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**Correspondence Address:**

Editor, JBUMDC, Bahria University Medical & Dental College, Adjacent PNS SHIFA,  
DHA Phase II, Karachi Pakistan

+92-21-35319491-9

<https://jbumdc.bahria.edu.pk>

[editor.bumdc@bahria.edu.pk](mailto:editor.bumdc@bahria.edu.pk)

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## COVID19 - A Daredevil or A Blessing In Disguise

Inayat Thaver, Fouzia Naeem Effendi, Fareeha Shahid

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COVID19 starting as an epidemic last year (2019) from Wuhan, China got converted into a pandemic within months with its devastating ravages throughout the world. The pandemic and its spread with its severity affected both poor and rich countries equally, which had a larger population. The measures taken by China, though, were initially challenged and even termed against the 'human rights' for the complete lockdown but soon were adopted by many countries. Suddenly, the need for ICUs and ventilators in them jumped throughout the world<sup>1</sup>, the value and demand for doctors, especially the clinicians managing the emergencies was brought to the limelight; all types of borders within and between the countries were closed for any movements and above all the social media became active with all the myths, misinformation and warnings about COVID19. The WHO, amidst all this chaos, took up the steering role for addressing and managing the pandemic. Various SoPs (standard Operating Procedures) were prepared, which by and large focused on a) social distancing b) wearing masks, and c) cleaning or sanitizing the hands regularly.<sup>2</sup> Suddenly, the soaps, sanitizers, and masks became expensive to the extent that at many places, they were not available. All the intuitions or areas where there was a potential of the larger gathering were closed, including offices, educational intuitions, markets, malls, and even parks and playgrounds were closed. Initially, it meant getting locked at home or getting necessary essential items, including food from someone else, or taking the risk of going out and getting these essential items. The various scientists related to Pathology/virology, public health experts, and health policy and planners also joined the bandwagon to address this pandemic. All the businesses, both local and international, plunged, and countries showed a downward trend.<sup>3</sup> Each

day, the number game of in-country and other countries globally was flashed on TV and social media, giving the counts of those infected and those admitted in the ICU and the ones who died. Soon, we came to know some of the potential risk factors and various theories about the natural history of the disease and its multiple causations. Various 'trials' and/or experiments were conducted claiming a drug or an approach's success. Initially, a phase of denial and conspiracy prevailed among many, including the developed countries' leaders. Lack of adequate emergency facilities prompted the riots, protests, and criticism by political opponents. Domestic violence, closure essential, and many other emergencies and surgical services, laying off of workers in various offices and institutions, were noticed, including increased sufferings faced by the daily wage workers, vulnerable population, and the poor.<sup>4</sup>

Against all these backdrops, there was a silver lining, seizing the opportunities and demonstration of philanthropy to address all these devastations and human sufferings. The frontline doctor- young, adult, and experts went out of the way to play their role by working long hours and risking their own lives. Various educational intuitions and offices and businesses started converting into digital approaches, and suddenly, the demand for connectivity increased everywhere.<sup>5</sup> Online businesses were launched, especially by many young startups and entrepreneurs. The use of new and existing software and programmes were being recommended, followed by their training and then active use, especially for teaching purposes. Various volunteers mobilized themselves for helping the poor, unemployed, and those who were quarantined but did not have any support at home or in hospitals.<sup>6</sup> The clinicians, especially the Infectious disease specialists, Pulmonologists, ICU and emergency specialists, pathologists/virologists, and other clinical disciplines, jumped in to manage and identify the treatment of the COVID19 dynamic but also for vaccination. The Public Health experts, especially the Epidemiologists and Infectious diseases experts, commenced their modeling about diseases' behaviour and how it can be prevented and then ultimately controlled.<sup>7</sup> Various laboratories and big commercial pharmacological and bio-medical companies started producing more cost-effective and quick detection tests. The WHO, including many other international bodies, made standard guidelines for managing the COVID19 and other related issues such as reproductive health, routine

#### Inayat Thaver

Professor and HoD, Department of Community Health Sciences,  
Bahria University Medical and Dental College, Karachi  
Email: [inayat.bumdc@bahria.edu.pk](mailto:inayat.bumdc@bahria.edu.pk)

#### Fouzia Naeem Effendi

Senior Lecturer, Department of Community Health Sciences,  
Bahria University Medical and Dental College, Karachi

#### Fareeha Shahid

Assistant Professor  
Department of Community Health Sciences,  
Bahria University Medical and Dental College, Karachi

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immunization, and reporting and monitoring system. State of the art reports and data management for recording cases followed by monitoring the cases were developed, including various local apps, quick fever detection systems, and mass screening. Thus, it seemed that there is war throughout the world, and all countries are global, though individually are participating in defeating that unforeseen enemy. All the countries organized various approaches some standard (as recommended by WHO or had been tried out successfully by others) or innovated their indigenous techniques. Thus, besides the terminology of ‘lockdown, others were coined, such as “smart lockdown” or “mini-lockdown,” etc. The strange behavior of the spread of the virus in various countries has puzzled many scientists, especially in Asian countries, including that of Pakistan.<sup>8</sup> This is in stark contrast to our immediate neighbor India where the situation is still out of control. The success observed in Pakistan may be due to the policies and programmes, or having some inherent immunity or striking at the right moment. New family reunions have been a very welcoming change for various societies, getting to disintegration. This only happened due to the lockdown forced by COVID19. People are getting more mindful of each other; the role of counsellors, psychologists, and psychiatrists could not be undermined who had proactively played their role due to lockdown consequences, including many mental health problems. Suddenly, we saw the surge of many ‘YouTube channels’ and so many potential stars who are active in sharing their knowledge, experiences, and reflections on various topics.<sup>9</sup>

In that context, the role of religious scholars should also be mentioned who had actively participated in spreading relevant health education messages, especially in the Muslim world. The most famous buzz word among these “new norms” (as they say)<sup>10</sup> is the WFH, i.e., working from home. The WFH appears to be highly practiced and has been successful in many circumstances; however, some barriers or potential issues have also been noted. For the first time, we should consider whether we need to physically go to the office or other places instead of doing it whole sitting from home. The WFH benefitted the crumbling economy and has improved the overall situation mainly because of decreased smoke from vehicles and being on the roads for quite a time while going to the offices. The participation in home chores besides by the women only at home has been another welcoming change. There had been reports that the men and children have started participating in some household chores; of course, there are exceptions to another extreme of domestic violence.<sup>11</sup>

Most governments have suddenly realized that they need to invest more and put a bigger pie of the budget for health. This has also been supported by various development partners and international non-government organizations. The decline in the cases and morbidity and mortality in many countries

has been reported for a few months, but they say that war is not over. There are potential dangers of a resurgence, especially with winter; some countries have reported the emergence of the virus in various places and gone back to lockdown or, to be more precise, smart or selective lockdown; this is now true for Pakistan, also. Based on the previous downwards trend of COVID19 cases, the Pakistan government has decided to open educational institutions; this has though followed after allowing the multiple businesses, especially the markets and malls, with the recommendations to observe SoPs.<sup>12</sup> However, in countries where there is a continuous downward trend, the people (or even government) are going into complacency and not fully observing the SoPs. The fears of resurgences of COVID19 is getting true, especially in Western countries where the winter has already commenced. In Pakistan, are also getting the resurgence, and it has been reported that the nation again has positive cases what it used to have back in July. We have yet to wait and see how things will turn out. However, we are passing through history after the last pandemic of plague, and we still need to know much more about the disease. However, various claims have been made for remarkable progress in producing and testing out the vaccine. But some scientists do tell us that the vaccine may not be the answer. The bigger question is, do we have to follow the ‘new norm,’ or we can go back to the era of BC, i.e., “before Corona.” Amid so many deaths and miseries, humanity is still alive. Thus, we have developed resilience, forbearance and have demonstrated so many untapped potentials to work around and keep the life and businesses moving on. Imagine a situation of BC (Before Corona). In the ‘BC’ period, we may not have advanced so much in utilizing digital technology and the health advances including the innovations to address a pandemic. The blessing in disguise has been to capture opportunities for getting nearer to family members (especially to the old ones) and the Almighty Allah and divine power Who controls and takes care of us.

**Author Contribution:**

**Inayat Thaver:** Agreement to be accountable for all aspects of work in ensuring that questions related to accuracy or integrity of any part of the work are appropriately investigated and resolved

**Fouzia Naeem Effendi:** Drafting the article or revising it critically for important intellectual content

**Fareeha Shahid:** Substantial contributions to conception and design, or acquisition of data, or analysis and interpretation of data

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## Phototherapy Induced Hypocalcemia in Neonates with Unconjugated Hyperbilirubinemia

Amna Khan, Anila Farhat, Hamayun Anwar, Sajid Shamim, Mujeeb Ur Rehman, Irfan Khan

### ABSTRACT:

**Objective:** To determine the frequency of hypocalcemia in neonates with unconjugated hyperbilirubinemia receiving phototherapy.

**Study design and setting:** Cross sectional study conducted at neonatal intensive care unit, King Abdullah Teaching Hospital, Manshehra for one year from December 2017 to November 2018.

**Methodology:** Total 213 full term stable neonates of either gender with jaundice were studied in this study. Out of which, 143 with unconjugated hyperbilirubinemia were exposed to phototherapy while 70 neonates with exaggerated physiological hyperbilirubinemia taken as control were not exposed to phototherapy. Serum calcium level was determined through blood test before and after 24 hours of phototherapy. SPSS version 22 was used to analyze the data. Frequency and percentages were used to describe categorical variables like gender and hypocalcemia. Hypocalcemia was stratified by age and gender to see effect modifiers. Post stratified chi-square test was applied in which p value = 0.05 was considered as significance value.

**Results:** In study group, 143 neonates who received phototherapy had mean age of 7 days  $\pm$  2.62 SD. Total 65% neonates were male and 35% neonates were female. Mean serum calcium level of neonates before and after provision of phototherapy was 9.28 mg/dl  $\pm$  0.23 and 8.54 mg/dl  $\pm$  0.68 respectively, which is statistically significant. The frequency of hypocalcemia was 40% in neonates with unconjugated hyperbilirubinemia after 24 hours of phototherapy.

**Conclusion:** Hypocalcemia is an important complication in neonates with unconjugated hyperbilirubinemia after continuous phototherapy. Hypocalcemia has clinical impact and adds to morbidity, and if left untreated, can lead to mortality.

**Key words:** Hypocalcemia, Neonates, Patent ductus arteriosus (PDA), Phototherapy, Unconjugated hyperbilirubinemia.

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### INTRODUCTION:

Hyperbilirubinemia is one of the most frequent and benign problem in neonates. During first week of life, around 80%

of preterm neonates and 60% of full term neonates have hyperbilirubinemia. Severe unconjugated hyperbilirubinemia, if not treated timely, can lead to permanent brain damage in the newborn.<sup>1</sup> Hyperbilirubinemia can be managed either by phototherapy, exchange transfusion or pharmacological agents.<sup>2</sup> Phototherapy is the most effective therapy for management of neonatal hyperbilirubinemia which lowers serum bilirubin level by converting bilirubin through structural photo isomerization and photo-oxidation into non-toxic form that is excreted out of the body.<sup>3</sup>

Complications of phototherapy are dehydration, diarrhea, skin rash, hyperthermia, retinal degeneration, DNA damage to lymphocytes, patent ductus arteriosus (PDA), bronze baby syndrome, and hypocalcemia.<sup>4</sup> Melatonin concentration is reduced in newborns with phototherapy which in turn leads to hypocalcemia.<sup>5</sup> First of all the association between phototherapy and hypocalcemia was reported by Shafiq MB et al. in preterm infants.<sup>6</sup>

The pathophysiology and the underlying mechanism by which phototherapy causes Hypocalcemia was suggested by Hayat<sup>7</sup> and Hunter<sup>8</sup> and reported that phototherapy inhibit the secretion of melatonin by pineal gland and this results

#### Amna Khan

Senior Registrar, Department of Pediatrics,  
Abbottabad International Medical College, Abbottabad

#### Anila Farhat

Assistant Professor, Department of Pediatrics,  
Frontier Medical and Dental College, Abbottabad  
Email: [paeds\\_doctor@yahoo.com](mailto:paeds_doctor@yahoo.com)

#### Hamayun Anwar

Senior Registrar, Department of Pediatrics,  
Frontier Medical and Dental College, Abbottabad

#### Sajid Shamim

Senior Registrar, Department of Pediatrics,  
Frontier Medical and Dental College, Abbottabad

#### Mujeeb Ur Rehman

Registrar, Department of Pediatrics  
King Abdullah Teaching Hospital, Manshehra-Pakistan

#### Irfan Khan

Assistant Professor, Department of Pediatrics  
Nowshera Medical College, Nowshera, KPK

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in blockage of the effect of cortisol on bone calcium.<sup>8</sup> Study by Husain et al suggested that neonates receiving phototherapy have reduced level of parathyroid hormone which leads to hypocalcemia.<sup>9</sup> While Hooman in a study reported that urinary excretion of calcium was significantly higher in patients exposed to phototherapy.<sup>10</sup>

Hypocalcemia is a significant problem in neonates subjected to phototherapy and its prevalence in full term neonates is 8.7%.<sup>11</sup> Complications of hypocalcemia in newborns include apnea, convulsion, muscle cramp, tremor, and tetanus.<sup>5</sup> Hypocalcemia developed in 39% of term and 53% of pre-terms after being subjected to phototherapy for more than 48 hours.<sup>12</sup> Hypocalcemia, being a major complication of phototherapy, is associated with poor prognosis in terms of high mortality rate as compared to babies with normocalcemia, if not diagnosed timely and treated accordingly.<sup>12,13</sup> The treatment of hypocalcemia includes intravenous 10% calcium gluconate by slow intravenous infusion over 30 minutes and when oral feeding begins, calcium supplementation are provided for few days.<sup>12,14</sup> Therefore, the objective of this study was to evaluate the frequency of phototherapy induced hypocalcemia in full term neonates with neonatal hyperbilirubinemia.

#### METHODOLOGY:

This cross sectional study was carried out at neonatal intensive care unit, King Abdullah Teaching Hospital, in Mansehra for one year from 1<sup>st</sup> December 2017 to 30<sup>th</sup> November 2018 after approval from the ethical committee of King Abdullah Teaching Hospital, Mansehra (ERC# 1766-08/EC). Sample size was calculated by WHO software formula to estimate a population proportion with specific absolute precision is used with the following assumptions: Confidence level = 95%, Anticipated proportion of hypocalcemia after phototherapy = 39%, absolute precision = 8%. Samples were collected by using non-consecutive sampling technique. Written consent was taken from parents/guardians before enrolling the patients into this study.

Total 213 full term stable neonates (37 to 41 weeks) of either gender with jaundice were assessed in this study. Among them 143 neonates (93 males and 50 females) with neonatal jaundice were enrolled in study group who were exposed to phototherapy. Total 70 stable neonates (45 males and 25 females) with physiological hyperbilirubinemia were enrolled in control group who were not exposed to phototherapy. All the full term stable neonates delivered at 37 to 41 weeks of gestational age, of either gender with unconjugated hyperbilirubinemia were included in the study. Newborns with jaundice in first 24 hours of life, neonates of a diabetic mother, who already had exchange transfusion, babies with prolonged jaundice for more than 14 days, neonates with conjugated hyperbilirubinemia were excluded from study.

Hypocalcemia was defined as serum calcium level less than 8mg/dl whereas hyperbilirubinemia was defined as total

serum bilirubin level above 95<sup>th</sup> percentile for age on hournomogram. A 4cc venous blood sample for serum calcium level and bilirubin level was sent to laboratory before starting conventional phototherapy and after 24 hours of continuous phototherapy. All the information including gestational age, gender, weight, age, mode of delivery, and serum calcium levels (pre and post phototherapy) were recorded on a pro-forma. SPSS version 22 was used to analyze data. Quantitative variables like age and serum calcium were described in terms of mean  $\pm$  standard deviation. Frequency and percentages were used to describe categorical variables like gender and hypocalcemia. Hypocalcemia was stratified by age and gender to see effect modifiers. Post stratified chi-square test was applied in which p value = 0.05 was considered as significance value.

#### RESULTS:

Among 143 neonates in the study group that received phototherapy, 93 (65%) neonates were male and 50 (35%) neonates were female while among 70 neonates of control group, 45 (64%) neonates were male and 25 (36%) neonates were female (Table 1). The frequency of hypocalcemia in neonates of the study group after 24 hours of phototherapy was 57 (40%), out of which 37 were male patients and 20 were female patients (Table 2). Distribution of hypocalcemia after phototherapy in different age groups is illustrated in (Table 3). 41 children out of 103 in age range of 1-10 days, 14 children out of 36 in age range of 11-20 days and 2 children out of 4 in the 21-28 days age range had hypocalcemia. The serum calcium levels of neonates before phototherapy of studied group and control group were 9.28 mg/dl  $\pm$  0.23 and 9.14 mg/dl  $\pm$  0.87 respectively (Table 4). There was no statistically significant difference between these two groups regarding serum calcium level on arrival ( $P>0.05$ ). Mean serum calcium levels of neonates of the studied group before and after provision of phototherapy were 9.28 mg/dl  $\pm$  0.23 and 8.54 mg/dl  $\pm$  0.68 respectively (Table 5). There is statistically significant decrease of serum calcium after phototherapy in the study group ( $P<0.001$ ).

