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COMPARISON OF RECOVERY CHRACTERISTIC OF EVOFLURANE WITH ISOFLURANE IN ADULT PATIENTS UNDERGOING CANCER SURGERY

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ABSTRACT

Inhaled volatile anesthetics are used for maintenance of general anesthesia because of their ease of administration, predictable intra-operative hemodynamic changes and recovery characteristics. Rapid recovery from anesthesia is beneficial to ensure quick return of protective airway reflexes, better respiratory drive to improve patient outcome and decrease post-operative complications. We compared recovery characteristics of two inhaled anesthetic agents sevoflurane and isoflurane in adult cancer surgical patients. We hypothesized that sevoflurane has less mean emergence time than isoflurane in adult patients undergoing cancer surgical procedures of intermediate duration. The objective of this study is to compare the mean emergence time of sevoflurane with isoflurane in adult patients. It was a randomized controlled trial conducted in a tertiary care cancer hospital over a period of 6 months. A total of 80 patients equally divided in two group were included. Mean and standard deviation was calculated for emergence time and age, gender was presented in frequency and percentage. Emergence time (in minutes) was compared in both groups and student t- test was applied as a test of significance. Results showed that emergence time of 7.1 ± 1.1 minutes with sevoflurane in group (A) patients and emergence time of 11.1 ± 1.4 minutes with isoflurane in group (B) patients with p value= 0.000. We concluded that Sevoflurane has less mean emergence time than Isoflurane in adult patients undergoing cancer surgical procedures of intermediate duration.

Key Words: emergence time, sevoflurane, isoflurane

Inhaled volatile anesthetics remain the most widely used drugs for maintenance of general anesthesia because of their ease of administration through specially designed chambers (vaporizers) and predictable intra-operative hemodynamic changes and recovery characteristics[1,2]. Rapid recovery from general anesthesia is beneficial to ensure quick return of protective airway reflexes, better respiratory drive to improve patient outcome and to decrease post-operative complications and ultimately decreasing morbidity due to different pulmonary complications as a consequence of delayed recovery from anesthetic agents[3,4].

Inhalational anesthetic agents can also be used as induction agents especially in pediatric patients and in adult patients in selective cases[5,6]. These agents are also used for sedation as an adjunct to regional anesthesia[7]. The choice of anesthesia and anesthetics has a profound impact on peri-operative course, and on post anesthetic recovery of patient[8]. The use of new inhalational anesthetic agents is on rise because of their favorable recovery characteristics, measured in terms of emergence time, extubation time and orientation time[9,10]. None of the currently available inhaled volatile anesthetic agents has all the properties of an ideal inhaled agents[11]. Sevoflurane is a rapidly acting, fluorinated ether inhaled anesthetic agent. It has predictable pharmacokinetic and pharmacodynamics properties that favors rapid emergence from anesthesia thus enhancing patient safety and comfort. It has a low blood gas partition coefficient of 0.69[12]. Sevoflurane is claimed to have rapid recovery profile, as compared to isoflurane, measured as mean and

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standard deviation of recovery characteristics in sevoflurane and isoflurane, the measurement of the emergence time, extubation time, cognition time for both the agents clearly expresses it [13]. The low blood gas partition coefficient of sevoflurane mainly imparts this quality and confers it to be an ideal anesthetic agent as compared to isoflurane in the form of good anesthetic agent for inhalational induction as well as better recovery profile [14,15].

Because of increased risk of pulmonary complications in early recovery period after general anesthesia, I compared recovery characteristics of sevoflurane and isoflurane in adult patients under-going cancer surgical procedures of intermediate duration so that these complications can be avoided in early post-operative period. The data from this study would help the health care professionals to use a better agent for early recovery from anesthesia, therefore the patients can be prevented from early post-operative pulmonary complications due to delayed recovery from general anesthesia.

Recovery from anesthesia [16,17]

Recovery is a continual process, the early stages of which overlap the end of intra-operative care. Patients cannot be considered fully recovered until they have returned to their preoperative physiological state. Recovery process commences on discontinuation of anesthetic agent, which allows the patient to awaken, recover protective airway reflexes, and resume motor activity and continues in post anesthesia care unit (PACU).

Patients are likely to begin responding to verbal stimuli when alveolar anesthetic concentrations are decreased to about 0.5 MAC for the volatile anesthetic drug (MAC awake) if unimpeded by other factors. Increased ventilation results in a more rapid decline in alveolar anesthetic concentration which hastens recovery, provided that the arterial carbon dioxide pressure is not so low that it diminishes cerebral blood flow and the removal of anesthetic agent from the brain.

Recovery from neuromuscular blockade may be monitored by peripheral nerve stimulation and by clinical indices. Recovery from intravenous opioids and hypnotics may be more variable and difficult to quantify than recovery from inhalation and neuro-muscular blocking agents. Transport from the operating room is usually complicated by the lack of adequate monitors, access to drugs, or resuscitative equipment. Patients should not leave the operating room unless they have a stable and patent airway, have adequate ventilation and oxygenation, and are hemodynamically stable.

All patients should be taken to the PACU on a bed that can be placed in either the head down or head up position. The PACU should be located near the operating rooms. A central location in the operating room area, Proximity to radiographic, laboratory, and other intensive care facilities on the same floor is also highly desirable. Every effort should be made to diminish unnecessary noise in PACU.

Immediate recovery from anesthesia is a concept of care during not just a place to put the patient after surgery. Responsibility can never be fully delegated by the anesthetist to others. Most problems relate to Airway, Breathing and/or Circulation; with delayed return of consciousness and inadequate analgesia being other common related issues. All these should be anticipated.

METHODS

STUDY DESIGN: Randomized Controlled Trial.

STUDY SETTING: Operation theaters, Shaukat Khanum Memorial Cancer Hospital & Research Center, Lahore.

DURATION OF STUDY: Six months from July 2011 to January 2012.

SAMPLING TECHNIQUE: Non-probability purposive sampling.

SAMPLE SIZE: A total of 80 patients, divided in two groups A and B of 40 each.

SAMPLE SELECTION:

INCLUSION CRITERIA:

1. Patients having American Society of Anesthesiologists (ASA) grade I, II

ı ASA grade I. A normal otherwise healthy patient with no associated medical problems.

ı ASA grade II. A patient with mild systemic disease (No functional limitations).

2. Surgery of intermediate duration (2-3 hours) such as hysterectomy, modified radical mastectomy, gastrectomy, abdominoperineal resection etc.

3. Patients having an age between 20 to 60 years.

4. Patients having BMI less than 30 kg/m2.

5. Elective surgery

6. Both genders.

EXCLUSION CRITERIA:

1. Patient refusal

2. Patients having a history of allergy to volatile anesthetics.

3. Patients with medical history of CNS disease on previous medical record e.g. anticipation for increased intracranial pressure, but if record is not available then any clinical signs of raised intracranial pressure.

4. Pregnant patients.

OPERATIONAL DEFINITIONS:

Emergence time: It is the time in minutes from discontinuation of inhalational anesthetic to opening of eyes, either spontaneously or on verbal prompting, repeated every minute.

DATA COLLECTION PROCEDURE:

After approval of hospital ethical committee and informed written consent, a total of 80 patients i.e. 40 patients in each group selected from elective surgery list fulfilling the inclusion criteria were included in the study. By using lottery method, the participants were assigned to receive either sevoflurane (Group-A) or isoflurane (Group-B) as their primary anesthetic agent. The subjects did not receive any pre-medication before arriving in the operating room. All patients were monitored by continuous ECG lead II, heart rate, an automated oscillometric blood pressure, pulse oximeter, oxygen analyzer, capnograph and temperature. General anesthesia was induced with propofol (2mg/kg) and fentanyl (2ug/kg) and atracurium (0.5mg/kg) all intravenously. After securing airway with cuffed endotracheal tube, anesthesia was maintained with 60% nitrous oxide, 40% oxygen and predetermined end-tidal concentration of either 0.65 MAC (1.3%) sevoflurane or 0.65 MAC (0.8%) isoflurane for duration of surgery and ventilator settings adjusted to maintain an end tidal pCO_2 of 30-35 mmHg. Morphine 0.1mg/kg & ketorolac 0.5mg/kg both intravenously were used as analgesic. Ondansetron 0.1 mg/kg was used as antiemetic agent. Atracurium was given in incremental doses of 0.1mg/kg every 20 minutes for maintenance of muscle relaxation. At the moment of last skin suture nitrous oxide and volatile anesthetics were discontinued simultaneously with no tapering. Lungs were manually ventilated with 100% oxygen at fresh gas flow of 6 L/min until spontaneous ventilation resumes. Atracurium was reversed with neostigmine (40 ug/kg) I/V and glycopyrolate (10 ug/kg). The endotracheal tube was removed when the extubation criteria are met. Emergence time (in minutes), as per operational definition was recorded.

DATA ANALYSIS:

Data obtained was entered into SPSS version 11.0. Mean and standard deviation were calculated for emergence time and age, Gender was presented in frequency and percentage. Emergence time (in minutes) was compared in both groups and the student T-test was test of significance with $p \pounds 0.05$ as level of significance.

RESULTS:

80 adult surgical patients participated in this study, 40 received Sevoflurane (group A) and 40 received Isoflurane (group B) as a maintenance anesthetic. The two groups were comparable with respect to age (Table IV). Recovery from anesthesia, (Emergence time) as determined by eye opening either spontaneously or in response to verbal prompting, were significantly shorter in patients

receiving sevoflurane than in patients receiving isoflurane. The mean emergence time was 7.1±1.1 minutes for Sevoflurane and 11.1±1.4 minutes in Isoflurane group as (p value 0.000). Mean age for sevoflurane group was 38 ± 8.1 years, and mean age for isoflurane group was 39.6 ± 11.2 years. The frequency and percentage of gender was as total 32 males (40%) and 48 female patients (60%).

DISCUSSION

Induction and maintenance of general anesthesia is often managed with an inhaled anesthetic, which should provide rapid & smooth induction,

Table 1: *Mean and Standard Deviation Values for Emergence Time (in minutes) and Age (in years)*

Variable	Sevoflurane n= 40	Isoflurane n= 40	p Value
Emergence time	7.1 ± 1.1	11.1 ± 1.4	0.000
Age	38 ± 8.1	39.6 ± 11.2	Not applicable

Data shown as Mean±SD

Table 2: *Age Range of the Patients in both Sevoflurane and Isoflurane Groups*

Age range (years)	Sevoflurane (group A) Number of patients	Isoflurane (group B) Number of patients
20-30	08	10
31-40	14	11
41-50	15	10
51-60	03	09

Table 3: *Gender Frequency and Percentage in both Sevoflurane and Isoflurane Groups*

Gender	Sevoflurane n= 40		Isoflurane n= 40		Total in both groups n= 80	
	Number	%	number	%	number	%
Male	12	30 %	20	50 %	32	40 %
Female	28	70%	20	50%	48	60 %

emergence and hemodynamic stability. The choice of anesthesia and anesthetics has a profound impact on peri-operative course, and on post anesthetic recovery of patient. As might be predicted from its lower blood/gas solubility, my studydemonstrated that adult patients anaesthetized for surgery of intermediate duration (2-3 hour) recovered significantly more rapidly after sevoflurane anesthesia than after isoflurane anesthesia. The emergence time,

Figure I: *Mean Emergence Time for Sevoflurane and Isoflurane*
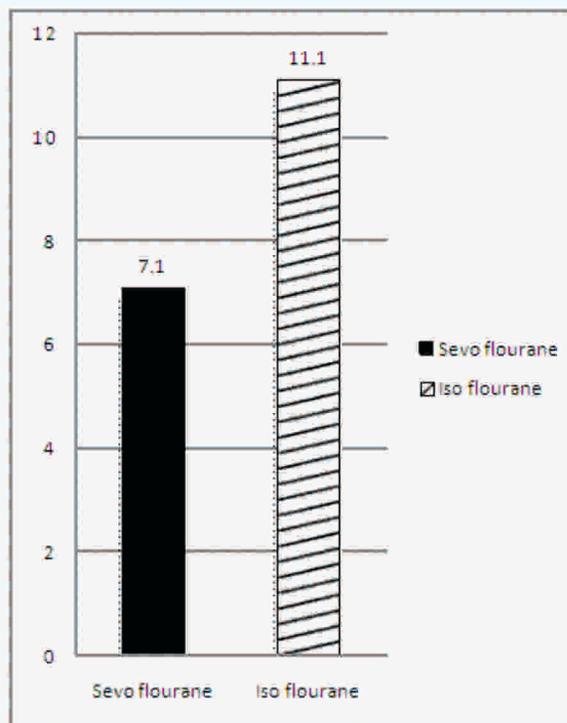
Values shown as time in minutes
Sevoflurane: mean emergence time 7.1 minutes
Isoflurane: mean emergence time 11.1 minutes

significantly shorterafter sevoflurane anesthesia as compared to isoflurane anesthesia.

Pharmacokinetic and pharmacodynamics differences among anesthetics may be important considerations, depending on the surgical setting, anticipated duration of surgery, whether endotracheal intubation is used, and other patient-specific factors such as body weight and age. The duration of surgery is an important consideration for most patients because differences between inhaled anesthetics in offset of effect vary with the duration of the procedure. Prolonged exposure has been associated with significantly delayed recovery. Nordmann GR and others, determined that the rate of recovery in children after exposure to desflurane was faster than those patients receiving isoflurane. Prolonged duration of exposure to isoflurane was associated with delayed recovery. This effect was insignificant in case of desflurane.[18] Desflurane or

sevoflurane may be preferred for obese patients because of a faster recovery and greater respiratory safety compared with isoflurane.[19] Sevoflurane is preferred for pediatric patients undergoing induction by inhalation because of its low propensity to cause respiratory tract irritation.[20]

Sevoflurane anesthesia had the clinical advantages of maintaining stable hemodynamics and rapid recovery when compared with isoflurane when compared in the form of heart rate, blood pressure and emergence time after anesthesia. Chen TL and others determined these effects in ASA-I and ASA-II Chinese adult patient with similar extent of exposure to anesthetics in both groups. Sevoflurane and isoflurane caused similar alterations in systolic and diastolic arterial pressure during maintenance. During emergence, time of response to command was significantly shorter in patients receiving sevoflurane than patients receiving isoflurane (5.6 +/- 0.4 min versus 15.2 +/- 3.0 min, p < 0.001).[21] Our results are very much comparable to above mentioned studies proving sevoflurane having faster emergence time as compared to isoflurane.

Patients receiving Sevoflurane showed earlier discharge time from the post-anesthesia care unit (PACU)-1 as compared to patient groups receiving isoflurane and also isoflurane has more incidences of mild airway hyper reactivity when compared to sevoflurane. This proves sevoflurane to be agent of choice as compared to isoflurane for maintenance of general anesthesia in daycare surgical procedures.[22] Sevoflurane and desflurane have shorter emergence times compared to isoflurane based anesthesia. Because of its pharmacological properties, desflurane appears to yield a rapid early and intermediate recovery compared with sevoflurane. The early recovery time seems to be shorter after maintenance of anesthesia with desflurane compared with sevoflurane. The intraoperative haemodynamic characteristics were comparable with both sevoflurane and desflurane. Both sevoflurane and desflurane provide a similar time to home readiness despite a faster early recovery with desflurane[23] again proving the need for an anesthetic agent having fast recovery profile and stable hemodynamics.

But on comparing inhalational anesthetics with intravenous agents like propofol for maintenance of general anesthesia, intravenous agents has been has been proved to be having faster recovery profile as compared to few inhalational agents like isoflurane as measured in terms of eye opening, time of extubation, orientation and mobility and frequency of postoperative nausea and vomiting in a Quasi-experimental study in patients undergoing laparoscopic cholecystectomy.[24] Another study proved isoflurane having fast recovery for few short surgical procedures, as Chiu CL and others conducted a prospective, randomized, controlled study to determine the maintenance and recovery characteristic of sevoflurane-nitrous oxide against isoflurane-nitrous oxide anesthesia in un-premedicated ASA I or II patients (aged 18-50 years). The speed of recovery was measured by time to eye opening, time to following simple command, and time to correctly giving own names and address and concluded that sevoflurane is a safe alternative to isoflurane but in these short surgical procedures.[25] A meta-analysis examined the recovery profiles of adult patients and compared the maintenance of general anesthesia with sevoflurane, isoflurane and propofol. The analysis considered 13 randomized controlled trials (RCTs) comparing sevoflurane with isoflurane and seven similar studies comparing sevoflurane with propofol. There was statistically significant reduction in times to recovery variables with the use of sevoflurane compared to isoflurane and propofol[26]. This is strongly in favor of our study providing an evidence as sevoflurane having better recovery profile as compared to isoflurane.

CONCLUSION

We concluded that Sevoflurane has less emergence time as compared to isoflurane in adult patients undergoing cancer surgery of intermediate duration.

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IRRATIONAL BELIEFS & PSYCHOLOGICAL DISTURBANCES: A CROSS-CULTURAL VALIDATION OF ELLIS' HYPOTHESIS

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ABSTRACT

The purpose of present study was to validate the Ellis' hypothesis that irrational beliefs lead to psychological problems, in Pakistani culture. For this purpose, a correlation study was conducted on female college students (intermediate to graduation) of Lahore city. The study was consisted of two phases. In first phase, the construct validity of Irrational Belief Questionnaire was computed by translating of Mahmood Rational Thought Test (a tool to measure irrational beliefs) into urdu language and taking experts rating on translation and for construct validity. The items with mean of 3.5 (maximum rating=4 0n 0-4 scale) were selected. The reliability of questionnaire was found to be significant with alpha co-efficient 0.72 (n=308). In second phase, the IBQ was correlated (n=200) with Siddiqui-Shah Depression Scale(SSDS), Siddiqui Anxiety Scale (SAS),Trait Anger & Expression Scale (TAES), Rifae Self-esteem Scale (RSES) & Student Problem Checklist (SPC).The results indicated significant (positive) correlation with RSES, TAES & SPC while no correlation could be found with other two scales. Although results has questioned the ABC theory of REBT but as results related to RSES, SSDS, SAS are refuting the Ellis' hypothesis to obtain current validity of questionnaire as well as use of more appropriate measures of psychological disturbances is needed to question the application of theory of REBT in Pakistani culture. Other possible reasons and application of study is discussed in detail.

A core hypothesis of Rational Emotive Behavior Theory & Therapy (REBT) is that irrational beliefs lead to psychological disturbance (Harris, davies & Dryden, 2006). Many studies were conducted to examine this hypothesis and find a significant correlation between measures of acuity depression and low self esteem (Harris, Davies & Dryden, 2006).

Rational Emotive Behavior theory & therapy is considered one of most important and influential theory among cognitive theory. According to Ellis's "cognitive theory of emotion formation" (Ellis, 1994; Ellis with Harper, 1975; as cited in Harris et al, 2006) people experience undesirable activating event about which they have rational (RBs) and irrational beliefs (Ibs). Not the activating event (A) but the rational and irrational beliefs lead to emotional consequences (C). Ellis theorized that rational beliefs (RBs) lead to functional and adaptive consequences while Irrational beliefs (IBs) lead to dysfunctional and maladaptive consequences (David,

Schnur, Belloiy,2000). Based on the concept of irrational and rational beliefs, Ellis presented his A-B-C model of personality which assumes that not the activation event but our beliefs (interpretations) related to that specific event result in healthy or unhealthy emotional consequences.

The model can be pictorially explained as following:
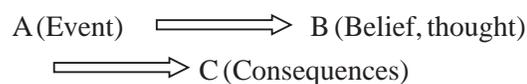
A (Event) $\Longrightarrow$ B (Belief, thought)
$\Longrightarrow$ C (Consequences)
(Source: Ellis & MacLaren,2000).

Ellis founded his personality theory on certain philosophical ideas which should be understood in order to understand the ABC theory and IBs hypothesis of REBT. Among those ideas following are important:

i. Ellis pointed out that there may not be such thing exist as objective reality but we can only know/see it through our fallible, biased affected

by prior experiences perception, so the achievement of objective reality is almost impossible (Ellis & MacLaren, 2000).

ii. Based on George Kelly's concept of personal social constructions, Ellis theorized that our views related to morality, good/bad, right/wrong are largely affected by our personal beliefs and social values so "all ethical beliefs have a constructive nature", (as cited in Ellis & MacLaren, 2000).

iii. Ellis emphasized much upon influence of social and cultural values on individual's beliefs system and he clammed that our beliefs are much less individualistic then are commonly thought, while these beliefs are rather innate and rigid/fixed (Ellis & MacLaren, 2000).

iv. Ellis said that people learn their values by their culture practices and there is no evidence which culture is good or bad. Elaborating this concept he cited that things and processes exist on a both/and an also basis (Ellis & MacLaren, 2000). Just like no solution is absolute, Ellis claimed that no goal/aim in life can be absolute but it always is open for argument, alternatives, and change.

In short the philosophical hypotheses of personality theory of REBT lie in shunning the absoluts but emphasizing on thinking pattern which is more flexible and adaptive (rational beliefs) (Ellis & MacLaren, 2000).

1. Based on these philosophical hypotheses, REBT postulated 12 irrational ideas prevalent in American society, although Ellis claimed that these ideas are not restricted to any specific society but shared cross-culturally. These irrational ideas are considered by Ellis as root of the "neurotic" disturbances among humans (Ellis,1962).

As REBT focuses on a "unique" type of beliefs, namely irrational beliefs (IBS), research data has narrow down these 12 irrational ideas into four core irrational beliefs although it was observed that these

core beliefs are usually presented by clients through above mentioned irrational ideas. But these core beliefs are the themes underlying these ideas.

Ellis collectively defines irrational beliefs as beliefs which are important to that individual and are being stated in absolute terms such as "should", "must", "ought". "have to", etc.(Dryden, 1999). while rational beliefs are elements of personal Significance being stated in non-absolute manners which manifest themselves inform of desires, preferences rather then in form of demands, as in case of irrational beliefs.

Windy Dryden (1984) said that in REBT rational beliefs mean "that which helps people to achieve their basic goals and purposes", and irrational means that "which prevents them from achieving these goals and purposes", (as cited in Ellis and MacLaren, 2000).

Ellis mainly discussed 4 components of irrational beliefs which are also known as core irrational beliefs of REBT. These four categories/components of irrational beliefs are– Demandingness, Awfiluzing/ catastraphizing, Low Frustration Tolerance, and Global Evaluation of Human worth and self and/or others downing.

1- Demandingness: It means "believing that certain things must or must not be happen". Believing that certain conditions, such as success and approval, are necessary (as cited in wessler & wessler, 1980).

This core belief implies that certain laws of nature must be adhered to and violation and negation of these laws is simply out of question-awful (wessler & wessler, 1980).

2. Awfulizatiing/Catastrophizing: It implies the belief that something is totally bad, as bad as it possibly could be, and not at all beneficial (Ellis, 2001).It is 100% bad, it could not possibly be worse (Nottingham, 1994).

3. Low Frustration Tolerance (LFT): It consists of the idea that "I can't stand" the discomfort of the situation.

4. Global Evaluation of Human worth and self and/or others downing: GE/SD appears when individuals tend to be excessively critical of themselves (i.e., to make global negative evaluations of themselves) and also of others and life conditions.

Ellis combined his concept of irrational beliefs with ABC model of personality theory and claimed that irrational beliefs lead to unhealthy negative emotions which are according to Ellis can be broadly divided into three types of emotional problems or disturbances, i.e., Depression, Anxiety and Anger (Davies & Dryden, 2006).

Studies on irrational beliefs have been related to its relationship with psychological problems, construction of scales and questionnaires to measure irrational beliefs and extraction of core beliefs, and cross-cultural validity of the concept of irrational beliefs conceptualized by Ellis. The research data collectively supported the Ellis's hypothesis that irrational beliefs lead to psychological problems (Bond & Dryden, 1996, 1997, 2000;

Bond, Dryden, & Briscoe, 1999; Dryden et al., 1989a; Dryden, Ferguson, & Hylton, 1989; Dryden, Ferguson, & Teague, 1989; David, Szentagotai, Eva & Macavei, 2005). While different cross-cultural studies have provided not only different measures of assessing irrational beliefs but also proved Ellis's assumption that these core irrational beliefs cannot be considered as present only in any specific society but are prevalent all over the world (Matsumura, 1991; Hassan & Ismael, 2004; Taghavi, Goodarzi, Kazemi & Ghorbani, 2006).

The aim of the present study is to validate the Ellis's hypothesis that irrational beliefs lead to psychological problems in Pakistani population by correlating Irrational Beliefs Questionnaire with various measures of psychological problems/ disturbances.

The study is highly beneficial in the sense that it is aimed to question the applicability of the concept of using irrational beliefs given by Albert Ellis in a culture like Pakistan which is heavily dominated by religious as well as diverse cultural backgrounds. While Ellis also admitted that our beliefs are result of our upbringing, our culture and result of learning. He also emphasized upon importance of semantics or words used in any culture to manifest the theme of these beliefs. So one can question whether the beliefs extracted from patients belong from a western, industrialized, modern country (America) can be as it is applicable to a culture very much different to first one. This study will help to not only validate the theory of irrational beliefs in our culture but also may provide a questionnaire in Urdu language which can be hopefully used for majority of our people rather than using questionnaire in English of translating it word to word. Because, in present study, the theme of items/ beliefs is aimed to be taken rather than translating it grammatically. This study will provide an empirical support to REBT from eastern culture and will open more doors to researches towards the theory and therapy of REBT related to our culture.

OBJECTIVES:

1. To assess the relationship between irrational beliefs and various dimensions of psychological problems such as anxiety, depression, anger and self-esteem.
2. To assess the relationship between irrational beliefs and academic problems faced by student population in Pakistan.
3. To adapt a questionnaire for the measurement of irrational beliefs in Pakistani population.

Hypotheses:

1. There will be significant positive correlation between Irrational Belief Questionnaire and Saddiqui-Shah Depression Scale (SSDS).
2. There will be positive correlation between Irrational Belief Questionnaire and Anger Scale.
3. There will be positive correlation between Irrational Belief Questionnaire and Saddiqui-Shah Anxiety Scale.
4. There will be negative correlation between

Irrational Belief Questionnaire and Self-esteem Scale.

5. There will be positive correlation between Irrational Belief Questionnaire and Student Problem Checklist.

METHOD

Research Design:

In present study Correlation design was used to assess the relationship between Irrational Beliefs and various dimensions of mental health.

The study was divided into two main phases. The first phase was conducted mainly to obtain construct validity of Irrational Belief Questionnaire while in 2nd phase, the correlation between Irrational Belief Questionnaire and other correlational measures was assessed.

Phase I:

The aim of this phase was to translate and adapt the Mahmood Rational Thought Test (MRTT) for Pakistani population and to obtain construct validity of Urdu questionnaire. For this purpose following procedure was followed.

Procedure:

(i) The Mahmood Rational Thought Test (MRTT) was translated by 3 bilinguals into urdu from english.

(ii) The translated items were discussed with a group of 5 bilinguals to select the most appropriate items.

(iii) The selected items were given to experts to rate on two measures, i.e., validation of Ellis's Irrational Beliefs' theory and on appropriateness of translation. The rating scale was based on 5-point scale of Likert type.

(iv) The items which gained mean rating of 3.5 and more on validation of theory measure were selected while same criteria was followed for translation measure.

(v) These finally selected items constituted the final form of Irrational Belief Questionnaire.

Sampling Strategy:

The Purposive Sampling technique of non-probability sampling was used to select the experts for the rating of questionnaire as ratings required certain qualification and experience related to clinical psychology and REBT.

Sample:

In first phase the sample consisted of 11 experts who were practicing clinical psychologist, had learned Rational Emotive Behavior Therapy (REBT) formally during their professional training as clinical psychologist and are practicing REBT in Pakistan.

Researcher's Instrument:

The instrument used in this phase was Mehmood Rational Thought Test (MRTT) which was developed and standardized by Dr. Zahid Mehmood on nurses of Britain (n= 400). This Test is based on 12 Irrational Beliefs of Albert Ellis and has 77 items. The factor analysis produced 5 factors with 50 items while remaining 27 items were excluded.

Statistics:

The statistics applied in this phase was Descriptive analysis (Average rating of each item rated by 11 experts) which has provided a mean value for each item to let researcher decide about finalization of items.

Phase II:

The aim of 2nd phase was to assess the correlation between Irrational Belief Questionnaire and other correlates in order to assess the relationship between Irrational Beliefs and various dimensions of mental health. Another objective was to assess the scale reliability of researcher's questionnaire.

Procedure:

(i) Sample was selected.

(ii) Data was collected.

(iii) Data analysis.

Sampling Strategy:

The Systematic Random Sampling technique of probability sampling was used to select the subjects to administer the researcher's questionnaire

and other validation measures.

In 2nd phase the sample consisted of 308 female college students of intermediate to graduation (age = 17years to 22 years) from different colleges of Lahore city. On 200 subjects, all the questionnaires were administered but Irrational Belief questionnaire was administered on more 108 subjects (N= 308).

Statistics:

The data was analyzed on SPSS and following test were used.

(i)   The Biveriate Correlation (Pearson Product Moment correlation)was administered to assess the correlation between Irrational Belief Questionnaire and other measures.

(ii) The Alpha Coefficient was computed to obtain the internal consistency (reliability) of Irrational Belief Questionnaire.

Instruments:

Siddiqui-Shah Depression Scale (SSDS): The Siddiqui-Shah Depression Scale is an indigenous tool developed by Siddiqui & Husnain consisted of 36 items to assess the symptoms of depression. The scale has been standardized on clinical and non-clinical population (n= 400) which indicated Spearman-Brown correlation of 0.84 & 0.89, respectively. While for these groups, the split-half reliability of scale is 0.79 & 0.80, respectively. Its concurrent validity with Zung Depression Scale was found to be 0.55.

Siddiqui Anxiety Scale (SAS) The indigenous scale developed by Siddiqui & Husnain in 1993 is consisted of 25 items of 4-point scale measuring the somatic symptoms of anxiety. The validity found with Beck Anxiety Inventory is 0.77 with 83% sensitivity and 69% specificity of the scale.

Trait Anger & Expression Scale(TAES): As an indigenous tool to measure intensity on anger, the Trait Anger & Expression Scale has 32 items rated on 5-point scale and was standardized on Pakistani

population. The mean score was 51.53 with std of 12.22. The Cronbach's alph was found to be 0.82 while Guttman's split-half relibilty was 0.80. The convergent validity with Buss 7 Perry Aggression Questionnaire was found to be significant.

Rifae Self-esteem Scale: It is a 29 item scale devised to measure self-esteem. The items are rated on 5-point scale. The split-half reliability of scale is 0.72 while internal reliability is significant with alpha coefficient of 0.83.

Student Problem Checklist: The Student Problem Checklist is an indigenous devise to assess the nature and intensity of problems faced by college students in Pakistan. The checklist developed by Mahmood & Hafeez (2006) on 800 students of Government College University has 58 items rated on 4-point scale.

Table 1: *Table is Showing Correlation of IBQ Dimensions of Psychological Disturbances (i.e., SSDS, SSAS, RSES, TAES & SPC).*

Scales	RSES	TAES	SSDS	SSAS	SPC
IBQ	0.34**	0.17 *	0.039	.088	0.21 *

Note: N= 200 , df= 198, *p<0.05, **p<0.001 (two tailed)

Table 2: *Table is Showing Reliability Analysis of the IBQ.*

Scale	N	No. of Items	Alpha
IBQ	308	59	0.72

Table is indicating significant internal consistency (reliability) of IBQ.

Table 3: *The Correlation Among other Scales Assessing Various Dimensions of Psychological Disturbances (i.e., SSDS, SSAS, RSES, TAES & SPC).*

Scales	RSES	TAES	SSDS	SSAS	SPC
RSES		.20**	-.02	. 01	-.06
TAES			.24 **	.27 **	.23**
SSDS				.68**	.55**
SSAS					.66 **
SPC					

Note: N: 200, df: 198, **p<0.01 (2-tailed)

RESULTS

Table 4: *Table is Showing Mean and Standard Deviation of IBQ and Other Correlates (i.e., SSDS, SSAS, RSES, TAES & SPC).*

Scales	MEAN	SD
IBQ	161.36	16.82
TAES	60.97	17.07
SSDS	27.84	14.55
SSAS	19.93	11.25
SPC	64.40	27.98
RSES	71.57	8.41

DISCUSSION

The present study was conducted to investigate the relationship between irrational beliefs and psychological disturbances (i.e., depression, anxiety, anger, self-esteem and problems faced by student population). The main aim was to validate the REBT theory of emotion formation which assumes that irrational beliefs lead to psychological disturbances in Pakistani culture and to construct a questionnaire in Urdu language in order to assess the irrational beliefs of our people. Rich research evidence based on mainly western studies with few support from eastern world, supported that assumption. To study this assumption, the Mahmood Rational Thought Test (MRTT) was translated into Urdu and its construct validity was obtained by taking experts rating on each item The Irrational Belief Questionnaire (IBQ) was then based on those selected items (59 items) which was correlated with Siddiqui-Shah Depression Scale(SSDS), Siddiqui Anxiety Scale (SAS), Trait Anger & Expression Scale (TAES), Rifae Self-esteem Scale(SES), and Student Problem Checklist (SPC). The hypothesis was that IBQ will have significant correlation with each scale. The IBQ has Alpha co-efficient of 0.72 which is indicative of significant scale reliability.

The result findings are diverse as some results are in line with previously conducted studies but three findings are contradictory to previous data.

The correlation between IBQ and TAES was found to be significantly (positively) correlated (r = 0.17) which can be supported by previously conducted researches that found positive correlation between aggressive thoughts/cognitions, behavior and irrational beliefs (Jones & Trower, 2004; Ziegler & Smith, 2000; Dve & Ecker, 2000). The correlation between IBQ and SPC was also found to be significantly (positively) correlated ® = 0.21) which again supported the Ellis' theory that irrational beliefs have connection/correlation with distress and stress. This correlation between IBQ & SPC is only indicative of equal intensity irrational beliefs with equal intensity of problems faced/perceived by students. Although those two results can not say whether irrational beliefs caused anger/problems for students or vice versa. But these results are inline with previous research data (DiLorenzo, David & Montgomery, 2007; Clorinda & Nagoshi, 1995).

The correlation with RSES was found to be significant (positive) correlation (r = 0.34) which is contradictory and refuted the researcher's hypothesis. The previous studies conducted on relationship between self-esteem and irrational beliefs found negative correlation between these two variables (Daly & Burton,1983) or no correlation between unconditional self acceptance, an important part of rational belief (Davies, 2006). But findings of this research have been contradictory. Combining it with other two contradictory results which had refuted the researcher's hypotheses related to SSDS and SAS, some possible explanation can be given. Firstly, the IBQ should be validated with another standardized tool of measuring/assessing irrational beliefs because the questionnaire has this very shortcoming. The other possible reason can be that Ellis although said that core irrational beliefs are universal but he at the same time said that not the words/semantics of these beliefs but their theme is universal. So it is possible that by translating, the MRTT has lost its quality to assess the irrational beliefs accurately. As far as SAS is concerned the scale is measuring only somatic symptoms of anxiety which are usually very rare in population to which this study is concerned (APA,1995). Same is the case with SSDS which is measuring somewhat clinical symptoms of depression which are usually uncommon in student population. Subjectively as researcher I experienced that subjects showed reluctance to complete these two scales as they felt them for mental patients. So a factor of desirability might have compelled them to rate items on lower ends. Another reason of this insignificant correlation can be the fact that usually in adolescent people tend to be more aggressive rather than having problems of depression and anxiety and this fact became stronger when scales assessing depression and anxiety are more of diagnostic nature. Another explanation of these contradictory results could be that study has been failed to exclude the effect of social desirability in subject's responses. Another explanation for this positive correlation with self-esteem with IBQ could be taken by Ellis argument that self-esteem is not an healthy concept because underlying this concept is

people's desire to rate themselves using overgenera- lization and other's approval while unconditional self acceptance is a healthy concept. So, this is may be reason that even self-esteem is not a healthy concept but depicting a fake positive image. Another reason can be that in our culture not only these beliefs (irrational beliefs) are given value but considering one-self as positive and high is also desirable in our society, so that social desirability might have affected the scores.

Although the correlation between TAES and SPC was found to be statistically significant with IBQ but psychologically the correlation of both scales with IBQ is not much high, that again question not only the validity of questionnaire but to the validity of the Ellis' ABC model and concept of irrational beliefs. Another point in favor of all these arguments are positive correlation among SSDS, SAS, TAES, SPC which indicate that all these are measuring psychological problems but may be choice of these measures for this population with respect to this study's aim was not appropriate, and that IBQ needs validation. In short, beside the high inter consistency, the validity of questionnaire is still questionable and if we ignore it then we can say that the Ellis's hypothesis and concept of irrational beliefs could not be validated satisfactorily in Pakistani population as far as results of this study are concerned.

RECOMMENDATIONS

The concurrent validity of IBQ should be computed before generalizing the results as only construct validity and internal consistency are not good enough for a tool to be taken as valid tool. The study should be replicated with clinical population with same scales as the diagnostic characteristic of the SSDS and SAS can be overruled. To validate the Ellis' hypothesis, the scale should be amended by changing the semantics according to our culture and for this purpose, the verbal reports given by psychiatric patients will be very useful. The data should be improved by including male population also.

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DIAGNOSTIC ACCURACY OF MRI IN PITUITARY MACROADENOMA

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Abstract

Introduction: Pituitary macroadenomas may cause hypopituitrism and visual disturbance due to their pressure effects as well as hyper pituitrism due to over production of certain hormone. MRI has evolved as a useful tool in the non-invasive imaging of sellar region with sensitivity and specificity reported as high as 72% and 90% respectively .

Objective: The objective of this study was to determine the diagnostic accuracy of MRI for pituitary macroadenoma using histopathology as gold standard.

Study design: Cross sectional survey.

Setting: Department of Diagnostic Radiology, Sir Ganga Ram Hospital, Lahore.

Duration: Six months from 30/09/2014 to 29/03/2015.

Subject and Methods: This study involved 140 patients suspected of pituitary macroadenoma referred for MRI from other departments of the hospital. A written informed consent was taken from all the patients.

Results: The mean age of the patients was 42.62 ± 15.72 years and 53.6% of the patients were male while 46.4% were female. On MRI, 55.7% patients had Pituitary Macroadenoma while MRI revealed normal pituitary gland in 44.3% patients. On Histopathology, Pituitary Macroadenoma was confirmed in 79.3% patients while normal pituitary tissue was reported in 20.7% cases. When cross tabulated, MRI with Histopathology, there were 75 True Positive cases, 36 False Negative cases, 3 False Positive cases and 26 True negative cases for MRI. The resulting sensitivity, specificity, positive predictive value, negative predictive value and accuracy of mri was 67.57%, 89.66%, 96.15%, 41.94% and 72.14% respectively.

Conclusion: The sensitivity, specificity and diagnostic accuracy of MRI in pre-operative detection of pituitary macroadenoma in suspected cases was found to be 67.57%, 89.66% and 72.14% respectively by taking histopathology as gold standard.

Key words: *Diagnostic Accuracy, Magnetic Resonance Imaging, Pituitary Macroadenoma*

The pituitary gland is the master gland of the body because it controls most of the body's endocrine functions by means of the hypothalamic-pituitary axis.[1] The most common pituitary tumors are adenomas with an estimated prevalence of 16.7% (14.4% in autopsy studies and 22.5% in radiologic studies), the other tumors constitute approximately 5 to 10% of all sellar and parasellar lesions.[2,3] Pituitary adenomas can be micro or macro adenomas depending on their size. By definition a

pituitary microadenoma is less than 10 mm in size. If the same tumor is greater than 10mm in size it is then considered a pituitary macroadenoma. Differences imaging are related to a difference in size rather than fundamental difference in biology.[4]

The clinical features of pituitary adenoma vary depending on the location and size of the tumor and its secretary capability. They typically appear during early adulthood, and no sex predilection is known. Secretary pituitary adenomas are usually small and

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generally do not cause neurologic symptoms or hypopituitarism, though they can. The symptoms of functioning tumors are related to the specific hormone secreted by the tumor.[3,5] These tumors become symptomatic earlier because they secrete hormones, and they are less likely than like null-cell tumors to become large enough to compress adjacent structures.[6,7]

As pituitary tumors grow, destruction of normal pituitary tissue results in various hormonal deficiencies. In rare cases, these tumors may spontaneously hemorrhage or become infarcted. The pressure they exert on nearby structures such as optic chiasm can produce double vision and progressive visual loss.[6,7] Thus patients with macroadenomas should be evaluated for hypopituitarism and other mass effects.[8]

Introduction of newer imaging modalities and of modern methods of neurosurgery and pharmacotherapy have revolutionized diagnosis and therapy of pituitary tumors.[9,10] CT and MRI have largely replaced plain radiography because conventional radiography is poor for delineating soft tissues.[11] Currently, MR is the method of choice for imaging of the pituitary gland and the parasellar area due to its ability to provide strongly contrasted high-resolution, multiplanar and spatial images.[12] Advanced MR techniques - MR diffusion, MR spectroscopy and MR perfusion - have been increasingly applied.[9,10,13] MR examination enables visualization of many anatomic details of pituitary gland, such as: the anterior lobe (adenohypophysis), the posterior lobe (neurohypophysis), pituitary infundibulum, parasellar structures (cavernous sinuses, sphenoid sinus, suprasellar cisterns) and optic chiasm.[9] In cases of pituitary hormone hypersecretion, MRI can demonstrate the causal lesion, which is often small (microadenoma). In pituitary adenomas with suprasellar extension, MRI shows the tumor's relation to the surrounding structures: the optic chiasm, the internal carotid artery, the sphenoidal sinus, etc. MRI usually makes it possible to confirm or rule out any cavernous sinus invasion by the pituitary adenoma, a determination essential for planning treatment.[14] MRI has approximately 90% sensitivity and a similar specificity for pituitary tumors in patients with most syndromes of pituitary hormone excess.[12] MRI is 61% to 72% sensitive and 88% to 90% specific for sellar masses.[15,16] The natural course of these adenomas is such that lifelong follow-up is necessary. MRI is the appropriate investigation to follow up these patients.[17]

This study is done in our setting to identify the role of MRI in diagnosis and management of pituitary macroadenomas. This will help the clinicians to identify these lesions planning surgery earlier or to avoid unnecessary surgeries.

Methods

This cross sectional survey was conducted at Department of Diagnostic Radiology, Sir Ganga Ram Hospital, Lahore over a period of 6 months from 30/09/2014 to 29/03/20. A total of 140 cases were selected using non-probability, purposive Sampling. The patients of age (10-75 years), of both sexes, referred from outdoor or indoor of Sir Ganga Ram Hospital Lahore having clinical suspicion or provisional diagnosis of pituitary adenoma or the patients having positive findings regarding Pituitary tumors on other modalities like X rays or CT scan and those whom tumor detected incidentally on any of imaging modalities without exact symptoms regarding pituitary were included in this study. All patients referred to our department meeting the inclusion criteria were included in the study. Informed consent for MRI was taken from all the patients included in the study. All the patients were recorded for their demographic features i-e. age, gender and address. MRI brain was performed by using 1.5 Tesla Toshiba Excelart Vantage MRI System. The QD C/T/L spin coils were used in all patients. Axial T1 & T2 weighted, FAT Suppression, sagittal T2 weighted and dynamic MR imaging after administration of 0.1 mmol of gadolinium per kilogram body weight was performed. The patients were followed then in collaboration with the neuro-

surgery department of our hospital after operation of tumor. Histopathological diagnosis after surgery was obtained. Post-operative histopathology correlation was made taking histopathology as gold standard. All this information was collected through a specially designed Performa. All the collected data was entered into SPSS version 11. Numerical variables such as age has been presented by mean ±SD. Categorical variables i-e gender, Pituitary macroadenoma on MRI and Histopathology has been presented as frequency and percentage. A 2×2 contingency table has been generated to calculate the sensitivity, specificity, positive predictive value, negative predictive value and accuracy of MRI in diagnosing pituitary macroadenoma by taking histopathological findings as gold standard.

RESULTS

The age of the patients ranged from 10 years to 75 years with a mean of 42.62±15.72 years as shown in Table 1. Majority of the patients were male (53.6%) while 46.4% were female as shown in Table 2. On MRI, 55.7% patients had Pituitary Macroadenoma while MRI revealed normal pituitary gland in 44.3% patients as shown in Table 3.

On Histopathology, Pituitary Macroadenoma was confirmed in 79.3% patients while normal pituitary tissue was reported in 20.7% cases as shown in Table 4.

When cross tabulated, MRI with Histopathology, there were 75 True Positive cases, 36 False Negative cases, 3 False Positive cases and 26 True negative cases for MRI as shown in Table 5.

The resulting sensitivity, specificity, positive predictive value, negative predictive value and accuracy of MRI was 67.57%, 89.66%, 96.15%, 41.94% and 72.14% respectively as shown in calculations following Table 6.

DISCUSSION

Pituitary macroadenomas are intrasellar masses usually with extrasellar extension. They may grow upwards causing the optic chiasm compression and indent the floor of the third ventricle. These tumors can also extend downward into the sphenoid sinus, back into the dorsum sellae or laterally into the cavernous sinus. Involvement of the cavernous sinus can modify the prognosis; therefore the correct diagnosis is of high clinical importance, although it

may remain difficult to differentiate compression and involvement.[9]

MRI has been found to be a valuable investigation in diagnosing piyuitary tumors due to its inherent ability to delineate various soft tissues. Its sensitivity, specificity and diagnostic accuracy has been well established.[15,16] However, there was no local research available on the diagnostic accuracy

Table 1: *Descriptive Statistics for Age*

	N	Minimum	Maximum	Mean	Std. Deviation
Age of the Patient	140	10	75	42.62	15.721
Valid N (listwise)	140				

Table 2: *Frequency Table for Gender*

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	Male	75	53.6	53.6	53.6
	Female	65	46.4	46.4	100.0
	Total	140	100.0	100.0	

Table 3: *Frequency of Pituitary Macroadenoma on MRI.*

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	Pituitary Macroadenoma	78	55.7	55.7	55.7
	Normal	62	44.3	44.3	100.0
	Total	140	100.0	100.0	

Table 4: *Frequency of Pituitary Macroadenoma on H/P*

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	Pituitary Macroadenoma	111	79.3	79.3	79.3
	Normal	29	20.7	20.7	100.0
	Total	140	100.0	100.0	

Table 5: *MRI Stage * H/P Crosstabulation*

		Diagnosis on H/P		Total
		Pituitary Macroadenoma	Normal	
Diagnosis on MRI	Pituitary Macroadenoma	75 a	3 b	78
	Normal	36 c	26 d	62
Total		111	29	140

Table 6: *Diagnostic Accuracy of MRI in Pituitary Macroadenoma*

Type of allergy	Number	Percentage
Sensitivity	$\dfrac{A}{a+c}$	= 67.57 %
Specificity	$\dfrac{D}{b+d}$	= 89.66 %
Positive Predictive Value	$\dfrac{A}{a+b}$	= 96.15 % (*)
Negative Predictive Value	$\dfrac{D}{c+d}$	= 41.94 % (*)
Accuracy	$\dfrac{a+d}{a+b+c+d}$	= 72.14 % (*)

of MRI in pituitary macroadenomas, which required the current study.

In our study, the sensitivity, specificity, positive predictive value, negative predictive value and accuracy of MRI was 67.57%, 89.66%, 96.15%, 41.94% and 72.14% respectively. Our results match closely with those of Gao et al.[15] (2001) who reported the sensitivity and specificity of MRI to be 61.1% and 88.9% respectively. However Famini et al.[18] (2011) did a similar study on 2598 patients and reported a very high sensitivity (99%) but very low specificity (29%) as compared to our study. A possible explanation for this conflict can be limited sample size of our study.

The present study is first of its kind and advocates the routine use of MRI in the pre-operative detection of pituitary macroadenomas in suspected cases owing to high positive predictive value (96.15%) along with its plus points of quick, safe (radiation free) and non-invasive nature. However, there is need to repeat this study over a larger sample size to further confirm the diagnostic accuracy of MRI in pituitary macroadenomas.

