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EDITORIAL

Responding to Coronavirus (COVID-19) Disease

Tariq Butt[1], Erum Butt[2]

In early December 2019, few pneumonia cases were identified caused by some unknown agent in the Wuhan, capital city of Province Hubei of China.[1] The agent was later on identified as an enveloped RNA beta Coronavirus[2] which was subsequently named by WHO as COVID-19 and the coronavirus disease 2019.[3,4] Till March 12, 2020, the worldwide 125048 cases and 4613 (3.69%) deaths in 117 countries have been reported[5] However, Guan et al.[6] reported 1099 patients with confirmed Covid-19 with death rate of 1.4%. It is pertinent to note that during 1918-19 flu (H1N1) pandemic about 500 million people or one-third of the world's population became infected with flu virus with about 50 million deaths worldwide. In February 1957, H2N2 virus triggered a pandemic ("Asian Flu") which result 1.1 million deaths worldwide. Then in 1968 new flu (H3N2) pandemic cause about 1 million deaths worldwide.[7-10] Although death rate of COVID-19 disease appears to be less as compared to similar corona virus diseases like SARS (9.6%), MERS (36%) and flu,[10,11] the rapidity of the virus to spread within community make it alarming challenge and the Covid-19 epidemic has created serious issues for the general and medical communities as regard to health & research.

Coronavirus has gripped the nations globally which resulted into the development of a lot of anxiety and panic. The people across the globe are infected through respiratory droplets. In response to the outbreak, various countries issued temporary travel restrictions, which may have slowed the spread of COVID-19 somewhat. The efficiency of transmission of a respiratory virus depends on basic reproduction number which has been estimated as 2.2 for this virus by recent studies which result in extreme capability of virus transmission and thus there is dire need to be prepared against this virus to establish worldwide until at least reproduction number has reduced to less than one.[12,13] In Pakistan till March 12, there were 20 confirmed cases of COVID-19 infections and all of them came from Iran. Two of them has already been cured of the disease and sent home.[14] However, because of high transmission capability; we must be ready to prevent this virus to establish in Pakistan.

Community spread in Pakistan could require adopting certain policies such as avoidance of gatherings to minimize spread. These include isolating diseased individuals (even at home), closing schools, and working from home when possible.[15] Centre for Disease control and Prevention (CDC), Atlanta has advised to avoid visiting areas like China, Korea, Iran and Italy where there are increased number of infected persons. These travel restrictions by various countries have definitely helped to reduce the spread of this virus. Public awareness is essential in controlling of any outbreak, however, these awareness campaigns lead to the development of panic among public. Panic has already been spread worldwide and World Health Organization (WHO) warned that increasing demand, buying due to fear and irrational use of personal protective equipment (PPE) has compromised supply globally and resulted in rising risk from COVID-19 and other infective agents.[16] Although we are still in the process of learning the actual pathogenesis, epidemiology and clinical presentation of this disease, Li and colleagues[17] have shown a comprehensive description of the patients with the disease who reported sick infected with this virus in Hubei province (Wuhan city), China. They demonstrated that the old age and patients with some coexisting other diseases were predisposing factors for high mortality and morbidity. Younger children were minimally affected. This type of information is essential to provide appropriate response to this outbreak.

Research has already been started to develop a vaccine against this virus[18] but this would require certain essential time period before launching for

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public use. Moreover, vaccine may not be useful to contain the current outbreak. Enrolling of participants on February 21, 2020 has already been started for the trial of the experimental antiviral drug remdesivir. Preventive measure and certain therapeutic agents including antiviral drugs lopinavir-ritonavir, RNA polymerase inhibitor remdesivir, interferon-1β and Chloroquine[19] are being used in getting this goal. One more option for trial could be use of hyperimmune globulin from recovered individuals and monoclonal antibodies.[20] The incubation period as determined by Li et al.[17] are important in that it provide some opportunity for intervention to attack the virus by some measures to reduce the spread of the virus. Genomic studies would be useful to determine host factors that predispose individuals to acquire infection of this virus.

In Pakistan this disease was already anticipated however, we should still expect a number of outcomes. First, domestic population and community take the epidemic seriously; therefore the situation demands public should be ensured confidence in dealing with the virus. Second, there is a need to declare warfare on the disease. The Government has to make it clear to the public whether our country is fully or partially prepared or just unprepared. The positive result of tests for COVID-19 in 20 people has raised anxiety of public tremendously and they are worried about the capabilities of the Government in dealing with the virus. Third, infected people in the country there is always a possibility of spreading the disease from man to man, it is time for us to focus on curing those infected and minimizing the spread of the virus. So now we should keep emphasis on the treatment of them and thus decreasing the spread of COVID-19. The Government has to take measures nationally to win the war against this disease. Health measures should include allocation of more funds and all resources to the disposal for Government to fight against the coronavirus. COVID-19 has crushed the economy worldwide, but it will be more damaging as it will shake global trust if we show poor response against this virus. There is always a chance of collaboration between various authorities and other countries, if we want to win the war.

WHO initially tried to hold back the description of outbreak as pandemic because in China, for example the spread of disease seems to be slowing and it could yet be contained worldwide if the correct measures are adopted. Moreover, countries are already on high alert. However, when there is endless spread of the disease worldwide, WHO on March 11, 2020 declared the outbreak as Pandemic. Researchers are collaborating across the borders to communicate virus genome sequences and vaccine development is under way. There is need for continuous reconnaissance, rapid diagnosis and vigorous research to understand the actual characteristics of this organisms and human vulnerabilities to them and to develop operative measures to protect ourselves.

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ORIGINAL ARTICLE

Dengue Infection in Pediatric Patients Admitted in A Tertiary Care Hospital in Rawalpindi

Najaf Masood[1], Muddassar Sharif[2], Juneda Sarfraz[3], Khushdil Khan[4], Muhammad Khalid Masood[5], Riffat Omer[6]

ABSTRACT

Objective: To review clinico-pathological data of Dengue infection in paediatric patients admitted during epidemic of 2015.

Study Design: This was a cross-sectional study.

Place and Duration of Study: The study was conducted at Department of Pediatrics during the epidemic from 1st July to 31st December, 2015.

Materials and Methods: Febrile patients, aged 1-12 year of both genders (fulfilling the criteria of dengue infection according to the reporting form designed by Dengue Advisory Expert group for dengue infection) were included. Their clinical features, blood counts and dengue markers were recorded and followed up during hospital stay. Findings were subjected to SPSS 20 for statistical analysis.

Results: A total of 133 febrile patients, half of them were male, were included after confirmation of diagnosis on dengue markers. More than two third 79.7% patients were above five years of age with mean age 8.5± 3.2 year and mean duration of fever was 5.88±2.14 days. Headache was the most prominent symptom in 54.9% febrile patients followed by vomiting 52.6%. Hepatomegaly was seen in 36.8% patients. Dengue fever was the most common presentation followed by Dengue Haemorrhagic fever and Dengue Shock Syndrome. Patients with Dengue Haemorrhagic Fever and Dengue Shock Syndrome had restlessness, abdominal pain and cold clammy skin on presentation. Leukopenia was more frequent than thrombocytopenia.

Conclusion: This study depicts that children more than five year of age more commonly suffer from dengue fever with full recovery within 96 hours of admission. As vaccine is not available in Pakistan, these patients need timely diagnosis and critical monitoring during disease course to prevent mortality.

Key Words: *Dengue Fever, Dengue Hemorrhagic Fever, Diagnosis of Dengue.*

Introduction

Dengue fever (DF) is caused by mosquito borne viruses and clinically results in biphasic fever, myalgia, arthralgia, rash, leukopenia, thrombocytopenia and lymphadenopathy, whereas Dengue Hemorrhagic fever (DHF) is severe often fatal febrile disease which results in increased capillary permeability, abnormalities of hemostasis and in some cases, cause of Dengue Shock Syndrome (DSS) is considered to have immune-pathologic basis.[1]

Dengue infects around fifty million people annually around the globe.[2,3,4] Incidence of dengue fever has increased by thirty folds over the last fifty years and there is an estimation that 390 million people in 128 countries are at risk of this dreadful viral disease.[5,6] Pakistan had its first outbreak of dengue in 1994 and since then few epidemics were reported till 2011 when a major epidemic of dengue fever occurred in Punjab especially in Lahore and adjoining areas. In this outbreak more than 21580 confirmed cases and 317 deaths were recorded.[7]

Diagnosis of dengue fever is usually based on its clinical presentation, hematological abnormalities and positive viral serology. Clinical manifestations of dengue fever are variable and are influenced by the age of the patient.[8] It remained throughout the year in this region and different clinical manifestations have been observed during different epidemic

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periods as described in study conducted in north India.[9] Rawalpindi also experienced high disease burden since 2011, therefore this study was conducted on pediatric patients to review clinico-pathological data of Dengue infection admitted in a tertiary care Hospital in Rawalpindi during the epidemic of 2015.

Materials and Methods

This was cross-sectional study, conducted at Pediatric Department of a Tertiary Care Health facility after approval from research and ethical committee RMC and Allied hospital Rawalpindi.

Febrile patients aged 1-12 year of both gender were included according to the Reporting form designed by Dengue Advisory Expert group.[10]

The children suffering from fever 2-9 days with two or more symptoms (headache, myalgia, arthralgia, retro-orbital pain, abdominal pain, rash, bleeding manifestations, irritability and reduced urine output with positive dengue markers were included in the study.

Patients who had previous history of leukopenia, thrombocytopenia or prolonged history of fever and patients with negative dengue markers were excluded.

Patients with fever and two or more symptoms according to reporting form were admitted in pediatric ward. Blood complete picture was sent to the haematology department of hospital. On the basis of leukopenia (Total Leucocyte Count <4000/cmm) or thrombocytopenia (Platelet <100,000/cmm) patients were classified as probable dengue fever. Later on the presence of dengue markers NS1, IgM and IgG positivity for dengue infection was confirmed by enzyme linked immune-sorbent assay from hospital laboratory. All patients were admitted in pediatric dengue ward and monitored for vital signs, urine output, and ultrasound chest/abdomen to rule out any evidence of plasma leak. They were followed up till time of discharge for improvement of symptoms and platelet count.

Results

This study included total 133 febrile patients, half of them were male, after confirmation of diagnosis on dengue markers. More than two third 79.7% patients were above five year of age with mean age 8.5$\pm$3.2 year. Demographic data of patients according to disease spectrum is described in table I. Duration of fever was 2-9 days with mean duration 5.88$\pm$2.14 days. Headache was the most prominent symptom in 54.9% febrile patients followed by vomiting 52.6%, myalgia 45.1%, abdominal pain 41.4% , retro-orbital pain and sore throat 21.8% each, arthralgia 19.5%, rash 14.3%, cough 13.5% and diarrhoea 10.5% . Majority of the patient 88.7% did not bleed during course of illness. Only 11.3% patients had bleeding in form of epistaxis, hematemesis, malena, hematuria or petechie, hence it was not found statistically significant in our study. Mean pulse rate was 93.4$\pm$17.3 beats/min. Most of the patients were maintaining their blood pressure with mean systolic and diastolic pressure of 92.3$\pm$14.2 and 58.9$\pm$12.7 respectively. Hepatomegaly was seen in 49 patients while splenomegaly was present in 11 patients. Patients with DHF and DSS had restlessness 3.75% and abdominal pain 7.5% while 3.8% patients had cold clammy skin on presentation. Clinical manifestations are described according to disease spectrum in table II. Blood complete picture revealed mean haemoglobin 12.07$\pm$1.73 gm %, mean total leukocyte count 4809$\pm$3091/mm^3 and platelet count 103936$\pm$65687.97/ mm.^{3} Leukopenia (total leukocyte count less than 4000/mm^3) was observed in 48.87% patients while thrombocytopenia less than 50,000 /mm^3 was seen in only16.54 %. Non-structural protein 1(NS1) was positive in 63.9% and IgM for dengue was detected in 41.27% patients. DF was the most common presentation in 72.2%, DHF was diagnosed in 19.5% while DSS was in 7.5% patients. DSS was observed more frequent in older age group, among ten patients of DSS, 7 were of more than ten year of age. Ultrasound was normal in patients with Dengue fever. Findings of fluid leak were observed in DHF and DSS patients. Among 36 patients 10 (7.5%) developed pleural effusion and gall bladder wall oedema. Pelvic ascites was as frequently observed as abdominal ascites. Laboratory findings are further described in table III. Patients with dengue fever improved with antipyretics and oral fluids. About 30.1% patients received intravenous normal saline and dextran 40 was administered in 4.5% patients. Blood transfusion was done in 8.3% patients. Platelet count improved within 4 days in 88.7% patients. More than two third 85.7% patients discharged from hospital within 96

hours with no mortality observed during epidemic period in the tertiary care hospital of the study. Features of disease regarding management and course of illness, according to severity of illness are further described in table IV.

Table I: Demographic Features of the Sample

Demographic Features	Dengue Fever n	Dengue Hemorrhagic Fever n	Dengue Shock Syndrome n	Total n
Age in years				
0-5 year	20	6	1	27
6-10 year	45	9	2	56
> 10 year	31	11	8	50
Sex				
Male	44	15	7	66
Female	52	11	4	67

Table II: Clinical Manifestations in Dengue Patients

Clinical Features	Dengue Fever n	Dengue Hemorrhagic Fever n	Dengue Shock Syndrome n	Total n
Fever	97	26	10	133
Headache	52	14	7	73
Vomiting	47	18	5	70
Myalgia	40	13	7	60
Abdominal Pain	36	15	4	55
Arthralgia	18	5	3	26
Retro orbital pain	24	2	3	29
Sore throat	22	4	3	29
Rash	16	2	1	19
Cough	13	5	0	18
Diarrhea	9	4	1	14
Epistaxis	7	3	0	10
Petechie	1	0	1	2
Hematemesis	1	0	0	1
Malena	1	0	0	1
Hematuria	1	0	0	1
Abdominal Tenderness	2	6	4	12
Restlessness	7	1	4	12
Cold Clammy Skin	0	2	3	5
Hepatomegaly	26	17	6	49
Splenomegaly	5	6	0	11

Table III: Laboratory Data in Dengue Patients

Laboratory Data	Dengue Fever n	Dengue Hemorrhagic Fever n	Dengue Shock Syndrome n	Total n
Ultrasound Findings				
Normal	96	0	0	96
Pleural effusion	0	5	5	10
Abdominal Ascites	0	5	3	8
Pelvic Ascites	0	8	1	9
Gall bladder wall thickness	0	8	2	10
Hematological Indices				
Hemoglobin in gm%				
10 or less	9	6	0	15
More than 10	87	20	11	108
Total leukocyte count(mm/3)				
Less than 4000	54	9	3	65
More than 4000	42	17	8	67
Platelet count (mm/3)				
Less than 50000	15	4	3	22
50,000-100,00	45	14	5	64
More than 100,000	41	8	3	52
Dengue Markers				
NS1	84	21	8	113
IgM	50	15	8	73
IgG	31	14	9	54

Table IV: Management Variables in Dengue Patients

Management Variables	Dengue Fever n	Dengue Hemorrhagic Fever n	Dengue Shock Syndrome n	Total n
Fluid Administered				
Normal Saline	3	26	11	40
Dextran 40	0	1	5	6
Blood transfusion	0	5	6	11
Improvement in Platelet				
Within 4 days	90	20	8	118
More than 4 days	6	6	3	15
Hospital Stay				
Within 4 days	90	17	7	114
More than 4 days	6	9	4	19

Discussion

Dengue is an epidemiologically important mosquito borne viral disease. Significant population of various age groups has suffered from the disease in last two decades in Pakistan. In this study 133 patients were included during six months of epidemic in Rawalpindi. We found two thirds of study population between 5-12 years of age. Same age group is found more affected from dengue infection in different studies conducted in Pakistan[11,12] and India.[13] We had no gender difference in this study which is contrary to a study conducted at southern India where 77.31% patients are male.[14] Fever was present in 100% patients followed by headache, vomiting, myalgia, abdominal pain, retro-orbital pain, sore throat, arthralgia, rash, cough and diarrhoea. Frequency of symptoms are consistent with other studies.[11,14.] Rash is one of the prominent clinical feature of dengue also noted in 64.5% patients in one study conducted in India[15] but we observed rash only in 4.3% patients. Bleeding in dengue infection is a common event. Its causes are multifactorial. In this study majority of the patient (88.7%) did not bleed during course of illness which is contrary with the study conducted in Indonesia and Philippines.[16,17] Hepatomegaly was present in 36.8% in our study that is not as frequent as in study done by Joshi R in Mumbai in which hepatomegaly is present in more than half (66%) patients.[13] Age less than five year, spontaneous bleed, Hepatomegaly, free fluid in serosal cavities, leukopenia less than 4000/ mm^3 and thrombocytopenia <50,000/mm^3 are significant risk factors in pediatric patients suffering from DHF.[18,19] None of these findings were found significant in this study.

We found two third of patients with dengue fever with mean duration of fever 5.88$\pm$2.14 days. Therefore, Non-structural protein 1(NS1) was the most frequent marker of dengue fever as compared to IgM for dengue fever. This observation is on par with finding of different studies.[14,19] Pleural effusion and gall bladder wall edema were the most frequent ultrasound findings in this study which is consistent with study conducted in India.[20] Normal Saline and dextran found useful in dengue haemorrhagic fever and dengue shock syndrome patients.[21,22] Same was observed in this study. Blood transfusion was done in 8.3% patients in current study which is not comparable with one of the Indian study in which only 1.8% children receive blood transfusion.[23] Early detection and timely management of the disease can prevent mortality. In our study more than half of patients 85.71% discharged from hospital within 96 hours with no mortality observed during epidemic period. These findings are concordance with another Indian study.[24]

Conclusion

This study depicts that children more than five year of age more commonly suffer from dengue fever with recovery within 96 hours of admission. As vaccine is not available in Pakistan, these patients need timely diagnosis and critical monitoring during disease course to prevent mortality.

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ORIGINAL ARTICLE

A Retrospective Analysis of Risk Factors and Fetomaternal Outcome of Placental Abruption

Rakhshanda Mushtaq, Uzma Afridi, Fozia Muhammad Bakhsh

ABSTRACT

Objective: To determine the risk factors, fetal outcome and maternal outcome of placental abruption.

Study Design: Retrospective observational study

Place and Duration of Study: January 2017 to June 2018, Gynaecology Department, Bolan medical complex Quetta.

Materials and Methods: During the study, 189 patients with placental abruption Data wes collected from records of labor room, obstetrical ward and Neonatal Intensive Care Unit. All diagnosed placental abruption cases were included in this study. The clinical data of the patients presented with placental abruption in our facility was reviewed and the fetomaternal outcome was analyzed. Information collected from record included demographics, parity, gestational age, HB% at arrival and risk factors for placental abruption. Data was analyzed using MS Excel version 13 and results were presented as averages and percentages.

Results: During study period 189 cases of placental abruption were recorded. Grandmultiparity (94.17%) and Anemia (83.59%) were identified as major risk factors for placental abruption. The frequency of PIH as a risk factor for placental abruption was recorded in (8.9%) cases and history of trauma was noted in [2.6%] cases. Maternal deaths were found to be (2.11%) and the women undergone surgical intervention were (15.87%) with (14.28%) developed PPH. Only (28.57%) fetuses survived in this study population. Intrauterine death was diagnosed at arrival in (60.84%) cases. Early neonatal deaths were recorded in (13.22%) cases.

Conclusion: Abruption is a frequent and major cause of maternal morbidity and perinatal mortality. Anemia and grand multiparty are identified as major risk factors. The frequency of PIH and Trauma as a risk factor for placenta abruption is found lower than expectation.

Key Words: *Anemia, Maternal Outcome, Placental Abruption, PIH, Fetal Outcome.*

Introduction

Placental Abruption is defined as complete or partial separation of placenta prior to birth. Placental Abruption is an important cause of maternal and fetal morbidity and mortality. It occurs in around 1% of all pregnancies.[1] Placental abruption is a major cause of maternal morbidity and perinatal mortality globally and specially in the developing world.[1,2] The rates of abruptio placentae as high as 4.4-4.5% have been reported in developing countries.[2,3] A study conducted by Dar A et al reported an incidence of 3.5 -3.8 % in Pakistan.[4] The incidence appears to increasing in the USA, Canada, and several Nordic countries possibly due to increase in prevalence of risk factor.[5]

It is one of the major causes of obstetric haemorrhage and common cause of maternal morbidity and mortality.[6] It is also a significant cause of perinatal mortality.[7] Although etiology of Abruptio placentae is not fully understood, its generally multifactorial, that is, abnormal placentation, placental insufficiency, vascular malformations and increased fragility of vessels predispose to hematoma formation resulting in separation of the placenta.[8] The risk factors for placental abruption are hypertensive disorders of pregnancy, polyhydramnios, advanced maternal age, maternal trauma, cigarette smoking, alcohol consumption, cocaine abuse, short umbilical cord, sudden decompression of the uterus, retro placental fibro myoma, amniocentesis, previous miscarriage, grand

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multiparity, preterm rupture of membranes (PROM),low socioeconomic status and/or low pre pregnancy body mass index.[9,10,11,12] The clinical hallmarks of abruption include vaginal bleeding accompanied by tetanic uterine contractions, uterine hypertonicity, and a non-reassuring fetal heart rate pattern.[13] The signs and symptoms of Abruptio Placentae vary depending on the severity of bleeding and degree of separation of the placenta.[14]In two third of cases placental abruption is classified as sever due to associated fetomaternal morbidity and mortality.[15] The most common presentations include vaginal bleeding, uterine and abdominal pain and tenderness, abnormal uterine contractions, premature labor, maternal hemodynamic instability, fetal distress, and fetal death.[14] Ultrasound examination is useful in diagnosis of placental abruption with reported accuracy of 87.5% due to improved technology.[16] The risk of recurrence of abruptio placentae is reported as 4%-12%.[17] Receiving increasing number of women with this grave complication and non-availability of reliable data about Baluchistan was the motivation to carry out this study. As BMCH Quetta is a tertiary care hospital and we receive patients referred from most of the peripheral hospital, so the results of study to some extent may reflect the situation in Baluchistan. The objective to conduct this study was to determine the risk factors for abruptio placentae in women of Baluchistan seen at BMCH emergency ward with placental abruption and to describe the fetomaternal outcome for these patients.

Materials and Methods

This retrospective observational study was conducted to analyze all the cases of placental abruption seen at gynecological department of BMCH Quetta between January 2017 to June 2018.189 cases of placental abruption were included in this study. Data was collected from records of labor room, obstetrical ward and Neonatal Intensive Care Unit (NICU) by authors. Permission of ethical review board was obtained and all ethical issues were addressed. All diagnosed placental abruption cases were included in this study and other patients presented with antepartum haemorrhage due to other causes like placenta Previa were excluded. We reviewed the clinical data of patients presented with placental abruption in our facility and analyzed the fetomaternal outcome. Information collected from record included demographics, parity, gestational age, HB% at arrival, risk factors for placental abruption i.e. History of trauma, PIH, PROM, Previous abruption, Anemia, socioeconomic status, fetal outcome i.e. intrauterine death, early neonatal death, prematurity and maternal outcome i.e. Shock, massive transfusion, operative intervention, PPH and mortality. Data was analyzed using MS Excel version 13 and results were presented as averages and percentages.