Table : Gender distribution of neonates in studied group with hypocalcemia and control group

	Gender	Frequency	Percentage
Studied Group (n=143)	Male	93	65%
	Female	50	35%
Control Group (n=70)	Male	45	64%
	Female	25	36%

Table 2: Frequency of hypocalcemia in neonates with respect to gender of the studied group (n=143) after phototherapy

Hypocalcemia	Frequency			Percentage		
	Male	Female	Total	Male	Female	Total
Yes	37	20	57	26%	14%	40%
No	56	30	86	39%	21%	60%
Total	93	50	143	65%	35%	100%

Table 3: Distribution of hypocalcemia after phototherapy in the neonatal age-group

Hypocalcemia	1-10 days	11-20 days	21-28 days	Total
Yes	41	14	2	57
No	62	22	2	86
Total	103	36	4	143
Mean ± SD (days)	7 ± 2.62			

Table 4: Comparison between studied group and control group regarding results of serum calcium on arrival

	Studied Group (n=143) (mean ± SD)	Control Group (n=70) (mean ± SD)	t-test	P-Value
Serum calcium (mg/dl)	9.28 ± 0.23	9.14 ± 0.87	1.28	>0.05

Table 5: Comparison between serum calcium levels before and after phototherapy treatment among studied group

	Before Phototherapy	After Phototherapy	Paired t-test	P-Value
Serum calcium (mg/dl)	9.28 ± 0.23	8.54 ± 0.68	8.25	<0.001

**DISCUSSION:**

Neonatal jaundice is one of the very common conditions with which pediatrician deal with and presents especially during the 1<sup>st</sup> week of life<sup>13</sup> and it is highly prevalent and dangerous during this stage of life.<sup>14</sup>

Jaundice is present in 60% of term and 80% of preterm infants and in most of cases it is benign condition. In Pakistan it affects 39.7% babies per 1000 live birth.<sup>15</sup> Unconjugated bilirubin is potentially neurotoxic and can cause neurologic and behavioral impairment. Thus main aim of therapy for neonatal jaundice is to prevent neurotoxic effect of unconjugated bilirubin.<sup>16</sup> The management options for newborn jaundice include phototherapy which can be divided into conventional phototherapy or intensive phototherapy, exchange transfusion and pharmacologic options like phenobarbitone, metalloporphyrins and intravenous immunoglobulin (IVIG).<sup>17</sup>

Phototherapy is the most effective therapy for management of neonatal hyperbilirubinemia which lowers serum bilirubin level by converting bilirubin into non-toxic excretable form.<sup>3</sup> Phototherapy converts unconjugated bilirubin to more polar stereoisomer by a process called photo isomerization. The substance formed cannot cross the blood brain barrier and is not neurotoxic and later on excreted out of the body via urine and bile.<sup>17</sup>

Blue fluorescent light with wavelength in the band of 460-490 nm are widely used for phototherapy and babies are kept at distance of 15-20 cm from light with eye pads for protection of eyes. Phototherapy reduces bilirubin level and

also the risk of exchange transfusion. Although phototherapy is safe way of treating neonatal jaundice but has some side effects like skin burn, diarrhea, hyperthermia, fluid loss, retinitis, thrombocytopenia, bronze baby syndrome. One of the important side effect but infact a complication of phototherapy is hypocalcemia.

Post phototherapy prevalence of hypocalcemia is 8.7% in this study. It results due to inhibition of pineal gland via transcranial illumination which decreases melatonin which in turn inhibits cortisol effect on bone calcium. Cortisol induces hypocalcemia by increasing calcium uptake by the bones.

Hypocalcemia leads to apnea, convulsion, muscle cramp, tremor, tetanus and increased mortality rate.<sup>5</sup> Therefore, it should be timely diagnosed by monitoring serum calcium level in neonates receiving phototherapy and appropriately treated with intravenous 10% calcium gluconate along with calcium supplementation. Our study will help pediatricians to plan prompt interventions to avoid complications of hypocalcemia in neonates receiving phototherapy.

In our study, the frequency hypocalcemia was 40% in neonates with unconjugated hyperbilirubinemia after completed continuous phototherapy for at least 24 hours. Study conducted by Jain SK et al<sup>12</sup> showed that hypocalcemia was developed in 39% of term and 53% of preterm neonates after being subjected to phototherapy for more than 48 hours. Analogous results were observed in another study conducted in Karachi by M et al<sup>20</sup> in which the frequency of hypocalcemia in term jaundiced neonates receiving phototherapy was 22.76% (28/123). Another study conducted by Rozario CI et al<sup>21</sup> had comparable results with our study, in which 67% of babies developed hypocalcemia after phototherapy. Alike results were also observed in another study conducted by Arora S et al<sup>11</sup> in which the frequency of hypocalcemia was found to be 42% in neonates with unconjugated hyperbilirubinemia after completed continuous phototherapy for at least 24 hours. In a study conducted in Iran,<sup>22</sup> the frequency of hypocalcemia was 7.5% after phototherapy which is contradictory to our study. In an Indian study by Goyal S et al,<sup>23</sup> the frequency of hypocalcemia was 35% in neonates after receiving phototherapy. Shrivastva et al<sup>24</sup> in a study observed that the frequency of hypocalcemia was 30% in term neonates while Haq et al<sup>25</sup> reported hypocalcemia to be present in 75% of the neonates exposed to phototherapy.

A study conducted in Egypt in 2015 by Bahbah et al<sup>26</sup> showed post phototherapy hypocalcemia was present in 26% of term neonates, in which 50 term neonates received phototherapy and 25 neonates were taken as control with physiological jaundice needing no phototherapy. This is analogous to our study in which we took 70 neonates as control with physiological jaundice needing no phototherapy and among 143 neonates exposed to phototherapy for 24 hours, 40% developed hypocalcemia.

In our study, the mean calcium level before and after 24 hours of continuous phototherapy was  $9.28 \pm 0.23$  mg/dl and  $8.54 \pm 0.68$  mg/dl respectively.

Mean calcium level before and after phototherapy in the local study conducted by Khan M et al<sup>20</sup> was  $8.73 \pm 0.68$  mg/dl and  $7.47 \pm 0.8$  mg/dl which is comparable with our study. Similarly, mean calcium level before and after phototherapy in the study conducted by Bahbah et al<sup>26</sup> was  $9.36 \pm 0.29$  mg/dl and  $8.58 \pm 0.76$  mg/dl which is also comparable with our study.

Phototherapy is also one of the effective therapies for neonatal hyperbilirubinemia with potential complication of hypocalcemia.<sup>27</sup>

This study is conducted on small group of subjects so further studies on larger scale should be conducted so that results can be extrapolated to larger population. Our study also explains this effect on calcium levels of neonates receiving phototherapy. Further studies are required to elaborate this aspect further, and to find out ways to avoid hypocalcemia after phototherapy either by using calcium supplements or refining application of phototherapy. Hence, results of this study will be useful for practitioners to devise meaningful early interventions to avoid complications of hypocalcemia in neonates receiving phototherapy at neonatal intensive care units.

## CONCLUSION:

Hypocalcemia is an important complication in neonates with unconjugated hyperbilirubinemia after continuous phototherapy. Hypocalcemia has clinical impact and adds to morbidity, and if left untreated, can lead to mortality.

### Authors Contribution:

**Amna Khan:** Conception and design, collection and assembly of data, final approval and guarantor of the article

**Anila Farhat:** Conception and design, collection and assembly of data, statistical expertise, final approval and guarantor of the article

**Hamayun Anwar:** Analysis and interpretation of data, drafting of article, statistical expertise

**Sajid Shamim:** Drafting of article, critical revision of the article for important intellectual content

**Mujeeb Ur Rehman:** Analysis and interpretation of data, statistical expertise

**Irfan Khan:** Drafting of article, critical revision of the article for important intellectual content

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## Efficacy of Ahmed Glaucoma Valve and Trabeculectomy With Mitomycin-C in Pediatric Glaucoma

Manzoor Ahmed Khan, Sadia Bukhari, Zafar Ahmed Khan, Mahtab Mengal, Muhammad Afzal Khan, Aimal Khan Panezai

### ABSTRACT

**Objective:** To compare the efficacy between Ahmed glaucoma valve surgery and Trabeculectomy with Mitomycin-c in pediatric glaucoma.

**Study design and setting:** Quasi-experimental study was conducted at Pediatric Ophthalmology Department, ISRA Post graduate Institute of Ophthalmology/ Al-Ibrahim Eye Hospital, Karachi. Duration of study was February to August 2016.

**Methodology:** Samples were divided into two groups. Group A Trabeculectomy with Mitomycin-C and Group B with Ahmed Glaucoma valve surgery. Inclusion criteria were children (above 2 years and less than 15 years of age) visiting Pediatric Ophthalmology OPD irrespective of gender, glaucoma diagnosed with the duration of symptoms > 4 weeks. Exclusion criteria were patient with repeat surgery for glaucoma, combined ocular surgery i.e penetrating keratoplasty or cataract, Preoperative keratitis, uveitis or conjunctivitis, as determined by slit-lamp examination. Paired sample t-test was applied to compare the pre and post IOP examination findings. P-value = 0.05 considered as statistically significant.

**Results:** A total of 110 patients were recruited in this study in which 97 patients were analyzed. Mean age of Group A was  $6.73 \pm 2.7$  and mean age of Group B was  $7.05 \pm 2.3$ . Mean pre-operative IOP in "Group A" was found to be  $31.59 \pm 5.4$  and post-operative IOP was reduced to  $17.95 \pm 4.8$  with statistically significant P-value  $< 0.0001$ . In "Group B" Mean pre-operative IOP was  $30.60 \pm 5.3$  and post-operative IOP was  $18.43 \pm 3.8$  with statistically significant P-value  $< 0.0001$ .

**Conclusion:** A significant difference found between efficacy of Ahmed glaucoma valve surgery and Trabeculectomy with Mitomycin-C in pediatric glaucoma after 4<sup>th</sup> week of surgery.

**Keywords:** Ahmed Glaucoma, Glaucoma, Mitomycin-C, Pediatric, Trabeculectomy, Valve.

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### INTRODUCTION:

Glaucoma is a progressive optic neuropathy resulting in optic nerve head damage with peripheral visual field defects,

in which raised intraocular pressure (IOP) is the one of major risk factor, which might result in complete blindness if untreated.<sup>1</sup> Therefore it is a common ocular disease with irreversible optic nerve damage that results in blindness.<sup>2</sup> Glaucoma accounts for 3.9% causes of blindness in Pakistan.<sup>3</sup> Glaucoma is treated with anti-glaucoma medications, laser and surgery. The treatment for pediatric glaucoma is mostly surgical.<sup>4</sup> The surgical procedures (Goniotomy, Trabeculotomy and Trabeculectomy with Mitomycin-C) are associated with good early success rates, but 20% of these patients require additional surgery to control IOP such as Ahmed glaucoma valve (AGV) surgery.<sup>5,6</sup> AGV is a tube shunt device with unidirectional flow restrictive mechanism to decrease intraocular pressure.<sup>7</sup> It is implanted sub-conjunctively over the globe with a tube inserted into the anterior chamber. Trabeculectomy with Mitomycin-C is another surgical treatment in which a shunt is produced in between anterior chamber of eye ball and sub-conjunctiva. But surgical failure has been observed over time with raised intraocular pressure.<sup>8</sup> Mitomycin is used as anti-fibrinolytic agent to decrease the rate of surgical failure.<sup>9,10</sup> The efficacy of both procedures in terms of control of intraocular pressure. It is labeled positive if it is in range of 8 to 21mm Hg measured on Perkins/ Goldmann applanation tonometer

**Manzoor Ahmed Khan**  
Senior Registrar,  
Bolan Medical and Health Sciences /  
Helper Eye hospital, Quetta  
Email: [khanmanzoorahmed@gmail.com](mailto:khanmanzoorahmed@gmail.com)

**Sadia Bukhari**  
Professor, Department of Ophthalmology  
ISRA Post Graduate institute of Ophthalmology /  
Al-Ibrahim Eye Hospital Karachi

**Zafar Ahmed Khan**  
Assistant Professor,  
Bolan Medical and Health Sciences, Quetta

**Mahtab Mengal**  
Senior Registrar,  
Bolan Medical and Health Sciences, Quetta

**Muhammad Afzal Khan**  
Assistant Professor,  
Bolan Medical and Health Sciences, Quetta

**Aimal Khan Panezai**  
Assistant Professor,  
Bolan Medical and Health Sciences, Quetta

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after 6 months of surgery.<sup>11</sup>The present study is aimed to compare the efficacy between Ahmed glaucoma valve surgery and Trabeculectomy with Mitomycin-C in pediatric glaucoma.

**METHODOLOGY:**

This was a quasi-experimental study conducted at Pediatric Ophthalmology OPD, ISRA Post graduate Institute of Ophthalmology/ Al-Ibrahim Eye Hospital, Karachi. Duration of study was February to August 2016. Study was conducted after ethical permission taken from the institute numbered A00061. A sample size of 110 patients (55 in each group) was calculated using estimated sample size for two-sample comparison of percentages. Keeping power of the test 80% with frequency of prevalence P1=75% and P2=50%<sup>11</sup> with margin of error 5%. Non-probability convenience sampling method was used to recruit patients in two groups. Group A was assessed with Trabeculectomy with Mytomycin-C and Group B with Ahmed Glaucoma Valve Surgery. Inclusion criteria were children (above 2 years and less than 15 years of age) visiting pediatric ophthalmology OPD irrespective of gender and glaucoma diagnosed with duration of symptoms > 4 weeks. Exclusion criteria were patients with repeated surgery for glaucoma, combined ocular surgery i.e penetrating keratoplasty or cataract, Preoperative keratitis, uveitis or conjunctivitis as determined by slit-lamp examination. History of patient was taken from parents or from patients with informed consent. Complains were gradual decrease in vision and slit lamp examination was performed to see retina clearly. After fundus examination for increase cup disc ratio, IOP measurement with Perkins/ Goldmann Applanation Tonometer was done to diagnose primary open angle glaucoma. Selection of patients were divided in two groups one by one in each group. In group A patients underwent trabeculectomy with mitomycin-C by experienced surgeon having more than 5 years of post-fellowship experience. Group B (Ahmed glaucoma valve surgery) was also treated by the same surgeon. The eyes were pad under aseptic measures in both groups. Next day dressing was done under aseptic measures and IOP was recorded by fourth year resident with applanation tonometer. Final outcome was measured at 4 week postoperatively. If IOP was less than or equal to 21 mmHg, it was taken as positive efficacy. Statistical analysis was done through SPSS version 23.0. For continuous variables mean + SD was calculated. Categorical variables were presented as frequencies and percentages. Chi square test was applied for two categorical variables like efficacy of IOP and gender. Paired sample t-test was applied to compare the pre and post IOP examination findings. P-value = 0.05 was considered as statistically significant.

**RESULTS:**

A total of 110 patients were recruited in this study in which 97 patients were analyzed. Missing follow-ups were 6

patients in “Group A” and 7 patients in “Group B”. In “Group A” 49 patients out of 55 and in “Group B” 48 patients completed their follow-up. Mean age of Group A was 6.73±2.7 and mean age of Group B was 7.05±2.3. “Group A” had 29 (59.2%) males and 20 (40.8%) females whereas “Group B” had 28 (58.3%) male and 20 (41.7%) female. (Figure 1)

Mean pre-operative IOP in “Group A” was found to be 31.59±5.4 and post-operative IOP at 4<sup>th</sup> week was reduced to 17.95±4.8 with statistically significant P-value <0.0001. In “Group B” mean pre-operative IOP was 30.60±5.3 and post-operative IOP at 4<sup>th</sup> week was 18.43±3.8 with statistically significant P-value <0.0001. (Table 1)

Efficacy was found positive in 41 (71.9%) males and 32 (80%) females with non-significance P-value 0.365. Age group of = 8 years had positive efficacy in 57 (76%) and < 8 years had 16 (72.7%) patients with non-significant P-value 0.754. More efficacy was found in Group B with 40 (83.3%) patients whereas Group A had 33(67.3%) patients with positive efficacy with significant P-value of 0.038. Table 2

Figure 1: Gender distribution Group wise (n=97)

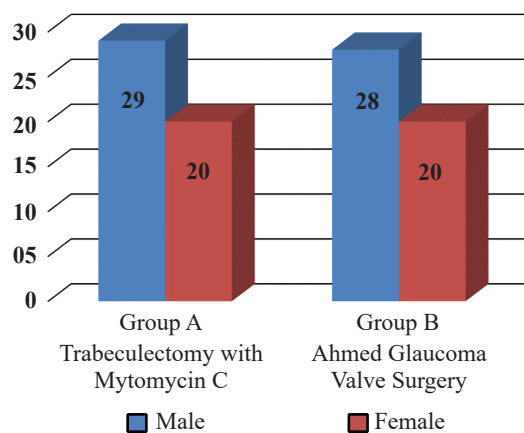


Table1: Comparison of Mean Intra ocular Pressure (IOP) Pre & Post-operatively in both groups

"Group A" Trabeculectomy with Mytomycin C	Mean±Standard Deviation	P-value
Pre-operative IOP	31.59±5.4	0.000*
Post-operative IOP	17.95±4.8	
"Group B" Ahmed Glaucoma Valve Surgery		
Pre-operative IOP	30.60±5.3	0.000*
Post-operative IOP	18.43±3.8	

\*P-value = 0.05 considered to be statistically significant via Paired Sample T-Test



Table 2: Efficacy according to Age, Gender &amp; Group

Parameters	Efficacy		Total (n=97)	P-value
	Positive (n=73)	Negative (n=24)		
<b>Gender</b>				
Male	41	16	57	0.365
	71.9%	28.1%	100.0%	
Female	32	8	40	
	80.0%	20.0%	100.0%	
<b>Age (years)</b>				
< 8 years	57	18	75	0.754
	76.0%	24.0%	100.0%	
> 8 years	16	6	22	
	72.7%	27.3%	100.0%	
<b>Group</b>				
"Group A" Trabeculectomy with Mytomycin C	33	16	49	0.038*
	67.3%	32.7%	100.0%	
"Group B" Ahmed Glaucoma Valve Surgery	40	8	48	
	83.3%	16.7%	100.0%	

\*P-value = 0.05 considered to be statistically significant via Chi-square Test

\*Positive Efficacy was measured as Intra ocular Pressure (IOP) = 21mmHg

## DISCUSSION:

Many studies had been done to compare the efficacy of Ahmed glaucoma valve surgery and Trabeculectomy with Mitomycin-C and the success rate for glaucoma drainage devices which are reported in different studies vary from 31% to 97%.<sup>12-14</sup> In present study the overall success rate in Trabeculectomy with Mitomycin-C "Group A" was 67.3% while it was 83.3% with Ahmed glaucoma valve implant surgery "Group B". A study done by HaiBo T et al compared the efficacy of Ahmed glaucoma valve and Trabeculectomy with Mitomycin-C in pediatric glaucoma.<sup>15</sup> They showed Trabeculectomy having a success rate of 50% while patients undergoing Ahmed glaucoma drainage implants had the overall success of approximately 75%<sup>16</sup> as compared to present study which showed greater efficacy for Ahmed glaucoma valve implants than Trabeculectomy with Mitomycin-c. Riva I et al reported an overall success of 73.3% in patients who underwent Trabeculectomy with Mitomycin-c and 86.7% in patients who underwent Ahmed glaucoma valve surgery<sup>17</sup>. Unfortunately this study was done on only aphakic patients. Similarly O Malley<sup>18</sup> et al showed a success rate of 72% in patients with refractory primary congenital glaucoma with glaucoma drainage device surgery<sup>18</sup>. Author used Baerveldt implant rather than Ahmed glaucoma valve.<sup>19</sup>

Fulcher et al<sup>20</sup> retrospectively reviewed 20 eyes with PCG that had undergone trabeculectomy without MMC with 5–14 years of follow up and reported an overall success of 92.3%

after 1 single trabeculectomy and 100% success with two trabeculectomies at the last follow-up visit. The authors reported no serious complications in any patients.

Theoretically the Ahmed glaucoma valve implant had significant benefit of controlling post-operative IOP and reducing the risk of hypotony due to restricted valve like mechanism compared to Trabeculectomy.<sup>21, 22</sup>

In summary different studies shows different results. This difference in success rate with our study may be due to the different age at presentation, race and gender, types of glaucoma, different surgical techniques or different surgical devices and length of follow ups. In general practice, Trabeculectomy is still preferred as the initial incisional glaucoma procedure in our country due to the affordability by patients. Glaucoma drainage implants (like AGV) are usually used in eyes at high risk for filtration failure.