CONCLUSION

Preoperative assessment using MRI brain with contrast on pituitary protocol is of value not only in diagnosing pituitary macroadenoma but also in assessment of its extension into cavernous sinuses, involvement of optic chiasma and encasement of carotid vessels. This information is helpful in deciding the extent and mode of resection as well as predicting and planning the expected complications of resection like bleeding or visual loss.

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TRANS-VAGINAL ULTRASOUND; AN ADJUNCT TO TRANS-ABDOMINAL ULTRASOUND IN ECTOPIC PREGNANCY

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ABSTRACT

INTRODUCTION: Historically, ectopic pregnancies were diagnosed on the classical triad of symptoms: pain, vaginal bleeding and a history of amenorrhea. Advances in diagnostic radiology brought Trans-abdominal Scan (TAS) as an important diagnostic tool in such patients. Recently Transvaginal scan (TVS) has been claimed to be more sensitive and accurate although data is limited. OBJECTIVES: The objective of this study was to determine the diagnostic accuracy of trans-abdominal and trans-vaginal ultrasound in the diagnosis of ectopic pregnancy by taking histopathology as gold standard.

STUDY DESIGN: Cross-sectional survey.

SETTING: Department of Diagnostic Radiology, Sir Ganga Ram Hospital, Lahore

DURATION: Six months (25/06/2014 to 24/12/2014).

SUBJECT AND METHODS: This study involved 195 women who presented in the emergency department with suspicion of ectopic pregnancy.

RESULTS: The mean age of the patients was 29.64±4.75 years while the mean gestational age was 7.26±2.28 weeks. Most of the patients were para 2 (38.5%), followed by para 3 in 23.6% cases. Out of 195 patients who presented with suspicion of ectopic pregnancy only 35(17.9%) were actually diagnosed to have ectopic pregnancy on histopathology (gold standard). TVS labeled ectopic pregnancy in 42 (21.5%) cases. There were 32 True Positive cases, 10 False Positive cases, 3 False Negative cases and 150 true negative cases. It yielded sensitivity (91.43%), specificity (93.75%), accuracy (93.33%), positive predictive value (76.19%) and negative predictive value (98.04%) of TVS for ectopic pregnancy taking histopathology as gold standard. TAS labeled ectopic pregnancy in 39 (20%) cases. There were 29 True Positive cases, 10 False Positive cases, 6 False Negative cases and 150 true negative cases. TAS yielded 82.86% sensitivity, 93.75% specificity, 91.79% accuracy, 74.36% positive predictive value and 96.15% negative predictive value of for ectopic pregnancy taking histopathology as gold standard.

CONCLUSION: TAS and TVS are both specific for diagnosis of ectopic pregnamncy, however TVS is more sensitive and accurate than TAS in the diagnosis of ectopic pregnancy. It can b used to complement the TAS to improve overall diagnostic accuracy of ectopic pregnancy.

KEY WORDS: trans-abdominal Scan, trans-vaginal scan, ectopic pregnancy

Ectopic pregnancy is the implantation of a fertilized ovum outside the endometrial lining of the uterus. First described in the 11th century, ectopic pregnancy is a major health problem for women of childbearing age and a leading cause of pregnancy-related deaths (4-10%) in the first trimester.[1] The overall incidence of ectopic pregnancy is 1.2 – 1.4% of all the reported pregnancies. Untreated, ectopic pregnancy can result in massive and fatal hemorrhage, infertility and maternal death.[2]

Historically, ectopic pregnancies were diagnosed on the classical triad of symptoms: abdominal pain, vaginal bleeding and a history of amenorrhea. However, advances in diagnostic ultrasound and the rapid immunoassay of serum human chorionic gonadotropin, has enabled the diagnosis at an earlier stage.[3] Findings which strongly suggest ectopic pregnancy on ultrasound include absence of

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gestational sac in uterus, presence of extra uterine mass, thickening of endometrial lining (pseudo gestational sac) and presence of fluid in the pouch of Douglas.[4] Trans-abdominal Scan (TAS) is most common-ly employed in such patients. However, in the past decade there has been increased advocacy for the use of trans-vaginal Scan (TVS) in suspected patients instead of trans-abdominal scan.[4] Kirk et al. in 2007 showed that trans-vaginal scan had a sensitivity and specificity of 98.3% and 99.9% respectively in the detection of ectopic pregnancy.[5] Malik et al. in 2010 showed that uterine gestational sac was absent in 94% cases along with the presence of extra uterine mass, pseudo gestational sac and fluid in the pouch of Douglas in 91%, 35% and 67% cases respectively in patients with ectopic pregnancy on ultrasound scan. They also observed that TVS had better sensitivity (92.94 % vs. 82.35 %) while both TAS and TVS were equally specific 93.33%.[6]

Trans-vaginal scan is thus better than trans-abdominal scan in establishing the accurate diagno-sis of ectopic pregnancy.[5,6] The evidence is however limited; only 1 local research paper is available.[6] Also, this obvious benefit is doubtful because Mahmoud et al. in 2012 showed that trans-vaginal scan was only better in revealing the presence or absence of gestational sac in the uterine cavity and had limited significance for lesions outside pelvis and that a preliminary trans-abdominal scan aided in the better interpretation of trans-vaginal scan.[7] The current trend in the emergency department of tertiary care units in Pakistan is transabdominal scan in patients suspected of ectopic pregnancy. The purpose of this study is to evaluate the accuracy of trans-vaginal scan and trans-abdominal scan to establish early and accurate diagnosis of ectopic pregnancy. This will in turn enable early and timely management of such patients, reducing the morbi-dity and mortality associated with this condition.

OBJECTIVE

The objective of this study was to determine the accuracy of trans-abdominal and trans-vaginal ultrasound in the diagnosis of ectopic pregnancy by taking histopathology as gold standard.

METHODS

This cross-sectional survey was conducted at Department of Diagnostic Radiology, Sir Ganga Ram Hospital Lahore over a period of 6 months from 25/06/2014 to 24/12/2014. A total of 195 female patients of reproductive age group (16-40 years) were selected by Non-probability Consecutive Sampling. Patients selected were those presented in emergency department with clinical suspicion of ectopic pregnancy i.e. history of conception/ amenorrhea, lower pelvic pain, vaginal bleeding and collapse and with raised serum HCG level (1500 to 2000 mIU/mL) as per routine investigations. Written informed consent and detailed history was taken from each patient. All the patients underwent TAS and TVS. TAS was performed with full bladder and 3.5 MHZ convex probe. The bladder was then emptied and TVS was performed using standard technique with 7 MHZ probe. Ectopic Pregnancy was diagnosed when any 3 of the following 4 ultrasound criteria were met.

a.   Absence of gestational sac in uterus

b.   Presence of extra uterine mass

c.   Presence of pseudo gestational sac

d.   Presence of fluid in the pouch of Douglas

The diagnosis was finally confirmed by the presence of embryonic and placental tissue on histopathology of the specimen taken during surgery from uterine/ extra uterine gestational sac.

Ultrasound findings along with ultrasono-graphic diagnosis were recorded. The final diagnosis after histopathology was also noted. All the data was entered into the attached proforma. All the scans were performed by the same consultant over the same machine to eliminate bias. Confounding variables were controlled by exclusion. All the collected data was analyzed with SPSS version [10].

RESULTS

The age of the patients ranged from 20 years to

38 years with a mean of 29.64±4.75 years as shown in Table 1. The gestational age of the patients ranged from 3 weeks to 11 weeks with a mean gestational age of 7.26±2.28 weeks as shown in Table 2. Most of the patients were para 2 (38.5%), followed by para 3 in 23.6% cases as shown in Table 3.

The frequency of ectopic pregnancy diagnosed on histopathology (gold standard) was 17.9% as shown in Table 84. TVS labeled ectopic pregnancy in 42 (21.5%) cases as shown in Table 5. A 2×2 contingency table was generated for TVS and histopathology which revealed there were 32 True Positive cases, 10 False Positive cases, 3 False Negative cases and 150 true negative cases as shown in Table 6. It yielded sensitivity (91.43%), specificity (93.75%), accuracy (93.33%), positive predictive value (76.19%) and negative predictive value (98.04%) of TVS for ectopic pregnancy taking histopathology as gold standard.

TAS labeled ectopic pregnancy in 39 (20%) cases as shown in Table 7. A 2×2 contingency table was generated for TAS and histopathology which revealed there were 29 True Positive cases, 10 False Positive cases, 6 False Negative cases and 150 true negative cases as shown in Table 8. It yielded sensitivity (82.86%), specificity (93.75%), accuracy (91.79%), positive predictive value (74.36%) and negative predictive value (96.15%) of TAS for ectopic pregnancy taking histopathology as gold standard.

DISCUSSION

Historically, ectopic pregnancies were diagnosed on the classical triad of symptoms: pain, vaginal bleeding and a history of amenorrhea. Advances in diagnostic radiology brought Trans-abdominal Scan (TAS) as an important diagnostic tool in such patients.[3] However, in the past decade there has been increased advocacy for the use of trans-vaginal Scan (TVS) in suspected patients instead of trans-abdominal scan. There are studies which show TVS to be more sensitive and specific than TAS in the diagnosis of EP.[5,6,8-12] The findings of

Table 1: *Descriptive Statistics for Age*

	N	Minimum	Maximum	Mean	Std. Deviation
Age	195	20	38	29.64	4.749
Valid N (listwise)	195				

Table 2: *Descriptive Statistics for Gestational Age*

	N	Minimum	Maximum	Mean	Std. Deviation
Age	195	3	11	7.26	2.279
Valid N (listwise)	195				

Table 3: *Frequency Table for Parity*

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	1	37	19.0	19.0	19.0
	2	75	38.5	38.5	57.4
	3	46	23.6	23.6	81.0
	4	37	19.0	19.0	100.0
	Total	195	100.0	100.0	

Table 4: *Frequency Table for Histopathological Diagnosis*

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	Yes	35	17.9	17.9	17.9
	No	160	82.1	82.1	100.0
	Total	195	100.0	100.0	

Table 5: *Frequency Table for TVS Diagnosis*

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	Yes	42	21.5	21.5	21.5
	No	153	78.5	78.5	100.0
	Total	195	100.0	100.0	

Table 6: *TVS * Histopathology Crosstabulation*

		Histopathology		Total
		Yes	No	
TVS	Yes	32	10	42
	No	3	150	153
Total		35	160	195

Table 7: *Frequency Table for TAS Diagnosis*

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	Yes	39	20.0	20.0	20.0
	No	156	80.0	80.0	100.0
	Total	195	100.0	100.0	

TP(a) = 32	FP(b) = 10
FN(c) = 3	TN(d) = 150

Sensitivity	$\dfrac{a}{a + c}$	= 91.43 %
Specificity	$\dfrac{d}{b + d}$	= 93.75 %
Accuracy	$\dfrac{a+d}{a+b+c+d}$	= 93.33 %
Positive Likelihood Ratio	$\dfrac{\text{Sensitivity}}{100 - \text{Specificity}}$	= 14.63
Negative Likelihood Ratio	$\dfrac{100 - \text{Sensitivity}}{\text{Specificity}}$	= 0.09
Disease prevalence	$\dfrac{a + c}{a + b + c + d}$	= 17.95 %
Positive Predictive Value	$\dfrac{a}{a + b}$	= 76.19 %
Negative Predictive Value	$\dfrac{d}{c + d}$	= 98.04 %

Table 8: *TAS * Histopathology Crosstabulation*

		Histopathology		
		Yes	No	Total
TAS	Yes	29	10	39
	No	6	150	156
Total		35	160	195

TP(a) = 29	FP(b) = 10
FN(c) = 6	TN(d) = 150

Sensitivity	$\dfrac{a}{a + c}$	= 82.86 %
Specificity	$\dfrac{d}{b + d}$	= 93.75 %
Accuracy	$\dfrac{a+d}{a+b+c+d}$	= 91.79 %
Positive Likelihood Ratio	$\dfrac{\text{Sensitivity}}{100 - \text{Specificity}}$	= 13.26
Negative Likelihood Ratio	$\dfrac{100 - \text{Sensitivity}}{\text{Specificity}}$	= 0.18
Disease prevalence	$\dfrac{a + c}{a + b + c + d}$	= 17.95 % (*)
Positive Predictive Value	$\dfrac{a}{a + b}$	= 74.36 % (*)
Negative Predictive Value	$\dfrac{d}{c + d}$	= 96.15 % (*)

these studies have been summarized in Table 9.

However, Mahmoud et al. in 2012 showed that trans-vaginal scan was only better in revealing the presence or absence of gestational sac in the uterine cavity and had limited significance for lesions outside pelvis and that a preliminary trans-abdominal scan aided in the better interpretation of trans-vaginal scan.[7]

Due to conflicting and limited local data on TAS and TVS, the purpose of the current study was to determine the diagnostic accuracy of these two ultrasound modalities in ectopic pregnancy. In the current study, the sensitivity and specificity of TVS was found to be 91.43% and 93.75% respectively. Our results match closely with those of Malik et al.6; sensitivity (92.94%) and specificity (93.33%). Our results also agree with those of Hopp et al.[10] and Condous et al.[11]. Timor-Tritsch8 and Kirk et al.[5] documented relatively higher sensitivity and specificity as compared to our study. Valenzano et al.[9] documented a very low sensitivity (88.4%) while Nahar et al.[12] documented a very low specificity (75%). These differences can be attributed to inter-operator bias (observer's skills) and hardware differences (probes used).

We observed a comparatively low sensitivity of TAS (82.86%) as compared to TVS (91.43%) while both of them were equally specific (93.75%). Our results match with those of Malik et al.[6] who observed sensitivity and specificity of TAS to be 82.35% and 93.33% respectively. Valenzano et al.[9] and Nahar et al.[12] observed very low sensitivity and specificity of TAS as shown in Table 9.

Thus trans-vaginal scan (TVS) is more sensitive (91.43% vs. 82.86%) and accurate (93.33% vs. 91.79%) than trans-abdominal scan (TAS). In the light of current evidence, it is recommended that

Table 5: *Summary of Existing Literature on TAS and TVS*

Author	Year	TVS		TAS	
		Sensitivity	Specificity	Sensitivity	Specificity
Timor-Tritsch[69]	1989	100%	98.2%		
Valenzano et al.[70]	1991	88.4%		76.9%	
Hopp et al.[71]	1997	96%	88%		
Condous et al.[72]	2005	90.9	99.9%		
Kirk et al.[5]	2007	98.3%	99.9%		
Malik et al.[6]	2010	92.94%	93.33%	82.35%	93.33%
Nahar et al.[73]	2013	92.3%	75%	73.1%	75%
Current Study	**2014**	**91.43%**	**93.75%**	**82.86%**	**93.75%**

patients who present with lower abdominal pain, amenorrhea and first trimester vaginal bleed should be evaluated by trans-vaginal scan along with other

investigations to confirm ectopic pregnancy.

However, a critical limitation observed in the present study was limited field of view of TVS; therefore it is recommended that trans-abdominal scan should be performed in addition to trans-vaginal scan.

CONCLUSION

Trans-vaginal scan is more sensitive and accurate than trans-abdominal scan in the diagnosis of ectopic pregnancy.

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BIOCHEMICAL ANALYSIS OF BONE PARAMETERS IN PATIENTS OF BETA THALASSEMIA MAJOR CHILDREN IN LAHORE, PAKISTAN

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Abstract

Background: Thalassemia is a complex group of genetic blood disorders resulting from defective or reduced rate of synthesis of one or more types of hemoglobin polypeptide chain that leads to severe anemia. To correct the anemia, hemoglobin level is tried to maintain minimum to 10 g/dl, and for that, thalassemia patients require repeated blood transfusion on regular basis that leads to iron deposition in many organs. Many studies have shown the disturbed liver and renal functions in these patients in Pakistan. No such study has been documented in which status of parathyroid gland and their related disorder was assessed. Hence the present study was designed to evaluate the functions of parathyroid gland with its effects on biochemical bone profile by measuring the levels of parathyroid hormone (PTH), calcium, phosphate (PO4), magnesium, alkaline phosphatase (ALP) and vitamin D in blood.

Subjects and Methods: It was a cross sectional descriptive study in which seventy patients with beta-thalassemia major and twenty healthy individuals matched by age as control were included. Venous blood was collected from each subject and biochemical analysis of various parameters was done through semi-automated analyzer through commercial kits. Data was analyzed using SPSS version 16.

Results: The thalassemia patients who were receiving packed cell volume (PCV) were found to have significantly higher levels of serum ferritin, phosphorous, alkaline phosphatase (ALP), magnesium (Mg) and lower levels of Vitamin D, parathormone (PTH) and calcium in comparison to healthy individuals.

Conclusions: Our study demonstrates that thalassemia patients have hypoparathyroidism with disturbed biochemical bone profile in comparison to control subjects of same age group.

Keywords: Alkaline phosphatase, parathyroid hormone, ferritin, thalassemia.

Thalassemia is a complex group of inherited autosomal recessive blood disorders[1]. It results from reduced or defective synthesis of one or more types of normal hemoglobin polypeptide chain in which beta chain defect is more common that leads to severe anemia [2].

The prevalence of the disease is more observed in North African countries and Southeast Asia. In Pakistan, large population size, cousin marriages and increased birth rate are considered the major prevalent factors for the disease[3]. In Pakistani population, overall carrier frequency rate of the disease is 5.5-6.5 % whereas homozygotic thalasse-mic children born are approximately 9000 each year. The carrier rate for beta thalassemia major varies from 1.4 to 8.0% in different regions of Pakistan. The maximum prevalence of beta thalassemia is reported in the province of Sind, coastal areas of Baluchistan and Khyber Pakhtunkhwa, where the population from various parts of world has settled during different period in history[4].

Blood transfusion is required on regular basis in thalassemia patients to attain ~10mg/dl hemoglobin levels. Repeated blood transfusions and use of chelating agents i.e., parenteral deferoxamine mesylate and oral deferasirox, result to organ

dysfunctions including endocrine glands[5,6,7]. This glandular damage occurs via formation of free radicals and lipid peroxidation which ultimately causes damage to cell surface receptors, mitochondrial membrane and lysosomes[8]. Chronic hypoxia, iron accumulation, chelating therapy, hormonal insufficiency and impaired calcium homeostasis also leads to growth & maturational delay and early osteoporosis[9,10,11]. Insulin-like growth factor-1 (IGF1), a major mediator of (GH)-stimulated somatic growth and a mediator of GH-independent anabolic responses in many cells and tissues is seen low in these patients[12]. However, most patients of beta thalassemia major with hypoparathyroidism usually remain asymptomatic; low calcium levels being detected during routine laboratory examinations[13].

Few studies in general, have focused on this aspect of beta thalassemia[14]. A very limited data in Pakistani population prompted us to plan a study in which we can evaluate the biochemical bone parameters and related growth & stress markers such as IGF1, vascular endothelial growth factor (VEGF), C-reactive protein (CRP)[15,16,17] collectively, to assess growth and maturation delay in thalassemic patients and then to prevent this delay and early development of osteoporosis.

METHODS

The study was performed according to the cross sectional descriptive study design.

An approval for this study was granted by the Ethical Committee of the University of Lahore, Research Center, Pakistan. Another official authorization was obtained from the Sundas Foundation Thalassemia Centre Shadman, Lahore. The purpose and objectives of the study were explained to the parents of all the participants and then written consent was obtained.

A total of seventy thalassemic children (aged from 2 to 21 years) receiving blood transfusion twice a week and chelating therapy consisting of 30 to 50 mg/Kg deferoxamine subcutaneously, were included for the study. Twenty apparently healthy children of same age and sex were also enrolled for the study as control. Patients of poor compliance which were suffering from DM type I, hepatic diseases, cardiac diseases, renal disorders, malnutrition disorders and malignancy were excluded from the study.

A full history taking with thorough clinical examination, paying particular attention to pallor, jaundice, hepato-splenomegaly, and manifestations of hypoparathyrodism was taken into account for all study participants.

The data of study was collected via using close-ended questionnaire which was constructed and conducted in Urdu and English languages and also from laboratory investigations of blood samples for the biochemical analysis of beta thalassemic children. Five ml of venous blood was collected from each subject (cases and controls). One ml of collected blood was added in EDTA containing tubes for hemoglobin estimation. Withdrawal of blood from the patients was performed just before the scheduled blood transfusion of the patients. Remaining 4ml of blood was then centrifuged for separating the serum for about 10-15 minutes at 3000 rpm. Serum obtained was stored at -20°C till further study of required parameters on semi-automated analyzer through commercial kits.

Data was analyzed statistically through SPSS version 16.

RESULTS AND DISCUSSION

The total annual incidence of symptomatic individuals of beta thalassemia is estimated at 1 in 100,000 throughout the world[18] which is more prevalent in North African countries and Southeast Asia. In Pakistan, large population size, cousin marriages and increased birth rate are considered as the major prevalent factors for the disease. In Pakistani population, overall carrier frequency rate of beta thalassemia is 5.5-6.5 % that varies from 1.4 to 8.0% in different regions of the country whereas the number of homozygotic thalassemic children born is about 9000 per annum[3].

Present study shows significantly (p<0.05) decreased levels of vitamin D, PTH and calcium in patients of -thalassemia major, whereas the levels of phosphate, alkaline phosphatase (ALP), and ferritin were found to be increased in thalassemic patients as compared to control subjects. These findings are in line with the work of Khalda et al., and Hagag[18,19] as they found decreased levels of vitamin D, PTH and calcium and increased levels of phosphorus, ferritin and ALP in -thalassemia major patients during the investigation of prevalence of hypoparathyroidism.

When serum level of malondialdehyde (MDA) and catalase were measured in these patients, significantly (p<0.05) high levels of these parameters were observed with decreased levels of superoxide dismutase (SOD), reduced glutathione (GSH) and hemoglobin, as compare to normal control subjects. These outcomes are in accordance with the studies of Elham and Shazia et al [20,21].

Glandular damage occurrs via iron overload and various mechanisms have been proposed which include free radicals formation and lipid peroxidation. These lead to destruction of lysosomal, sarcolemmal and mitochondrial membrane. Not only that this also damages cell surface transferrin recep¬tors and the cells' ability of protection against inorganic iron [22].

In present study serum magnesium level were also measured which was low as was agreed with the study of Ali et al [23]. They also observed significantly lower levels of serum magnesium level in patients of beta thalassemia major. Serum total proteins and albumin levels were found low in present study in accordance with the studies of Sameh et al[24]. In our study CRP and VEGF levels were found significantly (p<0.05) increased in conformity with the work of Rukhsana et al., and Farzane et al., respectively[15, 16]. In present study serum IGF1, level were measured in patients of beta thalassemia major significantly (p<0.05) low levels of IGF1 was observed as compare to normal control subjects. These results show the mechanism lying behind the glandular damage and were in accordance with the study of Mona et al, [25]. They observed significantly lower levels of serum IGF1 level in patients of beta thalassemia major which can lead to glandular dysfunction.

CONCLUSION

On the whole it is concluded that persistent iron overload leads to organ function damage which is further aided by increased oxidative stress, mainly caused by peroxidative damage due to secondary iron overload. Production of free radicals cause rise in serum antioxidant enzymes status which play an important role in pathogenesis of dysfunctional glands in Thalassemia. All these factors lead to delayed growth and maturation and development of weak bones.

Table 1: *Comparison of Mean Concentration of Ferritin, Hemoglobin, Vitamin D3 and PTH Blood Levels in Control and Thalassemic Subjects.*

Parameters	Control Subjects	Thalassemic Subjects
Hemoglobin (g/dl)	6.84±1.33	13.73±1.29
Ferritin (ng/dl)	168±10.00	3254.10±1728.38
PTH (pg/mL)	24.74±11.68	8.31±3.18
Vitamin D3 (pg/mL)	30.22 ±6.29	15.63±8.40
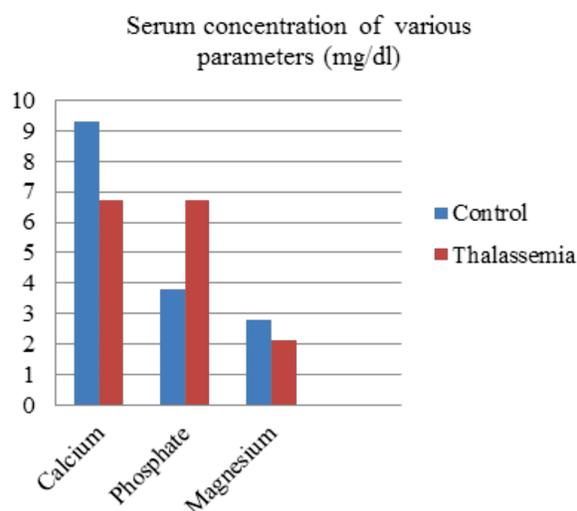
Figure1. *Comparison of Mean Concentration of Hemoglobin, Ferritin and Magnesium Blood Levels in Control and Thalassemic Subjects.*

The administration of essential antioxi-dant

enzymes and replacement of calcium, vitamin D, and growth related hormones is recommended in beta thalassemic patients in order to reduce existence of oxidative damage and related complications after performing a large scale assessment and evaluation.

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DIAGNOSTIC ACCURACY OF DOPPLER ULTRASONOGRAPHY FOR DIAGNOSIS OF PLACENTA ACCRETA TAKING SURGICAL FINDINGS AS GOLD STANDARD

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Abstract

Background: Placenta accreta is the abnormal implantation of the placenta into the uterine wall. The incidence of placenta accreta has increased with the rising number of cesarean deliveries. Prenatal diagnosis of placenta accreta can help minimize the complication rate by enabling a surgeon to plan for the type of resources needed at the time of delivery. Prenatal diagnosis of placenta accreta has historically been difficult, and the accuracy of sonography remains in question. The accuracy of sonography using gray scale and color Doppler techniques for prenatal diagnosis of placenta accreta varies widely in different studies.

Objective: Objective of this study was to determine the diagnostic accuracy of Doppler USG for diagnosis of placenta accreta in females presented with abnormal adherent placenta taking surgical findings as gold standard.

Method: The cross-sectional survey was conducted at Department of Obstetrics and Gynecology, Unit I, Lady Willingdon Hospital, Lahore for the period of 6 months. 100 cases were enrolled in study through non-probability, purposive sampling. Data was entered and analyzed through SPSS 17.0.

Results: The mean age of patients was 28.22+3.71 years. The mean gestational age was 28.15+3.37 weeks. There were 31% females with parity 3, 39% were with parity 4, 26% were with parity 5 and there were 4% females with parity 6. Out of 65 cases, positive on operative findings, there were 60(92.3%) cases positive on Doppler USG. Out of 35 cases, negative on operative findings, there were 26(74.3%) cases negative on Doppler USG. Thus the sensitivity, specificity, PPV and NPV of Doppler USG for placenta accreta were 92.3%, 74.3%, 87% and 83.9% respectively. The overall diagnostic accuracy of Doppler USG was 86%. Conclusion: Study concluded that sensitivity of Doppler USG was high enough and in future we can rely on Doppler USG for evaluation of placenta accreta.

Keywords: *placenta accreta, doppler ultrasonography, operative findings, abnormal adherent placenta.*

W hen the placenta is attached to myometrium but it does not invade the uterine muscle, it is called placenta accreta. It is increta when it invades myometrium and percreta when it penetrates through the uterine wall due to abnormal development of deciduas basalis. Placenta accreta is the most common comprising 80%.[1]

The presence of placenta accreta in patients with a previous cesarean section is associated with accreta in 10% to 35% cases. With multiple cesarean sections, the risk may be as high as 60-65%.[2]

The major risk factor is uterine scarring. Prior manual removal or uterine curettage may also cause scarring. Post-partum hemorrhage will occur in most cases, particularly if the accreta is partial where non-contracted portions of myometrium are adjacent to adherent placenta. Women with major placenta previa or placenta accreta are at high risk of preterm delivery and severe morbidity therefore early diagnosis of abnormally adherent placenta is desired to anticipate the management of patient and prevention of PPH.[3]

Placental tissue is easily distinguishable from myometrium deciduas on USG. Routine USG scanning at 20 weeks of gestation should include placental localization. 2D-ultrasonography is a useful tool to diagnose placenta accreta. The most reliable sign is the presence of abnormal placental lacunae. The presence of at least two ultrasound findings decreases the number of false-positive

diagnosis and increases the performance of 2D-Doppler ultrasonography.[4] Surgeons delivering the baby by cesarean section in the presence of a suspected placenta previa accreta should consider opening the uterus at a site distant from the placenta, and delivering the baby without disturbing the placenta, in order to enable conservative management of the placenta or elective hysterectomy to be performed if the accreta is confirmed. Going straight through the placenta to achieve delivery is associated with more bleeding and a high chance of hysterectomy and should be avoided.[5]

According to one study, the sensitivity and specificity of antenatal ultrasound diagnosis of placenta previa accreta during antenatal visit of pregnant female was 100%.[6]

One more study done in 2006, the sensitivity and specificity of Doppler USG was found to be 77% and 96% antenatally.[7] While one study showed very small variation in sensitivity and specificity of Doppler USG in detection of placenta accreta i.e. 90% and 100% respectively during antenatal visit of females.[8] But in another study, USG had 93% sensitivity and 71% specificity.[9]

Rationale of this study is to find the diagnostic accuracy of Doppler USG for diagnosis of placenta accreta in females after 20 weeks of gestation. It was observed that the accuracy of Doppler varies according to different studies. That's why this study is aimed to find the exact accuracy rate in our population. If accuracy rate of Doppler USG yields to be high in our study results, then in future we will use Doppler USG for detection of placenta accreta in such type of patients. Doppler is inexpensive and easily available.

METHODS

The cross-sectional survey was conducted at Department of Obstetrics and Gynecology, Unit I, Lady Willingdon Hospital, Lahore for the period of 6 months. 100 cases were enrolled in study through non-probability, purposive sampling. Informed consent was obtained not only for their data to be used in the study but also for hysterectomy if needed and patient demographic information (name, age, contact) was recorded. Patients were assessed for placenta accreta with the help of 2D-Doppler USG by researcher himself. If RI=0.25 and high velocity pulsatile venous-type flow is 15cm/s then cases were labeled as positive otherwise they were labeled as negative. All patients then underwent cesarean section and hysterectomy if required to stop bleeding and positive and negative cases of Doppler USG was then confirmed. All this information was recorded on proforma. Data was entered and analyzed through SPSS 17.0. Sensitivity, specificity, positive predictive value, negative predictive value, and accuracy of Doppler ultrasonography were calculated taking operative findings as gold standard.

RESULTS

In this study, we included 100 pregnant females who had suspicion of placenta accreta with mean age of 28.22+3.71 years. The minimum age of patients was 20 years while maximum age was 35 years (Table-1).

Table 1: *Descriptive Statistics of Age of Patients*

	N	100
	Mean	28.22
Age (Years)	SD	3.71
	Minimum	20
	Maximum	35
	Range	15

The mean gestational age was 28.15+3.37 weeks. The minimum gestational age was 21 weeks while maximum gestational age was 34 weeks (Table-2).

Table 2: *Descriptive Statistics of Gestational Age*

	N	100
	Mean	28.15
Gestational Age (Weeks)	SD	3.37
	Minimum	21
	Maximum	34
	Range	13

There were 31 (31.0%) females with parity-3,

39 (39.0%) with parity-4 and 26 (26.0%) with parity-5 while 4 (4.0%) females were with parity-6 (Table-3).

Among 65 cases, positive on operative findings, there were 60 (92.3%) cases positive on Doppler USG. Among 35 cases, negative on operative findings, there were 26 (74.3%) cases negative on Doppler USG. Thus the sensitivity, specificity, PPV and NPV of Doppler USG for placenta accreta were 92.3%, 74.3%, 87.0% and 83.9%, respectively. The overall diagnostic accuracy of Doppler USG was 86.0% (Table-4).

Table 3: *Distribution of Parity of Patients*

Parity	Frequency	Percentage
3	31	31.0%
4	39	39.0%
5	26	26.0%
6	4	4.0%
Total	100	100.0%

Figure-1: *Distribution of parity of patients*
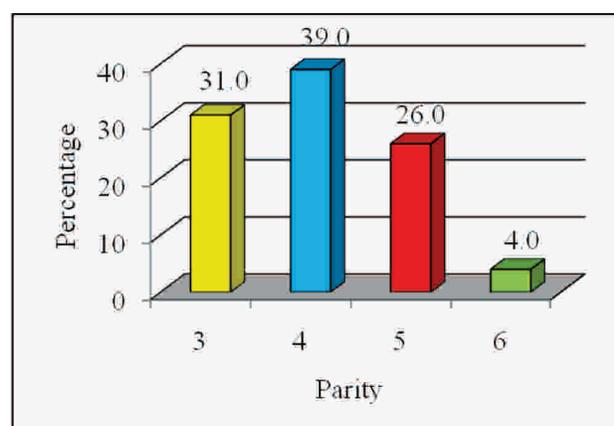
Table 4: *Comparison of Doppler USG and Operative Findings of Placenta Accreta*

		Operative Findings		Total
		Positive	Negative	
Doppler USG Findings	Positive	60 (92.3%)	9 (25.7%)	69 (69.0%)
	Negative	5 (7.7%)	26 (74.3%)	31 (31.0%)
Total		65 (100.0%)	35 (100.0%)	100 (100.0%)

Sensitivity	92.3%
Specificity	74.3%
PPV	87.0%
NPV	83.9%
Diagnostic Accuracy	86.0%

DISCUSSION

The study was conducted to find the diagnostic accuracy of Doppler USG in our population. To obtain adequate results, 100 pregnant females were included in the study who had suspicion of placenta accreta with mean age of 28.22+3.71 years. The mean gestational age was 28.15+3.37 weeks.

Among those with previous cesarean deliveries who have placenta previa or a low-lying anterior placenta, the risk of placenta accreta increases from 24% for a single cesarean delivery to 67.0% for 4 cesarean deliveries.[10] In our study, there were 31.0% females with parity 3, 39.0% with parity 4, 26.0% with parity 5 and 4.0% females were with parity 6.

In our study, we found the sensitivity, specificity, PPV and NPV of Doppler USG for placenta accreta were 92.3%, 74.3%, 87.0% and 83.9%, respectively. The overall diagnostic accuracy of Doppler USG was 86.0%. These results match with one study which reported that Doppler sonography had sensitivity of 93.0% and specificity of 71.0%.[9] But another study reported that sonography had sensitivity of 77.0% and specificity of 96.0%.[11]

The ultrasonographic features suggestive of placenta accreta include irregularly shaped placental lacunae (vascular space) within the placenta, thinking of the myometrium overlying the placenta, loss of the retroplacental "clear space", protrusion of the placenta into the bladder, increased vascularity of the uterine serosa-bladder interface and turbulent blood flow through the lacunae on Doppler USG. The presence and increasing number of lacunae within the placenta at 15-20 weeks of gestation have been shown to be the most predictive ultrasonographic signs of placenta accreta, with a sensitivity of 79.0% and a positive predictive value of 92.0%. These lacunae may result in the placenta having a "moth-eaten" or "Swiss cheese" appearance.[11-13]

Overall, grayscale ultrasonography is sufficient to diagnose placenta accreta, with a sensitivity of 77-87%, specificity of 96-98%, a PPV of 65-93% and a NPV of 98%. The use of power Doppler, color Doppler, or three-dimensional imaging does not

significantly improve the diagnostic sensitivity compared with that achieved by grayscale ultrasonography alone.[11,13,14]

CONCLUSION

Study found sensitivity of Doppler USG as 92.0% and specificity of 74.0%. This was high enough that in future we can rely on for evaluation of placenta accreta. Thus it was concluded from the results of this study that Doppler USG is enough to diagnose placenta accreta. Doppler USG is inexpensive and easily available technique. So in future we can rely on this technique to diagnose placenta accreta to avoid costly and invasive procedure.

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DIAGNOSTIC ACCURACY OF MRCP IN DIFFERENTIATING BENIGN AND MALIGNANT CAUSES OF OBSTRUCTIVE JAUNDICE TAKING HISTOPATHOLOGY AS GOLD STANDARD

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ABSTRACT

Background: It is difficult to differentiate between Benign and malignant biliary obstructions with imaging alone. MRCP is a well-established modality in differentiating the benign and malignant causes of obstructive jaundice. However in few cases, it is difficult to differentiate whether the obstruction is caused by inflammatory cause or a stricture is malignant in nature. Hence, we carried out a study to detect the diagnostic accuracy of MRCP in differentiating benign and malignant causes of obstructive jaundice.

Methods: The study design opted was observational prospective cohort, where the patients with obstructive jaundice were assessed for the diagnostic accuracy of MRCP in differentiating benign and malignant causes. The exclusion criteria included patients with metallic implant insertion, cardiac pacemakers, metallic foreign body in-situ, also patients having history of claustrophobia and who required sedation or ventilation whereas all the patients with clinical and laboratory finding suggestive of biliary obstruction causing obstructive jaundice were included in this study.

Results: A total of 70patients were recruited. The mean age of the patients was   51+11.9 with range 18-65. All the obstruction was imaged by MRI/MRCP. Out of the total, 58 (82.8%) cases were benign and 12 (17.2%) were malignant in nature. While comparing the lesions types, malignant lesions were found more in older ages than the benign lesions. The MRCP sensitivity, specificity and accuracy in benign stricture case were 91.7%, 96.1% and 94% respectively. Also In cases of malignant stricture, the MRCP sensitivity, specificity and accuracy was 85%, 96% and 93% respectively.

Conclusion: MRCP is an accurate means of differentiating benign and malignant causes of obstructive jaundice.

Keywords: Magnetic resonance cholangiopancreatography (MRCP), Magnetic resonance imaging (MRI), Sensitivity encoding (SENSE), choledocholithiasis

It is difficult to differentiate between Benign and malignant biliary obstructions with imaging alone. The most commonly cause for benign obstruction is choledocholithiasis, whereas the post cholecystectomy stricture, inflammatory, stricture formation secondary to pancreatitis are other causes. Few more causes of benign obstruction are choledochal cyst, primary sclerosing cholangitis, and Mirrizi syndrome[1,2]. On the other hand, cholangiocarcinoma commonly caused the malignant obstruction. Other causes involvedwere carcinoma gall bladder, carcinoma head of pancreas, lymph nodes and metastasis[2-4]. MRCP is a well-established modality in differentiating the benign and malignant causes of obstructive jaundice. However in few cases, it is difficult to differentiate whether the obstruction is caused by inflammatory cause or a stricture is malignant in nature. Hence, we carried out a study to detect the diagnostic accuracy of MRCP in differentiating benign and malignant causes of obstructive jaundice.

METHODS

The study design opted for the present research was observational prospective cohort, where the patients suggestive with obstructive jaundice or biliary obstruction were assessed for the diagnostic accuracy of MRCP in differentiating benign and

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malignant causes. The study duration was of twelve months starting from Dec 2015. The venue of the study was Sheikh Zayed Hospital. The exclusion criteria included patients with metallic implant insertion, cardiac pacemakers, metallic foreign body in-situ, also patients having history of claustrophobia and who required sedation or ventilation whereas all the patients with clinical and laboratory finding suggestive of biliary or jaundice obstruction were included in this study. All patients were underwent for imaging that was done on GE 1.5 Tesla MRI machine. The test was carried out after 4 hours fasting to stimulate gall bladder filling. Pineapple juice was provided to the patients before the examination. This improves the imaging quality and contrast. Selected MRCP sequences were used. The observations taken from MRCP and MRI were biliary channels, their asymmetrical/ symmetrical dilatation, pancreatic duct, calculus, stricture's site, margins (regular/irregular), tapering (abrupt/ gradual), length of stricture (long/short), Gall Bladder, lymph nodes, metastasis. A benign stricture was differentiated from a malignant one if it showed regular, symmetric and short segment narrowing. Irregular, asymmetric and long segment narrowing was more commonly found in malignant stricture. The patients were followed after surgical resection for histopathology of the specimen and grouped into benign and malignant groups. The sensitivity, specificity of MRCP/MRI were calculated with the histopathology report taken as gold standard for differentiating malignant from benign lesions. Demographic information along with diagnostic history of all the participants was collected. All the required diagnostic values were collected from the blood samples and imaging by following their standard operating procedures in hospital laboratory. An informed consent was also taken from the patients or attendant of the patient. Ethical consideration was taken in to account by taking approval Hospital ethical Committee.

Statistical analysis: All the collected data was stored electronically & analyzed later by using SPSS version 20. Descriptive statistics were applied to calculate mean and standard deviation. Frequency distribution and percentages were calculated for qualitative variables like matrix size, Benign stricture and p values less than 0.05 was considered statistically significant.

RESULTS:

A total of 70patients were recruited for this study. The mean age of the patients was 51+11.9 with range 18-65. 25 (31.3%) of the patient were in the age category of 36 to 45. Whereas 15 (18.7%) belong to 18-35 and 40(50%) were above and equal 45 years of age. All the obstruction was imaged by MRI/ MRCP. Out of the total, 58 (82.8%) cases were benign and 12 (17.2%) were malignant in nature. While comparing the lesions types, malignant lesions were found more in older ages than the benign lesions. The Benign obstruction patients were having the meanage of 48.9±12.03 years and of malignant obstruction was 54 ±10.3years. Abdominal pain and yellowish tinting of skin and sclera was commonest symptoms were observed in all the patients. While comparing the obstruction groups i.e. benign and malignant, Vomiting and fever were more common in benign and loss of appetite and weight loss was commonest in malignant group of obstruction. A detail summary of the biliary or jaundice obstructive diseases was given in the Figure 1.
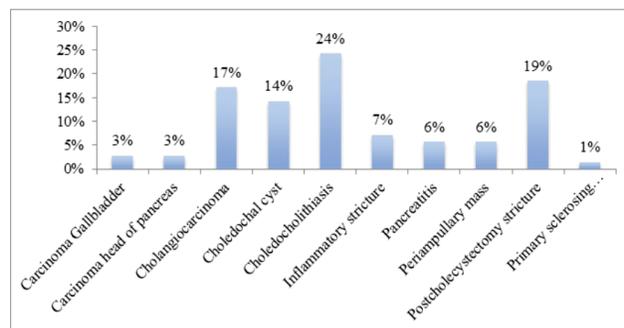
Figure 1 *Various Biliary Obstructive Diseases on the Basis of Final Diagnosis.*

Choledocholithiasis[17] (24%) was the commonest cause of benign obstruction in our study, followed by postcholecystectomy strictures 13

(19%). Other benign causes were choledochal cyst 10(14%), inflammatory strictures 5 (7%), pancreatitis 4(6%) and primary sclerosing cholangitis 1(1%). More on the details of benign strictures causes were given in table 1.

While in malignant obstructions, the commo-

Table 1: *Etiology of Benign Strictures*

Etiology of benign strictures	n(%)
Iatrogenic (post cholecystectomy)	18(69%)
Inflammatory stricture	5(19%)
Pancreatitis	3(12%)
Total	26(100%

nest cause was cholangiocarcinoma 5(41.67%), others were periampullary carcinoma 3(25%), carcinoma gall bladder and carcinoma head of pancreas each 2(16.67%). Finally, based on surgical, histopathological or ERCP correlation diagnosis was made. The final diagnosis was than correlated to MRCP findings and MRCP diagnostic effectively was calculated for individual group of diseases and for overall Jaundice/ biliary obstructive diseases. All the cases of choledocholithiasis were correctly diagnosed by MRCP. MRCP also diagnosed correctly all other cases of choledochal cyst. We also observed that 1 case of cholangiocarcinoma was falsely diagnosed as choledochal cyst on MRCP. Type of choledochal cyst was correctly diagnosed in all the cases by MRCP. We report in our study the MRCP sensitivity for detection of choledochal cyst as 100%,specificity 98.4%, and diagnostic accuracy 98.7%. Whereas, MRCP also diagnosed the entire benign stricture correctly but only two cases of periampullary carcinoma were wrongly diagnosed as benign strictures. Two cases of benign strictures were wrongly diagnosed as malignant strictures on MRCP. The MRCP sensitivity, specificity and accuracy in this case were 91.7%, 96.1% and 94% respectively. Also In cases of malignant stricture, the MRCP sensitivity, specificity and accuracy was 85%, 96% and 93% respectively.

DISCUSSION

The study was planned to determine the diagnostic accuracy of MRCP in differentiating benign and malignant causes of obstructive jaundice. We not only estimated the diagnosis accuracy but specificity and sensitivity also for both benign and malignant stricture/causes. Though this was a great challenge to differentiate benign obstruction from malignant obstruction and the reported differentiation varied from 30-80% in many other published studies,[6-9] thus we have conducted this prospective study to differentiate both obstruction by using MRCP. We report in our study that malignant obstruction patients have higher average age than benign obstruction patients. Our finding was supported by other published studies i.e. Saluja et al.[10] Considering gender ratio for jaundice diseases, men are more commonly effected by this disease than women and the ratio is given by 13:12. In case of benign disease; it is equally found in men and women but the malignant diseases were more common in men. This finding of our study was also supported by other published study findings.[10-11] We reported in our study with commonest symptoms in our sampled patients were, upper quadrant pain and yellowish discoloration of skin and sclera. In malignant pathologies, loss of appetite and weight loss were commonest symptoms. This finding is supported by a similar finding of Saluja et al.[10] Moreover in benign stricture commonest cause in our study was postcholecystectomy stricture, also the commonest cause in malignant stricture in our study was cholangiocarcinoma. The sensitivity, specificity and diagnosis accuracy reported in our study for choledocholithiasis cases were similar to that in study done by Varghese et al.[12] Another finding of our study was one case of primary sclerosing cholangitis that exhibit multiple strictures, irregularities of bile ducts and bile duct wall thickening on MRCP. This finding was supported by other similar findings by Katabathina et al., on MRCP[2]. We reported in our study with most cases with benign stricture. The sensitivity, specificity and diagnosis accuracy of benign strictures through MRCP were similar to study by Hintze et al. [14] Lee et al., in their study found that sensitivity of MRCP in diagnosis of benign lesions was 81%, specificity 92% and accuracy 87% [15]. In Malignant strictures cases, The MRCP detected all cases correctly with sensitivity 85.7%, specificity 96.3% and accuracy 93.3%. Similar results were seen in studies done by Reinhold et al., and Lopera et al.,[16,17]. While summarizing the overall results of our study, out of 70 patients 65 were accurately diagnosed by MRCP.

The sensitivity, specificity and diagnostic accuracy of MRCP for differentiation of benign from malignant causes of biliary obstruction was 85.7%, 96.3%, and 93.3% respectively. In other previous studies, sensitivity of MRCP for detection of cause of benign and malignant obstruction ranged from 92-100%. Saluja et al., found sensitivity, specificity and diagnostic accuracy of MRCP for biliary obstructive diseases in their study to be 87.5%, 85.3% and 82.7% respectively similar to our study[10]. Park et al., found that the sensitivity, specificity, and accuracy of MRCP for differentiation of malignant from benign causes of biliary stricture were 81%, 70%, and 76% respectively [9]

CONCLUSIONS

We conclude that MRCP is an accurate means of differentiating benign and malignant causes of obstructive jaundice.

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FREQUENCY AND DETERMINANTS OF DIGITAL DEMENTIA CAUSED BY OVERUSE OF DIGITAL TECHNOLOGY AMONG STUDENTS OF KING EDWARD MEDICAL UNIVERSITY, LAHORE

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ABSTRACT

Background: Digital dementia is the decline in brain functioning due to excessive use of digital technology including smart phones, internet and computers. It is a newly recognized disease and mostly young generation in their teens is affected by it. With advancement of technology in the past few years, digital dementia has become an uprising issue causing general dementia symptoms as loss of memory, lack of concentration, physical inactivity, emotional instability and insomnia among users of digital devices. Objective: To determine the frequency and determinants of digital dementia due to overuse of digital technology among the students of King Edward Medical University (KEMU), Lahore. Study Design: Descriptive. Cross sectional study. Place: King Edward Medical University, Lahore. Study period: 3 months (March 1st, 2017 to May 31st, 2017)

Patients and Methods: A described cross sectional study was conducted in King Edward Medical University, Lahore. A total of 100 students doing overuse of digital technology were selected. Sampling was convenient. Consent was taken. Then, selection was done according to the decided criteria. Data collection was done through pretested questionnaire. Data was analyzed through SPSS version 20.2.