Results

During study period 189 cases of placental abruption were recorded. Most of the cases were unbooked 165 (87%) Table I. Average Gestational age at presentation was 35, 72 weeks (Range, 28-41 Weeks) Table IV. Grand multi parity 178 (94.17%) and Anemia 158 (83.59%) were identified as major risk factors for placental abruption. 145 (76.71%) women belonged to poor socioeconomic strata. The frequency of PIH as a risk factor for placental abruption was recorded in 17(8.9%) cases and history of trauma was noted in 5(2.6%) cases. 25(13.22%) women presented with history of PROM and 4(2.1) had previous history of abruption.(Table I). Average Maternal age was recorded as 36 years (range 22-45). Table 4. Placental abruption resulted in 4 (2.11%) maternal deaths during study period. 92 [48.67%] presented in labor room in the state of shock and 105(55.55%) required massive transfusion.30 (15, 87%) women needed surgical intervention and 27(14.28%) developed PPH (Table II) Only 54 (28.57%) fetuses survived in this study population. Intrauterine death was diagnosed at arrival in 115 (60.84%) cases of placental abruption. Early neonatal deaths were recorded in 25 (13.22%) cases.35 (18.51%) babies were delivered prematurely as a result of placental abruption. Table III.

Table I: Risk factor for Placental Abruption

Risk factor for Placental Abruption	No. of Cases	Percentage
PIH	17	8.99%
Trauma	5	2.64 %
PROM	25	13.22%
Un booked	165	87 %
Previous history of abruption	4	2.11 %
Poor socioeconomic status	145	76.71%
Anemia	158	83.59%
Multiparty	178	94.17 %

Table II: Maternal Outcome of Placental Abruption

Maternal outcome	No. of cases	Percentage
Shock	92	48.67%
Massive transfusion	105	55.55%
surgical intervention	30	15.87%
PPH	27	14.28%
Maternal mortality	4	2.11%

Table III: Fetal Outcome of Placental Abruption

Fetal outcome	No. of cases	Percentage
Intrauterine death	115	60.84 %
Early neonatal death	25	13.22 %
Prematurity	35	18.51 %
Alive	54	28.57 %

Table IV: Average Maternal Age and Gestational Age of Fetus at the Time of Presentation

	Average	Range
Gestational age	35,72 %	28-41 weeks
Maternal age	36 years	22-45 years

Discussion

Abruptio placenta occurs in 0.8 - 1.0% of all pregnancies and 1.2% in twin pregnancies worldwide.[8,19,20] Hossain et al reported an incidence of 3.7% among Pakistanis women.[21] Placental abruption is a major cause of obstetrical haemorrhage and perinatal deaths. Increased maternal mortality and morbidity associated with placental abruption is due to haemorrhage.[22]

During this study period 189 women presented to BMCH emergency with placental abruption. 2.11% maternal deaths due to abruptio placentae were recorded. One mother was received dead in emergency with the diagnosis of placental abruption made by a general practioner. Another woman developed DIC after placental abruption and died. Two women died as a result of irreversible shock and uncontrolled PPH. Like other developing countries, maternal deaths due to hemorrhage are common in our country due to either delay in reaching the health facility or non-availability of blood. 48.67% presented in labor room in the state of shock and received active resuscitation. 55.55% required massive transfusion both due to antepartum and postpartum haemorrhage.15, 87% women needed surgical intervention in the form of emergency caesarean section (24), application of B-Lynch suture (7) and internal Iliac artery ligation (3) for sever PPH 27 women (14.28%) developed PPH Table II. In the Western world, maternal deaths due to placental abruption are rare; for instance a study done in Finland found that, between 1972 and 2005 placental abruption had a maternal mortality rate of 0.4 per 1,000 cases (which means that 1 in 2500 women who had placental abruption died); this was similar to other Western countries during that period. Without any form of medical intervention, as often happens in many parts of the world, placental abruption has a high maternal mortality rate. The prognosis of this complication depends on whether treatment is received by the patient, on the quality of treatment, and on the severity of the abruption.[23] only 28.57% fetuses survived in this study population. Intrauterine death was diagnosed at arrival in 60.84% cases of placental abruption. Early neonatal deaths were recorded in 13.22% cases. 18.51% babies were delivered prematurely as a result of placental abruption. Table III Poor perinatal outcome characterized by high intrauterine deaths observed in our study is consistent with other reports from developing countries.[24,25] The intrauterine death rate, maternal death rate, mean gestational age and PPH rates reported by H. Nazli et el are consistent with results of our study.[25] Another study conducted by Ohhashi M. et. al. reported that placental abruption accounts for 58% of perinatal deaths and 26 % of cases involving brain damage.[26] The fetal prognosis is mostly worse in case of placental abruption. Currently, in the UK, about 15% of fetuses die following this event.[23] The maternal effect of abruption depends primarily on its severity, whereas its effect on the fetus is determined both by its severity and the gestational age at which it occurs. Fetal morbidity is caused by the insult of the abruption itself and by issues related to prematurity when early delivery is required to alleviate maternal or fetal distress. Delivery is required in cases of severe abruption or when significant fetal or maternal distress occurs, even in the setting of profound prematurity. In some cases, immediate delivery is the only option, even before the administration of corticosteroid therapy in this premature infants.[27] Average Gestational age at presentation was 35, weeks (Range, 28-41 Weeks). Table IV Grand multiparty (94.17%) and Anemia (83.59%) are identified as major risk factors for placental abruption in our study. 83% women with placental abruption were found anemic (HB% less than 8) according to their blood samples drawn at arrival before the commencement of treatment.

Knowing the fact that HB% will remain unchanged initially (as both plasma and RBCs are lost equally during haemorrhage, before the commencement of intravenous fluids, 4 women, though anemic were not included among these women as they had been received treatment outside and referred to BMCH for management of placental abruption, in order to avoid the Bias that whether the Anemia is the cause or consequence of the placental abruption. Most of the cases were unbooked 87% and 76.71% women belonged to poor socioeconomic strata. This seems that the lack of antenatal care and poor socioeconomic status are significant contributory factors. The frequency of PIH as a risk factor for placental abruption was recorded in 8.9% cases and history of trauma was noted in 2.6% cases. The frequency of PIH and Trauma as a risk factor for placenta abruption are found lower than expectation. The 8.9% incidence of hypertensive disorder observed in our study may be an underestimate owing to masking of hypertensive disorder by lower blood pressures due to vaginal bleeding in patients with Abruptio Placentae. 13.22% women presented with history of PROM and 2.1 had previous history of abruption. Table I A review article by Downes et el confirm our study results that placental abruption is associated with significant risk of maternal mortality, perinatal mortality, PPH and caesarean section.[28] We acknowledge the limitations of our study that it doesn't describe the long term effects of placental abruption on fetus and mother as it is a retrospective study involving the record's analysis and most of these women are lost from follow up. The second limitation of this study was small sample size. A greater sample size is needed to better investigate the causal relationship between the risk factors of placental abruption. To conclude, Abruptio Placentae is a potentially serious obstetrical complication that tends to compromise maternal wellbeing and fetal viability. Increased frequency of Placental abruption is observed in women with low socioeconomic status, no antenatal checkup, and poor nutritional status. The results of our study provide important information to the obstetrician regarding the early identification of risk factors for placental abruption and developing individual antenatal care plans for women at risk of developing this complication. Proper management of these risk factors may reduce the risk of placental abruption and associated adverse outcome for mother and fetus. Furthermore, the results of our study highlighted the need for better equipped labor rooms and NICU to improve fetomaternal outcome in high risk pregnancies like placental abruption. Poor socioeconomic status, lack of antenatal care and delay in getting medical help due to long distances were found to be the major contributory factors in bad outcome in our study. The results of this study reflect insufficiencies of our health care management system. As morbidity and mortality associated with placental abruption can be decreased by good antenatal care, correction of Anemia, provision of contraceptive services and development of hospitals at far areas. The results of our study can be used to convince the policy makers to take in account the special circumstances of our province keeping in view the dynamics of this area.

Conclusion

Abruption is a frequent and major cause of maternal morbidity and perinatal mortality. Anemia and grand multiparty are identified as major risk factors. The frequency of PIH and Trauma as a risk factor for placenta abruption is found lower than expectation. Results of maternal and fetal outcome warrant the establishment of well-equipped labor rooms and NICU at tertiary care centers.

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ORIGINAL ARTICLE

The Association of Total Antioxidant Capacity with Metabolic Syndrome

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ABSTRACT

Objective: To determine the association between Total antioxidant capacity (TAC) with metabolic syndrome

Study Design: A cross sectional study design.

Place and Duration of Study: The study was conducted at department of Chemical Pathology, Islamic International Medical College Pakistan Railways Hospital, Rawalpindi. One year (2nd Sep 2018 to 2nd September 2019).

Materials and Methods: A total of 88 subjects, 44 with metabolic syndrome and 44 controls were recruited through non probability convenient sampling. Group I comprised of 44 metabolic syndrome individuals from both genders. Patients having FPG ≥ 100mg/dl were investigated for TG and HDL-C and their waist circumference and BP was measured. According to AHA/NHLBI guidelines, the individuals were labeled with MS on fulfilling three or more than three criteria i.e Fasting Plasma Glucose ≥ 100mg/dl, Serum Triglycerides ≥ 150mg/dl, HDL-C ≤ 40mg/dl in men and ≤ 50 in women, Blood Pressure ≥ 130/85 and waist circumference ≥ 40" in men or ≥ 35" in women.[8] Group 2 comprised of 44 healthy individuals.

In addition to the above mentioned lab tests, Total Antioxidant capacity (TAC) was measured for both the groups. Statistical Package for Social Sciences (SPSS) version 23.0 was used for entering and analyzing all data. Descriptive statistics were described for nominal data; mean and standard deviation were described for quantitative variables which included serum TAC, FBG, serum HDL-C, serum triglycerides, waist circumference and BP measurement.

Results: The mean age of metabolic disease group was 48.14 ± 10.48 years, and that of control group was 23.04 ± 5.82 years. TAC recorded levels were found to be considerably higher in the control group (18.13 ± 12.90 mmol/L) as compared to the Metabolic Syndrome group (4.56 ±.7.43). Serum HDL-C (37.09 ± 6.37 mg/dl) vs (43.09 ± 46.15 mg/dl) levels were lower in MS individuals. Whereas, Triglycerides (240.03 ± 93.19) vs (107.41 ± 56.50), FPG (139.43 ±57.56) vs (69.66 ± 30.46), BP (133.86 mm Hg + 13.59) vs (120.00 ± 0.00) were found to be higher in MS patients as compared to control group.

Conclusion: TAC gets depleted in MS individuals more as compared to healthy individuals. Estimation of TAC at an early stage can be useful for early detection of Metabolic Syndrome and further to prevent its complications such as DM, CVD and other metabolic disorders.

Key Words: *Cardiovascular Disease, Diabetes Mellitus, High Density Lipoprotein Cholesterol, Metabolic Syndrome, Total Antioxidant Capacity.*

Introduction

A group of disorders including hypertension, insulin resistance, dyslipidemias and abdominal obesity collectively contribute to the condition termed as Metabolic Syndrome (MS).[1] The incidence of MS is on the rise globally.[2] The individuals who are labeled to have metabolic syndrome are more prone to adverse cardiovascular incidents and death due to CVD.[3] Classical cardiovascular risk factors include low HDL-C, hypertriglyceridemia, hypertension and dysfunctions in glucose metabolism.[4] In addition, metabolic syndrome also causes a significant impact on health care cost and resource utilization.[5] A stringent clinical criteria, described by the American Heart Association and the National Heart, Lung and

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Blood Institute (AHA/NHLBI, 2009)used to define MS is described below. If any three of the following are met, the patient would be classified as having Metabolic Syndrome;

1. Serum triglyceride rising above 150 mg/dl (or the patient is on drug therapy for hypertriglyceridemia).
2. Circumferential waist of patients rises above around 102 cm in affected males and around 88 cm in affected females.
3. High Density Lipoprotein Cholesterol (HDL-C) levels ≤ 40 mg/dl for males (or the patient is on drug therapy for improving HDL-C level); or ≤ 50 mg/dl for females (or the patient is on drug therapy for improving HDL-C level).
4. Glucose levels rise above 100 mg/dl in the fasting state (or the patient is on drug therapy for hyperglycemia).
5. Blood pressure readings are higher than 130/85 mm Hg (or the patient is on drug therapy for hypertension).[6]

Moreover, the contribution of oxidative stress phenomenon in the pathology of the metabolic disorders is considerably significant in relation to MS.[7] Oxidative stress, can be understood as a disturbance in balance between free radicals genesis and the physiological capacity to counter the destructive process brought about by antioxidants. Oxidative stress has an integral contribution towards the progression of MS, Diabetes mellitus (DM) and cardiovascular diseases (CVD).[8] To manage the oxidative stress, many antioxidant defense systems operate through enzymatic or non-enzymatic systems. Non-enzymatic antioxidant comprises of glutathione, beta-carotene, vitamin A, C and E, Whereas enzymatic pathways include intracellular antioxidant enzymes catalase (CAT), glutathione reductase (GR), glutathione (GPx), and superoxide dismutase (SOD).[9] Total antioxidant capacity (TAC) is used as an instrument for diagnostic purposes and for treating CVD and DM.[10] Moreover, the levels of TAC are used as biological marker to monitor oxidative stress in humans.[11] Rationale behind the study, measurement of TAC can play a significant role in assessing oxidative stress and taking timely action to prevent MS complications such as DM, CVD and other metabolic disorders.[11] This study was aimed to determine the association between Total antioxidant capacities (TAC) with Metabolic syndrome

Materials and Methods

A cross-sectional study was conducted at the Department of Chemical Pathology at the Pakistan Railways Hospital Rawalpindi over the period of one year (2nd Sep 2018 to 2ndSep2019). Study started after the approval from the Ethical Review Committee, Riphah International University, Islamabad. An overall of 88 subjects, 44 cases and 44 controls were included in this study. Adults from both genders having MS were included. Patients with acute infections, chronic diseases like RA, SLE, pregnant and lactating women were excluded. Patients already on antioxidant and lipid lowering drugs were also excluded. Two groups of subjects were recruited for the study.

Group 1 This group comprised of 44 metabolic syndrome individuals from both genders. Patients having FPG ≥ 100mg/dl were investigated for TG and HDL-C and their waist circumference and BP was measured. According to AHA/NHLBI guidelines, the individuals were labeled with MS on fulfilling three or more than three criteria i.e. Fasting Plasma Glucose≥ 100mg/dl, Serum Triglycerides≥ 150mg/dl, HDL-C ≤ 40mg/dl in males and ≤ 50 in females, Blood Pressure ≥ 130/85 and waist circumference ≥ 102cm in males or ≥ 88cm in females.

Group 2 A total of 44 healthy individuals of both genders was recruited from faculty and lab staff of PRH as controls.

Patient was seated comfortably and 5ml of venous blood was taken in plain sample vacutainer. The collected blood sample was centrifuged at 1000xg for 15 min to extract serum and then this serum was stored at -70C.

All of the data was then entered and analyzed using, Statistical Package for Social Sciences (SPSS) version 23.0.Descriptive statistics (frequencies and percentages) weredescribed for nominal data, such as age and gender. Mean and standard deviation values were described for quantitative variables including the serum Total Anti-Oxidant Capacity, Fasting blood glucose, serum HDL-C, serum triglycerides, waist circumference and blood pressure measurements. Kolmogrov-Smirnov test was then applied to test the normality of the

distribution of the data. Since all variables were found to be irregularly distributed, the non-parametric Mann Whitney U test was applied to compare the various variables between the two groups, one with the metabolic diseases and the other control group of normal individuals. *P* value <0.05 was found to be statistically significant.

Results

A total of 88 subjects were encompassed according to the inclusion criteria of the study. Descriptive statistics of age (in years) were calculated as mean and standard deviation. Mean age of all the recruited subjects was 38.59 ± 15.19 years. The recorded mean age of Metabolic Syndrome group was 48.14 ± 10.48 years, and the mean age of control group was 23.04 ± 5.82 years.

Majority of subjects 36.3% were between 41-50 years, 31.3% participants were between 51-60 years. About 8.5% participants were between 33-40 years and 11.1%participants were between 61-70 years.Only2.27% participants were between 21-30 years in (Table I).

Table I: Descriptive Statistics of Age (N = 88)

	Mean	Standard Deviation
Metabolic Syndrome Group(n = 44)	48.14	10.48
Control Group (n = 44)	23.04	5.82
Total (n = 88)	38.59	15.19

A significant difference was found between values of different risk factors of MS (obesity, hypertension; and high Fasting plasma glucose, Triglycerides and HDL-C levels). The results showed that the values for MS patients were found to be considerably raised than those recorded for the control group.

The affiliation between the Total Antioxidant Capacity with HDL-C showed a positive correlation whereas TAC showed negative correlation with abdominal obesity, blood pressure, triglycerides and fasting blood glucose. (Table II).

TAC values were found significantly high in the control group (18.13 ± 12.90 mmol/L) as compared to the MS group 4.56 ± 7.43mmol/L in (Table III)

A valid instrument to quantify MS is by measuring TAC levels (Table III). The comparison was done between the MS and control groups. TAC levels were found to be severely depleted in the MS patients, in comparison to the control group.

Table II: Kolmogrov Smirnov Significance Values for Different Variables for Normality Tests

Variable	P Value
HDL-C	< 0.001
TGL	0.002
FPG	< 0.001
Systolic BP	< 0.001
Diastolic BP	< 0.001
Waist Circumference	0.011
Total Antioxidant Capacity	< 0.001

Table III: Mean, SD and *p* Values for Different Elements of MS (N = 88)

Metabolic Syndrome Indicators	Metabolic Syndrome Group	Control Group	P Value
HDL-C (mg/dl)	37.09 ± 6.37	43.09 ± 46.15	0.008
TGL (mg/dl)	240.03 ± 93.19	107.41 ± 56.50	< 0.001
FPG (mg/dl)	139.43 ± 57.56	69.66 ± 30.46	< 0.001
Systolic BP (mm Hg)	133.86 ± 13.59	120.00 ± 0.00	< 0.001
Diastolic BP (mm Hg)	87.27 ± 8.52	80.00 ± 0.00	< 0.001
Waist Circumference(cm)	37.84 ± 3.67	31.91 ± 3.12	< 0.001
TAC (mmol/L)	4.56 ± 7.43	18.13 ± 12.90	< 0.001

*$p \leq 0.05$ was taken as level of significant

Discussion

The present study has been carried out to determine the association between TAC with MS. Both Males and female between those 18-65 years of age were recruited. These results depict that incidence of MS increases with age. Ervin RB has also documented the increased incidence of MS in middle and old aged people.[12] However, Weiss et al found that MS is also common among children and young adults. Zhiyan Li et al has documented similar findings about the increased prevalence of MS among male population.[13] In our study it has been found that serum HDL-C levels were suggestively lower in MS group (37.09 ± 6.37 mg/dl) as compared to control group comprising of healthy adults(43.09 ± 46.15 mg/dl). In present study we have found that HDL-C has a positive correlation with Total (TAC). This positive correlation indicates the antioxidant activity. HDL-C exerts its anti atherogenic and anti-inflammatory properties, including anti oxidative activity by scavenging reactive oxygen species ROS.[14] In our study, the mean serum TG(>150 mg/dl) in MS patients and control subjects was 240.03 ± 93.19 and 107.41 ± 56.50 respectively. The raised levels of triglycerides in MS individuals indicate reverse correlation between triglycerides and TAC. Bitla et al, Abbasian et al and Zheng et al have also reported an inverse relation between triglycerides and TAC.[15] In

present study it has been found that the levels of FPG(≥ 100mg/dl) were much higher in MS individuals (139.43 ± 57.56 mg/dl) as compared to healthy adults (69.66 ± 30.46 mg/dl). Exposure to prolonged periods of hyperglycemia causes non-enzymatic glycation of extracellular proteins.[16] The study, by Maxwell et al and Ceriello et al have reported similar findings raised plasma glucose levels in MS subjects.[17] In present study, the mean and SD of systolic BP(mmHg) was 133.86 ± 13.59, and 120.00 ± 0.00 in MS patients and control groups respectively. The difference of systolic and diastolic BP was evidently raised in MS group as compared to control group due to increased ROS production, redox-signaling and decreased TAC in MS.[17] Sanchez-Rodriguez et al, in his study reported a negative correlation amongst BP and TAC similar to our study.[18] In this study the mean waist circumference (cm) was 37.84 ± 3.67, and 31.91 ± 3.12 in MS and control group respectively. Increased waist circumference in MS subjectis due to dysregulations of adipokines and development of MS which further reduces TAC. The waist circumference showed an inverse correlation with TAC. Research work conducted and documented by Chrysohoou et al and Hartwich et al reached to similar conclusions.[19]According to the results of this study TAC has a positive correlation with HDL-C; however it has an inverse correlation with TG, FPG, BP and waist circumference. TAC levels were found significantly increased in the control group (18.13 ±12.90 mmol/L) in comparison to the MS group (4.56±7.43mmol/L).A number of studies have been done to study the relationship between the components of MS & MDA i.e an oxidant bio-marker.[20]To conclude, this study, it can be stated that the oxidative stress in MS is worsened as a result of increased activity of the biochemical pathways which in turn influences increase in the rate of transport of ROS and thus enhancing the changes in antioxidant protection.[21] This study has certain limitations. The sample size was small and study was conducted at single center, hence, restricting us to generalize the findings of our study.

Conclusion

TAC gets depleted in Metabolic Syndrome individuals more as compared to healthy individuals. Estimation of TAC at an early stage can be useful for early detection of Metabolic Syndrome and further to prevent its complications such as DM, CVD and other metabolic disorders.

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ORIGINAL ARTICLE

Association of N-Terminal Pro Brain Natriuretic Peptide with Ventricular Ectopy

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ABSTRACT

Objective: This study aimed to determine the association of premature ventricular contractions burden of less than 20% with NT-pro BNP levels in patients with preserved left ventricular function.

Study Design: Case control analytical study.

Place and Duration of Study: It was conducted in physiology department of Islamic International Medical College (IIMC) in collaboration with Armed Forces Institute of Cardiology (AFIC) during the period of 18th April 2016 to 20th March 2018.

Materials and Methods: The study comprised a total of fifty participants which included 40 diagnosed patients of premature ventricular contractions (PVCs) and 10 healthy subjects (with no PVCs). PVCs burden was calculated by Holter monitoring report and echocardiography was done to determine left ventricular ejection fraction. Patients with burden>20% and Ejection fraction<50% were excluded. In all these patients NT-proBNP levels were measured and statistical analysis was done using SPSS version 25. Student's t-test and Pearson correlation tests were applied to see its association with PVCs burden.

Results: Ventricular ectopic burden<20% has NT-proBNP higher than controls but the increase is insignificant with p value of 0.056. Pearson correlation test showed no correlation of Premature ventricular contractions <20% with NT-pro BNP levels with r value of 0.1.

Conclusion: It can be concluded that the patients with PVCs burden less than 20% has no correlation with NT-pro BNP so they should not be considered as high risk patients.