## CONCLUSION:

A significant difference found between efficacy of Ahmed glaucoma valve surgery and Trabeculectomy with Mitomycin-C in pediatric glaucoma after 4<sup>th</sup> week of surgery. For patients with appropriate follow up and affordability Ahmed glaucoma valve implantation can be an effective and safe procedure for the treatment of pediatric glaucoma.

### Authors Contribution:

**Manzoor Ahmed Khan:** Conceived the study, Manuscript writing, Data collection, correspondence in replying reviews of manuscript & final review.

**Sadia Bukhari:** Supervision of work & Final Review.

**Zafar Ahmed Khan:** Methodology, Proforma development, Data collection & Final review.

**Mahtab Mengal:** Designing the study, Proforma development, Data collection & Final review.

**Muhammad Afzal Khan:** Statistical analysis and interpretation of data & Final review.

**Aimal Khan Panezai:** Proforma development, Designing the manuscript & Final review.

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## Correlation of Maternal Hemoglobin with Birth Weight: A Hospital Based Study

Hamzullah Khan, Khalid Khan, Neelum Shehzadi, Huma Riaz

### ABSTRACT:

**Objectives:** To determine the correlation of maternal Hemoglobin concentration in labor with birth weight.

**Study design and setting:** This was cross sectional study conducted in Qazi Hussain Ahmed Medical Complex, (QHAMC) Medical Teaching Institution Nowshera, from 20<sup>th</sup> April 2019 to 31<sup>st</sup> Jan 2020.

**Methodology:** A total of 254 deliveries were assessed. All pregnant ladies in labor, presenting to labor room of QHAMC Nowshera, irrespective of age were included. The weight of babies was recorded at birth. Pearson correlation and logistic regression and relative risk analysis were used to show the relationship and probability of occurrence of low birth weight babies in anemic and non anemic patients.

**Results:** The mean with standard deviation of hemoglobin in mothers was 10.76+1.63 g/dl. The mean with standard deviation of birth weight was 2.71+0.6 kg. The frequency of low birth weight babies was 68(26.77%) with weight less than 2500g at birth. A positive linear correlation of birth weight with level of hemoglobin of mother in labor was statistically significant ( $p=0.001$ ,  $r=0.35$ ). Using logistic regression analysis, it was observed that the probability of LBW in pregnant women with hemoglobin<11g/dl was 3.31 times higher ( $p=0.001$ ,  $OR=3.31$ ).

**Conclusion:** The frequency of LBW is 26.7% markedly higher and maternal anemia is a risk factor for it. The relative risk is 2.4 times higher in anemic pregnant ladies as compared to the non anemic mother.

**Key words:** Low birth weight, Iron deficiency anemia, Risk analysis

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### INTRODUCTION:

The causes of low birth weight are multifactorial and many factor including; maternal, genetic and fetal can contribute and play vital role in this regard. These factors interplay with each other and contribute individually as well as in combination.<sup>1</sup> A meta-analysis from different cohort and case control studies carried out in several countries of the world concluded that there is a statistically strong relationship of the maternal anemia with low birth weight.<sup>2</sup> In general practice maternal anemia is defined as maternal hemoglobin less than 11g/dl during the gestational period.<sup>1,3,4</sup> Regarding

the prevalence and definition of the low birth weight deliveries, a textbook William obstetrics reports 7 to 10% of the infants in the United States weigh less than 2500grams irrespective of gestational age/anemia<sup>4</sup>. The prevalence of low birth weight in Pakistan is reported as 10.04%.<sup>5</sup>

In general, the biochemical parameters of maternal nutrition have minimal effects on the birth weight of offspring. However mean birth weight of the non anemic and anemic groups have statistically significant difference.<sup>1,4</sup> Bhargava V et al reported that the desired weight of the babies is achieved in the body of the mother, that has a strong correlation with the maternal Hb%.<sup>6</sup>

The anemia of different gestational period has been reported to have an impact on the outcome, some have reported even the maternal anemia of the first trimester of pregnancy has a relationship to the deliveries of low birth weight babies, and the risk increases with the progression of anemia in next trimesters.<sup>7</sup> A study from Turkey reported that low Hb% of mother during the third trimester of pregnancy were strongly associated with low birth weight babies. They further reported that maternal anemia can be a direct cause of the deterioration of in-utero fetal growth due to lack of oxygen supply from the placenta to the fetal tissues. They extended their study and further reported that treatment of anemia during pregnancy is directly correlated with better outcomes in

#### Hamzullah Khan

Professor, Department of Hematology,  
Nowshera Medical College, Nowshera Pakistan  
Email: hamzakmc@gmail.com

#### Khalid Khan

Assistant Professor, Department of Pediatrics,  
Nowshera Medical College, Nowshera Pakistan

#### Neelum Shehzadi

Associate Professor, Department of Gynecology & Obstetrics,  
Nowshera Medical College, Nowshera Pakistan

#### Huma Riaz

Assistant Professor, Department of Hematology,  
Hayatabad Medical Complex, Peshawar.

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terms of birth weight.<sup>8</sup> A cross sectional study from India reported 4.86 time higher risk of preterm and low birth weight babies in pregnant women with severe anemia, followed by a risk of 3.18 time in pregnant ladies with moderate anemia.<sup>9</sup>

The prevalence of anemia in pregnant ladies in Pakistan reported as 29%.<sup>10</sup> Considering the high prevalence of anemia present study was aimed to determine the correlation of maternal hemoglobin concentration with birth weight of the newborn in a tertiary care hospital of Nowshera.

#### METHODOLOGY:

A cross sectional study was conducted in the Pathology department in collaboration with the Department of Gynecology and Obstetrics, Qazi Hussain Ahmed Medical Complex, Medical Teaching Institution Nowshera, from 20<sup>th</sup> April 2019 to 31<sup>st</sup> Jan 2020. Ethical approval for the survey was obtained from the Ethical Review Committee of Nowshera Medical College/QHAMC. ERC letter with reference number No-102, Dated 19 June 2019 was issued. Total number patients studied were 254. The calculated sample size was 139 on the basis of 10.04% prevalence of low birth weight in Pakistan.<sup>5</sup> The inclusion criteria was all expecting women in labor, presenting to the labor room of QHAMC Nowshera, irrespective of age. While the expecting women taking oral or intravenous iron therapy for their already diagnosed Iron deficiency anemia were excluded. Blood samples were collected from these women. The technique for the blood sampling collection was to collect 3 ml of venous blood using disposable syringes under aseptic techniques. The blood was added in an EDTA vacutainer and mixed gently. Complete blood count was calculated on hematology analyzer. Anemia was labeled when the pregnant women had a hemoglobin level of < 11 g/dl in accordance with the definition of World Health Organization<sup>11</sup>. This study was conducted in collaboration of gynecology department and pediatric/nursery department. The weight of the baby (in kg) after deliver was noted using manual weight machine and recorded in the patient file. The low birth weight was taken as weight less than 2.5 kgs as defined by the World Health Organization (WHO).<sup>12</sup>

Data was entered in SPSS Version 25. Descriptive statistics were used for numerical variables like Hb and ferritin of mother and weight of babies. The independent t-test was used for hemoglobin and ferritin levels in gender groups. Nominal variable were the mode of delivery and gestational age were presented with frequency and percentages using pi-charts. The Pearson Correlation test was used to determine the correlation of hemoglobin concentration of mother with weight of babies. Regression analysis was used to determine the probability of low birth weight in anemic and non anemic groups. Relative risk (RR) was calculated for stratification of anemic and non anemic groups based on the concentration of hemoglobin in group with deliveries of low birth weight babies using risk analysis statistics.

#### RESULTS:

Total of 254 cases were studied. The mean with standard deviation of hemoglobin in mothers was 10.76+1.63 g/dl. The minimum Hb% recorded was 6.2g/dl to a maximum of 18g/dl with a range of 11.8. The mean with standard deviation of birth weight was 2.71+0.6 kg. The minimum birth weight recorded was 1.5kg to a maximum of 4.6kg with a range of 2.1kg. (Table 1). It was observed that 68(26.77%) of the new born had weight less than 2500g, while 186(73.22%) had equal or more than 2500g weight. Out of total 254 cases 229(90.2%) were in full term with gestation period of more than 37weeks. 19(7.5%) were preterm with gestational history of less than 37 weeks, while 6 (2.4%) were post-term. Figure1. Similarly, 234(92.1%) cases delivered through Normal vaginal delivery (NVD), 14(5.5%) through Cesarean -section) and 6(2.4%) through forcep assisted deliveries (Figure 1)

The correlation of mother's hemoglobin with baby weight was assessed using Pearson correlation test and found a moderate uphill positive linear relation of birth weight with level of hemoglobin of mother at labour that was statistically significant ( $p= 0.001$ ,  $r=0.35$ ). (Table 2)

Using logistic regression analysis to show the probability of occurrence of LBW in relation with hemoglobin concentration dividing the patients in 2 categories. One groups with Hb% less than 11g/dl and another with more than 11 g/dl. It was observed that the probability of LBW in pregnant ladies with hemoglobin<11 was 3.31 times more than cases with Hb>11g/dl. (p-value 0.001, OR=3.31). (Table 3) The risk analysis for low birth weight deliveries in anemic and non anemic categories taking Hb% concentration in consideration were assessed. It was noted that the risk of low birth weight for cohort (category with Hb <11g/dl) was 2.4 times as compared to 0.56 times in cohort (category with Hb>11g/dl). The Odds ratio was 4.2 when measured with anemic mothers only. (Table 4)

#### DISCUSSION:

Intrauterine growth and development is most vulnerable process that affects and has a profound and lasting influence on the physical, mental and developmental growth after birth and in later life that largely depends on the maternal health and well being. we observed that the mean of hemoglobin in pregnant ladies in labor was 10.76+1.63 g/dl, that falls in anemic group as per definition of the WHO.<sup>11</sup> Likewise 68(26.77%) of the new born had weight less than 2500g. Many studies from Pakistan have reported low birth weight to have an established association with a group of maternal factors like weight and height of mother, social-economic status and maternal anemia.<sup>13,14</sup> Our findings are higher than Khan A<sup>15</sup> reported from Karachi as 10.6% of LBW deliveries and Najmi RS<sup>16</sup> reported the prevalence of total LBW deliveries from Lahore as 19%. UNDP reports the incidence of LBW deliveries as reported globally varies

Table 1. Descriptive Statistics of Hemoglobin and birth weight

	Hb of Mother	Babies weight at birth
Number of patients	254	254
Mean	10.76	2.71
Median	11	3
Mode	11	3
Std. Deviation	1.63	0.6
Range	11.8	3.1
Minimum	6.2	1.5
Maximum	18	4.6

a. Multiple modes exist. The smallest value is shown

Figure 1. Gestational history and Mode of Delivery

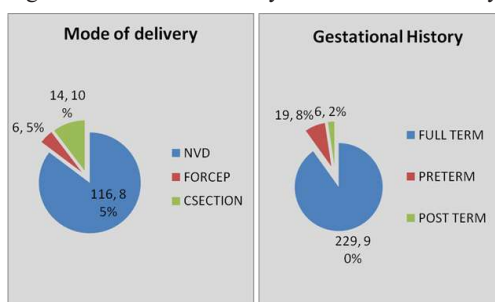


Table 2. Pearson Correlation of hemoglobin of mother with baby weight

		Birth weight
Hb%	Pearson Correlation	.347**
	Sig. (2-tailed)	0.001

\*\* . Correlation is significant at the 0.01 level (2-tailed)  
 \* . Correlation is significant at the 0.05 level (2-tailed)

Table 3. Regression analysis of the birth weight with anemia of mother

Observed		Predicted				
		Hb Categories				
		Hb<11	Hb>11			
Birthweight	<2.5kg	49	44			
	>2.5kg	24	137			
Variables In Equation						
	B	S.E.	Wald	df	Sig.	Exp(B)
Birthwt	1.197	0.244	24.055	1	0	3.311
Constant	-2.637	0.653	16.296	1	0	0.072

with 19% in developed countries, 31% from South Asia, followed by Africa & north America 15%.<sup>17</sup>

UNICEF reports that across the globe neonatal mortality increases by 20 times in newborn with low birth weight as compared to normal or heavier babies more than 2.5kg.<sup>13</sup> In Pakistan the prevalence of LBW births varies from 5 to 23% in different parts.<sup>18</sup>

Table 4. Risk Estimate of low birth babies in anemic and non anemic groups

	Value	95% Confidence Interval	
		Lower	Upper
Odds Ratio for Weight categories (1.00 / 2.00)	<b>4.288</b>	2.488	7.390
For cohort Hb% category-1 = Hb<11g/dl	<b>2.409</b>	1.733	3.350
For cohort Hb% category-2 = Hb>11g/dl	<b>.562</b>	.440	.718

The correlation of mother’s hemoglobin using Pearson correlation test was assessed and found a moderate uphill positive linear relation of birth weight with level of hemoglobin of mother at labor (P-value 0.001, r=0.35). Lumbanraja SN et al<sup>19</sup> observed that LBW was the only indicator out of multiple variables that statistically significantly correlated with Maternal anemia (p<0.05) that matches our findings. Our findings also matched with a study from Rawalpindi that reported that a total of 64% LBW deliveries with a statistical correlation with anemia in the third trimester of gestation (p=0.001).<sup>19</sup>

The same way, the probability of LBW in mother with hemoglobin<11 at labor, was 3.31 times more than mothers with Hb>11g/dl. Lone et al reported from a multivariate analysis that the risk of LBW babies in anemic population is 1.9 times higher than non anemic population(95% CI= 1.0–3.4) that was in concordance with our findings.<sup>20</sup>

An article published in the Bulletin of world health organization revealed an increased in incidence of LBW babies in anemic mothers, however the difference in anemic and non anemic mother in term of LBW deliveries was not statistically significant (p=0.112). Failure to control a decline in Hb below 10g/dl was also associated with preterm deliveries and was considered as high risk for LBW outcome.<sup>21</sup>

The risk of low birth weight for the cohort category with Hb <11g/dl) was 2.4 times. Another local study from Punjab reported a higher risk of LBW in pregnant ladies with low hemoglobin in their last trimester.<sup>22</sup> Another metaanalysis where 7243 articles were found in Medline, out of which 68 were selected for the study, revealed an increase in risk of LBW of 1.43 times associated with maternal anemia.<sup>23</sup>

There are few study limitations. Firstly, we were unable to check the serum ferritin levels of all the pregnant women in labor, therefore future studies should focus on the correlation of serum ferritin with the fetal weight at birth. Similarly, second limitation is that we were unable to separately explain the low birth weight and pre-term babies in both anemic and non anemic, so therefore the future

research studies should focus on these two different groups (Pre-term and LBW) and identify its correlation with maternal Hb and ferritin that can help the decision maker to decide best in the interest of mother and child.

### CONCLUSION:

The frequency of LBW is 26.7% markedly higher and maternal anemia is a risk factor for it. The relative risk is 2.4 times higher in anemic pregnant ladies as compared to the non anemic mother.

#### Authors Contribution:

**Hamzullah khan:** Concept design, data collection, data analysis, manuscript writing

**Khalid Khan:** Data Collection, manuscript writing, critical review

**Neelum Shehzadi:** Data collection, manuscript writing, critical review

**Huma Riaz:** Manuscript writing, critical review

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## Effect of Ginger-Naproxen on Knee Osteoarthritis: A Clinical Study

Mehtab Munir, Khalid Mustafa Memon, Sajid Abbas Jaffri, Hasan Ali

**Objective:** To evaluate clinical efficacy and safety of ginger with naproxen, in treating knee osteoarthritis.

**Study design and setting:** Randomized clinical trial conducted in medicine department OPD of National Medical Center, Karachi from 21<sup>st</sup> September 2018 till 31<sup>st</sup> March 2019.

**Methodology:** This study was conducted on 60 patients of knee osteoarthritis. After written informed consent, the patients were randomized to two groups. Group A received tablet naproxen 500mg and capsule ginger 550mg, twice daily and group B was given tablet naproxen 500mg twice daily. Total 53 patients finished the study (group A: n=27 and group B: n=26). Baseline pain (Visual Analogue Scale) and Western Ontario and McMaster Universities Osteoarthritis index (WOMAC) scores were noted at the beginning of study and reassessed after 6 weeks of the intervention. Safety profile of the drugs was assessed by observing adverse effects. Independent t-test was applied to check difference between the two groups. Statistical analysis was performed using SPSS version 23.0. P-value < 0.05 was considered as statistically significant.

**Results:** Before the intervention no significant difference was observed in two groups. However significant difference was observed between the groups in pain (p=0.019) and WOMAC (p=0.020) scores after 6 weeks of intervention. Moreover there was no significant difference (p=0.914) in occurrence of adverse effects between the two groups at the end of 6 weeks of study.

**Conclusion:** Ginger with naproxen can effectively treat pain and stiffness in knee osteoarthritis without added adverse effects when compared with naproxen alone.