Results: Out of 100 subjects included in study, majority (96%) were of age group 18-22 with 56% of the subjects being male and 44% being females. 15% of subjects were categorized as normal use of technology, 20% as above normal use, 25% as high use and 25% as very high use of technology. Among these, 75% of the subjects said they required checklist for memory support, 70% had difficulty remembering events, 87% had difficulty in finding kept items; 63% had difficulty in remembering familiar faces or names and 71% said they had difficulty remembering familiar road directions, 58% had difficulty in following conversation, 68% said they had difficulty in understanding reading, 37% said they had problem following storyline on TV,66% had the problem of repetitive questioning, 64% subjects were unable to perform household chores, 44 % had difficulty in taking self-care and 60% had physical restlessness, 50% showed inappropriate response to external stimuli, 63% had obsession towards emotional events, 76% had apathy, 71% had sleep pattern disturbances and 65% had restlessness at night, 78% of students had confusion after moving houses and 75% said that others were aware of changes in their behavior and appearance. Our study showed that greater the use of technology, greater the symptoms of digital dementia.

Conclusion: The overuse of digital devices and internet was found to affect mental and physical health of students. The dementia symptoms were exaggerated in those who were involved in significant overuse of modern technological tools.

Key words: digital dementia, technology, overuse, young generation.

Dementia is a medical condition mostly seen in the elderly or those suffering from some psychiatric illness or head trauma. However, there is a new cognitive disorder among the younger generation that is being discoursed known as "Digital Dementia". Digital dementia is defined as "the deterioration in brain function due to overuse of digital technology, such as smartphones, computers and internet".

With advent in the field of digital world, the

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tremendous increase in the use of social networking and entertainment technology has replaced the conventional methods of social interaction resulting in rising proportion of young generation prone to psychological and behavioral disorders; hence raising concerns about issues like addiction, physical inactivity, and lack of concentration, emotional blunting and memory impairment. In September 2013, a survey conducted by Pew Internet Projects Research, showed that 73% of adults on internet are using social networking sites and 71% of them are on Facebook.[1]. World conference on educational media and technology 2013 concluded that increased use of internet leads to loss of ability to memorize as we store information more on web than minds.[2] In a South Korean study, the mobile usage among aged 10-19 has risen to 18.4 % from 11.2 % in 2003.[3] According to internet world stats, in Pakistan overall usage of digital devices and internet among its population has risen from 10.4 % in 2016 to 22.2 % in 2018 (almost doubled in 2 years). Spitzer, a German neuroscientist who published a book titled DIGITALE DEMENZE (Digital Dementia), used MRI scans, neural network models and statistics showing that digital media has deleterious effects on learning capacity and mental growth. Marcel O'Gorman argued that, at the very least, this new disease should be taken up as a thought experiment, one that requires due attention in the face of a situation that might best be approached speculatively.[4] Moreover, children spending more than 1-2 hours per day on television or recreational computer have greater probability of increase in psychological problems. Viewing television and playing video games is also associated with shortened attention span and impulsiveness.[5] There is increased comorbidity between usage of digital devices and psychiatric illnesses shown in a study done in 2014[6]. Behavioral problems like alexithymia has been associated with overuse of digital devices.[7]

A study by Andrew Przybylski has introduced an anxiety disorder "fear of missing out" (FOMO) present in people who use social media excessively resulting in a vicious cycle with one condition feeding the other.[8]

A study has found that overuse of technology may cause the grey matter atrophy resulting in memory insufficiency and concentration problems. The parts of brain not being used while using digital devices remain under-developed and may cause early onset of dementia symptoms.[9]

A meta-analysis of 31 nations done in 2014 showed that higher the use of internet, greater the decrease in quality of life.[10]

The aim of this study is to introduce and analyze the harmful effects of the excessive use of digital technologies especially the smart phones and social network sites with particular reference to the issue of Digital Dementia.

METHODS:

A cross-sectional study was conducted to find out the frequency and determinants of digital dementia caused by overuse of digital technology among students of King Edward Medical University, Lahore. The research was extended over a period of three months (March 1st, 2017 to May 31st, 2017). The sample size consisted of 100 students selected by simple random technique. The study subjects included both male and female students who spent five or more hours daily using smart phones and/or social network sites like Facebook, Twitter, Instagram, online videogames etc. The students who were suffering from congenital neuropsychiatric conditions, drug addiction or past history of head trauma and brain tumors were excluded from the study. Written consent was taken from all the selected study subjects. Data was collected from a pre-tested and close ended questionnaire. Data entry and analysis was done by statistical software SPSS version 20. Descriptive analyses were used for demographic and categorical data. The variables shown to be associated with dementia were examined using bivariate analysis. DIGITAL DEMENTIA: Digital dementia is defined as the deterioration of brain function as the result of overuse of digital technology such as com-

puters, smart phone and internet.[17] DEMENTIA is labeled when there are cognitive or behavioral (neuropsychiatric) impairment that involves a minimum two of the following: 1. Impaired ability to acquire and remember new information.2. Impaired reasoning and handling of complex tasks, poor judgment. 3. Impaired visuospatial abilities. 4.Change in personality, behavior 5. Impaired language function (speaking, reading, writing)[18]. The diagnosis of early symptoms of dementia was made according to the Early Dementia Questionn-aire[19] incorporated in our own questionnaire.

RESULTS:

One hundred students participated in the study. Majority (96%) of the participants were from age group 18-22 and among them 56 % of the subjects were male and 44% were females.

Table 1: *Percentage of Respondents to Question-naire Regarding Over Usage of Technology.*

Sr. No.	Question	Response	Frequency	Percen-tage
1	Do you have a smartphone?	Yes	100	100
2	Do you feel absorbed in the internet?	No	52	52
		Yes	48	48
3	Satisfaction with the internet use?	No	73	73
		Yes	27	27
4	Attempts to reduce use?	No	61	61
		Yes	39	39
5	Depressed by failing to give up net use	No	81	81
		Yes	19	19
6	Stay online longer than intended?	No	34	34
		Yes	66	66
7	Risked losing significant Relationship?	No	78	34
		Yes	22	66
8	Lie about net use?	No	78	78
		Yes	22	22
9	Internet as means of escape	No	54	54
		Yes	46	46

Table 2: *Percentage of RespondentsFalling Under Various Categories of Overuse of Technology*

		Frequency	Percentage
Category of Technology Use	Normal use	29	29
	Above Normal	35	35
	High Use	11	11
	Very High	25	25

Table 3: *Percentage of Respondents to Dementia Score Questionnaire.*

Sr. No.	Dementia symptoms	Responses	Fre-quency	Perce n-tage
1	Require checklist as memory support.	Never	27	27
		Seldom	25	25
		Sometimes	36	36
		Always	12	12
2	Forgetting recent events	Never	32	30
		Seldom	35	
		Sometimes	27	27
		Always	6	6
3	Unable to find kept items.	Never	13	13
		Seldom	37	37
		Sometimes	43	43
		Always	7	7
4	Forgetting names/familiar faces.	Never	37	37
		Seldom	26	26
		Sometimes	31	31
		Always	6	6
5	Forgetting familiar road directions.	Never	29	29
		Seldom	22	22
		Sometimes	31	31
		Always	18	18
6	Difficulty in following conversation.	Never	42	42
		Seldom	30	30
		Sometimes	26	26
		Always	2	2
7	Difficulty in understanding reading.	Never	32	32
		Seldom	41	41
		Sometimes	22	22
		Always	5	5
8	Difficulty following stories on television.	Never	63	63
		Seldom	25	25
		Sometimes	11	11
		Always	1	1
9	Repetitive questioning.	Never	34	34
		Seldom	35	35
		Sometimes	26	26
		Always	5	5

10	Difficulty in daily household chores	Never	36	36
		Seldom	35	35
		Sometimes	27	27
		Always	2	2
11	*Difficulty in taking care of self*	*Never*	*54*	*54*
		Seldom	23	23
		Sometimes	16	16
		Always	7	7
12	Disrupted movement	Never	40	40
		Seldom	29	29
		Sometimes	27	27
		Always	4	4
13	Unsuitable reaction to stimuli	Never	50	50
		Seldom	28	28
		Always	3	3
14	Obsession towards emotional event	Never	37	37
		Seldom	27	27
		Sometimes	25	25
		Always	11	11
15	Apathy/ no passion	Never	24	24
		Seldom	35	35
		Sometimes	35	35
		Always	6	6
16	Night-day rhythm disruption.	Never	29	29
		Seldom	19	19
		Sometimes	31	31
		Always	21	21
17	Restlessness at night.	Never	35	35
		Seldom	31	31
		Sometimes	32	32
		Always	2	2
18	Confusion after moving houses/in a new environment.	Never	22	22
		Seldom	33	33
		Sometimes	33	33
		Always	12	12
19	Outsiders are aware of changes in you	Never	25	25
		Seldom	32	32
		Sometimes	30	30
		Always	13	13

Fig 1: *Dementia Score Plotted Against Over Usage*

of Technological Devices Showing Direct relationship between two variables.

DISCUSSION:

Technology and science are the emblems of modern day world, however the advancement in this field on one hand is providing an opportunity for an easy access to all the information and fast communication all around the globe while on the other hand is giving rise to problems of social awkwardness, emotional instability, cognitive impairment and physical inactivity among new generations. A meta-analysis study done by Cheng Cecilia and Li Angel Yee-lam showed the global prevalence of IA (internet addiction) to be 6.0% with highest prevalence being in the Middle East and the lowest being in Northern and Western Europe showing an inverse relationship between internet addiction and quality of life[10]. This study is an attempt to determine the prevalence of digital dementia characterized by cognitive and behavioral impairment due to excessive usage of technology in daily life among students of King Edward Medical University, Lahore.

Our study included five presenting symptoms of dementia among students affected by technology overuse: memory impairment, concentration deficit, emotional and physical health deterioration and sleep pattern disturbances. A study done by Lin & Zhou suggests that internet addiction results in abnormalities in white matter of brain that may cause such behavioral impairments. [9]

A vast majority of students in our study had memory problems like difficulty in remembering past events, familiar faces, names and road directions as well as requiring checklists as a memory support. Since all the students used internet / smart phones for over 35 hours a week, overuse of these technologies might be a contributing factor for their memory problems. The result can be compared with a 2014 study that showed over usage of social media has led to digital dementia which further led to increased demand for cognitive and thinking process
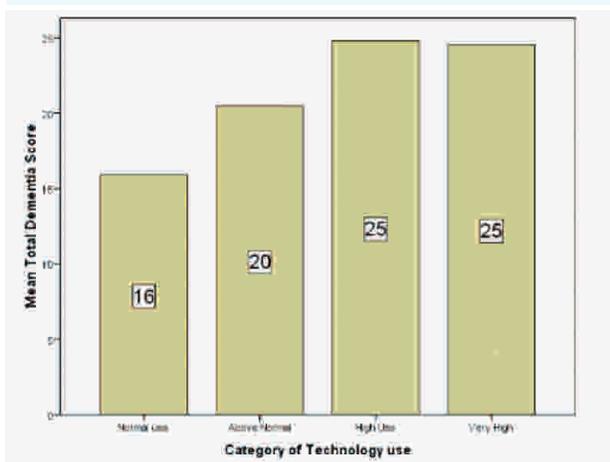
of brain.[4] Nicholas Carr, the bestselling author, also blames the technology for the change in thinking capacity of minds. [11]

The proportion of students having difficulty in concentration though lesser compared to memory problems, was still very high. More than half of the study population had difficulty in following conversation, understanding written material and complained of repetitive questioning. Many a studies support the theory that over use of technology including internet, smart phones and other digital media are the cause of shortened attention span and lack of concentration among the young people. The research review studying the effect of technology on child development, behavioral changes, and academic performance by Cris Rowan showed that the more time students spend on social media, the worse are their marks at school, even when vital factors such as family, educational, or immigrant background are controlled. (Mossle T 2010). In 2010 American society of pediatricians conducted a study and showed that children using television and video games were found to be more susceptible to attention disorders. [5]

Physical inactivity was the third variable studied, and our study showed that difficulty in daily chores, taking personal care and physical restlessness was significant among our study population. Social networking, playing online video games and watching TV leads to a sedentary lifestyle and detachment from the physical world. Our study can be compared with another study that showed that physical inactivity and obesity was seen more in those children who spent most of their time in sedentary behaviors like leisure time internet and computer use[13]. Increase in day time sleepiness and not taking active part actively work was found to be associated with increased internet use in 2009. [14]

In our study, emotional blunting and apathy was present in more than half of the subjects. Online communication with other internet users though gives an idea of global interaction, it deprives from personal contact and empathy. According to a research, Mood disorders showed a significant correlation with Internet Addiction Test.[27] A 2010 University of Michigan study showed that present day college students were significantly less empathetic than those of the 1980s and 1990s as determined by an analysis study of the past 30 years of students who were included in the Davis Interpersonal Reactivity Index which looked at factors like empathic concern, emotional response to the distress of other people, and "perspective-taking" or the ability to comprehend another person's perspective. This study cites that the increasing influence of callous reality television shows and the growing indulgence in social networking and texting are the causal factors for the decline in empathy among young people of today. (Globe and Mail). A 2014 study showed decreased wellbeing of individuals and behavior of escaping from real life problems and challenges in video gamers. [12]

Sleep-rhythm disturbances and restlessness at night was another factor studied and our data showed more than half subjects facing problems in this regard. The sleep pattern disturbances due to technology overuse is supported by the study conducted by Kwisook Choi PhD, Hyunsook Son, according to which Internet-addicted students were more likely to be sleep-deprived than non-addicted students as more day time sleepiness was noted in them.[14]

Our study showed that greater the use of technology, higher the score on EDQ[15]. The students who scored 0-4 on young's IAD scale showed progressive increase on dementia score from 15-25; and those scoring 5 showed dementia score of 24-40.

CONCLUSION:

The overuse of technological devices and internet was found to affect mental and physical health of students. The dementia symptoms were exaggerated in those who had significant over usage of technology

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RELATIONSHIP OF URINARY NEUTROPHIL GELATINASE ASSOCIATED LIPOCALIN WITH BASELINE PROTEINURIA IN CONTRAST INDUCED NEPHROPATHY

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Abstract

Objective: Urinary neutrophil gelatinase associated lipocalin has come across as one of the most promising biomarker to detect kidney injury. Our study was aimed to evaluate the role of baseline proteinuria as a risk factor for contrast induced nephropathy by finding the relationship between urinary neutrophil gelatinase associated lipocalin (uNGAL) and baseline proteinuria in patients undergoing coronary angiography.

Study design: This was a cross sectional study conducted in Sheikh Zayed Hospital Lahore.

Methodology: A total of fifty patients undergoing coronary angiography were selected for this study. Study subjects were both males (n=33) and females (n=17) and had no evidence of kidney disease at the start of study.

Results: Urinary NGAL which was positively correlated with baseline proteinuria as measured by albumin creatinine ratio (ACR). Our study suggests that baseline proteinuria is a strong predictive factor for developing contrast induced nephropathy as indicated by its strong correlation with Urinary neutrophil gelatinase associated lipocalin.

Conclusion: Our study suggests that urinary NGAL can be used to predict kidney involvement in patients undergoing contrast media administration as shown by its significant positive correlation with baseline proteinuria at 4 hours after contrast media. Proteinuria is a significant risk factor for developing CIN and precautions should be taken in patients with proteinuria undergoing contrast involving imaging procedures

Keywords: *contrast induced nephropathy, neutrophil gelatinase associated lipocalin, coronary angiography, proteinuria.*

Intravascular contrast media administration can result in acute kidney injury due to exposure to iodinated contrast medium.[1] Contrast induced nephropathy (CIN) is the third most common cause of renal damage in hospitalized individuals.[2] Imagining techniques enhanced by contrast are in great demand nowadays for more accurate diagnosis. These imaging techniques involve investigations like coronary angiography, angioplasty and CT scan. Moreover, due to increased number of percutaneous coronary interventions (PCI), the risk of contrast induced nephropathy has also been increased.[3] Decreased blood flow to kidney and direct renal toxicity are two primary mechanisms responsible for contrast induced nephropathy.[4] In general population, the risk of contrast induced nephropathy is very low, but there is high risk in patients with advanced kidney disease, diabetes mellitus, old age and those undergoing PCI. Because of limited options of treatment, prevention and early recognition of CIN is one of the main interests of clinicians and radiologists[5]. One of the efforts in managing CIN at an early treatable stage is introducing new biomarkers having significant correlation with routine kidney injury markers. These new biomarkers should be able to predict renal damage at initial stages so that appropriate management can be started timely. [6]

NGAL was initially isolated from human neu-

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trophils and has emerged as one of the promising sensitive, non-invasive biomarkers to detect kidney injury at an early stage.[7,8] CIN is routinely diagnosed by serum creatinine which is a late indicator of kidney damage.[9] CIN can be prevented and treated if detected at an early stage after renal insult which cannot be possible with the routinely used bio-markers. Therefore, it is utmost importance to high-light the risk factors which can help to detect kidney injury early in its course leading to appropriate treatment. Recent studies have shown NGAL as an effective indicator of kidney injury with close correlation with renal function.[10] In CIN, urinary NGAL can effectively predict the onset of kidney injury at an early treatable stage which is not possible with the help of routine markers.[11]

Numerous studies have shown that patients with proteinuria are at greater risk of developing kidney injury after administration of contrast media.[12] We designed our study to find out the correlation between uNGAL and baseline protein-uria of patients undergoing coronary angiography. This correlation can help us to assess the eligibility of NGAL as a predictor of worsening of renal function after administration of contrast media.

Objective:

To assess the correlation between urinary NGAL and baseline proteinuria in adult male and female patients undergoing contrast media adminis-tration.

METHODS:

Estimated sample size was 50 adult male and female patients. Patients with normal baseline serum creatinine undergoing procedures like coronary angiography or angioplasty were selected. Those having history of previous renal disease, pregnancy or contrast media administration during last seven days were excluded from the study. Consent was taken and details were recorded on a pre-designed Proforma. Spot urine samples were taken before contrast administration and at 4 hours after contrast

administration. Tests before contrast included uri-nary NGAL, Urinary creatinine, Urinary albumin and Urinary albumin/creatinine ratio (ACR) was calculated. Tests 4 hours after contrast included Urinary NGAL only. Creatinine was determined using Jaffe's method, albumin was estimated using turbidimetric method. Urinary NGAL was measured by rapid ELISA kit. ACR was calculated as milli-gram of albumin per gram of creatinine. Data was entered and analyzed using SPSS 20.0. Correlation between NGAL and baseline proteinuria was assessed using Pearson correlation coefficient.

RESULTS:

The mean age of study subjects was 59 ± 10 years and the weight was normally distributed. The spot urinary samples taken from cases before the administration of contrast showed uNGAL levels of 1.84 ± 0.43mg/ml and uNGAL levels four hours after contrast administration reached to 6.79 ± 6.41 mg/ml (p value <0.001). Before the administration of contrast media, uNGAL showed insignificant corre-lation with albumin-creatinine ratio (r=0.035, p value 0.807) However this correlation was signifi-cantly positive at 4 hours after contrast adminis-tration (r=0.617, p value <0.001).

Table 1: *Baseline Proteinuria of Patients before Contrast Administration*

Urinary sample before contrast	Mean	Standard Deviation	Min.	Max.
albumin(mg/L)	55	55	5	176
creatinine (g/L)	0.67	0.20	0.28	1.02
Albumin to creatinine ratio (mg/g)	82.2	85.7	6.0	299.0

Table 2: *Urinary NGAL Status of Patients before Contrast and 4 Hours after Contrast Administration*

Urinary NGAL (ng/ml)	Mean	SD	Min	Max	Q1	Median	Q3
before contrast	1.84	0.43	1.00	3.0	1.5	1.75	2.00
4 hours after contrast	6.79	6.41	1.75	29.0	3.0	4.00	7.63

Table 3: *Correlation of Urinary NGAL with Baseline Proteinuria before and after Contrast Administration*

	Correlation Coefficient	P-value
Correlation with baseline proteinuria before contrast(mg/g)	0.232	0.104
Correlation with baseline proteinuria 4 hours after contrast administration	0.617**	< 0.001

DISCUSSION:

This study was aimed to find out the correlation between urinary NGAL and baselineproteinuria as a risk marker for developing contrast induced nephropathy. This correlation can help to identify uNGAL as a reliable marker of contrast induced nephropathy. Numerous studies have shown proteinuria as a risk factor for CIN. Our study showed significant correlation between uNGAL and baseline proteinuria four hours after contrast administration and this shows that patients with evidence of renal impairment at baseline are more prone to developing acute kidney injury due to contrast media. A study done on Indonesian population showed similar results in which baseline proteinuria markedly increased the risk of CIN.[13]

Proteinuria is a strong indicator of renal disease involvement and many cross sectional studies have shown that urinary NGAL increases along with proteinuria in glomerular diseases[14]. Kuwabara et al showed in their study that NGA: significantly reduced in patients with kidney disease after treatment of proteinuria.[15] Many mechanisms are responsible for strong correlation between urinary NGAL and baseline proteinuria like loss of NGAL via damaged glomeruli, impaired reabsorption of NGAL in proximal tubular cells, direct tubular toxicity and nephron loss. One other hypothesis is increased NGAL production to compensate for tubular cell damage due to proteinuria.[14]

To decrease the risk of CIN careful screening of patients at risk of CIN is needed and thus by taking proteinuria as risk factor of CIN we can decrease morbidity and mortality associated with this iatrogenic condition.

CONCLUSION:

Our study suggests that urinary NGAL can be used to predict kidney involvement in patients undergoing contrast media administration as shown by its significant positive correlation with baseline proteinuria at 4 hours after contrast media. Proteinuria is a significant risk factor for developing CIN and precautions should be taken in patients with proteinuria undergoing contrast involving imaging procedures.

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COMPARISON OF CA-125 IN FIRST TRIMESTER OF PREGNANCY WITH NON PREGNANT WOMAN: COMPARITIVE CROSS SECTIONAL STUDY

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ABSTRACT

BACKGROUND: There is a strong relationship of CA125 level in first trimester of pregnancy. Serum level of CA125 is considered a valuable parameter not as a marker of ovarian carcinoma but also in other field of Obstetrics and Gynaecology. CA-125 measurements appear to be higher prognostic marker in viable pregnancy at an abortion risk.

AIMS AND OBJECTIVES: To compare the CA125 level in first trimester of pregnant and non pregnant females.

MATERIAL AND METHODS: Comparative Cross sectional study. The study was conducted in Department of pathology in collaboration with OBSTETRICS GYNAECOLOGY department of Jinnah Hospital Lahore. Collection of 40 blood samples of first trimester of pregnant females and 40 samples of non pregnant females were done after informed consent. Two groups were included in study, one group was normal pregnant women, second group was non-pregnant menstruating women of child bearing age. All women were underwent venipuncture, a blood was drawn in plain vial without any anticoagulant, CA 125 was measured in serum through ELISA and values were recorded along with their history. Data were analysed in SPSS 23 and expressed in form of graphs and tables.

RESULTS: 40 pregnant and 40 non pregnant (Controls) females were included in my study. CA125 levels were found to be raised in 40% of the pregnant woman i.e. greater than 35units/ml whereas 60% had normal CA125 value (less than 35units/ml). In control group, 92.5% females had normal value of CA125 and 7.5% females had raised value of CA125.

CONCLUSION: There was a strong relationship of CA125 in first trimester of pregnancy. The normal value of CA125 is 0-35 units/ml, which was exceeded in first trimester of pregnancy. There is a great significance of CA 125 in first trimester of pregnancy. In our study P value is less than 0.05 which is significant. Monitoring of CA 125 will help the clinicians for early detection of impeding abortion in first trimester.

Key words: *cancer antigen 125 , first trimester, ELISA* .

Cell-surface antigen CA-125 (cancer antigen-125) is high molecular weight antigen. CA-125 is coelomic antigen which is like a mucin. In 80% of cases of non-mucus epithelial carcinomas of ovary it is detected. This cell-surface antigen is secreted normally from coelomic epithelium, amnion and their derivatives such as respiratory system, epithelium of female genital system and mesenteric organs. Serum CA-125 level is secretary function of these organs[1]. Non- genital causes of high serum CA-125 include hepatic diseases, renal failure, peritonitis, breast, colon, tuberculosis and lung cancer. Genital causes of high serum CA-125 level are pelvic inflammatory diseases, adenomyosis, endometriosis, leiomioma, ectopic pregnancy, endometrial and ovarian cancer.

During pregnancy CA-125 increases in the first trimester[2,3]. Serum CA125 level is considered as a

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valuable parameter not only as a marker of ovarian carcinoma but also in other field of Obstetrics and Gynecology[4]. During pregnancy, CA-125 is secreted from tissues derived from embryonic epithelium of coelom throughout development5 and found in high concentration in human amniotic fluid[7], considerable quantity is seen in the deciduas and chorion which are the main source of CA-1256. In pregnancy, disturbance of the epithelial basement membrane of the fetus or disturbance of the deciduas are main causes of increase in the maternal serum level of CA 125 level.

In normal menstruating women there is a cyclic change in the serum concentration of CA 125 which demonstrates that it is a product of normal endometrium[8]. This means that CA 125 is synthesized by regular endometrium in non pregnant female and by deciduas in pregnant women[9].

Serum CA 125 level is higher in the first trimester of pregnancy with median level 53.6 U/ml (15.6 - 268.3 U/ml) as compared to non pregnant women with median level 19.3 U/ml (7.2 – 27.0 U/ml). In second trimester median level is 18.5 U/ml (12.0 – 25.1 U/ml) and in third trimester median level 19.2U/ml (16.8 – 43.8 U/ml).

Serum CA-125 level is now being used to observe the efficacy of treatment for ovarian cancer. High levels of serum CA-125 often point toward that the cancer is not responding to treatment[11]. Decline in serum CA-125 levels during treatment shows that the cancer is responding to treatment[12].

METHOD

Comparative Cross sectional study. The study was conducted in Department of pathology in collaboration with OBSTETRICS GYNAECO-LOGY department of Jinnah Hospital Lahore. Collection of 40 blood samples of first trimester of pregnant females and 40 samples of non pregnant females. Two groups were included. one group was normal pregnant women with no previous history of malignancy. Second group was non-pregnant menstruating women of child bearing age. All women were underwent venipuncture, a blood was drawn in plain vial without any anticoagulant, CA 125 was measured in serum through ELISA and values were recorded along with their history. Data were analyzed by SPSS 23 and expressed in form of graphs and tables.

STATISTICAL ANALYSIS

Data was analyzed by using SPSS 23. Quantitative variables were expressed as mean and standard deviation. The categorical variables will be expressed in the form of frequency and percentage. Appropriate statistical tools were applied to analyze the data and to calculate p-value and level of significance. A p-value of 0.05 was considered as statistically significant

RESULTS

Regarding comparison of age between pregnant and non pregnant females, mean age of pregnant females and non pregnant females was 25.35 SD ±4.73 and 27.15 SD ±5.05 respectively. (Table 1)

Frequency of pregnant women in the age group

Table 1: *Comparison of Age between Pregnant and Non Pregnant Females*

Age	Pregnant (n=40)	Non pregnant (n=40)
Mean	25.35±4.73	27.15±5.05
Minimum	19.0	18.0
Maximum	38.0	39.0

15 – 30years was 34 and in the age group >30 years was 6. On the other hand, non pregnant women there were 29 women in the age group of 15 – 30 years and 11 women were having age of >30years.
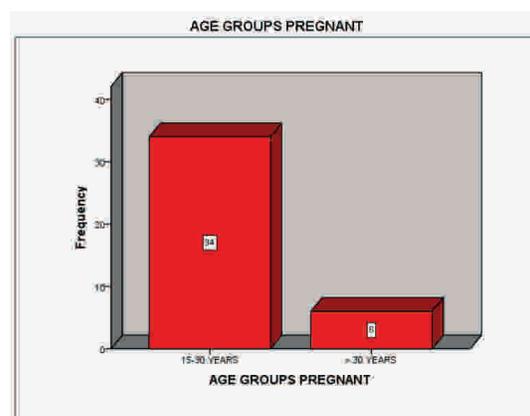
Figure No. 1. *Age Groups in Pregnant (cases)*
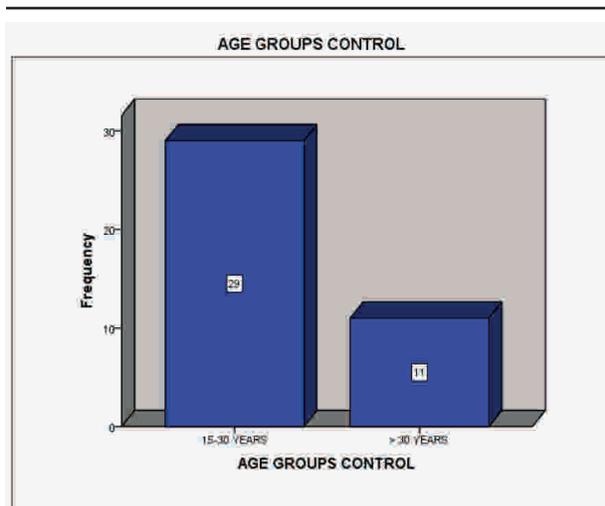
Figure No. 2: *Age group in Non Pregnant (control)*

Regional distribution in pregnant female shows that 42 % of the females belong to rural area and the rest of the females were belonging to urban area. Among non pregnant females 52% females belong to rural area and 48% belong to urban area .(Table 3)

Table 3: *Regional Distribution between Pregnant and Non Pregnant Females*

Region	Pregnant	Non pregnant
Urban	58%	48%
Rural	42%	52%

Out of 40 pregnant women 31(77.5%) were ailment free and 9(22.5%) were having other ailments (like hypertension etc). Among non pregnant women 38(95%) were ailment free and 2(5%) were having other ailments.

There was no past family history of malignancy among pregnant women whereas among non pregnant females, there was only 1(2.5%) female having past family history of malignancy .

Pregnant females showed that 22.5% of the females were using birth control pills whereas in non pregnant females only 15% have ever used birth control pills.

The frequency of taking alcohol in pregnant women showed that only 1(2.5%) female out of 40 was found to be an alcoholic whereas in non pregnant women no female was alcoholic .

Pregnant females showed that 4(10%) females

were smokers and 36(90%) were non smokers whereas among non pregnant women only 1(2.5%) female was found to be a smoker, rest were non smokers .(Table 4:)

Table 4: *Showing Personal Habits and Co-Morbidities in Cases and Control.*

Questions	Pregnant	Non pregnant
History of hypertension/diabetes or other chronic ailment	9/40 (22.5%)	2/40 (5%)
Malignancy	0.0 (0%)	1/40 (2.5%)
Birth control pills	9/40 (22.5%)	6/40 (15%)
Alcohol abusers	1/40 (2.5%)	0.0 (0%)
Smoker	4/40 (10%)	1/40 (2.5%)

40 pregnant and 40 non pregnant women were included in our study. The value of CA125 was found to be raised in 16(40%) of the pregnant women i.e. greater than 35units/ml whereas 24(60%) had normal CA 125 value (less than 35units/ml).In control group, 37(92.5%) females had normal value of CA125and 3 (7.5%) females have raised value of CA125 which is statistically significant as P value is <0.05.(table 5)

Table 5: *Comparison of CA 125 Level between Pregnant and Non Pregnant Females*

CA 125 level	Pregnant females	Non pregnant females
Raised (>35u/ml)	16 (40%)	3(7.5%)
Normal(<35u/ml)	24 (60%)	37 (92.5%)

Mean values of CA125 in pregnant and non pregnant are 125.5 ±164.4 and 17.3 ±7.1respectively showing significantly high values in pregnant. (Table 6)

Table 6: *Comparison of Means of CA125 In Pregnant and Non Pregnant*

CA-125	N	Mean	SD	p-value
Pregnant	40	125.5887	164.49220	.000
Non-pregnant	40	17.3930	7.18593	

P value is .000 in our study which is less than 0.05 that is statistically significant.

DISCUSSION

During pregnancy CA-125 increases in the first trimester.[2,3] Serum CA125 level is considered as a valuable parameter not only as a marker of ovarian carcinoma but also in other field of Obstetrics and Gynecology4. There were 40 pregnant and 40 non pregnant women in our study. In pregnant females 16(40%) of the subjects were having high levels of CA125. The current study is in accordance with Aslam. N, Ong. C, et al (2000), who observed that level of CA-125 was higher in 34% females in first trimester as compared to non-pregnant women.[16] Similar results were also shown by another study of Sersam. L. W, Mahmood. R. S, (2013), who noted significantly elevated CA-125 level in ruptured tubal ectopic pregnancy as compared to normal intrauterine pregnancy.[13]

Women with threatened abortion who eventually miscarried had constant or increasing concentration of CA125 over 5-7 days, whereas those who continued with pregnancy had a constantly low or steeply declining CA125 concentartion.[17] Also a single CA125 concentration of at least 43.1IU/ml was associated with greater risk of miscarriage in 200 women who had vaginal bleeding in their first trimester.[18]

There are some studies suggesting the predictive value when estimating the risk of miscarriage at early stages of pregnancy. The authors prove that women with threatening abortion revealed higher values of serum CA125 than those in control group. The patients who presented the highest value of antigen later miscarried.[19]

Another study conducted by Ayaty. S, Roudsari. V.F et al. (2007), compared normal pregnant women with threatened abortion group, they stated that serum CA-125 measurements appear to be higher prognostic marker in viable pregnancy at an abortion risk.[14]

According to Revankar V M, Aggarwal. A, et al. (2015), out of 12 patients only 4 patients aborted (33.3%) due to high serum CA 125 values. These all above mentioned studies are in favor of our study which predict that patients with high CA125 are at risk of abortion.[15]

The limitation of our study was that we could not do follow up of the pregnant females with higher levels of CA125 in first trimester, who were at risk of threatened abortion or miscarriage.

Another study is required to predict the final verdict.

CONCLUSION

There was a strong relationship of CA125 in first trimester of pregnancy. The normal value of CA125 is 0-35 units/ml, which was higher in first trimester of pregnancy. Our study consists of 40 patients (cases) and 40 controls. The value of CA125 was raised in 40% of the pregnant women (cases) as compared to control group in which only 7.5% of the females have raised CA125 value. There is a great significance of CA 125 in first trimester of pregnancy to predict impending abortion.

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EFFECT OF MEBENDAZOLE THERAPY DURING PREGNANCY ON BIRTH OUTCOME IN PATIENTS PRESENTING TO CH. REHMAT ALI MEMORIAL TEACHING HOSPITAL

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Abstract

BACKGROUND: Routine antenatal mebendazole therapy in pregnancy can be of great help in reducing the prevalence of anemia. At the moment this drug is not a widely used because of a lack of data on the safety of the drug especially in our population. We assessed the effect of mebendazole therapy during pregnancy on birth outcome.

METHODS: We observed the effect of mebendazole on the birth outcomes in Ch Rehmat Ali teaching hospital to the pregnant patients during second and third trimester of pregnancy. We observed the birth weight (low being classified as <2000g), perinatal mortality, still births, major congenital abnormalities and anemia (Hb < 10g/dl) among babies of mothers who had taken mebendazole during pregnancy.

FINDINGS: The rate of the proportion of low-birthweight babies 5.7% and anemia 16.2% was very much less effected while prevalence of congenital abnormalities, still birth and perinatal mortality was none in patients taking mebendazole.

INTERPRETATION: Mebendazole therapy during pregnancy is not associated with a significant increase in adverse effects in term of congenital defects, low birth weight, anemia and still births. This therapy could offer beneficial effects to pregnant women in developing countries, where intestinal helminthiases are endemic.

KEY WORDS: *Mebendazole, pregnancy, birth outcome, anemia, hemoglobin level, low birth weight*

The pinworm is a nematode that mostly infects children. In Pakistan, the prevalence among children of worm infestation was found to be 77.31% of which 64% were the female children.[1] This worm easily spreads across the family members and a common cause of anemia in females especially in pregnant ladies. The studies conducted in Babile, east of Ethiopia and Waikagul, recorded 6.7% and 18.5% respectively of the yearly prevalence of hookworm infestation.[2,3] Worldwide, hookworms infect an estimated 440 million people. Although most of those affected are asymptomatic,[4,5] approximately 10% experience anemia due to this worm infestation. The pregnant female is already susceptible to anemia due to excessive need of diet and consuming less resulting in clinical anemia which becomes more severe in the presence of hookworm infestation. This emphasis the need of treating the pregnant patients for helminth infestations properly and timely.

The World Health Organization (WHO) reco-mmends any of the following 4 drugs for the treatment of hookworm infection in pregnancy: albendazole, levamisole, mebendazole and pyrantel.[6] Because of the ease of use of their single-dose format, the benzimidazoles (albendazole and mebendazole) are the drugs most widely used in helminth control programs targeted to school-aged children and pregnant women.[7-9]

Despite the recognized benefits of deworming, it is possible that fear of adverse birth outcomes has limited its inclusion in routine antenatal care.

Mebendazole is said to be the treatment of choice for the treating pinworms during pregnancy. And treating the pregnant ladies with anti helminths lead to increase in mean Hb levels as well clinical wellbeing of the patient.[10]

Treatment of these worms in pregnancy has also been shown to reduce early infant mortality[11] apart from the prevention of anemia. These drugs, administered after the first trimester, have been found to be safe and effective, having few and minor,

if any, side effects.[12-14]

There are number of international studies in pregnant women which have shown that there is no adverse effect of mebendazole on pregnancy or birth outcome.[15-18] But mebendazole is considered category C pregnancy drug. So we aim this study to look for the adverse effects on birth outcome of the drug so that we may be sure to use it safely in pregnancy in our population.

OBJECTIVE

To find the effect of single dose of mebendazole therapy during pregnancy on pregnancy outcome

METHODS

STUDY DESIGN

Quasi experimental trial

SETTING

Pregnant patients coming to Chaudhary Rehmat Ali Memorial hospital, Lahore during the period of May 2017 to May 2018 were enrolled in the study after written informed consent.

INCLUSION CRITERIA

• Second & third trimester of pregnancy
• No previous treatment with Mebendazole in previous 6 months.

EXCLUSION CRITERIA:

• 1st trimester of pregnancy
• Severe anemia (Hb < 7g/dl) requiring treatment with Iron/Blood transfusion

DATA COLLECTION:

Each of the participant was given a single dose of mebendazole 500mg and her particulars were noted. Each was then followed till delivery approx. 5 months. Assessments were made at baseline (second trimester), at third trimester and at the delivery. The parameters including birth weight, any major congenital abnormality, still birth, perinatal mortality and improvement in Hb were noted. Low birth weight was defined as baby weight <2000gms at birth. While anemia was defined as Hb level < 10g/dl at time of delivery.

RESULTS

In this study, the mean age of patients was 29.8 years. There were 36 (17.1%) female of age 20-25years, 79 (37.6%) were aged between 26-30years while 95 (45.2%) aged between 31-35years. There were 121 (57.6%) females who belonged to low socioeconomic status while 45 (21.4%) belonged to middle class family and 44 (20.95%) belonged to high socioeconomic status. Out of 210 females, 76 (36.2%) were residing in a rural area while 134 (63.8%) resides in urban area. There were 196 (93.3%) were Muslim females while 14 (6.7%) were Christians. There were 66 (31.4%) primiparous and 144 (68.6%) were multiparous. Table 1

In the whole sample, only 2 (0.95%) had still birth, but there was no perinatal mortality or

Table 1: *Maternal Baseline Characteristics*

Characteristics	Frequency	Percentage
Age(years)		
20-25	36	17.1%
26-30	79	37.6%
31-35	95	45.2%
Mean Age	29.8	
Socioeconomic Status		
Low	121	57.6%
Middle	45	21.4%
High	44	20.95%
Residence		
Rural	76	36.2%
Urban	134	63.8%
Religion		
Islam	196	93.3%
Christian	14	6.7%
Parity		
Primi	66	31.4%
Multi	144	68.6%

congenital malformation (0%). Mean Hb of females at baseline was 10.7±0.6g/dl which remain almost unchanged (10.6±0.5g/dl) after treatment with single dose of mebendazole. At time of delivery, 176 (83.8%) females had Hb in normal range (10-14g/dl), while only 34 (16.2%) had Hb=7-10g/dl, but no female had Hb below 7g/dl. The mean birth weight of neonates was 2429±49grams. There were 198 (94.3%) neonates with normal birth weight

while there were only 12 (5.7%) neonates who were LBW (<2000grams). Table 2

Table 2: *Effects of Deworming on Birth Outcomes*

Still Birth	02	0.95%
Perinatal Mortality	00	0.0%
Congenital malformation	00	0.0%
Mean Baseline Hb level G/dL	10.7 g/dl	
Mean Hb level after treatment	10.6 g/dl	
10-14g/dl	176	83.8%
7-10 g/dl	34	16.2%
<7 g/dl	00	0.0%
Mean Birth weight	2429gms	
Normal birth weight 2000gms	198	94.3%
LBW <2000gms	12	5.7%

DISCUSSION

Anemia predisposes to severe morbidity in pregnant women and reduces tolerance to normal blood loss during child birth, which can be devastating. Still births and low birth weights are also related to anemia as well. Apart from other causes, hookworm is an important cause of anemia causation especially in endemic areas and low socio-economic parts with poor hygiene[19-20] like Pakistan.

Mebendazole was chosen as a treatment of choice for management for deworming the pregnant patients because it is very poorly absorbed from the gut (only 2-10%) so having very little effect on the baby[21] and its beneficial effect during pregnancy shown by Atukorala et al.[22] and low incidence of congenital effects[23]

A double-blind randomized controlled trial of antenatal mebendazole to reduce low birth weight in a hookworm-endemic area of Peru[24] and a study done by de silva NR at el.[25] showed almost the same results as our study though we didn't have controls but our study showed that incidence of still birth is negligible with mebendazole use in pregnancy.

There came out no teratogenic effect of antihelminth after its use in 2nd and 3rd trimester which also correlates with a Hungarian study indicating no correlation of their use and incidence of teratogenic or fetotoxic effects.[26]

A 2001 study in Sierra Leone showed that albendazole treatment during pregnancy successfully reduced the prevalence of maternal anemia which is a bit in contrast to our study which showed a stable level of Hb even after with the treatment of the mebendazole showing neither increase nor decrease in mean Hb level.

So our study showed that single use of Mebendazole use in pregnancy after 1st trimester is safe and effective leaving no adverse effects on both fetus and mother. There are though soe other tjings to consider like hygiene of the surroundings, mother with good washing/scrubing of hands, useable things. Proper deworming of the family members especially the children must be ensured. Eradication of the larva reservoirs be done. So all these measures will aid in community health as primary prevention is should always be at the top.

CONCLUSION

Mebendazole therapy during pregnancy is not associated with a significant increase in adverse effects in term of congenital defects, low birth weight, anemia and still births. This therapy could offer beneficial effects to pregnant women in developing countries, where intestinal helminthiases are endemic.

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PERCEPTION AND PRACTICES REGARDING ADVERSE DRUG REACTION AMONG DOCTORS WORKING IN TERTIARY CARE HOSPITAL OF LAHORE

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Abstract

Background: Any drug/medicine during its normal therapeutic use has a potential to produce adverse reaction(s). It is very difficult to get any medicine which is absolutely safe. Adverse drug reactions (ADRs) contribute to a significant number of morbidity and mortality all over the world. Underreporting of spontaneous adverse drug reaction (ADR) is a threat to pharmacovigilance. Various factors related with the knowledge and attitudes are responsible for underreporting of ADRs.

Objectives: The objective of this study was to evaluate perception and practices regarding adverse drug reaction among doctors working in tertiary care hospital in Lahore.

Subjects and Methods:

Study Design: Cross sectional study

Study Setting: Department of Pharmacology Rahbar Medical and Dental College Lahore

Study Duration: From January 1, 2018 – March 31, 2018

Sampling Technique: Non probability / purposive sampling

Inclusion Criteria: Doctors including house officer, medical officers, postgraduate trainee and consultants working in tertiary care hospital in any specialty.

Data Collection Procedure: 97 doctors those fulfilling the inclusion criteria were included in the study. A structured questionnaire was designed for assessment of perception and practices of doctors regarding ADR were evaluated. Data was entered and analyzed in SPSS ver: 17.0. Frequency and tabulation was calculated for perception and practices regarding ADR.

Results: 97 doctors including house officers, MO, SR and Consultant were interviewed. Mean age was 28.2 + 7.7 years. 54.6% were male. Regarding knowledge, 76.3% of respondent believe that ADR can be prevented. 91.8% thinks that training about ADR reporting should be given and reporting of ADRs is your professional duty/obligation.. 60.8% supports that direct ADR reporting by the patients instead of physicians.

Conclusion: ADR reporting rate was very low among the health care professional working in tertiary care hospitals especially in younger age group. Doctors are aware of importance of ADR reporting; their perception toward ADR reporting is right but it is not reflected when it comes to the act of reporting of ADRs. The is gap between knowledge, perception and practices which need to be addressed not only to improve ADR reporting by younger health care workers but also will be beneficial for patients.

Key words: *Adverse Drug Reaction, perception, practices, ADR.*

Adverse drug reaction (ADR,s) is defined by World Health Organization (WHO) as "a response to a drug which is noxious and unintended, and which occurs at doses normally used in man for the prophylaxis, diagnosis or therapy of disease or for the modification of physiological function."[1] ADRs are one of the major health care issues encounter at all level of health care system and is occurring throughout the world regardless of their economic parity. They affect patients in every health care setup and its magnitudes vary according to circumstances and it cause greater morbidity and mortality and increasing burden of disease.[2,3]

Adverse Drug Reactions (ADRs) constitute an important cause of morbidity and mortality affecting all age groups. An ADR is any noxious, unintended and undesired effect of a drug, which occurs at doses normally used in humans for prophylaxis, diagnosis, or therapy of disease or the modification of physiological functions.[3,4] It is known that ADR may occur with any drug even when used correctly.[3,4] However, certain factors may predispose or contribute to development of ADR and these may include: irrational use of drugs and poor prescribing patterns; promotional activities by pharmaceutical company; inadequate access to objective sources of information; liberal drug outlets and unhealthy pharmaceutical practices; self-medication practices; "drug gifts" from overseas; lack of public awareness and low literacy level.[4]

Preventing ADRs is an integral part of routine clinical work of any physician. Their active involvement in spontaneous eporting of ADRs is essential for establishing a system that improve phamacovigilence and reporting of ADR so that medical undergraduate are trained at early level to give attention to this important aspect. Present study was conducted among doctors working in tertiracy care hospitals to assess the pereception and practices of physicians regarding reporting of ADRs, and pharmacovigilance as well as to identify the reasons for not reporting ADR with suggestion for improvement in the reporting system.

METHODS

A cross sectional study was conducted at Department of Pharmacology Rehbar Medical and Dental College Lahore, from January 1, 2018 – March, 2018. 97 doctors including house officer, medical officers, postgraduate trainee and consultants working in tertiary care hospital in any specialty were included in the study through Non probability / purposive sampling with 95% confidence interval and 10% margin of error assuming 50% had knowledge regarding ADR. A structured questionnaire was designed for assessment of perception and practices of doctors regarding ADR were evaluated. Data was entered and analyzed in SPSS ver: 17.0. Frequency and tabulation was calculated for perception and practices regarding ADR.