Key Words: *Cardiomyopathy, NT-ProBNP, PVCs, PVCs Burden, Ventricular Ectopy.*

Introduction

Ventricular ectopy or premature ventricular contraction is defined as an extra heartbeat, originating from the ventricles and comes before the normal heart beat.[1] Premature ventricular contractions (PVCs) is common with an estimated prevalence of 1% to 4% in the general population.[2]

The mechanisms for ventricular ectopy production include re-entry, triggered activity and automaticity.[3] Occurrence of re-entry takes place due to presence of one way block and an area of slow conduction. During ventricular activation slow conduction area activates the blocked area after ventricular recovery, resulting in an ectopic beat.[4] In the triggered activity, the preceding action potential produce after depolarizations which results in ectopic beat. Automaticity points to presence of an ectopic focus of pacemaker cells in the ventricle with sub threshold potential for firing. Basic rhythm of heart raises these cells to potential resulting in an extra beat.[3,1]

Frequent ventricular ectopic beats have a high risk of developing dilated type cardiomyopathy.[5] Rapid pacing due to PVCs results in LV dyssynchrony resulting in LV dilatation and ultimately reduced ejection fraction.[6] During this process changes in neurohormonal pathway occurs which bring about release of bioactive peptides.[7] ProBNP splits into BNP (32 amino acid) and N-Terminal proBNP (76 amino acid). ProBNP is mainly synthesized and secreted by cardiac myocytes in response to myocardial wall stretch.[8] NT-proBNP levels are found to be raised in patients of left ventricular dysfunction and ventricular dilatation.[9] In comparison of diagnostic significance of BNP with NT-proBNP, for left ventricular dysfunction, both are equivalent, but in some groups NT-proBNP is found to be superior.[10,9]

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PVCs were long considered benign until they were found to be associated with risk of developing PVCs induced cardiomyopathy.[11] High PVCs burden is associated with development of cardiomyopathy but sometimes high burden patients do not develop cardiomyopathy and patients with the burden of 4% can develop cardiomyopathy. Currently no risk profile defines a group of patients at high risk of PVCs induced cardiomyopathy.[12] Role of NT-proBNP as a biochemical marker to predict cardiomyopathy needs to be studied.

This study aimed to determine the association of moderate ventricular ectopic burden (less than 20%) with N-Terminal proBNP levels in patients with preserved left ventricular function, thus assessing it's importance as a determinant to stratify high risk patients.

Materials and Methods

A case control study was conducted in Physiology department of Islamic International Medical College Rawalpindi, in collaboration with Electrophysiology department of Armed Forces Institute of Cardiology (AFIC) from 18th April 2016 to 20th March 2018 after approval from ethical review committee (ERC). A total of 50 patients were taken among which 40 were diagnosed patients of premature ventricular contractions with PVCs burden≤20%. Patients were diagnosed on 24 hours Holter monitoring report and their PVCs burden was calculated by dividing total number of PVCs by total analyzed beats in 24 hours. Echocardiography was done in all the patients to assess their heart status. Inclusion criteria were specified as, age between 18-60 years, LV ejection fraction less than 50% and patients with PVCs burden less than 20. Patients with PVCs burden >20% and ejection fraction <50% were excluded from the study. Patients out of age range of 18-60 years were excluded from the study. Ten age matched healthy subjects with no PVCs were taken as controls. In all these patients, venipuncture technique was used to collect the blood sample. NT-proBNP levels were measured in all blood samples using ELISA kit and statistical analysis was done by using SPSS version 25. Data was normally distributed so parametric tests were applied. Pearson correlation test was applied to determine the correlation of NT-proBNP with moderate PVCs burden (burden<20%) and Student's t-test was applied to compare mean NT-proBNP levels of PVCs patients with control subjects (having no PVCs).

Results

Baseline characteristics are shown in Table I which shows 47±6 years as the mean age of the PVCs patients. Among the total of 40 patients 18 were females and 22 were males.

Table I: Baseline Characteristics of Participants

Baseline and Clinical characteristics		PVCs Patients	Control	Total(n)
Age(years)		47±6	45±4	
Gender	**Male**	22	6	28
	Female	18	4	22
Total(n)		40	10	50

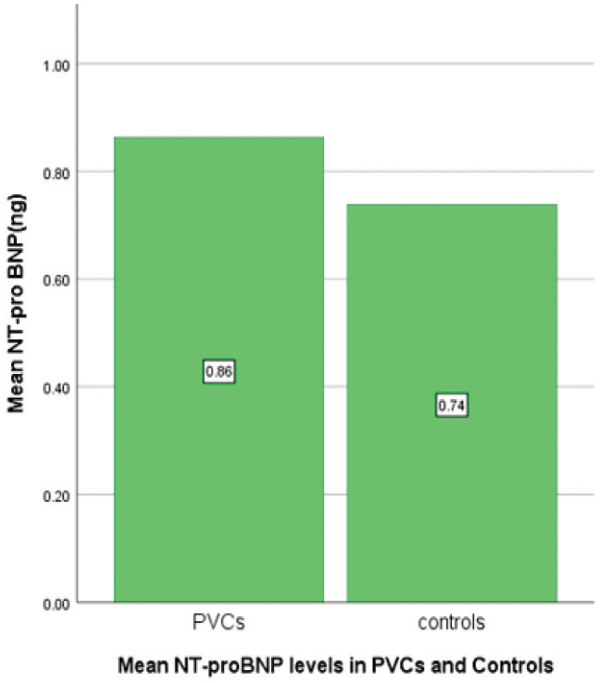

Fig 1: Comparison of Mean NT-Pro BNP in PVC's Patients and Controls

Figure 1 Mean NT-proBNP levels in PVCs patients are 0.86±0.47ng and in control group 0.74±0.49ng which shows that NT-proBNP levels are high in PVCs as compared to controls but the increase is insignificant with p value of 0.56.p value ≤0.05 was considered to be significant.

Table II shows correlation of PVCs burden <20% with NT-proBNP. Pearson correlation test was applied and r value of 0.1 shows no correlation of ventricular ectopic burden < 20% with N-Terminal pro BNP levels.

Table II: Correlation of Ventricular Ectopic Burden <20% with NT-ProBNP Levels

NT-pro BNP levels (ng/ml)		
Ventricular Ectopy	**r value**	**p value**
<20%	0.1	0.6

r is Pearson correlation coefficient

P value<0.05 was considered to be significant.

Discussion

The current study was aimed to evaluate the association of NT-proBNP with PVCs burden less than 20% in patients with preserved LV function left (Left ventricular ejection fraction <50%). Levels of NT-pro BNP were not significantly raised in PVCs patients as compared to control groups. Hence the results suggest no correlation of NT-proBNP with PVCs burden less than 20%.

A study by Skranes et al, illustrates the association of N-Terminal pro BNP with PVCs which contradicts the present study findings. The contradiction may be due to the reason that current study is done on patients with PVCs burden less than 20% while that study was done on frequent PVCs (PVCs>24%) patients. That study also differed from the current study as it was done in community based population.[13] In another study conducted on animals (dogs), NT-proBNP and Interleukin 6 (IL-6) were measured in all PVCs burden (25%, 33% and 50%). In all these PVCs burden of 25%, 33% and 50%, PVCs induced cardiomyopathy (LVEF<50%) was present among 11.1%, 44% and 100% of animals but no increase in NT-proBNP or IL 6 was observed in any of these burdens.[14] This finding is in line with present study.

Another study aimed to identify the risk factors shows that the individuals with low socioeconomic status, increased waist hip ratio, body height>median and sokolow-Lyon Index have higher frequency of PVCs. At the same time the study demonstrates that the patients with higher NT-proBNP levels have frequent PVCs (PVCs burden>24%).[15] But the present study showed no association of NT-pro BNP with PVCs which could be due to the fact that present study determined the NT-proBNP levels in patients of mild to moderate PVC burden (PVCs<20%) rather than frequent PVCs burden.[15]

Sajadieh et al conducted a study on middle aged and elderly patients which demonstrates that in the absence of any known cardiac disease, the NT-proBNP levels are higher in patients with frequent PVCs as compared to those with no PVCs.[16]

In present study myocardial wall stress was not measured as this facility was not available in the center.

Conclusion

It is concluded from the present study that NT-proBNP levels are not raised in PVCs patients with burden of less than 20% as well as no correlation of NT-proBNP is found with PVCs in burden of less than 20%. Thus declining its importance as a determinant to stratify the patients at high risk

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ORIGINAL ARTICLE

To Compare the Effect of Nepafenac versus Prednisolone on Post-Operative Inflammation and Intraocular Pressure after Cataract Surgery

Asim Mehboob[1], Muhammad Usman Arshad[2], Faran Bin Afzal[3], Sohail Zia[4], Aneeq Ullah Baig Mirza[5], Masud Ul Hassan[6]

ABSTRACT

Objective: To compare the effect of topical 0.1% Nepafenac and 1% prednisolone in control of inflammation and maintenance of Intraocular Pressure (IOP) after cataract surgery.

Study Design: Randomized control trial.

Place and Duration of Study: Department of Ophthalmology, from 4th June 2018 to 30th June 2019.

Materials and Methods: Total sample size of study population was 400, including all patients getting phacoemulsification cataract surgery. Study population was equally divided in two groups. Group 1 was Nepafenac group, and Group 2 was Prednisolone group. Both groups underwent cataract extraction, and were started on topical 0.1% Nepafenac or 1% Prednisolone along with topical antibiotics after surgery. Post-operative IOP and activity and flare was checked in all patients on day 1, 7 and 28 after surgery and compared between both groups.

Results: The study population had a mean age of 60.97±4.91 years. The proportion of male and female patients in study population was 51% and 49% respectively. Difference in mean post-operative IOP and mean change from pre-operative value between both groups was statistically significant (p=0.003 and 0.004 respectively). There was statistically significant difference between both groups in terms of anterior chamber cells and flare respectively at 1st week post-operatively (p=0.002, and 0.003). However, there was no statistically significant difference between both groups in terms of anterior chamber cells and flare respectively after 28 days post-operatively (p=0.12, and 0.71).

Conclusion: Nepafenac is superior to prednisolone in controlling IOP after cataract surgery, with adequate and comparable control of post-surgical inflammation.

Key Words: *Intraocular Pressure, Nepafenac, Prednisolone.*

Introduction

Cataract surgery is the most commonly performed surgery all over the world in ophthalmic eye care.[1] However like any other surgical procedure; it is also associated with a number of complications. Commonly observed post-operative complications are inflammation, infection and refractive errors.[2] Post-operative inflammation after cataract surgery remains a grave concern. This manifests as cells in Anterior Chamber (AC), proteins (flare), corneal edema and iritis.[3] This is responsible for sufficient stress to patient as well as surgeon, as post-operative surgical outcome remain compromised till settling of inflammation, which usually requires a long term management with topical and local or systemic drugs. Inflammation is managed by variety of therapeutic agents like drugs corticosteroids and other anti-inflammatory drugs. Corticosteroids are commonly used agents, which manage inflammation very well with reasonable safety. Post-operative inflammation is managed by prescription of topical corticosteroids or local steroid injections, former being commonly practiced. The drugs are safely discontinued, upon return of eye to inflammation-free state, manifested by variety of clinical signs.[4] Different corticosteroids are commonly used to treat post-cataract surgery inflammation, with different

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safety and therapeutic profiles.[5]

Conventionally, topical dexamethasone, prednisolone, loteprednol etabonate and flouromethalone are given to control inflammation after cataract surgery. A commonly observed side effect of these agents is raised Intra Ocular Pressure (IOP). Although a number of factors can result in raised IOP after cataract surgery, but in un-eventful and complication free surgery with restoration of visual acuity within days, steroids can result in raised IOP. Increased IOP can result in compression of the optic nerve leading to progressive irreversible neuropathy.

Researches are being carried out internationally to recommend a safe compound which can provide anti-inflammatory effects but with no side effects as compared to traditional steroids. Non-Steroidal Anti Inflammatory Drugs (NSAID) is widely prescribed to manage post-operative inflammation and also to provide analgesia after phacoemulsification cataract surgery. They are also shown to be beneficial in control of IOP while managing inflammation. The role of NSAIDS is also well established in prevention of post pseudophakic surgery macular oedema.[6,7]

Therefore we tried to conduct a study on comparison of efficacy and safety of Nepafenac and Prednisolone after cataract surgery. The aim of the study was to compare the effect of topical 0.1% Nepafenac and 1% prednisolone in control of inflammation and maintenance of Intraocular Pressure (IOP) after cataract surgery.

Materials and Methods

This randomized control trial was carried out after permission from hospital ethical review board in the Department of Ophthalmology, from 04 June 2018 to 30 June 2019. Written informed consent was mandatory from all patients prior to inclusion in the study. Approval from hospital's ethical review committee and written informed consent was taken from all participants. The sample size was calculated keeping level of significance as 5%, and power of the test as 80%, using World Health Organization calculator. For ease of analysis, a total sample size of 400, with 200 patients in each group was strength of study. Non-probability consecutive sampling technique was used, and all patients divided in Group 1 or 2 using lottery method. Patients with visually significant cataract undergoing cataract surgery, aged between 40-60 years from either gender were included. Patients with pre-existing glaucoma or uveitis, complicated cataract, prolonged surgery, increased phaco time, per and post-operative complications, systemic diseases e.g., diabetes, hypertension, asthma, arthritis, were excluded. All patients underwent thorough eye examination and IOP measurement was by the single researcher to exclude bias. All the patients underwent a slit lamp examination of anterior segment and assessment of IOP using applanation tonometer. All patients underwent radical and conventional phacoemulsification surgery, and all were implanted with posterior chamber intraocular lens after surgery by a single surgeon. Both groups were prescribed with 0.5% topical Moxifloxacin eye drops, three times daily for 2 weeks. Group 1 was co-started with topical 0.1% Nepafenac eye drops, thrice daily for four weeks after cataract surgery. Group 2 was started with topical 1% Prednisolone eye drops thrice daily after cataract surgery for four weeks. IOP, AC cells and flare were checked on day 1, 7 and 28 after surgery. The data collected was entered in pre-devised proforma. The data was entered and analyzed using SPSS software version 20.0. The mean and standard deviations were used to evaluate ordinal data while frequencies and percentages were calculated for nominal data variables. Normality of data was checked. Post stratification, independent't' test was used to compare mean IOP and mean change in IOP between both groups. IOP of <19mmHg after cataract surgery was considered efficacy of topical drug to control IOP. Chi square test was used to compare grading of cells and flare between both groups. p value of ≤ 0.05 was taken as statistically significant.

Results

In this study a total of 400 cases meeting the inclusion criteria were evaluated and analyzed. The groups had equal number of participants (200 each). Group 1 was Nepafenac group, in which patients were given Nepafenac and Group 2 was Prednisolone group. The clinical data of study population is given in Table (I) The comparison between both groups in terms of age, gender and laterality of eyes was statistically unremarkable. Mean pre-operative IOP and post-operative IOP along with mean change in IOP in both groups is

given in Table(I) Difference between both groups in terms of post-operative IOP and mean change in IOP was statistically significant (p=0.003 and 0.004 respectively). A higher number of patients (102/200) showed IOP control efficacy (IOP<19mmHg) in group 1 as compared to group 2 (88/200). However, the difference was not statistically significant (p=0.182). The comparison of AC cells and Flare between both groups at 1 week and 28 days is given in Table (III) The difference in AC flare and cells grading between both groups at 1 week was statistically significantly different (p=0.023 and 0.002 respectively). However, the difference in flare and cells grading at 28 days (4 weeks) after surgery was not statistically significant (p=0.216 and 0.137 respectively).

Table I: Demography and Clinical Data of Study Population (n=400)

Variable		Group 1 Loteprednol etabonate Group (n=200)	Group 2 Dexamethasone Group (n=200)	p Value Groups)
Age (Years) Mean±SD	60.97±4.91	61.3±4.89	60.63±4.99	0.603**
Gender (Male/Female)	204 /196 (51%)/ (49%)	103 /97 (51.5%)/ (48.5%)	101 /99 (50.5%)/ (49.5%)	0.297*
Laterality of eye (Right/left)	198/202 (49.5%)/(50.5%)	98/102 (49%)/ (51%)	100/100 (50%)/ (50%)	0.762*

Table II: Comparison of Pre and Post-Operative IOP

Variable	Group 1 Nepafenac Group (n=200)	Group 2 Prednisolone Group (n=200)	p Value
Mean pre - operative IOP (mmHg) Mean±SD	18.17±2.11	18.18±2.17	0.438*
Mean post - operative IOP (mmHg) Mean±SD	19.04±1.86	21.31±2.07	0.003*
Mean change in IOP (mmHg) Mean±SD	1.23±0.18	2.79±1.19	0.004*
Frequency of IOP–Pre-Operative			
12-15mmHg	22(12.2%)	17 (9.4%)	0.713**
16-19 mmHg	94(51.9%)	93 (51.4%)	
20-23 mmHg	65(35.9%)	71 (39.2%)	
Frequency of IOP –Post-Operative			
12-15mmHg	4(2%)	10 (5%)	0.182**
16-19 mmHg	98(49%)	78(39%)	
20-23 mmHg	96(48%)	104(52%)	
24 27mmHg	2(1%)	8(4%)	

Table III: Comparison of Post-Operative AC Cells and Flare between Group (n=400)

Variable	Group 1 Nepafenac Group (n=200)	Group 2 Prednisolone Group (n=200)	p Value
AC Flare – 1 week			
Grade 0	76(382%)	162 (81%)	0.023*
Grade 1	88(44%)	22 (11%)	
Grade 2	36(18%)	16 (8%)	
AC Flare – 28 days			
Grade 0	164(82%)	192(91%)	0.216*
Grade 1	36(18%)	8 (4%)	
AC Cells – 1 week			
Grade 0	86(43%)	120 (60%)	0.002*
Grade 1	62(31%)	36 (18%)	
Grade 2	42(21%)	30 (15%)	
Grade 3	10(5%)	14(7%)	
AC Cells – 28 days			
Grade 0	166(83%)	186 (93%)	0.137*
Grade 1	32(16%)	14 (7%)	
Grade 2	2(1%)	-	

Discussion

The corticosteroids are widely used after cataract surgery to control post-operative inflammation, but rise in IOP is a known complication of their use. Injudicious and prolonged use, especially in already compromised individuals puts optic nerve at risk of damage. This has been managed by limited use or use of alternative therapeutic agents.[8] We observed a mean rise of 1.23±0.18 mmHg in IOP in patients receiving Nepafenac eye drops, while a mean rise of 2.79±1.19 mmHg was observed in Prednisolone group. In a study conducted for evaluation of IOP rise after Prednisolone use after cataract surgery, it was observed that 3% of patients has high IOP after cataract surgery.[9] Since the difference in change in IOP was significant between groups, we recommend use of Nepafenac in patients particularly susceptible to glaucomatous damage. There have been multiple researches evaluating safety, performance and analysis of NSAIDS after phacoemulsification

surgery. In a study evaluating post-operative inflammation by laser photometry, it was observed that Nepafenac was superior to other NSAIDs in controlling post-operative inflammation.[10] We used topical Nepafenac in concentration of 0.1%, given thrice daily for four weeks. Some studies evaluated the dose of Nepafenac, and found out that 0.1% Nepafenac was equally effective to 0.3% Nepafenac with less adverse effects.[11] In another study comparing efficacy of Nepafenac with placebo drug, it was observed that Nepafenac was far superior in managing post-surgical inflammation.[12] In the most reliable meta-analysis evaluating 19 controlled trials, it was observed that Nepafenac was superior to all NSAIDs in managing post-operative pain, while management of AC inflammation after cataract surgery was superior by Diclofenac followed by nepafenac eye drops.[13]

There have been some studies mentioning the superiority of steroids in maintaining mydriasis during cataract surgery if used before surgery. However some studies have shown equal efficacy of Nepafenac and Prednisolone in maintaining mydriasis during phacoemulsification.[14] This is to prove non-inferiority of NSAIDs to steroids in managing per-operative mydriasis.

In another study conducted for comparison of Nepafenac and Prednisolone in controlling inflammation after small gauge vitrectomy, it was observed that Nepafenac was superior to Prednisolone in managing post-operative pain, and was equal in efficacy in management of post-operative inflammation.[15] In other studies comparing safety profile of NSAIDs and steroids in management of inflammation after cataract surgery, it was observed that Diclofenac was equal to Prednisolone in management of inflammation, and was equally safe and well-tolerated.[16] Similar findings were observed by Malik A and colleagues, who observed that NSAIDS like nepafenac, bromfenac and ketorolac are a good alternative to steroids in management post-operative ocular inflammation.[17]

We observed that there was statistically significant difference in grading of AC cells and flare between both groups at 1 week after surgery. However, the difference was not statistically significant at 4 weeks after surgery. This is in connection with results found out by Simone JN et al who found out that Prednisolone was superior to Nepafenac in management of ocular inflammation at 1 week, which was comparable at one month after surgery.[18] We used either Nepafenac or Prednisolone along with antibiotic after surgery. In another study, it was revealed that Diclofenac alone, or used in combination with Dexamethasone was superior to Dexamethasone alone in prevention of development of pseudophakic macular edema, and change in central retinal thickness.[19]

There have been conflicting results with regards to superiority of NSAIDs in post-operative pain and inflammation. In one meta-analysis, gross results showed the superiority of NSAIDS in management of post-operative inflammation as compared to corticosteroids. However, the results also showed the better results of NSAIDS in prevention of Irvine Gass syndrome (pseudophakic cystoid macular oedema).[20] In one meta-analysis evaluating 48 randomized control trials, no conclusion was found regarding superiority of NSAIDs to steroids in management of post-operative inflammation or pain.[21]

Our study has limitation of not having a group using combination of NSAIDS and steroids for management of inflammation and evaluation of IOP. The management of post-operative pain using visual analogue score could also have been beneficial. The follow up time of 4 weeks after surgery was also slightly shorter, considering that inflammation might continue for 6 to 8 weeks after surgery.

Conclusion

We conclude that Nepafenac was safer in control of IOP after phacoemulsification cataract extraction surgery. The control of post-operative inflammation is better with use of steroids immediately after cataract surgery. However, in long term, both drugs show equal efficacy in management of post-operative inflammation. Nepafenac is thus a safe and efficient alternative to Prednisolone in patients undergoing un-eventful cataract surgery.

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ORIGINAL ARTICLE

Proximal Convoluted Tubules as the Primary Target of Renal Histopathological Injury by Ingestion of Pesticide-Residue-Laden Fruits and Vegetables

Lubna Shahper[1], Shagufta Nasreen[2], Muhammad Qasim Muneer[3], Nazia Ayyub[4], Sadia Hassan[5]

ABSTRACT

Objective: To determine the potential adverse renal histopathological effects on the proximal convoluted tubules in male, *Wistar* rats due to ingestion of subchronic dose of triazophos.

Study Design: Randomized controlled trial.

Place and Duration of Study: A study of 3 weeks duration (plus 1 week for slide preparation & histological study), was held in the animal house-PGMI, Bird wood road, Lahore.

Materials and Methods: Two equal groups were made, of 6 *Wistar*, male rats each. Group A was control while experimental group B was given triazophos, in a dose of 8.2 mg/kg-subchronic dose ($1/10^{th}$ of LD 50), a commonly used pesticide, as 1:100 dilution solution through oral gavage for 21 consecutive days. On day 22, the rats were sacrificed and tissues preserved for histological examination and measurement of proximal and distal tubular diameters by using micrometric grid.

