ISSN: 199-7124 (Print)
NLM ID: 101184601
www.bmcjournal.com

Bangladesh Medical College Journal

Vol. 25 January 2020 No.1

Contents

BANGLADESH MEDICAL COLLEGE JOURNAL

Vol. 25 No. 1 January 2020

Official Publication of Bangladesh Medical College
(Recognized by BMDC)

EDITORIAL BOARD

MEMBERS

Address for Correspondence: Prof. Sharmeen Yasmeen, Professor & Head, Dept. of Community Medicine
Bangladesh Medical College, House # 34, Road # 14A, Dhanmondi R/A, Dhaka-1209
Phone: (88-02) 44812101-6, Fax: (88-02) 9125655
E-mail: sharmeenbmc@yahoo.com, Web: www.bmcjournal.com

Bangladesh Medical College Journal

INFORMATION FOR CONTRIBUTORS

- This peer reviewed journal publishes original papers, case reports and reviews in all branches of medical science. The style of the papers should be in the modified Vancouver style (Ref: New England Journal of Medicine 1991; 324 : 424-8).

- Paper should be submitted to the Editor, Bangladesh Medical College Journal, Road No.14/A, House No. 34, Dhanmondi R/A, Dhaka-1209. Papers should be written in English and three copies must be submitted with three sets of illustrations. Manuscripts should be typed on one side of white paper (size-A4) with margins of at least one inch.

Paper should be accompanied by a soft copy or preferably CD in Microsoft Word

- Double spacing should be used throughout. Each of the following sections should begin on separate pages as: title, abstract and key words, text, acknowledgements, references, individual tables and legends. Pages should be numbered consecutively beginning with the title page. The title page should carry (a) the title of the article, (b) name of each author with highest academic degree (s) and institutional affiliation, (c) name of the department and institute where the work was carried out, and (d) name and address of the authors to whom correspondences should be addressed.

- Original articles should have following headings:
  Abstract, Introduction, Materials and Methods, Results, Discussion, Acknowledgements (if any), References. Manuscripts must be accompanied by a covering letter. This must include: (a) a statement that the work has not been published or submitted for publication elsewhere, (b) a statement that the manuscript has been read, approved and signed by all authors. Any work which has been carried out in part or fully abroad, must be accompanied by a letter from the head of the institution where the work was done stating that the work has been carried out in that institute and that there is no objection to its publication in this journal.

- If the article is a whole or a part of the dissertation or thesis submitted for a post graduate degree should be mentioned in which case the name of the worker and the guide must be mentioned and must be permitted for publication by the competent authority of the institute where the work has been done.

- The abstract of the work should be of less than 200 words. Each table should be typed double spaced on a separate sheet. A brief title of each table should be supplied. Figures should be professionally drawn and photographed. Photographs should be on glossy papers (usually 5 x 7 inch). These should not be inserted into the text but marked on the back with the figure numbers, title of the paper and name of author. The top of the figure should be indicated. All photographs, graphs, diagrams should be referred to as figure and numbered consecutively in the text in Arabic numerical. The legends for figures should be typed on a separate sheet.

- Ethical aspects will be considered in the assessment of papers and authors should indicate in methods whether permission of relevant ethical committee has been taken if needed (see the World Medical Association's code of ethics. Brit Med J 1964; 2: 177). Statistical methods used should be described in enough detail to enable a knowledge- able reader with access to the original data to veri- fy the reported results. Study design should be stated with details about randomization.

Editorial

COVID-19: A Global Health Crisis of 21st Century

Begum N

The coronavirus, COVID-19 pandemic is the defining global health crisis of our time and the greatest challenge we have faced since World War II. First emerging as a small outbreak of viral pneumonia of unknown aetiology from a sea food market in China ultimately was announced by World Health Organization (WHO) in January 2020 as a novel Coronavirus to be associated with the disease. A novel coronavirus (nCoV) is a new strain that has not been previously identified in humans. Based on clinical criteria and available serological and molecular information, the new disease was called coronavirus disease of 2019 (COVID-19), and the novel coronavirus was called SARS Coronavirus-2 (SARS-CoV-2), emphasizing its close relationship to the SARS virus (SARS-CoV) of 2002, causative agent of Severe Acute Respiratory Syndrome. The WHO declared the outbreak as a Public Health Emergency of International Concern on 30 January 2020.

Coronavirus is a positive-sense RNA virus having four main subgroups—alpha, beta, gamma, and delta—based on their genomic structure. Alpha and beta coronaviruses infect only mammals. In 2002–2003, the severe acute respiratory syndrome coronavirus (SARS-CoV) caused a SARS epidemic in China that resulted in 10% mortality. Similarly, the Middle East respiratory syndrome coronavirus (MERS-CoV) caused a devastating pandemic in 2012 with 37% mortality rate in Middle East. All coronaviruses that have caused diseases to humans have had animal origins. In the case of SARS-CoV and MERS-CoV, detailed investigations suggest these viruses have likely to be originated from bats and then jumped into another amplification mammalian host, Himalayan palm civet cat for SARS-CoV and Dromedary camel for MERS-CoV. Recent SARS-CoV2 which is the agent of COVID-19 is presumed to originate in bat & gain access to human via Pangolin, an exotic animal.