RESULTS

97 doctors including house officers, MO, SR and Consultant were interviewed. Mean age was 28.2 + 7.7 years. 88.7% were less than 35 years. 54.6% were male and 45.4% were females. 53.6% of interviewee were from medicine, 24.7% were from surgery and 12.4% from Gynecology and obstetrics department. 50.4% were house officer, 34.0% were PG trainees and 10.3% were consultant in study. (Table no: 1)

Regarding knowledge, 76.3% of respondent believe that ADR can be prevented. 91.8% thinks that training about ADR reporting should be given and reporting of ADRs is your professional duty/ obligation.. 60.8% supports that direct ADR reporting by the patients instead of physicians and 51.5% came across with ADR during their job / training and only 36.1% had once in life time experience in their personal life and only 39.2% knows how to report ADR. 56.7% thinks that ADR should be reported to Hospital Administration, 21.6% to ADR reporting Center. 6.2% thinks that it should be reported to the concerned pharmaceutical

Company and 5.5% thinks that it should be reported to all three places. Regarding knowledge about Department dealing with ADRs within your Hospital 43.3% thinks that it sould be concerned Unit / Department, 19.6% thinks that it should be medical superintendent office and 15.5% to ADRs Centre within hospital. (Table no:2).

Regarding responsible person for reporting ADR in a hospital 52.6% thinks it should be the doctor in charge, 27.8% thinks its responsibility of pharmacist and 19.6% it should be the nurse incharge. Knowledge was assessed about place of reporting of ADR 24.7% thinks it should be health department and 60.8% thinks that it is within hospital where ADR are reported and 8.2% think the Director General Health office is place of reporting ADR. Reason for not reporting ADR was also evaluated 40.2% have no idea where and how to report ADR, 21.6% had legal / professional liability and 14.4% say they don't have time to report ADR. (Table no:3).

DISCUSSION

The burden of ADRs is enormous and it effects all populations, community throughout the world is expected to be higher in developing countries because of ignorance, poverty, self-medication and increase prevalence of fake and adulterated medi-

cines. The economic burden of ADRs on the society is enormous, for example, in the US, an estimated annual cost of drug-related problems is 30 billion Dollars.[5,6]

Many developed countries have strong pharma-

Table 1: *Demographic and Professional Information Regarding Respondents.*

Variables n= 97	Frequency	Percent
Age Mean = 28.22 SD= 7.67 Min 23 Max = 48		
< 35 years	86	88.7
> 35 years	11	11.3
Gender		
Male	53	54.6
Female	44	45.4
Specialty		
Medicine	52	53.6
Surgery	24	24.7
Psychiatry	1	1.0
Obstetrics & Gynecology	12	12.4
Pediatrics	8	8.2
Designation		
House officer	49	50.5
Postgraduate trainee	33	34.0
Mo	5	5.2
Consultants	10	10.3

covigilance systems.[2] The systems are established to report suspected ADRs that medical practitioners encounter in their clinical practice. However, there

Table 2: *Knowledge Regarding ADR's among Health Care Professionals*

Variables	Yes		No		Don't Know	
	Frequency	Percent	Frequency	Percent	Frequency	Percent
ADRs be prevented	74	76.3%	15	15.5%	8	8.2%
Do you know about national reporting centers for ADR?	13	13.4%	75	77.3%	9	9.3%
Do you think that it is necessary that training about ADR reporting should be given to you?	89	91.8%	4	4.1%	4	4.1%
Do you think reporting of ADRs is your professional duty/obligation?	89	91.8%	4	4.1%	4	4.1%
Do you support 'Direct ADR reporting by the patients instead of physicians?	59	60.8%	37	38.1%	1	1.0%
Have you come across with ADRs in your training/job?	50	51.5%	47	48.5%	0	0.0%
Have you come across with ADRs in your life (personal Experience)?	35	36.1%	62	63.9%	0	0.0%
Do you know how to report ADRs?	38	39.2%	56	57.7%	3	3.1%

Table 3: *Perception Regarding ADR's among Health Care Professionals*

Variables		Frequency	Percent
Where ADRs should be reported?	Hospital Administration	55	56.7%
	ADR reporting Center	21	21.6%
	Pharmaceutical Company	6	6.2%
	All of them	15	15.5%
Is Any Department dealing with ADRs within your Hospital?	Concerned Unit-Department	42	43.3%
	Medical superintendent	19	19.6%
	ADRs Centre within hospital	15	15.5%
	None of the above	21	21.6%
Responsible person for reporting ADR in a hospital	Doctor	51	52.6%
	Pharmacist	27	27.8%
	Nurse	19	19.6%
Where should be reporting Centre for ADRs?	Don't Know	4	4.1%
	Health Department	24	24.7%
	Within a hospital	59	60.8%
	Director General Health	8	8.2%
	All of them	2	2.1%
Reasons for not reporting ADRs?	No idea where/how to report	39	40.2%
	Legal/professional liability	21	21.6%
	No time to report ADR	14	14.4%
	Many Drugs in treatment chart difficult to assess ADRs due to which medicine	23	23.7%

are considerable differences in the patterns of ADR reporting phenomena. A serious limitation with all ADR reporting methods all over the world is an under reporting. Even in high-rated ADR reporting countries, merely 10% of the total ADRs are seen to be reported.[1,2,4]

The level of awareness of ADR reporting process came out be low and was similar to findings from other studies done in developing countries.[6] A study done by Adedeji et al also showed major information gaps in perception and practices. The study showed that no pharmacovigilance committee and no official performa ADRs reporting is in knowledge of health care professional which is main reason for the respondents' low level of awareness. Awodele et al.reported a dissimilar finding in a study that involved doctors in private hospitals in Lagos. No immediate reason(s) could be proffered for this but an interaction of theenvironment, the attitude and awareness of patients may be a possible explana-

tion.[7]

In a study by Nahar N et al reported that majority of physicians (93%) perceived that among health care professional doctors are the most responsible persons who will report ADRs. Among the agents which report should be done are allopathic drugs (89%) and vaccines (70%) were given most important to report. Events like reaction to a new drug (86%), serious event (78%) and death of patients (83%) given importance to report by the physicians.[12] In our study 52.6% thinks it should be the doctor in charge, 27.8% thinks its responsibility of pharmacist and 19.6% it should be the nurse incharge. Knowledge was assessed about place of reporting of ADR 24.7% thinks it should be health department and 60.8% thinks that it is within hospital where ADR are reported and 8.2% think the Director General Health office is place of reporting ADR.

In a study be Pushkin R listed many possible

reasons for physicians not reporting ADRs. Main reasons reported are possibility of physicians being uncertain about association between an ADR and drug and physicians' perception that others in the hospital like pharmacists report such events to authorities. Our study also had similar findings.[13]

In a study by Chatterji et al showed According to this study there exists a good knowledge about ADR reporting among clinicians. However, the two quotients – attitude and perception/practice are still gray zones amongst the clinicians. The study also showed that there is a need to create awareness about drug safety and pharmacovigilance by incorporating it in medical teaching and training. Similar findings were depicted in studies done in Saudi Arabia showing a limited knowledge of pharmacovigilance that could have affected reporting incidence. Educational intervention and a practical training program need to be applied by the drug regulatory body as well as health authorities to enhance the pharmacovigilance and drug safety culture.[15,16]

Our study in accordance with other studies suggests that there is a reasonable amount of knowledge or awareness in the medical practitioners about importance of ADRs yet in practice there is lot of lethargy toward reporting of ADRs. There is a need for suitable changes in the undergraduate teaching curriculum and also that prescribers need a periodic reinforcement regarding ADR monitoring.

CONCLUSION

ADR reporting rate was very low among the health care professional working in tertiary care hospitals especially in younger age group. Doctors are aware of importance of ADR reporting; their perception toward ADR reporting is right but it is not reflected when it comes to the act of reporting of ADRs. The is gap between knowledge, perception and practices which need to be addressed not only to improve ADR reporting by younger health care workers but also will be beneficial for patients.

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PREVALENCE OF GASTRIC VARICES, THEIR TYPES AND ASSOCIATIONS AMONG LIVER CIRRHOSIS PATIENTS

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Abstract

Objective: To determine the prevalence of gastric varices, their types and associations in patients suffering Liver cirrhosis who underwent upper gastrointestinal endoscopy (UGIE) at Liver Clinic, Lahore, Pakistan.

Study Design: Retrospective cohort study

Methodology: In a retrospective analysis of patients who underwent UGIE from July 2010 to June 2014, presence gastric varices, types of gastric varices, gender, age groups, grade of esophageal varices (EV), presence of portal hypertension gastropathy (PHG), gastric vascular ectasia (GVE), and hiatal hernia + reflux esophagitis (HH+RE) were the qualitative variables, while age of the patients was a quantitative variable. The data was evaluated on SPSS version 25, where means and standard deviations were calculated for quantitative variable, and frequencies and percentages were computed for qualitative variables. The bivariate analysis was performed to determine the significant relation of different predictive factors with presence of gastric varices. While applying chi-square test of independence, a p value of equal to or less than 0.05 was considered as significant. The odds ratio along with their 95% confidence interval (CI) were also calculated for each association.

Results: Out of the total of 2463 chronic liver disease (CLD) patients who underwent UGIE, 64.4% were male and 35.4% were female. Their mean age was $51.03 + 10.18$ years, and the mean weight was $72.70 + 15.55$ Kilogram. The prevalence of fundal varices was 12.4% (n=305); amongst which 22.6% (n=69) had GOV1, 13.1% (n=40) had GOV2, 58% (n=177) had IGV1, 1% (n=3) had IGV2, 0.7% (n=2) had GOV1 along with GOV2, and 4.3% (n=13) had GOV2 along with IGV1. 12.5% males and 12.2% females had fundal varices. Similarly, in different age groups, 0% adolescents, 11.8% young adults, 12.2% middle aged adults and 16.1% older adults had fundal varices. The association of finding fundal varices with gender (p=0.898), different age groups (p=0.456) was not statistically significant. 12.6% patients without EV, while 10.2% with grade I EV, 12.6% with grade II EV and 15.1% with grade III EV had fundal varices. Amongst the patients with PHG, 12.8% had fundal varices, while amongst the patients without PHG, only 4.9% had fundal varices. Similarly, amongst the CLD patients without GVE, 12.9% (n=289) had fundal varices, and 7.1% (n=16) patients with GVE had fundal varices. 12.9% CLD patients without HH+RE had fundal varices, while only 0.9% (n=1) patients with HH+RE had fundal varices. The occurrence of fundal varices had a statistically significant association with different grades of esophageal varices (p=0.023), presence of PHG (p=0.007), absence of GVE (p=0.011), and absence of HH+RE (p=0.000).

Conclusion: Gastric varices were prevalent in liver cirrhosis patients, amongst which IGV1 were the most common in our population. GV were more prevalent in association with grade III EV as compared to grade I and II EV. However, their prevalence in different age groups and gender had no statistical significance. Presence of GV in liver cirrhosis patients may have a protective or inhibitory role for the development of HH+RE and GVE.

Keywords: *gastric varices, sarin categories, retrospective analysis, statistical associations*

Gastric varices (GV)[1] are dilated submucosal veins that occurs secondary to portal hypertension or splenic vein obstruction.[2] Sarin classified GV into 4 types.[3] Gastroesophageal varices (GOV) type 1 and GOV type 2 are the esophageal varices that extend below cardia into stomach along lesser curvature and greater curvature respectively. Isolated gastric varices (IGV) type 1 and IGV type 2 are in the fundus and elsewhere in the stomach respectively. The prevalence of GV in cirrhosis is estimated to be 15-17%.[3,4,5] GOV1 are more frequent approximately 75%, and IGV2 are extremely infrequent among all GV. GV have a lower risk of bleeding than EV. However, their bleeding tends to be more severe with a higher mortality, approximately 45%.[3]

Left gastric vein, a branch of portal vein, is involved in the formation of EV and GOV1. The branches of splenic vein in posterosuperior part of the gastric wall, short gastric vein and posterior gastric vein, are involved in the formation of GOV2 and IGV1. Some branches of splenic vein and superior mesenteric vein are responsible for IGV2.[6] GV are drained by portosystemic collaterals. EV and GOV1 drains via azygous veins, while IGV1 drains via left inferior phrenic vein (IPV) into left renal vein or inferior vena cava. GOV2 drains via both EV and IPV.[7]

GOV1 share the vascular anatomy as that of EV, so treatment plan for both is same. Primary prophylaxis includes non-selective beta blockers (NSBB) for high risk small EV/GOV1 (with red sign or in CTP-C patient), and NSBB or carvedilol, or endoscopic variceal band ligation (EVBL) for medium or large EV/GOV1. Secondary prophylaxis includes combination of NSBB and EVBL (1st line) and TIPS (2nd line). For GOV2 or IGV1, primary prophylaxis includes NSBB while secondary prophylaxis includes TIPS or BRTO. Similarly, for actively bleeding GOV2 or IGV1, TIPS is the treatment of choice. Cyanoacrylate glue injection is an option if TIPS or BRTO are not technically feasible in secondary prophylaxis or actively bleeding GOV2

or IGV1.[8,9,10] Dual venous connection makes the management of GOV 2 difficult. BRTO eradicates its posterior (fundal) part drained by IPV, and may remain its anteromedial (cardiac) part which is drained by esophageal varices. This part may need transhepatic embolization or EVBL.[11]

When we see gastric varices in liver cirrhosis patients, additional endoscopic findings like esophageal varices (EV), portal hypertension gastropathy (PHG), gastric vascular ectasia (GVE), and hiatal hernia + reflux esophagitis (HH+RE) are also found. The available international data is scarce about any association of gastric varices with these additional findings.

The objective of this study was to find the prevalence of gastric varices, their types and associations in patients suffering Liver cirrhosis who underwent upper gastrointestinal endoscopy (UGIE) at Liver Clinic, Lahore, Pakistan.

METHODS

This was a retrospective cohort study carried out at Liver clinic, 250 Shadman Lahore. Amongst the CLD patients who underwent UGIE from July 2010 to June 2014, the patients with gastric varices were evaluated. GV were divided into 4 types according to Sarin classification.[3] The esophageal varices extending below the cardia into stomach along lesser curvature and greater curvature were named as GOV1 and GOV2 respectively, while isolated gastric varices are in the fundus and elsewhere in the stomach were named as IGV1 and IGV2 respectively. The age of the patients was categorized into childhood if < 13 years, adolescence if 13-18 years, young adults if 19-44years, middle aged adults if 45-65 years, and older adults if >65 years.[12,13]

EV were graded from I to III as follow: small and straight EV were Grade I, EV, tortuous varices occupying <1/3 of the esophageal lumen were grade II, and larger occupying >1/3 of the esophageal lumen were grade III EV.[14]

The presence gastric varices, types of gastric varices, gender, age groups, grade of esophageal

disease, presence of portal hypertension gastropathy, GVE, and HH+RE were the qualitative variables, while age of the patients was a quantitative variable. The entire data was evaluated on SPSS version 25. During descriptive interpretation of data, means and standard deviations were calculated for the presentation of quantitative variable, and frequencies and percentages were computed for qualitative variables. The bivariate analysis was performed to determine the significant relation of different predictive factors with presence of gastric varices. While applying chi-square test of independence, a p value of equal to or less than 0.05 was considered as significant. Moreover, odds ratio along with their 95% confidence interval (CI) were also calculated for each association.

RESULTS

A total of 2463 chronic liver disease (CLD) patients underwent UGIE, out of which 1587 (64.4%) were male and 876 (35.4%) were female. Their mean age was $51.03 + 10.18$ years with a range of 14 to 95 years, while their mean weight was $72.70 + 15.55$ Kilogram with a range of 29-131 kilogram. 305 (12.4%) patients had fundal varices; amongst which 22.6% (n=69) had GOV1, 13.1% (n=40) had GOV2, 58% (n=177) had IGV1, 1% (n=3) had IGV2, 0.7% (n=2) had GOV1 along with GOV2, and 4.3% (n=13) had GOV2 along with IGV1. (Picture 1-3)

Amongst the CLD patients who underwent UGIE, 12.5% males and 12.2% females had fundal varices. The association of finding fundal varices with gender was not statistically significant (p= 0.898). Amongst the CLD patients who underwent UGIE, 0% adolescents, 11.8% young adults, 12.2% middle aged adults and 16.1% older adults had fundal varices. The association of occurrence of fundal varices in different age groups was also not statistically significant (p=0.456). 12.6% (n=22) CLD patients without esophageal varices, while 10.2% (n=100) CLD patients with grade I esophageal varices, 12.6% (n=68) with grade II esophageal varices and 15.1% (n=115) with grade III esophageal

varices had fundal varices. The occurrence of fundal varices had a statistically significant association with different grades of esophageal varices (p= 0.023) Amongst the patients with PHG, 12.8% (n=299) had fundal varices, while amongst the patients without PHG, only 4.9% (n=6) had fundal varices. The occurrence of fundal varices in CLD patients with portal hypertensive gastropathy had statistically significant association (p=0.007). Similarly, amongst the CLD patients without GVE, 12.9% (n=289) had fundal varices, while only 7.1% (n=16) CLD patients with GVE had fundal varices. The association of occurrence of fundal varices in CLD patients without GVE was statistically significant (p=0.011). 12.9% (n=304) CLD patients without hiatal hernia + reflux esophagitis had fundal varices, while only 0.9% (n=1) CLD patients with hiatal hernia + reflux esophagitis had fundal varices. The association of occurrence of fundal varices in CLD patients without hiatal hernia + reflux esopha-
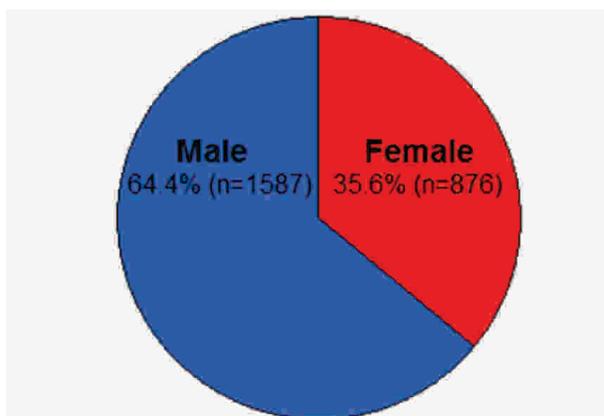
Picture 1: Gender wide distribution of Fundal varices
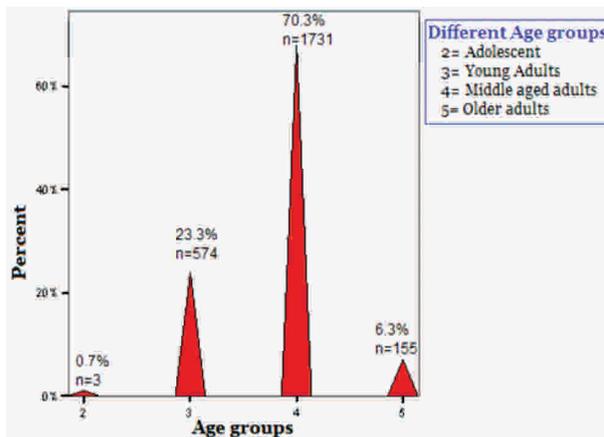

Picture 2: Distribution of fundal varices in different age groups

Table 1: *Correlation of Presence of Gastric Varices with different Parameters (n = 305/2463)*

Parameters /Categories	Gastric varices		Total	p-value	Odd ratio with 95% Confidence interval
	Yes	No			
Gender:					
Male	198 (12.5%)	1389 (87.5%)	1587	0.898	1.024 (0.797-1.317)
Female	107 (12.2%)	769 (97.8%)	876		
Age groups:					
Adolescent	0 (0%)	3 (100%)	3	0.456	
Young Adults	68 (11.8%)	506 (88.2%)	574		*
Middle aged adults	212 (12.2%)	1519 (87.8%)	1731		
Older adults	25 (16.1%)	130 (83.9%)	155		
Grade of Esophageal varices:					
No	22 (12.6%)	152 (87.4%)	174	0.023	
Grade I	100 (10.2%)	885 (89.8%)	985		*
Grade II	68 (12.6%)	472 (87.4%)	540		
Grade III	115 (15.1%)	649 (84.9%)	764		
Portal hypertensive gastropathy:					
Yes	299 (12.8%)	2042 (87.2%)	2341	0.007	2.831 (1.235-6.489)
No	6 (4.9%)	116 (95.1%)	122		
Gastric vascular ectasia:					
Yes	16 (7.1%)	210 (92.9%)	226	0.011	0.514 (0.304-0.867)
No	289 (12.9%)	1948 (87.1%)	2237		
Hiatal hernia + Reflux esophagitis:					
Yes	1 (0.9%)	105 (99.1%)	106		0.064 (0.009-0.463)
No	304 (12.9%)	2053 (87.1%)	2357	0.000	

* Odd ratio can only be computed for 2 X 2 tables

gitis was statistically significant (p=0.000).

Picture 3: Frequency of different types of Fundal varices

Types of Fundal varices
A = IGV1
B = GOV1
C = GOV2
D = GOV2 plus IGV1
E = IGV3
F = GOV1 plus GOV2
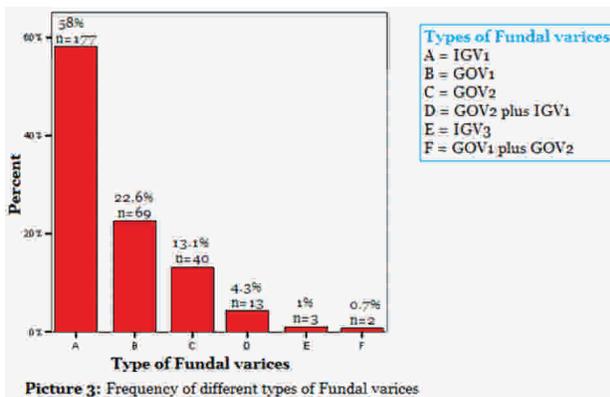
DISCUSSION

Gastric variceal bleed is a serious complication in decompensated liver cirrhosis and the endoscopist should be familial of its different types, their location, and management. Type of GV (IGV1> GOV2> GOV1), large size, presence of red sign, and severity of liver dysfunction are the factors associated with higher risk of bleeding.[15]

In a study, Mudawi, Ali and Tahir found 16.8% prevalence of GV. Similarly, in 2007, Khalid

Mumtaz and his colleagues reported the prevalence of GV of 15% (220/1436) in portal hypertension patients in Karachi. In our study of 2463 CLD patients, the prevalence of GV was 12.4%. Perhaps, the prevalence of GV in liver cirrhosis patients of our population was decreasing. This hypothesis requires further studies to validate these findings.

In 1992, Sarin and colleagues reported that amongst GV, GOV1 were the most common (75%) while IGV2 were extremely infrequent. In our study, IGV1 were most prevalent (58%) followed by GOV1 (22.6%). IGV2 were least prevalent (0.7%). This prevalence variation may be due to difference in distribution of portal hypertension in our population.

Mudawi and colleagues also noted that GV were more prevalent in patients with grade I and grade II EV. However, reverse was found in our data. The prevalence of GV was 10.2%, 12.6%, and 15/1% in patients with grade I, II, and III EV respectively.

Whether, gastric varices have protective role in the development of HH + RE in cirrhotic patients. International data is scarce on this hypothesis. In our

data, 0.32% (1 out of 305) cirrhotic patients with gastric varices had HH + RE, while 4.8% (105 out of 2158) cirrhotic patients without gastric varices had HH + RE. In past, multiple studies showed high prevalence of GERD in liver cirrhosis patients.[16] No one study correlated Hiatal hernia in cirrhosis patients with gastric varices. Our observation of less prevalence of HH + RE in conjunction with gastric varices may point the protective role of gastric varices in occurrence of HH + RE in cirrhotic patients. This hypothesis may require further studies to be validated.

In our study, 5.2% (16 out of 305) cirrhotic patients with gastric varices had GVE while 9.7% (210 out of 2158) cirrhotic patients without gastric varices had GVE. Perhaps, development of gastric varices in cirrhotic patients has an inhibitory effect on development of GVE. No reference evidence was found in literature discussing this effect. I think, further larger studies are required to validate these findings.

CONCLUSION

Gastric varices are prevalent in liver cirrhosis patients, amongst which IGV1 are the most common in our population. The GV are more prevalent in association with grade III EV as compared to grade I and II EV. However, their prevalence in different age groups and gender has no statistical significance. The occurrence of gastric varices in liver cirrhosis patients had a protective or inhibitory role for the development of HH+RE and GVE.

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TERATOGENIC EFFECTS OF DELTAMETHRIN ON THE DEVELOPING MICE

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Abstract

Objectives: Deltamethrin is a synthetic pyrethroid pesticide used globally in agriculture, domestic pest control, foodstuff protection, and disease vector control. Initially thought to be less toxic, quite a large number of recent reports have shown its toxic effects in animals. The current study was designed to evaluate the teratogenic effects of deltamethrin on the developing mice.

Material and Methods: 30 pregnant female mice of Swiss Webster variety of Mus musculus were chosen for the experiment and divided into control (C, 05 animals) and deltamethrin treated (DM, 25 animals) groups. The animals in DM group were divided into DM-I, DM-II, DM-III, DM-IV, and DM-V subgroups each consisting of 05. Each experimental subgroup animals were given 1.25, 2.50, 5.00, 10.00 and 15.00 µg of deltamethrin per g body weight orally on day 6, 8, and 10; and the control group animals were given 0.1 ml of corn oil (the vehicle used). The fetuses were recovered and examined on day 18 of gestation.

Results: In-utero deltamethrin treated fetuses revealed significantly decreased body weight, crown rump length; sizes of brain, eyes, limbs and tails. The severity of these changes found to be dose dependent. Morphological studies revealed some abnormalities including distorted axis, sacral teratoma, microcephaly, anencephaly, micromelia and dysplasia of limbs, club foot, microgonathia and short tail.

Conclusion: Deltamethrin is potentially harmful to the developing fetuses of mice, and may be equally harmful for the developing human too.

Key Words: *pyrethroids; deltamethrin; insecticide metabolism; teratogenicity; in-utero; mice;*

Pesticides play an important role in modern agriculture and their use has been increased steadily.[1] Presently, large quantities of pesticides are being used word wide to eradicate pests in agriculture and public health. Hence, humans may expose to pesticides at all stages of their life, prenatal and postnatal, especially children who are not adequately protected from the adverse effects of pesticides.[2] Large-scale usage of pesticides to crops and forests may lead to the presence of these toxic substances in the environment and can pollute the water reservoirs, streams and rivers, thus endangering the marine life, animals and human health.[1] Various epidemiological studies have shown relationship between spontaneous abortions and fetal death after maternal exposure to organochlorine and organophosphorous pesticides.[3] Because of this concern, pyrethroid pesticides have emerged as a major class of highly active insecticides having high bioefficacy and relatively low toxicity.[4] The use of pyrethroids as antipesticidal agents have markedly increased during the last a few decades.[5,6] Pyrethroids increase embryonic resorption and fetal mortality and fetotoxicity in animals. Maternal exposure to cypermethrin, for example, was found to affect the body and organs weights of offsprings.[2] Exposure to pyrethroids has been extensively documented in pregnant women, infants and children.[7] Pyrethroid ingestion leads within minutes to sore throat, nausea, vomiting and abdominal discomfort; convulsions and coma

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are the life-threatening features.[8] Pyrethroids are reported to cause hepatic and renal toxicity.[9] The pyrethroid act by modifying the gating characteristics of voltage-sensitive sodium channels to delay their closure[10,11] and causes hypersensitivity[12], tremors[13] and paralysis.[14]

Deltamethrin is a a-cyano type-II fourth generation pyrethroid insecticide [(S) alpha-cyano-3-phenoxybenzyyl-(1R)-cis-3-(2.2-dibromovinyl)-2,2 -dimethylcyclopropane-carboxylate] which was synthesized in 1974 and marketed in 1977.[15] It is odorless and colorless crystalline powder.[16] It is found in a variety of commercial insecticide products such as Butoflin, Butoss, cislin, Crackdown and K-Othrin.[17,18,19] It is extensively used in agriculture and forestry because of its high activity against broad spectrum of insects[20] and pests of glasshouse and field vegetables such as leeks and salad onions.[21] It is also being used as an alternative pesticide in malaria control[22,23], and triatomine (bugs) control, the causative vectors in Chagas disease.[24] Deltamethrin ingestion is associated with decreased sperm count, motility, and abnormal spermatozoa in mice.[25] Deltamethrin, also, exhibits an immunosuppressive effect which causes negative impact on the host resistance to Candida albicans infection.[26] The most important sources of the animal and human exposure to deltamethrin are polluted food and water, and it is readily absorbed by the oral route.[27] Deltamethrin, after oral administration, is rapidly absorbed; about half is hydrolyzed into acid and alcohol moieties by liver microsomal enzymes, the acid component is conjugated and secreted in urine; and the remaining portion is excreted unchanged through feces within 24 hours in rats.[9] During its metabolism, reactive oxygen species (ROS) are also produced which can induce oxidative stress in tissue and cause chronic permanent damage in intoxicated animals.[28] In commercial formulations, the activity of pyrethroids (deltamethrin) is usually enhanced by the addition of a synergist such as pipronyl butoxide which inhibits metabolic degradation of the active ingredient.[8] As deltamethrin is being extensively used as insecticidal agent, this study was planned to evaluate the teratogenic effects of deltamethrin on the developing mice.

METHODS

Sixty adult sexually mature mice [20 male and 40 female (non-pregnant)] Swiss Webster variety of Mus musculus were used in this study. Males and females were placed in separate cages and fed on commercial diet, water ad libitum, and reared at optimal light, temperature ($26+2°C$) and relative humidity 40-55% for acclimatization for 15 days. After this, the animals were kept in a ratio of one male and two females in separate cages for one week for conception under controlled conditions. Pregnancy day "0" was determined by the presence of vaginal plug. 30 pregnant female mice were chosen randomly for the experiment and divided into control (C) (05 animals) and deltamethrin treated (DM) (25 animals) groups. The animals in DM group were divided into DM-I, DM-II, DM-III, DM-IV, and DM-V subgroups each consisting of 05. All the animals were given respective identification marks and the animals of each subgroup were housed in separate cages. Each experimental subgroup animals were given respective dose of deltamethrin orally on day 6, 8, and 10 as shown in fig. 1; and control group animals were given 0.1 ml of corn oil (the vehicle used).

On day 18 of gestation, the pregnant mice were weighed; fetuses were recovered by cesarean section and counted. Each fetus was dried and weighed to a 0.01 mg precision. A total of 18 fetuses were chosen at random from pregnant mothers of control group as well as from each deltamethrin treated subgroup. The fetuses were placed in Bouin's fixative for 48 hours and then preserved in 70% alcohol for teratological study. The data was analyzed by using one way ANOVA through SPSS software, and post hoc multiple-comparison test. P-value <0.05 was considered significant.
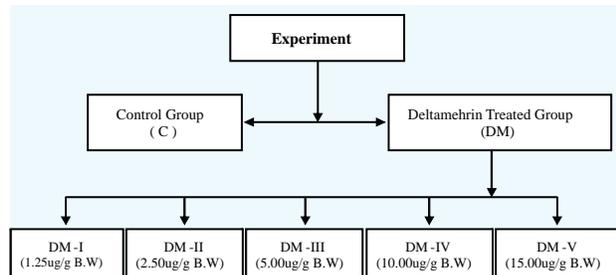
Fig 1: *Schematic Diagram Showing the Dosage Pattern of Deltamethrin. All treatments were applied on days 6, 8 and 10. Control animlas were given 0.1 ml of corn oil*

RESULTS

Control group ©

In this group, the fetuses were uniform in appearance, well developed and well grown morphologically. Each fetus had well developed and prominent head, trunk, limbs and tail. All the sense organs of the animals were quite distinct in craniofacial region. The fore, mid and hind brain were distinctly seen. Well developed telencephalon was indicated by laterally protruding cerebral hemispheres. The rhombencephalon was well developed and divided into metencephalon and myelencephalon (Fig. 2).

The basic sense organs- nose, eyes and ears were well developed. Two nostrils were seen close to each other at the anterior end of the snout. The snout had distinct lines of vibrissal development. The eyes were well developed with distinct upper and lower eyelids. Well developed pinna and a distinct auditory meatus indicated well developed external ear. In many cases, the pinna was so developed that it covered the opening of auditory meatus. At this stage, the heads were irregular in shape as the skulls had not developed fully. The jaws were well developed especially the lower jaw. Slight flattening of the thorax was apparent with protruded abdomen. Skin was thick but still unpigmented. It was wrinkled which camouflaged the internal viscera (Fig. 2).
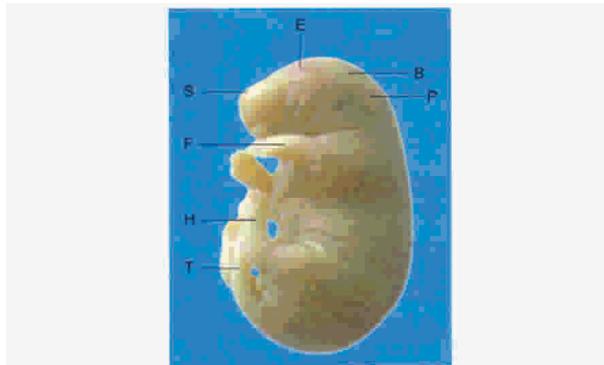
Fig. 2: *A Macrophotograph of 18-day Mouse fetus of Control (Vehicle Treated Group) given a 0.1µg/g Corn Oil B.W Showing Normal Development. Note: Normal development of snout (S); Eye (E); Brain (B); Pinna (P); Tail (T); Hind limb (H) and Fore limb.*

Experimental group

Subgroup DM-I: There were slight remarkable differences in the external morphology of the fetuses (Fig. 3). The basic sense organs and ears were well developed. Micro-ophthalmia was observed in 5.55% of the fetuses and club foot was also seen in 5.55% of the cases. Hence the overall percentage of the malformed fetuses in this group was 11.11% (Table 1) and the morphometric changes are shown in table 3.
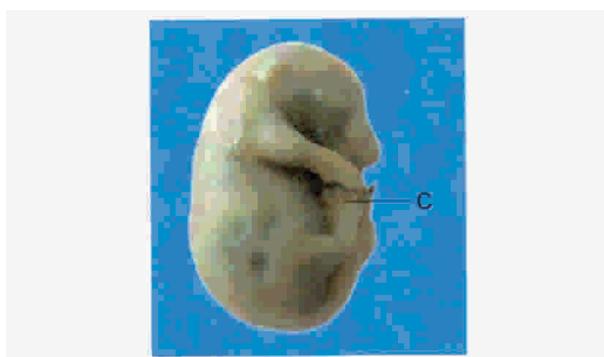
Fig. 3: *A Microphotograph of 18-day Mouse Fetus of Recovered from Mothers given a Dose of 1.25µg/g B.W (DM-1) on Day 6, 8 and 10 of Gestation. Abnormalities Induced by the Deltamethrin including. Club Shaped pes ©.*

Subgroup DM-II

This group animals showed remarkable diffe-

rences in the external morphology of the fetuses. 5.55% of the fetuses showed anencephaly with microgonathia (fig. 4). 5.55% showed short tail, and 11.11% were with dysplasia. No resorbed uterus was seen in the animals of this group. Hence the overall percentage of malformed fetuses in this group was 44.44% (table 1) and the morphometric changes observed are shown in table 3.
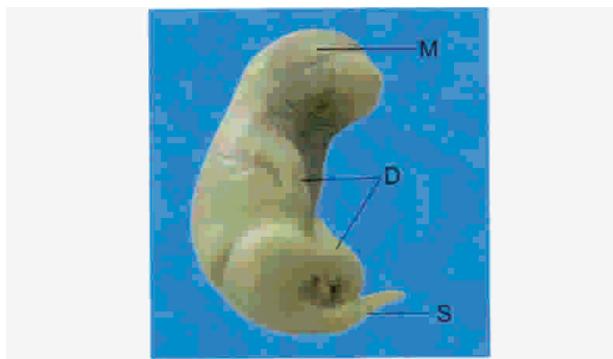

Fig. 4: *A Microphotograph of 18-day Mouse Fetus of Recovered from Mothers given a Does of 2.50 µg/g B.W (DM-II) on Day 6, 8 and 10 of Gestation. Abnormalities Induced by the Deltamethrin including, Dysplasis (D); Microphthalmia (M); S (Short tail).*

Subgroup DM-III

Remarkable differences were noted in the external morphology of the fetuses in this group. Brain defects were seen in 5.55% of the fetuses. The fetuses with tail defects were 5.55. Malformed sacral region were seen in 5.55% and some of the fetuses were distorted axis (Fig. 5 & Table 1). Anencephaly was seen in 5.55% of the fetuses; microphthalmia in 5.55; anophthalmia in 11.11%; micromelia in 5.55%; and dysplasia in 11.11%. Short tail was seen in 5.55% and microgonathia were present in 11.11% of the fetuses. Thus the overall percentage of malformed fetuses in this group was 66.66% (Table 1). No resorbed uterus was seen in this group. The morphometric changes observed are shown in table 3.
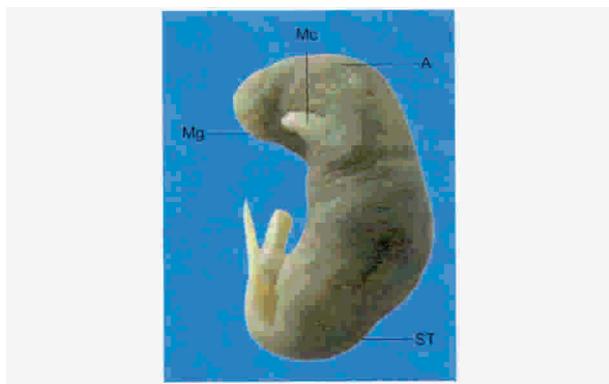
Fig. 5: *A Microphotograph of 18-day Mouse Fetus of Recovered from Mothers given a Doese of 5.00 µg/g B.W (DM-III) on Day 6, 8 and 10 of Gestation. Abnormalities Induced by the Deltamethrin including Micrognathia (Mg); Micromelia (Mc); Anencephaly (A); Sacral Teratoma (ST).*

Subgroup DM-IV

It was noted that there were remarkable difference in the external appearance of the fetuses in this group (Fig. 6). The microcephaly was seen in 5.55% of the fetuses; malformed sacral region in 2.77%; distorted axis in 2.77%; dysplasia of limbs in 11.11%; and meromalia in 5.55%. No fetus with jaw defect was seen in this group but tail defect were present in 5.55% of the fetuses. Resorbed uteruses were seen to be 22.22% in this group (Fig. 6B & Table 1). Hence overall percentage of the malformed fetuses in this group was 77.77%. The morphometric changes observed are shown in table 3.
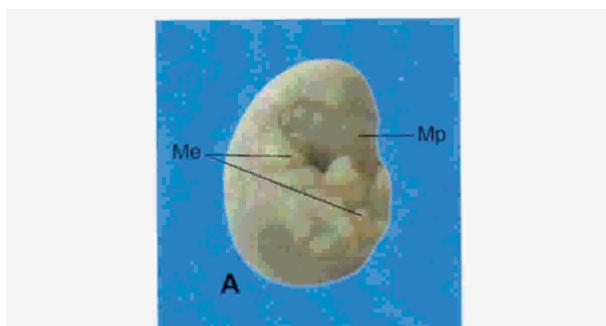
Fig. 6A: *A Microphotograph of 18-day Mouse Fetus of Recovered from Mothers given a Doese of 10.00 µg/g B.W (DM-IV) on Day 6, 8 and 10 of Gestation. Abnormalities induced by the Deltamethrin including Micrognathia (Mp); Meromelia (Me).*
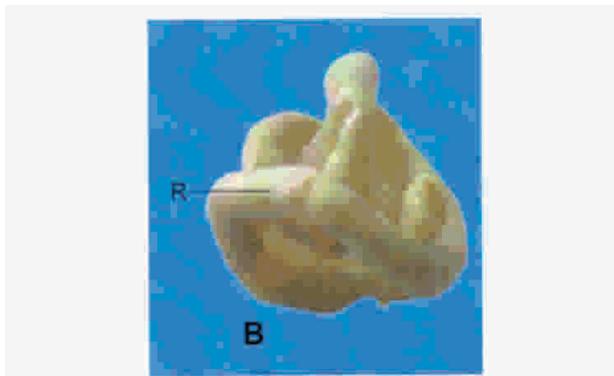
Fig. 6B: *Microphotograph of 18-day Old Resorbed Uterus from Mother given a Dose of 10.00 µg/g B.W (DM-IV) on 6, 8 and 10 day of Gestation. Note: Resorbed uterus (R).*
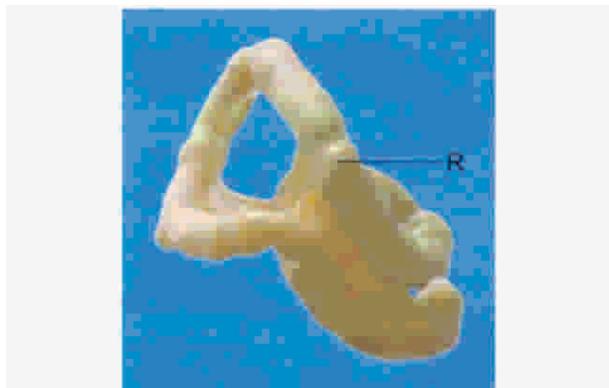
Fig. 7: *Macrophotograph of 18-day Old Resorbed Uterus from Mother given a Dose of 15.00 µg/g B.W (DM-V) on 6, 8 and 10 day of Gestation. Note: Resorbed uterus ®.*

Subgroup DM-V

Remarkable differences in the external morphology of the fetuses in this group were noted. Microcephaly was seen in 11.11% of the fetuses; eye defects in 5.55%; micromelia in 11.11%; and agenesis of tail in 11.11%. Resorbed uteruses were noted in 22.22% in this group (Fig. 7). Hence the overall percentage of malformed fetuses in this group was 83.33% (Table 1). The morphometric changes seen are shown in table 3.

DISCUSSION

Usages of synthetic pyrethroids have been increased in the near past because of its outstanding target oriented pesticidal action.[9] This widespread use has significantly increased chances of human exposure to these pesticides.[29] They have a wide spectrum of insecticidal potency, vertebrate toxicity, and environmental stability.[30] Their acute toxicity is dominated by pharmacological actions upon the

Table 1: *Developmental Anomalies Induced by Deltamethrin on 18-day Old Fetuses Recovered from Pregnant Mice Administrated Orally with different Concentrations on days 6, 8 and 10 of Gestation.*

Dose [D] Groups	Axis defects (%)	Brain defects (%)	Eye defects (%)	Limbs defects (%)	Jaw defects (%)	Tail defects (%)
C	normal	normal	normal	normal	normal	normal
DM-1	distorted (5.55)	(0.00)	microphthalmia (5.55)	club shaped (5.55)	(0.00)	(0.00)
DM-II	sacral teratoma (2.77) distorted (2.77)	anencephly (5.55)	malformed (5.55)	dysplasia (11.11)	micrognathia (5.55)	short (5.55)
DM-III	sacral region malformed (5.55) distorted (5.55)	anencephly (5.55)	microphthalmia (5.55) anophthalmia (11.11)	micromelia (5.55) dysplasia (11.11)	micrognathia (11.11)	agenesis short (5.55)
DM-IV	malformed (11.11)	microcephaly (5.55)	micophthalmia (11.11)	dysplasia (11.11) meromelia (5.55)	(0.00)	agenesis (5.55)
DM-V	distorted (5.55)	microcephaly (11.11)	malformed (5.55)	meromelia (11.11)	(0.00)	agenesis (11.11)

ᴅ: For explanation see figure 1

Table 2: *Complete Percentage Data of Morphological Abnormalities Induced by Deltamethrin on 18-day Old Fetuses Recovered from Pregnant Mice, Administrated Orally with different Concentrations on days 6, 8 and JO of Gestation.*

Dose D Groups	No. of fetuses observed	Malformed Fetuses %	Resorbed uterus %	Eye defects %	Jaw defects %	Brain defects %	Limb defects %	Axis distortion %	Tail defects %
C	18	00.00	00.00	00.00	00.00	00.00	00.00	00.00	00.00
DM-I	18	11.11	00.00	5.55	00.00	00.00	5.55	00.00	00.00
DM-II	18	44.44	00.00	5.55	5.55	5.55	11.11	5.55	5.55
DM-III	18	66.66	5.55	16.66	11.11	5.55	16.66	5.55	5.55
DM-IV	18	77.77	22.22	11.11	00.00	5.55	16.66	11.11	5.55
DM-V	18	83.33	27.77	5.55	00.00	11.11	11.11	11.11	11.11

D: For explanation see figure 1

Table 3: *Effects of Deltamethrin on 18- day Fetuses Recovered from Pregnant Mice, Administrated Orally with different Concentrations on days 6,8 and 10 of Gestation.*

Dose D Groups	Weight (mg±S.E.)	CR Length (mm±S.E.)	Brain Size (mm±S.E.)	Eye Lenght (mm±S.E.)	Eye Width (mm±S.E.)	Fore Limb Lenght (mm±S.E.)	Hind Limb Lenght (mm±S.E.)	Tail Length (mm±S.E.)
Control	1687.48± 60.54(a)	22.75± .13 (a)	8.25± .08 (a)	3.3± .05 (a)	2.83± .057 (a)	8.41± .073 (a)	8.80± .06 (a)	11.91± .19(a)
DM-I n =18	1313.87± 17.76(b)***	21.41±.108 (a)	7.44±.06 (ab)	3.05±.03 (b)	2.30±.06 (b)***	7.80±.06 (ab)	8.22±.10 (a)	11.66± .12(a)
DM-II n=18	148.89±16.74 (c)***	19.72±.14 (b)***	7.16±.05 (bc)*	2.50±.07 (c)***	2.13±.05 (b)***	7.11±.10 (ab)	7.72±.06 (ab)	10.41±.14 (b)*
DM-III n =18	841.4±51.70 (d)***	16.00±.24 (c)***	6.47±.07 (d)***	2.02±.06 (d)***	1.58±.04 (c)***	6.44±.09 (bc)***	7.00±.07 (bc)***	8.52±.25 (c)***
DM-IV n =18	48.99±18.26 (e)***	5.56±1.08 (d)***	1.94±.53 (e)***	.667±.18 (e)***	.778±.15 (d)*'*	1.80±.55 (d)***	1.89±.541 (d)***	1.52±.46 (d)***
DM-V n=18	.912±.31 (e)***	2.14±.60 (e)***	.853±.31 (f)***	.088±.08 (f)***	.17±.09 (e)***	.47±.32 (e)***	.73±.40 €***	.61±.33 (e)***

D: For explanation see figure 1

(DMRT, comparison of the categories within a group; any two category within the same group do not having a common small alphabet parentheses differ significantly from each other)DMRT, category wise inter associated paretheses differ significantly from each other {DMRT= Duncan's Multiple Range Test (P 0.05)}

Significant differences (P <0.05, P<0.01, P<0.001) indicated by * ,** , *** respectively when compared with vehicle-treated animals.

central nervous system, predominantly mediated by prolongation of the kinetics of voltage regulated sodium channels, although other mechanisms also operate.[29] One of the main mechanisms of action of pyrethroids is through formation of reactive oxygen species (ROS) which induce oxidative stress leading to tissue damage.[31] Several pesticides have been reported to possess hormonal activities as well, and thus classified as endocrine disrupters.[32] Keeping in view the large scale use of insecticides now a day, and their reported toxic effects on mammalian and non mammalian animal species, the present study was designed to see the effects of deltamethrin on mice fetuses.

Bhaumik and Gupta[33] treated female albino rats with deltamethrin on day 6 through 15, and noted minor malformation(s) such as focal subcutaneous hemorrhages and retarded growth in both the treated and control animals. The only skeletal variation seen was bilateral wavy ribs in one of the fetuses. There were quite low incidences of microphthalmia and hypoplastic kidney but theses but these variations were not significant. Saillenfait et al[34] noted that deltamethrin had no statistically significant effect on the incidence of post-implantation loss, fetal weight or anogenital distance in the male fetuses. Dose

related reduction in weight gain but no effect on number of implants, fetal mortality, fetal malformations was noted by Hallenbeck et al[35] when they treated pregnant mice with deltamethrin on day 7 to 16 of gestation. Almost similar findings has been reported by El-Gerbed.[1]

Abdel-khalik et al[36] investigated the effects of deltamethrin on the fetuses of pregnant rats. They noted retardation of growth, hypoplasia of the lungs, dilatation of the renal pelvis and increase in placental weight but no skeletal changes were seen. Schardein[37] treated pregnant rats with deltamethrin on day 6 through 15 of gestation and found changes as folded retina, vertebral malformations and fused sternebrae, but no effect on body weights of the fetuses were seen.