Results: The micrometric measurement of diameters of PCT in group A and B indicated that they increased significantly from 38.90 ± 2.72µm in group A to 50.35 ± 2.61µm in group B (p-value <0.001). The mean diameter of DCT in both the groups was also measured and increased in group B from 34.48 ± 2.58µm in group A to 48.03 ± 3.42µm in group B (p-value <0.001). In group B, inflammatory changes like basement membrane interruption, loss of brush border and severe vacuolar cellular degeneration of proximal convoluted tubules were seen.

Conclusion: The results confirm the potential adverse renal histopathological effects on the proximal convoluted tubules in male, *Wistar* rats due to ingestion of triazophos, a commonly used pesticide. Pesticides induce inflammatory changes in convoluted tubules leading to tubular dilatation and hyperplasia more in PCT owing to the extensive exposure of toxic substances in the proximal tubules and resultant increased PCT mean diameter.

Key Words: *Food Chain, Harmful Residues, Insecticides, Pesticides, Renal Damage, Triazophos.*

Introduction

The scientists claim that organophosphorus pesticides like triazophos rapidly degrades and do not tend to persist or bioaccumulate in the environment or food chain but unfortunately pesticide residues in food are regularly detected at low levels in the food chain in a range of food items and water.[1] Triazophos is an organophosphorus pesticide, sprayed rampantly on crops to get rid of the pests infesting on them and to improve the crop yield.[2] It is widely used in agriculture, veterinary medicine and public health all over the world due to its rapid biodegradability and good control over the pests.[3] In spite of all the claims of pesticides' non-persistence in the food chain, their residues' presence in food items cannot be denied. Thus, not only the nutritional value of the food is compromised, pesticides' presence adversely affects the environment as well as the consumers' health.[4] Liver & kidneys are the primary organs to be affected due to the conjugative metabolism & excretion of the pesticides through these organs.[5] In kidneys, proximal convoluted tubules are the primary target of histological injury owing to their greater length than the distal convoluted tubules & greater

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exposure of all kinds of toxins to them.[6]

The unfortunate extension of pesticides' harmful effects, from the target of pest control to involvement of non-target spectrum of other living organisms as well has led to a confusion whether pesticides are more harmful or useful for the mankind.7 The rationale of present study aimed at observing renal damage especially in the proximal convoluted tubules when the experimental animals ingested subchronic dose of triazophos for a period of 3 weeks. The main objective of the study was to determine the potential adverse histopathological effects on the proximal tubules in male, *Wistar* rats due to ingestion of subchronic dose of triazophos.

Materials and Methods

The study was randomized controlled trial of 3 weeks duration (plus 1 week for slide preparation & histological study) held in the animal house of PGMI, Lahore, in which 12 male, *Wistar* rats of age 6-8 weeks (excluding the females, < 6 weeks old, < 150 g weight, sick and ailing rats), weighing 175-200 g were selected. Rules and regulations laid down by the Ethical review board of Postgraduate medical institute, Lahore were followed & their ethical permission taken. The sampling technique adopted was by simple random sampling, with the help of Stat Trek's Random Number Generator. Group A was kept as control and group B as experimental.

The animals were acclimatized for a week; food and water were made available *ad libitum,* with maintenance of 12-hour light and dark cycle and temperature maintained at 25-30°C. Triazophos was given in the sub chronic dose, 8.2 mg/kg body weight ($1/10^{th}$ of LD50)[8] to the group B as dilution solution through oral gavage while same quantity of distilled water was given to the group A for 21 consecutive days.[9] Parametric data was noted on weekly basis. The rats were sacrificed on day 22, their kidneys dissected out and preserved for H & E slides preparation and histological examination for micrometric measurement of tubular diameters.

Four proximal and four distal convoluted tubules (sub capsular, mid-cortical, juxtamedullary and medullary) [10] were selected per high power field (40X); for each slide; both the vertical and horizontal diameter between the opposite basement membranes of each tubule was measured and then average taken. Finally, the mean diameters of PCT and DCT were determined for each animal.[11] For micrometry**,** an eyepiece micrometer scale and a stage micrometer slide were used. On the stage micrometer slide, a 1 mm scale was engraved. This 0.01 mm scale was divided into 100 equal divisions. 15 divisions of eyepiece micrometer were equal to 4 stage micrometer divisions.[12]

100 stage divisions = 0.01mm = 1000 µm

1 stage division = 1000/100 = 10 µm

15 divisions of eyepiece micrometre = 4 stage divisions (40 µm)

1 division of eyepiece micrometre = 40/15 = 2.66 µm

The measured average diameter of each tubule was multiplied by 2.66 to get the exact tubular diameter.[13]

Data was analyzed by SPSS version 22.0. Independent sample t-test was used to compare the mean diameters of PCT and DCT in both groups. Fisher's exact test was used to analyze the proximal and distal tubular epithelial cells for cytoplasmic vacuolization and loss of brush border.

Results

Diameter of PCT/DCT: The mean diameters of PCT and DCT in both group A and B were taken.

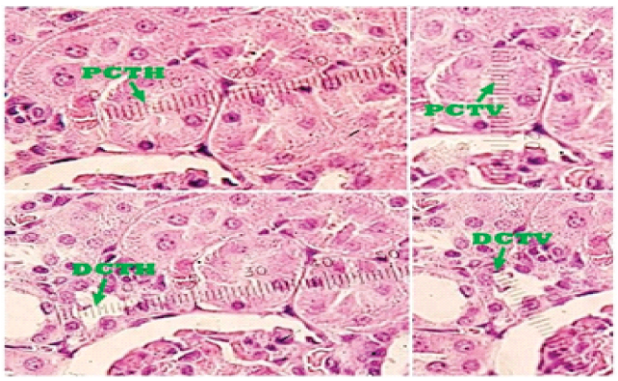

Fig 1: Photomicrograph Showing the Horizontal and Vertical Proximal Convoluted Tubular Diameter (PCTH/ PCTV) and Distal Convoluted Tubular Diameter (DCTH/ DCTV) through Micrometer. H&E X400

Table I: Mean Diameter Comparison PCT and DCT among Groups

Parameters	Group A	Group B	p-value
Mean diameter PCT of all rats in a group	38.90 ± 2.72	50.35 ± 2.61	< 0.001*
Mean diameter DCT of all rats in a group	34.48 ± 2.58	44.03 ± 3.42	< 0.001*

Independent sample t test

**p value* ≤ 0.05 is considered statistically significant

Loss of Brush border

Fisher's exact test showed that there was statistically significant association between loss of brush border PCT and groups (Table II Figure 2, 3)

Table II: Distribution of Loss of Brush Border (PCT) Among Groups

Brush Border loss	Group A N=6 (%)	Group B N=6 (%)	*p-value*
Normal	6 (100%)	0 (0.0%)	0.002*
Mild 25-50%	0 (0.00%)	0 (0.0%)	
Moderate 50-75%	0 (0.00%)	2 (33.3%)	
Severe 75-100%	0 (0.00%)	4 (66.7%)	

Fisher's exact test

*p value ≤ 0.05 is considered statistically significant

Cytoplasmic Vacuolization (PCT/DCT):

Fisher's exact test showed that there was statistically significant association between cytoplasmic vacuolization in PCT and DCT among groups. (Table III, IV; Figure 2, 3)

Table III: Distribution of Cytoplasmic Vacuolization (PCT) Among Groups

Cytoplasmic vacuoles in PCT	Group A N=6 (%)	Group B N=6 (%)	*p-value*
Normal	6 (100%)	0 (0.0%)	0.002*
Mild 25-50%	0 (0.00%)	0 (0.0%)	
Moderate 50-75%	0 (0.00%)	1 (16.7%)	
Severe 75-100%	0 (0.00%)	5 (83.3%)	

Fisher's exact test

*p value ≤ 0.05 is considered statistically significant

Table IV: Distribution of Cytoplasmic Vacuolization (DCT) Among Groups

Cytoplasmic vacuoles in DCT	Group A N=6 (%)	Group B N=6 (%)	*p-value*
Normal	6 (100%)	0 (0.00%)	0.002*
Mild 25-50%	0 (0.00%)	0 (0.00%)	
Moderate 50-75%	0 (0.00%)	2 (33.3%)	
Severe 75-100%	0 (0.00%)	4 (66.7%)	

Fisher's exact test

*p value ≤ 0.05 is considered statistically significant

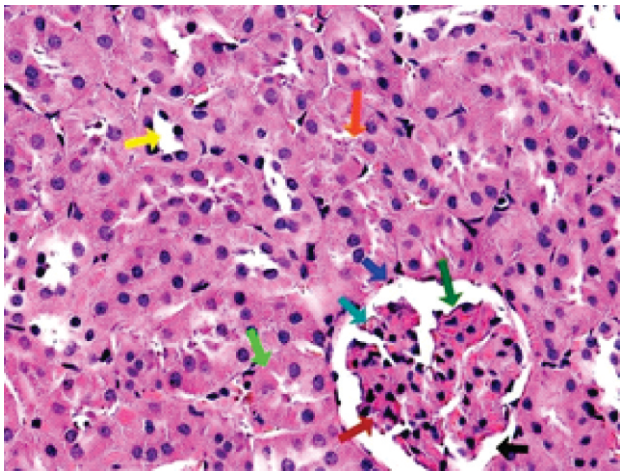

Fig 2: Photomicrograph of group A kidney cortex showing glomerulus **(Red)**, parietal **(Blue)** and visceral **(Dark-Green)** layers of Bowman's capsule **(Black)**, tuft of capillaries **(Aqua-Blue)**, proximal tubules (**Light-Green**) with brush border **(Orange)** and distal convoluted tubules **(Yellow)**. H&E stain X400.

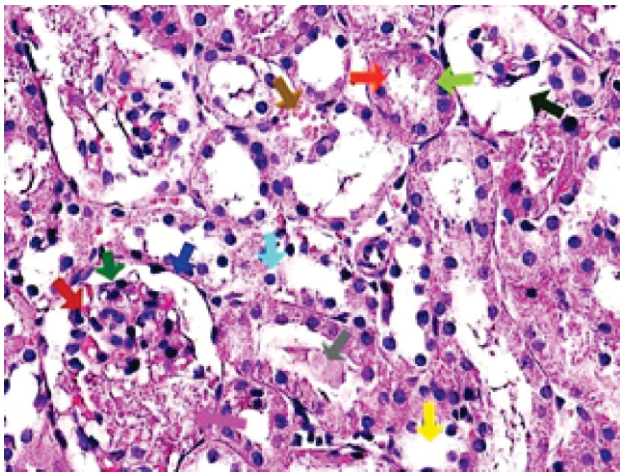

Fig 3: Photomicrograph kidney cortex in group B showing glomerulus **(Red)**, parietal **(blue)** and visceral layers **(Dark-Green)**, Bowman's space **(Black)**, glomerulus **(Pink),** distal **(Yellow)** & proximal tubules (**Light-Green**) loss of brush border (**Orange),** protein cast **(Grey)**, congestion in the blood vessel (**Brown**) and vacuole **(Aqua Blue**). H&E stain X400.

Discussion

In the present study, subchronic dose of triazophos induced nephrotoxicity evidenced by histopathological changes in the kidneys.[14] The most marked change observed in the H & E kidney slides of rats of group B was increased tubular diameter measured by using micrometric grid under light microscope (Table I, Fig. 1), due to cellular hyperplasia leading to tubular dilation & ultimate

epithelial necrosis, degeneration and desquamation with granular debris in the tubular lumen. This increase in diameters was statistically significant (p-value <0.001).

Pesticides exhibit their harmful effects due to induction of oxidative stress in the cells and generation of free oxygen radicals.[16] The reactive oxidative radicals cause anatomical and functional alterations in the mitochondria of cells.[17]

In group B, all rats had moderate to severe interrupted brush border (Table II, Fig 3).[15]This loss of brush border was statistically significant (p value< 0.002). Cytoplasmic vacuolization of PCT (Table III, Fig 3) and DCT (Table. IV, Fig 3) in the rats of group B was also statistically significant.

The loss of brush border results when lysosomal degradative enzymes damage the glycocalyx thus disrupting the microfilaments making the structure of microvilli onto the cytoskeleton of cells as well as cell membrane disruption.[19] Disturbed ionic balance in the organelles underlie the formation of multiple membrane vesicles which fuse to form vacuoles causing breakdown of organelles and finally cell death as already explained by Elhalwagy in 2016 in a study on effects of triazophos on liver and kidneys of rats.[20]

Commonly used pesticides like triazophos, persist in the environment and food chain.[21] Jain et al, in 2010.[17] Ghaffar et al, in 2014[22]and Mohineesh et al, in 2014[23] conducted studies on triazophos and its subchronic dose's effects on body tissues. They all proved that triazophos adversely effects the body organs. Rahman and Sattar in 2018 conducted a study on effects of different doses of pesticides on body tissues.[24]

The present study was conducted to observe the persistence of organophosphorus pesticides in the food chain of Pakistan, the present status of which is quite alarming for the health of mankind, as rampant usage of pesticides on crops is tenfold high in Pakistan as compared to other countries. The limitations of the present study were the unawareness among the general population about the hazards of the rampantly-used pesticides and insecticides on almost all the crops and the persistence of their residues in the fruits and vegetables. The gravity of the situation and the unawareness towards its seriousness seems like a hidden iceberg and need further probing into the matter.

Conclusion

The results confirm the potential adverse renal histopathological effects on the proximal convoluted tubules in male, *Wistar* rats due to ingestion of triazophos, a commonly used pesticide. Pesticides induce inflammatory changes in convoluted tubules leading to tubular dilatation and hyperplasia more in PCT owing to the extensive exposure of toxic substances in the proximal tubules and resultant increased PCT mean diameter.

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ORIGINAL ARTICLE

Dexamethasone versus Prednisolone in Relapse of Symptoms in Children with Acute Exacerbations of Asthma

Hijab Shaheen[1], Shagufta Sohail[2], Noshina Riaz[3]

ABSTRACT

Objective: To determine effectiveness of single dose of oral dexamethasone with multiple doses of oral prednisolone in relapse of symptoms in children with acute exacerbations of asthma.

Study Design: This was a randomized controlled trial.

Place and Duration of Study: The study was conducted from 1st January to 31st December 2016 at the emergency department of Children's Hospital, Pakistan Institute of Medical Sciences (PIMS), Islamabad.

Materials and Methods: Total 302 patients were included in the study with 151 children in each group receiving either dexamethasone or prednisolone. Sampling technique was consecutive and non-probable. Children of age 2 to12 years with previous history of asthma diagnosed by a physician presenting with acute exacerbations in emergency were included after consent. After assessment of Pediatric respiratory assessment measure (PRAM) score by the study physician, the patient was either given a single dose of dexamethasone 0.3mg/kg with maximum dose of 12mg or 1mg/kg of oral prednisolone with maximum dose of 40mg followed by two doses for next 2 days after discharge. Patients were reassessed for PRAM score at day 4. The patients were then called at day 14 for the assessment of relapse of symptoms of asthma like cough, wheeze and breathing difficulty. Data was documented by the study physician on a proforma. SPSS version 20 was used for entry and analysis of data. Data was presented as mean with standard deviations. Percentage was calculated from descriptive variables. Chi-square test was used for nonparametric data. P value was significant if less than 0.05.

Results: There was no significant difference in relapse of symptoms of asthma on day 14 between dexamethasone and prednisolone.10 patients i.e. 6.6% in Prednisolone and 12 i.e. 7.9% in Dexamethasone group had relapse of symptoms of asthma on Day 14 with a 'p' value of 0.65 which was not significant.

Conclusion: Single dose dexamethasone is as effective as multiple doses of prednisolone as measured by relapse of symptoms in children with acute exacerbation of asthma.

Key Words: *Asthma, Dexamethasone, Prednisolone, Relapse.*

Introduction

Asthma is one of the common pediatrics illnesses.[1] It is a frequent cause of presentation in the emergency department and hospitalization. In children it is estimated that asthma causes an estimated loss of 14.4 million school days.[2] Asthma is a worldwide problem with an estimated 300 million affected individuals.[3] Global Initiative of Asthma (GINA) reports a prevalence of 4-5% in Pakistan.[4] Asthma is a chronic inflammatory disorder characterized by airway hyper responsiveness.[5] Bronchoconstriction leads to airway edema in response to certain triggers leading to cough, shortness of breath, chest tightness and wheeze along with variable limitation of expiratory airflow.[6] Patients with asthma experience exacerbations with worsening of their symptoms. In 2019 British Thoracic society (BTS) guidelines recommend inhaled β_2 agonist as first line treatment for asthma along with early use of steroids.[7] Systemic corticosteroids for shorter duration are mainstay for asthma exacerbations which are moderate to severe.[8] Corticosteroids decrease relapses of illness, admission to hospitals and the requirement for bronchodilators. The steroid recommended is prednisone/prednisolone orally for five days, as oral is as effective as intramuscular and intravenous route.[9] However; prolonged duration of treatment with prednisolone

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for 3-5 days and its bitter taste leading to vomiting may decrease compliance with it.[10]Dexamethasone is tried as an alternative to prednisolone. It has a long half-life (36 to 72 hours) as compared to prednisolone (12 to 36 hours) so it requires fewer doses as compared to prednisolone.[10] Furthermore it tastes better and costs less. It can be given orally or via intramuscular route ensuring compliance.

A number of studies have published which compared single or two days per oral or intramuscular dexamethasone with 3 or 5 days of prednisone or prednisolone. There is increasing documentation that short duration of treatment with dexamethasone is as effective as prednisolone in asthma exacerbations which are mild or moderate in severity.

Asthma is a common illness in our community. Although there are multiple trials available in the literature to support equivalence of dexamethasone versus prednisolone, there is no study conducted in this regard locally. Secondly the available guidelines are still supporting use of prednisolone in asthma exacerbations. So we decided to carry out this comparative study in our local population in the emergency department to compare the relapse rate of symptoms in children with acute exacerbations of asthma receiving either oral dexamethasone or prednisolone.

Materials and Methods

It was a Randomized control trial conducted at the Emergency Department, Children's Hospital, Pakistan Institute of Medical Sciences (PIMS), Islamabad from 1st January 2016 till 31st December 2016.Total sample size was 302 cases and 151 patients were included in each group receiving either dexamethasone or prednisolone. Consecutive, non-probable sampling technique was used. Permission from the hospital ethical committee was taken before the commencement of study. Inclusion criteria was children of age 2 to 12 years, both male and female with previous history of asthma as diagnosed by a physician , who present with acute exacerbation of asthma in emergency department. Asthma exacerbation was interpreted as acute attack of asthma with symptoms of cough, wheeze, dyspnea and oxygen saturation of less than 95% and with Pediatric Respiratory Assessment measure(PRAM) score of more than or equal to 6.[11] This score takes into account 5 items to evaluate severity of asthma. Suprasternal retractions, scalane muscle contraction, air entry in chest, wheeze and oxygen saturation with individual score of 0-4 for each sign. Total score from 1-3 shows mild exacerbation, 4-7 shows moderate exacerbation and 8-12 reveals severe exacerbation of asthma. Patients with silent chest, cyanosis, drowsy, unable to verbalize, having marked tachycardia and respiratory distress, having known exposure to tuberculosis, fever more than 39.5C°,use of corticosteroids in previous 4 weeks and those having significant co-morbid were excluded from the study .

Eligible participants were identified during clinical consultation in emergency department and PRAM score was assessed by the study physician. Informed written consent was obtained from parents/guardians. Randomization was done by lottery method. The study physician was responsible for randomization, dispensing, accountability and collection of medicinal products and maintenance and documentation of patient's record and data. Study packs of the medicines were made; each labeled clearly with name of the medication "PREDNISOLONE" or "DEXAMETHASONE."The randomized patient was either given a stat dose 0.3mg/kg dexamethasone orally (maximum 12mg) or prednisolone orally in 1mg/kg dose (maximum 40mg) followed by two doses after discharge. If the patient was randomized to the group of dexamethasone that was the only dose. If the patient was randomized to have prednisolone, two doses were provided to the patient prior to discharge from emergency department for next two subsequent day intake to complete 3 days of treatment. Subjects and parents/guardians were trained to administer prednisolone on second and third day of treatment. Patients were asked to bring the empty (dose) packs on the fourth day and were reassessed for PRAM score .Patients were then called after two weeks and enquired about symptoms of relapse of asthma. A relapse was interpreted as a visit to physician for symptoms of wheeze, breathing difficulty and cough within two weeks of inclusion in the study.[10] Patients who vomited after oral steroids, whose condition deteriorated and required hospitalization, those did not appeared for Day 4 PRAM score reassessment or

were lost to follow up at two weeks were excluded from the study.

SPSS version 20 was used for entry and analysis of non-parametric data. Data was presented as mean with standard deviations. Percentage was calculated from descriptive variables. Chi- square test was used. P value was significant if less than 0.05.

Results

Total 302 patients were finally enrolled in the study and 151 children were included in each group. Regarding age of patients, 71 i.e. 47% in Prednisolone and 93 i.e. 61.5% in Dexamethasone group were between 2-7 years of age while 80 i.e. 52.9% in Prednisolone and 58 i.e. 38.4% in Dexamethasone group were between 8-12 years of age. Mean age was 7.48± 2.53 years in Prednisolone and 7.07± 2.16 in Dexamethasone group. 96 i.e. 63.5% in Prednisolone and 80 i.e. 52.9% in Dexamethasone group were male while 55 i.e. 36.4% in Prednisolone and 71 i.e. 47.02% in Dexamethasone group were female. PRAM Score for each patient either in the dexamethasone or prednisolone group at time of induction in study was calculated and distribution of all patients according to the score is shown in Table I. Majority of the patients either in dexamethasone or prednisolone group had a score of 9 or 10 at induction. No patient having PRAM score of 12 was included in either group because of associated co-morbidities.

Table I: Distribution of Patients According to Pram Score

Pram Score At Baseline	Dexamethasone Number (%)	Prednisolone Number (%)
6	12(7.9%)	10(6.6%)
7	22(14.5%)	19(12.5%)
8	19(12.5%)	23(15.2)
9	42(27.8%)	40(26.4%)
10	33(21.8%)	42(27.8%)
11	23(15.2%)	17(11.2%)
12	0	0
Total	151	151

The mean PRAM score at baseline was calculated as 8.90 ± 1.40 in Prednisolone and 8.86 ± 1.49 in Dexamethasone group. It was 0.92± 0.33 for Prednisolone and 0.96 ± 0.25 for dexamethasone group on 4th day of treatment. The mean change in PRAM score from baseline to reassessment at day 4 was 7.98 for prednisolone and 7.90 for dexamethasone group.

Only 10 patients i.e. 6.6% in Prednisolone and 12 patients i.e. 7.9% in Dexamethasone group had relapse of symptoms of asthma like cough, wheeze or breathing difficulty documented on day 14 follow up, whereas 141 i.e. 93.3% in Prednisolone and 139 i.e. 92% in Dexamethasone group had no relapse of symptoms. This difference was not statistically significant with 'p' value of 0.65.

Discussion

This study suggests that in children with acute exacerbation of asthma, there was no significant difference in relapse of symptoms either treated with prednisolone or dexamethasone on a 14th day follow up. Dexamethasone is as effective as prednisolone and can be used as an alternative to prednisolone in management of exacerbations of asthma. It requires lesser/fewer doses than prednisolone; effects are equivalent but not inferior to prednisolone.