**Key words:** Ginger, Knee osteoarthritis, Naproxen, Pain, Stiffness, WOMAC score.

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### INTRODUCTION:

Osteoarthritis (OA) is an inflammatory and degenerative disease of joints. Most frequently, hand and weight bearing joints are affected. It is marked by the breakdown of the cartilage; this causes bones to rub against each other, causing pain and loss of movement.<sup>1</sup> Globally 9.61% of men and 18.0% of women, greater than 60 years of age have symptomatic osteoarthritis as claimed by WHO.<sup>2</sup> Prevalence of OA in Northern area of Pakistan was established to be 37 / 1000 and there was preponderance of knee joint involvement that is 95%. India revealed the prevalence to

be 5.8% and typically community above 65 years of age was affected.<sup>3</sup> Among all the joints, knee joint is affected most of all from osteoarthritis. Worldwide 3.8% of people suffered from knee osteoarthritis in contrast to 0.85% prevalence of hip osteoarthritis. 2.2 % of males and 3.8% of females were found to have knee OA in South East Asia.<sup>4</sup>

Progressive and chronic degeneration of articular cartilage and abnormal joint remodeling are hallmark of osteoarthritis, leading to pain and limitation of movement. In synovial joints, whole joint is involved including cartilage, sub-chondral bone, synovial membrane, ligaments and peri-articular musculature.<sup>5</sup>

People suffering from osteoarthritis mostly gain medical consideration for the reason of joint pain that is classically localized around knee and distal femur. With progression in joint degeneration, a steady decline in functional activities and trouble in performing simple daily jobs such as walking, climbing stairs and housekeeping is observed by the patient. Muscle wasting and adhesive capsulitis may occur in knee joint.<sup>6</sup>

Classic radiographic findings are joint space narrowing, sub-chondral bone sclerosis, osteophytes and cyst formation. OA can be divided into five grades (0-4) on plain radiograph according to Kallgren Lawrence grading system.<sup>7</sup>

#### Mehtab Munir

Senior Lecturer, Department of Pharmacology,  
Bahria University Medical and Dental College, Karachi  
Email: [drmehtabmunir@hotmail.com](mailto:drmehtabmunir@hotmail.com)

#### Khalid Mustafa Memon

Professor, Department of Pharmacology,  
Bahria University Medical and Dental College, Karachi

#### Sajid Abbas Jaffri

Professor and Head, Department of Medicine,  
Bahria University Medical and Dental College, Karachi

#### Hasan Ali

Professor and Head, Department of Biochemistry,  
Bahria University Medical and Dental College, Karachi

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American College of Rheumatology (ACR) has given comprehensive guidelines for knee OA diagnosis. Clinical plus radiographic criteria requires knee pain with 1 of these three findings age > 50 years, morning stiffness < 30 minutes and crepitus + presence of osteophytes.<sup>8</sup>

Knee osteoarthritis treatment is categorized into; non-pharmacological, pharmacological and surgical intervention.<sup>9</sup> Non-steroidal anti-inflammatory drugs (NSAIDs) are corner stone for the pharmacological treatment of osteoarthritis. Naproxen sodium is commonly employed for treatment of knee osteoarthritis. It is an established non-selective NSAIDs and is a prescription drug.<sup>10</sup> Naproxen non-selectively inhibits both iso-forms of cyclo-oxygenase enzyme. Hence it prevents inflammation in osteoarthritis through inhibition of COX-2 enzyme. But it has been found that COX-1 (also known as prostaglandin endoperoxide synthase-1) enzyme is over expressed by synovial cells in OA patients. Naproxen shows more selectivity for COX-1 iso-form.<sup>11</sup>

Although diverse pharmacological modalities are available for management of OA but none of these offer treatment other than symptomatic relief and are associated with many adverse effects. Hence for chronic disease like OA, increasing trend for using alternate medicines has been observed.<sup>12</sup> Moreover herbal medications are mostly of low cost, widely available and more tolerable. Many patients around the world prefer to use herbal medicine; thereby; it is important to evaluate the efficacy and safety of these herbs.<sup>13</sup>

Scientific name of ginger is *Zingeriber officinal* and rhizome is the part of plant that is commonly used. Ginger is a commonly used spice all over the world with origin from southern China or south-east Asia.<sup>14</sup> Characteristic pungent flavor of ginger is because of non-volatile molecules like gingerols, shagoals, paradols, and zingerone. The active ingredients in ginger include gingerol and shagoal have anti-inflammatory, anti-oxidant and some other pharmacological activities. Mechanism of action is through inhibition of cyclo-oxygenase enzyme, lipo-oxygenase pathway, interleukin-1 $\beta$  (IL-1 $\beta$ ), IL-6 and tumor necrosis factor- $\alpha$  (TNF- $\alpha$ ). Activation of NF  $\kappa$ B and inhibition of inflammatory cell infiltration may also be involved. Ginger has shown to have chondro-protective role in osteoarthritis in animal model. This role is due to its anti-inflammatory and anti-oxidant activity.<sup>15</sup>

Ginger has analgesic and anti-inflammatory role, moreover it is readily available and commonly used in culinary in Southeast Asia. Hence its acceptance as treatment of osteoarthritis is anticipated to be effortless. Therefore, this study was aimed to evaluate clinical efficacy and safety of ginger with naproxen in comparison with naproxen alone for management of knee osteoarthritis.

#### **METHODOLOGY:**

It was a randomized clinical trial that was conducted in medical OPD of National Medical Center in Karachi from

21<sup>st</sup> September 2018 till 31<sup>st</sup> March 2019. The study was approved from ERC of Bahria University Medical and Dental College numbered 49/2018. Sample size was estimated using the method of sample size “Comparing Two Means” on Openepi. Minimum sample sizes in each group was calculated to be n1= 23, n2=23, hence 46 in total. However 60 patients were registered in this study with 30 patients in each group after informed written consent.

Inclusion criteria were; males and females > 50 years of age suffering from knee osteoarthritis requiring regular medical treatment. Clinical and X-ray findings of the patients were as stated by the American College of Rheumatology criteria for knee osteoarthritis<sup>8</sup> and radiographic evidence of knee OA in concordance with Kallgren-Lawrence grade of 1 to 3.<sup>7</sup> Patients having known history of hypersensitivity to the study drugs, Kallgren-Lawrence grade of 0 or 4, concurrent other inflammatory or traumatic joint disease, recent or concurrent major illness of hepatic, renal, cardiovascular, gastrointestinal, hematopoietic or endocrine systems, terminal illness or cancer, overweight defined as a BMI >30, pregnancy or lactation (women) and intra-articular or systemic corticosteroid therapy in 3 months preceding enrolment for the study were excluded from the study.

Patients fulfilling the inclusion criteria were given wash out period of 72 hours for any medication before start of the study. By using simple systematic randomization, these 60 patients were divided into two groups: Group A (n=30) received tablet Naproxen 500 mg + capsule Ginger 550 mg orally twice daily for 6 weeks. Group B (n=30) patients were prescribed tablet Naproxen 500mg orally twice daily for 6 weeks. A pre-designed evaluation form was used to record demographic profile and study parameters of the patients. The clinical efficacy of the drugs was evaluated by composite Western Ontario and McMaster Universities Osteoarthritis (WOMAC) index and Visual Analogue Scale (VAS) at the beginning and end of the study.<sup>7,8</sup> WOMAC index evaluates pain and stiffness in knee OA. VAS was used to assess pain at movement. Safety profile of the drugs was assessed by noting the adverse effects like heart burn, epigastric pain, diarrhea, flatulence, abdominal distension, rash, allergic reactions and fluid retention during the study. Statistical analysis was done using SPSS version 23.0. Normality of the data was assessed by plotting histogram. Independent t-test was applied to check difference between the two groups. P-value < 0.05 was considered as statistically significant.

#### **RESULTS:**

Initially 60 patients were registered for the study with 30 patients in each of the two groups. However 03 patients dropped out in group A and 04 patients in group B failed to follow-up. Hence 53 patients finished the study (group A: n=27 and group B: n=26).

No significant difference was found for demographic



Table 1: Demographic data of patients in group A and group B

Demographic Variable	Group A (n=27) Mean ± Standard deviation	Group B (n=26) Mean ± Standard deviation	P-value $\Phi$
Age	57.07±4.44	57.03±4.84	0.97
BMI	28.07±1.53	27.71±1.39	0.33
Gender			0.77
Females	21(70%)	22(73.3%)	
Males	9(30%)	8(26.7%)	
Involved Knee joint			0.78
Right knee	20(66.7%)	21(70%)	
Left knee	10(33.3%)	9(30%)	

$\Phi$ independent t-test

Group A treated with Naproxen + ginger Group B treated with Naproxen

Table 2-A Comparison of the pain scores (VAS) between group A (Naproxen + ginger) and group B (Naproxen) before and after intervention

Intervention	Mean ± Standard deviation of group A	Mean ± Standard deviation of group B	P-value $\Phi$
Before	5.43 ± 0.69	5.27 ± 0.78	0.383
After	2.48 ± 0.64	2.92 ± 0.68	0.019

$\Phi$ independent t-test VAS = visual analogue scale

Table II-B Comparison of WOMAC scores between group A (Naproxen + ginger) and group B (Naproxen) before and after intervention

Intervention	Mean ± Standard deviation of group A	Mean ± Standard deviation of group B	P-value $\Phi$
Before	36.70 ± 7.17	36.83 ± 10.04	0.953
After	17.17 ± 4.18	20.12 ± 4.65	0.020

$\Phi$ independent t-test

WOMAC score= Western Ontario and McMaster Universities Osteoarthritis index

Table 3 Adverse effects of Patients in group A and group B after 6 weeks of intervention

Adverse effects	Group A (n=27) (Percentage %)	Group B (n=26) (Percentage %)
Heart burn	3 (11.11%)	8 (30.76%)
Epigastric pain	0 (0%)	1 (3.84%)
Diarrhea	6 (22.22%)	1 (3.84%)
Rash	0 (0%)	0 (0%)
Allergic reaction	0 (0%)	0 (0%)

Group A treated with Naproxen + ginger  
Group B treated with Naproxen

variables such as age, gender, BMI and affected knee in two groups. (Table 1) Before intervention, difference between pain and WOMAC scores of the two groups was not significant (p-value >0.05). Means of pain scores were 5.43 ± 0.69 in group A and 5.27 ± 0.78 for group B before intervention. After 6 weeks of intervention means of pain scores decreased in both groups but more in group A (2.48

± 0.64) than group B (2.92 ± 0.68) (p-value = 0.019) (Table 2a). Means of WOMAC score were group A; 36.70 ± 7.17 and group B 36.83 ± 10.04 before intervention. After intervention the scores were also observed to be decreased in group A (17.17 ± 4.18) and group B (20.12 ± 4.65) but statistically significant (p-value = 0.020) decrease in group A. (Table 2b)

Regarding adverse reactions, it was noted that heart burn was more common in group B (8 /26) and diarrhea (6 /27) was observed more in group A. However no significant difference was found in occurrence of adverse effects between the two groups that is p-value = 0.914. Rash, allergic reactions, abdominal distension or fluid retention were not reported by any of the participants. Eight patient in group B suffered from heart burn and only one had severe epigastric pain at 5<sup>th</sup> week of the study. (Table 3) The patient was advised to stop the regimen at once and was managed accordingly.

**DISCUSSION:**

This study was conducted on 53 patients suffering from primary knee osteoarthritis with age equal and more than 50 years. Percentage of female patients (71.66%) was more than males (28.33%). This is similar to an Indian study in which females above 50 years (31.6%) were found to be suffering from primary knee OA more than males with comparable age (28.1%).<sup>16</sup> A study conducted in Sri Lanka also demonstrated that knee OA was more prevalent in females above 50 years of age (20.1%).<sup>17</sup> In this study most of the patients were overweight (mean BMI > 25). The similar results were found in the Indian study where primary knee OA was more common in overweight/ obese as compared to normal or underweight people.<sup>16</sup>

The present study patients of knee osteoarthritis were randomized to group A and group B. Baseline pain (VAS) and WOMAC scores were noted before intervention and showed no significant difference between the groups. After receiving 6 weeks of intervention both pain and WOMAC scores of the participants showed decline but it was more in group A (p-value >0.05). Gastrointestinal adverse effects were more in both groups but no significant difference was found between the groups. Notable adverse effect in group A was diarrhea but that was mild in nature (1-2 episodes of loose stools / day) and did not lead to quitting the study.

A similar study was conducted in Iran<sup>18</sup> on 90 patients of knee OA for 12 weeks to assess effect of ginger on pain and satisfaction of the patients. Randomization was done to divide the patients into ginger and control groups. The ginger group participants took osteoarthritis treatment prescribed by orthopedic specialist and ginger with the dose of 1000mg / day (2 tablets of 500mg). The control group only took treatment given by the orthopedic specialist. A decline in pain scores (VAS) was observed in both groups but more in the ginger group (p-value = 0.001). Adverse effects were found to be same in both groups and were more related to gastrointestinal tract similar to our study.<sup>18</sup>

Another study was conducted in India on 60 patients of knee OA. The patients were divided into 3 groups. Group I was given tablet diclofenac 50 mg and capsule placebo, group II received capsule ginger 750 mg and capsule placebo and group III was given capsule ginger 750 mg and tablet diclofenac 50 mg. The patients were assessed fortnightly till 12 weeks. Group III demonstrated marked improvement in WOMAC index and VAS as compared to other groups (p-value <0.001). Regarding adverse effects, no significant variation was seen among the groups that was in accordance with the present study.<sup>19</sup>

A meta-analysis was conducted by Osteoarthritis Research Society International (OARSI) conducted a meta-analysis in 2015.<sup>20</sup> Objective was to assess efficacy and safety of ginger in osteoarthritis. This meta-analysis included randomized placebo controlled trials with duration ranging

from 3 to 12 weeks. 47 to 66 years was mean age of participants with higher percentage of women. The daily dose of ginger ranged from 500mg to 1000mg. A statistically significant decline in pain (p-value=0.005) and disability (p-value=0.01) was caused by ginger. Moreover no serious events were noted with ginger. Hence ginger was concluded to be efficacious and safe for reducing pain and inflammation of OA.<sup>20</sup>

This anti-inflammatory and analgesic effect of ginger is because of decline in pro-inflammatory cytokine as demonstrated by a double-blinded randomized placebo-controlled clinical trial. The patients were given 500mg capsules of ginger twice daily (GG) or placebo (PG) containing starch. Serum of participants was collected before and after administration of ginger. A significant decline in serum nitrous oxide and hs-C protein was observed in GG group.<sup>21</sup> In this study, tumor necrosis factor- $\alpha$  (TNF- $\alpha$ ) and interleukin-1 $\beta$  (IL-1 $\beta$ ) were also compared before and after administration of ginger or placebo. These parameters were also found to be less in ginger group as compared to group receiving placebo after 3 months of period.<sup>22</sup> Inhibition of several other inflammatory markers by ginger e.g. leukotrienes and prostaglandins, have also been shown in other studies.<sup>23, 24</sup>

Limited evidence is available to observe the effect of ginger on knee osteoarthritis. Hence future multicenter and long term studies are recommended.

**CONCLUSION:**

Ginger is more effective in reducing pain and stiffness in management of knee osteoarthritis when given with naproxen as compared to naproxen alone.

**Authors Contribution:**

**Mehtab Munir:** Designing the study, data collection, data analysis, literature search and article write up

**Khalid Mustafa Memon:** Designing the study, article write up and proof reading

**Sajid Abbas Jaffri:** Data collection, article write up and proof reading

**Hasan Ali:** Literature search, article write up and proof reading

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## Factors Associated with Sodomy Cases at a Tertiary Care Hospital of Karachi

Abdul Waheed, Mir Ghulam Ali Talpur, Iqbal Ahmed Khan, Hari Ram, Shahid Nezam, Syed Pervaiz Alam

### ABSTRACT

**Objective:** To observe the number of sodomy cases and their associated factors reported to Abbasi Shaheed Hospital for medicolegal examination in Karachi.

**Study design and setting:** The retrospective study design conducted at medicolegal section of Abbasi Shaheed Hospital Karachi from January 2016 till December 2018 reported from 45 different police stations of Karachi.

**Methodology:** This was a single centred study on sodomy conducted by using non-probability sampling technique. Data was collected from medico legal section of Abbasi Shaheed Hospital, Karachi, from a period of January 2016 till December 2018 reported from 45 different police stations of Karachi.

**Results:** A total of 102 sodomy cases were reported in various police stations of Karachi during this period. Majority of cases were reported in the police stations belonging to Surjani town (11) followed by Sir Syed (9), Sohrab Goth (9), North Naziamabad (8) and Gulbahar (7). Majority of the convicts belonged to the age range 21-30 years followed by 10-20 years of age. Majority of the accused were found to be living alone without family for earning purpose. All of them were usually of poor socio economic conditions and illiterate. Majority of the couples were found to be related to each other. Presence of semen stains, sexual potency and DNA analysis further confirmed their involvement.

**Conclusion:** Majority of the accused were of young age, poor, living alone without family, illiterate and from laborer class. These might be the factors responsible for their involvement in alleged sexual behavior.

**Keywords:** Anal Intercourse, Homosexual, Medico-legal Section, Police Stations,

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### INTRODUCTION:

Anal sex is defined as inserting the penis into somebody's anus, or rectum for the purpose of sexual pleasure.<sup>1</sup> Additional practices encompassing anal sex can be comprised

of fingering the anus, using sex toys for anal insertion, oral sex executed on the anus, and pegging.<sup>2</sup> Although<sup>3,4</sup> anal intercourse generally means penile-anal penetration, whereas anal sex depicts any sort of anal sexual activity performed between couples.<sup>2-4</sup>

Although anal sex is generally allied with male homosexuality, various researches indicate that it can also be associated with heterosexual relationships.<sup>5</sup> People may feel sexual satisfaction from anal sex mainly by stimulating anal nerve endings, and orgasm may be accomplished through anal penetration of the prostate in males, indirect stimulation of the clitoris or vagina in females, and other sensory nerves (specifically the pudendal nerve).<sup>2,5</sup>

As with vaginal sexual activity, anal sex candidates are also at danger of getting sexually transmitted infections (STIs).<sup>5</sup> Anal sex is believed to be a risky sex activity due to the hazard of damage to anus and rectum. Anus and rectum are very delicate body parts and do not have lubrication like the vagina gives, so they can be torn easily and can transmit infection, particularly if extra lubrication is not done.<sup>5,6</sup>

Strong opinions are often spoken about anal sex. It is controversial in various cultures, especially with respect to religious prohibitions. This is usually due to prohibitions against anal sex or instructions about the procreative purpose

#### Col (R) Dr Abdul Waheed TI(M)

Assistant Professor, HoD Forensic Medicine and Toxicology  
Karachi Institute of Medical Sciences (KIMS), Malir Cantt,  
Karachi  
Email: [chundrigarwaheed@yahoo.com](mailto:chundrigarwaheed@yahoo.com)

#### Mir Ghulam Ali Talpur

Medical Officer  
Sindh Government Hospital, New Karachi

#### Iqbal Ahmed Khan

Senior Lecturer, Department of Forensic Medicine  
Fazaia Ruth Pfao Medical College

#### Hari Ram

Demonstrator  
Shaheed Mohtarma Benazir Bhutto Medical College

#### Shahid Nezam

Senior Medico-Legal Officer  
Abbasi Shaheed Hospital, Karachi

#### Syed Pervaiz Alam

Associate Professor, Department of Forensic Medicine  
Liaquat College of Medicine & Dentistry

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of sexual activity. It may be considered taboo or unnatural, and is a crime in some countries, punishable by corporal or capital punishment.<sup>4,7</sup>

The rich nervous supply of anus and rectum can make anal sex more gratifying for men or women.<sup>2,5,7</sup> The internal and external sphincter muscles of anus are sensitive tissues enriched with many nerve endings thus provide pleasure or pain via.<sup>2,5</sup>

Heterosexual anal intercourse (HAI) is also not an uncommon behavior with 36% of women and 44% of men (25–44 years old) in the United States reporting ever having HAI in their lifetime. There is evidence that the prevalence of HAI may be increasing in recent years, which may be due to a true increase in the behavior over time or heterosexuals becoming more comfortable reporting the behavior.<sup>7,8</sup>

Reports concerning the prevalence of anal sex among gay and other men are found to be variable. A survey in *The Advocate* in 1994 specified that 46% of gay men desired to penetrate their partners, while 43% desired to be the receptive partner. Other links suggests that nearly three-fourths of gay men have performed anal sex at least one time, with similar percentage contributing as tops and bottoms.<sup>9</sup> According to the 2012 NSSHB sex survey in the U.S; high prevalence of anal sex among gay men has been reported with 83.3% of the men having performed anal sex in the insertive way and 90% in the receptive way. Majority reported recent performance even as within 30 days or less.<sup>10</sup>

Frequency of anal sex is increasing nowadays because of the increased viewing of anal pornography videos among men. Seidman *et al.* reported that "cheap, accessible and, especially, interactive media have allowed many more people to view pornography", and this modern way of producing pornography, in which buttocks and anus become more eroticized, has led to a significant increase in or obsession with anal sex among men.<sup>11</sup>

Assuming the increased prevalence of sodomy cases in our population, this study was especially designed to retrospectively observe the sodomy cases brought at medico legal department of Abbasi Shaheed Hospital for examination, from various police stations of Karachi, Pakistan and its associated factors.