The present study observations, however, have proved to be embryo toxic in mice at the doses that usually do not cause a perceptible maternal toxicity. It has been concluded undoubtedly that pre and peri-implantation embryonic resorptions increase as indicated by reduced number of implantation and average liter size depending upon the dose (Table 2). Growth retardation is indicated by reduced mean fetal weight (fig. 8) as well as crown rump length (fig. 9) and significantly decreased their values (p<0.001) and this situation becomes more and more worse with increase in dose (Table 3). Retorted growth of other organs like brain, eyes, limbs and tails is indicated by reduction in their sizes and significantly decreased values (P<0.001) which becomes more prominent with increasing dose (Table 3). A large number of fetal dysmorphologies such as microcephaly, paddle shaped manus; distorted axis and meromalia were seen. The neuro-cephalic and cranio-facial derangements included: anencephaly, microcephaly, anophthalmia, microphthalmia, microgonathia, improperly formed eye cups. Hygroma dorsalis was seen in upper cardiac region and congenital pulmonary emphysema was noted as the most prevalent microanatomical arrangements.

On the basis of the findings cited above, it is concluded that exposure to deltamethrin is teratogenic and embryo toxic, particularly if such exposure occurs at the beginning of organogenesis, at the dose levels used in this study which cause perceptible toxicological symptoms in dams. Thus it is recommended that the use of this particular insecticide having multitudes of systemic and developmental toxological effects must be curtailed to minimum possible level. Wherever its use seems unavoidable, this insecticide must be used under strict safety measures; particularly pregnant women and kids must be kept away from such places where deltamethrin is being used. As deltamethrin, which is possible cause of congenital abnormalities and inabilities in mammalian and non-mammalian species, is commonly used as mosquito repellent, for the control of ectoparasites in domesticated animals and poultry, should be minimized. Thus, it is possible to save our coming generations from an easily avoidable factor which may possibly lead to a horrible increase in the number of disables in our society.

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AN ASSOCIATION OF SERUM ZINC LEVELS WITH FEBRILE SEIZURES A CASE CONTROL STUDY IN CHILDREN (06 TO 36 MONTHS)

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Abstract

Aim: The aim of this study is to find the association between zinc deficiency and Febrile Seizures in children of 06 to 36 months of age.

Methods: Case control study was conducted at the department of Paediatrics, Sharif Medical and Dental College Lahore from 1stSeptember 2016 to 31st August 2017.Total 200 cases (100 each in cases and controls) were included in this study. The collected data was entered and analyzed with SPSS-17 software. Mean+standard deviation was calculated for quantitative data like age and serum zinc levels; while frequency and percentages were calculated for qualitative data like gender and zinc deficiency.

Results: In our study, out of 200 cases (100 each in cases and controls), mean+sd was calculated as 20.71+9.06 in cases and 21.62+9.77 months in controls, 70%(n=70) in cases and 65%(n=65) in controls were male while 30%(n=30) in cases and 35%(n=35) in controls were females, the meanseum zinc levels were calculated as 71.76+19.68 in cases and 79.34+16.46 in controls, p value was 0.003 showing a significant difference, comparison of zinc deficiency was recorded in 37%(n=37) in cases and 16%(n=16) in controls, odds ratio was calculated as 3.08, p value was 0.0008.

Conclusion: It is concluded that the frequency of zinc deficiency is significantly higher in patients presenting with febrile seizures as compared to the controls in children with 06 to 36 months of age.

Keywords: *children, 06 to 36 months of age, febrile Seizures, zinc deficiency, association*

Febrile convulsion is one of the most common seizure disturbances in children with an approximate incidence of 3-4%. Febrile convulsion is defined as seizure associated with fever as high as 38.5°C in children 6 months to 5 years without any infection in central nervous system or other factors explaining its incident.[1] The peak onset is age 18 to 22 months.[2] Pathogenesis of febrile seizures remain unknown. Several potential hypothesis such as genetic basis, immunological disorders, low serum iron level as well as serum and cerebrospinal fluid zinc levels, calcium, magnesium levels and low gamma-ammino butyric acid have all been proposed to explain pathophysiology of this condition.[3] Zinc is an important micronutrient that plays a significant role in growth and development, immune system response, enzymatic activity of different organs, proteins and cellular metabolism, neurological functions, nerve impulse transmission and hormone release.[4] Zinc deficiency lowers serum and CSF concentration of gamma amino butyric acid (GABA). This hypozantemia activates N-Methyl-D-Aspartate receptors one of glutamate family of receptor which may play an important role in induction of epileptic electrical discharges.[5] Low Zinc levels can play a role in pathogenesis of febrile seizures. Past studies have reported the low serum zinc level in children with febrile seizures.[6,7]

METHODS

The study was conducted at department of Paediatrics Sharif Medical and Dental College

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Lahore. Total 200 patients (100 in each group) case and control with history of fever and fits were enrolled from sep. 2016 to August 2017. The age range was from 06 months to 36 months. The study was conducted after approval from hospital ethical committee. Patients of 06 months to 36 months of age belonging to either sex with history fever and fits were included in the study. Patients with history of developmental delayed, known case of epilepsy and on zinc therapy were excluded from the study. The collected data was entered and analyzed with SPSS-17 software.

RESULTS

A total of 200 cases (100 in two groups) fulfilling the inclusion/exclusion criteria were enrolled to find the association between zinc deficiency and Febrile Seizures in children of 06 to 36 months of age. Age distribution of the patients was done, it shows that 44%(n=44) in cases and 36%(n=36) in controls were between 6-18 months of age while 56%(n=56) in cases and 64%(n=64) in controls were between 19-36 months of age, mean+sd was calculated as 20.71+9.06 in cases and 21.62+9.77 months in controls. (Table No. 1). Regarding gender distribution, 70%(n=70) in cases and 65%(n=65) in controls were male while 30%(n=30) in cases and 35%(n=35) in controls were females. Man zinc levels were calculated as 71.76+19.68 in cases and 79.34+16.46 in controls, p value was 0.003 showing a significant difference. (Table No. 2).Comparison of zinc deficiency was recorded in 37%(n=37) in cases and 16%(n=16) in controls while remaining 63%(n=63) in cases and 84%(n=84) in controls had no findings of the morbidity, odds ratio was calculated as 3.08, p value was 0.0008. (Table No. 3)

DISCUSSION

This study was conducted to see whether there is an association between serum zinc levels and febrile seizures as local data on association of zinc deficiency with febrile seizures is lacking. In our study, out of 200 cases (100 each in cases and

Table 1: *Age Distribution (n=200)*

Age (in months)	Cases (n=100)		Controls (n=100)	
	No. of patients	%	No. of patients	%
6-18	44	44	36	36
19-36	56	56	64	64
Total	**100**	**100**	**100**	**100**
Mean+sd	**20.71+9.06**		**21.62+9.77**	

Table 2: *Mean Zinc Levels In Both Groups (n=200)*

Zinc levels	Cases (n=100)		Controls (n=100)	
	Mean	SD	Mean	SD
	71.76	19.68	79.34	16.46

P value=0.003

Table 3: *Comparison of Zinc Deficiency (n=200)*

Zinc deficiency	Cases (n=100)		Controls (n=100)	
	No. of patients	%	No. of patients	%
Yes	37	37	16	16
No	63	63	84	84
Total	**100**	**100**	**100**	**100**

Odds ratio=3.08
P value= 0.0008

controls), mean+sd was calculated as 20.71+9.06 in cases and 21.62+9.77 months in controls, 70% (n= 70) in cases and 65%(n=65) in controls were male while 30%(n=30) in cases and 35%(n=35) in controls were females, man zinc levels were calculated as 71.76+19.68 in cases and 79.34+16.46 in controls, p value was 0.003 showing a significant difference, comparison of zinc deficiency was recorded in 37%(n=37) in cases and 16%(n=16) in controls, odds ratio was calculated as 3.08, p value was 0.0008.

We compared our results with a previous study done in Iran a significant statistical difference was observed between two groups regarding the average level of serum zinc(P=0.0001) thirty seven (53.81%) of children in case group and 10(9.6%) in control group were found to have hypozantemia.[8] In a study done by Mehri Taheryra, in patients group serum zinc level was significantly lower (70 ug/dl) than control group (90ug/dl) which is statistically significant (P<0.001).[9] The findings of our study are in agreement with the above studies.

In another study by Lee JHetal zinc levels in children with febrile seizures was significantly lower (60.5±12.7) than those in children with afebrile seizures (68.9±14.50) (P<0.0010).[10] These findings are in contrast with our results. Mollah MA et al[11], in 2008 published a study comparing serum and CSF Zinc levels of febrile seizure children to their matched non-seizure febrile peers. Mean Zn concentration in both serum and CSF was less in febrile seizure children than in their matched non-seizure febrile peers (p<0.001). Kumar L et al[12] in a recent case control study found that mean serum zinc level was significantly lower in cases as compared to control (p<0.05) in children having febrile seizure. Ganesh R et al[13] compared serum zinc levels in 38 cases of simple febrile seizure with 38 age matched controls with statistically significant results (p<.001). Amiri M et al,[14] Modarresi MR et al,[15] Hydarian F et al,[16] and Talebian A et al,[17] also gave similar results which are comparable with our study. In another study the serum Zn level was found significantly lower in cases of simple febrile seizures than in controls.[18] In summary, the current study, in accordance with above mentioned studies justify the hypothesis that "there is an association between deficiency of serum zinc and febrile seizures".

CONCLUSION

It is concluded that the frequency of zinc deficiency is significantly higher in children with febrile seizures as compared to the controls between 06 to 36 months of age.

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BULLYING AMONG MEDICAL STUDENTS OF AIMC AND ITS PSYCHOLOGICAL EFFECTS ON THEM

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Abstract

Objectives: The purpose of this study was to ascertain the incidence of bullying among medical students of Allama Iqbal Medical college and its psychological effects on their life

Methodology: This cross sectional study was conducted at Allama Iqbal Medical College, Lahore affiliated with Jinnah Hospital Lahore, Pakistan from April to May in 2016. 300 students were selected by stratified random sampling technique. All the data was collected through structured questionnaire. Data was analyzed by SPSS version 17.0.Frequency tabulation and percentages were generated for qualitative variables. Chi –square test was used to find out relation between bullying and psychological effects e.g. anxiety etc.

Results: Bul lying was common among medical students. Incidence of bul lying was 66%.Major form of bul lying was verbal abuse (68%) followed by mistreatment (19.6%) and physical abuse (11.6%). 111 students reported that they had been bullied at least once a month. There was positive association between being bul lied and development of anxiety and depression among its victims.

Conclusions: Bullying was common among medical students. Majority of it was done by seniors. It promoted development of anxiety and depression among its victims. In order to avoid this, anti bullying team should play its due role. Student must be educated about this issue.

Key words: *bullying. medical student. verbal abuse. anxiety. depression*

Bullying is the use of force, threat, aggressive and intimidating behavior to dominate others. It shatters the confidence and self-respect of recipient.[1] It has various forms such as physical abuse, verbal abuse, belittlement, sexual harassment and mistreatment.[2] Bullying is a global phenomenon. Various researches on this topic have shown that it is present in every walk of life in one form or other.[3]

Bullying is venomous for educational and learning environment and it effects the learning capability of students. Prevalence of bullying among American medical students was 98.69 %, While In contrary to that 87% of British students reported that they had never been bullied. This contrast may be due to strong anti-bullying policy and peer support.[1,4-6] The major form of bullying was verbal abuse and its frequency increase with increase in year of study.[3,4,6]

In contrast to USA and European countries, the incidence of bullying is less in Islamic Countries. 61% in Jordan, 28% in Saudi Arabia and 52% in Pakistan. This decrease in prevalence may be due to different culture background. The main form of bullying is same as that of USA and UK which is verbal abuse.[2,7-12] In Indo Pak region, bullying in form of physical ragging is common at college and university level especially of public sector. It is a social curse and has been reported by various newspapers at national level, but no effort is still in view from government sector.[13-15] Bullying has disastrous psychological impact. It may result in anxiety, depression and suicide thoughts as much as twice more than other kids. Workplace bullying especially in health care profession can cost self-respect and professional contentment.[16-21]

There has been one or two researches on this topic in Pakistan but none of these researches have been done in Allama Iqbal medical college and none of them have shown bullying psychological effect on medical students life.[2,9] The purpose of this study was

to ascertain the incidence of bullying among medical students of Allama Iqbal Medical College, Lahore and its psychological effects on their life.

METHODS

This cross sectional study was conducted at Allama Iqbal Medical College, Lahore affiliated with Jinnah Hospital Lahore, Pakistan from April to May in 2016. 300 students were selected by stratified random sampling technique.

SAMPLE SELECTION

Inclusion criteria:

ᴵ Medical Student of Allama Iqbal Medical college

Exclusion criteria:

ᴵ Staff and Teachers of Allama Iqbal Medical college

Variables:

Independent Variables:

ᴵ Bullying

ᴵ Age

ᴵ Sex

Dependent Variables:

ᴵ Psychological Impact

DATA COLLECTION PROCEDURE

300 medical students those fulfilling the inclusion criteria were included in our study. All the data was collected through structured questionnaire.

DATA ANALYSIS PROCEDURE

Data was analyzed by SPSS version 17.0. Frequency tabulation and percentages were generated for qualitative variables. Chi –square test was used to find out relation between bullying and Psychological effects e.g. anxiety etc.

RESULTS

A cross sectional study was conducted among the medical students of Allama Iqbal Medical College, Lahore .Number of students who participated in this study were 300.Out of 300,198 students reported that they had been bullied by other as shown in Graph no 1. 112(74.6%) of males and 86(57.3%) females were bullied as shown in table no.1. 75% of

final year study reported that they had been bullied as shown in table no.2. The major form of bullying was verbal abuse (68%) followed by mistreatment (19.6%) and physical abuse (11.6%). Majority of bullying was done by seniors. 111 students reported that they had been bullied at least once a month as shown in graph no.3. Most of the students reacted to bullying by giving a verbal reply (56%) followed by escape from scene (34.3%) and fighting (9%) as shown in graph no.4. There was a positive correlation between being bullied and development of anxiety, depression and bad academic performance.

Out of 192, 90(45.4%) students reported that it provoked anxiety them. It produced depression in 48 (24.2%) students. 45(21.7%) students said that it effected their grades .P value for anxiety, depression and bad academic performance was P<0.001 as shown in table no.4 which showed strong there is strong association between being bullied and anxiety, depression and bad academic performance.

Out of 251 students who told that anti bullying society existed in their college, but only 29(9%) students were satisfied with its response as shown in table no.5 and graph no.5 respectively.
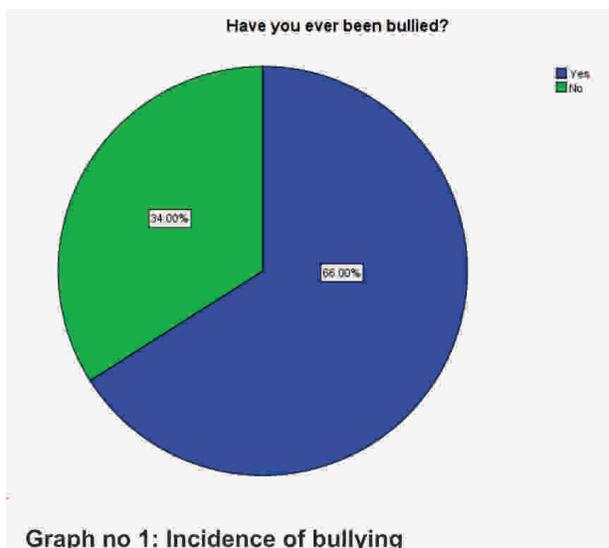
Graph no 1: Incidence of bullying

Table 1: *Incidence of Bullying among Males and Females*

Gender	Yes(Frequency and Percentage)	No (Frequency and Percentage)
Male	112(74.6%)	38(25.4%)
Female	86(57.3%)	64(42.7%)

Table 2: *Incidence of Bullying among Students of Different Classes*

Year of study	Yes (Frequency and Percentage)	No (Frequency and Percentage)
1st year	39(65%)	21(35%)
2nd year	39(65%)	21(35%)
3rd year	41(68.3%)	19(31.7%)
4th year	34(56.6%)	26(43.3%)
Final year	45(75%)	15(25%)
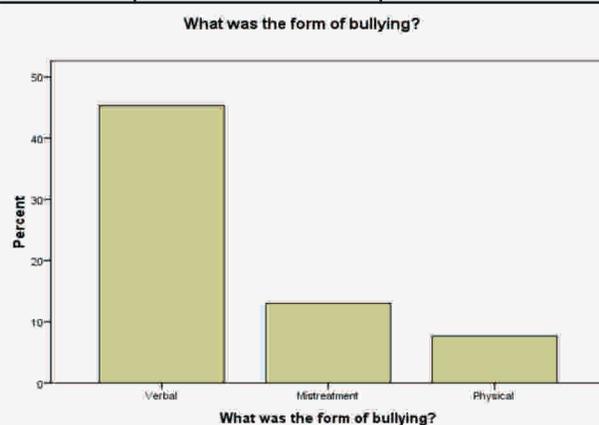
Graph no 2: Major form of bullying

Table 3: *What was the form of Bullying?*

Construct	Frequency	Percentage
Physical	23	11.6%
Verbal	136	68.68%
Mistreatment	39	19.6%
Total	198	100%
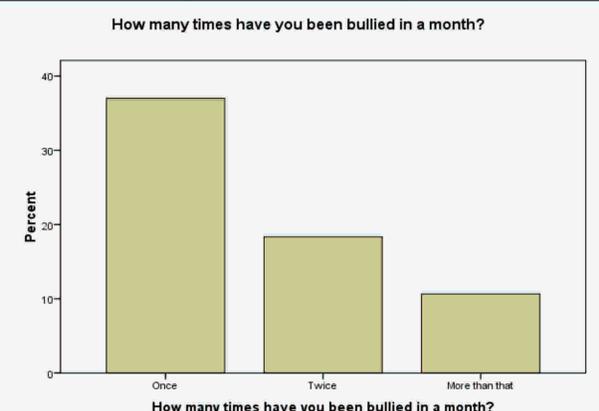
Graph no 3: Incidence of bullying in a month
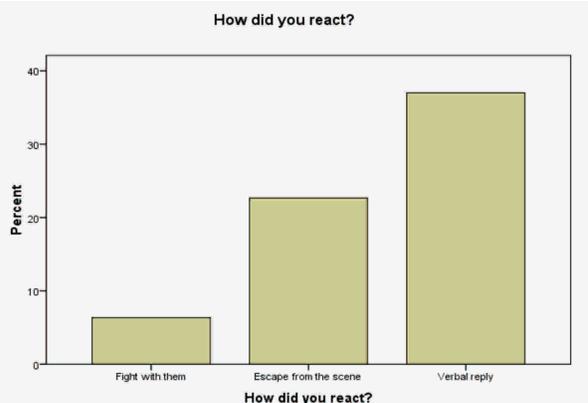
Graph no 4: Reaction to bullying

Table 4: *Psychological Effect of Bullying.*

Construct	Frequency	Percentage (%)	P value
Anxiety			0.001
Yes	90	45.45 %	
No	108	54.55%	
Depression			0.001
Yes	48	24.24%	
No	148	75.76%	
Effect on academic performance			0.001
Yes	43	21.71%	
No	155	78.29%	
Any change in life routine			0.001
Yes	37	18.68%	
No	161	81.32%	
Any thought of suicide			0.212
Yes	3	0.01%	
No	195	99.9%	

Table 5: *Any Anti Bullying Policy in your Institute?*

Gender	Yes (Frequency)	No (Frequency)
Male	124	26
Female	127	23
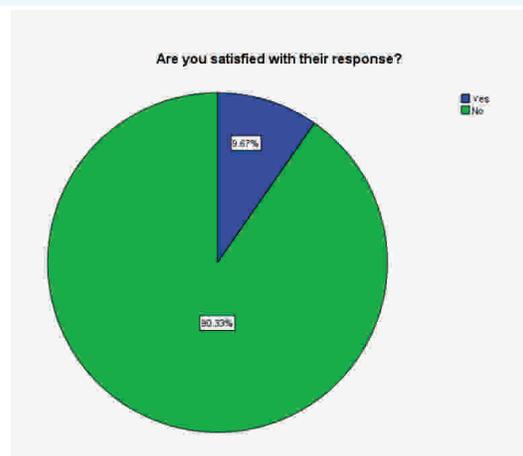
Graph no 5: Are you satisfied with anti bullying team response?

DISCUSSION

Our study suggested that bullying was common among medical students of Allama Iqbal Medical College, Lahore. Frequency of bulling was 66%. Interestingly, another research done on this topic in Pakistan had showed similar result.[2] Survey among medical students of 6 medical colleges showed that 52% of students had been bullied during their medical education.[9] In contrary to that, 28% of Saudi students reported exposure to bullying.[7] Prevalence of mistreatment was 61% in Jordan.[8] Research highlighted that prevalence of bullying was 98% among American students[4] and 98.5 % among Nigerian graduates.[11] Incidence of bullying was lesser than American studies but it was higher than study done in Saudi Arabia.[4,7,11] Males were bullied more than Females. In contrast to that, another study conducted in Pakistan had shown opposite results.[2] Study showed that major form of bullying was verbal abuse (69%) followed by mistreatment (20%) and physical abuse (12%). Studies performed globally have shown similar trend. International studies had shown High prevalence of sexual harassment, 34% in Nigerian study, 33% in Jordan study and 17% in study done in Oulu Finland. However, no such case was reported in our study. This was mainly due to Islamic cultural background.[11,8,3] Our study highlighted that majority of bullying was done by seniors. Studies done in other institutes had shown same results.[2,8,9] However study conducted among students of USA showed that majority of bullying was done by resident or fellows.[5] Our study showed that psychological effects in the form of anxiety, depression and bad academic performance were significantly associated with bullying. However, in our study suicidal behavior was not associated with bullying in contrast to that study had shown that there was a strong correlation between bullying and suicidal behavior.[17] Previous researches done in Pakistan had not highlighted this point. Our research added this point.

CONCLUSION

- Bullying was common among medical students. Majority of it was done by seniors.
- Verbal abuse was the most common form of bullying.
- There was positive correlation being bullied and development of anxiety, depression and bad academic performance. Recommendation:
- Anti bullying team should play its due role.
- Student must be educated about this issue.
- Students must be counseled about its psychological effects.

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COMPARISON OF HORMONAL ASSAYS WITH TRANSVAGINAL SONOGRAPHY IN POLYCYSTIC OVARIAN DISEASE

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Abstract

Objectives: To determine the diagnostic accuracy of hormonal assay in diagnosis of polycystic ovarian disease by taking findings of transvaginal sonography as gold standard.

Study design: Cross-sectional survey.

Setting: Study was carried out in the department of Radiology Jinnah Hospital / Allama Iqbal Medical College Lahore.

Duration of study: Six months (from March 2017 to August 2017)

Patients and methods: The calculated sample size was 250 cases of polycystic ovarian disease. Transvaginal sonography was mode of examination and at the same time blood sample was taken to measure the levels of serum prolactin, follicle stimulating hormone and luteinizing hormone.

Results: Mean age of the patients was found to be 26.2±4.0 years. Number of cysts showed 62.4% patients had 10-15 cysts, 16.8% had 16-20 cysts, 14.8% had <10 cysts and 6.0% patients had >20 cysts. According to arrangement of cysts, 25.2% were peripheral and 74.8% were random cysts. In comparison, findings of transvaginal sonography versus hormonal assay in detection of PCOs showed 227 positive cases on hormonal assays and 223 positive cases on transvaginal sonography (gold standard). Sensitivity was found to be 98.6%, specificity 74.0%, diagnostic accuracy 96.0%, PPV 96.9%, NPV 86.9%.

Conclusion: Hormonal assays are having minimal edge over the ultrasonography regarding the diagnosis of polycystic ovarian disease however ultrasound examinations are quick with immediate results.

Key words: PCOD, TVS, hormonal assay.

Polycystic ovarian disease is a condition that presents with ovarian dysfunction and endocrine problems. Polycystic ovarian disease is a heterogeneous condition, which is defined by the presence of two out of the following three criteria:

1. Oligomenorrhoea and or anovulation
2. Hyperandrogenism (clinical and or bio-chemical)
3. Polycystic ovaries.[1]

If ovaries are polycystic on ultrasonography and there are no clinical features suggestive of the polycystic ovarian disease then it is called polycystic ovaries. On the other hand if in addition to the polycystic ovaries there are other features like menstrual irregularity, infertility, acne, Hirsutism then it is called as polycystic ovarian disease or syndrome.[2,13]

The polycystic ovary has been defined as having 12 or more follicles per ovary or an ovarian volume greater than 10 ml as determined by ultrasonography.[3,11,12]

Using ultrasound examination criteria 20-30% of apparently healthy women in have been found to have polycystic ovaries in population study.[4]

Polycystic ovarian disease is one of the most common endocrinopathies, occurring in women in reproductive age and is the most common cause of infertility due to anovulation. There is no single

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criterion for the diagnosis of this syndrome.[5,14] It affects about 1 in 15 women worldwide.[6,15]

Regarding the diagnosis of polycystic ovarian disease tools, the clinician has the clinical features, ultrasound examination of the ovaries, hormonal assays and the laparoscopic examination of the ovaries. Laparoscopy is not routinely performed in most of the centers for the diagnosis of polycystic ovaries. It is ultrasonography and hormonal assays of the patients that are routinely employed for the diagnosis of the polycystic ovarian disease.[1] Fox et al (2008) reported diagnostic accuracy of hormonal assay 94%, sensitivity of 92% and specificity 96%.[7]

Prevalence of PCOs is 5-10% in women of reproductive age using the diagnostic criteria of the US National Institute of Health, reported by Norman et al in 2004.[8] In Pakistan prevalence of PCOD is 5%–10%.[16]

In hormonal assays, out of the long list of the hormones, which are disturbed in this condition routinely performed tests are serum follicle stimulating hormone (FSH) levels, serum luteinizing hormone (LH) levels and serum prolactin levels.[9]

Though the transvaginal sonography for the diagnosis of polycystic ovaries is quick and less expensive yet it is sometimes not possible to perform in unmarried patients, unwilling patients and sometimes ovaries were difficult to visualize when they are lying high in the pelvis; here the role of hormonal assays replaces the transvaginal sonography.

METHODS

Study Design: Cross-sectional survey.

Setting: Study was carried out in the department of Radiology Jinnah Hospital / Allama Iqbal Medical College Lahore.

Duration Of Study: Six months (from March 2017 to August 2017)

Sampling Technique: Non-probability purposive sampling.

Sample Size: The calculated sample size was 250 cases with 7% margin of error, 95% confidence level, taking expected percentage of polycystic ovaries i.e. in apparently healthy women and sensitivity and specificity of hormonal assays in the diagnosis of polycystic ovarian disease i.e. 92% and 96% respectively, and expected percentage of polycystic ovaries in apparently health women i.e. 25%.

Inclusion Criteria
1. Patients between 15-35 years of age.
2. Patients fulfilling two out of the following three criteria:
a. Oligomenorrhoea and/anovulation (on history)
b. Hyperandrogenism (clinical and / biochemical) on history and hormonal assays.
c. Polycystic ovaries (on ultrasound examination)

Exclusion Criteria
1. Patients receiving any sort of the hormone therapy like for ovulation induction, menstrual regularity (on history).
2. Any other concomitant chronic illness like tuberculosis, type-II diabetes (on history).
3. Unwilling patients for transvaginal ultrasonography.

Data Collection Procedure: 250 patients of polycystic ovarian disease referred from the department of the Gynaecology Units of Jinnah Hospital Lahore, which were fulfilling the inclusion criteria selected. An informed consent was obtained from them for the use of data in the research.

Transvaginal sonography was the mode of examination. Following information was recorded, ovarian size (in three dimensions) and volume (in ml), number of the cysts, and the arrangement of the cysts (random or peripheral). At the same time blood sample was withdrawn and sent for the hormonal assays of serum follicle stimulating hormone (FSH) levels, serum luteinizing hormone (LH) levels and serum prolactin levels and sent to the clinical laboratory.

Data Analysis: All the cases were evaluated regarding transvaginal sonographic findings and compared with the above-mentioned serum hormone levels.

The collected information was entered in the SPSS version 16.0 and analyzed through its statistical programme. Variables to be investigated were age, ovarian size and volume; hormonal levels, and arrangement of the cysts were presented as descriptive statistics giving mean and standard deviation for numerical values.

Arrangement of the cysts (peripheral or random), presence or absence of oligomenorrhoea,

anovulation, hyperandrogenism and polycystic ovaries were presented as frequency and percentages.

The comparison of the ultrasound findings with serum hormone levels were made by constructing 2×2 tables. This helped to calculate sensitivity, specificity, diagnostic accuracy, positive predictive value (PPV) and negative predictive value (NPV) of hormonal assay by taking transvaginal sonography as a gold standard.

RESULTS

This study showed that maximum number of patients 108 (43.2%) were in younger age group i.e. between 20-25 years. Minimum number i.e. only 16 cases (6.4%) in age group less than 20 years. Mean age of the patients was found to be 26.2±4.0.

Distribution of cases by number of cysts showed 156 patients (62.4%) had 10-15 cysts, 42 patients (16.8%) had 16-20 cysts, 37 cases (14.8%) had <10 cysts and 15 cases (6.0%) had >20 cysts.

According to arrangement of cysts, 63 (25.2%) were peripheral and 187 (74.8%) were random cysts.

Ovarian volume <10ml found in 78 cases (31.2%) and >10ml in 172 cases (68.8%).

Serum prolactin level in 91 patients (36.4%) was < 19.5ng/ml and in 159 patients (63.6%) it was > 19.5ng/ml.

FSH:LH ratio in 103 patients (41.2%) was <1.0 and in 147 patients (58.8%) ratio was > 1.0

Levels of serum prolactin and FSH:LH showed normal levels in 23 patients (9.2%) while raised levels of serum prolactin, deranged FSH:LH or both of these criteria were found in 227 patients (90.8%).

132 Patients were showing both raised serum prolactin levels and as well as deranged FSH:LH (52.8%).

According to ultrasonographic criteria, out of 250 patients 223 were showing either increased ovarian volume or increased number of the cysts in the ovaries or both of these criteria, (89.3%) of the patients.

Out of the 250 patients 157 showing ovarian volume 10 ml or more and having 10 or more cysts, 62.8% of the patients having both the criteria of polycystic ovaries.

In comparison, findings of transvaginal sonography versus hormonal assay in detection of PCOs showed 227 positive cases on hormonal assays and 223 positive cases on transvaginal sonography (gold standard).

Sensitivity was found to be 98.6%, specificity 74.0%, diagnostic accuracy 96.0%, positive predictive value (PPV) 96.9% and negative predictive value (NPV) 86.9%.

DISCUSSION

Polycystic ovarian disease is the most common endocrinopathy affecting the females at the prime of their age having diverse range of presentation ranging from infertility, obesity, menstrual irregularity, hirstuism, predisposition to the development of the diabetes mellitus and association with endometrial carcinoma.

Polycystic ovarian disease is a condition in which any two of the following three criteria are met.
- Oligomenorrhoes or Anovulation
- Hyperandrogenism (clinical / biochemical)
- Polycystic Ovaries

Polycystic ovaries is defined as either the presence of the 12 or more cysts measuring 2-8 mm in diameter in the ovary or the ovarian volume is greater than 10 ml or both of the above mentioned criteria.

In Polycystic ovarian disease there may be polycystic ovaries and usually they are but it is not mandatory in such patients that they have polycystic ovaries. Similarly in patients having polycystic ovaries it is not mandatory that they are having polycystic ovarian disease though they usually have polycystic ovarian disease.

Similarly if the patient is having either raised serum prolactin level or deranged FSH:LH ratio then the patient is showing the evidence of polycystic ovarian disease. Raised serum prolactin levels and deranged FSH:LH ratio may be present simultaneously.

Polycystic ovarian disease is a diagnosis, which is based on clinical findings, serum hormone assays and ultrasonographic findings.

Our study was designed such that all the sample volume patients were having polycystic ovarian disease.

By taking the isolated findings of blood biochemistry and ultrasonography i.e. increased serum prolactin levels, deranged FSH:LH ratio, increased ovarian volume and increased number of the cysts then finding the evidence of the disease is ranging between 58% to 69%, however if we combine the both biochemical findings i.e. raised serum prolactin level and deranged FSH:LH ratio then finding the evidence of the disease touches the figure of 90.8%, similarly if we combine the ultrasonographic findings i.e. increased number of the cysts and increased ovarian volume then finding the evidence of the disease is 89.3%.

In a study by Fox et al (2008) reported the diagnostic accuracy of hormonal assays in polycys-

tic ovarian disease is 94%.[7]

In 2015 Dumont et al. reported the specificity and sensitivity of hormonal assays to be 97 % and 92 % respectively.[17]

In another study regarding the prevalence of polycystic ovaries in women with anovulation and hirsutism, found polycystic ovaries in up to 92% of the patients.[10]

Polycystic ovaries were defined with ultrasound imaging in a series of 173 women who presented to a gynaecological endocrine clinic with anovulation or hirsutism. Polycystic ovaries were found in 26% of women with amenorrhoea, 87% with oligomenorrhoea, and 92% with idiopathic Hirsutism—that is hirsutism but with regular menstrual cycles. Fewer than half the anovulatory patients with polycystic ovaries were hirsute, but in 93% of cases there was at least one endocrine abnormality to support the diagnosis of polycystic ovaries i.e raised serum concentrations of luteinizing hormone, raised luteinizing hormone: follicle stimulating hormone ratio, or raised serum concentrations of testosterone or androstenedione. This study shows that polycystic ovaries, as defined by pelvic ultrasound, are very common in anovulatory women (57% of cases) and are not necessarily associated with hirsutism or a raised serum luteinizing hormone concentration. Most women with hirsutism and regular menses have polycystic ovaries so that the term "idiopathic" hirsutism no longer seems appropriate. [10]

CONCLUSION

Hormonal assays are having minimal edge over the ultrasonography regarding the diagnosis of polycystic ovarian disease however ultrasound examinations are quick with immediate results.

The other important aspect is while writing the report of the ultrasound both the ovarian volume and the number of the cysts should be mentioned.

Similarly asking for serum hormone assays both serum prolactin levels and FSH:LH ratio should be simultaneously ordered to maximize the finding the evidence of disease.

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DIAGNOSTIC ACCURACY OF COLOR DOPPLER SONOGRAPHY IN THE DIAGNOSIS OF THYROID NODULES

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Abstract

Objectives: To determine the accuracy of Color Doppler Sonography in the diagnosis of thyroid nodules using histopathology as gold standard.

Study Design: Cross-Sectional Survey.

Setting: Study was carried out in the Department of Radiology, Jinnah Hospital / Allama Iqbal Medical College Lahore.

Duration of Study: Six months (from January 2017 to June 2017).

Subjects & Methods: Total Number of 85 cases were included in this study with features of thyroid swelling, nodules, dysphagia, hoarsness of voice, palpitations and cervical lymph node enlargement.

Results: Mean age of the patients was 48.56.3 years. Considering the sensitivity, when the results are compiled 75.0% is the sensitivity rate, 96.9% is the specificity rate. Hence, the diagnostic accuracy is 91.7% while positive predictive value is 88.2% and negative predictive value is 92.6%.

Conclusion: Fine Needle Aspiration cytology is having minimal edge over the grey scale ultrasound and Color Doppler flow study regarding the diagnosis of thyroid nodules whether benign or malignant, however ultrasound examinations are quick, readily available, less time consuming, without employment of any radiation with immediate results.

Key Words: Thyroid nodules, malignant, Color Doppler Sonography.

The human thyroid gland develops in the fetus in the first trimester as an outgrowth of cells from the pharynx, which in adult life consists of two lobes and an isthmus. Fibrous septae divide the thyroid gland into pseudo lobules. In cease of malignant transformation these cells lead to papillary, follicular and aplastic carcinomas. Second set of cells in the thyroid gland (called C cells) that produce calcitonin which is involved in calcium homeostatis. If these cells undergo malignant transformation then lead to medullary carcinoma.[1]

Color Doppler sonography is an extremely valuable, non-invasive adjunct to the assessment of patients with thyroid nodules without any use of radiation (with higher sensitivity of 92.3% and specificity of 88%). The association of Color flow Doppler sonography and conventional ultrasound improves the diagnostic accuracy of thyroid carcinoma.[2] Prevalence of thyroid nodules is 25% worldwide[3] while it is 21% in Pakistan.[4] First task of ultrasound is to detect and characterize nodules and determine which lesions require biopsy.[5] Secondly the use of ultrasound can be highly effective in guiding fine needle aspiration biopsy of thyroid nodules that are difficult to palpate.[6] Patients presenting with nodular thyroid lesions are evaluated with features of Color Doppler Ultrasonography i.e. hypoechogeneity, ill defined margins, microcalcifications, cyst with solid components, thick incomplete halo, enlarged cervical lymph nodes with malignant feature and intranodular blood flow, which are highly suggestive of malignancy.[7] The results are compared with Histopathological diagnosis. To detect malignancy in follicular neoplasm

where fine needle aspiration cytology (FNAC) cannot diagnose malignancy and to guide FNAC needle in multinodular goiter and small thyroid nodules.[8]

Due to superficial location of thyroid gland, high frequency linear array transducers are employed in the range of 7-15 MHz.[9] Normal thyroid is of uniformly increased echogenicity, higher than overlying strap muscles.[10] The vascu-larity is symmetrical bilaterally on Color or Power Doppler.

Use of Color Doppler is particularly valuable in assessing thyroid lesions that may be predominantly cystic or have internal hemorrhage.[11] In patients with possible malignant thyroid nodules, an attempt should be made to search for cervical lymphadeno-pathy along the internal jugular chain.[12]

According to the American Association of Clinical Endocrinologists (AACE) and Association of Medical Endocrinology (AME) medical guide-lines for clinical practice for the diagnosis and management of thyroid nodules, FNAB should be performed on all hypoechoic nodules with at least one of the following additional US features: irregu-lar margins, intranodular vascular supply, taller-than-wide shape, or microcalcifications.[13] The British Thyroid Association (BTA) has recently produced a US classification (U1–U5) of thyroid nodules to facilitate the decision-making process regarding the need to perform fine-needle aspiration cytology (FNAC) for suspicious cases.[14]

Significant relationship was observed between malignancy and hypoechogenicity, irregular mar-gins, taller than wide, thick incomplete halo, micro calcifications, lymph node enlargement and local infiltration. Intranodular vascularity was a signi-ficant criterion to suggest malignancy in thyroid nodules on Color Doppler. Malignant nodules had a mean RI of 0.73 and mean PI of 1.3 which were significantly higher than the benign nodules. Accuracy of detecting malignant thyroid nodules by combining gray scale and Doppler is higher than either of them alone.[16]

Study conducted by Algin O, Algin E, et al reveals RI and PI values are useful in distinguishing malignant from benign thyroid nodules.[17]

The purpose of our study was that if use of Color Doppler ultrasound can help in differentiating the benign and malignant nodule, then the number of unnecessary multiple needle biopsies of the thyroid could be reduced.

Our objective was to determine the accuracy of Color Doppler sonography in the diagnosis of thyroid nodules using histopathology as gold standard.

METHODS

STUDY DESIGN: Cross-sectional survey

SETTING: Department of Radiology, Jinnah Hospital / Allama Iqbal Medical College, Lahore.

DURATION OF STUDY: Six months (from January 2017 to June 2017).

SAMPLE SIZE: The calculated sample size with 12% margin of error, 95% confidence level, 25% prevalence rate of thyroid nodules taking 92.3% sensitivity and 88% specificity of Color Doppler sonography is 81, rounded off 85 cases.

SAMPLING TECHNIQUE: Non-probability purposive sampling

SAMPLE SELECTION:

Inclusion Criteria

1. Male and female patients between ages of 15-70 years.
2. Patients with history of nodule in neck, dysphagia, hoarseness of voice, tachycardia, palpitation and duration.

Only those patients were included in which both Doppler study and surgery was carried.

Exclusion Criteria

1. Patients already diagnosed to have thyroid malignancy, which came for review US after surgery.
2. Patients who give previous history of thyroid lobectomy, presence of scar over thyroid site, cyst aspiration.

3. Patients with some other primary cancer suspected to have metastatic involvement taking into account of previous investigations.

DATA COLLECTION:

First consecutive 85 patients referred form the indoor department of surgery and medicine with features of thyroid swelling, nodules, dysphagia, hoarsens of voice, palpitations and cervical lymph nodes enlargement were included in the study. An informed consent, with promise of confidentiality, was obtained from them for using their data in research. The demographic information (age), family history and detailed clinical history was obtained from every patient regarding thyroid nodules. Effect modifiers e.g. age was controlled through stratification.

These cases were then subjected to Color Doppler ultrasound using 10MHz probe attached to GE logic pro Color Doppler machine. Grey scale and Color Doppler ultrasound of the thyroid was done to see hypoechogenicity, inhomogeneity, ill defined margins, microcalcification, cyst with solid components, thick incomplete halo, enlarged cervical lymph nodes with malignant features and intra-nodular blood flow, which are highly suggestive of malignancy.

All the cases were undergone biopsy and histopathology results were taken as gold standard. All thyroid nodules were evaluated for any area of abnormal blood flow pattern, microcalcifications, cysts with solid components. Diagnosis was made on this basis and compared with histopathology report.

DATA ANALYSIS:

The collected information was entered into SPSS version 11.0 and analyzed through its statistical program. The variables to be investigated were age, sex and color flow patterns type I (avascular), type II (peri-nodular) and type III (intra-nodular hypervascularity). Out of these variables age and size of nodule were quantitative variable and were presented as Mean SD (Standard Deviation).

Sex and Color Doppler evaluation of location of nodule (right lobe, left lobe, isthmus), number (solitary / multiple), margins (smooth/irregular), density (Solid/cystic), calcification (present / absent), blood flow measurement (resistive index, pulsatility index), color flow (Type I, Type II, Type III), all these variables were presented by frequency and percentage. The comparison of Color Doppler ultrasound with histopathology was made. This enabled to calculate sensitivity, specificity, diagnostic accuracy and predictive values of Color Doppler ultrasound taking histopathology as gold standard.

RESULTS

Out of total 85 cases, 13 (15.3%) patients were less than 20 years of age, 28 (32.9%) patients were between 21-40 year, 33 (38.9%) patients were between 41-60 year while 11 (12.9%) patients were more than 60 years of age with mean age of 48.5±6.3 years.

Majority of the patients were females i.e. 61 (71.8%) and remaining 24 (28.2%) were males.

Regarding the presenting complaints 23 (27.0%) patients had complaint of dysphagia, 22 (25.9%) patients had complaint of hoarseness, 29 (34.2%) had palpitation and 11 (12.9%) had weight loss.

Out of 85 cases those patients who presented with the presence of nodules in right lobe were 27 (31.8%). Those patients who had the nodule(s) in left lobe were 36 (42.4%), 3 patients (3.52%) had the nodules in isthmus and 19 patients (22.3%) had bilateral involvement.

Out of total 85 cases, 29 patients (34.1%) had solitary involvement and 56 patients (65.9%) had multiple involvement.

Distribution of cases by margins, 68 (80.0%) patients showed smooth margins while 17 (20.0%) patients had irregular contours.

Out of total 85% patients, 23 patients (27.0%) had solid nature, 39 patients (46.0%) had cystic appearance and 23 (27.0%) had both solid and cystic component.

Calcifications were seen in 13 (15.2%), while 84.8% were devoid of any calcifications.

Out of total 85 cases, 79 (93.0%) showed nodules which were confined and 6 patients (7.0%) had local invasion.

Out of 85 cases, 19 patients (22.3%) had type I color flow pattern (avascular), 45 patients (52.9%) had type II peri-nodular color flow type, 21 patients (24.8%) exhibited intranodular type III hypervascularity.

Out of 85 total cases when comparison with histopathology was carried out 15 patients proved to be malignant i.e. true positive. While 2 patients were false positive, 63 patients were true negative and 5 cases were false negative.

Considering the sensitivity when the results are compiled 75.0% is the sensitivity rate, 96.9 % is the specificity rate. Hence, the diagnostic accuracy is 91.7%. Positive predictive value is 88.2%. Negative predictive value is 92.6%.

DISCUSSION

Thyroid nodules are common findings in the general population; these can be either benign or malignant in nature. In iodine deficient countries like Pakistan especially in mountainous areas where the deficiency is more pronounced approximately 25% of the population have thyroid nodules. Whereas in western countries about 5% of the population is affected.[3] Patients present with diverse problems such as swelling in the neck, palpitation, dysphagia, hoarseness of voice and weight loss etc.

Thyroid swellings are usually slowly progressive or may show rapid increase in size of the nodule due to intranodular haemorrhage.

For diagnostic purposes; proper history, local examination, grey scale and Color Doppler evaluation are the main non-invasive, readily available adjuncts to make the diagnosis. Important findings like decreased echogenicity, irregular and ill-defined margins, cyst with solid components, incomplete halo, enlarged cervical lymph nodes with malignant features and intranodular blood flow are highly suggestive of malignancy.

In predicting malignancy with grey scale study, absent halo sign is the best single sign, whereas microcalcification is more specific. The most predictive echo patterns are a combination of two or three signs that have high specificity and sensitivity. These findings are comparable with other studies.

Histological examination demonstrated thyroid carcinoma in 17 patients: 9 Papillary carcinomas, 5 follicular carcinomas, 2 medullary carcinomas, 1 undifferentiated carcinoma and 68 were benign thyroid nodules.

On conventional sonography the absence of halo sign, presence of microcalcifications and hypoechogenicity of nodule were in favor of malignancy. Therefore, in diagnosing malignancy, the absence of halo sign, was most sensitive and presence of microcalcifications was most specific.

On the other hand absent halo sign was the most predictive and absent halo sign plus microcalcification were the most specific criteria.

On Color Doppler study three flow patterns were considered that is:

Type I: Avascular,

Type II: Perinodular hypervascularity,

Type III: Intranodular hypervascularity.

For the avascular type (Type I) no significant statistical difference was demonstrated between benign and malignant nodules.

But Type II vascularity was in favor of a benign nodule (36/68 of benign nodule vs. 3/17 of malignant nodules).

Type III hypervascularity was predictive of malignancy (11/68 of benign and 12/17 of malignant nodules).

The combination of halo sign, presence of microcalcifications and intranodular hypervascularity demonstrated the higher values to predict malignancy.

Out of 85 total cases 15 patients proved to be malignant that is true positive. While 2 patients had

false positive results. 63 patients were true negative and 5 cases were false negative.

In present study, Color Doppler sonography in the diagnosis of thyroid nodules using histopathology as gold standard was assessed in terms of sensitivity (75%), specificity (96.9%), positive predictive value (88.2%) and negative predictive value (92.6%), diagnostic accuracy of Color Doppler sonography was observed 91.7%. A study carried out by Sharma et al (2007) in the Department of nuclear medicine, Institute of nuclear medicine and Allied Sciences (INMAS), Delhi, India, demonstrated sensitivity of 53.5% & specificity of 86.4%, positive predictive value of 61.5% and negative predictive value of 82%. [15]

The results of present study were also comparable with a study carried out by Appetecchia and Solivetti in 2006. [2]

In another study regarding the outlook and appearances of the thyroid nodules on Ultrasonography and Color Doppler flow studies the results were quite comparable. [7]

CONCLUSION

Fine Needle Aspiration cytology is having minimal edge over the grey scale ultrasound and Color Doppler flow study regarding the diagnosis of thyroid nodules whether benign or malignant, however ultrasound examinations are quick, readily available, less time consuming without employment of any radiation with immediate results.