The SARS-related coronaviruses are covered by spike (S) proteins that contain a variable receptor-binding domain (RBD). This RBD binds to angiotensin-converting enzyme-2 (ACE-2) receptor found in various human tissues. Spread of SARS-CoV-2 is predominantly via respiratory droplet, contact and rarely via fecal-oral route. Primary viral replication is presumed to occur in mucosal epithelium of upper respiratory tract with further multiplication in lower respiratory tract and gastrointestinal mucosa, giving rise to a mild viremia. ACE-2 is broadly expressed in nasal mucosa, bronchus, lung, heart, oesophagus, kidney, stomach, bladder and ileum, and these human organs are all vulnerable to SARS-CoV.

Acute Respiratory Distress Syndrome (ARDS) is a life-threatening lung condition that prevents enough oxygen from getting to the lungs and into the circulation, accounting for mortality of most respiratory disorders and acute lung injury. In fatal cases of COVID-19, individuals exhibit severe respiratory distress requiring mechanical ventilation. Previous studies have found that genetic susceptibility, and inflammatory cytokines were closely related to the occurrence of ARDS.

Coronaviruses are in general spread most often by respiratory droplets and contacts. Droplet transmission is typically limited to short distances, generally less than 2 m. Once infected droplets have landed on surfaces, their survivability on those surfaces determines if contact transmission is possible. Based on our current understanding from other beta coronaviruses including SARS and MERS, they can survive and remain infectious from 2 hours up to 9 days on inanimate surfaces such as metal, glass or plastic, with increased survival in colder and dryer environments. Understanding of incubation period is very important as it allows health authorities to introduce more effective quarantine systems for suspected cases. The best current estimates of the SARS-CoV-2 infection incubation period ranges from 2 to 14 days.

For diagnosis of Corona virus RT-PCR is the gold standard test though its specificity is 100% and sensitivity is around 60-70%. This test detects RNA of the SARS-CoV-2 and is used to confirm very recent or active infections. RT-PCR test can be done with respiratory samples including nasopharyngeal swab, oropharyngeal swab or nasal swab obtained by various methods. For control of infection measures like aggressive testing for case detection, isolation, contact tracing, quarantine and supportive treatment are important.

The most important preventing measure is wearing face mask as the virus mainly spread through respiratory droplets. The type of mask varies according to occupation of individual; N-95 mask is mandatory for those health care professionals who are in direct contact with COVID-19 patients admitted in hospital whereas surgical mask or simple cloth mask may be enough for general people. Then maintenance of cough etiquette and social distance for at least 3-6 feet specially in public places and working environment, washing of hands often with soap and water for at least 20 seconds after blowing of nose, coughing, sneezing or touching any contaminated objects are other paramount of importance. Hand sanitizers containing at least 60% alcohol can be used as an alternative where washing facilities are not available. So far no specific treatment came out and countries across the globe have teamed up to develop an effective vaccine against the novel coronavirus.

We know that prevention is better than cure. The best policy to combat COVID-19 includes combined and coordinated preventive and control measures. Evidence based information should be disseminated to change the attitude and practice of people towards a healthy lifestyle and behaviour.

Prof. Dr. Nilufar Begum; MBBS, M. Phil, WHO Fellow
Professor and Head, Dept. of Microbiology
Bangladesh Medical College

References:

1. Zhu N, Zhang D, Wang W, Li X, Yang B, Song J, Zhao X, Huang B, Shi W, Lu R et al. A Novel Coronavirus from Patients with Pneumonia in China, 2019. N. Engl. J. Med. 2020; 382: 727-733
2. C Huang, Y Wang, X Li, L Ren, J Zhao, Y Hu et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. Lancet 2020; 395 (10223): 497-506
3) M Bassetti, A Vena, D Roberto Giacobbe. The Novel Chinese Coronavirus (2019-nCoV) Infections: challenges for fighting the storm. Eur. J. Clin. Invest. 2020; A3209
4) R Lu, X Zhao, J Li, P Niu, B Yang, H Wu et al. Genomic characterization and epidemiology of 2019 novel coronavirus: implications for virus origins and receptor binding. Lancet 2020; 395 (10224): 565-574
5) D S Hui, E IA, T A Madani, F Ntoumi, R Kock, O Dar et al. The continuing 2019-nCoV epidemic threat of novel coronaviruses to global health - the latest 2019 novel coronavirus outbreak in Wuhan, China.Int. J Infect Dis 2020; 91: 264-266
6) J Cui, F Li, Z L Shi. Origin and evolution of pathogenic coronaviruses. Nat Rev Microbiol 2019:17: 181-192
7) Managing epidemics, key facts about major deadly diseases. Geneva: World Health Organization; 2018. (https://apps.who.int/iris/handle/10665/272442).
8) World Health Organization Press Conference. The World Health Organization (WHO) Has Officially Named the Disease Caused by the Novel Coronavirus as COVID-19.
9) Gorbalenya AE, Baker SC, Baric RS, de Groot RJ, Drosten C, Gulyaeva AA, Haagmans BL, Lauber C, Leontovich AM, Neuman BW et al. Severe acute respiratory syndrome-related coronavirus: The species and its viruses- A statement of the Coronavirus Study Group. bioRxiv 2020. [Google Scholar]
10) Huang C, Wang Y, Li X, Ren L, Zhao J, Hu Y, Zhang L, Fan G, Xu J, Gu X et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. Lancet (Lond. Engl.) 2020; 395:497-506
11) Xiong C, Jiang L, Chen Y, Jiang Q. Evolution and variation of 2019-novel coronavirus. bioRxiv 2020.
12) Hui DS, Azhar E, Madani TA, Ntoumi F, Kock R, Dar O, Ippolito G, McHugh TD, Memish ZA, Drosten C et al. The continuing 2019-nCoV epidemic threat of novel coronaviruses to global health-The latest 2019 novel coronavirus outbreak in Wuhan, China. Int. Soc. Infect. Dis. 2020; 91: 264-266.
13) N Chen, M Zhou, X Dong, J Qu, F Gong, Y Han, et al. Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China**:** a descriptive study**.** Lancet 2020; 395 (10223): 507-513,
14) Guo YR, Cao QD, Hong ZS, Tan YY, Chen SD, Jin HJ, Tan KS, Wang DY, Yan Y. The origin, transmission and clinical therapies on coronavirus disease 2019 (COVID-19) outbreak- An update on the status. Mil. Med. Res. 2020; 7: 11.
15) Du L, He Y, Zhou Y, Liu S, Zheng BJ, Jiang S. The spike protein of SARS-CoV: a target for vaccine and therapeutic development. Nat. Rev. Microbiol. 2009; 7: 226-236.
16) Pardi N, Hogan MJ, Porter FW, Weissman D. mRNA vaccines- A new era in vaccinology. Nat. Rev. Drug Discov. 2018; 17: 261-279.
17) Ahmed SF, Quadeer AA, McKay MR. Preliminary identification of potential vaccine targets for 2019-nCoV based on SARS-CoV immunological studies. BioRxiv 2020; 12: 254.

Clinical presentation of ectopic pregnancy patients: Experience of 48 cases in a selected tertiary hospital in Dhaka city

Fatema N[a], Munira S[b], Hasan K A M M[c], Khatun S[d]

Abstract

Background: Ectopic pregnancy patients can be presented with different clinical features. It often poses the greatest diagnostic problem. The early diagnosis of a tubal pregnancy before tubal rupture would significantly reduce mortality or morbidity of mothers.

Objective: The objective of the present study was to evaluate the clinical presentations of ectopic pregnancy patients aiming at quick management.

Methods: This cross-sectional study was carried out in the inpatient Department of Obstetrics and Gynaecology at Bangladesh Medical College Hospital, Dhaka, Bangladesh from January 2012 to December 2012 for a period of one year. All clinically suspected cases of ectopic pregnancy within the reproductive age admitted in the study place were included in the present study. After taking detailed history with particular scrutiny of the menstrual, obstetric and contraceptive histotry, a thorough physical examination was performed and ectopic pregnancy was diagnosed clinically in a large number of cases.

Results: A total number of 48 cases were confirmed as ectopic pregnancy. All the cases had abdominal pain and 94.0% patients had a period of amenorrhoea; 50.0% patients had early pregnancy symptoms, 44.0% had per vaginal bleeding and 42.0% had syncope. Among all ectopic pregnancy cases majority 27(56.2%) patients had amenorrhea of 6 to 8 weeks. All the cases had abdominal tenderness. Most of the cases 28(58.3%) had pain on movement of cervix. However, 22(45.8%) patients presented with abnormal per vaginal bleeding. Among all cases 40(83.3%) cases had severe pain. About 45(93.7%) cases of the patients of ectopic pregnancy had radiation of pain. Of all cases 21(43.7%) cases had associated per vaginal bleeding and 27(56.3%) cases had no per vaginal bleeding.

Conclusion: Abdominal pain, vaginal bleeding, abdominal tenderness, amenorrhoea for 6 to 8 weeks and pain on movement of cervix are the most common clinical features of women with ectopic pregnancy. Prompt evaluation of clinical manifestation is the key component for appropriate management of ectopic pregnancy without any sufferings.

Keywords: Ectopic pregnancy, Clinical presentation, Fallopian tube, Amenorrhoea.