The results of our study are comparable to a trial done by Cronin et al. comparing dexamethasone to prednisolone for acute exacerbations of asthma.[10] They concluded that a single oral dose of dexamethasone (0.3mg/kg) was non inferior to a 3 days treatment of prednisolone (1mg/kg/day) as measured by mean PRAM score on day 4.No significant difference was also observed in both groups receiving either dexamethasone or prednisolone in hospital admissions or number of return unscheduled visits after treatment to hospital. Keeney et al.in their analysis regarding risk of relapse of symptoms between dexamethasone and prednisolone at day 5 and 10-14 days found no significant difference.[12] However they included studies comparing both oral and intramuscular dexamethasone with oral prednisolone in their analysis.

A double blind, randomized controlled trial was conducted in India to compare the efficacy of oral dexamethasone to prednisolone in treatment of moderate exacerbation of bronchial asthma in children.[2] They also concluded that single dose of dexamethasone was as effective as three doses of prednisolone as no significant difference was observed in mean time in hours to attain a PRAM score of less than 2 and number of bronchodilator nebulization in both groups randomized to receive either dexamethasone or prednisolone.

Paniagua et al in a randomized, non-inferiority trial

compared efficacy of two doses dexamethasone (0.6 mg/kg/dose) to five days of oral prednisolone (1.5 mg/kg/day, followed by 1mg/kg/day on days 2-5) in children with asthma exacerbations.[13]Both groups showed no difference related to persistence of symptoms and unscheduled emergency department visits at day 7. They also suggested dexamethasone as an effective alternate to prednisolone.

A Cochrane review by Norman sell et al which reviewed 18 randomized studies comparing dexamethasone to prednisolone suggested a comparable (not superior) efficacy and safety of dexamethasone to prednisolone.[14] However, it suggested larger studies with oral steroids to make conclusions as different studies had used different doses and duration of steroids and different methodologies to measure results.

Our study suggests dexamethasone as a potential alternate for prednisolone. Longer half-life as compared to prednisolone leading to less frequent dosing, better taste, lesser cost and similar efficacy as documented by insignificant difference in relapses of both groups makes it a better alternative therapy.

Limitation of our study was small sample size in each group and only children of two to twelve years were included in our study so findings are required to be confirmed with a larger trial. Secondly this study was conducted in the emergency department of the hospital and further studies are required to apply this management to ambulatory outpatient clinics as well.

Conclusion

Single dose dexamethasone is as effective as multiple doses of prednisolone as measured by relapse of symptoms in children with acute exacerbation of asthma.

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ORIGINAL ARTICLE

Cord Blood Albumin as a Predictor of Significant Hyperbilirubinemia in Term Neonates

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ABSTRACT

Objective: To determine the frequency of jaundice at a cut off level of ≤2.8 gm/dL of the cord blood albumin in full term babies.

Study Design: Descriptive case series study.

Place and Duration of Study: This Research was done in Pediatric Department, Holy Family Hospital, Rawalpindi from 27th July 2013 to 27th January 2014.

Materials and Methods: Seventy term neonates, delivered by any mode of delivery and normal birth weights were included. Cord blood albumin level was sent. Neonates were divided into two groups. Group I was having cord blood albumin levels equal to or less than 2.8gm/dl and group II had level above 2.8gm/dl. They were followed in OPD at 72 hrs of life for development of jaundice. Jaundice was assessed clinically by Kramer dermal zones method and confirmed by serum total bilirubin level estimation. All information was recorded in predesigned proforma. Data was analyzed by using SPSS Version 23. Chi square was used to calculate frequency of jaundice in two groups of neonates.

Results: Mean cord blood albumin level was 3.23±0.86 gm/dL. Frequency of jaundice was significantly high in group I-71.9% versus 15.8% in group II (p=0.0005). Stratification analysis was performed with respect to gender for frequency of jaundice. It was again significantly high in group I compared to group II, irrespective of sex. (p=.001 and.002 respectively).

Conclusion: It is concluded that full term babies having cord blood albumin level ≤2.8 gm/dL are at risk to develop neonatal jaundice.

Key Words: *Albumin, Cord blood, Jaundice Neonatal.*

Introduction

Jaundice is the visible manifestation in skin and sclera of elevated serum bilirubin. Neonatal jaundice may not appear until serum bilirubin exceeds 5 to 7 mg/dL. Significant neonatal jaundice means any level of bilirubin requiring intervention like phototherapy and exchange transfusion.[1]

Jaundice is observed during the first week of life in approximately 60% of term and 80% of preterm neonates.[2] A study in West Indies showed the incidence of clinically significant jaundice in this age, as 4.6%.[3]

Nearly 8% to 11% of neonates develop hyperbilirubinemia.[4] It is one of the commonest cause of admission in neonatal units worldwide.

Bilirubin is produced in reticuloendothelial system as the end product of heme catabolism. Biliverdin is formed from heme and is reduced to water insoluble bilirubin. It is then transported bound to albumin to the liver.[5]

A study done in Karachi reported that neonatal jaundice was the third common cause, accounting for 13.5% of all neonatal admissions.[6]

Extreme neonatal hyperbilirubinemia has long been known to cause the clinical syndrome of kernicterus, or chronic bilirubin encephalopathy (CBE). Kernicterus is commonly characterized by choreoathetoid cerebral palsy (CP), impaired upward gaze, and sensorineural hearing loss, whereas cognition is relatively spared. The chronic condition of kernicterus may be, but is not always, preceeded in the acute stage by acute bilirubin encephalopathy (ABE). This acute neonatal condition is also due to hyperbilirubinemia, and is characterized by lethargy and abnormal behavior, evolving to frank neonatal encephalopathy, opisthotonus, and seizures.[7]

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It is already established from literature, that low levels of serum albumin at the time of birth are a predictor of significant hyperbilirubinemia. The early prediction of jaundice can help in timely intervention and reduction in morbidity and mortality associated with hyperbilirubinemia. In our country less work has been done on this subject. The aim of our study was to determine the frequency of jaundice at a cut off level of ≤2.8 g/dL of cord blood albumin in full term babies.

Materials and Methods

This descriptive Case Series study was done in Pediatric department, Holy Family Hospital (HFH) Rawalpindi from 27th July 2013 to 27th January 2014. Seventy neonates delivered in Holy Family Hospital, were included by using consecutive sampling technique.

After approval from hospital ethical committee and informed consent from each parent, 2 ml of cord blood was taken for serum albumin and sent to the laboratory.

Term neonates with gestational age between 37 to 42 weeks, born by any mode of delivery, of both genders and normal birth weights were included. Prematurity, Rh, or ABO incompatibility, already admitted patients and those having CRP >6 were excluded from the study.

On the basis of cord blood albumin levels, neonates were divided into two groups, one having cord blood albumin less than or equal to 2.8gm/dL(Group I) and the other having cord blood albumin more than 2.8gm/dL (Group II). They were followed in OPD at 72 hrs of life for development of jaundice. Jaundice was assessed clinically by Kramer dermal zones method and confirmed by serum total bilirubin level estimation. Neonates were assessed for the need of phototherapy/exchange transfusion.

Data was analyzed by using SPSS Version 23. For qualitative variables like gender and jaundice, frequency and percentages were calculated. Chi square was used to calculate frequency of jaundice in two groups of neonates. *p* value less than 0.5 was significant.

Quantitative variable, albumin level was represented as mean and standard deviation. Stratification was done with respect to gender and observed effect on outcome.

Results

Out of 70 neonates, 44(62.86%) were male and 26(37.14%) were female. Spontaneous vaginal delivery (SVD) was the mode of delivery of 49 (70%) and 21(30%) were born by Lower Segment Caesarean Section (LSCS). The neonates were divided into two groups on the basis of cord blood albumin level. They were followed in OPD at 72 hrs of life for development of jaundice. Clinically jaundice was observed in 29 (41.43%) neonates at 72 hours of life.

Mean serum albumin level was 3.23±0.86 gm/dl (2-5.8 gm/dL) as shown in (Table I). There were 32(45.71%) neonates in group I and 38(54.29%) in group II. Comparison of frequency of jaundice among neonates in two groups of cord blood albumin is shown in (Table II). It was significantly high in group I [71.9% (23/32) versus 15.8% (6/38)] as compared to group II (p=0.0005).

Stratification analysis was performed with respect to gender for frequency of jaundice. It was again significantly high in group I in both male and female neonates. [p=.001 and.002 respectively (Table III)].

Table I: Mean Serum Albumin Level in Full Term Neonates

Statistics		Serum Albumin Level (gm/dl)
Mean		3.23
Std. Deviation		0.86
95% Confidence Interval for Mean	Lower Bound	3.03
	Upper Bound	3.44
Minimum		2.0
Maximum		5.8

Table II: Comparison of Frequency of Jaundice in Group I &II on Basis of Cord Blood Serum Albumin. (N = 70)

Cord blood Albumin levels	Frequency Of Neonates with Jaundice at 72 Hours	Total	P-Value
≤ 2.8 gm/dl Group I	23(71.9%)	32	0.0005
>2.8 gm/dl Group II	6(15.8%)	38	

SPSS Version 23 (Chi-Square test = 22.51)

Table III: Comparison of Frequency of Jaundice in Male and Female Neonates in Group I and II

Cord Blood	Jaundice at 72 hours		P-Value
Albumin levels	MALE	FEMALE	
≤ 2.8 gm/dl Group I	12(66.7%)	11(78.6%)	0.001 (M)
>2.8 gm/dl Group II	4(15.4%)	2(16.7%)	0.002 (F)
Total	16	13	

SPSS Version 23 [Chi-Square test = 12.088 (M), 9.905(F)]

Discussion

In the present study, we assessed the ability of cord blood albumin as a predictor of significant hyperbilirubinemia in neonates. Out of 70 babies 32 were in group I and 38 in group II. Frequency of jaundice was significantly high in group I (71.9%) as compared to group II (15.8%). Sex and mode of delivery had no significant correlation with hyperbilirubinemia.

Jaundice is a common clinical condition and constitutes one of the major causes of morbidity during the neonatal period.[8] Neonatal hyperbilirubinemia (NH) needs appropriate and timely treatment, no matter whether it arises from physiological or pathological causes.[9] Physical examination is not a reliable measure of the blood level of serum bilirubin. The concept of prediction of jaundice offers an attractive option to pick neonates at risk of significant neonatal hyperbilirubinemia. In these situations, it would be desirable, to implement early treatment and thereby minimize the risk of bilirubin dependent brain damage.[10]

Maisels and Kring showed that male sex has more risk of readmission for neonatal hyperbilirubinemia. It could be explained on the basis that in developing countries male children are given more care in comparison to the females, because of the gender discrimination prevalent in the society.[11] Our study resembles the study done by Taksande et al, which also states that there is no relation between neonatal hyperbilirubinemia and the sex of the baby.[12]

In this study 70% neonates were delivered by SVD and 30% were born by LSCS. Taksande et al and Aiyappa's studies state that there is no significant association between the mode of delivery and neonatal hyperbilirubinemia, as is seen in our study.[10,12]

In our study, frequency of jaundice in neonates was 41.43% at 72 hours of life. In Trivedi et al's study, it was 33.88%, who followed full term neonates till seventh day of life.[13]

In our study, frequency of jaundice was significantly high in group I- 71.9% versus group II-15.8%. ($p<0.0005$).

Aiyappa also divided neonates into two groups, based on cord blood serum albumin, but those with serum albumin level >than 2.8gm/dL were labelled as group I, different from our group I. In his study 126 babies were under Group 1 and 39 under Group 2. Jaundice was observed in 34% of neonates from group I and in 71.7% from group II. The total bilirubin levels were significant in Group II, ($p<0.001$) [12]. This was consistent with our study.

In Trividi et al's and Reshad M et al studies, cord blood albumin ≤ 2.8gm/dL, like in our study was also a risk indicator in predicting neonatal hyperbilirubinemia.[13,14]

In studies of Choudhary RE, Meena KJ and Mishra AK, neonates were divided into 3 groups based on serum levels of <2.8g/dL, 2.8-3.3gm/dL and >3.3gm/dL. In these studies it was found that most of the neonates with albumin less than 2.8 gm/dL developed jaundice within 72 hrs after birth, which was again similar to our study.[15,16,17] In these studies it was concluded that it is probably safe to discharge neonates with levels more than 3.3gm/dl.

Neeraj Rajpurohit et al, in their study found that cord blood serum albumin ≤ 2.6 gm/dL was associated with increased risk of neonatal hyperbilirubinemia[18]. They also took cord serum bilirubin and found it more sensitive than cord serum albumin in predicting significant neonatal hyperbilirubinaemia. Cord blood serum bilirubin was not taken in our study.

Bhat JA and Khairy MA in their studies found cord blood albumin as a better and early, indicator of hyperbilirubinemia compared to cord blood bilirubin and bilirubin/albumin ratio. Neonates with cord blood albumin < 2.4g/dl and ≤3 g/dl were at risk in their studies respectively.[19,20] Neonatal hyper bilirubinemia remains the most common cause for readmission.[21]

By predicting the newborns, who are likely to develop significant neonatal jaundice early, we can effectively design and implement the follow-up plan.

Neonatal hyper bilirubinemia is a cause of concern for the parents as well as the pediatricians. Early discharge of healthy term newborns after delivery has become a common practice because of medical and social reasons and economic constraints.

As far as the limitations of our study are concerned, we could have followed the neonates longer, and measured both cord blood bilirubin and albumin levels. So, future studies are suggested comparing cord blood albumin with cord blood bilirubin.

Conclusion

It is concluded from our study that full term babies having cord blood albumin level ≤2.8 gm/dL are at risk of developing significant hyperbilirubinemia. Cord blood albumin can be used as a predictor for hyperbilirubinemia, and for early review of jaundice especially in developing countries, where regular follow up is difficult.

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ORIGINAL ARTICLE

Medication Non-Adherence in Anxiety and Depression

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ABSTRACT

Objective: To find out the frequency of non-adherence in patients with anxiety and depression, receiving treatment in teaching hospitals.

Study Design: A cross-sectional descriptive study

Place and Duration of Study: The study was conducted at Pakistan Railway Hospital, Rawalpindi and Riphah International Hospital, Islamabad from 1st June 2018 to 31st December 2018.

Materials and Methods: After approval from Ethics review committee (ERC) and informed consent of the participants, those meeting inclusion criteria; 310 patients (n=310) were included in this study. Out of these 151(n=151) patients were suffering from depression, while 159(n=159) were having anxiety. Patients with mixed anxiety and depression were excluded. Demographic details (age, gender, education, marital status) were recorded. International classifications of diseases (ICD-10) diagnostic guidelines and clinical assessment was used to confirm diagnosis of anxiety and depression. The Morisky Medication Adherence Scale (MMAS-8) was used to measure levels of non-adherence. Data was analyzed using SPSS-20 and results compiled accordingly.

Results: Out of 151(n=151) depressed patients 81.4% have low to medium adherence to pharmacological treatment, while out of 159(n=159), patients with anxiety 78% have medium to low adherence to prescribed treatment. Medication non-adherence was statistically significant in both anxious and depressed patients.

Conclusion: Patients suffering from anxiety and depression show significant non- adherence to pharmacological treatment.

Key Words: *Anxiety, Depression, Medication Adherence, Medication Non-Adherence.*

Introduction

The WHO (World Health Organization) defines adherence as "the extent to which a person's behavior (including medication-taking) corresponds with agreed recommendations from a healthcare provider".[1] It includes the initiation of the treatment, implementation of the prescribed regime, and continuation of the pharmacotherapy.[1] Non-adherence to prescribed medicines is common in patients with chronic diseases, which leads to adverse consequences.[2] The WHO, in its 2003 report stated that non- adherence may have a far more profound effect on the recovery of the patients.[2] As per WHO, the different components contributing to poor adherence can be classified into five categories: financial issues, treatment related elements, patients-related variables, condition-related elements, and services related elements.[2]

Non-adherence may be intentional or unintentional behavior.[3] If a patient does not take the medicine because of forgetfulness or lack of access, it is called unintentional. In contrast, if the patient does not follow the prescription because of his or her personal beliefs or perception of medicine, then it is known as intentional non-adherence.[3] With respect to depression, studies have clearly shown that patients who are non-adherent are more likely to have increased severity of the illness, experience more relapses, have greater number of hospital emergency visits/hospitalizations and decreased remission rates.[4] Those factors which have consistently been demonstrated to have a negative impact on medication adherence rates in patients suffering from psychiatric disorders include patient related factors (young, unmarried, male), psychological factors (i.e. poor insight, denial of illness), medication-related factors (i.e. side effects),

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and social/environmental factors (i.e. quality of therapeutic alliance, family support).[5,6] Non-adherence leads to poor clinical outcome, increased morbidity, mortality and wasteful increase in health care expenditure.

Mental health issues are common around the world. In this respect anxiety disorders account for 16% of the worldwide prevalence of mental disorders, whereas, the prevalence of mood disorders is around 12%. Another dimension of this issue is the fact that more severe psychiatric disorders have higher association with non-adherence.[8] A Systematic literature review revealed that adherence depended on the type and severity of psychiatric disorders (Major depressive disorder: 28– 52%, bipolar disorder 20–50 %, schizophrenia: 20– 72% and anxiety disorder 57%).[8] The importance of adherence was emphasized in another paper which had been widely cited in the literature.[9] Thus measuring and monitoring adherence is important for both researchers and clinicians.[10] Also, exact assessments of adherence will help to enhance proper medicine use in patients with mental disorders.

Despite the fact that non-adherence to prescribed treatment leads to excessive morbidity and mortality, this issue has not been given due attention by researcher in Pakistan; therefore there is a need to study this domain of clinical services in patients with common mental disorders. The objective of this study was to find the frequency of non-adherence in patients with anxiety and depression receiving psychiatric treatment in hospital setting.

Materials and Methods

This cross sectional descriptive study was conducted in Pakistan Railways Hospital, Rawalpindi and Riphah International Hospital, Islamabad which are teaching hospitals of Islamic International Medial College, Rawalpindi. The duration of study was from 1st June 2018 to 31st December 2018. Approval was obtained from the Ethics review committee (ERC) of Islamic international medical college; Riphah International University and informed consent was obtained from the participants. Data collection was done by the teaching faculty with help of final year medical students and students of psychology, who were undergoing internship training and were working under direct supervision of the teaching faculty. By using convenient sampling technique, three hundred and ten (n=310) patients from both genders between ages 18-60 years, meeting the inclusion criteria were invited to participate in the study. Out of these 151(n=151) patients were suffering from depression, while 159(n=159) were having anxiety. Patients with mixed anxiety and depressive disorders, other psychiatric disorders or having co-morbidities were excluded. Demographic details (age, gender, education, marital status) were recorded and International classifications of diseases (ICD-10) diagnostic guidelines and clinical assessment, was used to confirm diagnosis of anxiety and depression. After 3-6 months of out-patient follow up, the Morisky Medication Adherence Scale (MMAS-8) was used to measure levels of non-adherence. Data was analyzed using SPSS-20 and results compiled accordingly.

The Morisky Medication Adherence Scale (MMAS-8) consists of eight items with two types of responses to detect barriers to adherence. Items 1-7 are dichotomous (yes/no response), and item 8 is a 4-point Likert scale (from “never” to “always”) to measure factors such as forgetfulness. MMAS-8 has been validated with good sensitivity and specificity in patients with chronic diseases.[11,12] Hence, it is an acceptable self-report measure for adherence to medication. Patients who required assistance were provided guidance to understand the questionnaire.

Results

Table: I Demographic & Clinical Variables of Depressive Patients (n=151)

Gender	**Frequency/Percentage**
Female	103(68.2%)
Male	48(31.8%)
Age group in years	
18-25	14(9.3%)
26-40	67(44.4%)
41-60	70(46.4%)
Education	
No formal school education	30(19.9%)
Under matric	43(28.5%)
Matric/Intermediate	48(31.8%)
Graduates	18(11.9%)
Post-graduates	12(7.9%)
MMAS Scores	
High	28(18.5%)
Medium	63(41.7%)
Low	60(39.7%)
Depression scores	
Mild	68(45%)
Moderate	33(21.9%)
Severe	50(33.1%)

As shown in table I, out of 151 (n=151) depressed patients 68.2% were females and 31.8% were males. Similarly 90.8% of the participants were between age 26-60 years and 60.3% have educational level below intermediate. 39.7% have low adherence (MMAS score<6), while 41.7% had medium adherence (MMAS score <8). As far as severity of depression is concerned 45% had mild depression while 55 % moderate to severe depression.

Table: II Demographic & Clinical Variables of Anxiety Patients (n=159)

Gender	Frequency/Percentage
Female	113(71.1%)
Male	46(28.9%)
Age group in years	
18-25	28(17.6%)
26-40	75(47.2%)
41-60	56(35.2%)
Education	
No formal school education	40(25.2%)
Under matric	49(30.8%)
Matric/Intermediate	55(34.6%)
Graduates	9(5.7%)
Post-graduates	6(3.8%)
MMAS Scores	
High	35(22.0%)
Medium	75(47.2%)
Low	49(30.8%)
Anxiety scores	
Mild	117(73.8%)
Moderate	28(17.6%)
Severe	14(8.8%)

As shown in table II out of 159 (n=159) patients with anxiety disorder, 71.1%) were females and 28.8% were males. Similarly 82.4% were between age 26-60 years and 65.4% had education below intermediate. 30.8% of the patients had low adherence (MMAS score<6), while 47.2% had medium adherence (MMAS score <8). Out of the total sample 117(73.8%) had mild anxiety while26.4% had moderate to severe anxiety.

Table: III Pearson Correlation MMAS-8 & Depression (n= 151)

Pearson correlation	Depression
MMAS-8	-.309**
Level of sig.	0.00

**P<0.01

As shown in tables III there is a negative relationship between medication adherence and depression. It means as the severity of depression increases the medication adherence decreases. The relationship is highly significant.

Table: IV Pearson Correlation MMAS-8 & Anxiety (n= 159)

Pearson Correlation	Anxiety
MMAS-8	-.179*
Level of sig.	.02

*p< 0.05

As shown in tables IV there is a statistically significant negative relationship between medication adherence and anxiety. As the anxiety increases the medication adherence decreases.