The other important aspect while writing the report of ultrasound Color Doppler flow study, combination of three or more features like absent halo sign, microcalcifications and increased intra-nodular blood flow pattern should be documented because these features enhance the diagnostic accuracy.

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PREVALENCE OF DEPRESSION IN ASTHMATIC FEMALES OF LAHORE. PAKISTAN

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Abstract

Objective: To assess the association between the severity of asthma and its level of control and depression by using Hamilton Depression Rating Scale (HDRS).

Methodology: observational study was conducted at department of Pulmonology Mayo hospital Lahore for 6 months. Random sampling technique was use. Informed consent was obtained. Demographic details were obtained. Questionnaire was filled up .A Sample size was estimated as 84, by using a software G-power, Considering 5 % level of significance, power of the test is 80%, and 0.3 effect size.

Results: In this study 85 female subjects with asthma were asked to fill the questionnaire mean age of the subjects was 40.86 ± 4.76 with 95% C.I 39.83-41.89 Among asthmatic patients 41(56.9%) felt angrier as well as feel depressed. There was association between feeling angrier for being asthmatic and depression (p-value 0.021)

Conclusion: findings explained that there is positive association between depression and asthma in females living in Pakistan.

Key words: *depression , anxiety , asthma ,breathing problem*

Depression and asthma are two very common chronic diseases all over the world, imposing unacceptable social and economic burdens on the public healthcare system.[1,2] According to survey it is very common in females. and causing severe problems with healthcare system even in Pakistan. Approximately 16% of adults in the United States are diagnosed with major depression disorder, and 5.8% of men and 9.5% of women will likely experience an episode of depression within a 12-month period.[3] Because both depression and asthma compel to behave in a certain way for substantial public health burdens, the relationship between these two conditions has attracted attention over the past few years in our society. Many potential studies had been assessed the characteristic connection between depression and asthma; however, indeterminate results were obtained. Equally detrimental, asthma affects 39.5 million Americans, 29.0 million adults of them , and 300 million individuals all over the world[4], with increasing preponderance in many countries.[5]

Rates of depression or depressive symptoms are often found to be higher among persons with chronic health conditions.[6,7] psychological effects are very dominant in females and males with long term abnormal health related conditions. This finding has generally been substantiated among adults with asthma[8,10] In many chronic health conditions, symptom severity appears to be an important determinant of depression.[11,12] Consistent with this, more frequent and/or severe asthma symptoms have been associated with depression.[13] Estimates of psychopathology in severe asthmatics range from 30% to 63%.[14,15] Exposure to stress and strong emotions can make asthma worse, while having asthma can give patient an increased vulnerability towards the development of anxiety disorders[16] Chronic disease patients with an additional psychia-

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tric disorder such as sad feeling of gloom and inadequacy or depression typically put into health care services more often compared to chronic disease patients without additional psychiatric disorders.[17]

METHODOLOGY

Observational study was conducted at department of Pulmonology Mayo Hospital Lahore for 6 months. Random sampling technique was use. Informed consent was obtained. Demographic details were obtained questionair was filled up. A Sample size was estimated as 84, by using a software G-power, considering 5 % level of significance, power of the test is 80%, and 0.3 effect size.

Results

In this study 84 female subjects with asthma were asked to fill the questionnaire mean age of the subjects was 40.86 ± 4.76 with 95% C.I 39.83-41.89. Among asthmatic patients 41(56.9%) felt angrier as well as feel depressed. There was association between feeling angrier for being asthmatic and depression (p-value 0.021)

DISCUSSION

Rates of depression or depressive symptoms are often found to be higher among persons with chronic health conditions.[6, 7] This finding has generally been substantiated among adults with asthma[8, 10] in the present study there is positive correlation between asthma, depression and anxiety. Chronic health condition impedes the activities of daily life. In the recent study 56.9% patients felt depressive and angrier. Due to prolonged exposure to medication and health endangerment with chronic asthma, patients felt depressed and angrier. Esti-

mates of psychopathology in severe asthmatics range from 30% to 63%.[14,15] With the progression of time asthmatics develop psychopathologic attitude. Due to prolong exposure to asthmatic stress and condition their behavior changes with time. Exposure to stress and strong emotions can make asthma worse, while having asthma can give patient an increased vulnerability towards the development of anxiety disorders[26, 27]. Stress worsens the asthma .it aggravates the symptoms of asthma and anxiety. The probability of asthma attacks increasesas level of stress increases. Due to use of steroids and other inhalers asthmatics face more health problems like muscular weakness. As far as this study is concerned 75.3% females feel angrier and depressed by not able to come up with their responsibilities and duties. There is strong association between asthma and depression in females of Pakistan.

Depression and Angriness was found associated with feeling insecure when you forget to bring inhaler along with you while going to market, Poor appetite or overeating, Feeling tired or fatigued, Little interest or pleasure in doing things, Feeling bad about yourself or that you are failure or have yourself down, Do you feel your asthmatic medicines affect your voice?

CONCLUSION

According to research and previous literature review there is positive association between asthma and depression in females. Asthma causes the depression and anxiety in females. Due to chronic illness patients feel hazards in activities of daily life (ADL). Prolong exposure to chronic asthma, impedes the quality of life that enhances the depression in asthmatics.

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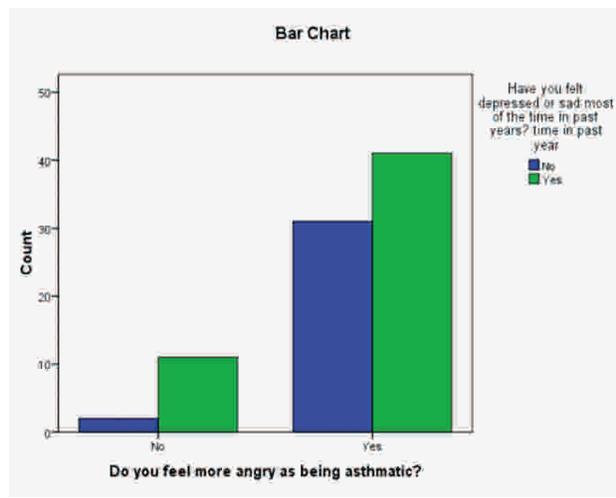
Table 1:

	Do you feel angrier as being asthamtics		Total	
	No	Yes		P-value
Do you feel angry when you get asthmatic attack after having some product?	14(15.4%)	70(97.2%)	84(84.7%)	<0.001 *
Do you feel insecure when you forget to bring inhaler along with you while going to market?	15(30.8%)	69(95.8%)	73(85.9%)	<0.001 *
Poor appetite or overeating?	21(53.8%)	63(87.5%)	70(82.4%)	0.009*
Feeling tired or fatigued?	(61.5%)	53(73.6%)	61(71.8%)	0.504
Little interest or pleasure in doing things?	11(84.6%)	45(62.5%)	56(65.9%)	0.203
Feeling bad about yourself or that you are failure or haveyourself down?	12(92.3%)	40(55.6%)	52(61.2%)	0.013*
Do you feel your asthmatic medicines affect your voice? time in past year?	12(92.3%)	43(59.7%)	55(64.7%)	0.028*
Have you felt depressed or sad most of the time in past years? time in past year	11(84.6%)	41(56.9%)	52(61.2%)	0.021
Do you think it is wonderful to be alive now?	11(84.6%)	47(65.3%)	58(68.2%)	0.211
Do you feel anxiety most of the time in a day?	10(76.9%)	47(65.3%)	57(67.1%)	0.531
Do you think this disease interferes with carrying duties andresponsibilities?	9(69.2%)	55(76.4%)	64(75.3%)	0.727
Do you have constipation problem?	9(69.2%)	54(75.0%)	63(74.1%)	0.662
Do you have any digestive problem?	8(61.5%)	54(75.0%)	62(72.9%)	0.325
Do you prefer to stay home at home rather than going out anddoing new things?	11(84.6%)	53(73.6%)	64(75.3%)	0.504
Are you afraid that something bad is going to happen to you?	9(69.2%)	47(65.3%)	56(65.9%)	0.526
Do you feel pretty worthless the way you are now?	10(76.9%)	52(72.2%)	62(72.9%)	0.510
Do you think this disease interferes with carrying duties and responsibilities?	11(84.6%)	57(79.2%)	68(80.0%)	0.492
Do you feel anxiety most of the time in a day?	11(84.6%)	56(77.8%)	67(78.8%)	0.447
Do you feel lack of reactivity to pleasant events?	10(76.9%)	55(76.4%)	65(76.5%)	>0.999
Do you feel loss of motivation to do things?	10(76.9%)	54(76.1%)	64(76.2%)	>0.999

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ANTIMICROBIAL SUSCEPTIBILITY PATTERN OF UROPATHOGENS AT A TERTIARY CARE HOSPITAL, LAHORE

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Abstract

Objective: To determine the antimicrobial susceptibility pattern of uropathogens in the patients at a tertiary care hospital.

Study Design: Laboratory based study.

Place and Duration of Study: Department of Microbiology, Sharif Medical City Hospital, Lahore from November 2016 to December 2017.

Methodology: A total of 508 positive urine cultures out of 1054 urine samples over a period of fourteen months were included in this study. The microorganisms were identified by gram staining and standard biochemical tests. The antibiotic sensitivity of isolated bacteria was assessed by Kirby-bauer disk diffusion technique in accordance with guideline of Clinical Laboratory Standard Institute (CLSI).

Results: Out of the 508 positive urine culture specimens, 377 (74.4%) were from outdoor patients and 131(25.7%) were from indoor patients. Gram negative bacteria were more prevalent as 364 (71.6%) of the total isolates were gram negative, 88(17.3%) were gram positive bacteria and 56 (11%) were candida albicans. Escherichia (E.coli) accounted for 255(50.1%) of the total positive cultures followed by Klebsiella pneumoniae 60 (11.8%) and then candida 56 (11%). Carbapenems, aminoglycosides and nitrofurantoin showed promising results for gram negative bacteria as shown by their susceptibility pattern. 96.8% of the E.coli isolates were sensitive to imipenem, 93.7% to meropenem, 80 % to amikacin, 51.7% to piperacillin/tazobactam and 51% to nitrofurantoin. In case of Klebsiella pneumoniae 70% isolates were sensitive to imepenem, 67.2% to meropenem, 65% to amikacin, and 28.3%to sulbactam/ cefoperazone and tazobactam/piperacillin and 50% to nitrofurantoin. Pseudomonas aeruginosa exhibited 72.7% susceptibility to piperacillin/tazobactam and amikacin, 63.6 % to imipenem and 57.6% to meropenem. Out of Staphylococcus aureus, 45.8 % isolates were MRSA and 54.2% were MSSA. 100% of S. aureus isolates were susceptible to vancomycin and linezolid. Only 33.9% enterococcus were sensitive to imepenem and pieracillin/tazobactam, 45.2% to fosfomycin, 54.7% to nitrofurantoin and 100% sensitive to vancomycin and linezolid

Conclusion: Majority of the gram negative isolates were sensitive to imipenem, amikacin and piperacillin/tazobactam while susceptibility to most of commonly used antibiotics like cephalosporins and fluoroquinolones was very low. Among the oral antimicrobials, nitrofurantoin showed good results for enterobacteriaceae and enterococcus responded well to both fosfomycin and nitrofurantoin.

Key Words: *uropathogens, kirby-bauer disk diffusion technique, antimicrobial susceptibility. urinary tract infection.*

U rinary tract infection (UTI) is one of the most common bacterial infections in both community and health care settings being responsible for most hospital visits.[1,2]

It refers to the presence of microbial pathogens affecting the urinary tract and may be classified by the site of infection as cystitis in urinary bladder and pyelonephritis in kidneys.[3] Bacteria in the urinary bladder might remain silent or lead to symptomatic UTI presenting with ,back pain, urinary frequency and urgency.[4]

Urinary tract is a very common route of nosoco-

mial infection, particularly for catheterized patients. Patient's own colonic flora mostly leads to catheter-associated UTIs and the duration of catheterization is a very important risk factor[5] The most prevalent pathogen of UTI is Escherichia coli followed by Klebsiella pneumoniae and other pathogens like Staphylococcus, Proteus, Pseudomonas, Entero-coccus, and Enterobacter.[6,7] Management of UTI is most commonly begun empirically. However, an increase in antimicrobial resistance has raised challenges in treating outpatients.[8] This is because of injudicious and indiscriminate use of antibiotics. The susceptibility profile of bacteria vary consider-ably in different areas. Hence determining local etiology and antimicrobial susceptibility pattern of the uropathogens would help the clinicians to the most effective empirical treatment and would prevent the undue use of drugs.[3]

Thus the aim of this study was to determine bacterial pathogens causing UTI presenting in a tertiary care hospital in Lahore and to assess their in vitro susceptibility to the commonly used antibio-tics.

METHODS

This laboratory based study was conducted in the Department of Microbiology in Sharif Medical City Hospital, Lahore. Institutional ethical and research committee approved the project for research purpose. All urinary specimens received in laboratory for culture from patients suspected to have UTI from November 2016 to December 2017 were included in this study. Repeated samples from the same patient and mixed growth with no predominant organism were excluded from the study. 0.2 ul of each urine specimen was inoculated on Cysteine Lactose Electrolyte deficient agar (CLED, Oxoid UK) using calibrated loop surface streak method and bacterial colony count of 105 cfu/ml was recorded as significant. The inoculated culture plates were then incubated at 37°C for 24 to 48 hours.[9] The microorganisms were identified by Gram staining and biochemical tests. Analytical

profile index API-20E (Biomerieux, France) was used to identify members of Enterobacteriaceae family according to manufacturer's protocol. Anti-microbial sensitivity of the bacterial isolates was assessed by Kirby-Bauer disk diffusion technique according to CLSI guidelines. Cefoxtin (30μg) was used for identifying MRSA. The sensitivity plates lawned with Staphylococcus aureus were incubated at 35°C for 24-48 hours. The isolates with an inhibition zone of cefoxitin of 22mm were labeled as MSSA and < 22mm as MRSA.

Commercially available discs (Oxoid UK) of the following antibiotics were used in the study.

Amoxicillin/clavulanic acid (20/10μg), Cefi-xime (5μg), ceftriaxone (30μg), cefotaxime (30μg), ceftazidime (30 μg), cefipime (30 μg), imipenem (10 μg), meropenem(10 μg), nitrofurantoin (300 μg), gentamicin (10 μg), Amikacin (30 μg), ciprofloxacin (5 μg), trimethoprim/sulfamethoxazole (1.25/23.75 μg), tetracycline (30 μg), cefoperazone/sulbactam, piperacillin/tazobactam (100/10 μg) , penicillin (10 units), ampicillin (25 μg), cefoxitin (30 μg), vanco-mycin (30 μg), linezolid (30 μg), fosfomycin (200 μg) were used. The zones of inhibition of all drugs for the isolated bacteria were measured and reported according to the CLSI guidelines.[10] S. aureus (ATCC 25923) and E. coli (ATCC 25922) were used as reference strains.

STATISTICAL ANALYSIS:

The data obtained was entered and analyzed using Statistical Package for Social Sciences (SPSS) version 24. Frequencies and percentages were calculated for the study variables. The p-value of 0.5 was considered statistically significant.

RESULTS

A total of 1054 urine specimens were inocula-ted and out of these 508 (48.2%) exhibited positive cultures. 340 (67%) positive urine cultures were from female patients and the remaining 168 (33 %) from male patients. Around 74.4% (377) positive cultures were from outdoor patients and 131(25.7%) from indoor patients. The age of the patients presen-

ting with UTI ranged from 1 to 75 years and the majority were around 45 years old. Gram negative bacteria were predominant as a total of 364 (71.6%) isolates were gram negative. 88(17.3%) were Gram positive bacteria and 56 (11%) were candida albicans. Escherichia coli (E.coli) accounted for 255(50.1%) of the total positive cultures followed by Klebsiella pneumoniae 60 (11.8%) and then candida albicans 56 (11%).33 (6.5%) of positive cultures yielded Pseudomonas aeruginosa, 35(6.9%) yielded Staphylococcus aureus and enterococcus was isolated in 53(10.4%) cultures.

Table 1 shows the susceptibility pattern of enterobacteriaceae. It is evident from this table that carbapenems, amikacin, tazobactam/piperacillin and cefoperazone/sulbactam are good treatment options for enterobacteriaceae. However, commonly used drugs like cephalosporins, amoxicillin/ clavulanate and even ciprofloxacin are less effective. Among oral drugs nitrofurantoin has shown better results except for Klebsiella pneumoniae.

Table 2 is showing antimicrobial susceptibility pattern of Pseudomonas aeruginosa and acinetobacter. Piperacillin/tazobactam and amikacin exhi-

bited highest sensitivity (72.7%) for Pseudomonas aeruginosa followed by carbapenems. 21(63.6%) isolates of Pseudomonas were sensitive to imepenem and 19(57.6%) were sensitive to meropenem. Only 12(36.3%) isolates showed sensitivity to cefipime. Similar results were obtained for ciprofloxacin and levofloxacin. Two isolates of acinetobacter were isolated. One isolate did not respond to any of the tested antibiotic and the other was sensitive to imepenem, meropenem and doxycycline only. Cephalosporins, fluoroquinolones and aminoglycosides were not effective at all.

The susceptibility pattern of Staphylococcus aureus and enterococcus is shown in table 3. Out of Staphylococcus aureus,16(45.8 %) isolates were MRSA and 19(54.2%) were MSSA. 35 (100%) isolates of S. aureus isolates were susceptible to vancomycin and linezolid. Only 18(33.9%) enterococcus were sensitive to imepenem and pieracillin/ tazobactam, 45.2% to fosfomycin, 54.7% to nitrofurantoin and 100% sensitive to vancomycin and linezolid.

Table 1: *Susceptibility Pattern of Enterobacteriaceae*

ANTIBIOTICS	E.COLI n=255	K.PNEUMONIAE n=60	ENTEROBACTER CLOACAE n=5	PROTEUS SP. n=9
AMOXICILLIN/CLAVULANATE	13(5.1%)	11(18.3%)	0(0%)	2(22.2%)
CEFIXIME	21(8.1%)	7 (11.7%)	2(40%)	4(44.4%)
CEFOTAXIME	23(9.0%)	12(20%)	2(40%)	4(44.4%)
CEFTRIAXONE	23(9.0%)	12(20%)	2(40%)	4(44.4%)
CEFTAZIDIME	23(9.0%)	14(23.3%)	3(60%)	4(44.4%)
CEFIPIME	31(12.2%)	14(23.3%)	3(60%)	5(55.5%)
PIPERACILLIN/TAZOBACTAM	132(51.7%)	17(28.3%)	4(80%)	7(77.8%)
GENTAMICIN	54(21.2%)	26(43.3%)	5(100%)	5(55.5%)
AMIKACIN	204(80%)	39(65%)	5(100%)	6(66.7%)
CIPROFLOXACIN	21(8.2%)	20(33.3%)	0(0%)	3(33.3%)
TETRACYCLINE	47(18.4%)	9 (15%)	0(0%)	0(0%)
SULFAMETHOXAZOLE/TRIMETHOPRIM	52(20.4%)	7 (11.6%)	0(0%)	0(0%)
CEFOPERAZONE/SULBACTAM	119(46.7%)	17(28.35%)	4(80%)	7(77.8%)
NITROFURANTOIN	130(51%)	30(50%)	0(0%)	3(33.3%)
IMIPENEM	247(96.8%)	42(70%)	5(100%)	5(55.5%)
MEROPENEM	239(93.7%)	41(67.2%)	5(100%)	5(55.5%)

DISCUSSION

Urinary tract infection accounts for majority of bacterial infections in community as well as health care settings. The treatment of UTI depends upon detecting the pathogens and assessing the antibiotic effective against those pathogens. The management of UTI is getting harder because of rising antibacterial resistance among bacteria. This has led to heavy economic burdeon.[11] Hence identification of regional bacterial pathogens and their susceptibility pattern is of utmost importance so that empirical drug therapy, antibiotic policies and infection control plans can be established.[12]

In our study, 340 (67%) positive urine cultures were from female patients and the remaining 168 (33 %) from male patients, females being more prone to UTI because of having proximity of short urethra and genital tract as the bacteria may be pushed up the urethra during sexual activity.[13,14]

In current study, major bulk of the positive cultures was constituted by gram negative rods as 364 (71.6%) of the total isolates were gram negative. Out of these E.coli (50.1%) is the predominantly isolated pathogen followed by Klebsiella pneumoniae (11.8%). Similar findings were obtained in a study conducted at AFIP in 2012. However, contrary to Klebsiella pneumoniae in our study, the second most common pathogen in AFIP research turned out to be Pseudomonas aeruginosa.[14] In present study, 255(50.1%) of the positive cultures revealed E.coli. The results agree with similar study conducted in Peshawar, Khyber pukhtunkhwa, Pakistan reporting even higher frequency with 77% cultures yielding E.coli as the predominant uropathogen.[15]

In this study 96.8% E.coli isolates were sensitive to imepenem, the results are consistent with a study carried out at AFIP and a study in Peshawar. (15.16) Contrary to our results, 44% E.coli showed resistance to carbapenems in another study conducted in Lahore.[17] This proves indiscriminate and undue use of antibiotics that has led to limited drug options for the treatment of UTIs.

As far as susceptibility to to fluoquinolones is concerned, a very high resistance is observed in this study. 91.8% E.coli , 66.6% Klebsiella and 100% Enterobacter and Proteus were resistant to ciprofloxacin. These results are comparable to another study at AFIP where 78.5% E.coli,85.8% Klebsiella,71.4% Enterobacter and 100% Proteus exhi-

Table 2: *Susceptibility Pattern of Pseudomonas and Acinetobacter*

Antibiotics	Pseudomonas aeruginosa N=33	Acinetobacter sp. N=2
Ceftriaxone	-	0
Cefotaxime	-	0
Ceftazidime	12(36.3%)	0
Cefepime	10(30.3%)	0
Piperacillin/tazobactam	24(72.7%)	0
Cefoperazone/sulbactam	14(42.4%)	0
Gentamicin	14(42.4%)	0
Amikacin	24(72.7%)	0
Ciprofloxacin	12(36.3%)	0
Levofloxacin	12(36.3%)	0
Imipenem	21(63.6%)	1(50%)
Meropenem	19(57.6%)	1(50%)
Doxycycline	-	1(50%)
Sulfamethoxazole / trimethoprim	-	0

Table 3: *Susceptibility Pattern of Staphylococcus Aureus and Enterococcus*

Antibiotics	Staphylococcus aureus N=35	Enterococcus species N=53
Penicillin	10(28.5%)	18(33.9%)
Ampicillin	10(28.5%)	18(33.9%)
Amoxicillin	10(28.5%)	18(33.9%)
Amoxicillin/ clavulanate	19(54.2%)	18(33.9%)
Cefoxitin	19(54.2%)	-
Cefotaxime	19(54.2%)	-
Ceftriaxone	19(54.2%)	-
Imepenem	19(54.2%)	18(33.9%)
Tetracycline	23(65.7%)	13(24.2%)
Gentamicin	16(45.7%)	-
Tazobactam/ pipercillin	19(54.2%)	18(33.9%)
Fosfomycin	12(34.2%)	24(45.2%)
Nitrofurantoin	13(37.1%)	29(54.7%)
Ciprofloxacin	7(20%)	5(9.4%)
Vancomycin	35(100%)	53(100%)
Linezolid	35(100%)	53(100%)

bited ciprofloxacin resistance. Similar pattern is observed in another study in India.[14,18] These findings are quite unlike a study carried out in London where 94% of isolated E.coli were suscep-tible to ciprofloxacin.[19] These contrasting reports owe to injudicious use of fluroquinolones in our part of the world resulting in poor susceptibility to a very important antimicrobial group.

The susceptibility of Enterobacteriaceae to trimethoprim/sulfamethoxazole was found to be very low in current study. Only 20.4 % and 11.6% E.coli and Klebsiella were found to be sensitive respectively. These results are consistent with other local studies.[15,16] Contrary to the local study results, studies conducted in Tunisia and other parts of the world showed higher sensitivity of enterobacteria-ceae to this very important oral antimicrobial.[11,20]

Another commonly used oral antimicrobial used for empirical treatment of uncomplicated UTI in our setup is Nitrofurantoin. It has a wide spectrum against Gram positive as well as gram negative bacteria. Above all it's a very cost effective drug. 51% and 50% E.coli and Klebsiella exhibited susceptibility to nitrofurantoin. These results are quite promising. However none of the Enterobacter was sensitive. 54.7% Enterococci were also suscep-tible to this oral drug. Even better results are obtained in a study in Bangladesh where only 28.1% E.coli were resistant and none of the Enterococccus isolated exhibited nitrofurantoin resistance.[21] Hence, nitrofurantoin is still a good prophylactic drug for recurrent UTI.

Out of 88 isolates of gram positive bacteria, 35(6.8%) were Staphylococcus aureus. 16(45.8 %) isolates were MRSA and 19(54.2%) were MSSA. Hence, a significant population of S.aureus could not be treated with Beta–lactam drugs. The results are a little different from a study conducted in Peshawar in 2014. 54.35% of urinary pathogens were S.aureus in their study and only 29.68% were MRSA. The frequency of MRSA in our study is quite high as compared to the study in Peshawar.[22] Another study at Nigeria showed 33.6% S. aureus isolated from urine cultures and all the isolates were MRSA[23] This rising incidence of MRSA necessitates the judicious use of antibiotics.

The antibiogram of Enterococci and S.aureus showed very poor susceptibility to ampicillin, amoxicillin, amoxycillin/clavulanic acid and cipro-floxacin. However,all isolates were susceptible to vancomycin and linezolid. And none of the isolates in the population studied were vancomycin resistant. 45.2% Enterococci were susceptible to fosfomycin. Sofia et al conducted a research on urinary patho-gens in Greece and the results showed good suscep-tibility of E.coli as well as enterococcus to fosfo-mycin, suggesting it to be a good oral choice for UTI[24]

As for as the susceptibility profile of Pseudo-monas aeruginosa is concerned, 72.7% exhibited susceptibility to piperacillin/ tazobactam and amika-cin. The results are comparable to another study conducted in Karachi showing 74.7% sensitivity to amikacin and 80.4% to piperacillin/tazobactam. However, 89.6% isolates were susceptible to imipe-nem which is quite high as compared to our study as only 63.6% isolated pseudomonas in our study were susceptible to imepenem.[25] 36.3% and 30.3% Pseudomonas isolates in the current research were susceptible to ceftazidime and cefipime respec-tively. These results for anti-pseudomonal cephalo-sporins are quite similar to other studies carried out in AFIP and in Karachi. [14,25]

Only two cultures yielded Acinetobacter spe-cies. Both the isolates were highly resistant to the tested antimicrobials. None of these isolates exhibi-ted susceptibility to cephalosporins, ciprofloxacin, amikacin or tazobactam/piperacillin. Only one isolate was susceptible to imepenem ,meropenam and doxycycline. This is a real alarming situation. Contrary to our results, a study conducted previously in India revealed more sensitive antibiogram of acinetobacter species. None of the strain in Indian study was imepenem resistant.[26] The worsening susceptibilty pattern drags our attention to antibiotic stewardship. However, further studies with large

number of Acinetobacter isolates are required to design antimicrobial panel against this pathogen.

Out of 508 positive cultures, 56 (11%) turned to be candida albicans. For candiduria, the predisposing factors should be identified. Addressing these factors usually resolve the infection and antifungal might not be needed. [27]

CONCLUSION

Majority of the gram negative isolates were sensitive to imipenem, amikacin and piperacillin/ tazobactam while susceptibility to many of the commonly used antibiotics like Amoxicillin/ clavulanate, cephalosporins and fluoroquinolones, trimethprim/ sulphamethoxazole, was very low. Among the oral antimicrobials, nitrofurantoin showed good results for enterobacteriaceae and enterococcus responded well to both fosfomycin and nitrofurantoin.

Out of Staphylococcus aureus, 45.8 % isolates were MRSA. And 100% S.aureus and enterococci were susceptible to vancomycin and linezolid.

Recommendation

It is recommended that hospitals should gather data and recognize the uropathogens and their resistance pattern to various antimicrobials. This regional data should be used to design new antibiotic policies and infection control strategies in health care set ups

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CLINICOPATHOLOGICAL FEATURES OF CHRONIC MYELOID LEUKEMIA

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Abstract

Chronic myeloid leukemia (chronic granulocytic leukemia) is a myeloproliferative neoplasm characterized by Philadelphia (Ph) chromosome, creating the fusion oncogene BCR–ABL1 that encodes for active tyrosine kinase, which occurs in a haemopoietic progenitor and confers proliferative and anti-apoptotic effects. The presenting features of chronic myeloid leukemia are variable ranging from silent disease to nonspecific symptoms and signs including fatigue, weight loss, night sweats, hyperleucocytosis and splenomegaly.

Objective: To determine the frequency of clinicopathological features in Chronic myeloid leukemia patients

Material and Methods: Descriptive cross sectional study conducted at department of AIMC. Fifty five patients of all age groups, both genders and all the three clinical phases were included. A detailed history and physical examination was entered in a proforma. In every patient about 5ml EDTA blood sample was collected. Complete blood counts were performed on hematology analyzer (Sysmex KX-21) Peripheral blood smears were prepared and stained using Giemsa stain. Differential count was performed. Bone marrow aspiration was done. The diagnosis of Chronic myeloid leukemia was made by complete blood count, examination of peripheral blood smear and bone marrow findings.

Result: The mean age at time of diagnosis was 38.1±11.5 SD years (range 17-66). The patients were divided into three age groups and majority of patients, 29(52.7%) were between 20-40years age group. Out of 55, 21(38.2%) were male and 34 (61.8%) were females . The most common symptoms were fever (43%), weakness (30.9%), abdominal distention (27.3%) and pain left hypochondrium (20%). Forty two(76.3%) had enlarged spleen and 23(41.8%) had enlarged liver. Complete blood count revealed anemia (HB<10g/dl) in 25(45.4%), hyperleucocytosis (WBC>100x109/l) in 41(74.5%) and marked thrombocytosis (platelets >600x109/l) in 9(16.3%).The mean hemoglobin was 9.9g/dl, Mean leucocyte count (TLC) was 176 x103/ul , mean platelet count was 419 x103/ul. Mean percentages of neutrophils, lymphocytes, monocytes, eosinophils, basophils, metamyelocytes, myelocytes, promyelocytes and blast were 50, 7, 2.9, 2.6, 1.7, 11.5, 16.2, 2, and 5 respectively

Conclusion: Chronic myeloid leukemia affects people at young age in this region, mostly in third decade . Splenomegaly followed by fever, hepatomegaly and weakness were the commonest clinical features. Majority of patients were in chronic phase with high white blood cell counts.

Chronic myeloid leukemia (chronic granulo-cytic leukemia) is a myeloproliferative neoplasm characterized by rearrangement of the long arms of chromosome 9 and 22, resulting in the Philadelphia (Ph) chromosome, creating the fusion oncogene BCR–ABL1 that encodes for active tyrosine kinase, occurs in a haemopoietic progenitor and confers proliferative and antiapoptotic effects.[1]

The incidence of CML appears to be constant worldwide. It accounts for about 1-2 per 100,000 of population per annum, with slight male predo-minance.[1,3]

The disease is most commonly diagnosed in the fifth and sixth decades of life in developed countries. In the developing world, presentations in the third and fourth decades are more common, possibly reflecting younger population demographics. CML is rare in the paediatric population.[1,3]

CML usually runs a biphasic or triphasic course.[5] This process includes an initial chronic phase and a terminal blastic phase, which is preceded by an accelerated phase in 60-80% of patients.[2,5]

The presenting features of chronic myeloid leukemia are variable[2,3] ranging from silent disease to nonspecific symptoms and signs including fatigue, weight loss, night sweats, hyperleucocytosis and splenomegaly mostly.[3] Splenomegaly is documented in 30-70% of cases. The liver is enlarged in 10-40% of cases.[5,6]

The confirmation of diagnosis of chronic myeloid leukemia is the demonstration of cytogenetic abnormality called Philadelphia chromosome or its molecular equivalent (BCR-ABL fusion) by Polymerase Chain Reaction(PCR) and/or FISH, the hallmark of diagnosis is demonstration of leucocytosis with basophilia, immature granulocytes, mainly metamyelocytes, myelocytes, promyelocytes and few or occasional myeloblasts in the peripheral blood. Bone marrow aspiration findings and clinical features will support the diagnosis.[7]

OBJECTIVE

The objective of this study is to determine the frequency of clinicopathological features in CML patients.

METHODS

Descriptive cross sectional study conducted during period from Ist July 2017 to 31st December 2017 at department of AIMC. A total of 55 consecutive patients with suspicion of chronic myeloid leukemia referring from oncology department to hematology department of AIMC belonging to all age groups, both genders and all the three clinical phases were included. Patients who had received cytotoxic treatment previously (except hydroxyurea) were excluded from the study. A detailed account of history and physical examination was entered in a proforma specially pertaining to age, sex, address, clinical symptoms like fever, weight loss, fatigue, tiredness, pain in left or right hypochondrium , abdominal distention, and night sweat, mass in abdomen, clinical signs like pallor, lymphadenopathy, splenomegaly, hepatomegaly, skin changes. Then laboratory features like complete blood count including hemoglobin, total WBC counts and its differentials (Blasts, promyelocytes, myelocytes, metamyclocytes, mature neutrophils, eosinophils and basophils) and platelet counts were also noted in a separate table in the proforma. In every patient about 5ml EDTA blood sample was collected. Complete blood counts were performed on a fully automated hematology analyzer (Sysmex KX-21). Peripheral blood smears were freshly prepared and stained using Giemsa stain. The slides were examined under a microscope and differential count was performed. Bone marrow aspiration was performed; multiple smears were made. The smears were examined and at least five hundred cells were counted for myelogram. The diagnosis of CML was made by complete blood count, examination of peripheral blood smear and bone marrow findings. Patients were placed in chronic, accelerated and blastic phases according to WHO criteria. Cytogenetics and molecular studies could not be done due to lack of these facilities at AIMC.

Operational definitions:

Anemia was defined as hemoglobin concentration less than 10g/dl.

Fever was defined as body temperature greater than 37°c.

Weight loss as reduction in weight as evidenced by looseing of cloth, shoes, belt.

Night sweat was defined as a drenching of night cloth / pyjamas by sweat.

Hepatomegaly or splenomegaly when liver and spleen were palpable below the right or left costal margin respectively.

The data was analyzed using SPSS version 23. Variable were analysed as mean and percentages. P value was determined and value of <0.05 was take as statistically significant.

RESULTS

A total of 55 patients were diagnosed as chronic myeloid leukemia, over a period of six months. The mean age at time of diagnosis was 38.1±11.5 SD years (range 17-66). The patients were divided into three age groups and majority of patients, 29(52.7%)

were between 20-40years age group (Table No.1).

Out of 55, 21(38.2%) were male and 34 (61.8%) were females with male to female ratio 0.6:1

Table 1: *Age Groups in Chronic Myeloid Leukemia.*

AGE GROUPS	Frequency	Percent
<20YEARS	4	7.3
20-40 YEARS	29	52.7
>40 YEARS	22	40.0
Total	55	100.0
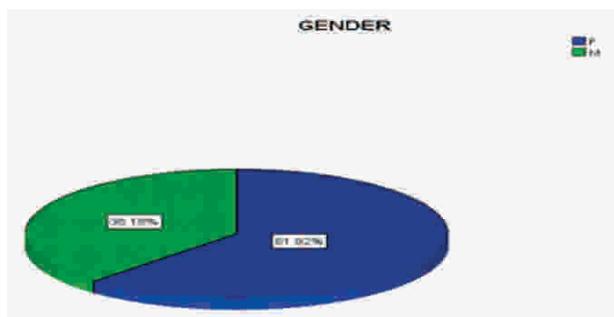
Figure: *Shows Gender Distribution.*

At time of diagnosis, chronic phase was seen in 49 patients (89.1%), 5(9.1%) had accelerated phase and 1(1.8%) was in blast crisis of chronic myeloid leukemia, according to WHO criteria for phases of disease. Table No. 2

The laboratory and clinical parameters observed at first time of presentation are shown in Table No. 3

The most common symptoms were fever (43%), weakness (30.9%), abdominal distention (27.3%) and pain left hypochondrium (20%). 42(76.3%) had enlarged spleen and 23(41.8%) had enlarged liver (Table No: 3).

Complete blood count revealed anemia (HB<

Table 2: *Showing Phases of CML According to WHO Criteria*

CML PHASES	Frequency	Percent
CHRONIC PHASE	49	89.1
ACCELRATED PHASE	5	9.1
BLAST PHASE	1	1.8
Total	55	100.0

10g/dl) in 25(45.4%), hyperleucocytosis (WBC> 100×109/l) in 41(74.5%) and marked thrombocytosis (platelets >600x109/l) in 9(16.3%) of cases

Table 3: *Showing Clinical Features*

SIGNS & SYMPTOMS	Count	Percent
Fever	24	43.6%
Pallor	1	1.8%
Weakness	17	30.9%
Pain Abdomen	5	9.1%
Mass Left Hypochondrium	2	3.6%
Pain In Lymphnodes	1	1.8%
Priapism	1	1.8%
Nausea,vomiting	3	5.5%
apetite	2	3.6%
Burning Micturition	1	1.8%
Weight Loss	7	12.7%
Shortness Of Breath	3	5.5%
Pain In Joints	1	1.8%
Brusing	3	5.5%
Epistaxis	3	5.5%
Menorrhagia	4	7.3%
Pr Bleeding	1	1.8%
Cough	2	3.6%
Pain Left Ypochondrium	11	20.0%
Pain Epigastrium	1	1.8%
Abdominal Distention	15	27.3%
Splenomegaly	42	76.3%
Hepatomegaly	23	41.8%

as shown in table no.4

The mean hemoglobin was 9.9g/dl, Mean TLC was 176 x10^3/ul, mean platelet count was 419 x10^3/ul. Mean percentages of neutrophils, lymphocytes, monocytes, eosinophils, basophils, metamyelocytes, myelocytes, promyelocytes and blast were 50, 7, 2.9, 2.6, 1.7, 11.5, 16.2, 2, and 5 respectively. Table no.5

DISCUSSION:

The incidence of CML is approximately 1 per

Table 4: *Showing Frequency of Anemia, Hyperleucocytosis and Thrombocytosis*

PARAMETER	Frequency	Percent
ANEMIA	25	45.5
HYPERLUCOCYTOSIS	41	74.5
THROMBOCYTOSIS	9	16.4

100,000 population per year. In 2002, it is estimated that there will be 4,400 new cases with 2,000 estimated deaths.[3,8] Local data reveals an incidence of CML in Karachi (1995-2002) is 1.2/100,000 in males and 0.8/100,000 in females[3,23]; the results are consistent with international studies.[9,10]

The mean age in this series is 38.1 years which

Table 5: *Showing Lab Paramteres.*

PARAMETER	Mean	Std. Deviation
HB(g/dl)	9.995	1.6831
TLC(/ul)	176.0985	125.84843
PLT(/ul)	419.64	230.798
POLY(%)	50.18	14.278
LYMP(%)	7.29	5.937
MONO(%)	2.93	2.316
EOS(%)	2.65	1.965
BASO(%)	1.76	1.688
META(%)	11.58	6.082
MYELO(%)	16.29	8.839
PROMY(%)	2.00	2.411
BLAST(%)	5.35	9.264

is significantly younger than reported in Europe (median age 55years),[11] America literature (median age 66 years),[16] France(55years)[11] and India (43 years)[13], but similar to that earlier reported in Pakistan[17] and Niegeria.[19] Reasons for this early incidence of CML in Pakistan are not fully known.

In our study there is a predominance of females as compared to males with a male to female ratio of 0.6:1. In another local study at AKU this ratio was 1.69:13, our study is not consistent with this study, which is consistent with studies from other parts of the world.[2, 10, 22]. A female preponderance among elderly with Philadelphia positive cases have been reported[15] which is in accordance with our study. This difference may be attributed to difference in the local environment, majority of our females population lives in rural areas and exposed to pesticides in fields.

The frequency of all three phases of CML in this series is 89.1%, 9.1% and 1.8% in chronic phase (CP), accelerated phase (AP) and blast phase (BP) respectively. A local study conducted in CMH,

Rawalpindi revealed the frequency of CP, AP and BP as 77.8%, 15.5% and 6.7% respectively.[17] In another local series, which included 275 cases, the frequency of CP, AP and BP were 87.3%, 8.1% and 4.7% respectively.[12] The results of above mentioned studies favor our results. In a large multi-centered French study, at the time of diagnosis, the frequency of CP, AP and BP were 96.8%, 2.2% and 0.9% respectively.[17,11] Comparing our data with this study, the frequency of CP was lower than this case series, while AP and BP are higher.

Splenomegaly, similar to other reports[7,14] was the commonest clinical feature in our study followed by fever, hepatomegaly, weakness, abdominal distention and pain left hypochondrium.

The mean HB in our study was 9.9g/dl which is similar to Syed NN et al (10g/dl),[3] but higher than a study of a series of 46 cases by Shittu AO et al (7.3g/dl).[7] Markedly raised WBC ($>100 \times 10^9$/l) is common in this series (mean 176×10^9/l), similar to findings in other studies.[2,20,3,7] but complication arising from leucostasis like priapism, retinopathy deafness and mental disturbance were not seen . This is because the syndrome of leucostasis is more common in the blast phase because of large and rigid blast cells in peripheral blood.[7]

The mean platelet count in our study (418×10^9/l) which is comparable to a local study at AKU (408×10^9/l).[3] Faderl et af.18 and Savage et al.[21], reported splenomegaly (48 and 76 percent), anemia (45 and 62 percent), white blood cell count above 100,000/cmm (52 and 72 percent), and platelet count above 600,000 to 700,000/cmm (15 and 34 percent) at the time of diagnosis. Although, presence of enlarged spleen at the time of diagnosis was more prevalent in our population, but the frequency of hyperleucocytosis, anemia or thrombocytosis are almost comparable with the international studies cited above.[10,18,21]

Presence of enlarged spleen is unexplainable in our population; it might be because of delay in presentation or might be due to high white blood cell count and co-existant infectious etiology like

hepatitis B and C etc.

CONCLUSION

Chronic myeloid leukemia affects people at young age in this region, mostly in third decade. Splenomegaly followed by fever, hepatomegaly and weakness were the commonest clinical features. Majority of patients were in chronic phase with high white blood cell counts.

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ROLE OF CT (FESS PROTOCOL) IN DIAGNOSIS OF FUNGAL SINUSITIS IN IMMUNOCOPROMISED PATIENTS KEEPING HISTOPATHOLOGY AS GOLD STANDARD

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Abstract

Background: Allergic fungal sinusitis (AFS) is more noninvasive fungal disease. In actual this is an allergic retort of the extra mucosal fungi presence in the sinuses. The bone remodeling is due to the propensity of allergic mucin and mucocele establishment. On preoperative diagnosis of disease, a CT scan of nose and paranasal sinuses is an indispensable and prerequisite.

Methods: This was a prospective cohort study with total of 60 patients. These patients were selected randomly while visiting the department of Radiology, Sheikh Zayed Hospital. The exclusion criteria include all patients with diabetes mellitus (DM), and those on long-term antibiotic or steroid therapy whereas all patients with chronic rihnosinusities as per definition of Lanza and Kennedy et al were included in this study.

Results: We recruited a total of 60 patients for this study. The average age of all the patients was 28 + 8.9 with range 10-65. 30 (50%) of the patient were in the age category of 21 to 30. 10 (16.67%) belong to 10-20 and 20 (33.33%) were above and equal 31 years of age. 38 (63.33%) of the patients were female and 22(37.7%) were male. The incidence of AFS was more in females than males i.e. 54% females and 46% males respectively. Conclusion: We may conclude from our study findings that CT is the best tool to diagnose AFS whereas with the advent of endoscopic sinus surgery the diagnosis can be better and clearer.

Keywords: Allergic fungal sinusitis (AFS), mucocele establishment, immunucompetency, paranasal sinuses, CT scans.

In Rhinology, Allergic fungal sinusitis (AFS) is a disease that occupies huge attention and discussions. This is more noninvasive fungal disease. In actual this is an allergic retort of the extra mucosal fungi presence in the sinuses. The bone remodeling is due to the propensity of allergic mucin and mucocele establishment.[1,2] More Frequently the young adults with atopic immunucompetency; and who lived in warm and humid climates were affected by this disease.[3-4] On preoperative diagnosis of disease, a CT scan of nose and paranasal sinuses is an indispensable and prerequisite.[2] Although the CT scan findings are of considerable importance but absolute diagnosis can only be completed once after histopathological investigations. As Intraoperative and histopathological, the existence of allergic mucin and fungal debris is said to be the sine qua non for diagnosis of AFS.[5] The primary objective of the study was to identify the role of CT in diagnosis of fungal sinusitis in immunocopromised patients keeping histopathology as gold standard.

METHODS

We opt a prospective cohort design for this study. A total 60 patients were recruited for the study; these patients were selected randomly while visiting in the Out patient department of the abc hospital. The study duration was of eight months starting from Jan 2016. The venue of the study was Sheikh Zayed Hospital. The exclusion criteria include all patients with diabetes mellitus (DM) , and those on long-term antibiotic or steroid therapy whereas all patients with chronic rihnosinusities as per definition of Lanza and Kennedy et al were included in this study. Firstly all the results were evaluated from the CT scan for allergic fungal sinusitis characteristics that are mainly consisted completely unilateral or bilateral opacification of multiple sinusitis with central hyperattenuation, sinus mucosal formation and pressure erosions of laminia papyracea or skull base.

One more selection criterion was the patients who were diagnosed as allergic fungal sinusitis (AFS) on prospective CT scan. Later these patients underwent surgeries and the intraoperative findings were evaluated as AFS evidence. Other demographic information with necessary diagnostic history was collected for all the patients time to time. For the diagnostic values their standard operating procedures (SOPs) were strictly followed in hospital laboratory. Additionally an informed consent was taken from the patients or attendant by acknowledging them the study outputs and ensuring the confidentiality. Ethical approval was taken from the hospital ethical Committee.

Statistical analysis: The information collected from patients were entered electronically, stored and analyzed later by using SPSS version 18. Descriptive statistics were applied by calculating mean and standard deviation. Frequency distribution and percentages were performed for all qualitative variables like gender sinusitis type etc. P values less than 0.05 was considered statistically significant in all inferential statistics.

RESULTS

We recruited a total of 60 patients for this study. The average age of all the patients was $28 + 8.9$ with range 10-65. 30 (50%) of the patient were in the age category of 21 to 30. 10 (16.67%) belong to 10-20 and 20 (33.33%) were above and equal 31 years of age. 38 (63.33%) of the patients were female and 22(37.7%) were male. The incidence of AFS was more in females than males i.e. 54% females and 46% males respectively. More of the baseline characteristics of all the patients were given in table 1.

Table 1: Baseline Characteristic for all the Participants

Characteristics	n(%)
Number of patients	60
Age (mean+ SD)	28 + 8.9
Gander	
Female	38(63.3%)
Male	22(37.7%)
Residence	
Urban	18(30%)
Rural	42(70%)
AFS symptoms	
Nasal obstruction	58(96.67%)
Nasal Discharge	55(91.67%)
Nasal polyposis	50(83.3%)
Telecanthus	4(6.67%)

The Allergic rhinitis was observed in 51 (85%) and atopy was seen in 52(86.67%) cases. Preoperatively the CT scan showed 100% mucosal hypertrophy and intrasinus hyperattenuation in all patients. More on the CT scan diagnosis and histopathological findings were given in table 2.