Introduction:

Ectopic pregnancies could be occurred in any segment of the fallopian tube, uterine horns which includes the interstitial portion of the tube, cervix, ovary, and abdominal cavity.[1] The commonest site of ectopic implantation is fallopian tube, which is about 95.0% cases to 98.0% cases; however, other sites are the uterine horns 2.0% to 2.5% cases; the ovary, cervix and abdominal cavity are less than 1.0% case.[2]

The problem of ectopic pregnancy is essentially a diagnostic one, as it can present in a different number of ways-acute, silent or chronic.[3] It is often chronic group which poses the greatest diagnostic problem. The emphasis today is on the early diagnosis of a tubal pregnancy before tubal rupture, for this would significantly reduce mortality or morbidity and also improve the conception rate by permitting conservative tubal surgery.[4] A high index of suspicion and modem diagnostic methods are necessary to identify an ectopic pregnancy. Serum beta-hCG, ultrasound and laparoscopy are the confirmatory diagnostic methods.[5]

Chronic presentation can frequently give rise to diagnostic confusion.[6] The quiet or chronic picture is seen when intraperitoneal bleeding from the tube is small in amount, however, recurrent as the tubal abortion or mole. This patient

a. Dr. Naheed Fatema; FCPS, MCPS, MBBS
Resident Surgeon, Department of Obstetrics and Gynecology
Bangladesh Medical College Hospital, Dhaka

b. Dr. Sherajum Munira; MBBS
Assistant Registrar, Department of Obstetrics and Gynecology
Kurmitola General Hospital, Dhaka

c. Dr. K. A. M. Mahbub Hasan; MD, MBBS
Medical Officer, Department of Cardiology
National Institute of Cardiovascular Diseases, Dhaka

d. National Professor Dr. Shahla Khatun; FRCOG, FCPS, FICS, MBBS
Chairman, Green Life Medical College Hospital, Dhaka

Correspondence to:
Dr. Naheed Fatema; FCPS, MCPS, MBBS
Resident Surgeon, Department of Obstetrics and Gynecology
Bangladesh Medical College Hospital, Dhaka
Email: dr.naheedkoly@gmail.com

has a short period of amenorrhoea with early pregnancy symptoms. The menstrual period is over due by few weeks, distension or contraction of the tube may cause pain to one illiac fossa.[7] The seventy of pain depends on the amount of blood loss and there is nearly always associated syncope. The combination of pain and syncope is the most constant and characteristic symptoms of ectopic pregnancy.[8] There may be referred pain to the shoulder. Slight vaginal bleeding may follow lower abdominal pain. Once this bleeding has begun it tends to continue without intermission. This is a diagnostic feature. Tenderness, abdominal muscle guarding over the lower abdomen, especially on the affected side is a striking feature. Haemoperitoneum of 2 or 3 weeks standing can cause the appearance of bruising around the umbilicus.[9] This present study was undertaken to evaluate the clinical presentations of women with ectopic pregnancy**.**

Material and Methods:

This was a descriptive type of cross-sectional study. The study was carried out in the inpatient Department of Obstetrics and Gynaecology at Bangladesh Medical College Hospital, Dhaka, Bangladesh from January 2012 to December 2012 for a period of one year. All clinically suspected cases of ectopic pregnancy within the reproductive age admitted in the department of Obstetrics and Gynaecology at the Bangladesh Medical College Hospital, Dhaka during the study period were included in this study. Patients other than ectopic pregnancy were excluded from this study. The sampling technique was non-probability purposive sampling. After taking detailed history with particular scrutiny of the menstrual, obstetric and contraceptive history, a thorough physical examination was performed and ectopic pregnancy was diagnosed clinically. In some cases, investigations like pregnancy test, βhCG and ultrasonography were done to support the clinical diagnosis. Hemoglobin estimation and blood grouping was done in all cases. Data were collected on initial presentation, chief complaints, past obstetrics and gynaecological history, history of previous surgeries (tubal, ovarian and/or uterine), history of infertility and use of ovulation induction and history of contraception and were documented on a pretested semi-structured questionnaire and a checklist. Laboratory findings and treatment history was also recorded. Data collection were conducted by the researcher herself. All data were compiled and edited meticulously by thorough checking and rechecking. All omissions and inconsistencies were corrected and were removed methodically. Quantitative data were expressed as mean and standard deviation and qualitative data were expressed as frequency distribution and percentage. Statistical analysis was performed by using SPSS for windows version 12.0. Probability value <0.05 was considered as level of significance with a 95% confidence limit. Prior to the commencement of this study, the research protocol was approved by the ethical committee (Local Ethical committee) of the Bangladesh Medical College Hospital, Dhaka. Informed consent was taken from the respondents prior to interview.

Results:

In this study a total of 48 cases were confirmed as ectopic pregnancy based primarily on clinical presentations.

Table 1: Distribution of ectopic pregnancy cases according to age (n=48)

Age Group	Frequency	Percent
Less than 20 years	14	30.55
21 to 25 years	20	41.66
26 to 30 years	10	19.44
More than 30 years	4	8.33
Total	**48**	**100.0**

Mean age=24±2.87

Majority of the cases 20(41.66%) were in 21 to 25 years' age group followed by < 20 years and 26 to 30 years of age group which were 14(30**.**55**%)** cases and 10**(**19.44%) cases respectively. The mean age with SD of the study population was 24.0±2.87 years (Table 1).

Table 2: Distribution of presenting symptoms among the ectopic pregnancy cases

Presenting Symptoms	Frequency	Percent
Abdominal pain	48	100.0
Period of Amenorrhoea	40	94.4
P/V Bleeding	20	44.4
Early Pregnancy Symptoms	24	50
Syncope	18	41.7
Shock	12	25

All the cases (100.0%) had abdominal pain and 94.0% patients had a period of amenorrhoea, 50.0% patients had early pregnancy symptoms, 44.4% had per vaginal bleeding and 42**.0%** had syncope and 25.0% of patient presented with shock (Table 2).