#### **METHODOLOGY:**

This was a single centered retrospective study and data was collected from medico legal section of Abbasi Shaheed Hospital, Karachi, from a period of January 2016 till December 2018. An inclusion criterion was all the anal sex cases performed without consent irrespective of age and gender based on Karachi population. Sodomy performed with consent was excluded. All the other type of sexual behaviours were also excluded. There are about 150 police stations in Karachi. Medicolegal cases of more than 45 police stations cases are reported at Abbasi Shaheed Hospital

(ASH). ASH deals from district central, east & west of Karachi, the important police stations included were Nazimabad, North Nazimabad, Hydri Market, Paposh Nagar, Gulbahar, Rizvia, Taimorea, Sir Syed, Shakra-e-Noor Jahan (SNJ), Orangi Town, Pakistan Bazaar, Iqbal Market, Mominabad Town, Peerabad, Manghopir, Khawaja Ajmir Nagri, New Karachi, Surjani Town, Site Area, Pakistan Colony, Pir Islamb bux Colony (PIB), Sohrab Goth, Site Super Highway Industrial Area (SSHIA), Sachal Goth, Gadap City, Federal B. Industrial Area (FBIA), Gabol, New Karachi Industrial Area (NKIA), Smanabad, Gulberg, Ysuif Plaza, Azizabad, Johar Abad, Aziz Bharti, Gulshan-e-Iqbal, Mobin Town, Sharifabad, Gulistan-e-Johar, Gulshan-e-Maymar, Bilal Colony.

A total of 102 cases of sodomy were reported in the above police stations of Karachi in the specified time period.

Detailed information regarding time and place of incidence, area of residence, bath history and relationship with the passive agent was gathered from the register for Accused. Findings of physical examination such as any signs of local injury, scratches & bruises marks, development of secondary sexual organs, presence of any abnormality like hernia, hydrocele, varicocele was also collected. Penile erecting capacity was also evaluated and mentioned in the register. Evidences were also collected for presence of any trace elements like semen, hairs were taken from anal region both superficial and deep. Preliminary clinical examination was also conducted. In case of disappointing results of the clinical examination, DNA test of suspicious active agents/accused was carried out for confirmation. Data was entered and analysed using SPSS version 22 by calculating simple frequencies and percentages.

#### **RESULTS:**

A total of 102 sodomy cases were found to be registered at medico legal department of Abbasi Shaheed Hospital, Karachi brought from various police stations of Karachi during a period of Jan 2016 till Dec 2018. Total 99 % cases were found to be homosexual in nature while only 1 case was registered as heterosexual in nature. All were residents of Karachi. Sodomy cases were reported to hospital on same day (the day the anal sex was performed). Time elapsed between anal sex and examination was observed to be ranged from 2 to 12 hours. Majority of cases were examined within 3-4 hours. Majority of the convicts belonged to the age range of 21-30 years followed by 10-20 years of age. (Fig-1) Mean age of the convicts was calculated to be 23.19 years. All the active agents were usually of poor socio economic conditions and illiterate. Majority of the active agents were found to be living alone without family for the earning purpose. Detailed demographic features of the agents are shown in Table-1. Table-2 shows the findings of preliminary physical and clinical assessment of active agents. Semen stains were found on the cloths of 30 (29.4%) whereas

Table 1 - Demographic Features of the accused N=102

Characteristics	N (%)
<b>Age Range</b>	
10-20	26 (25)
21-30	52 (50.9)
31-40	4 (3.92)
41-50	10 (9.8)
51-60	4 (3.92)
61-71	6 (5.82)
<b>Gender</b>	
Males	101 (99)
Females	1 (1)
<b>Socioeconomic conditions</b>	
Good	00 (00)
Poor	102 (100)
<b>Education</b>	
Nil	80 (78.43)
Primary	17 (16.6)
Secondary	5 (4.90)
<b>Employment status</b>	
Employed	99 (97.05)
Unemployed	3 (2.94)
<b>Living</b>	
With Family	14 (13.72)
Alone	88 (86.27)

Table 2- Preliminary Physical and clinical assessment of accused (N=102)

Findings	Positive	Negative
<b>Semen stain</b>	30 (2.94)	72 (70.5)
<b>Blood stain</b>	12 (11.7)	90 (88.2)
<b>Bruise/scratch marks</b>	14 (13.7)	88 (86.2)
<b>Penile erection capacity</b>	102 (100)	0 (0)
<b>Any disease e.g., hydrocele, hernia</b>	0 (0)	102 (100)
<b>Secondary sexual characteristics</b>	102 (100)	0 (0)
<b>Potency/Penile erection</b>	102 (100)	0 (0)

blood stains were found in 12(11.7%) out of 102 active agents. Scratch marks were observed in 14 active agents. On preliminary clinical assessment, all the convicts were found to be sexually potent. Secondary sexual characteristics were well developed in all. DNA of only suspicious 14 accused was sent for laboratory analysis out of 102. (Table 2). Majority of cases were reported in the police station belonging to Surjani town (11) followed by Sir Syed (9), Sohrab Goth (9), North Nazimabad (8) and Gulbahar (7). Majority of the cases were brought to ASH by the Police. However, few cases were also brought by relatives with police letters. It was also observed that majority of cases

Table-3 Information gathered from register related to Accused

Associated Factors	No (%)
<b>Place of incident</b>	
Victim's house	5 (4.9)
Accused house	3 (2.9)
Isolated Place	89 (87)
Hotel	5 (4.9)
<b>No of partners</b>	
Single	93 (91)
Multiple	10 (9.8)
<b>Relationship with Passive partner</b>	
Related	95
Non-Related	7
<b>Employment type</b>	
Labourer	78
Fruit seller	4
Driver	4
House-Servant	11
Shopkeeper	5

were not brought on time by Police as they usually try to negotiated with both parties. Table-3 shows some more information related to accused gathered from register.

**DISCUSSION:**

According to this study, 102 cases of sodomy were reported to medico legal section of a tertiary care hospital for medico legal examination from various police stations of Karachi. 99 % cases were homosexual in nature while only 1 case was of heterosexual in nature. Of the data that are available, it appears a significant and increasing minority of heterosexuals have ever practised anal intercourse. Among homosexual men, most, but not all, report anal sex, with large proportions of men engaging in both insertive and receptive anal intercourse.<sup>12</sup>

In our country's Khyber Pakhtoon Khawa Province (KPK), it is outwardly common that Pashtun males do sexual activity with young boys which is suggested by IRIN as a "a practice now deeply rooted in the local culture."<sup>13</sup> The Internet is promoting "solidarity" among homosexuals in Pakistan.<sup>13,14,15</sup> Online chat rooms offer a protective and unidentified platform for middle and upper class gay men.<sup>14</sup> According to a British Broadcasting Corporation (BBC) article (2005), increased number of homosexual couples are residing together in Pakistan's big cities such as Karachi and Islamabad.<sup>15</sup> However, one of *Guardian* article published in 2006 reported that it is "rare" for same sex couples to reside together ad majority have to finally marry women so as to avoid from any scandal in their family. It is well stated that the environment in larger cities such as Islamabad, Karachi and Lahore is more bearable as compared to rural areas where the extreme conservatism is present and homosexuals remain

"closeted".<sup>16</sup> There are no reports on female homosexuality, in Pakistan, the females inhabit mainly, a strictly private realm.<sup>17</sup>

Homosexuals who are not liked by their families also have to establish themselves on their own. This growth is impossible in the homosexual environment or in rural areas of country. The country's intentional blindness has provided space sufficient for gays and lesbians. They live together as couples, though discreetly.<sup>18</sup>

In this study, mainstream population of the active agents/accused fitted to the age range of 21-30 years followed by 10-20 years of age which is quite a young age. Researches on the premarital sexual activity of adolescents has shown that it is potentially risky and harmful<sup>19</sup>, because of the risk of sexually transmitted infections (STIs) and unwanted teenage pregnancies as identified in countries such as Great Britain and the United States.<sup>20,21,22</sup> Risky sexual activities of young adults, usually executed as precocious sexual onset (*i.e.*, first intercourse before the age of 15; erratic condom use, and many sexual partners can directly lead to the incidence of STIs including HIV.<sup>23,24</sup>

In this study, majority of the cases were of homosexual. Only 1 case of heterosexual anal case was reported. Still strict social customs are present for females, which keep them away from any sex activity and avoid indulging in multiple sex partners<sup>25</sup> whereas boys have more liberty for sex. Boys are generally socialized in more sex-positive peer contexts and are pressurized by their fellow friends to indulge in sexual activity.<sup>26</sup> This is the reason boys are more reported to be involved in sexual activities. Gender differences in sexual behaviors found in our societies are basically due to cultural and socialization factors.<sup>27</sup>

In our study, majority of cases were reported in the police station belonging to Surjani town (11) followed by Sir Syed (9), Sohrab Goth (9), North Nazimabad (8) and Gulbahar (7). The reason for more incidences of sexual abuse cases in these areas could be because of low socio demographic type of these areas.<sup>28</sup>

Reasons of accused for involving in unnatural sex activities identified by this study were living alone without family, lack of education as majority of the active agents were living alone in the city for earning purpose but were illiterate. Disturbed family relationships can cause disturbances in emotions which are assumed to be developed in early childhood and which in a majority of cases can cause the anti-social, sexual and violent behavior at a young age.<sup>29</sup> Delayed reporting of sexual assault cases can result in loss of essential evidences required. Hence; early reportage and inspection of cases must be done.<sup>30</sup>

It is highly recommended to conduct this study gathering data from interior areas of Pakistan. Furthermore, more demographic characteristics of accused *i.e.* race and family atmosphere should also be incorporated. Smaller sample

size and data collection from single center are major limitations of present study.

## CONCLUSION:

Majority of the accused were of young age, poor, living alone without family, illiterate and from labour class. These might be the factors responsible for their involvement in alleged sexual behavior.

## Authors Contribution:

**Abdul Waheed:** Conceived the idea, writing of manuscript, SPSS analysis and supervised the study

**Ghulam Ali:** Proposed the study design and collection data

**Iqbal Ahmed Khan:** Helped in data collection procedure and entry of data in Excel

**Hari Ram:** Critically analyzed the manuscript, Bibliography

**Shahid Nezam:** Helped in data analysis and critically analyzed the manuscript

**Pervaiz Alam:** Helped in data entry and analysis

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## Asymptomatic Carotid Artery Stenosis among Patients with Type II Diabetes Mellitus

Sadia Shahid, Abdul Latif Khattak, Karamat Hussain Shah Bukhari, Raffi Uddin, Raees Iqbal Khan, Mohammad Shahbaz Amin

### ABSTRACT

**Objectives:** To assess Carotid artery intima-media thickness in patients with type II diabetes mellitus.

**Study design and setting:** This descriptive cross-sectional study was conducted at Department of Medicine, CMH Quetta from June 2018 to May 2019.

**Methodology:** Total 176 known type II diabetes mellitus (DM) patients were included in study. Age ranged from 30-70 years. Patients using statin drugs, chronic kidney disease and decompensated liver cirrhosis were excluded. Carotid artery ultrasonography was carried out by radiologist. Carotid artery intima-media thickness (CIMT) was achieved with a 7 MHz B-mode ultrasound system. The intima-media thickness (IMT) was demarcated as the distance between the leading edge of the luminal echo to the leading edge of the adventitia of the media. This distance was measured during the diastolic phase. This was measured 3 cm before the carotid bifurcation. Also, carotid bifurcation and internal carotid artery 2 cm distally from the carotid bifurcation was scanned.

**Results:** Mean age was  $47.86 \pm 6.46$  years. Most of the patients 125 (71.02%) were consisted of 30 to 50 years of age. Among them the 176 patients, 92 (52.27%) were male and 84 (47.73%) were females. Male to female ratio comprised of 1.1:1. Results further revealed that 43(24.43%) patients showed asymptomatic Carotid artery intima-media thickness. Rest there was no asymptomatic Carotid artery intima-media thickness in 133 (75.57%) patients.

**Conclusion:** This study determined that the frequency of asymptomatic Carotid artery intima-media thickness in patients with type II diabetes mellitus is quite high.

**Keywords:** Asymptomatic, Carotid artery intima-media thickness, Type 2 diabetes.

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### INTRODUCTION:

Main types of diabetes mellitus (DM) includes: type I or

**Sadia Shahid**

Senior Registrar, Department of Medicine  
Combined Military Hospital, Quetta

**Abdul Latif Khattak**

Associate Professor, Department of Medicine  
Combined Military Hospital, Quetta

**Karamat Hussain Shah Bukhari**

Assistant Professor, Department of Medicine  
Combined Military Hospital, Lahore

**Raffi Uddin**

Assistant Professor, Department of Medicine  
Combined Military Hospital, Lahore

**Raees Iqbal Khan**

Senior Registrar, Department of Medicine  
Combined Military Hospital, Quetta  
Email: [iqbalraees@yahoo.com](mailto:iqbalraees@yahoo.com)

**Mohammad Shahbaz Amin**

Associate Professor, Department of Pathology  
Lahore Medical and Dental College, Lahore

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Accepted: 05-Nov-2020

insulin dependent DM or juvenile diabetes, type II or non-insulin dependent DM or adult-onset diabetes and gestational diabetes.<sup>1,2</sup> Occurrence of diabetes mellitus is 10-14% throughout world.<sup>2</sup> Diabetes mellitus type 2 (formerly noninsulin-dependent diabetes mellitus (NIDDM) or adult-onset diabetes refers to a metabolic disorder. It is considered as high blood glucose levels in the presence of comparative insulin resistance and deficiency and in Type I disorder due to absolute insulin deficiency<sup>3</sup>. This critical insulin deficiency is due to destruction of islet cells in pancreas.<sup>4</sup>

Destructive effects of hyperglycemia can be categorized as macro-vascular complications. Macrovascular complications include coronary artery disease, peripheral arterial disease, and stroke. While micro vascular complications are diabetic nephropathy, neuropathy and retinopathy.<sup>5</sup> Altered platelet morphology and functions have been found in diabetic patients. This pathology is related to the pathological processes. This pathological process poses high risk of vascular disease.<sup>6</sup> Diabetes Mellitus (DM) has emerged as most prevalent non-communicable diseases worldwide.<sup>7</sup> It has become the fourth or fifth important cause of mortality among high-income countries.<sup>7</sup> From 2009 till 2034, count

of people with diagnosed and undiagnosed diabetes would go on rise from 23.7 million to 44.1 million in United States.<sup>8</sup> It is anticipated that by 2025 about 380 million people would suffer from type 2 diabetes. Population having impaired glucose tolerance in the world would count about 418 million.<sup>9</sup> Major risk factor for cerebrovascular events is stenosis of the internal carotid artery. Those individuals with signs and symptoms of ischemic stroke plus a carotid stenosis showed 50% high risks of a recurrent event. These patients have a risk of stroke equal to 21% at 2 weeks after the first transient Ischaemic stroke or stroke. Also, risk is 32% at 12 weeks.<sup>10</sup> Asymptomatic Carotid artery intima-media thickness is directly proportional to a higher risk of stroke. Recent research revealed stroke risks of about 0.5% per year for 70% to 99% ACAS transient ischemic stroke patients.<sup>11</sup> Therefore; the rationale of the study is to estimate the Carotid artery intima-media thickness in our local diabetic patients. The outcome of this study will be a parameter for developing forthcoming research approaches. This will also guide us for developing mechanisms of avoiding future cerebrovascular events in type 2 Diabetes Mellitus patients.

#### METHODOLOGY:

This descriptive, cross-sectional study was performed in outpatient and indoor patients in Department of Medicine, CMH Quetta cantonment from June 2018 to May 2019 for one year. Approval of Combined Military Hospital, Quetta ethical committee has been obtained numbered IRB/019. Sample Size was calculated by keeping 20.8% proportion of carotid artery intima-media thickness in patients with DM<sup>12</sup> with 95% confidence interval and 6% margin of error using World Health Organization (WHO) sample size calculator. Hence 176 was the calculated sample size. Non-probability, consecutive sampling technique was carried out in both outpatient and indoor admitted patients. Informed and written consent was taken from all patients included in the study. Patients fulfilled inclusion criteria by history and examination. Patients with type-II DM for two years duration, without signs or symptoms of focal or global neurological deficit, male and female with age range between 30 to 70 years, patients without target organ damage like retinopathy, left ventricular hypertrophy and nephropathy were included in study. Patients having history of using statins, fibrate drugs, and multivitamins especially thiamine supplements, diagnosed history of renal failure, diagnosis of decompensated liver failure on medical records and laboratory investigations were excluded from the study. Carotid artery ultrasonography was done by an experienced specialist radiologist for the vascular ultrasonography performed by Doppler. Carotid artery intima-media thickness was assessed with a 7 MHz B-mode ultrasound system. The IMT stands for the distance between the foremost edges of the luminal echo to the inner edge of the adventitia of the media. This distance were measured during the diastolic phase. The B-mode scanning procedure comprised the scanning of the right and left

common carotid arteries (3 cm before the carotid bifurcation). It also includes the internal carotid artery 2 cm distally from the carotid bifurcation. It was measured in mm and a value exceeding 7mm was considered as carotid artery stenosis. All data was endorsed on the Performa. Data entered and analyzed in SPSS version 22. Mean + SD were calculated for quantitative variables like age and extent of DM. Frequencies and percentages were obtained for categorical variables like gender and Carotid artery intima-media thickness. Carotid artery intima-media thickness was stratified among age, gender and duration of diabetes. It was performed to calculate effect modifications by chi square test. The p value of < 0.05 was considered as statistically significant.