Discussion

The current study shows that 81.4% of depressed patients have low adherence to pharmacological treatment, while 78% of patients with anxiety also have low adherence to prescribed treatment. Moreover medication adherence has a negative correlation with anxiety and depression severity, which means when the level of anxiety and depression increases the adherence to medication decreases. The exact cause of this association cannot be pin pointed because of the cross-sectional study design; however, the lack of interest and motivation and poor concentration in depressed patients may be a contributory factor. Similarly fear of medication and possible side effects or dependence may be a reason for non-adherence in patients with anxiety. A study carried out in Pakistani population showed that out of 100 psychiatric patients receiving outdoor treatment 18(18%) were non-compliant. This study defined non-compliance as attending the OPD after a lapse of 15 days or more from the recommended date of follow up visit. The main reasons for non-compliance to follow-up treatment were denial of disease and non-affordability of treatment.[13] The sample size in this study was small and no particular diagnosis was mentioned, which meant that patients with all mental disorders were included in that study. In our study only patients with anxiety and depression were included and frequency of low adherence to medication was quite significant as already mentioned. Previous studies on this subject had also shown that non-adherence was common in patients with depression.[14-18] In a study on non-adherence in 367 males patients with major depressive disorder receiving outpatients care, 63.1% of the participants stopped taking

medications without consulting their physicians.[14] However, this study was based upon a retrospective chart-review, while our study involved direct interaction with patients and we measured non-adherence with a valid and reliable scale. In a systematic review of thirty-two observational studies, it is found that white ethnicity and older age is associated with better adherence to treatment, while severity of depression does not play an important role in predicting compliance.[15] However, this review was limited to studies in the English and Spanish populations. In another cross sectional study involving 103 psychiatric patients, 72(69.9%) patients were non-adherent.[16] In this study the sample size was small and different measurement tools other than MMAS-8 were used for adherence. Patients with a variety of psychiatric diagnosis were included. In yet another qualitative study, 30 patients with depression were interviewed in depth and it was found that the factors specific to patients and side effects of antidepressants were the main contributory factors towards non-adherence.[17] In contrast, our study has a descriptive design and depression severity is inversely related to non-adherence. In a recent study depression with recurrent episodes, decrease or loss of interest and atypical symptoms were found to be risk factors for non-adherence, whereas selective noradrenaline reuptake inhibitor (SNRI) treated first episode was a protective factor against non-adherence.[18] The authors in this study did not mention any association with severity of depression. Our study is focused on anxiety and depression severity and their relationship with non-adherence, as there was no local evidence available on this subject. However, both studies indicate that clinical characteristics of the patient may play an important role in medication non-adherence. In another recent study stressed that the management of major psychiatric disorders is highly affected by medication non-adherence.[19] The authors recommended an integrated approach to reduce the burden of medication non-adherence and stressed that doctors should pay much more attention on educating patients with risk of non-adherence.

The above mentioned discussion clearly shows that non-adherence is a major issue in psychiatric patients, particularly those suffering from depression. In Pakistan, there is a knowledge gap regarding various demographic and clinical variables involved in treatment non-adherence in psychiatric patients. Studies in Pakistan have found that the prevalence of anxiety and depression ranges from 22 -60%.[20] In order to deliver effective treatment, we need to fully understand the issue of non-adherence by generating local evidence on this subject. In clinical practice it is a common observation that an empathetic relationship and medication related education of patients can improve adherence to treatment. However, we need to carry out more studies in order to understand and manage non-adherence related factors in patients with anxiety and depression.

Conclusion

Patients with anxiety and depression show significant non- adherence to treatment. This non-adherence is highly significant in patients with depression, and its severity shows an inverse relationship with adherence. Further studies are needed to clarify the role of psycho-education, therapeutic alliance and the role of socio-cultural factors in non-adherence to treatment in patients with anxiety and depression. By generating local evidence and better understanding on medication non-adherence, the clinician will be better able to identify this issue and prevent its adverse consequences on patients and health care delivery.

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ORIGINAL ARTICLE

Medical Errors and the Prevalence of Phenomenon of Second Victim in A Tertiary Care Hospital in Islamabad

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ABSTRACT

Objective: To determine the frequency of medical errors committed by doctors and the prevalence of second victim phenomenon in a tertiary care hospital, and to find out the effects of the error on the second victim's life.

Study Design: Cross sectional study

Place and Duration of Study: This study was conducted in a tertiary care hospital of Islamabad from 1st February to 30th September 2016.

Materials and Methods: A total of 200 male and female doctors were selected from a tertiary care hospital in Islamabad, Pakistan, through convenient sampling technique in order to fill a pretested structured questionnaire, for a period of six months. Questionnaire was adapted from a previous study and alpha reliability of the variables checked. Data was collected via face to face interviewing. It was analyzed using SPSS version 21.

Results: Out of the 200 study participants, 62.5% belonged to the age group of 24-31 years, 53% of them were males and 43% were females. Major errors were 13.2 %, minor 57.2 %, near miss were 29.6%. The prevalence of second victims came out to be76 %, and it was almost equal in males (80.6%) and females (71.7%) and was the highest in Medicine department (35-40%). The main cause of errors was documented to be overwork by 72.5% of the participants. The major emotional effect as perceived by 50.5% participants was guilt, followed by sadness in 21.6%, embarrassment in 16.5% and sleep disturbance in 16%. Around 75.5%of the participants were of opinion that an organization should be in place to help second victims come out of their trauma. According to 83% study participants, medical errors should be disclosed to patients and their families.

Conclusion: The study concludes that there is a high prevalence of medical errors in the tertiary care hospital and male and female doctors are equally becoming second victims of their errors. The major effects of medical error on the second victim's life are feeling of guilt, sadness, embarrassment and sleep disturbance.

Key Words: *Cross Sectional, Medical Errors, Phenomenon, Prevalence, Sampling, Second Victim.*

Introduction

Humans commit mistakes but the brunt of mistakes done by doctors is faced by the patients and they are the prime or first victims of doctors' errors. They may have to bear all sorts of trauma ranging from a minor harm to disability or even death. Doctors themselves are the second victims of their own errors as they have to face the consequences of their mistakes, which can be a range of effects like frustration, distress, self-doubt, emotional trauma, anger, a sense of incompetence in profession, insult, and even loss of job.[1] They also receive a very harsh reaction if, at all, they share their mistakes with fellow colleagues or with the patients and their families. The term 'second victim' refers to the healthcare professional who experiences emotional distress following an adverse event which was unanticipated.[2]

Studies show that minor to major medical errors affect many patients worldwide every year.[3] The cases of doctors' negligence have been highlighted in various newspapers but not from the angle of second victims. The mistakes of doctors have been attributed to under qualification, indifferent approach towards the patient due to their private practices, lack of professional ethics as well as faulty health policies.[4]

According to a study from Johns Hopkins, more than 250,000 deaths per year are related to medical errors

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which suggests that deaths from medical errors comprise roughly 10 percent of all deaths in America every year[5] which makes medical errors the third leading cause of death in the U.S.[6] One of the leading causes of *errors* is communication barrier between patient and doctor.[7] The increasing death toll over last six years is alarming, and proves that errors are consistently occurring. In neighboring countries like India, 5.2 million patients are effected each year due to medical errors.[8] In Pakistan, medical errors are not reported frequently due to fear of embarrassment in front of peers, fear of medico-legal action, fear of punitive action by patients and complaints to governing bodies but around half a million error-related deaths are occurring each year. Many patients lose their life or face other serious health problems and disabilities because of the poorly structured healthcare system.[9] No sympathy is shown towards the second victims, although they are equally affected by trauma. Improving patient safety requires more than voluntary reporting. Organizational changes need to be implemented and institutionalized as well.[10] Researchers figured out three ways doctors choose to cope with the stress: (1) to abandon the profession, (2) to leave the incident behind and carry on with their duty, (3) learn lesson from their mistakes and try to avoid them in future.[11]

Physicians all over the world, irrespective of their competence, are bound to commit medical errors as human error cannot be ruled out. Various circumstances affect their state of mind and they may make mistakes unintentionally. Researchers while attending a conference found that 60% of the physicians present there recalled at least one adverse patient event that left a huge negative impact on their lives. Among anesthesiologists, 84% suffered at least one such event that affected them emotionally and among these, more than 70% reported stress and self-doubt. Nineteen percent of these anesthesiologists admitted that they still were not able to recover from the emotional trauma.[12]

According to a report on the growing issue of medical negligence in Pakistan, the medical training of doctors in Pakistan needs special attention. Work hours need to be regulated and deficiencies in legal protection for doctors and patients need to be rectified. Reasonable salaries and working hours for doctors, and adequate training and skills might lead to decreased errors, and in turn, decrease in the number of second victims.[13]

The second victim phenomenon has been highlighted and researched in various developed and developing nations of the world but extensive literature survey indicates no significant study conducted in any tertiary care hospital of Islamabad. The study fills an identified gap in the body of knowledge and proves to be a contribution to the domain of public health. Its main objective was to determine the frequency of medical errors committed by doctors and the prevalence of second victim phenomenon in a tertiary care hospital, and to find out the effects of the error on the second victim's life.

Materials and Methods

A cross-sectional study was conducted from1st Feb – 30th Sep, 2016, and 200 male and female doctors from a tertiary care hospital in Islamabad were selected through convenient sampling technique. The research was ethically approved from ethical committee of the hospital and the confidentiality of the name of hospital and the respondents was ensured. Written informed consent was taken from all the participants and they were allowed to withdraw any time during the study.

Medical officers, registrars and consultants from Medicine, Surgery, Pediatric, Eye, Gynecology / OBS , ENT, Derma, &ICU department who had worked in the hospital for at least one year or more after house job were included in the study. House officers were excluded since they were under training and learning phase and had less than one year experience**.** Data was collected using a pretested structured questionnaire. The tool was adapted from a previous study in this regard with modifications. Alpha reliability of the variables was checked. Sample size was obtained using WHO sample size calculator taking the following study as reference:

Waterman A D et al, The Emotional Impact of Medical Errors on Practicing Physicians in the United States and Canada. The Joint Commission Journal on Quality and Patient Safety, August 2007; 33 (8):467-476.[14]

Before entering data into computer, all questions were checked for mistakes and omissions. Data was analyzed using SPSS version 21, and presented mainly as frequencies and percentages using bar

charts, and frequency tables. In order to see the gender difference of second victim phenomenon prevalence, chi-square test was applied taking p-value of <0.05 as significant.

Results

Out of the total 200 study participants, 106 (53%) were females and 94 (47%) were males. Majority belonged to the age group of 24-31yrs (62.5%), (Table1). The prevalence of second victims came out to be 76%.It was almost equal in males 76/94 (80.8%), and females 76 /106 (71.7%). The value of chi square was 0.139 at p < 0.05, (Table II). Prevalence was highest in department of medicine 38(25%),followed by surgery 27(17.8%) and gynecology 25(16.44%)(Fig 1)

Majority of the second victims, 87(57.2%) were involved in minor error. Out of these, 48 (55.1%) disclosed the error to the authorities, and 39 (44.8%) disclosed it to the patient.(Table III,IV)

According to participants' responses, major barrier towards disclosure of error was fear of loss of professional reputation, declared by 93 (30.8%). Major emotional effect on second victims was guilt in 98 (24.9%), followed by sadness in 85 (21.6%), and embarrassment in 65(16.5%) respondents. Around 42 (40%) of participants' responses revealed that family life was affected due to an error, About 81 (25.8%) responses showed that job dissatisfaction was a major effect on occupational life, followed by 43 (13.7%) responses that pointed to negative effect on confidence as physicians.(Table V). The main cause of error according to the study population was overwork in 140 (72.5%), followed by lack of experience 82(42%), lack of knowledge 56 (28%), and panic 43 (21.5%).

According to 166 (83.0%) of the participants, patients and their families should be told about the adverse events. Among all,153 (76.5%) were of the opinion that error disclosure training should be provided to doctors, and 152(76%) wanted provision of counseling services to second victims. Majority, 151 (75.5%), of the participants were of the opinion that there should be some organization for support of second victims in order to solve their issues. Among all, 70 (35%) participants disagreed with the statement that hospitals support second victims.

The following hypothesis was made for chi square application to see the difference of gender in second victim phenomenon.

H_0: There is no significant difference between the frequencies of male and female second victims.

H_1: There is a significant difference between the frequencies of male and female second victims.

p value: 0.139

Level of Significance: <0.05

The application of Chi-square Test indicates that p-value is 0.139 which is higher than the level of significance that is 0.05 hence accepting the null hypothesis and rejecting the alternate hypothesis, the results of the analysis indicate that medical errors equally affect both male and female doctors, in this tertiary care hospital.

Table I: Demographic Profile of Study Participants (n=200)

		Frequency	Percentage %
Gender	Female	106	53
	Male	94	47
Department	Medicine	50	25
	Gynae/Obstetrics	37	18.5
	Surgery	33	16.5
	Eye	22	11.0
	Paediatrics	19	9.5
	ENT	14	7.0
	Others (Derma,ICUetc)	25	12.5
Age(In Years)	24-27	65	32.5
	28-31	60	30.0
	32-35	40	20.0
	36-39	23	11.5
	40 and above	12	6.0
Marital Status	Married	133	66.5
	Un-married	67	33.5
Designation	Medical officer	117	58.5
	PGT(postgraduate trainee)	36	18
	Consultant	21	10.5
	Senior registrar	26	13

Table II: Cross Tabulation Showing the Frequencies of Male And Female Second Victims

Gender	**Been A Second Victim**		**Total**	**P value at < 0.05**
	yes	no		
Male	76	18	94	0.139
Female	76	30	106	
Total	152	48	200	

Table III: Type of Medical Error (n=152)

Type of Error	Frequency	Percentage%
Near miss	45	29.6
Minor Error	87	57.2
Major Error	20	13.2

Table IV: Error Disclosure by the Participants (N=152)

	Major Error (n= 20)		Minor Error (n= 87)		Near Miss (n=45)	
	Frequency	Percentage %	Frequency	Percentage %	Frequency	Percentage %
Error Disclosure to the Authority	17	85	48	55.1	40	88.9
to the patient	3	15	39	44.8	5	11.1

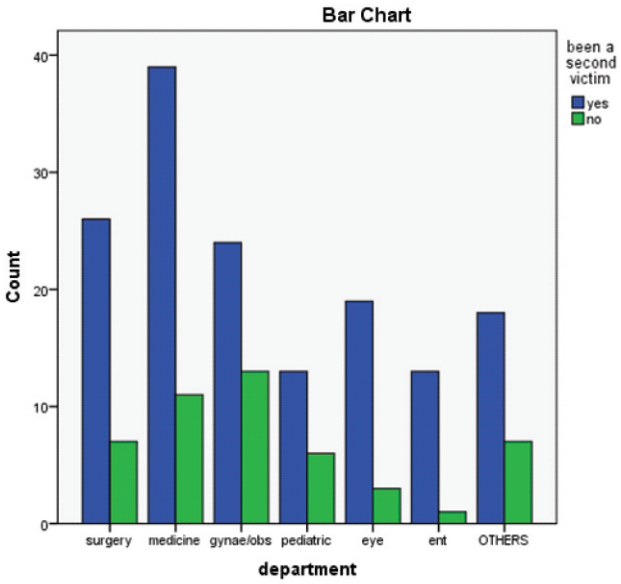

Fig 1: Bar Chart Showing Second Victim Prevalence in Different Departments

Table V: Participants 'responses About Effect of Error on Life and Barriers to Disclosure

Effect on Personal Life	**Frequency**	**Percentage %**
Sleep disturbance	63	16
Doubt about the potential for future errors	40	10.1
Anger	43	10.9
Embarrassment	65	16.5
Guilt	98	24.9
Sadness	85	21.6
Effect on Social Life		
Family life affected	42	40
Children affected	16	15.2
Friendship affected	18	17.1
Other relations in society affected	29	27.6
Effect on Occupational Life		
Job dissatisfaction	81	25.8
Affected confidence as physician	43	13.7
Professional reputation affected	41	13.1
Insult from authority	41	13.1
Monetary set back	28	8.9
Effect on productivity	30	9.5
Team work with colleagues affected	28	8.9
Litigation	22	7
Barriers Towards Error Disclosure	**Frequency**	**Percentage %**
Fear of embarrassment	31	10.3
Fear of patient's reaction	72	23.8
Fear of litigation	55	18.2
Fear of loss of professional reputation	93	30.8
Lack of peer and institutional support	51	16.9

Table VI: Participant's Response on How Errors Should Be Managed by Authorities (n=200)

	Response	**Frequency**	**Percentage %**
Error Disclosure Training Should Be Provided	Yes	153	76.5
	No	47	23.5
Counseling Should Be Provided To Second Victims	Yes	152	76
	No	48	24
Need For Society Or Organization To Solve The Issue	Yes	151	75.5
	No	49	24.5
Errors Should be Disclosed to Patients and their Families	YES	166	83
	NO	34	17

Discussion

Doctors, as second victims, have to face emotional trauma in an adverse situation. This research was designed to determine the prevalence of the second victim phenomenon and effect of medical errors on doctors' lives.

In our research on 200 participants, 76% declared that they had been a second victim somewhere along their medical career in this hospital after committing an error. Major errors committed were 13.2 %, minor 57.2 %, near miss were 29.6%. In a similar research conducted by Attia Bari and fellows in Lahore, 130 residents were included to study this phenomenon and majority of respondents (98.5%) described some form of error. Major errors that occurred were 19%, minor were 48% and 19% were near miss. [13]Most of the participants recalled that they were medical officers or trainees when they experienced this phenomenon, which is similar in

both studies. In our study 69% disclosed medical errors to their senior authorities, and 31% to patients, while these results are in line with their study where 57% residents disclosed medical errors to their senior physician but disclosure to patient's family was negligible (11%).This points to similar socio-cultural conditions in major cities of our country. The major cause of error was declared to be fatigue in 65%, due to long duty hours, which was similar to our research, and guilt was the most felt emotional setback.

In contrast study done on residents of USA & canada[14] revealed that 92% of participants were involved in errors including major (57%), minor (36%) and near miss. (7%).This is higher as compared to ours, and the difference may be due to higher chances of disclosure of errors. In that study, 89% reported disclosing major error to patients and 54% disclosed minor error to patients, which is 15% for major and 44.8 % for minor error in our setting, hence explains the difference. Our physicians are reluctant to disclose errors. A good majority (83%) of the participants of our study believed that patients and their families should be told about the adverse events, but contrastingly, disclosure to the patients is much lesser (15%).Such a low percentage is seen mostly because of fear of loss of professional reputation and fear of patients' reactions and dissatisfaction with the overall system of the hospitals. Doctors should be able to tell the patient and the authority about such adverse events openly. Our findings emphasize the need for establishment of proper support system and societies for doctors to cope with the stress of such events. About 76.5% of the participants believe that there should be error disclosure training given to health care professionals. Also in our setting, male and female doctors were equally affected by the second victim phenomenon, while in their study, females were more affected. It might be due to the fact that our females are either more resilient and can handle stress in a better way or afraid to admit and disclose errors. In Maeve O'Beirne's research done on Canadian health professionals, the top five reported emotional responses were frustration (48.3%), embarrassment (31.5%), anger (12.6%), guilt (10.1%), and sadness (2.1%).In our study results for embarrassment (16.5%) anger (10.9%) guilt (24.9%) and sadness (21.6%) clearly show that our respondents were left with a heavy heart and felt more guilty and sad after the incident. It was revealed that 52% of 264 participants talked to someone to deal with an emotional response.[15] In our study 76% of the respondents wanted access to counseling after serious errors, which seems to lack in our system, as no one lends a shoulder for emotional venting and counseling. Proper training should be provided to the doctors to disclose such information to the patients and their families. Among our study participants, 35% disagreed with the statement that hospitals support second victims. In USA & Canadian study, 90% of physicians disagreed that hospitals and health care organizations support physicians and help them in coping with trauma and stress linked to medical errors. Hence the indifferent and non-sympathetic approach of healthcare organizations seems to exist universally regardless of whether the country is developed or developing. A majority (82%) of physicians showed interest in receiving counseling after a medical error.[14] Researchers at the University of Missouri Health Center found that almost 1 in 7 staff members declared in a survey that they had experienced a patient safety event within the past year that affected personal life causing anxiety, depression, or doubt in professional confidence. A major two thirds of them denied any support from their institute.[16] In most health care settings, healthcare providers do not receive care, support or guidance when they commit an error, and most suffer in silence.[17]

A research conducted in a tertiary care hospital in India concluded that errors related to medication were 50.26%, related to treatment procedures were16.23% and related to clerical procedures were 28.27%.[18] Hence, errors are inevitable. They are occurring globally and need attention in order to prevent psychological, physical, and emotional setback in the physicians. At present medical errors have become great challenges for healthcare professionals, and health policy makers.[19]

The study was limited because of convenient sampling technique and small sample size. As it was carried out in only one tertiary care hospital hence results can't be generalized. Further studies are suggested to know the actual prevalence of second victim phenomenon and the magnitude of medical

errors occurring in major hospitals.

Conclusion

The study concludes that there is a high prevalence of medical errors in the tertiary care hospital and male and female doctors are equally becoming second victims of their errors The major effects of medical error on the second victim's life are feeling of guilt, sadness, embarrassment and sleep disturbance. The main cause of error identified is overwork.

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ORIGINAL ARTICLE

Exploring the Challenges and Barrier of Delivering and Receiving Effective Feedback in Clinical Environment: A Qualitative Inquiry

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ABSTRACT

Objective: To explore the teachers and undergraduate medical students' perceptions regarding the challenges of feedback in their educational process during clinical rotation.

Study Design: It was an institution based exploratory qualitative study.

Place and Duration of Study: The study was conducted at Islamic international medical college Islamabad from 1st January to 30th June 2016.

Materials and Methods: Purposive sampling technique with maximum variation was adopted to select a total of six assistant professors from six different clinical specialties and six final year MBBS students on clinical rotations. The data was collected through structured interviews. The written consent was taken from all the respondents before conducting the interviews. Themes and sub themes were emerged through the combination of open and axial nodes.Thematic analysis of the transcribed data was done using Nvivo software.

Results: A number of challenges to effective feedback were perceived by the teachers and also by the medical students during clinical clerkship in institution. The emergent themes were: time pressure, discouraging attitude of the teachers, defensive attitude of students, the inappropriate process and contents of feedback. These challenges of feedback should be addressed in order to improve the learning of the students as the ultimate beneficiaries are our patients.

Conclusion: The study concluded that there were several barriers to effective feedback that were hampering the development of competent clinician. Effective constructive feedback will enhance the learning of students during their clinical rotations. It is only promising when it is specific, in time, constructive, follow appropriate structured process and encourage student involvement. Constructive feedback helps in motivating but does not dampen their learning.

Key Words: *Barriers, Clinical Clerkship, Feedback, Perception, Students, Teachers*

Introduction

Constructive feedback is an essential feature of effective teaching that facilitates the learning of medical students.[1] In medical education, feedback is provided by clinical supervisors who have direct interaction and closely observe the student's clinical activities.[2]

It is evident the feedback which has been provided by an experienced clinical instructor who directly observes the learner's attitude have a greater impact on student learning.[3,4] Most of the students feel that both positive and corrective feedback is essential for gaining competence in clinical practice.[5]

In clinical setting, feedback provides information about the performance of the learners in a given clinical activity that helps them to improve their future performance in the same activity. If not provided effectively during clinical training, it produces detrimental results.[6,7]

Increasingly in medical education, a large number of health professionals are providing feedback especially at the end of formal assessments, either in the workplace or in clinical settings.[8]

Several barriers have been identified by the teachers while giving feedback; and by the students while receiving the feedback.[9] It is emphasized that feedback is useless if it does not bring a positive change in students' behavior.[10,11] Feedback was considered to be unhelpful and unfair, when it is

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judgmental.[12,13] Respondents also disliked receiving feedback in front of others. These are some of the issues which need to be addressed for making feedback effective.[14]

The challenges reported by Bing and others i.e. insufficient training of supervisors, negative reaction to feedback, unfamiliarity of the faculty with the process of feedback; time and place constraints and the lack of favorable educational environment.[15,17] The critical point, is no formal training of clinician who provides feedback in clinical setting. There is need to develop feedback structure before its process of application.[18]

It is important to identify the challenges faced by Pakistani medical teachers and students during their feedback process. There is need to overcome the existing barriers that will help to produce the competent medical graduate. This study was intended to explore the views of teachers and undergraduate medical students regarding the challenges while giving and receiving feedback in the clinical settings.