Table 3: Distribution of duration of amenorrhea among ectopic pregnancy cases

Amenorrhoea	Frequency	Percent
6 to 8 weeks	27	56.2
More than 8 weeks	19	39.6
No period	2	4.2
Total	**48**	**100.0**

Among all ectopic pregnancy cases 19(39.6%) patients had more than 8 weeks amenorrhoea; 27(56.2%) patients had amenorrhea of 6 to 8 weeks and 2(4**.**2%) patients had no period of amenorrhoea (Table 3).

Table 4: Distribution of different signs of ectopic pregnancy cases

Various signs	Frequency	Percent
Abdominal tenderness	48	100.0
Abdominal rigidity	12	25.0
Muscle guard	0	0.0
Adnexal mass	8	16.7
Rebound tenderness	6	12.5
Pain on movement of cervix	28	58.3
Per vaginal Bleeding	22	45.8

All the cases (100%) had abdominal tenderness. Most of the cases had pain on movement of cervix which was 28(58.3%) cases. However, 22(45.8%) patients presented with abnormal per vaginal bleeding; 8(16.7%) patients had adnexal mass and 12(25.0%) patients had presented with abdominal rigidity (Table 4).

Table 5: Distribution of cases according to character of pain

Character of pain	Frequency	Percent
Severe pain	40	83.3
Dull pain	8	16.7
Total	**48**	**100.0**

Among all cases majority 40(83.3%) cases had severe pain only while 8(16.7%) patients had dull pain (Table 5).

Table 6: Distribution of study cases according to radiation of pain

Radiation of Pain	Frequency	Percent
Yes	45	93.7
No	3	6.3
Total	**48**	**100.0**

Table 6 shows that most of the cases 45(93.7%) had radiation of pain and 3(6.3%) cases had no radiation.

Table 7: Distribution of cases according to per vaginal bleeding

Per vaginal bleeding	Frequency	Percent
Present	21	43.7
Absent	27	56.3
Total	**48**	**100.0**

Of all cases 21(43.7%) cases had per vaginal bleeding and 27(56.3%) cases had no per vaginal bleeding (Table 7).

Discussion:

In this study, the presenting symptoms of ectopic pregnancy were analyzed. All (100.0%) cases had lower abdominal pain; 94.0% patents had a period of amenorrhoea; 44.0% patients had per vaginal bleeding; 50.0% patients had early pregnancy symptom and 42.0% patients had syncope attack. Archibong et al[4] found that the presenting symptom in order of frequency were abdominal pain 93.0% cases, vaginal bleeding 61.0% cases, amenorrhoea, fainting attack and shock were 46.0% cases, 5.0% cases and 2.0% cases respectively. In this present study, 25.0% cases are in shock which is higher in Zabin[9] study (94.0%), Kulsum[10] study (45.0%); however, this is almost similar to Parveen[11] study (28.0%). These studies clearly figure out that, patients presented with shock are reducing day by day which indicates that the patients are getting aware of the situation.

In this study, history of amenorrhoea of 6 to 8 weeks was about 56.0% cases which is similar to another finding by Kulsum[10] which was 53.0% cases. In another local study, Parveen[11] shows 62.5% patients with 6 to 8 weeks amenorrhoea. Besides this, it had been found that 6.0% cases had no history of amenorrhoea, which was close to finding by Kulsum.[10]

The clinical features of ectopic pregnancy are not unique to the condition. It has been found that 75.0% women presents with sub-acute symptom and 25.0% or less with acute abdomen. The common presenting features are lower abdominal pain delayed or irregular menstruation followed by vaginal bleeding or brown discharge and syncope.

Clinical finding of these cases showed many important signs. Among them, abdominal tenderness is present in 100.0% cases of ectopic pregnancy. Archibong et al[4] have found the above stated sign in 90.8% cases in their series. Zabin[9] and Kulsum[10] have mentioned in their study 100% of the cases had abdominal tenderness while Parveen[11] has found 96.6% in the cases. Therefore, signs of ectopic pregnancy in this study and other's observation show a constant and similar rate. Adnexal mass is present in 17.0% cases, while movement of cervix producing pain in 39.0% cases in this present study. Kulsum[10] has observed 13.0% cases with adnexal lump and 81.0% of cases produced pain on movement of the cervix. Archibong et al[4] have found that palpable adnexal mass is present in only 2.0% cases while cervical excitation test is present in 56.0% cases. This may be due to the fact that, cases may have been diagnosed earlier due to the presence of better investigation facilities.