#### RESULTS:

Age range was between 30 to 70 years with mean age of  $47.86 \pm 6.46$  years. Main stream of the patients 125 (71.02%) were among age 30 to 50 years as revealed in Table I. Total patients were 176 patients out of which 92 (52.27%) were male and 84 (47.73%) were females. Male to female ratio is 1.1:1. Mean period of disease was  $7.11 \pm 3.89$  years. Asymptomatic Carotid artery intima-media thickness was observed in 43 (24.43%) patients, whereas no evidence of asymptomatic carotid artery intima-media thickness in 133 (75.57%) patient (Table II). Also, presence of asymptomatic carotid artery intima-media thickness was calculated on age groups. It was observed that there was no significant difference between different age groups. Stratification of asymptomatic carotid intima-media thickness with respect to age, gender and duration of diabetes mellitus type II is shown in Table II. This study also showed no significant

Table-I: Age distribution of patients (n=176).

Age (in years)	N(%)
30-50	125(71.02)
51-70	51(28.98)
Total	176 (100)

Table II: Stratification of asymptomatic carotid artery intima-media thickness with age, gender and duration of diabetes mellitus

Age (years)	Asymptomatic carotid artery stenosis		P-value
	Yes	No	
30-50	32	93	0.572
51-70	11	40	
Gender	Yes	No	0.604
Male	21	71	
Female	22	62	
Duration (years)	Yes	No	0.805
<5	23	74	
>5	20	59	

Table-III: Distribution of patients according to duration of DM (n=176)

Duration (in years)	No. of Patients(%)
<5	97 (55.11)
>5	79(44.89)

Mean  $\pm$  SD = 7.11  $\pm$  3.89 years

difference between male and female. Table III has shown the distribution of asymptomatic carotid intima-media thickness with reference to span of disease.

### DISCUSSION:

Diabetes has been demarcated as an independent risk factor for the occurrence of high-grade carotid artery intima-media thickness in the general population.<sup>13</sup> Type-II Diabetes (T2D) carries a considerable risk factor for the advancement of atherosclerosis. It is measured by increase in carotid intima-media thickness (CIMT). It is expressed in length unit per patient in 1 year. It is associated with the incidence of plaques on the internal carotid artery in 1–2 years.<sup>14,15</sup> We have performed this study to estimate and determine the frequency of asymptomatic carotid artery intima-media thickness in patients with type II diabetes mellitus.

Age in this study ranged between 30 to 70 years. Mean age calculated as 47.86  $\pm$  6.46 years. Most of the patients 125 (71.02%) were in range of 30 to 50 years of age. Among 176 patients, 92 (52.27%) were male and 84 (47.73%) were females. Male to female ratio remained 1.1:1. Asymptomatic carotid artery intima-media thickness was observed in 43 (24.43%) patients. However, there was no evidence of asymptomatic carotid artery intima-media thickness in 133 (75.57%) patients. In one study, 19.2% of diabetic patients had significant carotid artery intima-media thickness compared to 9% in non-diabetic patients.<sup>16</sup> In another study, 20.8% of patients with Diabetes mellitus were reported to have carotid artery intima-media thickness.<sup>12</sup> Asymptomatic significant stenosis was lesser in few areas of the world such as 1.2% from Austria,<sup>17</sup> 1.3% in Australia,<sup>18</sup> 1.4% in Netherlands,<sup>19</sup> 1.5% from Taiwan,<sup>20</sup> and 2.1% from France.<sup>21</sup> The incidence of asymptomatic significant carotid artery intima-media thickness was found as being 5.4% in the Dutch population,<sup>22</sup> 3.9% in Italians,<sup>23</sup> 4.6% from USA,<sup>24</sup> and 4.2% from Russia.<sup>25</sup> Ethnicity and basic genetic makeup with alteration from external factors such as diet, lifestyle, and stress may contribute to this pathological process. This study displayed an obvious increment in the risk (6.2 times) of developing ICA stenosis with diabetes of more than 15-year duration (OR = 6.2; 95% CI: 3.41–11.3).

In diabetic individuals, carotid artery disease is often noticed at more advanced stages of the disease as compared with the overall population. It is observed that in diabetic subjects, the arteriosclerotic process grows at faster rate and much earlier as compared to non-diabetic patients. Diabetic patients

remain asymptomatic for carotid artery disease for longer periods. Diabetic patients have large volume atherosclerotic plaques and are usually characterized by their large lipid cores. This pathologic process leads to large remodeling rates in the involved vascular segment. These segments have thin fibrous caps with strong inflammatory process which make them more susceptible to rupture. This process becomes basis for an acute coronary event. Diabetic patients also have additional extensive, diffuse and severe coronary artery involvement. All above mentioned are features are associated with a bad prognosis. Multivariate analysis showed that non-obstructive and even obstructive CAD analyzed by coronary CTA points towards prognostic indicators for asymptomatic T2DM patients<sup>26</sup>. Prospective, long duration clinical studies<sup>27</sup>, revealed that acceptable glycemic control related with early management of other cardiovascular risk factors. These cardiovascular risk factors include such as obesity, hypertension and dyslipidemia. Their early management is linked with lower morbidity and mortality in diabetic patients. Precise screening methods are essential for evaluating diabetic patients who are vulnerable for Stroke development. It will lead to reduction of the cost and morbidity related with conventional carotid angiogram. Duplex Doppler ultra-sonography has been turned out as broadly recognized noninvasive screening method.<sup>28</sup> In routine patient follow up only symptomatic patients are evaluated for carotid duplex examination. But fresh data displays that those patients with asymptomatic carotid artery stenosis of 60% or more have a reduced 5 years risk of ipsilateral stroke on elective carotid endarterectomy.<sup>29</sup> In the context of these results, it has turned out to be an essential to assess carotid artery disease in all Type 2 Diabetics. It should be done in all diabetic patients whether they are symptomatic or asymptomatic to evaluate cerebrovascular disease. This will aid in risk stratification and developing sophisticated management plan.

### CONCLUSION:

This study concluded that the frequency of asymptomatic carotid artery intima-media thickness in patients with type II diabetes mellitus is fairly high. It is recommended that proper screening should be carried out to estimate frequency of asymptomatic carotid artery intima-media thickness incidence in patients with type II diabetes mellitus. This will help in reduction of their morbidity and will have significant impact on mortality.

#### Authors Contribution:

**Sadia Shahid:** Idea, design, data collection  
**Abdul Latif Khattak:** Data collection, data analysis  
**Karamat Hussain Shah Bukhari:** Introduction, manuscript writing  
**Raffi Uddin:** Data interpretation, abstract writing  
**Raees Iqbal Khan:** Data interpretation, discussion  
**Mohammad Shahbaz Amin:** Data analysis and interpretation

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## Comparison of Team Based and Traditional Teaching Methods in Forensic Medicine: on the Basis of Assessment Tools

Shahid Kamran, Muhammad Sajid Khan, Jamil Ahmed Siddiqui, Natasha Mustafa, Waqar Shaikh, Hina Khan

### ABSTRACT

**Objective:** To compare two different teaching methods in Forensic Medicine on the basis of assessment tools.

**Study design and setting:** A cross sectional analytical study was conducted at the Department of Forensic Medicine at Al-Tibri Medical College and Hospital, from February to August 2019

**Methodology:** Total 100 students of third year MBBS were included in this study after taking ethical approval from the ethical review committee. These students were randomly divided into two groups of 50 students each, with Group A being taught through the traditional didactic lectures and Group B by Team Based Learning (TBL). Both groups were assessed using different assessment tools. Each assessment was of 25 marks and for comparison of marks, independent “t” test was applied comparing the mean value through SPSS version 20.0 and the level of significance was taken at  $< 0.05$ .

**Results:** The student’s involved in Team Based Learning performed superior than teacher centered strategy. In Group A, the students were taught via traditional lecture-based method and Group B was introduced to Team Based Learning. The mean score of assignment in Group A and Group B showed P value  $< 0.001$  that showed significantly higher grades in student-centered teaching.

**Conclusion:** Team based learning showed significant successful results in all assessment methods, therefore, it has been concluded through our study that Team Based Learning is a more effective method of teaching Forensic Medicine and it helps in making learner autonomous.

**Key word:** Andragogy, Self-directed learning, Team Based Learning

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### INTRODUCTION:

Several medical universities across Asia use conventional, orthodox teaching methods that largely do not encourage the notion of active learning or student participation.<sup>1</sup>

Pakistan, being a third world country is marred by its own set of problems and financial constraints, which allows for a very restricted budget to be utilized towards medical education.<sup>2</sup> Most of the medical universities across the country are still relying on the traditional didactic lecture based learning method calling for a large, passive audience instead of inspiring student engagement or team work. However, efforts are being made to incorporate newer methods of teaching such as Team Based Learning (TBL) so as to keep the level of medical education being provided in Pakistan, at par with the international standards.<sup>3</sup> In Team Based Learning, a class of students is divided into multiple small groups and assigned with tasks ensuring their involvement and a know-how regarding the application of the facts, with the teacher functioning as the facilitator to the small groups. These teams are then assigned with small tasks or tests to gauge the clarity of their concepts regarding the topic, which is followed by a discussion and feedback from the faculty. Finally, the students are evaluated via examination.<sup>4,5</sup>

TBL has proven to be quite effective in several of the disciplines of medical sciences as recorded in various researches.<sup>6,7,8</sup> Forensic Medicine is a clinically oriented subject assimilating knowledge from a variety of other

#### Shahid Kamran

Assistant Professor, Department of Forensic Medicine, Al-Tibri Medical College & Hospital, Karachi

#### Muhammad Sajid Khan

Assistant Professor, Department of Physiology, Al-Tibri Medical College & Hospital, Karachi

#### Jamil Ahmed Siddiqui

Assistant Professor, Department of Biochemistry, Al-Tibri Medical College & Hospital, Karachi

#### Natasha Mustafa

Lecturer, Department of Forensic Medicine, Al-Tibri Medical College & Hospital, Karachi

#### Waqar Shaikh

Lecturer, Department of Forensic Medicine, Al-Tibri Medical College & Hospital, Karachi

#### Hina Khan

Associate Professor, Department of Anatomy  
Deputy Director Research  
Al-Tibri Medical College & Hospital, Karachi  
Email: [drhinasalman@gmail.com](mailto:drhinasalman@gmail.com)

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medicinal disciplines such as pathology, emergency medicine, orthopedics and surgery. In Pakistan, the legal framework is such that it frequently requires collaboration from the medical fraternity to solve various criminal cases amidst the dearth of forensic experts. Therefore, on an undergraduate level, forensic medicine requires a diversity of new teaching methods so as to effectively impart the knowledge of forensic medicine among the medical students and to help them acknowledge the importance of this dynamic subject.<sup>9</sup> Team Based Learning is a teaching methodology which was introduced in 1970 by Michaelson to improve student participation and performance in business schools. Since then, this learning tool has been embraced by various medical universities globally.<sup>10</sup>

Keeping this in perspective; Team Based Learning was introduced in Forensic Medicine to see its effectiveness as far as the academic progress of the students is concerned. Therefore; this study was aimed to compare two different teaching methods in forensic Medicine on the basis of assessment tools.

**METHODOLOGY:**

Cross sectional analytical study was conducted at Department of Forensic Medicine for a period of six months from February 2019 to August 2019 after taking ethical approval from the ethical review committee. A total of 100 students of third year MBBS of Forensic Medicine were included in study and were randomly divided into two groups by using two color flags on the basis of teaching methods. Each group comprised of 50 students with one group of students being taught through traditional didactic lectures which is a teacher centered method and the students in the second group were engaged in team-based learning which is a student-centered teaching method. Four different topics were taught by applying either of the two methods in their respective teaching groups. Students were later assessed by using four different assessment tools: multiple choice questions (MCQs), short essays, observed structured practical examinations (OSPE) and assignments.<sup>11</sup> To exclude bias as much as possible, same faculty member was appointed to teach both the groups and students were randomly selected irrespective of their gender and past academic record.

Each assessment was of 25 marks and to measure the grading, a scoring scale was designed, with score 1 representing less than 5 marks, score 2 representing marks between 6 to 10, score 3 representing marks between 11 to 15, score 4 representing marks between 16-20, and score 5 representing marks between 21 to 25. This grading method was designed to evaluate the marks of the students participating in these two different teaching methodologies. Assessment were taken by facilitator and using a checklist for marking. Data was analyzed using the SPSS 20 version. Independent “t” test was applied to compare the mean value of the scores and P-value of less than 0.05 was considered significant.

Frequency and percentage were used for representation of grades among the class.

**RESULTS:**

Total of 100 students were divided into two groups labeled as group A and group B. Mean age for both the groups was 21.34 ± 1.32 and 51 students were males and 49 students were females being randomly divided into either of the two groups.

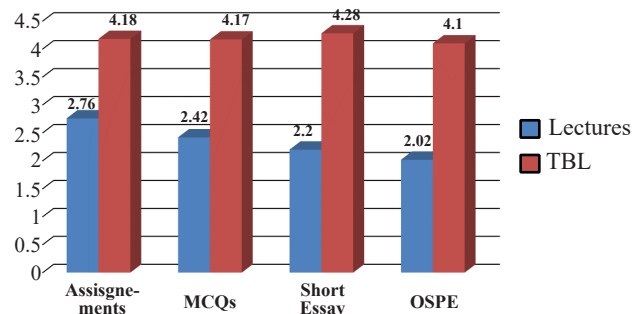
Frequency and Percentage of grades among two different groups were showed in Table I

In Group A, the students were taught via traditional lecture-based method and Group B was introduced to Team Based Learning. The mean score of assignment in Group A was and Group B showed P value <0.001 that showed significantly higher grades in student-centered teaching. The mean score of Group A in MCQs based assessment and in Group B its p value was <0.001, showing higher achievement of marking in Group B as compared to A. Mean score of Group A in short essay and in Group B, which is a significantly higher number as compared to that of Group A with p value <0.001. In Group A the grading of OSPE and in Group B was again a higher number of marking in comparison to that of Group A with p value <0.001 as shown in Figure 1.1

Table I Comparison of Grades among the groups

Assessment Tool	Grading	(Group A) Traditional lecture based n (%)	(Group B) Team based n (%)
Scoring Assignments	<5	6(12%)	-
	6-10	14(28%)	-
	11-15	21(42%)	9(18%)
	16-20	4(8%)	23(46%)
	21-25	5(10%)	18(36%)
Scoring MCQs	<5	15(30%)	1(2%)
	6-10	13(26%)	2(4%)
	11-15	13(26%)	5(10%)
	16-20	4(8%)	21(42%)
	21-25	5(10%)	21(42%)
Scoring OSPE	<5	19(38%)	1(2%)
	6-10	13(26%)	2 (4%)
	11-15	16 (32%)	8(16%)
	16-20	2(4%)	19(38%)
	21-25	-	20 (40%)
Scoring Short Essay	<5	15(30%)	-
	6-10	16(32%)	-
	11-15	15(30%)	8(16%)
	16-20	2(4%)	20(40%)
	21-25	2(4%)	22 (44%)
	Total		50(100%)

Figure: 1.1 Mean of grading among different groups and Level of significance between different assessment tools



### DISCUSSION:

Team Based Learning is a teaching methodology which was introduced in 1970 by Michaelson to improve student participation and performance in business schools. Since then, this learning tool has been embraced by various medical universities globally.<sup>11</sup>

In this study; it was observed that the group introduced to TBL did remarkably well as compared to the group being taught by traditional lectures. Another study reported that medical students taught via team based learning were better able to retain the knowledge gained.<sup>12</sup> Our study also exhibited similar finding as our students showed an improvement in remembering and recalling the content taught to them through TBL which also boosted their level of confidence during exams.

A study published on clinical neurology education on undergraduate level reported that students engaged in Team Based Learning performed far better academically and scored higher as compared to those engaged in passive learning.<sup>13</sup> This is a finding which is analogous to our study. Several other studies in the past have also recorded the superiority of Team Based Learning Method over the passive lecture based learning method.<sup>14,15</sup> Another study was done among the students of engineering and Nursing and they observed the positive effects among the students using flipped class and TBL sessions. Similarly in this study the TBL induced highly positive scores.<sup>16,17</sup> In accordance with the study results there was an effective learning among the multiprofessionals groups of medical students taught through TBL, as in this study the student centered approach was highly effective as compare to teacher centered.<sup>18</sup> One of the study conclusion revealed that there was highest grading among the students those taught through TBL in comparison with traditional teaching method among the students of optometry.<sup>19</sup>

Our study, however, had its own limitations with regards to the limited number of topics covered during this study and also that it did not compare TBL with any other active learning methods. For more favorable outcomes a research study covering all the topics of Forensic Medicine should

be conducted and other active learning methods in andragogy should also be explored. It was recommended that flipping the 2 groups teaching them from both the strategies and assessing them so if you haven't done that you should include in your study design. Therefore, this teaching strategy should be made an integral part of the curriculum devised for the subject of Forensic Medicine and for other disciplines being taught at undergraduate level to the MBBS students across the medical universities of Pakistan. Along with that, other active learning methods must also be researched and experimented upon.

### CONCLUSION:

Team based learning is a better learning tool compared to the traditional didactic lecture based learning for students as it has been found to improve the students' performance in exams, enhance their confidence and also inspires cooperation and teamwork amongst classmates.

#### Authors Contribution:

- Shahid Kamran:** Experimentation / Study conduction
- Muhammad Sajid Khan:** Manuscript writing
- Jamil Ahmed Siddiqui:** Analysis / Interpretation / Discussion
- Natasha Mustafa:** Facilitated for reagents / Material analysis
- Waqar Shaikh:** Critical review
- Hina Khan:** Conception of study / Designing / Planning

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## Perception of Halitosis among General Population

Mahnoor Khawaja M. Saleem, Abhishek Lal, Sabeen Masood, Dinaz Ghandhi, Anum Arif Sitai, Naseer Ahmed

### ABSTRACT

**Objective:** To assess the self-perception of halitosis among general population of Karachi along with the oral hygiene methods used. Secondly, the self-perception of halitosis was compared with predictor variables such as age, gender, level of education, and occupation.

**Study design and setting:** Cross-sectional survey; a total of 401 participants of Karachi were recruited in September 2020, Pakistan.

**Methodology:** Using Google Forms, an online questionnaire was developed and consisted of 27 questions regarding demographics and self-perceived halitosis, which was filled by the participants. For the statistical analysis, a multiple linear regression test was used to analyze any significant relation between predictor variables and self-perceived halitosis.

**Results:** Out of the 401 participants, 168 (41.9%) were males and 233 (58.1%) were females. A total of 184 (45.9%) participants suffered from halitosis, with more prevalence in males. Mostly, 251 (62.6%) participants perceived to have halitosis themselves, with tooth brushing the most common (44.9%) way to reduce it. About 340 (84.8%) respondents brushed daily, with twice a day selected by 250 (62.3%). The coated tongue was seen by 124 (30.9%) of participants themselves. Age was found to be significantly associated with self-perceived halitosis.

**Conclusion:** Halitosis is a frequent problem most prevalent in male gender. It has medical and psychosocial impact. Although in general, people are aware of perceiving bad breath themselves, there is still a need for public awareness campaigns to disseminate more knowledge and management options regarding halitosis. Frequent visits to dental and medical healthcare professionals should be encouraged to mitigate this problem.