Materials and Methods

This was a simple qualitative, exploratory study. The duration of study was six months that was conducted at Islamic International Medical College from 1st January to 30th June 2016. A total of 12 participants who fulfilled the selection criteria were interviewed. Purposive sampling technique with maximum variation was used to select the sample. The study was started after obtaining the ethical approval from ethical committee of Riphah International University Islamabad. The six experts who participated were assistant professors from six different clinical specialties, and were providing regular feedback at the end of each clinical task. The Six were MBBS final year students interviewed who were high achievers, average and at borderline. They had a better understanding of the feedback process and receiving feedback in their clinical clerkship. The medical experts and students who were not involved in feedback process were excluded. Anonymity of all the participants was ensured throughout the study.

The interviews were audio recorded. After thorough interview content review it was manually transcribed. The transcript data was triangulated with the available literature for accuracy and validity. The software Nvivo version 11 was used for qualitative data analysis. Themes were selected and subthemes were identified. Six steps were followed for data analysis and interpretation. Transcripts were coded and themes confirmed. After identifying open codes, axial coding performed to find out subthemes. Selective codes were identified, and interpretation of results was done.

Results

Ten key categories were elicited from the transcripts of twelve participants i.e. Time constraint, Departmental policy, spoon feeding, student disinterest, Teacher student relationship, Generalized and non-specific feedback, insulting attitude, proper and constructive feedback each are described with quotes and codes in the following (Table I). Five Themes with 18 sub –themes were emerged i.e. related to feedback: teacher factors, learner factors, feedback process, feedback content, and educational context shown in (Table II).

Teacher factors

Major issue reported by students that were about the clinical faculty's insulting attitude during clinical task that damage student's self-esteem and hinders their learning. Clinical faculty reported that they had a feeling of uneasiness when they provided negative feedback to students. It damages the student teacher positive relationship during teaching and learning process.

"The students appreciate positive feedback more and it is conceived to be as praise, on another hand they take negative feedback as criticism."[Participant Table I]

Learner factors

Teachers highlighted that students had a defensive attitude while receiving corrective feedback. They showed disinterest, disrespect to the teachers. Sometime the students show poor reaction to negative feedback as result of which feedback being disregarded subsequently.

"While receiving negative feedback, some of the students defend themselves immediately during criticism "no this is not true "No that is because". [Participant Table IV]

Feedback Process & Feedback Content

One another barrier related to the feedback is its delivery and inappropriate content that influence its affectivity. Student faced difficulty in their clinical learning due to the delayed feedback on observed

performance and lack of departmental policy existence for feedback process.

"Some department does not give feedback frequently and immediately after performance even the content of the feedback is not specific; some teachers give general feedback in form of comments."[Participant S#10]

Educational Context

Inconsistent feedback from multiple sources and time pressures due to clinical and teaching work are also a marked barrier to effective feedback.

"There are lot of tasks, running around in all directions, we're surrounded by patients in clinical setting at one time and deal with number of the students, at the same time and we have not ample of time and proper place to give individual feedback."[Participant Table IV]

Two perception models were developed one was related to the teachers' perceptions about the challenges of feedback in clinical rotation. According to teachers major barriers they faced while giving feedback in clinical clerkship i.e. Disinterest of the students, Time constraints, Inadequate training of supervisors and Dissatisfaction with the process of feedback that is shown in (Fig.1).The second developed model related to the students' perceptions about the challenges of feedback in clinical rotations. According to students major barriers they faced while receiving feedback in clinical clerkship were Inappropriate content of the feedback, Insulting attitude of the teachers and Lack of continuity with the teaching that is shown in (Fig.2).

Table I: Representative Quotes from the Participants, Categories Identified, and Codes Given to them in Descending Order of Frequency

S.No	Quotes from interviews	Categories	Coding
1.	*"It is a work load and the time constraint that they do not give feedback on direct observation."(Participant 4)*	Time constraint	TC
2.	"*There is no well -defined departmental protocol and guidelines to provide feedback."* (Participant 3)	Departmental policy	DP
3.	*"Medical students are mature and independent, feedback is spoon feeding for them instead of change in their behavior"*(Participants 6)	Spoon feeding	SF
4.	*"Student's disinterest hinders the effectiveness of the process of feedback"* (Participant 5).	Student disinterest	SD
5.	"*Negative and corrective feedback harm the teacher - students relationship".* (Participant 2)	Teacher - student relationship	TSR
6.	"*Mostly the teachers give generalized feedback in written form like satisfactory or non - satisfactory."* (Participant 8)	Generalized feedback	GF
7	*"Some of the teachers give non relevant and non - specific feedback not related to direct observation."(*Participant 11)	Nonspecific feed back	NSF
8	*"Insulting attitude of the some of the teachers reduce our self -esteem instead of foster of learning behavior."* (Participant 9)	Insulting attitude	IA
9	*"I think feedback definitely can change the behavior of the students if given properly "* (Participant 6)	Proper feed back	PF
10	*"I think feedback should be constructive as it is helpful in giving information to a trainee about strengths and weakness of their performance."(* Participant 5)	Constructive feed back	CF

Table II: Themes and Sub Themes

Themes	Sub themes
Teacher factors	• A fear of losing the student - teacher relationship • lack of attention • in humiliating attitude of the teachers • Lack of training • Insensitive
Learner factors	• disrespect to the teachers • Disinterest • Defensive reaction of the students
Feedback process	• Lack of timely feed back • Lack of individual feed back • Feedback through other individual • No specific departmental policy of giving feedback
Feed content	• Generalized content of feed back • Written feed back • Verbal feedback not binding • Discouraging feed back
Educational context	• Limited time for feedback • Feedback from multiple teachers

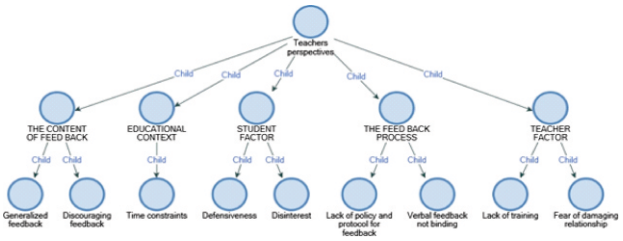

Figure 1: Teachers' Perceptions Model about the Challenges of Feedback in Clinical Rotation

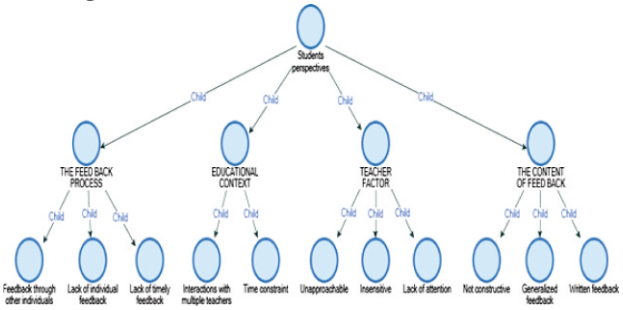

Figure 2: Students' Perceptions Model about the Challenges of Feedback in Clinical Rotations

Discussion

The result of this study showed that the effective utility of feedback is highly dependent on its process of delivery acknowledgeable differences have been seen in the teachers' and under graduate medical students' perception on the feedback provided or received during clinical clerkship.

In our study, the barrier highlighted by teachers were their unwillingness to provide a feedback to students who have negative attitude, don't pay attention and reluctant to receive feedback. According to them such disrespectful attitude cannot rectify their learning behavior.[19,20] Some time student become unreceptive to negative feedback due to feel of embarrassment.[21] According to Rahimi M, feedback with generalized approach doesn't matter for students even they didn't remember what they pointed out for improvement that is similar to current study results.[22] According to Duckworth A, lack of acceptance of feedback by the student and unwillingness from teachers hinders learning process during clinical clerkship that is similar to the results of current study that's why need to build self-control and grit in both teachers and students that is key to success of learning. [23] Al-Haqwi reported student poorly perceives teacher's intentions at the time of feedback upon that they build argument.[9,24] .Gonzalo JD in (2014) emphasised that it is necessary for a good teacher to be courageous and give good feedback to a student and continue it especially to those who expressed a negative attitude. It is needed to rectify their learning behaviour and be able to objectively improve their performance.[25]

Brief interaction of the teachers with learners due to busy schedules, time constraint and workload results in less opportunity for direct observation of learners. In addition to these issues, clinicians sometimes may not be able to find the opportunities for feedback in clinical settings, and feedback as a teaching tool is neglected.[24,26]

During clinical clerkship period direct observation is necessary of the student's patient encounters by clinical supervisor for good clinical teaching.[17.18,24,27]

Our study observed that there were variations within the departments because there is no clear departmental policy about the process of providing the feedback. It is clearly defined that the medical teachers who are dedicated for feedback are un-trained and didn't know about the process of feedback that's why feedback not effective as we consider.[28]

One another barrier related to the affectivity of feedback that was highlighted in our study is about its inappropriate content and multiple sources that is also highlighted in Hesketh E,work as Inconsistent feedback from multiple sources[29] and by Chaou CH in (2017) the variety and complexity of feedback content and its source is a big challenge.[30]

Conclusion

In conclusion, identified barriers in perception of teachers and students about the feedback were following i.e. inappropriate feedback & content, teacher's insulting attitude, negative feedback, unreceptive attitude towards receiving the feedback etc. There is need to deal with all these existing barriers by the joint collaboration of clinical departments and medical education department so the feedback can be utilized effectively in the learning process of medical students during clinical clerkship.

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ORIGINAL ARTICLE

Emotional Intelligence of Medical and Dental Doctors with Different Clinical Experiences: A Cross Sectional Study

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ABSTRACT

Objectives: To measure Emotional intelligence scores of medical and dental doctors with different years of clinical experience.

To establish a correlation between domain specific Emotional Intelligence scores and years of clinical experience of medical and dental doctors.

Study Design: A Quantitative; Cross-sectional Survey was conducted at Fatima memorial college of Medicine & Dentistry, Lahore.

Place and Duration of Study: Study was conducted from August 4th, 2019 to October 6th, 2019 i.e. (2 months) duration.

Materials and Methods: A total of 150 medical and dental doctors were selected using convenience sampling in 3 different categories according to clinical experience. After ethical approval & informed consent of participants, data was collected using pre-validated "Leadership Toolkit Emotional Intelligence Questionnaire." Data was summarized using descriptive statistics in SPSS 23. Mean and standard deviation for each group was calculated. Comparison between groups & five domains of EI was using cross tabulation & Pearson's chi-square test.

Results: A total of 150 doctors with 55.3% females and 44.7% males participated in the study. Emotional quotient was assessed based on 5 domains by plotting responses on 5-point Likert scale. Majority of the participants scored, well in self-awareness (63%), empathy (66%), while low in managing emotions (37.3%), self-motivation (45%) and social skills (38%). Total global-EI score increases with years of experience. Consultants scored statistically higher in all domains except managing emotions. House-officers scored lowest in managing emotions while post-graduates scored lowest in social skills.

Conclusion: There is a positive correlation between global EI scores and years of clinical experience with a downward trend in scores of self-motivation and social skills among post graduate trainees.

Key Words: *Consultants, Emotional Intelligence, House-Officers, Post-Graduate Trainee, Years of Experience.*

Introduction

Over the early part of the last century the concept of Intelligent Quotient (IQ) i.e. cognitive proficiencies and mental aptitudes were the prime source for prediction of academic and non-academic successes.[1] The research over the last 3 decades have highlighted the importance of socio-emotional capabilities affecting the daily life and hence performance of an individual.[2] The concept of EI was first given by Peter Salovey & John D Mayer as mental abilities model. They traced the emotional hierarchy as ability to correctly perceive, use, understand and manage emotions.[3,4] Daniel Goleman in 1990's highlighted the importance of emotional intelligence over Cognitive intelligence. He rationalized emotional intelligence in the domains of self-awareness, self-management, social awareness and social skills.[5,6] So, EI is social intelligence that enmeshes one's ability to assess, monitor & discriminate between one's emotions as well as others, correctly label the emotions and use this ability in guiding one's own thinking and actions.[7] A fine interplay of cognitive intelligence, empathy and emotions, i.e. Emotional Intelligence, is needed to

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enhance beliefs and philosophies of personal dynamics. There are three main models of EI. Ability Model focuses on the balance between discrete mental abilities and emotion processing abilities, Mixed model incorporates multiple attributes like assertiveness, flexibility, motivation etc. in regulation of emotional abilities, Integrative model combines multidimensional skills from different domains of EI to mental abilities to describe a performance framework.[8]

EI is the driver of success vehicle in both our personal and professional lives. Cognitive intelligence and emotional intelligence are not foes, they are acquaintances which work hand in hand for a holistic success.[9] Studies have shown that people with high EI performs better at workplace and personal life because they are equipped with the power of regulating their emotions which help them in managing conflicts, taking decisions and adapting to the situation.[10,11] EI has a strong effect on communication skills, job satisfaction, academic and workplace performance, stress and burnout which then exerts a string effect on doctor patient relationship and patient satisfaction.[12,13,14] General intelligence (Emotional + Cognitive) is a dynamic entity which varies with time, and environment and can be improved.

The attributes of EI are integral to health professional role, especially doctors and nurses. Both formal and informal efforts are being made at different levels of health sector to increase awareness about emotional intelligence and its effects on performance. In Pakistan various studies have been conducted to assess the level of emotional intelligence, describe its relation to workplace performance and to establish a correlation between IQ and EQ. But little research has been done to understand the relationship between different time frames of clinical experience in relation to the specific domains of emotional intelligence. Moreover, only a couple of studies in this context have been done on dental doctors in Pakistan. In general, Emotional intelligence improves with the experience and training but literature is scarce on how it varies across different domains. The study is directed to assess the 5 different domains of emotional intelligence in correlation to the years of clinical experiences. This will ultimately help us in devising targeted interventions to improve emotional intelligence. A study was planned to measure EI scores of medical and dental doctors with different years of clinical experience & to establish a correlation between domain specific EI scores and years of clinical experience of medical and dental doctors

Materials and Methods

A cross-sectional survey was conducted at Fatima Memorial college of Medicine & Dentistry, Lahore for time duration of 2 months i.e. Aug 4th 2019 to Oct 6th 2019.

A sample of 150 medical and dental doctors was selected using convenience sampling. Data collection was completed within 1 week. The doctors were selected in 3 different categories according to clinical experience i.e. 50 each from House officers, Post-graduate trainees and consultant's category. Both males and females in clinical practice were included in the study. Medical and dental undergraduate students & basic sciences post-graduate trainees and consultants were excluded from the study.

Ethical approval was sought from Institutional Review Board. After taking informed consent of the participants, data was collected using pre-validated 'Leadership Toolkit Emotional intelligence questionnaire'. The participants recorded their response on a 5-point Likert scale for each question. The questionnaire consisted 50 questions; 10 from each emotional competency of Self-awareness, managing emotions, motivating oneself, Empathy, Social skills. Individual results of questions of each domain were aggregated to give a consolidated score for the said domain which was then re-categorized into 3 classes i.e. strength, needs attention and developmental priority (as per the existing tool). No incentive or reward was given to the participants for inclusion in the study.

Collected data was entered into SPSS 23. The data for each group was summarized using descriptive statistics. As the data was symmetrically/ parametrically distributed so mean and standard deviation was calculated for each group. For the comparison between the 3 groups of participants and the five domains of EI questionnaire cross tabulation was done using Pearson's chi-square test.

Results

A total of 150 medical and dental doctors participated in the study with age group ranging from 25 to 44 years with mean age of 34.5 years. Equal number of participants was recruited in each category. There were 83 (55.3%) females and 67 (44.7%) male participants. Majority of the participants were in their thirties (83) while some juniors (42) were in twenties and some consultants (25) in forties. The detailed distribution of participants is given in table I.

Table I: Frequency Table of participants in HO, PG's & Consultant Categories

Clinical Experience	No. of Participants	Gender Distribution		Mean age (Years)
		Male	Female	
HO	50	28	36	26 ± 1.96
PG	50	18	26	34 ± 2.04
Consultant	50	21	20	42 ± 3.07

Majority of the participants 95 (63%) scored well while 55 (37%) needs improvement in domain of *self-awareness*. In the domain of self-awareness, consultants scored statistically higher than others (P value= 0.025). 38% house officers, 74% post graduate trainees and 78% consultants obtained scores in strength category. None of the scores were in developmental priority category. (Table II).

Majority of the participants 94 (62.6%) needs improvement in domain of *Managing emotions* while only 56 (37.3%) scored well. In the domain of managing emotions, Post Graduate Trainees scored statistically higher than others (P value= 0.05). 20% house officers, 48% post graduate trainees and 44% consultants obtained scores in strength category. (Table II)

Majority of the participants 83 (55%) needs improvement in domain of self-motivation while only 67 (45%) scored well. In the domain of self-motivation, consultants scored statistically higher than others (P value= 0.001). 24% house officers, 72% post graduate trainees and 78% consultants obtained scores between 34-50 (strength category). None of the scores were in developmental priority category. (Table II)

Majority of the participants 99 (66%) scored well while 51 (34%) needs improvement in domain of *empathy*. In the domain of empathy, consultants scored statistically higher than others (P value= 0.011). 38% house officers, 76% post graduate trainees and 84% consultants obtained scores in strength category. (Table I).

Table II: Emotional Quotient Interpretation & Comparison among House Officers, Residents & Consultants

Domains of EI	House Officers % Age of Participants		Post Graduate Trainees % Age of Participants		Consultants % Age of Participants		Pearson Chi-Square value	Likeli-hood Ratio value
	Need Improv-ment	Strength	Need Improve-ment	Strength	Need Improve-ment	Strength	(P-value)	(P-value)
Self-Awareness	62	38	26	74	22	78	7.38 (0.025)	8.02 (0.018)
Managing Emotions	80	20	52	48	56	44	6.60 (0.05)	6.86 (0.053)
Self-Motivation	76	24	68	72	22	78	13.63 (0.001)	14.13 (0.001)
Empathy	62	38	23	76	16	84	8.99 (0.011)	8.87 (0.012)
Social Skills	70	30	82	18	34	33	4.50 (0.005)	4.55 (0.031)

Majority of the participants 93 (62%) needs improvement in domain of *social skills* while only 57 (38%) scored well. In the domain of social skills, consultants scored statistically higher than others (P value= 0.005). 70% HO'S, 82% PG's and 34% consultants obtained scores between 18-34 (needs attention category). None of the scores were in developmental priority category. (Table II).

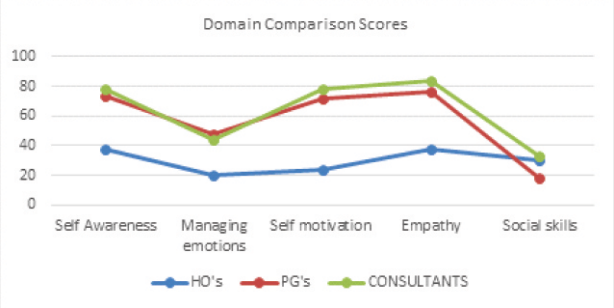

Fig 1: Line Diagram Showing Strength Scores In Each Emotional Domain

Discussion

In this study emotional intelligence is assessed across gender, years of experience and qualification categories with respect to domain specific scores in EI. A general positive trend in EI scores was noted however statistically significant lower scores were observed in managing emotions and social skills domain across all the categories, raising a question about what are the possible causes of such a finding. The total emotional scores in this study vary directly with the increase in years of experience i.e.

consultant scores > PG trainee scores > House officers scores. The consultants scored higher in domains of self-awareness, managing emotions and self-motivation while the scores are relatively less in domains of managing emotions and social skills. House officers need improvement in all the domains generally, however PG trainees scored well in managing emotions as compared to consultants but scored very poor in social skills.

In my study the female participants (55.3%) were more than (44.7%) male participants. This is in accordance with a similar study conducted in Lahore, Pakistan showing more prevalence of female doctors.[15] However, couple of Indian studies on emotional intelligence reported more male predisposition in hospital settings.[16,17] Generally in Pakistani context the ratio of female doctors is more than male doctors.

Overall the scores of HO's and PG's need drastic improvement in self-motivation, empathy & in social skills domain. Scores in managing emotions domain needs improvement in all categories of participants. The scores of PGs' are least in social skills domain while the scores of HO's are the least in managing emotions domain.

The overall scores of emotional intelligence in my study show a direct relationship with age and experience. The scores of consultants are more than that of PG'S, and PG's have scored well than HO's. Golman has also reported a positive correlation of age and experience with emotional intelligence due to physiological and mental maturity processes.[6] McKinley study has also shown that emotional intelligence increases with age and maturity.[18,19] Cabello also reported that extremes of age have low EI while mid population has higher EI (20). Literature suggests that health care providers may experience a negative physical and emotional toll when pre occupied with treating severely ill patient with high morbidity and mortality. This negative cuff may even be amplified for doctors in the initial phases of their clinical experience.[13] This literature evidence supports the results of this study, as the house officers have scored lowest while the consultants have scored highest in most of the domains. This positive trend in EI in relation to the years of experience should be reconfirmed with longitudinal re investigation to see for the effect size and confirmation of the said notion. A multi-level qualitative exploration is needed for reconfirmation of finding as these outcomes may be due to normal age maturation, varied life experiences, structured training, mentoring or other unidentified & unrevealed factors.

Although the total EI scores shows an increasing trend with years of training, yet postgraduate trainees show a downward trend in the domains of self-motivation and social skills. This downstream observation can be justified by the social and mental stresses, exams, depression, burnouts and financial problems encountered by trainees during the training phase. Satterfield has highlighted that decrease in EI during training phase in his study, due to depersonalization, stress, burnout and desensitization.[21] Papanagnou et al. has reported a mid-training downwards trend in overall emotional intelligence of medicine trainees.[22,23] Sarah has also reported a decrease in emotional intelligence in military surgical residents during mid-training phase.[24] The possible explanation for lower scores in managing emotions and social skills domain may be attributed to either poor baseline scores or other medicating variables like stress, depression, over commitment & self-doubt which could manifest as a deficit in the scores of these domains. Increased level of responsibility along with mental and physical stress may be another contributing factor towards the declining scores.[19] Residents are a wet soil, and training period is crucial to promote their emotional wellbeing and competency. So, efforts should be made to improve their stress tolerance, assertiveness, resilience, optimism , self-perception and self-expression which in turn will ensure development of emotionally intelligent consultants. Open lines of communication, accessible and broad learning culture, real time feedback and promotion of self-reflection and self-efficacy can further augment healthcare professional's wellness and hence emotionally intelligent providers and individuals.[17]

The scores in self-awareness and empathy domains are higher than other domains. This might be attributed to either good baseline EI scores or it might be a manifestation of other intervening variables. Structured training, regular medical education workshops, psychiatric counselling,

communication skills workshops, mentoring and support groups, stress management and conflict management exercises during weekly CPC's and portfolio development with reflective practice, may have contributed to the increasing trend in global EI scores and domain specific EI scores. Literature suggests that active learning sessions, hands-on practice and situated learning improves emotional skills. Deliberate and planned efforts for early clinical exposure, integrated teaching and learning, situated learning and workplace role modeling might have been an instrumental factor for improvement in empathy in doctors. Regular educational training workshops by medical education department in domains of self-reflection, self-efficacy, self-regulated learning and portfolio development might be a contributory factor to improved self-awareness. A multi-level re exploration is required for confirmation of findings.