The possible finding on vaginal examination include arterial pulsation in the fornix on the affected side, an irregular and tender enlargement of the appendage on the affected side and an ill-defined tender semisolid swelling in the pouch of Douglas, indicative of pelvic haematoma.[12] Tenderness in the pelvis is the most constant sign. The patient looks pale and the pulse is likely to be raised especially after an attack of pain. A long standing haemoperitoneum however, can cause a high leucocyte count; this in association with low haemoglobin level is a diagnostic point.[13]

During acute presentation there is a sudden massive intra peritoneal hemorrhage and is typical of tubal rupture rather than tubal abortion.[7] It may supervene on a previously chronic picture. After a short period of amenorrhoea and sometimes none, the patient is seized with sever lancinating pain in one illiac fossa or in the hypogastrium.[14] This is immediately followed by profound collapse marked by pallor, low blood pressure subnormal temperature and a weak rapid pulse. Usually however the haemorrhage is temporarily arrested and the general condition improve within few hours but pain persists. Pain is typically referred to shoulder tip or interscapular area due to irritation of the diaphragm by blood and this may be provoked by laying the patient down, raising the foot end of the bed.[11]

Examination reveals obvious signs of shock and anaemia.[15] The abdomen is tender; furthermore, the presence of free blood in the peritoneal cavity may be indicated by dullness in the flanks and intestinal distension in frontal.[12] Body temperature is normal and there may be a moderate leucocytosis. Vaginal examination should be done very gently. Acute tenderness and the production of pain by movement of the cervix are the characteristic sign (cervical excitation). Some enlargement of one adnexa may be detected but this sign in not so easy to elicit because of tenderness.

Conclusion:

In conclusion abdominal pain, amenorrhoea, early pregnancy symptoms, per vaginal bleeding and syncope are the most common symptoms associated with the ectopic pregnancy. However, in the majority of study population abdominal tenderness, pain on movement of cervix, abnormal per vaginal bleeding, adnexal mass and abdominal rigidity are found during examination. Most of the patients are presented with severe abdominal pain. Furthermore, most of the patients are presented with radiation of pain. Further large scale should be conducted to get the real scenario.

References:

1. Kumar P, Malhotra N. Ectopic Pregnancy. In: Jeffcoate's principles of Gynaecology 7th edition. Chapter 9. New Delhi/London Arnold.2008:142-160
2. Barnhart KT. Ectopic pregnancy. New England Journal of Medicine. 2009 Jul 23;361(4):379-87.
3. Gaddagi RA, Chandrashekhar AP. A Clinical Study of Ectopic Pregnancy. Journal of Clinical & Diagnostic Research. 2012 Jun 1;6(5):867-869
4. Archibong E, I Sobanda A. Ectopic pregnancy. In Abudhabi, Saudia Arabia. Saudia Medical Journal, 2000; Vol. 21(4): 330-334
5. de Bennetot M, Rabischong B, Aublet-Cuvelier B, Belard F, Fernandez H, Bouyer J, Canis M, Pouly JL. Fertility after tubal ectopic pregnancy: results of a population-based study. Fertility and sterility. 2012 Nov 1;98(5):1271-6.
6. Rotas MA, Haberman S, Levgur M. Cesarean scar ectopic pregnancies: etiology, diagnosis, and management. Obstetrics & Gynecology. 2006 Jun 1;107(6):1373-81.
7. Shetty S, Shetty AK. A Clinical Study of Ectopic Pregnancies in a tertiary Care Hospital of Mangalore, India. Innovat J Med Health Sci. 2014;4(1):305-9.
8. Shukla DB, Jagtap SV, Kale PP, Thakkar HN. Study of ectopic pregnancy in a tertiary care centre. Int J Reprod Contracept Obstet Gynecol. 2017 Mar 6;6(3):975-979.
9. Zabin F. Study on clinical presentations, management and operative findings of ectopic pregnancy. IPGMR Dhaka, 1998 [FCPS Dissertation].
10. Kulsum SU. Study on risk factors, clinical presentations and operative management of Ectopic pregnancy, IPGMR, Dhaka, 2002, [FCPS Dissertation]
11. Parveen R. Clinicopathological study of tubal ectopic pregnancy. A study of 60 cases, IPGMR, Dhaka 1992 [FCPS Dissertation]
12. Lawani OL, Anozie OB, Ezeonu PO. Ectopic pregnancy: a life-threatening gynecological emergency. International journal of women's health. 2013; 5:515
13. Wakankar R, Kedar K. Ectopic pregnancy-a rising trend. International Journal of Scientific Study. 2015 Aug;3(5):18-22.
14. Fathima ARN, Thangathai S**.** A Study on Clinical Trends of Ectopic Pregnancy in a Tertiary Care Hospital**.** Journal of Medical Science and Clinical Research 2016;4**(**11**):**13774**-**79
15. Udigwe GO, Umeononihu OS, Mbachu II. Ectopic pregnancy: a 5-year review of cases at nnamdi azikiwe university teaching hospital (NAUTH) Nnewi. Nigerian Medical Journal. 2010 Oct 1;51(4):160.

Original Article

Seventeen years demographic profile of cancer patients at a selected medical college hospital

Rahman M S[a], Tabassum F[b], Ghosh P K[c], Khanam F[d], Bhuiyan M E[e], Begum S[f], Mohal M[g], Masud Z M[h]

Abstract

Background: Globally cancer has higher trend of morbidity and mortality. The number of new cases is apprehended to rise by about 70% over the next 2 decades. According to cancer registry report 2008-2010, NICRH lung cancer topped the list in all patients followed by breast, cervix, oesophagus, stomach, liver, Gall bladder, rectum, larynx and ovary.