**Keywords:** Awareness, Halitosis, Prevalence, Self-perception.

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### INTRODUCTION:

Halitosis is an unpleasant odor or smell that is emitted from a person's oral cavity. Other terms that are frequently used

to denote halitosis is bad breath, fetor oris, or oral malodor. The primary substance that is responsible for causing halitosis is volatile sulfur compounds (VSCs) which are produced by gram-negative anaerobic bacteria (*Treponema denticola*, *Enterobacteriaceae*, *Prevotella (Bacteroides) melaninogenica*, *Porphyromonas gingivalis*, *endodontalis*, *Prevotella intermedia*, *Fusobacterium periodonticum*) from protein degradation.<sup>1</sup> Methyl mercaptan and hydrogen sulfide have been the most common substances isolated from malodor of individuals.<sup>2</sup> Halitosis is divided into three broad categories: factual halitosis, where either physiological or pathological halitosis is present; pseudo-halitosis, where a person thinks he or she might have halitosis although it's not present; and halitophobia, fear of having bad breath.<sup>3</sup> The factual halitosis is mainly the one that may require attention by the dentist if it is bothersome for the patient. Halitosis is a problem that affects multiple aspects of life such as social, medical, and psychological. About factors that can be associated with the development of halitosis,<sup>33</sup> categories have been formed which include intra-oral factors, extra-oral factors, and temporary factors, with intra-oral factors being the most common ones.<sup>4</sup> The main intra-oral factor that leads to the production of malodor is VSCs produced by gram-negative anaerobic bacteria. The yellowish-white coating of the tongue

**Mahnoor Khawaja M. Saleem**

Student,  
Altamash Institute of Dental Medicine, Karachi,

**Abhishek Lal**

Student,  
Altamash Institute of Dental Medicine, Karachi  
Email: [abhishekdarshan@yahoo.com](mailto:abhishekdarshan@yahoo.com)

**Sabeen Masood**

BDS (Graduated),  
Altamash Institute of Dental Medicine, Karachi

**Dinaz Ghandhi**

Associate Professor, Department of Oral and Maxillofacial  
Surgery,  
Altamash Institute of Dental Medicine, Karachi

**Anum Arif Sitai**

Demonstrator, Department of Oral Pathology,  
Altamash Institute of Dental Medicine, Karachi

**Naseer Ahmed**

Assistant Professor, Department of Community Dentistry,  
Altamash Institute of Dental Medicine, Karachi

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Accepted: 24-Dec-2020

has also been well established as an intra-oral factor leading to malodor.<sup>5</sup> Extra-oral factors include respiratory, gastrointestinal tract problems, sinusitis, diabetes, kidney problems, and sometimes side effects of some drugs. Temporary factors leading to malodor include foods containing onions, garlic, pepper, use of cigarettes, consumption of alcohol, and lastly morning bad breath. Furthermore, common etiologies related to dentistry leading to bad breath include dental plaque, dental caries, reduced salivary flow, and poor periodontal conditions.<sup>6</sup> Treatment of halitosis primarily depends on the underlying causative factors, which may be provided by the dentist, physician, or psychologist.

Halitosis is a very commonly encountered problem that may not have medical seriousness but has a serious social stigma.<sup>7</sup> Malodor if a person has, frequently leads to a decrease in self-confidence and avoidance behaviors particularly in social gatherings. Bad breath is commonly associated with a psychiatric disorder such as phobias, depression, worry and this adversely affects one's self-esteem.<sup>8</sup> Certain agents are commonly used by the general population to reduce or eliminate malodor such as tooth brushing, mouthwash, chewing gums, flossing, etc. Very rarely does the bad breath have any serious medical implications.

Most commonly, a person who does have bad breath may not notice it since they are not aware of the quality of their bad breath. There is a difference between objectively assessing and self-perception of bad breath which can lead to underestimation of the presence of bad breath. A frequently encountered factor regarding bad breath is that people avoid informing a person of having bad breath. Since it is difficult to judge the level of halitosis, some perceive it as nominal whereas some think of it as high enough to avoid social gatherings. Performing better oral hygiene methods have been proven to reduce bad breath and significantly increase one's self-confidence and self-esteem.<sup>9</sup>

Due to the serious social impact of halitosis perceived in generality, knowledge about this entity is important to reduce its impact on one's quality of life. Many times, individuals themselves know about having bad breath with their peers also suggesting it. Most of the time, poor oral hygiene of the population has been the main factor leading to the development of bad breath, with few people with underlying medical disorders.<sup>10</sup> Lack of knowledge about self-perception of halitosis leads to negligence to correct it. Therefore, from both social, medical, and psychological perspectives, it is necessary to increase the general population's knowledge of self-perception of halitosis which can be a definitive remedy for their concern.

It was aimed to assess the self-perception of halitosis among general population of Karachi along with the oral hygiene methods used. Secondly, the self-perception of halitosis was compared with predictor variables such as age, gender, level of education, and occupation.

## **METHODOLOGY:**

In this cross-sectional survey, total 401 participants that belonged to Karachi, Pakistan were recruited. The duration of data collection was from 1 Sept 2020 to 30 Sept 2020.

A questionnaire was formulated online using Google Forms, and the generated link was sent to the participants through different social media platforms such as WhatsApp, Emails, Facebook, and Twitter, and their responses were recorded. To calculate sample size, OpenEpi software was used keeping the desired percentile of 50 and a confidence interval of 95. The calculated sample size for this study was  $384(n=[Z12-\acute{a}/2.p.q]/d2)^{11}$ . A written consent was taken from the participants on the questionnaire. Primarily in our study, our focus was on self-perception of halitosis in the general population using validated tools.<sup>12</sup>

Secondarily demographic including age, gender, level of education, and occupation were also assessed. A questionnaire was designed in accordance with another study with some modifications considering the objectives of the current study.<sup>12</sup>

This questionnaire included questions such as whether the person feels he/she has bad breath or not, duration of awareness of bad breath, source of awareness of bad breath, measures to reduce bad breath, dental treatments, underlying systemic diseases which may lead to halitosis, oral hygiene habits, presence of dry mouth, symptoms of current systemic diseases and social habits which includes smoking. In the questionnaire, all these questions were formulated in English language. Adults who were above 18 and residing in Karachi, Pakistan, were part of this study.

Those who were below 18 years old and not residing in Karachi, Pakistan were excluded from the study. The information gathered from the participants through the filled questionnaires were kept anonymous and confidential. Ethics Review Committee of Altamash Institute of Dental Medicine, Karachi has approved this study (AIDM/EC/09/2020/02).

SPSS statistical software version 25 was used. Along with descriptive statistics, a multiple linear regression test was used to analyze any significant relation of the predictor variables, which are age, gender, education, and occupation with Halitosis. A p-value of <0.05 was considered to be as statistically significant.

## **RESULTS:**

In this study, a total of 450 questionnaires were received. On scrutiny, 49 forms were excluded based on being irrelevant and incomplete. A total of 401 participant's data was included in this study. The response rate was calculated to be 89.1%. Descriptive statistics and multiple linear regression tests were used to identify any significant relationship of predictor variables, which were age, gender, level of education, and occupation with Halitosis. Of the 401 participants, the majority of participants, about 222 (55.4%) belonged to the

age group of 18-30 years. Among the participants; majority were 233 (58.1%) female participants. Majority were 43.4% were graduates. Most of the participants in our study were students (35.7%) as shown in table 1. Regarding questions to assess halitosis, the majority that is 45.9% (184) of respondents self-perceived bad breath, with 40.9% (164) participants answering “No” and a few 53 (13.2%) not sure about it. Of the participants suffering from bad breath, most were aware of suffering from bad breath since “Weeks ago” (20.7%) and “Years ago” (19.7%). About finding out whether having bad breath or not, mostly 251 (62.6%) participants figured it out by themselves. Regarding measures opted to reduce bad breath, the majority of participants i.e. 44.9% chose “Toothbrush” as a measure to reduce bad breath as shown in figure 1. About 339 (84.5%) participants did not visit the dentist to have an examination performed for bad breath. Furthermore, 359 (89.5%) respondents did not have an examination performed for conditions that are associated with bad breath. Predominantly, 347 (86.5%) participants did not have any treatments performed either by a physician or dentist to treat their bad breath. Regarding oral hygiene, most of the 340 (84.8%) participants brushed their teeth regularly with a few 61 (15.2%) did not. About the frequency of brushing per day, 2 times a day was the most commonly select option by 250 (62.3%) number of participants. About flossing, 307 (76.6%) respondents did not floss their teeth with only a small number of 94 (23.4%) doing it. The majority of 275 (68.6%) participants did not use mouthwash every day, with those who used mouth wash, 93 (23.2%) of them using it “Once” a day.

Regarding bleeding gums, 250 (62.3%) respondents answered “No” when asked about bleeding from gums after brushing teeth. The majority of 313 (78.1%) participants did not have any loose teeth, with a small number of 60 (15%) having loose teeth. Most of the 311 (77.6%) participants did not suffer from dry mouth, few 56 (14%) reported to suffer from it. About suffering from dry eyes, the majority of 338 (84.3%) participants stated not to suffer from dry eyes. Most of the 283 (70.6%) participants did not have a bad taste in their mouths. Regarding the presence of coated tongue, 124 (30.9%) participants responded “Yes” to have their tongue frequently coated with yellowish or white deposits, with 221 (55.1%) answering “No”.

About the medical history of the respondents, 194 (48.4%) respondents had a positive medical history, with stomach problems (37.1%), emotional disturbance (38.7%), sinusitis (30.4%), and diabetes (28.4%) mainly selected. Regarding problems because of bad breath, the majority of 320 (79.8%) participants did not suffer from any problems due to the presence of bad breath with a small number of 52 (13%) reported hesitation of other people talking to them. Most of the 309 (77.1%) participants were not smokers. Asking other people other than healthcare professionals to judge bad breath, mostly 331 (82.5%) participants did not ask other

people’s opinion of their bad breath.

To analyze relation between age, gender, education, and occupation with Halitosis, multiple linear regression test was used with a p-value of =0.05 considered as significant. A significant relation was found of age (p-value=0.00) when compared with halitosis. Although similar was not seen with gender (p-value=0.89), education (p-value=0.56) and occupation (p-value=0.12) in relation to halitosis, as shown in table 2.

Table 1: Demographic characteristics of the participants

	Demographic Variables	n (%)
Age	18-30 years	222 (55.4%)
	31-40 years	81 (20.2%)
	41-50 years	49 (12.2%)
	51-60 years	32 (8.0%)
	Above 60 years	17 (4.2%)
Gender	Male	168 (41.9%)
	Female	233 (58.1%)
Education	Undergraduate	150 (37.4%)
	Graduate	174 (43.4%)
	Postgraduate	59 (14.7%)
	Below graduate	18 (4.5%)
Occupation	Student	143 (35.7%)
	Business	55 (13.7%)
	Healthcare Professional	82 (20.4%)
	Engineer	24 (6.0%)
	Teacher	27 (6.7%)
	Unemployed	34 (8.5%)
	Others	36 (9.0%)

Figure 1: Measures used to reduce bad breath (n=401)

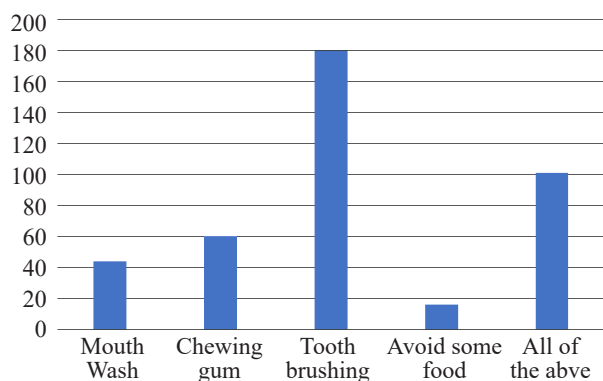


Table 2: Relation of age, gender, education and occupation with Halitosis using multiple linear regression test

Variables	Coefficient	Standard Error	T-value	p-value
Age	-0.254	0.233	-4.290	0.001
Gender	0.007	0.481	0.137	0.891
Education	0.034	0.330	0.567	0.567
Occupation	0.089	0.130	1.555	0.121

**DISCUSSION:**

Halitosis or Bad breath is a very common problem present worldwide with not only medical consequences but social and psychological as well. The prevalence of halitosis throughout the globe has been strongly established.<sup>11</sup> In our study, 45.9% of the participants self-perceived for having bad breath. Previous studies in the literature suggest 8-50% of the people self-perceived bad breath.<sup>13</sup>

Age has a significant impact on the self-perception of bad breath as reported in our study. The younger adults were more aware of their breath and if it appeared bad, they perceived it. One reason for this could be that younger adults are more vigilant of their breath as they are part of many social gatherings as compared to older adults.<sup>14</sup> Moreover, this study concluded that males suffered and perceived bad breath more as compared to females. One reason for this could be that females tend to take better care of their oral hygiene as compared to males according to literature.<sup>15</sup> However, the level of education played no significant role in judging one's bad breath in our study. This contrasts with previous studies that report lower education leads to poor self-perception of halitosis.<sup>16</sup>

Tooth brushing regularly, at least twice a day has been the standard protocol to keep oral hygiene optimum. Majority reported very good oral hygiene with brushing their teeth regularly and twice per day in this study. This, however, may be due to the majority of individuals in the sample belonging to good socioeconomic status, which plays a role in maintaining and performing optimal oral hygiene measures.<sup>17</sup> If oral hygiene is good and yet halitosis persists in an individual, then the coated tongue is most likely the cause.<sup>18</sup> This could be the reason individuals in this study reported bad breath despite having good oral hygiene. Although one study did conclude decreased long-term benefit of performing tongue cleaning such as with tongue scrapers.<sup>19</sup>

Most of the respondents in this study did not report to the dentist or physician despite having bad breath. In accordance with Hammad et al., most of the participants tried to solve their bad breath with a measure like chewing gums, mouth wash, and tooth brushing.<sup>20</sup> This means that most of the participants lack knowledge about halitosis regarding its causes and management plans. A study reports that chewing gums tend to decrease VSCs, thus individuals decrease their self-perception of bad breath.<sup>21</sup> In a Nigerian study where most of the participants chose a close friend to ask their opinion, these results contrast with our study where most of the individuals themselves evaluated whether they had bad breath or not.<sup>22</sup> To measure halitosis, the organoleptic score is the gold standard method.

Although rare, some systemic diseases are known to cause bad breath. Conditions like diabetes, tonsillitis, sinusitis, liver problems, and stomach problems are known to cause halitosis. Although this was correlation was not found in

our study. Similarly, no correlation was found in our study between the intake of medicines and halitosis, although previous studies do report a positive association.<sup>23</sup> Furthermore, improper breathing could also result in bad breath.<sup>24</sup>

Smoking was found among 92 participants in this study. It is concluded from previous studies that individuals use smoking as a method to overcome their halitosis problem.<sup>25</sup> This then leads to a strong smoker's breath, which can be smelled nearby. When patients with halitosis seek treatment for it, they are strongly encouraged to quit it.<sup>26</sup>

Flossing has been an adjunctive method to maintain and improve oral hygiene along with other modalities such as tooth brushing and mouthwashes. In our study, very few individuals used dental floss as part of their routine oral care. Although the importance of dental floss in oral health has been emphasized in literature.<sup>27</sup>

Strengths of this study includes the utility of a validated tool. Whereas, limitations of the study are as bad breath was assessed relying on self-perceived data without clinical examination. Since the questionnaire was in English language so illiterate individuals or people not using online tools got excluded from the study. Lastly, those participants who reported not to have halitosis, it was not clear whether they were free from it or afraid of telling as a result of embarrassment.

**CONCLUSION:**

Halitosis is a frequent problem most prevalent in male gender. It has medical and psychosocial impact. Although in general, people are aware of perceiving bad breath themselves, there is still a need for public awareness campaigns to disseminate more knowledge and management options regarding halitosis. Frequent visits to dental and medical healthcare professionals should be encouraged to mitigate this problem.

**Authors Contribution:**

**Mahnoor Khawaja M. Saleem:** Literature review and drafted the manuscript  
**Abhishek Lal:** Literature review, drafted the manuscript and data interpretation  
**Sabeen Masood:** Drafted the manuscript and performed data analysis  
**Dinaz Ghandhi:** Conducted final and critical review of the manuscript  
**Anum Arif Sitai:** Drafted the manuscript and collected data  
**Naseer Ahmed:** Performed final review and approval of the manuscript

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## PD-L1 in Breast Cancers and its Prognostic Significance

Sayher Kazmi, Sumayyah Shawana, Nighat Jamal

### ABSTRACT:

Breast cancer is the most common malignancy in females globally. Various factors are responsible for its development which include both genetic and hormonal causes. An important discovery is the role of the PD-1/PD-L1 axis in the development of cancers. The PD-1-/PD-L1 pathway plays a part in allowing tumour cells escape from the host's immune response and hence permits the proliferation of tumour cells. PD-L1 expression has been observed in various breast cancers at distinct levels such as in tissues and in blood. Different methods have been utilized for its detection including immunohistochemistry, RNA sequencing and ELISA, amongst others. The results have been conflicting regarding the expression of PD-L1 and the prognosis of breast cancer based on parameters such as overall survival and disease free survival. Different immunotherapies have also emerged as a new modality to treat breast cancer. This review intends to explore the prognostic significance of PD-L1 expression in breast cancers.

**Keywords:** Breast cancer, PD-L1, Prognosis

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### INTRODUCTION:

Breast cancer continues to be the leading malignancy in females worldwide. In 2018, the incidence of breast cancer was 2,088,849, which consisted 11.6% of the total cancers in both genders combined.<sup>1</sup> It is also the number one cancer reported in Pakistan amongst adults.<sup>1-2</sup> It is a heterogeneous disease resulting from a mixture of genetics and hormonal interplay. Around 12% of breast cancers emerge because of a mutated gene inheritance. Mutations in the tumour suppressor genes such as BRCA1, BRCA2, TP53 and CHEK 2 are liable in the causation of familial cancers, the most common being BRCA 1 and BRCA2 mutations. The risk factors for harboring breast cancer include diet, hormonal changes (early menarche, late menopause) radiation exposure, having a first degree relative with breast cancer and genetics.<sup>3</sup> Breast cancer can be divided according to its histological status and molecular subtypes, which include Luminal A, Luminal B, HER2 enriched and triple negative.<sup>3-5</sup>

Over the years the PD1/PDL1 pathway has gained enormous attention for the role it plays in tumour immune escape.<sup>6</sup> PD-1, also known as CD 279, was originally cloned in 1992,

and was primarily thought to be a part of the apoptotic pathway of cells.<sup>7</sup> It is a receptor located on T cells.<sup>8</sup> PD-L1, also known as B7-H1, is the ligand of PD-1.<sup>9</sup> Alongside being found on macrophages, dendritic cells and B cells, it is expressed on malignant cells.<sup>8</sup> The interaction of PD-1 and PD-L1 causes increased apoptosis of T cells, thus cancer cells have a route of evading the immune system.<sup>10</sup> It has been extensively studied that along with many other cancers, breast cancer cells overexpress the PD-L1 receptor.<sup>11-17</sup> PD-L1 has been found to be expressed in renal cell carcinomas,<sup>11</sup> non-small cell lung carcinomas,<sup>12</sup> colorectal carcinomas,<sup>13</sup> ovarian carcinomas<sup>14</sup> and melanomas.<sup>15</sup>

Prognosis can be defined as “the prospect of recovery as anticipated from the usual course of disease or peculiarities of the case”<sup>18</sup>. Prognosis in breast cancers is largely determined by the clinicopathological parameters. These include age, gender, tumor size, lymph node metastasis, lymphovascular invasion, neural invasion<sup>19</sup>, histologic subtype, grade, stage, mitotic figure count and hormone receptor status.<sup>20</sup> High expression or overexpression of PD-L1 can also influence prognosis as reviewed.