Perception, management, and utilization of emotions is a prime factor in patient care and hence ensures successful career of a doctor.[13, 25] Formal and informal training of emotional intelligence improves communication or social skills, empathy, attitude and patient care.[26] Small group teaching and workshops have been proven as the most effective way of letting people understand and label their emotions.[27] Mindfulness can be promoted by role modeling which is essential for patient care.[28]

Conclusion

There is a positive correlation between global EI scores and years of clinical experience. There is a downward trend in the scores in domains of self-motivation and social skills in post graduate trainees while House officers needs improvement in all domains. Consultants need to improve predominately in managing their emotions.

Limitations

This is a unicentric study with small sample size so some observations may be context specific however the findings of my study are parallel with the other international studies. This study is unique in incorporating both medical and dental doctors but it is a cross- sectional study, a more rigorous approach would be to conduct this study in a longitudinal design. The leadership toolkit emotional intelligence questionnaire used in the study is based on a 5-point Likert scale so it is difficult to know the real impact of the small differences in the scores.

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CASE REPORT

Retrieval of A Separated Endodontic Instrument Via Braiding Technique

Mehak Babar, Anum Moiz, Sohaib Siddique

ABSTRACT

A successful endodontic treatment of a tooth can be compromised by several causes, one such cause is a separation of an instrument within the canal. In order to increase the survival rate and prognosis of a tooth this mishap needs to be rectified. There are many nonsurgical and surgical ways available to deal with such a scenario. This case report presents a least invasive way of tackling this iatrogenic error that involves removal of the fractured instrument via braiding technique and also by passing of a ledge resulting in a successful outcome.

Key Words: *Braiding Technique Separated Instrument, Root Canal Treatment.*

Introduction

Dental clinicians performing endodontic treatment face variety of complications during this procedure, the most common of these are the iatrogenic errors occurring during root canal preparation.[1] Among these mishaps intracanal separation of an endodontic instrument is the most prevalent. This broken instrument might adversely affect the prognosis of the treatment by obstructing a thorough cleaning and shaping of the canal. [2] The long term prognosis of such teeth is determined by the pre-operative infection of the tooth, location and timing of the separated instrument.[3] In order to retain teeth with such mishap and to increase the longevity; several treatment options are available to overcome this incident. Among these options the first and the foremost is to try removing the separated fragment with the aid of ultrasonic, retrieval kits, hollow tubes or files. If these options fail the other options are to bypass the fragment or go for surgical treatments such as apicectomy, root resection, hemi section or extraction.[4] The choice for instrument retrieval technique should be the least invasive and is also operator dependent.[5]

This article presents a case report on minimally invasive way of file retrieval from a lower first molar. The technique used for retrieval was "braiding technique". In which 2 or 3 small sized files are twisted around the separated instrument after an initial attempt of by passing it. This preserves root dentin thus provides strength and functional support to the already weaken tooth.

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Case Report

A 22years old male patient presented to operative department of Islamic International Dental hospital with a complaint of radiating pain on chewing in lower right first molar. Upon clinical examination the tooth was heavily restored with amalgam, mild swelling in buccal vestibule was evident. (Fig.1) The tooth had undergone root canal treatment 1year back. The tooth was tender to percussion. Oral hygiene status was satisfactory. Medical history was non-significant.

Periapical radiograph was performed that showed an inadequate endodontically treated tooth. Distal canal was obturated at short length. A separated H-file was seen in one mesial canal at least 4-5mm in the coronal 2/3rd of root with the other mesial canal being missed. For identifying the canal with the separated instrument another X-ray with SLOB (Same Lingual Opposite Buccal) technique was done. The mesial shifting located the instrument to be in mesiobuccal canal, which was later confirmed after access opening.

Clinical procedure

The patient was notified about the condition of the tooth, and also the treatment to be done. The proposed treatment was initiated after taking the informed consent from the patient. Local anesthesia was given via inferior alveolar nerve block and rubber dam was applied. The amalgam restoration was removed with high speed hand piece using tungsten carbide 245 bur till the access opening.

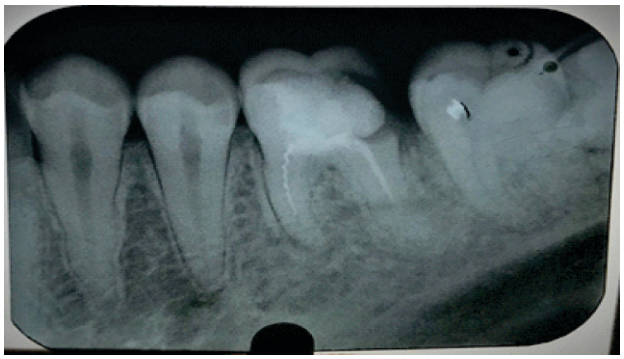

Fig 1: Pre Operative Periapical Radiographic Image

Coronal flaring was done with GG-drills 2 and 3 followed by 4. An attempt was made to bypass the separated instrument using H-files in a sequence from 20 to 40 numbers. The created space was used to employ "Braiding technique" in order to retrieve the file. Two number 10k files were inserted in the canal and twisted around the separated file and then pulled upwards towards the orifice. This led to the loosening of file in canal which was later removed with the aid of "Stieglitz forceps." (Fig 2 & Fig3)

During canal shaping and cleaning a ledge was encountered in outer wall of mesio-lingual canal. The ledge was bypassed with a small K- file with a watch-winding motion and the working length was achieved. (Fig.4) The root canal treatment was completed with laterally condensed obturation. (Fig.5) Coronal buildup was done with amalgam filling.

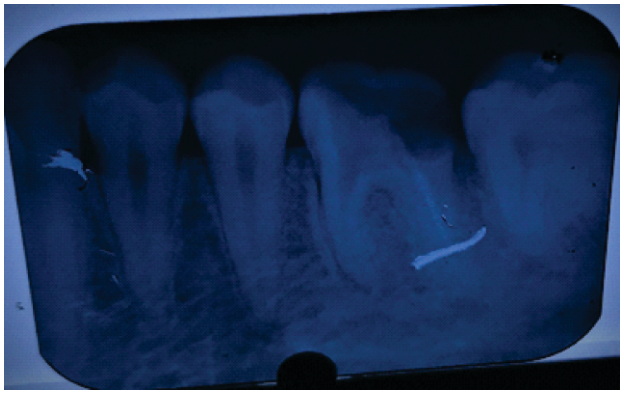

Fig 2: Periapical Radiograph Showing the Removal of Separated Instrument From the Canal

Fig 3: Retrieved Instrument from Canal

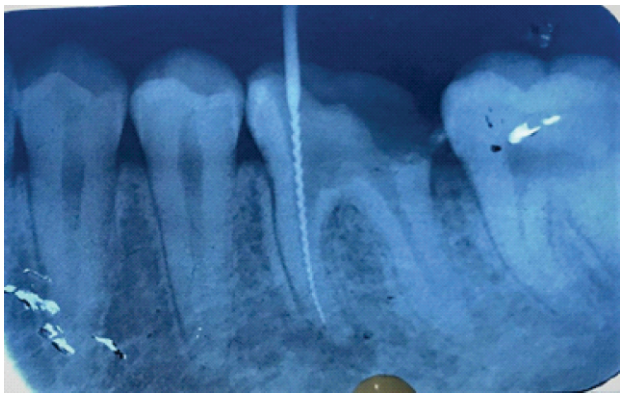

Fig 4: Ledge bypassed

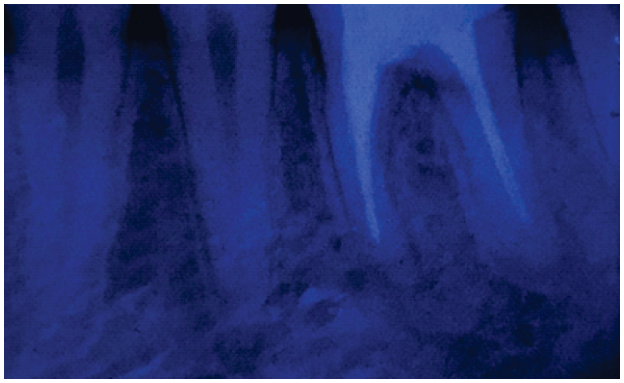

Fig 5: Post-Operative Periapical Radiograph of Obturated Root Canals

Discussion

The success and an overall prognosis of root canal treatment might be adversely affected by a separated instrument within a canal.[6] Instrument separation is a common mishap that can occur even by experienced endodontists as shown by a previous study results that incidence was (94.8%) in endodontists as compared to general dentists (85.1%).[7] The prognosis in such cases is dependent on root vitality, periapical status of a tooth, the level of separation and the status of cleaning and shaping of canal at the time of separation.[8] In order to increase the longevity of a tooth, every attempt must be made to bypass or remove the fractured instrument.

Orthograde instrument retrieval is a time taking procedure and requires a lot of effort with a 55-79%

success rate.[8] Among different retrieval methods braiding technique is the simplest one, limiting excessive removal of root canal dentin and also prevents tooth from iatrogenic errors such as perforation and fracture.[9]

In this case copious irrigation with sodium hypochlorite and 15% EDTA were used for lubrication. Researches have shown that if an instrument can be bypassed it can be retrieved with ease.[10] Same as in this case after accomplishing the bypassing, braiding method was implemented. That involves insertion of 2 or 3 H- files in the canal alongside the fractured object which is then withdrawn by gripping the object through twisting of these files. The above mentioned technique resulted in a successful retrieval of the instrument with least amount of destruction to the tooth and periapical tissues.

The advancement of technology had revolutionized the field of dentistry in every aspect, resulting in the development of newer techniques for retrieval of fractured instrument. The different techniques and armamentarium includes Masserann kit, Brasseler Endo extractor kit, Cancellier instrument and Mounce extractors, Instrument removal system, Ultrasonic removal with dental operating microscope/ dental loupes, laser, electrolysis and many more.[11,12] In comparison to the novel techniques mentioned above, the retrieval of a fractured instrument with the aid of braiding technique is a simple and low cost alternative. It does not require any special devices, and uses routine endodontic instruments in the dental clinic, it is fast to execute and less technique sensitive.[13] In order to achieve the beneficial result a dentist needs to charter patience, persistence and perseverance along with the least invasive method of instrument retrieval.[14]

Conclusion

As stated prevention is better than cure so every effort must be made to follow the proven strategies, implementing safe methods and have thorough knowledge during root canal procedure in order to prevent such mishaps from happening at first place. On the other hand if it does happen begin treatment with the simplest and least invasive methods to deal with such scenarios.

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JOURNAL OF ISLAMIC INTERNATIONAL MEDICAL COLLEGE (JIIMC)

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FOCUS AND SCOPE

We accept articles on clinical, basic medical sciences and articles on medical education from both local and international authors. To encourage and facilitate their contribution, the manuscripts submitted by the international authors are published on priority basis. Moreover, international authors are exempt from publication and processing charges. The journal follows the uniform requirements for manuscripts submitted to Biomedical Journals, (updated on *http://www.icmje.org/recommendations/*).

AIMS AND OBJECTIVES

The primary aim is promotion and dissemination of medical research which is achieved through following:

- To publish innovative, evidence based, peer-reviewed clinical, basic medical science and medical education research articles on a diverse range of topics.
- To publish both qualitative and quantitative researches in medical education.
- To encourage original researches related to combination of health and peace and prevention of ferocity through different health associated initiatives.
- To educate and update the knowledge of physicians, surgeons and other health care providers by publishing basic and clinical science based researches to support informed clinical decisions.
- To improve public health in developing countries by elevating the quality of medical care, disease prevention, and research provided by an informed readership.
- To enable physicians and surgeons to be informed in different areas of medicine.
- To encourage balanced and responsible debate on controversial issues that affect health care system and approaches.
- To forecast important issues and trends in medicine and health care.
- To highlight the non-clinical aspects of public health, including the legal, ethical, economic, political, environmental and cultural issues.
- To attain the maximum level of ethical medical journalism and to produce a publication that is appropriate, reliable, and easy to comprehend.
- To promote the integrity of science by publishing evidence based, latest, important and useful medical research articles.

FREQUENCY OF PUBLICATION

JIIMC is published quarterly and is also available on JIIMC Website.

HISTORY OF JOURNAL

The publication of JIIMC was started in print form only in 2004. However, the regularity in the publication of journal was achieved in 2008. The journal was published biannually till July 2013. Quarterly publication of journal was started from September 2013. In 2011, website of JIIMC was developed and online publication of journal was started in July, 2011. Since then our journal is published in time and on regular basis.

EDITORIAL POLICY

JIIMC is a peer reviewed medical journal published by Islamic International Medical College, Riphah International University Islamabad, Pakistan. JIIMC follows the International Committee of Medical Journal Editors (ICMJE) uniform requirements for manuscripts submitted to biomedical journals (updated on http://www.icmje.org/recommendations/). JIIMC also follows the policies of World Association of Medical Editors (WAME). The publisher and the members of the editorial board cannot be held responsible for errors or for any consequences arising from the use of the information contained in this journal. More than five years old data is not accepted for publication.

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SOURCES OF SUPPORT

Higher Education Commission (HEC), Islamabad, Pakistan.

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- Withdrawal of already published article (as the case may be).
- Barring the authors from further publication in the JIIMC for one year or permanent depending upon the nature of offence. The author will be on watch. HEC, PMDC and author's institute will also be notified for information and possible action.
- In case of multiple submissions, editors of other journals will also be informed. The author(s) will have to provide documentary proof of retraction from publication, if such a defence is pleaded.
- Those claiming intellectual/idea or data theft of an article must provide documentary proof in their claim

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We follow the double blind review process by a panel of peer-reviewers with diverse knowledge and expertise in their specialties, and having a vast experience as researcher.

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- To evaluate the manuscripts critically and provide comprehensive, speedy and unbiased but polite feedback to the author as well as to the editor regarding its suitability for publication.
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- To maintain the confidentiality of a manuscript forwarded for assessment.
- Shall not copy the manuscript submitted for assessment.
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- Reviewer shall not communicate directly with the author and even not to identify themselves to
- Reviewer shall make effort to meet the deadline (2 weeks) for the review of manuscript.
- To be aware of any probable conflicts of interest and to inform the editor about it, if needed withdraw themselves from the peer-review process if a conflict exists.

SELECTION OF REVIEWERS

- Seventy five percent of reviewers will be from Pakistan and 25% will be selected from abroad.
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Once the manuscript is received in the JIIMC office, acknowledgement letter is sent to the corresponding author along with JIIMC copy right , undertaking agreement performa and JIIMC declaration of conflict of interest performa. The CRUA should be duly filled-in and signed by all authors and returned to the JIIMC office. All manuscripts received are initially assessed by the editorial staff for worth of its publication. It is ensured that manuscript is prepared in accordance with the uniform requirements submitted to medical journal as approved by ICMJE guidelines. It is also assessed to see that it is written in accordance with the JIIMC format and technically correct. The manuscript is also assessed for statistical analysis by the Journal's statistician. Deficiencies found by editor and statistician are communicated to author for redressing the article at the initial stage.

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Once the article is received from the author, the manuscript is sent to at least two or three independent peer reviewers of the specialty the article belongs to. A sufficient time of 1 or 2 weeks are given to the reviewers to return their comments on a special designed proforma of JIIMC. Comments from two reviewers are mandatory for review of a manuscript. Once the reviewed manuscript is received from both the reviewers, their comments/suggestions are communicated to the author for revision.

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The assessment, external review process and editorial decision on a manuscript are usually longer.

Once all articles are corrected, pages are numbered, datelines, short titles and authors' names are inserted on each page, finally content page is made. The Managing Editor checks final proofs at the dummy stage before sending them for printing.

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The 'JIIMC' agrees to accept manuscripts prepared in accordance with the "Uniform Requirements submitted to the Biomedical Journals" published in the British Medical Journal 1991; 302: 334-41.

The material submitted for publication should be sent completely to the Journal of Islamic International Medical College, Pakistan. Research work that has already been reported in a published paper or is described in a paper sent or accepted elsewhere for publication should not be submitted. Duplicate submission of the same research work to other journal should be avoided as this fall into the category of publication misconduct. A complete report following publication of a preliminary report of a preliminary report, usually in the form of an abstract, or a paper that has been presented at a scientific meeting, if not published in a full proceedings, may be submitted.

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It is mandatory to submit online a duly filled-in copyright, authorship and undertaking proforma along with the manuscript. (https://jiimc.riphah.edu.pk/downloads/). The sequence/ order of name of authors submitted at the time of initial submission of manuscript shall not be changed at any stage.

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All those designated as authors should meet all four criteria for authorship as stated in ICMJE recommendations (http://www.icmje.org/icmje-recommendations.pdf). According to ICMJE recommendations authorship is based on the following four criteria: 1. Substantial contributions to the conception or design of the work; or the acquisition, analysis, or interpretation of data ; and 2. Have been involved in drafting the work or revising it critically for important intellectual content; and 3. Have given final approval of the version to be published; and 4. Agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Each author should have participated sufficiently in the work to take public responsibility for appropriate portions of the content. We strongly discourage gift or ghost authorship. Mere supervision, collection of data, statistical analysis and language correction do not grant authorship rights.

GENERAL ARCHIVAL INSTRUCTIONS

The manuscript should be typed in MS Word. Each manuscript should include a title page (containing email address, cell numbers, institution and postal address of the corresponding author), abstract, key words, text, acknowledgements (if any), references, tables (each table, complete with title and footnotes) and legends for illustrations and photo-graphs. Each component should begin on a new page. Sub-headings should not be used in any section of the script except in the abstract.

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SHORT COMMUNICATIONS should be about 1000 words, with a non-structured abstract, two tables or illustrations and 5 references.

CLINICAL CASE REPORT and brief or negative research findings may appear in this section. Clinical Case Reports should be of academic value and provide relevance of the disease being reported as rare or unusual. The word count of case report should not be more than 800 words with 3- 5 key words. The abstract should be non-structured of about 150 words (case specific) with maximum of 5 references. It should not include more than 2 figures and one table.

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LETTERS TO THE EDITOR should normally not exceed 400 words, have no more than 05 references and be signed by all the authors-maximum 3 are allowed. Preference is given to those that take up points made in contributions published recently in journal. Letters may be published with a response from the author of the article being discussed. Discussions beyond the initial letter and response will not be entertained for publication.

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An article based on dissertation/thesis submitted as part of the requirement for a postgraduate degree (M. Phil, FCPS, MS) can be sent for publication after it has been approved by the institution's ethical review board/committee and the college/university evaluation committee/board. The data should not be more than five years old. Thesis/dissertation based article will be assessed by proper review process. Once accepted for publication, then disclosure will be made that 'it is a Dissertation based article'.

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  - ✓ A warning letter will be issued to the author or reviewer covering the misconduct and as a warning to future behaviour.
  - ✓ Publication of a formal notice detailing the misconduct.
  - ✓ A formal letter to the head of the author's or reviewer's department and Institution.
  - ✓ Formal retraction or withdrawal of a publication from the journal.
  - ✓ Debarment of the authors(s) from further publication in the JIIMC for one year or permanent depending upon the nature of offence.

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ABSTRACT

Abstracts of original article should be in structured with following sub-headings: i. Objective, ii. Study Design, iii. Place & Duration of Study iv. Materials & Methods, v. Results, vi. Conclusion. Four elements should be addressed: why did you start, why did you do, what did you find and what does it mean. Why did you start in the objective. What did you do constitutes the methodology and could include design, setting, patients or other participants, interventions, and outcome measures. What did you find is the results, and what does it mean would constitute; our conclusions. Please label each section clearly with the appropriate sub-headings. Structured abstract for an original article, should not be more than 250 words. At least 3 key words should be written at the end of abstract. Review article, case report and other require a short, unstructured abstract. Commentaries do not require abstract.

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a. Give background information about the subject matter and the issues your study intends to address. Only strictly pertinent references should be cited and the subject should not be extensively reviewed.
b. Describe what is known (in the literature) and what is not clear about the subject with reference to relevant literature thus identifying the literature gap.
c. You write the rationale (justification) of your study.
d. Finally you mention the objective of your study

MATERIALS AND METHODS

Methodology is written in past tense.

Follow this sequence **without headings:**

- Study design
- Place and Duration of Study
- Sample size
- Sampling technique
- Mention about permission of ethical review board and other ethical issues addressed.
- Inclusion and Exclusion Criteria
- Data collection procedure-
- Type of data: parametric or nonparametric
- Data analysis; including Statistical Software used, and statistical test applied for the calculation of p value and to determine the statistical significance. Exact p-values and 95% confidence interval (CI) limits must be mentioned instead of only stating greater or less than level of significance. All percentages must be accompanied with actual numbers.

RESULTS

These should be presented in logical sequence in the text, tables and illustrations. All the data in the tables or illustrations should not be repeated in the text; only important observations should be emphasized or summarized. No opinion should be given in this portion of the text.

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This section should include author's comment on the results. Write in present tense, active voice- except for results, which are written in past tense. It should be written in following sequence:

a. First of all very briefly summarize, Interpret and discuss main results and don't merely repeat the results.
b. Discuss key studies relevant to your study.

c. Compare your work with other`s work.
d. Describe limitations of your study.
e. Suggest future work if necessary.

CONCLUSION

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REFERENCES

References must be given in the Vancouver Style only. References should be numbered in the order in which they are superscripted in the text. At the end of the article, the full list of references should give the names and initials of all authors (unless there are more than six when only the first six should be given followed by et al). The author's names are followed by the title of the article; title of the journal abbreviated according to the style of the Index Medicus (see "List of Journals Indexed", printed yearly in the January issue of Index Medicus); year, volume and page number; e.g. Hall, RR. The healing of tissues by C02 laser. Br J. Surg: 1970; 58:222-225. References to books should give the names of editors, place of publication, publisher and year. The author must verify the references against the original documents before the article. References to papers accepted but not yet published should be designated as "in press" or "forthcoming"; authors should obtain written permission to cite such papers as well as verification that they have been accepted for publication.

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Tables and illustrations should be merged within the text of the paper, and legends to illustrations should be typed on the same sheet. Table should be simple, and should supplement rather than duplicate information in the text; tables repeating information will be omitted. Each table should have a title and be typed in double space without horizontal and vertical lines on an 8 ½" x 11' paper. Tables should be numbered consecutively with Roman numeral in the order they are mentioned in the text. Page number should be in the upper right corner. If abbreviations are used, they should be explained in foot notes and when they first appear in text. When graphs, scattergrams, or histogram are submitted, the numerical data on which they are based should be supplied. All graphs should be made with MS Excel and be sent as a separate Excel file even if merged in the manuscript. For scanned photographs highest resolution should be used.

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Figures and Photographs should only be included when data cannot be expressed in any other form. Figures and photographs must be cited in the text in consecutive order. Legends must be typed on the same paper. Legends for photomicrographs should indicate the magnifications, internal scale and method of staining.

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All articles submitted to JIIMC are checked by antiplagiarism software TURNITIN. JIIMC follows the standard definition and description of plagiarism and follow the recommendations by Committee of Publication Ethics (COPE), ICMJE, Pakistan Association of Medical Editors (PAME), Higher Education Commission (HEC) of Pakistan policies about plagiarism available on www.cope.org.

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- Any manuscript submitted for publication

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