Objective: To assess the socio-demographic profile of cancer patients admitted in a selected Medical College.

Methods: In Bangladesh Medical College Hospital, we have documented total number of 16971 newly diagnosed cancer patients in 17 years from 2003 to 2019. All of the patients belonged to adult group.

Results: Among 16971 patients male: female was 1:1.06. About 56.6% of the patients belonged to age group 40-59 years. 50% of the patients were to lower middle to poor socioeconomic group. Forty percent of the total patients were smoker. Both in male and female the top most cancer were breast cancer which was 16.5 %, followed by Ovarian cancer 11%, lymphoma 10%, Colorectal Cancer 9.3%, lung cancer 9%. Among male leading cancer was lung cancer 18% followed by lymphoma 14.7%, Colorectal 11.5 %. Among female top was Breast cancer 31.3% followed by Ovary 21% and Colorectal 7% .

Conclusion: Epidemiology of cancer is changing and it is now prevailing as a modern or slow epidemic. Lifestyle and behavioral modification as an intervention can bring the desirable changes in the population characteristics.

Keywords: Cancer, Demographic profile.

Introduction:

Cancer is the most dreaded disease in the world. The incidence of cancer is increasing with each year and it is attributed to the changes in lifestyle and increase in life expectancy.[1,2,3] The cancer profile varies in different parts of the world and an epidemiological study helps to know the common cancers prevalent in particular segments of a population and the risk factors involved.[2,3] Cancers figure among the leading causes of morbidity and mortality worldwide,with approximately 14 million new cases and 8.2 million cancer related deaths in 2012. The number of new cases is expected to rise by about 70% over the next 2 decades.[4] Tobacco use is the most important risk factor for cancer causing around 20% of global cancer deaths and around 70% of global lung cancer deaths. Cancer causing viral infections such as HBV/HCV and HPV are responsible for up to 20% of cancer deaths in low- and middle-income countries.[5]

In 2002, 4.2 million new cancer cases, 39**%** of new cases worldwide were diagnosed among 3.2 billion persons **(**48**%** of the world population**)** living in the fifteen most highly developed countries in South, East, and Southeast Asia**:** Japan, Taiwan, Singapore, South Korea, Malaysia, Thailand, China, Philippines, Sri Lanka, Vietnam, Indonesia, Mongolia, India, Laos, and Cambodia**.** China and India, together accounting for 37**%** of the worldwide population, reported 3 million of these newly diagnosed cancer cases**.** Greater than 50**%** of the world's new cases of stomach cancer, and greater than 70**%** of newly diagnosed esophageal cancer worldwide occur in these Asian countries**.** In 7 of these Asian countries, lung cancer has the highest incidence rate **(**age**-**standardized**)** of all cancers in males, and breast cancer is the highest incident cancer for females**.**[6]

a. Dr. Md Saidur Rahman; MPhil, DCP, MBBS
Associate Professor, Department of Pathology
Bangladesh Medical College, Dhaka

b. Dr Farzana Tabassum; MD, MBBS
Associate Professor, Department of Pathology
Ibrahim Medical College, Dhaka

c. Prof. Paritosh Kumar Ghosh; M. Phil, MBBS
Professor & Head, Department of Pathology and
Principal, Bangladesh Medical College

d. Dr. Fatema Khanam; MRCP,MBBS,
Registrar, Department of Medicine
Bangladesh Medical College Hospital

e. Dr Md. Elias Bhuiyan; MRCP, FCPS, MBBS
Assistant Professor, Department of Medicne
Bangladesh Medical College Hospital

f. Dr Shahnaz Begum; MBBS
Medical Officer, Department of Oncology
Bangladesh Medical College Hospital

g. Momotaz Mohal
Senior Staff Nurse, Bangladesh Medical College Hospital

h. Dr. Zafor Md. Masud; FCPS, M. Phil
Professor & Head, Department of Oncology
Bangladesh Medical College Hospital

Correspondence to:
Dr. Zafor Md. Masud; FCPS, M. Phil
Professor & Head, Department of Oncology, BMCH
Email: zaformasud@yahoo.com

Globally, cancers in all forms are causing about 12% of all deaths. In developed countries cancer is the second leading cause of death accounting for 21% of mortality by other causes and in developing countries it ranks third, accounting for 9.5% of all deaths.[7]

Cancer has become one of the ten leading causes of death in India. Around, 1.5-2 million cancer cases occur at any given point of time. Over 700000 new cases of cancer and 300000 deaths occur annually due to cancer. Nearly 1500000 patients require facilities for diagnosis, treatment and follow up at a given time.[8]

The global community can expect an increase of incidence of about 1% each year, with larger increase in China, Russia and India. In 2030, incidence may increase to 20-26 million with around 13-17 million mortality. Cancer cases doubled globally between 1975 and 2000, will double again by 2020 and triple by 2030. The rapid increase in the global cancer burden represents a real challenge for health systems worldwide.[9]

According to Bangladesh Cancer Society the burden of new adult cancer patients is 250000/yr, and the total cancer burden is 10,00000/yr. This is an institutional based statistic, the actual picture probably far away from it due to many barriers. The majority of the patients cannot reach to final diagnosis or avail the treatment facilities.