### METHODOLOGY:

A methodically comprehensive search was performed using NCBI PubMed database and Google Scholar. 73 relevant articles from the years 2000 to 2019 were found from this literature search. The studies were scrutinized and evaluated further for the magnitude and significance of breast cancer, and the prognostic value of PD-L1. Out of these articles, 50 were ultimately selected. Articles which were unrelated to the topic and obsolete texts were excluded. Based on these criteria, this review article was devised.

**Sayher Kazmi (M. Phil Student)**

Department of Pathology,  
Bahria University Medical and Dental College, Karachi  
Email: [kazmi.s@hotmail.com](mailto:kazmi.s@hotmail.com)

**Sumayyah Shawana**

Associate Professor, Department of Pathology  
Bahria University Medical and Dental College, Karachi

**Nighat Jamal**

Assistant Professor, Classified Pathologist  
PNS Shifa Hospital, Karachi

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### Literature review:

The city of Karachi, Pakistan, is stated to have the topmost incidence of breast cancer in Asian populations, excluding Israeli Jews. The reasons for this are not all entirely obvious, however, certain risk factors make the women more vulnerable to harboring it. It also accounts for one third of all female cancers.<sup>21</sup> In the United States and Europe, breast cancer incidence rate is four to seven times higher as compared to other countries, but since developing countries are implementing Western lifestyles, such as decreased breastfeeding and fewer number of pregnancies, it is predicted that by this year, 2020, 70% of breast cancer cases would be found in the developing countries.<sup>3</sup>

The PD-1 and PD-L1 combination is an immune checkpoint. Working together, they prevent cytotoxic T cells from performing an excess of their function, thus maintaining a steady state of T cell function and preventing over stimulation. However, tumor cells can take advantage of this route by expressing PD-L1 themselves, hence avoiding the immune system and proliferating.<sup>22</sup>

PD-L1 expresses in a variety of forms in different regions. It is seen in tissues, where it can be detected as protein<sup>23</sup> or mRNA<sup>24</sup>. Current evidence has shown that the membrane bound PD-1 and PD-L1 have circulating forms as well and hence may be detected in blood in the soluble form<sup>25,26</sup> or as exosomes<sup>27</sup>.

Consequently, there are a variety of methods and procedures for its detection which include immunohistochemistry (IHC), flow cytometry & ELISA, in situ hybridization, PCR, DNA microarrays and RNA sequencing<sup>28-33</sup>. There is currently no set standard for the evaluation and expression of PD-L1 and many challenges exist. PD-L1 expression had initially been determined through IHC in tumours but detection through IHC comes with its own share of limitations. Some include differences in antibody clones of different companies, the method used to score the variables, and the small innate differences in PD-L1 expression in the different types of specimens like surgical resection and biopsies, fresh frozen and archives, and primary and metastatic tumours<sup>34-35</sup>. Besides IHC, analysis at the protein or messenger RNA level have different cells involved in expression such as tumour cells or tumour infiltrating lymphocytes. Hence the availability and utilization of different techniques may be responsible for the differing results in literature<sup>36</sup>.

Prognosis is usually based on various parameters which includes overall survival, when the cause of death is not specified; disease free survival, the time period after treatment when no disease, or cancer, can be identified; and metastasis free survival, defined as the time from the start of treatment for cancer in which the patient is alive with no metastasis.<sup>37</sup> PD-L1 can be used as a prognostic marker in breast cancer, however, the relationship among overall survival, clinicopathological features and prognosis in general amongst

breast cancer patients is conflicting.

Several commentaries have suggested that expression of PD-L1 in breast cancer patients can be a favorable prognostic marker<sup>17, 38-40</sup>. It has been linked to negative lymph node metastasis and an increased tumour infiltrating lymphocyte count, leading to a better overall survival<sup>17</sup> and disease free survival.<sup>17, 38</sup> Cytoplasmic expression of PD-L1 in tumour cells is associated with a lower risk of breast cancer specific deaths, and both PD-L1 expression and tumour infiltrating lymphocyte count are related to a better outcome<sup>39</sup>.

Amongst the subsets of breast cancers, PD-L1 is seen to be more significantly expressed in the triple negative group or basal like tumours<sup>28</sup>, and in this subcategory, PD-L1 expression is associated with a favorable prognosis due to a better disease free survival.<sup>38</sup> It has also been observed that PD-L1 expression, when linked to poor prognostic features such as high tumour grade, was associated with a good relapse free survival specifically in the basal type, and not with the outcome of breast cancers in general<sup>40</sup>. Remarkably, PD-L1 expression has led to a better overall survival in some breast cancer cases which presented with poor clinicopathological features, probably due to an anti tumour response<sup>16,41</sup>. The expression of PD-L1 has also been reported to activate immune-related pathways such as IFN  $\alpha$ , IFN  $\beta$  and TNF  $\alpha$ , hence leading to a good prognosis and it seems to be the only prognostic element in metastasis free survival<sup>42</sup>.

Some evidence has concluded an opposing relationship regarding PD-L1 expression in breast cancer and prognosis, with its expression being associated with a poor overall survival and an independent negative prognostic factor<sup>43</sup>. Higher PD-L1 expression has also been observed in patients who were younger than 35, who presented at an advanced stage and those with a larger tumour size and hence are linked with a poor disease free and overall survival<sup>44</sup>. A meta-analysis which comprised of 5 studies and a total of 2546 breast cancer patients also showed a link between PD-L1 expression and a reduced overall survival<sup>45</sup>. PD-L1 expression is a poor prognostic marker in those triple negative breast cancers which have a low tumour infiltrating lymphocyte count.<sup>46</sup>

Along with the traditional treatments of chemotherapy and radiotherapy for breast cancers, immunotherapies are also emerging which have encouraging results.<sup>47</sup> Drugs targeting PD-1 or PD-L1 have been discovered to improve the outcome of the patients; these drugs include Pembrolizumab, Atezolizumab, Avelumab and Nivolumab<sup>48</sup>. According to a review study, 500 studies were carried out on anti PD-1 and anti PD-L1, using nine types of antibodies from at least 8 pharmaceutical companies, on approximately 20 types of hematological and solid malignant tumors.<sup>49</sup> This study further mentioned that some of the anti PD-1 and anti PD-L1 drugs have already been permitted by the US Food and Drug Administration (FDA). Trials conducted have shown

that these drugs, when used alone, may enhance a more favorable prognosis, and when they are used in combination with other drugs such as chemotherapeutics, the response is strengthened.<sup>50</sup> Since there are conflicting results in literature regarding the prognostic significance of PD-L1 in breast cancers, and because very scarce data is available in Pakistan as well in this regard, there is a dire need for conducting further researches and clinical trials in this domain to gain coherent results. Doing so, the results will eventually aid in the selection of proper immunotherapeutic drugs for the treatment of breast cancer, alongside the existing therapies.

### CONCLUSION:

Breast cancer continues to rank number one across the globe. Researches have demonstrated conflicting results regarding the expression of PD-L1 as an indicator of prognosis of breast cancer; which strongly supports the intense need of globally standardizing the detections methods & techniques, cut off values, scoring systems and sample sizes for obtaining consistent results. A finding revealed in most studies is that PD-L1 expression may be a good prognosis of breast cancer if it is associated with an increased tumour infiltrating lymphocyte count. This outcome may be due to the fact that increased PD-L1 expression causes a compensatory reaction of additional tumour infiltrating lymphocytes, which in turn provide the anti- tumour response, hence leading to a good prognosis. More research is warranted in this domain. Since plenty of research has also led to the conclusion that PD-L1 expression is a poor prognostic marker in breast cancer as well, anti- PD-1/PD L1 therapy is gaining momentum and is an encouraging breakthrough for treatment of breast cancer. Further studies and clinical trials are needed in this regard to evaluate the effect of immunotherapeutic drugs on breast cancers.

#### Authors Contribution:

**Sayher Kazmi:** Conceiving the idea, literature search, writing of the article

**Sumayyah Shawana:** Literature review, critical analysis of article

**Nighat Jamal:** Critical review of article

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## Rectal Duplication Cyst Mimicking Rectal Prolapse

Asrar Ahmad, Eelaf Karar, Irum Saleem, Nisar Ahmad

### ABSTRACT:

Gastrointestinal tract duplications are rare congenital malformations that are benign, presenting usually in childhood. Most common sites include the distal ileum and oesophagus. Rectal presentation is quite uncommon and is usually cystic. This is a case of a three year old boy who came with rectal prolapse. On further examination and imaging investigations a pre-sacral cyst was located and a diagnosis of rectal duplication was made. The cyst was completely excised by a posterior sagittal approach.

**Keywords:** Gangrene, Ileostom, laparotomy, volvulus.

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### INTRODUCTION:

The incidence of gastrointestinal duplication cysts is 1 in 10,000 live births and hence it is quite a rare congenital abnormality. Rectal duplications represent 5% of all duplications in the alimentary tract.<sup>1</sup> Most rectal duplications are cystic (94%) and are usually recognized as perianal abscesses, fistulas or tumours.<sup>2</sup> Knudtson *et al*<sup>3</sup> assess that up to 45% of rectal duplications are associated with a fistula to the anus or perianal region.<sup>3</sup> Tubular duplications of the rectum are generally located posteriorly and have been anterior to the rectum in only a few reported cases.<sup>4</sup> Most patients present with constipation, rectal bleeding, urinary tract infection, rectal prolapse, haemorrhoids and perirectal abscess. Diagnosis starts with ultrasound examination, plain radiography of the abdomen, contrast enema, computed tomography and MRI study.<sup>5</sup>

### CASE REPORT:

In December 2017 a three years old male child was referred from a peripheral hospital to Combined Military Hospital Nowshera, where he had undergone examination under anaesthesia (EUA). The mother complained of something coming out of anus on defecation for the last four months. The mass would at times reduce spontaneously and at times

would cause pain and had to be reduced manually. Moreover, it will not comprise the whole circumference of the anus. There was no history of constipation, diarrhoea or bleeding per rectum. On EUA they found a large bulging mass in the posterior wall of the rectum. On digital rectal examination a cystic mass was palpable in the posterior wall of the rectum. The upper limit could be reached. The overlying rectal mucosa was normal. No communication with the rectum was visible. His complete blood counts, serum electrolytes and renal function tests were normal. Ultrasound pelvis was suggestive of a cystic lesion in the presacral space. CT scan pelvis was suggestive of a well-defined round to oval shaped, non-enhancing, cystic mass lesion in presacral region measuring about 3.7×3.3×3.5 cm. It was compressing the rectum antero-laterally with indistinct interface. The interface with sacrum was intact and there was no erosion of bone. A diagnosis of rectal duplication cyst was made (Figure.1). He was prepared for surgery. Gut preparation was done. The cyst was approached through posterior sagittal incision. The muscularis propria of rectum was opened and the cyst was excised completely without opening the mucosa of rectum (Figure.2). The muscularis propria was repaired with absorbable interrupted sutures and skin wound closure done with subcuticular suture. He made a smooth post-operative recovery and was discharged on the 4<sup>th</sup> post-operative day. The patient recovered completely and follow up revealed no complaints. A signed informed consent was obtained from the guardian of the child for writing and publishing this case report.

### DISCUSSION:

Gastrointestinal (GI) duplications are a very uncommon but complex set of embryological disorders that can involve any part of the alimentary canal from the tongue to the anus. Duplications of any kind share common characteristics like, they are hollow, lined with gastrointestinal tract epithelium and have a smooth muscle wall. Gastrointestinal duplications were initially believed to be more common in males but it was later confirmed that there is an equal male to female ratio.<sup>6</sup>

**Asrar Ahmad**  
Classified Paediatric Surgeon,  
PNS Shifa Hospital, Karachi  
E-mail: [drasrar.ahmad@yahoo.com](mailto:drasrar.ahmad@yahoo.com)

**Eelaf Karar**  
Medical Officer,  
PNS Shifa Hospital, Karachi

**Irum Saleem**  
Registrar, Department of Gynaecology  
Bahria University Medical Dental College, Karachi

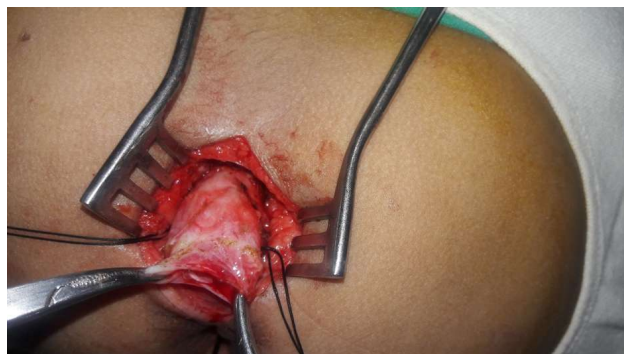
**Nisar Ahmad**  
Medical Officer,  
Hayatabad Medical Complex, Peshawar

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Figure.1 CECT Scan of abdomen showing pre-sacral cystic mass



Figure.2 Rectal duplication cyst from a posterior sagittal approach



Colonic duplications account for 15% and rectal duplications account for 5% of all alimentary canal duplications.<sup>7,1</sup> The exact pathogenesis of duplications is unknown and multiple theories have been put forward. According to the most credible theory, as the rapidly growing endothelial cells occlude the intestinal lumen, vacuoles form inside the cell masses due to the growth of the intestine. These vacuoles fuse to create a single lumen intestine. If one of these vacuoles pinches off, they can create a secondary lumen, which may entirely be separated from the main lumen but grows in proportion to the main lumen. Colonic duplications can be cystic or tubular involving a limited portion of the colon or be extensive. They are usually divided into two types, type I and II. Type I usually has partial involvement of the colon or rectum while type II has a wider spectrum as in addition to colon and rectum, there can also be associated congenital anomalies including duplication of the lower genitourinary tract, double appendices, situs inversus and neural tube defects. Ultrasonography and contrast studies are most widely used. Computed tomography (CT) and magnetic resonance imaging (MRI), although less often used, are helpful in localizing and diagnosing complex duplications.<sup>8</sup> Rectal Duplications are treated with complete surgical excision of the cyst by transanal, transcoccygeal or posterior sagittal approach. Other less invasive ways include transanal endoscopic microsurgery or transabdominal laproscopic surgery.<sup>9</sup> These duplication may mimic a tail gut cyst, anterior sacral meningocele, cystic sacrococcygeal teratoma, anal duct or gland cyst, necrotic rectal leiomyosarcoma, dermoid cyst, epidermoid cyst, cystic lymphangioma, neuroenteric cyst and necrotic sacral chordoma.<sup>10</sup>

Tail gut cysts are usually multilocular and present later in life. Epidermoid cysts are thin walled filled with clear fluid.

Dermoids are heterogenous with skin appendages. Sacrococcygeal teratomas are also heterogenous lesions with mixed cystic and solid components. Anterior sacral meningocele and neuroenteric cysts are better differentiated with MRI because of its communication with the subarachnoid space.

#### CONCLUSION:

Although rare, gastrointestinal tract duplications can present by various ways and have to be ruled out in case of suspicion by good imaging modalities and then be treated with complete surgical excision by a favourable approach to relieve symptoms and prevent complications.

#### Authors Contribution:

**Asrar Ahmad:** Operating surgeon & discussion

**Eelaf Karar:** Write up

**Irum Saleem:** Write up

**Nisar Ahmad:** Referencing Discussion

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## Online Learning is a Way Forward During Pandemic

Syeda Rida Baqir, Abida Arif

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COVID-19 or corona virus is a natural disaster which is provoking panic throughout the world. Against this new pandemic virus, no vaccine is available. Many countries are affected by this Pakistan a large number of cases observed throughout Pakistan were recorded.<sup>1</sup> Due to the COVID-19, colleges and universities is seriously affected since March 2020. Constraint recommended by the government and other organizations to address the educational process by strictly following protective measures against coronavirus for teachers, and learners. Several institutes have stopped all physical classes in universities and schools, including practical sessions. The educational process is facilitated through online in account of safety measures against coronavirus.<sup>2</sup>

Globally, many teachers and students show enthusiasm towards the delivery of education through online mode. Teachers have already making plans that how to provide effective online lessons to their students.<sup>3</sup>

There are many degrees awarding institutes which are authorized by Higher Education Commission (HEC) in Pakistan.<sup>4</sup> Online education, examinations and assessments are started by University of health Sciences (UHS), during this pandemic COVID -19.

Online education is also called electronic learning it is the interaction between educators and learners through internet service desktop, laptop or mobile. It comprises of multiple formats like video, audio, documents etc. Following are the online modalities through which online quality education can be maintained.

1) Online lectures which can be given through different applications like zoom, Microsoft teams, google classroom, hang out etc

2) Online tutorials (asynchronous) it comprises of online multimedia learning tutorials in which video, animations,

assignments and quizzes are used at the available resources for this purpose are: Aquifer, FOAMed, MedEdPortal, the New England Journal of Medicine video series or OpenPediatrics.<sup>5</sup>

3) Online videos is commonly available platform, through which practical skills can be studied or synchronous online video.

4) Tele school is the channel which is launched by education ministry of Pakistan in corona virus season of lockdown through PTV (Pakistan television). This channel work for the promotion of education in Pakistan. The Education Minister of Pakistan 2020 said that the channel will be accessible from 8am to 6pm for class 1 to class 12. The Prime Minister of Pakistan 2020 has given the suggestion that this channel ought to carry on afterward the ended. The Prime Minister said it will be beneficial for the promotion of education in distant zones of our country while the

### Authors Contribution:

| Syeda Rida Baqir: Final editing |

| Abida Arif: Final proof reading |

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**Syeda Rida Baqir**

Senior Lecturer  
Bahria University College of Physical Therapy  
Bahria University Medical & Dental College

**Abida Arif**

Senior Lecturer,  
Bahria University College of Physical Therapy  
Bahria University Medical & Dental College

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