Table 2: CT Scan Diagnosis Verses Histopathological Findings

CT scan findings (Preoperative)	n(%)	Endoscopic sinus surgery findings	n(%)	Histopathological findings	n(%)
Mucosal attropy	60(100%)	Fungal dabris and allergic mucin	42(70%)	Allergic mucin	49 (81.6%)
intrasinus hyperattenuation	60(100%)	Only Fungal debris	5 (8.3%)	Noninvasive fungal hyphae eosinophiliac infiltrates	48(80%)
Remodeling of sinus wall	50(83.3%)	Fungal debris and allergic mucin absent	13(21.67%)	Charcot leyden crystals	50(83.3)
Expansion of bone	37(61.67%)	Positive AFS cases on surgery	52(86.67%)	AFS confirmed cases	48(80%)
Orbit involvement	4(6.67%)	Unilateral involvement out of AFS positive	33(55%)		
Intracranial involvement	1(1.67%)	Bilateral involvement out of AFS positive cases	21(35%)		
Unilateral involvement of AFS	32(53.3%)	Multiple sinus involvement out of AFS positive cases	50(83.3%)		
Bilateral involvement of AFS	18(46.7%)				
Multiple sinus involvement	53(88.3%)				

DISCUSSION

This study was planned to determine the role of CT scan for the diagnosis of AFS disease by keeping histopathological findings as gold standard, moreover we aim to draw a comparison among different diagnosis methods. For almost recent three decades, AFS appeared as a clinical distinctive form of chronic rhinosinusitis. It was quite similar to the allergic bronchopulmonary aspergillosis in very initial studies, but recent advancements and more research enable us to identify AFS with inimitable radiographic, clinical, pathological characteristics.[7] This condition appeared when an atopic person inhaled fungal sporic air or when it is exposed with fungal spores in air and the process prolonged to the situation of sinus expansion.[8,9] The diagnosis of AFS may require a mixture of therapies based on radiographic, clinical and pathological information.[10] The set criteria for AFS diagnosis are still uncertain universally.[11] An essential modality for AFS diagnosis is CT scan, now a days not only diagnosis, but extension and treatment plan was also made through CT scan findings.[11-12] As per a study conducted by Schubert, on CT scan, the hyperattenuating signals in AFS may be instigated by the existence of inspissated allergic mucin and fungal hyphae (both) within para-nasal sinuses.[3] In our study and other published findings, the imaging of CT scan displays sinus mucocele creation, erosions, and lamina papyracea or skull base with insistent border.[10] Moreover in our findings the AFS exhibits more erosions than the other forms.[13] Accentuating the imperative role of histopathology in its diagnosis, an extensive overlap exists among AFS and related other forms. In our study findings the allergic mucin was thick, inflexible and of dark color. Histopathologically it actually consist of onionskin's lamination and in contextual a fungal hyphae with sporadic charcoal laden crystals.[10] We had observed among few of our study cases, the allergic mucin left from sinuses does not have recognizable fungal origins; similar findings were available in literature.[14-15] Rather to an organism related to fungus or the clinical predictive characteristics were important but its identification in mucin either via histopathological or CT scan is very important to diagnose the AFS.

CONCLUSIONS

We may conclude from our study findings that CT is the best tool to diagnose AFS whereas with the advent of endoscopic sinus surgery the diagnosis can be better and clearer.

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THE AETIOLOGICAL FACTORS OF EPISTAXIS IN PATIENTS PRESENTED IN A REFERRAL HOSPITAL IN SAUDI ARABIA

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Abstract

Introduction: Epistaxis is a common emergency problem in ENT practice. It is usually managed by simple conservative measures but for that its definitive cause is essential to find out. The objective of the study was to find out the cause of epistaxis which is a common emergency in otorhinolaryngology.

Objective: To find out different etiological factors causing epistaxis.

Materials and methods: A retrospective descriptive study from December 2015 to November 2016, for 137 patients admitted with epistaxis, in referral hospital, Saudi Arabia. Medical records were reviewed and results analysed. Detailed history, routine ENT and systemic examination along with nasal endoscopic examination to find out bleeding site and its possible local/general cause were found out. Routine laboratory investigations and specific radiological investigations requested for. Management plan was bi-fold including measures to stop bleeding and then treat underlying cause.

Results: The mean age of patient was 43.96. Males were 67% and females were 33%. In 77.37% of patients, it was anterior epistaxis and 22.63% were admitted with posterior epistaxis. The most common cause was trauma, in 39.41% followed by idiopathic (23.35%), inflammatory (17.51%), hypertension (12.40%), drugs (5.10%) and 2.18% of the patients were having tumours of nose and nasopharynx.

Conclusion: Nasal trauma topped the list of causative factors for epistaxis, followed by idiopathic group (though nose picking still important factor even denied by patients), inflammatory and hypertensive patients. Few patients taking Aspirin and NSAIDS and last in the list were patients having tumours of nose and nasopharynx.

Keywords: *epistaxis, endoscopic examination, idiopathic, nasopharynx.*

Epistaxis is among one of the most common emergency in otolaryngological practice seen in up to 60% of adults in their lives (at least one episode) but treatment is needed in only 6-10% cases.[1,2] Epistaxis is defined as bleeding from inside the nose.[3] The term 'Epistaxis' was coined by William Cullen. Until the period of middle age, nasal bleeding was considered to be a natural means of purification of internal diseases.[4] Although epistaxis is a common cause of hospitalization in otolaryngology department but surgical intervention is rarely needed. Refractory epistaxis can occur in some cases.[5]

Epistaxis can be classified into primary (where no definite cause found) or secondary (where causal factor present), Childhood (16 years) or adulthood (16 years), anterior (bleeding site anterior to pyriform aperture) or posterior (bleeding site posterior to pyriform aperture).[3]

Age distribution of epistaxis is bimodal, common in childhood but less common in early adulthood and then again peaks in 6th decade of life. 70-80% cases of epistaxis are idiopathic. Primary Epistaxis is the spontaneous bleed without any causal factor. Trauma, surgery and anticoagulant overdose accounts for a small proportion of cases, classified as secondary epistaxis.[6]

Treatment (Haemostasis) of posterior epistaxis is difficult comparing with anterior epistaxis and

recurrence is seen in many cases. There is no definite protocol for the management of epistaxis, although various treatment methods are available for the management ranging from local pressure (nose pinching), topical vasoconstrictor, nasal packing, and cauterization (chemical/electric) to embolization or ligation.[7]

METHODS

A retrospective study was carried out in Department of Otorhinolaryngology, Najran General Hospital, Najran, Kingdom of Saudi Arabia which is a referral hospital, from December 2015 to November 2016. Patients admitted during this duration with epistaxis were reviewed and aetiology, mode of presentation, associated medical conditions, drugs history, anterior rhinoscopy and endoscopic nasal examination, treatment and hospital stay were recorded in an excel sheet and analysed.

There were 137 patients of age 4 years to 85 years. There were 92 (67.15%) male patients and 45 (32.84%) female patients (Fig.1). Male to female ratio was 2:1. In 106 patients (77.37%), anterior epistaxis was seen while 31 patients (22.62%) were admitted with posterior epistaxis. (Fig.2) Out of these 112 (81.75%) patients were admitted through emergency department and 25 (18.24%) attended ENT outpatient clinic. (Fig.3)
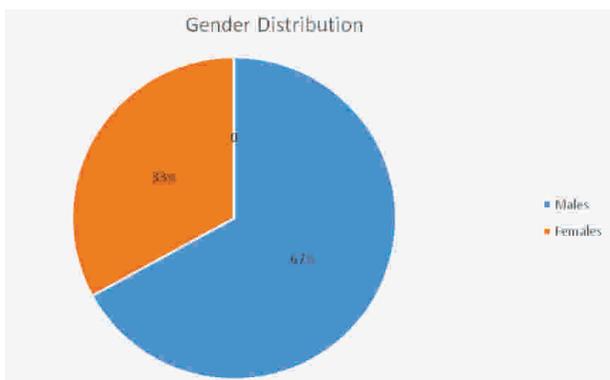
Fig. 1
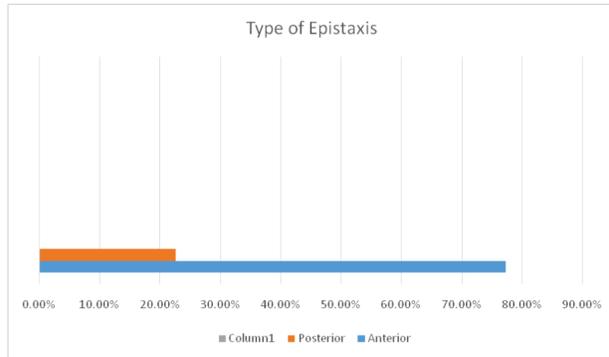
Fig. 2
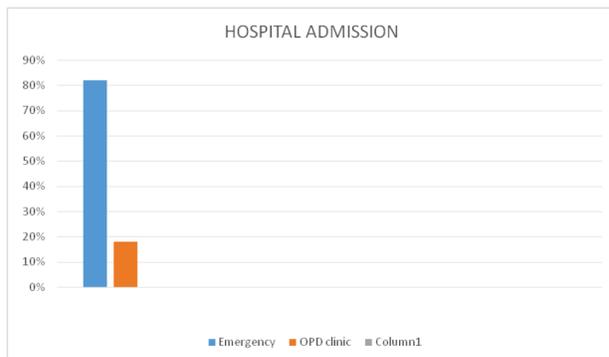
Fig.3

Trauma (39.41%) was the most common cause of epistaxis. Out of 54 patients, presented with history of trauma, 37 were due to road traffic accidents, 13 were brought to hospital after assaults and 4 got injury while playing football. Idiopathic group (27.35%) was second in list and in this group no definite causative factor was found but bleeding was anterior and Little's area was lacerated and ulcerated or bleeding point visible there so nose picking may be triggering factor though was not admitted by patients. Inflammatory (mostly viral upper respiratory tract infection) group (17.51%) was on third number in list, followed by hypertensive (12.40%) patients and on drugs (5.10%) mostly aspirin and

Table 1: *Causes of Epistaxis*
(Total no. of patients=137)

Sr.No.	Etiologies	No. of Patients	Percentage
1	Trauma	54	39.41%
2	Idiopathic	32	23.35%
3	Inflammation	24	17.51%
4	Hypertension	17	12.40%
5	Drugs	07	5.10%
6	Tumours	03	2.18%

NSAIDS and lastly were patients (2.18%) having nasopharyngeal carcinoma and bleeding polyp of nasal septum. (Table1)

Detailed history, routine ENT & systemic examination along with nasal endoscopy done in all patients to localise bleeding site and find out cause for epistaxis. Routing laboratory investigations including complete blood count (CBC), bleeding time and coagulation time, coagulation profile including Partial Thromboplastin Time (PTT) and activated Partial Thromboplastin Time (aPTT) were requested. CT scan of nose, nasopharynx and paranasal sinuses asked for patients having nasopharyngeal carcinoma for staging purposes & biopsy to confirm the diagnosis.

Those cases having inflammatory upper respiratory infections and using drugs were managed by nose pinching and by using vasoconstrictor nasal drops (Xylometazoline). As in these cases epistaxis was mild. In Trauma/idiopathic cases, chemical cautery controlled bleeding where bleeding point could be localised on routine or endoscopic examination. Otherwise anterior nasal packing was to be done. In 7 patients with hypertension and 2 patients with nasopharyngeal carcinoma, posterior nasal packing was required by Foley's catheter with anterior nasal packing with roll gauze.

DISCUSSION

Epistaxis is one of the commonest emergency encountered by ENT personnel. It has a male preponderance as in present study showed males (67%) more affected than females (33%). Reason being that more exposed to road traffic accidents and assaults, also more involved in sport injuries. Most studied have shown that males have outnumbered females regarding occurrence of epistaxis.[18,19]

Nasal cavity is highly vascular because of frequent anastomoses between external carotid and internal carotid system arteries. Terminal branches of these systems are supplying the mucosa of the nasal cavity. Plexus of vessels in the anterior nasal septum is called Kiesselbach's plexus at Little's area.

In the management of posterior nose bleeds, branching of sphenopalatine artery in the nasal cavity is a key point. The dividing line between "posterior" and "anterior" epistaxis is the maxillary sinus ostium.[1] Anterior epistaxis was more common than posterior epistaxis in this study which is found in other studies also.[6,11]

Road traffic accidents trauma and assaults is the commonest etiological factor, followed by idiopathic and hypertension.[12,13,14] A large number of patients (640) were included in a study by Mahmood et al. found accidental trauma as the most common cause of epistaxis.[15] In a study of 72 cases by Iseh KR et al. the most common cause of nose bleeding was idiopathic (29.2%), followed by trauma (27.8%).[16] Idiopathic is the most common aetiology of epistaxis in most of the patients followed by tumours and trauma or iatrogenic causes.[10]

Inflammatory diseases (mostly viral upper respiratory tract infections) caused epistaxis in 17.51% of patients in present study. Infections and inflammations of nose and paranasal sinuses have been implicated as source of epistaxis in many studies.[15,16]

Most international studies have shown hypertension as one of the important cause of epistaxis.[14,16,17,18] But many studies revealed no connection between epistaxis and hypertension.[19,20] Elderly people commonly have comorbidities like hypertension and diabetes mellitus which causes degenerative changes in blood vessels, making them more fragile which bleed easily on abrupt pressure changes such as straining during micturition and defecation in benign prostatic hypertrophy and constipation respectively; excessive coughing in chronic obstructive pulmonary disease and lifting heavy objects.[21]

Four patients on aspirin and 3 patients on NSAIDS (total 5.10%) were found to have epistaxis. It may be due to platelets function alteration.[22] Aspirin is a risk factor for nasal bleed is not proven by different studies.[23] Aspirin, alcohol abuse and

hypertension have been suggested as risk factors for recurrent epistaxis and posterior nasal cavity was the anatomical site for bleeding. Mucosal abnormality, spurring and septal deviation were predisposing anatomical factors.[24]

In present study, 3 cases were diagnosed as having tumours. Two were of nasopharyngeal carcinoma and one suffering from bleeding polypus of nasal septum. Accidently no case of juvenile nasopharyngeal fibroma was encountered during study period which is the most common tumour causing epistaxis.[25,26]

Bleeding disorders specially platelets disorders, Haemophilia, Von will ebrand disorder, hereditary telangiectasia, typhoid fever and cirrhosis of liver are also found culprit for epistaxis.[2 '2 '2

CONCLUSION

Epistaxis is one the most common emergency in ENT department anywhere in the world. As it has a variety of etiological factors so first-hand knowledge of these causes and prompt diagnosis along with control of bleeding and hemodynamically stable patient is the priority in each case. As trauma is the most common cause in Saudi Arabia also and road traffic accidents heading the list so proper traffic rules awareness and vehicle speed monitoring is urgently required because it is causing mortality also. Judicious use of endoscopes for nasal and nasopharyngeal examination with CT scan, ENT surgeons are in better position to properly diagnose the causative factor in epistaxis and specially site of bleeding. By proper diagnosing, idiopathic group number can be reduced and also recurrent epistaxis can be avoided as well. Recurrent epistaxis should not be taken lightly rather exclusive and comprehensive investigations are needed.

Acknowledgement

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MANAGING GIARDIA INTESTINALIS ASSOCIATED IRON DEFICIENCY ANEMIA, WITHOUT IRON SUPPLEMENTATION

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Abstract

Giardia intestinalis, etiological agent of Giardiasis, is the most frequently reported intestinal parasite worldwide. The fascinating cosmopolitan protist pathogen, which can be found from tropics to Arictic Greenland, has no respect for age, sex, ethnicity or socioeconomic status. The curious organism constitutes a significant public health problem because of its high incidence and prevalence. Since the site of absorption of iron is duodenum and it is a duodenal parasite, the resultant sub-optimal absorption leads to iron deficiency anemia (IDA). The present study was conducted to ratify the effects of successful anti-giardial therapy on iron status, in those cases having associated IDA. The research question was "Can successful anti-giardial therapy correct IDA, in proven cases of Giardiasis, without iron supplementation?" From amongst 14 proven cases of Giardiasis associated IDA, 10 (M:F 4:6…..71.4%), after having been instituted Secnidazole sodium, demonstrated significant improvement, in iron status, by day 45. Normal haematological picture was obtained in further 6 weeks.

Standard oral Ferrous Fumerate therapy instituted to the 4 non-responders (M:F 2:2….28.6%) resulted in complete resolution of the problem in two of them (M:F 0:2….50%). The remaing two (M:F 2:0…….50%) were found to be suffering from GERD, on long standing use of proton pump inhibitors (PPIs). It is well known that inhibition of gastric acid secretion, by PPIs, decreases the bioavailability of iron. Switching over to H2 receptor antagonists is the reliable solution. The research question we had formulated, was successfully addressed. A large multicenter study, by a team of consultants in Internal Medicine, Tropical Medicine, Gastroenterology and Hematology ,to investigate in details the impact of Giardiasis on hematological profile, is recommended.

Keywords: *giardia intestinalis, giardiasis, iron deficiency anemia, oral iron therapy, secnidazole, proton pump inhibitors.*

Giardia intestinalis, etiological agent of Giardiasis, is the most frequently reported intestinal parasite worldwide. Although its first ever description has been traced to Antony van Leeuwenhoek (1632-1723 CE), justifiably called "The Father of Microbiology"[1], the organism has been found in human coprolites (fossilized dung), as old as 1200 AD, from European and American archeological sites.[2] This cosmopolitan protist pathogen, which can be found from tropics to Arictic Greenland, has no respect for age, sex, ethnicity or socioeconomic status.[3]

It may infect neonates as early as 4th post-partum day and those as old as 94 years, according to the case reports from Guatemala and United Kingdom, respectively.[4,5] The fascinating organism constitutes a significant public health problem because of its high incidence and prevalence.[6] The prevalence rates may vary 3-10% in industrialized countries and 20-40% in resource-limited countries.[7]

It is an important cause of travellers' diarrhoea,[8] common cause of waterborne[9] and infrequent cause of foodborne epidemics.[10] The infections are common in children day care centres,[11] backpackers[12] and homosexuals.[13] Its zoonotic potential is well established.[14] In the past, it was

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relatively neglected partly due to the focus of the scientific community on more "fashionable disea-ses".[15] However, in 2004, the World Health Organi-sation included it in its "Neglected Disease Initia-tive".[16]

To date, Giardia organisms have been sub-classified into eights genetic assemblages (A-H). A and B appear to be the main (or possibly the only) assemblages that infect human beings.[17] Those with assemblage B were found to have higher number and frequency of symptoms as compared with people infected with assemblage A.[18] In an Egyptian Study, a significant correlation was found between assemb-lage A subtype distribution among IDA patients-91% in comparison to assemblage B where it was 9%.[19]

The case definition of Giardiasis (last updated 2011) by The Centers for Disease Control and Prevention, United States (CDC) is : "an illness caused by the protozoan Giardia lamblia (also known as G.intestinalis or G.duodenalis) and characterized by gastrointestinal symptoms such as diarrhoea, abdominal cramps, bloating, weight loss or malabsorption".[20]

The laboratory confirmed Giardiasis shall be defined "as the detection of Giardia organisms, antigen, or DNA in stool, intestinal fluid, tissue samples, biopsy specimens or other biological sample".[20]

Anemia (from the ancient Greek   μ , anaimia) means 'lack of blood'. Iron Deficiency Anemia (IDA), the most common cause of anemia in the world, is defined by a decrease in the total amount of hemoglobin or the number of red blood cells.[21] It is typically caused by inadequate intake of iron, sub-optimal absorption of iron, chronic blood loss, or a combination of all. The World Health Organization defines anemia as blood hemoglobin values of less than 7.7 mmol/l (13 g/dl) in men and 7.4 mmol/l (12 g/dl) in women.[21]

METHODS

Study Population:

One hundred and eighty individuals (M:F 101: 79….56%:44%) from amongst the attendees of the Adult Medicine Clinic of the principal investigator, after their free agreement to be enrolled in the study, were investigated for the presence of Giardia intes-tinalis, by stool microscopy. Those found positive (37….21%) were treated with specific anti-giardial therapy (Secnidazole sodium as single supervised dose). The results have already been reported and published.[1,6] The present study comprises of those 14 proven cases of Giardial infection (M:F 6:8 …. 37.8%) who had associated IDA, in addition to other clinical manifestations.

Type of Study:

Descriptive, Analytical, Interventional

Objective:

To ratify the effects of successful anti-giardial therapy on iron status, in those cases having associa-ted IDA.

Research Question:

Can successful anti-giardial therapy correct IDA, in proven cases of Giardiasis, without iron supplementation?

Inclusion Criteria:

All proven cases of Giardiasis associated IDA, in the study population.

Exclusion Criteria :

1. Those with polyparasitism
2. Those immunosuppressed
3. Those with overt blood loss
4. Those with occult blood loss
5. Pregnant and lactating females
6. Females with dysfunctional uterine bleeding

Study Instrument (Diagnostic Criteria):

For Giardiasis: Detection of Giardia intestinalis on stool microscopy.[20]

For IDA: WHO's criteria, as mentioned above.[21]

Laboratory Diagnostic Tool: Estimation of blood hemoglobin levels

Parasitological Cure:

Non-detection of Giardia intestinalis in three stool samples post-treatment, one week apart. .

Clinical Cure:

Complete resolution of Giardia related symptoms post-treatment, with no recurrence in follow up period of 6 weeks.

Complete Cure:

Combination of the two (Parasitological and Clinical Cures)

RESULTS

From amongst the 14 proven cases of Giardiasis associated IDA, 10 (M:F 4:6….71.4%), after having been instituted Secnidazole sodium, demonstrated significant improvement (from mean <9.7g/dL to > 11.5g/dL in females and from mean <10.2g/dL to > 12.8g/dL in males by day 45. Normal haematological picture was obtained in further 6 weeks.

Standard oral Ferrous Fumerate therapy instituted to the 4 non-responders (M:F 2:2….28.6%) resulted in complete resolution of the problem in two of them (M:F 0:2….50%). The remaing two (M:F 2:0….50%) were found to be suffering from GERD, on long standing use of proton pump inhibitors (PPIs). They were referred to the gastroenterologist for further action.

DISCUSSION

IDA is thought to affect the health of more than one billion people worldwide, with the greatest burden of disease experienced in lesser developed countries, particularly women of reproductive age and children. This greater disease burden is due to both nutritional and infectious etiologies.[22] The intestinal parasitic infections are one of 17th Neglected Tropical Disease listed by WHO and being the 4th top leading cause of communicable diseases, with a high percentage of disability.[23]

The main parasites causing blood loss in man and leading to direct IDA are the common worm infections. These include hookworm infection (Necator americanus and Ancylostoma duodenale);

whipworm infection (Trichuris trichiura); and schistosomiasis (Schistosoma mansoni, S. haematobium, and S. japonicum). The common protozoa ,causing IDA, are Giardia intestinalis and Entamoeba histolytica. Whereas the cause of IDA in the former (a duodenal parasite) is sub-optimal iron absorption, chronic blood loss is responsible in the later (a caecal parasite) .

Whereas in our study, 37.8 % of those harbouring Giardia intestinalis had associated IDA, the comparable figures, from other spots on the globe, were 25% in Brazil,[24] 26.5% in Iran,[25] 28.3% in rural Punjab[3] and 80% in an Italian study[26]. The successful anti-giardial treatment in our study resulted in significant improvement in the iron status of the individuals. Our results are in tune with those of the studies conducted in Carcase,[27] Ahwaz,[25] Udaipur[28] and rural Punjab.[3]

The four cases, in which IDA did not respond to eradication of the offending organism Giardia intestinalis, were chosen for iron supplementation. As justifiably concluded by Camaschella, oral iron replacement is the standard front-line therapy for IDA.[29] The estimated absorption rate of the ferrous salts is 10-15%, with no difference found in absorbability among the three main formulations (ferrous sulfate, ferrous gluconate, and ferrous fumarate).[30] However, we preferred Ferrous Fumerate because of its better tolerability. Two of the four responded while the remaining two cases, in whom IDA did not respond either to anti-giardial therapy or to oral Ferrous fumerate supplement, were found to be on long term PPIs. Since oral iron absorption occurs in the duodenum and requires increased gastric acidity to allow iron to remain in the more soluble ferrous form, Huang[31] and Tempel et al[32] have concluded that inhibition of gastric acid secretion decreases the bioavailability of iron. Humans are able to utilize two types of iron (heme and non-heme). The heme (from animal blood and muscle) being the most important nutritional source of iron is believed to be more readily absorbed.[33] The heme type is absorbed independently of gastric pH whereas the non-heme

type (from grains, plants, fruits, vegetables and nuts) requires an acidic pH for absorption.[34]

Hashimoto has documented that switching over to H_2 receptor antagonists, from PPIs, can normalize the absorption of oral iron supplement resulting in cure of IDA.[35] This was worth trial in our cases but giving due weightage to the assertion of Kitchenstein[36] and that of Jimenezk et al[37] that the recal-citrant IDA should preferably be managed by a gastroenterologist, we opted to refer the two non-responders to the first available gastroenterologist, for further action.

In addition to fall in hemoglobin and hemocrit levels in Giardia infected individuals, significant increase in TLC and DLC was noted in Anantnag Study.[38] This, we could not do in ours. However, we plan to study in detail the hematological profile in our upcoming research project.

CONCLUSION

The research question formulated for our study "Can, successful anti-giardial therapy correct IDA in proven cases of Giardiasis, without iron supplementation?" has been successfully addressed.

RECOMMENDATIONS

A large multicenter study, by a team of consultants in Internal Medicine, Tropical Medicine, Gastroenterology and Hematology, to investigate in details the impact of Giardiasis on hematological profile, is recommended. Giardia human genotypes studies, if made available, would add to the beauty of the research, as is evident from the Egyptian study.[19]

Ethical Considerations:

The procedures adopted in the present study were in accordance with the 1975 Declaration of Helsinki, as reviewed in 2000.

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Conflict of Interest:

None

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IMPROVED DETECTION OF INTRASCROTAL PATHOLOGIES BY COLOUR DOPPLER SCROTAL ULTRASOUND IN ADDITION TO SCROTAL PHYSICAL EXAMINATION IN PRIMARY INFERTILITY CASES IN MALES

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Abstract

Infertility is defined as a failure to achieve pregnancy after 1 year of frequent, unprotected intercourse. Scrotum is a cutaneous bag containing two testes, the epididymis and the lower part of the spermatic cord. Different scrotal pathologies have been found to be the cause of primary infertility in males which are usually missed on physical examination.

In this study, Grey scale ultrasound as well as doppler scrotal ultrasound were performed on 350 cases of primary infertility which are referred by consultant urologist and consultant physician along with the record of their physical findings. For convenience, number of these cases on ultrasound were tabulated separately under categories of different scrotal pathologies and the percentages were analysed in total and in each of the categories. Number of pathologies detected on imaging were 405 in total and out of these 188 were diagnosed first time by grey scale and doppler ultrasound imaging.

The results indicate increased number of new cases in each category of scrotal pathologies. The most commonly missed finding on physical examination alone was found to be right sided varicocele (20 cases out of 35 cases corresponding to 57%). All the cases of primary intrasubstance testicular pathologies such as testicular microlithiases, testicular cysts and testicular masses while most of the cases of small epidydimal masses (60%) and scrotal pearls (93%) were only diagnosed on ultrasound.

The results also indicate that, in cases of primary infertility, simple, cost effective, non-hazardous Grey scale as well as doppler ultrasound examinations provides improved outcome in detecting different scrotal pathologies. It leads to the conclusion that Grey scale as well as doppler ultrasound examination should always be done on every patients of primary infertility in addition to physical examination.

Key words: *grey scale ultrasound, scrotal doppler ultrasound, testes, epidydimus, varicocele*

Infertility is defined as a failure to achieve pregnancy after 1 year of frequent, unprotected intercourse.[1] Testicular failure or dysfunction, also referred to as primary hypogonadism, is the most common identifiable cause in males.[2]

Scrotum is a cutaneous bag containing two testes, the epididymis and the lower part of the spermatic cord. In self clinical examination of the scrotal swelling, physical evaluation may be inadequate due to tenderness, swelling or gross distortion of scrotal contents. Clinical signs and symptoms are usually nonspecific, variable and misleading.[3]

Ultrasound is the preferred imaging modality for the scrotum because of its low cost, lack of ionizing radiation, and ability to image in real time. The clinical history and examination of patients presenting with scrotal symptoms frequently overlap among multiple etiologies. A thorough understanding of the usual findings is required to accurately guide patient care and to aid in differentiating surgical from medical, and benign from malignant etiologies.[4] Having high sensitivity and specificity (97% and 94% when compared to venography),[5] non-invasive nature, and relative ease of perfor-

mance, scrotal ultrasound with Doppler examination has become the study of choice in evaluating scrotal and testicular pathology.[6]

OBJECTIVES

To find out improved detection of intra scrotal pathologies by scrotal colour Doppler ultrasound in addition to scrotal physical examination only and calculating the percentages of individual scrotal pathologies missed by scrotal physical examination only.

METHODS

This study was performed at Shalamar hospital and Polytest clinic from January 2014 to June 2017. There was convenient method of sampling used in this study. Total number of 350 primary infertility cases of age ranging from 25-50 years were included in this study. All the included patients were referred by consultant urologist and consultant physician along with the details of their physical findings. A copy of their physical examination findings was kept for record purposes.

The patients with previous scrotal intervention or surgery and with known medical history of chronic medical illnesses were excluded. Also the patients of secondary infertility were not included.

The study was performed using high-resolution real time grey scale ultrasonography and Doppler imaging using 7.5 to 10 MHz linear transducer of TOSHIBA NEMIO 20 Ultrasound Doppler machine.

Scanning was routinely performed in supine position after elevating the scrotum, using a towel draped over thighs, and the penis was placed on the patient's abdomen and covered with a towel. Each of scrotal sacs were examined in transverse, sagittal and oblique planes. Scanning was also performed with the patient in erect posture and during Valsalva manoeuvre. The inguinal regions were routinely included in the imaging of scrotum.

RESULTS

Out of 350 total infertile patients, scrotal pathologies were observed in 325 patients while 25 patients were found to be normal. A total of 405 abnormalities were detected upon ultrasound as in few cases, there were more than one significant finding on ultrasound, as shown in Table 1.

Out of these 405 abnormalities, 217 abnormalities were detected on physical examination and 188 were missed as shown by Table 2 (also showing percentages of individual pathologies missed by physical examination only).

For easy interpretation, the results of each of detected pathologies are individually explained below.

There were 230 total cases of varicocele and out of these 50 were bilateral. cases and These are included in the table as left and right varicocele. Total number of missed cases of left and right varicocele on physical examination were 54 and 20 corresponding to 28% and 57% respectively.

The pathologies related to Epidydimus were found to be 46 in total, out of which 36 were Epidydimal Cysts / Spermatoceles and 10 were Epidydimal masses (predominantly of Inflammatory etiologies). There were 17 (48 %) and 6 (60%) cases of small Epidydimal cysts / Spermatoceles and small Epidydimal Masses respectively which are missed by physical examination only.

The primary intrasubstance testicular pathologies such as Testicular masses (4 cases), Testicular Cysts (11 cases) and Testicular Microlithiasis[8] remained almost 100% undetected on physical examination in our study as evident in table 2.

Approximately 28% cases of mild Hydrocele were missed by physical examination only. This was evident by 17 additional cases which were detected by ultrasound out of total 60 cases of Hydrocele.

Scrotal pearls were predominantly missed by physical examination (93%) as reflected by 27 out of 29 cases which were detected by ultrasound only.

2 out of 5 Scrotal wall masses and 2 out of 12 Scrotal hernias were missed by physical examina-

tion only in patients with associated large hydroceles and marked varicoceles.

Table 1 shows the number of cases of different ultrasound findings.

The Table 2 shows the number of missed findings on physical examination in comparison with ultrasound examination.

DISCUSSION

Infertility is lack of pregnancy after unprotected intercourse of about one year[7]. A multicentre

Table 1:

Sr. No	Scrotal Pathologies on Ultrasound	Number of Cases
1	Varicocele	
1 (A)	Left Varicocele	195
1 (B)	Right Varicocele	35
2	Epidydimal Mass	10
3	Epidydimal Cyst / Spermatocele	36
4	Testicular Focal Mass	4
5	Testicular Focal Cyst	11
6	Testicular Calcifications	8
7	Hydrocele	60
8	Scrotal Pearls	29
9	Scrotal Wall Masses	5
10	Scrotal Hernias	12
	Total	405

Table 2:

Sr. No	Scrotal Pathologies on Ultrasound	Number of Cases on Ultrasound	Number of Cases Missed On Physical Examination	Percentage Of Escaped Cases
1	Varicocele			
1 (A)	Left varicocele	195	54	28
1 (B)	Right varicocele	35	20	57
2	Epidydimal mass	10	6	60
3	Epidydimal cyst / spermatocele	36	17	48
4	Testicular focal mass	4	4	100
5	Testicular cyst	11	11	100
6	Testicular micro calcifications	8	8	100
7	Hydrocele	60	17	28
8	Scrotal pearls	29	27	93
9	Scrotal wall masses	5	2	40
10	Scrotal hernias	12	2	16
	Total abnormalities	405	188	

study by World Health Organization in late 1980's showed that in about 20% of infertility cases, the cause was predominantly in male partner, and in 27% abnormalities were found in both partners; therefore, a male factor is present in approximately 50% of infertility cases supporting the importance of workup for male infertility.[8]

Physical examination has been the mainstay in evaluation of scrotal contents in patients with infertility.[9] It is worth mentioning that the result of physical examination is directly dependent upon experience of the physician. Moreover, the condition of patient such as associated hydrocele, hernia and obesity as well as previous surgical history directly influence the physical examination findings. The examination by ultrasound in such cases may be of prime importance in the diagnosis of the underlying disease.[10]

Previous studies using ultrasound as a routine examination in men with infertility demonstrate 38 to 57% incidence of intrascrotal abnormalities, including many non-palpable lesions.[11,12,13] Pierik et al reported that 67% of intra-scrotal findings in a series using ultrasound were not observed on palpation.[11] In our study, intra-scrotal ultrasound abnormalities were found in 88.5 % of 350 men with infertility, whereas 188 (46.0%) out of 405 findings were not observed on palpation. As in previous reports, varicocele was the most frequent finding; however, other lesions including testicular microlithiasis, epididymal cysts were also reported in those studies[11,12,13] as in our study.

In our study most frequent finding is varicocele as reported by previous studies[11,12-13]. Significant number of cases were missed by palpation especially mild predominantly single vessel varicocele, which is a significant cause of subfertility as reported by Naryan et all 1981 in one of studies.[14] An improved detection rate of varicocele by use of sonography compared with palpations has been demonstrated by McClure & Hricake.[15]

In one study, the incidence of epididymal pathologies (cysts and masses) and testicular cysts as

a cause of infertility was found to be 0.7-1.1%[14,15]. This incidence is significantly lower as compared to our study where it was 13.14 %.

Other testicular parenchymal pathologies especially the tumours were all missed by palpation but were detected by ultrasound (4 cases in our study). The tumours are risk factor for subfertility as reported by previous studies.[16,17] Studies routinely using ultrasound in infertile populations show tumor incidence of 0.5-1.4%, higher than that seen in general population.[11,18]

Previous studies showed incidence of testicular microlithiasis ranging from 0.6-9.0 % in healthy population and 0.8-20 % in subfertile populations and 16.9-48.3% in patients with testicular tumors[19,20] while in our study physical examination could not pick up a single case of testicular microlithiasis while ultrasound was able to diagnose 8 cases.

The improved sensitivity of ultrasound to detect scrotal pathologies as well as hydrocele as a cause of infertility was well described by Pierik FH et al.[11]

CONCLUSION

As evident by our study there is improved detection of intrascrotal pathologies by ultrasound examination of scrotum as compared to physical examination only. These include testicular tumors, epididymal and testicular cysts, varicoceles, and hydroceles, emphasizing that scrotal doppler ultrasound should always be done in primary infertility cases for diagnosing intrascrotal pathologies.

DECLARATION

The authors do not have any conflict of interest to declare.

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ASSOCIATION OF SERUM CHOLESTEROL LEVELS WITH DECOMPENSATED CHRONIC LIVER DISEASE

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Abstract

Introduction: Cirrhosis, a sequel of chronic liver disease is a common and major cause morbidity and mortality in world. Hepatitis B and C are leading causes of chronic liver disease in Pakistan with prevalence of 3-4% and 5-7% respectively. Various studies were published in past to establish an association of serum cholesterol levels with chronic liver disease.

Objectives: To determine the frequency of decreased serum cholesterol in cirrhotic liver disease.

Study design: Cross-sectional descriptive study.

Setting: Medical wards of Services Hospital Lahore.

Duration of Study: 11-12-2015 to 11-06-2016

Material and Methods: 170 patients meeting the inclusion criteria were included in the study. Patients were sorted according to Child Pugh class. Variables of interest i.e. age, sex, cholesterol levels were recorded on a standard proforma.

Results: In this study there were total 170 subjects. Out of these 170, there were 90 (52.94%) males and 80 females (47.06%). The mean age was 49.06±5.38 years and mean cholesterol level was 173.84±33.95 mg/dl. There were 88 (51.76%) case in the age group of 40 to 49 years while 82 (48.24%) in 50 to 60 years. The majority of the cases in our study presented in Child Pugh class C, affecting 79 (46.47%) cases, followed by Class B and then Class A affecting 49 (28.82%) and 42 (24.71%) cases respectively. Decreased level of cholesterol was seen in 111 (65.29%) and 63 (37.06%) patients had it in the range of 150 to 200 mg/d. Decreased cholesterol level was maximally seen in Child Pugh class C where it affected 58 (73.42%) of cases in their respective group showing significant difference in contrast to other groups with p value of 0.002.

Conclusion: Liver cirrhosis in its decompensated stage can lead to a variety of complications. Its numbers are on the rise due to increased incidence of hepatitis C in developing countries like Pakistan. Majority of the cases are admitted with Child Pugh class C. Hypocholesterolemia is an important entity. Child Pugh class B and C are significantly associated with it.

Key words: Cirrhosis, hypocholesterolemia, Child Pugh class.

Decompensated liver disease represents the final common clinical pathway for a wide variety of chronic liver diseases. It is also termed as cirrhosis which was first introduced by Laennec in 1826. It is derived from the Greek term scirrhus and refers to the orange or tawny surface of the liver seen at autopsy.[1]

Cirrhosis is defined histologically as a diffuse hepatic process characterized by fibrosis and the conversion of normal liver architecture into structurally abnormal nodules. The progression of liver injury to cirrhosis may occur over weeks to years.

Indeed, patients with hepatitis C may have chronic hepatitis for as long as 40 years before progressing to cirrhosis.

Many forms of liver injury are marked by fibrosis, which is defined as an excess deposition of the components of the extracellular matrix (i.e., collagens, glycoproteins, proteoglycans) in the liver. This response to liver injury potentially is reversible. By contrast, in most patients, cirrhosis is not a reversible process.

In addition to fibrosis, the complications of cirrhosis include, but are not limited to, portal

hypertension, ascites, hepatorenal syndrome, hepatic encephalopathy and dyslipidemias.[1,2]

Often a poor correlation exists between the histologic findings in cirrhosis and the clinical picture. Some patients with cirrhosis are completely asymptomatic and have a reasonably normal life expectancy. Other individuals have a multitude of the most severe symptoms of end-stage liver disease and have a limited chance for survival. Common signs and symptoms may stem from decreased hepatic synthetic function (e.g., coagulopathy), decreased detoxification capabilities of the liver (e.g., hepatic encephalopathy), altered metabolism (dyslipidemia) or portal hypertension (e.g., variceal bleeding).[1-2]

METHODS:

It was a cross sectional descriptive study, conducted in medical wards of Services Hospital Lahore, from 11-12-2015 to 11-06-2016. 170 patients of decompensated chronic liver disease were enrolled in this study. Sampling technique used was non-probability consecutive sampling.

Inclusion Criteria:

• Patients between 40-60 years were included.

• Both males and females were included.

• Diagnosed patients of cirrhosis as per operational definition diagnosed at least 6 months ago. Cirrhosis was defined by abdominal ultrasonography (coarse echo texture liver) and any of the laboratory parameters (reversal of ALT/AST ratio, thrombocytopenia defined as platelets <50,000/mm³, raised INR>1.2 and low serum albumin=<3.5).

Exclusion Criteria:

Causes of cirrhosis with history of:

• Alcoholism

• Autoimmune hepatitis, primary biliary cirrhosis, primary sclerosing cholangitis.

• Metabolic causes (alpha 1 antitrypsin deficiency, Wilson's disease, and hemochromatosis).

• Other causes of dyslipidemia which included the following were excluded:

a. Diagnosed cases of hypertension (systolic BP of more than 140 mmHg and diastolic blood pressure more than 90 mm Hg.

b. Diagnosed cases of diabetes mellitus (fasting blood sugar of more than 7.1mmol/L).

c. Diagnosed cases of cardiovascular disease.

d. Diagnosed cases of cerebrovascular diseases.

e. Diagnosed case of kidney diseases.

f. History of lipid regulating drugs.

DATA COLLECTION PROCEDURE:

After approval of synopsis and informed consent, 170 patients fulfilling inclusion criteria were included in the study from medical wards of Services Hospital Lahore. All participants will be explained the purpose of study. All patients will be sorted according to Child Pugh class. All variables of interest i.e. age, sex, cholesterol levels were recorded on a proforma. Fasting lipid cholesterol levels were determined after overnight 12 hours fast. 3 ml of venous blood will be drawn under aseptic measures and was sent to institutes' laboratory. Decreased serum cholesterol levels were labeled as per operational definition (<200mg/dl).

DATA ANALYSIS:

The data collected was entered and analyzed by SPSS version 18. Mean with standard deviation was calculated for quantitative variables i.e. age, serum cholesterol levels. Categorical variables like gender, Child Pugh class and decreased cholesterol levels were presented as frequencies and percentages. Chi square test was used to compare the frequency of serum cholesterol level among Child Pugh classes and p-value of 0.05 was considered as significant.

RESULTS:

In this study there were total 170 subjects. Out of these 170, there were 90 (52.94%) males and 80 females (47.06%) as in figure 01. The mean age was 49.06±5.38 years with minimum of 40 years and maximum 60 (figure 02). The mean cholesterol level in this study was 173.84±33.95 mg/dl and minimum was 109 and maximum 238 as showed in table 05. Figure 02 shows that 88 (51.76%) cases were in the

age group of 40 to 49 years while 82 (48.24%) in 50 to 60 years. The majority of the cases in our study presented in Child Pugh class C where it affected 79 (46.47%) of the cases. It was followed by Class B and then Class A affecting 49 (28.82%) and 42 (24.71%) cases respectively (figure 04). Decreased level of cholesterol was seen in 111 (65.29%) of the cases in contrast to 59 (34.71%) of cases in which normal cholesterol levels were observed as in figure 05. Regarding cholesterol levels the maximum reported cases were seen in the range of 150 to 200 mg/dl which was noted in 63 (37.06%) of cases. It was followed by more than 200 mg/dl in 58 (34.12%) and then less than 150mg/dl in 49 (28.82%) cases (figure 06).

Decreased cholesterol level was maximum seen in Child Pugh class C where it affected 58 (73.42%) of cases in their respective group showing significant difference in contrast to other groups with p value of 0.002 (table 6).


Figure 02: *Age Distribution Of Study Subjects n=170*
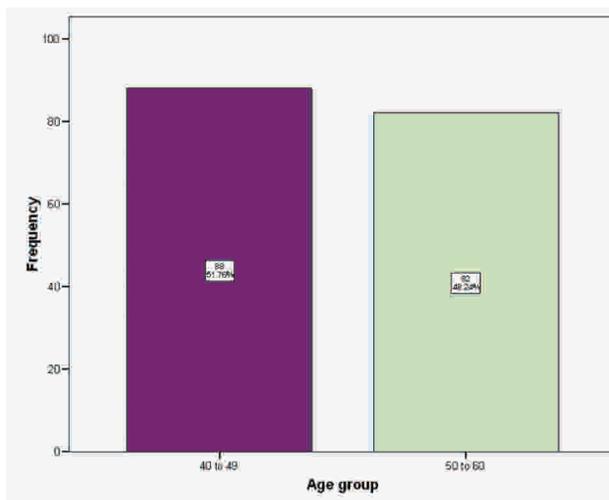
Figure 03: *Age Groups Of Study Subjects n=170*


Figure 01: *Gender Distribution of Study Subjects n=170*
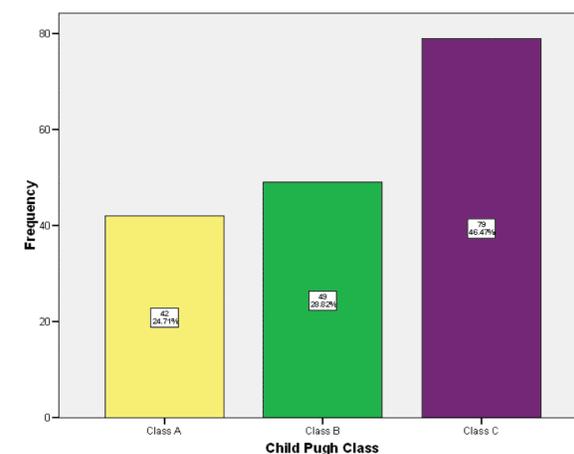
Figure 04: *Child Pugh Class Of Study Subjects n=170*
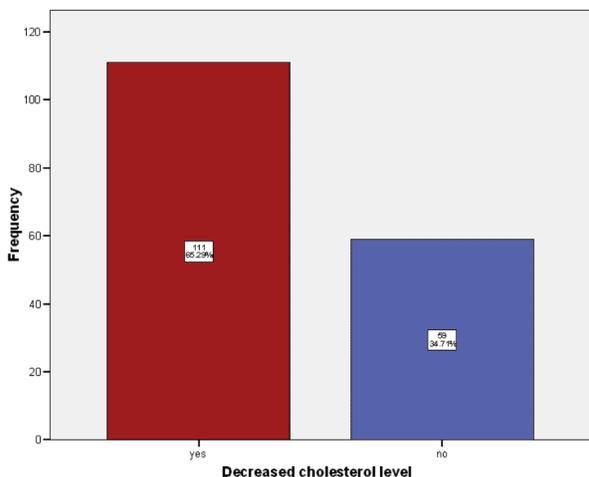
Figure 05: *Decreased Level Of Cholesterol In Study Subjects. n=170*
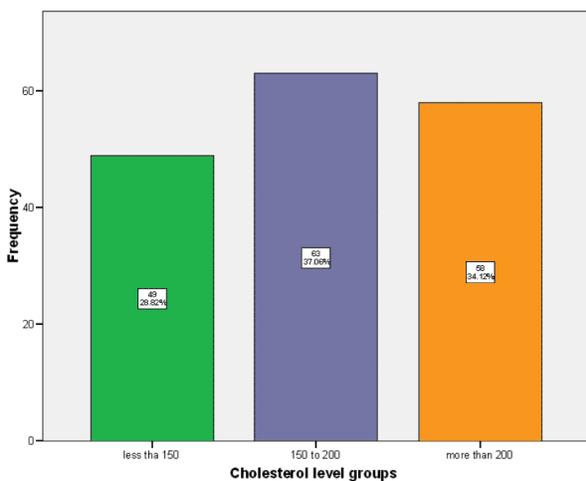
Figure 06: *Cholesterol Level Groups Of Study Subjects. n=170*

Table 1: *Child pugh class with Respect to Decreased Cholesterol. N=170*

Child Pugh Class	Decreased cholesterol		Total
	Yes	No	
Class A	18 (42.86%)	24 (57.14%)	42
Class B	35 (71.43%)	14 (28.57%)	49
Class C	58 (73.42%)	21 (26.58%)	79
Total	111 (65.29%)	59(34.71%)	170 (100%)

Chi-Square=12.45   p=0.002

DISCUSSION

The liver plays a crucial role in the synthesis, secretion, catabolism, and storage of lipids and lipoproteins. Therefore, the serum lipids and lipoproteins concentrations in liver diseases could be changed. Generally, the level of plasma lipids and lipoproteins tends to decrease with the severity of liver disease. However, the results of these studies were not the same. The reason for the discrepancy of the results could be the different etiology of liver injury. There is no information if alcoholic and nonalcoholic liver cirrhosis equally affect the lipids metabolism. It has been known that the major effects of high alcohol consumption on lipids metabolism are the excessive synthesis of triglycerides, hyper-triglyceridemia and hypercholesterolemia, defective esterification of plasma cholesterol, and decreased level of high-density lipoprotein cholesterol as compared to other pathologies leading to decompensated liver disease which may have resulted in lower levels of various lipids like cholesterol.

There was almost equal distribution of male and females in this study affecting 90 males and 80 females out of total 170 with slight male dominance. The similar higher number of males was also noted by Ooi K, Selimoglu MA and Baraona E et al who also observed this ranging from 1.3:1 to 2:1 with higher male number.[3-5] Why this number was high in their studies as compared to ours? It might be due to a higher rate of alcoholism in their region which was not common in our region and it was also excluded in this study.

The majority of the cases in our study presented in Child Pugh class C where it affected 79 (46.47%) of the cases. It was followed by Class B and then Class A affecting 49 (28.82%) and 42 (24.71%) cases respectively. Similar trends were seen in other studies done by Seidel D et al Cicognani C et al, Ghadir M et al and Irfan S et al who also found higher number in class C as compared to either class B or A.[6-9] Why the most cases presented in higher Child Pugh class is because, patients usually report to hospital when more symptomatic hence falling in higher scores. Secondly majority of these studies were done on indoor patients which obviously are suffering from severe disease hence raising the number of Child Pugh class C.

However, Burroughs AK and Goldeberg E et al

found relatively higher number in class B.[10-11] although there was not much difference in class B and C in their group again reflecting the pathophysiology that higher the severity of disease and higher are the chances to report.

On stratification of the different Child Pugh class groups it was seen almost equally in both the gender except slight higher male count in Class B affecting 27 (55.10%) cases, although this difference was not found statistically significant with p value of 0.89. Similar findings were observed by Siagris D and Burroughs et al who also had equal distribution of genders in different Child Pugh classes.[10,12]

On stratification of different age groups there was almost similar percentages in all the age groups with a slight higher number was seen in age group of 40 to 49 presenting in Class A with 24 (57.14%) cases. Moreover considering the other groups, there was either equal distribution or more number seen in age group of 51 to 60 years. This difference was not significant (p= 0.62). Other studies conducted by Roesch DF and Shimizu H et al also found it in age groups younger than 50 years but they included even younger patients as compared to this study starting from the age group of 15 years.[13,14] But they also did not find any significant association. Why this difference was not found significant, and why the younger patients had class A. This might be because as this decompensation is a chronic process, so younger patients presented with early stage like class A. Secondly at relatively younger ages the co-morbids are also at lower side so this might be the reason for a marginal higher number with milder disease.

Decreased cholesterol level was seen in all the classes of decompensated liver disease to different extent. It was noted that maximum seen in Child Pugh class B and C where it affected more than 70% each in their respective groups with significant p value of 0.002. These findings were seen similarly in other studies conducted by Irshad M et al and Siagris D et al who also found significant reduction in the cholesterol level.[12,15] However there was a slight

change in the cut off values in their studies but yet they found significant association. This reflects the pathophysiology of the disease process as the liver is decompensated; it is not able to effectively participate in the metabolism of the lipids leading to decreased level of it. This again was reinforced by the fact that higher the Child Pugh class and higher are the chances of its lower levels as seen in this study with maximum in Child Pugh Class C 73.43% then B 71.43% and then in A 42.86%. Similar findings were observed by the study conducted by Ghadir M et al who noted that higher the degree of Child Pugh Class and higher are the chances to lower levels of all the lipids along with the cholesterol level.[8] A study done by Irfan S et al at Bahawalpur even showed this derangement in 100% of the cases presenting in Child Pugh Class C.

A very higher percentage in contrast to other classes were observed with 33 (67.35%) of cases in their respective group in Class C where they had cholesterol level less than 150 mg/dl with a very high significance of 0.001. A study conducted by Mehboob F et al also revealed a very significant association of this cholesterol level with advanced disease where they found about 79.41% of the cases with cholesterol level of 100-150mg/dl as compared to other groups who had even less than 10% of the cases involved.[16] This was also noted by Rubbia-Brandt L et al and Jarmay K et al who also had found it but there difference was not found significant.[17,18]

There were few limitations of this study as it checked only for the cholesterol level and not the other lipid profile which are also likely to be disturbed in decompensated disease. Secondly all other effect modifiers i.e. comorbids in the form of DM, HTN, renal or cardiac disease were ruled out which should have been studied.

There were many strengths of the study too. It was a good sample sized study. Moreover, hypo-cholesterolemia is an under rated entity and not much work was done before in this context in Pakistan.

CONCLUSION

Liver cirrhosis in its decompensated stage can lead to a variety of complications. Its numbers are on the rise due to increased incidence of hepatitis C in developing countries like Pakistan. Majority of the cases are admitted with Child Pugh class C. Hypocholesterolemia is an important entity. Child Pugh class B and C are significantly associated with it.

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FREQUENCY OF PREDIABETES IN PATIENTS INFECTED WITH HEPATITIS C VIRUS

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Abstract

INTRODUCTION: Prediabetes as a proxy for insulin resistance is a predictor for success of interferon in treatment for chronic hepatitis C. Burden of prediabetes in patients with hepatitis C virus infection may help in tailoring therapy on an individual basis.

OBJECTIVE: To determine the frequency of prediabetes in patients with hepatitis C virus infection.

STUDY DESIGN: Cross Sectional survey

STUDY SETTING: The study was conducted in medical outpatient department, Services Hospital, Lahore.

DURATION OF STUDY: Six months from 9th May 2014 to 8th November 2014.

MATERIALS & METHODS: 181 patients with Hepatitis C virus infection without any sign of decompensation were included in the study. Patients were screened for prediabetes and checked for glucose intolerance. Body mass index was measured and BMI > 24.9kg/m2 was used as an effect modifier.

RESULTS: Mean age of patients was 40.4 ± 2.7 years. 54.1% were below 40 years of age. 83 patients (45.9%) were male and 28.7% were female. 12 (6.6%) had BMI >24.9kg/m2 while rest (93.4%) were not obese. 28 (15.5%) had prediabetes. Prediabetes was significantly associated with female gender and obesity.

CONCLUSION: It is concluded that prediabetes in chronic hepatitis C patients was found in 28 (15.5%) individuals among the sampled population in the study.

KEYWORDS: prediabetes, insulin resistance, interferon therapy, chronic Hepatitis C.

Globally 150 million people are suffering from hepatitis C Viral (HCV) infection and 350,000 people die from HCV related complications every year.[1] HCV infection is nowadays recognized as a disease of global importance and available data suggest that the prevalence of HCV infection is approximately 2.2–3.0% worldwide with the highest prevalence in the African and the Eastern Mediterranean region where Pakistan[1] and Egypt share the major chunk.[1-3] Diabetes is also very common globally[4] showing prevalence about 16.68% in males and 19.37% in females in Pakistan[5] quite different from world which was projected to be 7.7% by 2030.[4]

Prediabetes and HCV coexist with different age and gender distribution in different geographical areas.[6] This double burden of disease is a new phenomenon seen in developing countries now days. Same holds true for simultaneous presence of prediabetes in patients with chronic hepatitis C virus infection.[7]

In a Japanese study the prevalence of prediabetes in chronic hepatitis C patients came out about 13.6% showing almost double the rate present in non HCV healthy population.[8]

HCV is able to induce insulin resistance directly and has consistently been found to be closely linked to fibrosis in HCV infection.[9] Severe fibrosis is more likely in diabetic patients than those with no diabetes.[6] Insulin resistance may promote hepatic fibrosis in chronic hepatitis C and has emerged as a cofactor in failure to achieve sustained viral response (SVR).[10]

There is scarce local data available showing the coexistence of prediabetes and hepatitis C Virus (HCV) infection in our population. It is not our routine practice to screen every patient with HCV for prediabetes. As outcome of treatment depends highly on co existing prediabetes or diabetes, 7 local prevalence of prediabetes in HCV patients is essential to be known. Our population differs from

others in circulating genotype6 and sedentary lifestyle[3]. The rationale of my current study is that it will help devise some screening guidelines for all patients presenting to our hospitals as early detection of prediabetes in Hepatitis C can lead to early intervention with significant positive impact on two main things. Firstly, early detection of prediabetes in HCV patients may help us to control diabetes before its complication. Secondly it will help us to predict the success of antiviral therapy to attain sustained viral response.

METHODS

SETTING:

Medical outpatient department, Services Hospital, Lahore

DURATION:

Study was completed in six months from 9th May 2014 to 8th November 2014.

STUDY DESIGN:

Cross Sectional survey

SAMPLE SIZE:

Taking frequency of prediabetes among chronic hepatitis C 13.6% 7 and acceptable difference of 5%, required sample size is 181.

SAMPLING TECHNIQUE:

Non-probability purposive sampling.

INCLUSION CRITERIA

• Age: 18-60 years

• Either sex

• Patients with Hepatitis C virus defined as patients with positive qualitative polymerase chain reaction for HCV RNA

• Never diagnosed as diabetic or glucose intolerant determined by history

• No sign of decompensation i.e. history of hematemesis, ascites and splenomegaly (by ultrasonography) and hypoalbuminemia by chemical auto analyzer

EXCLUSION CRITERIA

• Body mass index (BMI) more than 35 kg/m²

• Relapse of HCV infection due to failed inter-feron treatment determined by history

• History of chronic kidney disease determined by serum creatinine and BUN

• Any other connective tissue disorder like rheumatoid arthritis and SLE determined by history.

DATA COLLECTION PROCEDURE

After approval of synopsis and informed consent, 181 patients according to selection criterion were included in the study from medical OPD of Services Hospital Lahore. All participants were explained the purpose of study. All variables of interest like age, sex, BMI and fasting & post glucose level were recorded on a standard questionnaire. Prediabetes was determined as per operational definition (if 8 hours fasting blood sugar levels were impaired i.e. between 100 to 126 mg/dl on two separate occasions 24 hours apart and was confirmed if blood sugar level came 140 to 200 mg/dl two hours after administration of 75g oral glucose solution) after administration of 75g glucose in solution form by standardized calorimetric method. Under aseptic conditions 3ml venous blood was drawn by phlebotomy and sent immediately to laboratory. Body mass index was measured and BMI $> 24.9 kg/m^2$ was used as effect modifier i.e. data was stratified for obese and non-obese.

DATA ANALYSIS

Data collected was entered and analyzed in the SPSS version 17. Mean with standard deviation was calculated for quantitative variables like age, weight, body mass index and blood glucose level and frequency and percentages in case of categorical variables like gender and prediabetes. Data was stratified by age, gender and BMI to determine the effect modification. Post stratification chi square test was applied. A p value <0.05 was considered significant.

RESULTS

Mean age was 40.4 ± 2.7 years ranging from 35-45. (Table I) 54.1% were below 40 years of age while

rest were above 40 years. (Table II). 181 patients according to inclusion criteria were included in the study 83 (45.9%) were male while rest (54.1%) were female. (Table III). 12 patients (6.6%) had BMI > 24.9kg/m² while rest (93.4%) were not obese. (Table IV). 28 (15.5%) had prediabetes according to operational definition while rest (84.5%) were free from prediabetes. (Table IV).

When we cross tabulated the age groups with prediabetes, we found a non-significant difference (p= 0.632, Table VI). When we cross tabulated the sex of respondents with prediabetes, we found a significant difference (p= 0.04, Table VII). 20.4% were female with prediabetes as compared to 9.6% male.

When we cross tabulated the obesity (Body mass index >24.9kg/m2) with prediabetes, we found a highly significant difference (p= 0.001, Table VIII).

Table 1: *Age Distribution of Sampled Population*

	N	Minimum	Maximum	Mean	Std. Deviation
Age	181	35	45	40.45	2.725

Table 2: *Frequency Distribution of Sampled Population by Age Groups*

	Frequency	Percent	Valid Percent	Cumulative Percent
Below 40 Years	98	54.1	54.1	54.1
40 Years & above	83	45.9	45.9	100.0
Total	181	100.0	100.0	

Table 3: *Frequency Distribution of Sampled Population by Sex*

	Frequency	Percent	Valid Percent	Cumulative
Male	83	45.9	45.9	45.9
Female	98	54.1	54.1	100.0
Total	181	100.0	100.0	

Table 4: *Frequency Distribution of Sampled Population by Prediabetes*

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	No	153	84.5	84.5	84.5
	Yes	28	15.5	15.5	100.0
	Total	181	100.0	100.0	

Table 5: *Frequency Distribution of Sampled Population by Body Mass Index >24.9kg/m²*

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	No	169	93.4	93.4	93.4
	Yes	12	6.6	6.6	100.0
	Total	181	100.0	100.0	

Table 6: *Crosstab between Age Groups & Prediabetes*

Age groups		Prediabetes No	Prediabetes Yes	Total
40 Years & above	Count	69	14	83
	% within Age groups	83.1%	16.9%	100.0%
Below 40 Years	Count	84	14	98
	% within Age groups	85.7%	14.3%	100.0%
Using chi square test, p value =.632 (Non-significant)				

Table 7: *Crosstab between Sex & Prediabetes*

Sex		Prediabetes No	Prediabetes Yes	Total
Female	Count	78	20	98
	% within Age groups	79.6%	20.4%	100.0%
Male	Count	75	8	83
	% within Age groups	90.4%	9.6%	100.0%
Using chi square test, p value =.04 (significant)				

Table 8: *Crosstab between Body Mass Index > 24.9kg/m² & Prediabetes*

Body mass index >24.9kg/m²		Prediabetes No	Prediabetes Yes	Total
Yes	Count	0	12	12
	% within Age groups	0.0%	100.0%	100.0%
No	Count	153	16	169
	% within Age groups	90.5%	9.5%	100.0%
Using chi square test, p value< 0.001 (significant)				

DISCUSSION

Hepatitis C virus (HCV) infection is associated with insulin resistance (IR) and subsequent poor response to antiviral therapy.[2] The clinical relevance of prediabetes in Hepatitis C virus arises from its ability to promote hepatic inflammation and fibrosis and to impair response to antiviral therapy. Several studies are focused on the relationship of insulin resistance and chronic hepatitis C (CHC). Different lines of evidence have found that IR is a common feature in patients with CHC.[3-5]

In our study, 28 patients (15.5%) had prediabetes according to operational definition while rest

(84.5%) were free from prediabetes. This is quite high prevalence showing the need to screen all patients with Hepatitis C virus infection to undergo screening for glucose intolerance and prediabetes. We may tailor antiviral therapy according to needs of individual patients.

Our results are comparable with previous studies. In a Japanese study the prevalence of prediabetes in chronic hepatitis C patients came out about 13.6% showing almost double the rate present in non HCV healthy population.[8]

Although Diabetes is very common globally showing a stage of global pandemic.[4] Excess prevalence i.e. almost double the projected (7.7% by 2030) shows association of Hepatitis C virus infection with development of prediabetes.[4]

Among included 181 patients, 83 (45.9%) were male while rest (54.1%) were female. It implies that female were more in our sampled population showing that it may be due to health seeking behavior or change in pattern for seeking advice in our sampled population but on the other hand they are more at the risk of contracting this disease by obstetric surgeries, by infected blood transfusion etc.[5,8]

The patients without prediabetes are more likely to achieve early viral response patients and subsequently sustained viral response at 6 months.[9]

When we cross tabulated the age groups with prediabetes, we found a non-significant difference (p= 0.632). The age of a patient is a common risk factor for developing prediabetes. Non-significant association may be due to younger population in our study sample. Mean age was 40.4 ± 2.7 years ranging from 35-45 years. 54.1% were below 40 Years of age while rest were above 40 Years.

Then we stratified the patients for gender and when cross tabulated the gender with prediabetes we found that there is a difference in prevalence of prediabetes among male and female patients. (p= 0.04, Table VII).

20.4% were female with prediabetes as compared to 9.6% male. The reason may be obesity, poor and sedentary life style along with malnutrition.

To determine the effect of obesity among patients with Hepatitis C virus infection, we stratified data for Body mass index $>24.9 kg/m^2$. When we cross tabulated the obesity (Body mass index $> 24.9 kg/m^2$) with prediabetes, we found a highly significant difference (p= 0.001). All obese patients had prediabetes. A preventive program may help reduce the double burden of disease i.e. prediabetes and Hepatitis C virus infection.

CONCLUSION

It is concluded that prediabetes in chronic hepatitis C patients was found in 28 (15.5%) individuals among the sampled population in the study. Prediabetes was found associated with female gender and obesity (Body mass index $>24.9 kg/m^2$). Further studies should be encouraged in this regard.

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FREQUENCY OF METABOLIC SYNDROME IN PATIENTS PRESENTING WITH CARDIAC SYMPTOMS AND MEAN SERUM GAMMA-GLUTAMYLTRANSFERASE IN PATIENTS WITH OR WITHOUT METABOLIC SYNDROME

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Abstract

Background: Metabolic Syndrome (MetS) is a complex disorder defined by a cluster of interconnected factors that increase the risk of cardiovascular diseases. Serum gamma-glutamyltransferase (GGT) plays a key role in the gamma-glutamyl cycle, a pathway for synthesis and degradation of glutathione and xenobiotic detoxification.

Objective: To assess the frequency of MetS in patients presenting in a tertiary care hospital with cardiac symptoms and to compare the mean serum gamma-glutamyltransferase (GGT) in patients with or without MetS.

Study Design: Cross sectional.

Setting: Medical Unit II, Department of Medicine, DHQ Hospital, Gujranwala.

Duration of study: 6 months from 05-10-2016 to 05-04-2017.

Methods: 130 patients were enrolled in this study according to inclusion criteria. Informed consent and demographic information was obtained. After evaluation, frequency of MetS was assessed and two groups were formed i.e. group I with MetS and group II without MetS. Serum GGT level was assessed in both groups. Data was entered and analyzed on SPSS version 21.

Results: The mean age of the patients was 58.40±15.68 years; male to female ratio of the patients was 1.5:1. The patients with MetS were 36.15% (n=47). Statistically significant difference (P-value=0.000) was found between the GGT levels in patients with MetS.

Conclusion: The frequency of MetS in cardiac patients was 36.15%, and the patients with MetS had significantly higher level of GGT as compared to patients without MetS.

Keywords: *MetS, Gamma-Glutamyltransferase.*

MetS is a syndrome described as a constellation of interrelated factors that increase the hazard of cardiovascular atherosclerotic diseases and type 2 diabetes mellitus.[1] In Pakistan, the incidence of MetS is approximately 63.7%, much less than figures quoted in India i.e. 73.3%.[2,3]

MetS stimulates coronary heart disease through multiple mechanisms. The thrombogenicity of circulating blood is increased partly by increasing plasminogen activator type 1 and adipokine levels, and triggering endothelial dysfunction. It may also raise the risk of coronary heart diseases by increa-

sing arterial stiffness. Further mechanisms include oxidative stress, which has been linked with numerous constituents of MetS.[4,5] In a study, it was stated that in patients exhibiting cardiac symptoms, 9.2% had MetS.[6]

Serum gamma glutamyltransferase (GGT) is an enzyme existing in serum and most cell surfaces. It is considered an oxidative stress marker. Increased serum GGT levels are associated with the development of hypertension. GGT may also contribute in the pathogenesis of cardiovascular disease, diabetes mellitus, obstructive sleep apnea syndrome, and

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MetS.[7]

GGT is an inexpensive, highly-sensitive and dependable laboratory test which is often used as a marker of hepato-biliary dysfunction and alcohol and as a diagnostic tool in many conditions. Recently, GGT has been shown to have an active role in oxidative and inflammatory mechanisms, and thus it can be used as a biomarker to determine risk for cardiovascular diseases and MetS.[8]

An increase in serum GGT predicts the start of MetS, occurrence of cardiovascular disease, and death suggesting that GGT is an important marker of metabolic and cardiovascular risk.[9] In a study, conducted by Bozbas et al., it was reported that in MetS patients (n=117), the mean GGT level was 21 (16-33)U/l (21±4.25U/l), whereas mean GGT value in patients without MetS (n=115) was 19 (14-26)U/l (19±3U/l), P-value=0.008.[10] This seems that whether an individual has MetS or not, there may be not much effect on GGT level as the level in MetS patients was in normal range. However, another study, conducted by Suma et al., showed that in MetS patients (n=30), the mean GGT level was 59.23±67.75U/l, which was significantly higher than without MetS (n=30) i.e. 23.53±5.27U/l, P-value<0.01.[11]

The rationale of this study is to compare the mean GGT in patients with or without MetS. Raised GGT is usually associated with cardiovascular events, as in cases with cardiovascular event, GGT is usually found to be raised. MetS is a leading factor of cardiovascular events and addition of raised GGT may also accelerate the development of atherosclerosis and lead to cardiac events. Literature has reported that the level of GGT does not vary very much whether patients develop MetS or not. But contradiction has also been reported in literature. So, it is important to know whether GGT level is high in MetS patients in our local population as there is no local data is deficient. Results of this study will help to improve our knowledge and practice and will guide the physicians to observe and manage the patients accordingly as raised GGT level may lead to more severe consequences like cardiac events including heart failure and increased mortality.

METHODS

It was a cross sectional study conducted in Medical Unit II, Department of Medicine, DHQ Hospital, Gujranwala. It was conducted over a period of 6 months from 05-10-2016 to 05-04-2017. 130 patients were included in the study. Sampling technique used was non-probability, consecutive sampling. Inclusion criteria

Patients of age 30 – 80 years of either gender, presenting with chest symptoms within last 24 hours
Exclusion criteria

- Patients with liver problems (AST> 40IU, AST> 40IU), renal problems (serum creatinine > 1.2gm/dl), taking barbiturates or phenytoin (as per medical record).

- Patients with history of smoking and alcohol abuse, Hepatitis B or C (as per medical record)

Data Collection

130 patients fulfilling the inclusion criteria were selected from OPD of Department of Medicine, DHQ Hospital, Gujranwala. Informed consent was obtained. Demographic information (name, age, gender) was also obtained. Then patients were evaluated for presence or absence of MetS. After evaluation, frequency of MetS assessed and two groups were formed i.e. group I with MetS and group II without MetS. Then blood sample was drawn from each patient through a BD syringe with the help of a staff nurse under aseptic measures. All samples were stored in a vial containing Ringer's solution. Samples were sent to the laboratory of the hospital for assessment of GGT level and GGT level was recorded.

Data Analysis

The collected information was entered into SPSS version 21.0 and analyzed. Quantitative variables like age, BMI, duration of cardiac symptoms and GGT level were calculated as mean & standard deviation. Qualitative variable like gender and MetS were calculated as frequency and percentage. GGT

levels were compared in patients with or without MetS. Independent t test was applied. P-value< 0.05 was considered as significant. Data was stratified for age, duration of cardiac symptoms, gender (male/female) and BMI. Post-stratification, chi-square for MetS and independent sample t-test was applied to control effect modifiers.

RESULTS

The mean age of patients with MetS was 58.40±15.68 years and mean age of patients without MetS was 54.72±14.03 years (Table1). The male to female ratio of the patients was 1.5:1. Gender distribution is depicted in Fig. 1. Descriptive statistics of BMI is illustrated in Table 2. Frequency distribution of MetS is shown in Fig. 2. Descriptive statistics of GGT level is illustrated in Table 3. Values of GGT in patients with and without MetS are shown in table 4. Statistically significant difference was found between the GGT levels with MetS i.e. P-value= 0.000. Table 5 depicts the relation of age with MetS. Statistically insignificant difference was found between the age with MetS i.e. P-value= 0.373. Relation of gender and MetS is depicted in table 6. Statistically insignificant difference was found between the sex with MetS i.e. P-value= 0.233. Table 7 depicts the relation between BMI and MetS. Statistically significant difference was found between the MetS with BMI i.e. p-value=0.000. Table 8 illustrates the relation of age, sex and BMI with GGT levels. Statistically significant difference was found between the GGT levels with BMI i.e. p-value= 0.000.
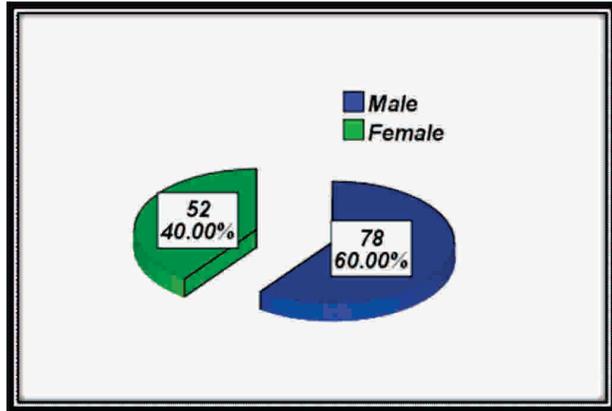
Fig 1: *Frequency Distribution of Gender*

Table 2: *Descriptive statistics of BMI (Kg/m^2)*

	n	130
	Mean	24.29
BMI (Kg/m^2)	SD	4.46
	Minimum	18.50
	Maximum	35.02
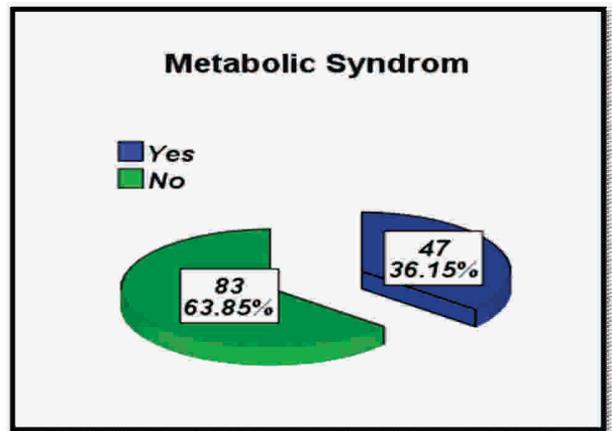
Fig 2: *Frequency Distribution of MetS*

Table 3: *Descriptive Statistics of GGT*

	n	130
	Mean	20.69
GGT	SD	6.611
	Minimum	10
	Maximum	35

Table 1: *Descriptive Statistics of Age (Years)*

		MetS	
		Yes	No
	n	47	83
Age (years)	Mean	58.40	54.72
	SD	15.68	14.03

Table 4: *Comparison of GGT with MetS*

		MetS	
		Yes	No
	n	47	83
GGT	Mean	26.15	17.60
	SD	6.24	4.49

Ind. t test=9.023
P-value=0.000*

Table 5: *Comparison of age with MetS*

		MetS		Total
		Yes	**No**	
Age (years)	**50**	15	33	**48**
	> 50	32	50	**82**
Total		**47**	**83**	**130**

Chi value=0.793
P-value=0.373

Table 6: *Comparison of Gender with MetS*

		MetS		Total
		Yes	**No**	
Sex	**Male**	25	53	**78**
	Female	22	30	**52**
Total		**47**	**83**	**130**

Chi value=1.42
P-value=0.233

Table 7: *Comparison of BMI with MetS*

		MetS		Total
		Yes	**No**	
BMI	**Underweight**	0	3	**3**
	Normal	0	78	**78**
	Overweight & Obese	47	2	**49**
Total		**47**	**83**	**130**

P-value=0.000

Table 8: *Comparison of Age, Sex and BMI with GGT Level*

GGT level		Mean	SD	P-value
Age (years)	**50**	20.79	6.56	**0.896**
	> 50	20.63	6.67	
Sex	**Male**	20.69	6.39	**1.000**
	Female	20.69	6.98	
BMI	**Underweight**	18.00	3.61	**0.000**
	Normal	17.56	4.56	
	Overweight &obese	25.84	6.34	

DISCUSSION:

This cross sectional study was conducted in Medical Unit II, Department of Medicine, DHQ Hospital, Gujranwala to assess the frequency of MetS in patients presenting in a tertiary care hospital with cardiac symptoms and the mean serum GGT in patients with or without MetS.

MetS is a complex of metabolic abnormalities that escalates the risk of cardiovascular diseases, diabetes mellitus and future athero-thrombotic events. Prevalence of MetS is on the increase world-wide also referred to as the insulin-resistance syndrome, syndrome X, and the deadly quartet. It has generated significant scientific interest in the past few decades. GGT is considered a marker of oxidative stress, fatty liver disease and alcohol consumption and it may be directly involved in the production of reactive oxygen species.[12]

In our study, the patients with MetS were 47(36.15%). The mean value of GGT level was 20.69±6.611U/L. This study elucidates that the mean value of GGT level in patients with MetS was 26.15±6.24U/L and its mean value in respondents without MetS was 17.60±4.49U/L. Statistically the patients with MetS had significantly higher level of GGT as compared to those without MetS patients i.e. P-value=0.000. A study by B. Kasapoglu et al.[13] presented a significant relationship between elevated GGT levels and MetS after adjustment for age, sex and BMI. In multivariance analysis, in MetS group, a high GGT was positively associated with cardiovascular disease prevalence (odds ratio: 2.011, 95% CI 1.10 - 4.57) compared to low GGT group independent of age, sex and smoking habits.

In adults, serum GGT levels are closely related with the increased number of the patients with MetS.[14] In a study, conducted by Bozbas et al., it was reported that in MetS patients (n=117), the mean GGT level was 21 (16-33)U/l (21±4.25U/l), which was significantly higher than without MetS (n=115) i.e. 19 (14-26)U/l (19±3U/l), p-value=0.008.10

Liu CF et al. (2012)15 conducted a meta-analysis of prospective cohort studies to systematically evaluate the exact relationship between GGT and risk of MetS. Results showed that GGT levels were positively associated with risk of MetS independently of alcohol intake. Similar results were observed by Kawamoto R et al. (2009)16 and Oda E et al. (2009)[17] in Japanese men and women.

Another study, conducted by Suma et al., illustrated that in MetS patients (n=30), the mean GGT level was 59.23±67.75U/l, which was notably higher than without MetS (n=30) i.e. 23.53±5.27U/l, p-value<0.01.[11]

Rantala et al. investigated the relationship between GGT and MetS and pointed out a highly significant relationship between GGT and the components of the MetS even after adjustment for age, body mass index and alcohol consumption.[18]

In another study of Sakugawa et al.[19], the serum GGT level was found to be correlated with components of MetS. Although this association between GGT and MetS is not clearly understood, some epidemiological studies[20] also advocate that higher serum GGT levels is associated with development of cardiovascular disease risk factors, including diabetes, hypertension, and the MetS. Prospective

studies have shown that high levels of GGT are an independent risk factor of MetS, diabetes and cardiovascular disease.[20-23]

CONCLUSION

According to this study the MetS was present in 36.15% patients presenting with cardiac symptoms, and it has been concluded in this study that the patients with MetS had significantly higher level of GGT as compared to without MetS patients.

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DIAGNOSTIC ACCURACY OF ULTRASOUND IN THE DIAGNOSIS OF INTUSSUSCEPTION IN CHILDREN

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Abstract

Objectives: To evaluate the diagnostic accuracy of ultrasound in the diagnosis of Intussusception in suspected children, taking operational findings as gold standard

Materials & Methods: 113 children with age <5 years of both gender having clinical features suggestive of intussusception were included in the study. Patients with history of previous surgery, patients with stomas, patients with known congenital intestinal anomalies and haemodynamically unstable patients were excluded. All these patients were undergone Ultrasonography abdomen and pelvis for evaluation of intussusception. The sonographic findings were recorded as positive and negative for intussusception. The criteria for positivity included visualization of target or doughnut sign on transverse view and the "pseudo kidney sign" in longitudinal view. Then all these patients have undergone Diagnostic laparoscopy and or exploratory laparotomy and intra-operative findings were recorded and correlated with ultrasonography.

Results: In this study age was ranges from 0 to 5 years with mean age of 01 ± 1.15 years. Out of these 113 patients, 69.02% were male and 30.98% were females with ratio of 2.2:1. Majority of patients 51.33% and 46.02% presented with bilious vomiting and intermittent screaming (abdominal pain) respectively. Ultrasound supported the diagnosis of intussusception in 76 (67.26%) patients. Operative findings confirmed intussusception in 79 (69.91%) cases whereas 34 (30.01%) patients revealed no intussusception. There was one false positive and four false negative results on ultrasonography. The sensitivity, specificity, positive predictive value, negative predictive value and diagnostic accuracy of grey scale ultrasonography in intussusception in children were 94.94%, 97.06%, 98.68%, 89.19% and 95.57% respectively.

Conclusion: This study concludes that ultrasonography (USG) is cost effective, non invasive and the imaging modality of choice with high sensitivity and specificity in diagnosing intussusception in children.

Keywords: *Intussusception, Ultrasonography, Diagnostic Accuracy.*

Intussuception is the invagination of a segment of the intestine (intussusceptum) into adjacent segment of intestine (intussuscipiens). The intussusceptum is composed of an inner wall and an outer wall.[1]

Intussuception is a common surgical emergency in children, according to recent review of World Health Organization (WHO) in developed countries, the baseline incidence of intussusception is between 0.5 and 4.3 cases per 1,000 live births or 0.7–1.2 cases per 1,000 children aged less than one year.[2] Accurate estimates of the incidence of intussusception in developing countries are not available.[3] Intussusception is seasonal, in UK commonly occur during late spring and autumn.[4]

Intussusception (IS) was first reported in 1674 by Barbette of Amsterdam.[5] In childhood intussusception is idiopathic in 90% of cases.[6] In the remaining 10%, it is secondary to a pathological lead point such as Meckel's diverticulum, polyp, enteric duplication cyst and small bowel lymphoma, etc.[12,14] The first successful operative reduction was reported

by Hutchinson in 1873.[7]

Clinical presentations of intussusception may include crying episodes, abdominal pain, bilious vomiting, and lethargy. "Currant jelly" stools, a late finding and marker for bowel ischemia, is observed in some cases.[8]

There are four types of intussusception; ileo-colic, ileo-ileo-colic, colo-colic and small bowel intussusception (jejuno-jejunal and ileo-ileal). Ileo-colic intussusception is the most common type, > 80% of cases in children.[9]

Intussusception is a rare disease. Due to delay in diagnosis, intussusception related mortality in the developing countries is higher as compared to the developed countries.[8] It can be diagnosed by history, clinical findings, ultrasonography, contrast studies (barium enema, air enema) and computed tomography.

With recent advancement in ultrasound technology (improved scanner technology and high-resolution transducers has provide image data of high temporal and spatial resolution), ultrasonography has been widely used in the diagnosis of gastrointestinal lesions. Ultrasonography has the advantage of being cheap, non invasive, portable, flexible and user- and patient-friendly.[10,11]

The sensitivity and specificity of ultrasound to diagnose intussusception in children has been reported as 93% and 99% respectively in tertiary care settings of developed countries.[12]

On USG the components of an intussusception produce characteristic appearances. In transverse section multiple alternating hyperechoic and hypo-echoic layers owing to the presence of three over-lapping mucosal and muscular layer of intussuscipiens (distal segment) and Intussusceptum (proximal segment) are seen, may described as "doughnut or target sign". In longitudinal section the mass is roughly ovoid in shape, with different tissues appearing layered longitudinally appeared like a sandwich may described as "pseudokidney sign". Enlarged lymphoid tissue or lymph nodes may be seen within the mass in transverse or longitudinal

section. Occasionally pathological lead points are also identified using this modality.[13]

In children, the primary method of treatment is hydrostatic or pneumatic reduction of the intussusception under radiologic control. However, pneumatic reduction should never be attempted where the bowel is necrotic or perforated. Prediction of bowel viability and reducibility is very important.[17] Ultrasound also plays a role in the evaluation of reducibility of intussusceptions, there are definite signs on US (trapped fluid and the absence of blood flow at Doppler imaging) that will influence non-operative management (i.e., hydrostatic or pneumatic reduction) and could lead to improved prognosis and timing for surgical intervention.

Methods:

This Cross-sectional study was conducted at Department of Radiology, Bahawal Victoria hospital, Bahawalpur. The calculated sample size was 113 cases with 5% margin of error, 25% prevalence of intussusceptions, 95% confidence level by taking p = 90%, sensitivity = 93%, specificity = 99% and d = 5%. Sampling technique was non-probability, consecutive sampling. Children with age ranges from 0-5 years of both gender having clinical features of suspected intussusception as per operational definition from 0-5 days duration were included in the study while Patients with history of previous surgery; Patients with stomas; Patients managed non operatively; Haemodynamically unstable patients; Patients with known congenital intestinal anomalies were excluded from study. After approval from the hospital ethical committee, an informed, written consent was taken from parents/guardian of the selected patients. After taking proper history , general data including age and sex (male/female) was collected. All the patients were underwent USG abdomen and pelvis for the evaluation of intussussception.

The ultrasound was performed by GE logic 500 color doppler ultrasound series machine with probe frequency ranging from 7.5 – 11 MHz by consultant

radiologist (assistant professor and above having 5 years experience). Grey scale USG of entire abdomen including the pelvis was performed in all patients by using convex array transducer. The sonographic findings were recorded as positive and negative for intussusception. The criteria for positivity included visualization of target or doughnut sign on transverse view and the "pseudo kidney sign" in longitudinal view. The criteria of negativity were non-visualization of above findings or visualization of normal gut with or without alternative diagnosis.

All these patients have undergone Diagnostic laparoscopy and or exploratory laparotomy and intra-operative findings were recorded. All those cases were considered for intussusception in which there was mass of gut having invagination of part of the intestine into adjacent distal segment on naked eye examination. These operative findings were correlated with ultrasonographic findings for evaluation of diagnostic accuracy of ultrasound in diagnosing intussusception. The collected information was analyzed using SPSS version 10.00. The qualitative data like demographics (sex; male or female), presenting complaints and USG findings and operative findings for intussusception (yes/ no) was presented as frequency distribution. Quantitative data in the study like age (in years) and duration of symptoms (in days) was presented as mean and standard deviations. The main outcome variable was correct findings on USG for presence of intussusception which was presented as diagnostic accuracy. 2×2 contingency table was used to calculate sensitivity, specificity, positive predictive values, negative predictive values, true positive, true negative, false positive, false negative and diagnostic accuracy of ultrasonography in intussusception taking operative findings as gold standard. Effect modifiers like age, gender and duration of symptoms were controlled by stratifications and Chi-Square test was applied to see the effect of these on outcome variable. P   0.05 will be taken significant.

RESULTS

Age ranges in this study was from 0 to 5 years with mean age of 01 ± 1.15 years. Majority of the patients 71.68% were between 0 to 2 years of age as shown in Table I. Out of these 113 patients, 78 (69.02%) were male and 35 (30.98%) were females with ratio of 2.2:1 (Figure 1).

Majority of patients 51.33% and 46.02% presented with bilious vomiting and intermittent screaming (abdominal pain) respectively followed by stool mixed with mucous and blood, palpable abdominal mass, abdominal distention and constipation as shown in Table II.

Stratification of age group and gender according to the presence of intussusception was shown in Figure 2. The duration of symptoms in patients ranged from 0 to 5 days with an average of 02 ± 0.65 days. Stratification of patients according to duration of symptoms was shown in Table V.

All the patients were subjected to grey scale ultrasonography of the abdomen. Ultrasound supported the diagnosis of intussusception in 76 (67.26%) patients. In these patients, intussusception could be visualized on grey scale ultrasound with multiple alternating hyperechoic and hypoechoic layers owing to the presence of three overlapping mucosal and muscular layer of intussuscipiens (distal segment)and Intussusceptum (proximal segment) which were considered as ultrasound positive.

Operative findings confirmed intussusception in 79 (69.91%) cases whereas 34 (30.01%) patients revealed no intussusception. In ultrasound positive patients, 75 (66.37%) (True Positive) had intussusception and 01 (0.88%) (False Positive) had no intussuscpetion on operation. Among, 37 ultrasound negative patients, 04 (3.54%) (False Negative) had intussusception on operation where as 33 (29.20%) (True Negative) had no intussusception (p<0.0001) as shown in Table III. Sensitivity, specificity, positive predictive value, negative predictive value and diagnostic accuracy of ultrasonography are calculated taking operative findings gold standard.

So, the sensitivity, specificity, positive predictive value, negative predictive value and diagnostic

accuracy of grey scale ultrasonography in intussusception in children were 94.94%, 97.06%, 98.68%, 89.19% and 95.57% respectively in Table V.

Table 1: *%age of Patients According to Age Distribution (n=113).*

Age (years)	Male		Female		Total	
	No.	%age	No.	%age	No.	%age
0-1	29	25.66	16	14.16	45	39.82
>1- 2	26	23.01	10	8.85	36	31.86
>2- 3	12	10.62	05	4.42	17	15.04
>3- 4	05	4.42	03	2.66	08	7.08
>4- 5	06	5.31	01	0.88	07	6.19
Total	78	69.02	35	30.96	113	100.0
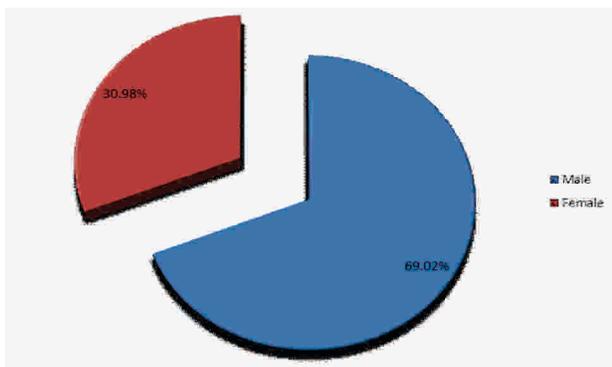
Figure-1: *%age of Patients According to Gender (n=113).*

Table 2: *%age of patients according to presenting complaints (n=113).*

| Presenting Complaints	No. of Patients	%age
Billious Vomiting	58	**51.33**
Intermittent Screaming (Abdominal Pain)	52	**46.02**
Stool mixed with mucous & blood	39	**34.51**
Palpable Abdominal Mass	37	**32.74**
Abdominal Distention	31	**27.43**
Constipation	27	**23.89**

Note: Patients were presented with two or more presenting complaints.

Table 3: *Summary of Results.*

	Positive result on Ultrasonography	Negative result on Ultrasonography
Positive Operative findings	75 (TP)*	04 (FN)***
Negative Operative findings	01 (FP)**	33 (TN)****

*-TP=True positive **-FP=False positive
-FN=False negative *-TN=True negative
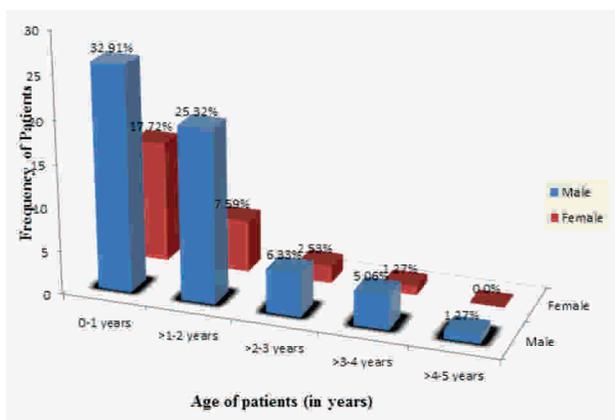
Figure-2: *%age of Patients with Intussusception According to Age Groups and Gender (n=79)*

Table 4: *%age of Patients with Intussusception according to Duration of Symptoms (n=113)*

Duration of Symptoms (0-5 days)	Intussusception			
	Present (n=79)		Absent (n=34)	
	No.	%age	No.	%age
< 3 days	66	**83.54**	23	**67.65**
>3 days	13	**16.46**	11	**32.35**

Table 5: *Evaluation of Ultrasonography in Intussusception.*

Evaluation of Ultrasonography	Values (%)
· **Sensitivity**	94.94
· **Specificity**	97.06
· **Positive Predictive Value (PPV)**	98.68
· **Negative Predictive Value (NPV)**	89.19
· **Diagnostic Accuracy**	95.57
· **Liklihood ratio for Positive test result**	32.28
· **Liklihood ratio for Negative test result**	0.52

Sensitivity: TP / TP + FN
Specificity: TN / TN + FP
Positive Predictive Value (PPV): TP / TP + FP
Negative Predictive Value (NPV): TN / TN + FN

DISCUSSION

In infants and toddlers Intussusception is very common type of intestinal obstruction. It is an occlusive-strangulation type of intestinal obstruction, and all necessary measures should be taken early to diagnose and treat in order to prevent gut ischaemia.[14]

Intussusception is usually diagnosed on brief history and physical examination. On Per rectal examination intussusceptum may be felt by the finger. A definite diagnosis always need confirmation by diagnostic imaging modalities.[15] The role of the abdominal x-ray is debatable. It may show signs of intestinal obstruction only. [16]

Definite Diagnosis of intussusceptions can be made with noninvasive imaging modalities such as ultrasound, CT and MRI . With recent improvement in ultrasound technology and device, ultrasonography has been widely used in the diagnosis of gastrointestinal pathologies. Ultrasound is useful to identify intestinal gross lesions as well as integrity of tract layers.[17]

Ultrasound (US) is the primary tool for initial diagnosis of intussusceptions. This is accurate in diagnosing intussusception with a certainty of up to 100% ,in addition can detect pathologies such as the presence of a PLP, presence of a lead point and incomplete reduction after enema.[16]

At presentation age of the patient plays an important role in differentiating type and pathology of the intussusception. Small bowel intussusceptions particularly ileoileal type is a common variety in adults.The mean age of children with small bowel intussusception ranged from 4 to 11 years in several studies.[18] In this study, age range was from 0 to 5 years with mean age of 01 ± 1.15 years which is very much comparable to study of Stanley A et al[19] who had observed mean age of 01 while much lower than Riera A et al[20] who had found mean age of 2.1 years.

Idiopathic intussusception is more common in children between 6 months and 2 years of age.[16] In the studies done by Riera A et al[20] and Munir A et al[21] intussusception was more frequent in males. So, this study has shown that children with intussusception were mostly males (69%) with 71.68% patients ranging between ages of 0–2 years.

Along with diagnosis of intussusception ultrasound can also be used to monitor its reduction without hazards of any ionising radiation. Intussusception has a characteristic appearance on ultrasound which make its diagnosis easy when properly performed by an experienced sonographer.[16] Intussusception can be missed when there is intestinal obstruction with gross gaseous distension.

The performance of ultrasonography in our study exhibited high specificity, which would make it an excellent test to rule in intussusception. Also the high sensitivity scores make ultrasonography useful as a screening test to rule out the condition. In this study, the sensitivity, specificity, diagnostic accuracy of ultrasonography in intussusception in children was 94.94%, 97.06% and 95.57% respectively. Justice FA et al[12] found sensitivity and specificity of ultrasonography as 97.5% and 99%, respectively, for diagnosing intussusception in children.

Riera A et al[20] in his study found the sensitivity of 85%, specificity of 97%, positive predictive value of 85%, and negative predictive value of 97% for the diagnosis of ileocolic intussusception. In 1987, Pracos et al[15] reported 100% accuracy of sonography for the diagnosis and exclusion of intussusception in 426 children, including 145 with intussusception. Stanley A et al[19] studied 24 patients and concluded that ultrasonography should be an essential diagnostic tool in children with intussusception. In a retrospective study, Susan D et al[23] in 151 patients has also supported the use of ultrasound as a screening examination for children with possible intussusception in all cases, except those with high-risk factors such as a palpable abdominal mass. Despite the fact that the advantages of ultrasound have been established for the diagnosis of intussusception,[24] its use has been somewhat slowly accepted throughout the world. This indicate the fact that many radiologists are not equally skilled with sonography.[25] There has been much discussion about

the operator dependant nature of ultrasonography and its interpretation. There is no doubt that the radiologist's experience and training are very important factors in performing and interpretation of ultrasonography. However, Verschelden et al[24] showed that a 100% accuracy rate could be achieved by third and fourth year residents.

CONCLUSION

This study concluded that Ultrasonography (US) has revolutionised the diagnosis and management of intussusceptions due to its high sensitivity and specificity in diagnosing intussusceptions in children. Being non invasive and a highly sensitive tool of investigation, early and timely diagnosis of intussusception in children could be made which would ultimately help in reducing the intussusception related mortality.

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