According to cancer registry report 2008-2010, NICRH lung cancer topped the list in all patients followed by breast, cervix, oesophagus, stomach, liver, Gall bladder, rectum, larynx, ovary.[10]

Material and Methods:

This cross sectional retrospective descriptive study was conducted in 2020 at the Department of Oncology, Bangladesh Medical College to find out the demographic distribution of the cancer patients from 2003 to 2019. Data was collected from hospital records (Register of Department of Oncology)

Results:

In Bangladesh Medical College Hospital, we have documented total number of 16971 newly diagnosed cancer patients from 2003 to 2019.

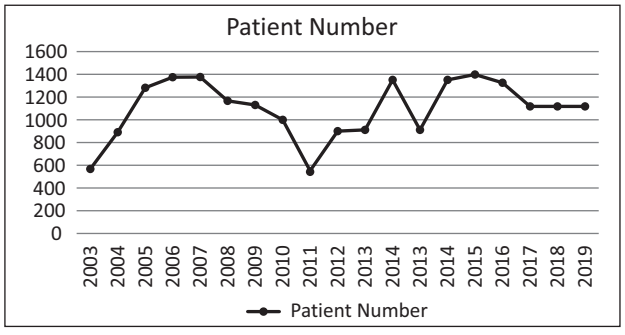


Fig 1: Distribution of the study population by gender and year from 2003-2019

Fig 1 shows incidence of cancer patients are increasing and it became three times in 5 years time.

Table 1: Socio demographic characteristic of the patients (n=16971)

Variables	Frequency	Percent
Age group		
Below 20 years	1452	8.5
20 -39 years	3502	20.6
40-59 years	9607	56.6
60 yrs and above	2410	14.3
Sex		
Male	8204	48.4
Female	8767	51.6
Educational status		
Illiterate	6788	40
Literate	10183	60
Socio economic status		
Lower Middle	8486	50
Middle	6788	40
Tobacco consumption		
Well to do	1697	10
Ever use	6789	40
Never use	10182	60
Tobacco consumption by gender (Both smoke and smokeless) n= 6789		
Male	5432	80
Female	1357	20

Table 1 shows that among the total 16971 cancer patients 8204 (48.4%) were male and rest 8767 (51.6%) were female. Male: Female ratio is 1:1.06. Majority 9607(56.6%) of the patients belongs to 40-59 years of age. More than half (60 %) of the patients were literate and rest 40% were illiterate. Fifty percent of the patients belonged to lower middle class, 40% middle class and only 1697(10%) belonged to well to do class. According to tobacco consumption history (both smoke and smokeless form), 6789(40%) ever consume tobacco where 60% never consume. Among the tobacco consumer majority (80 %) were male.

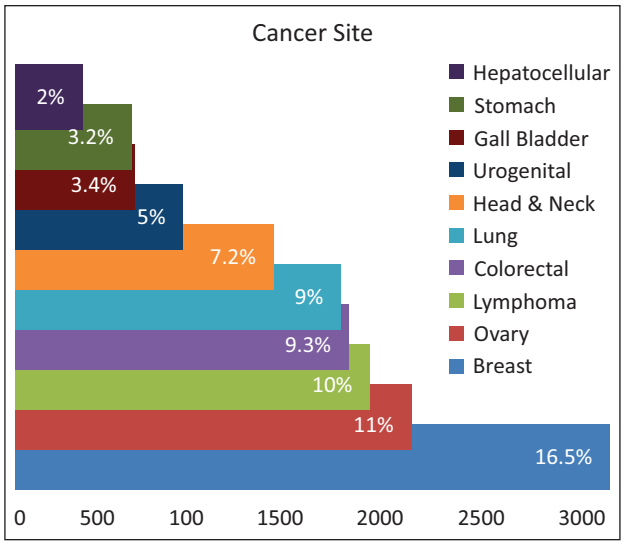


Figure 2: Distribution of patients by top ten malignancies in adult (N= 16971)

Figure 2: shows both in male and female the top most cancer were breast cancer which was 16.5 %, followed by Ovarian cancer 11%, lymphoma 10%, Colorectal Cancer 9.3% ,lung cancer 9% .

Table 2: Distribution of patients by top ten malignancies in Male (n= 8204)

Cancer sites	Number	Percent
Lung	1516	18
Lymphoma	1225	14.7
Colorectal	962	11.5
Head & Neck	752	9
Urogenital	690	8.3
Stomach	397	4.7
Gall Bladder	362	4.3
Hepatocellular Carcinoma	230	2.8
Oesophagus	196	2.3
Periampullary/Cholangio	119	1.5

Table 2 shows among male leading cancer was lung cancer 18% followed by lymphoma 14.7%, Colorectal 11.5 %, Head & Neck 9% .

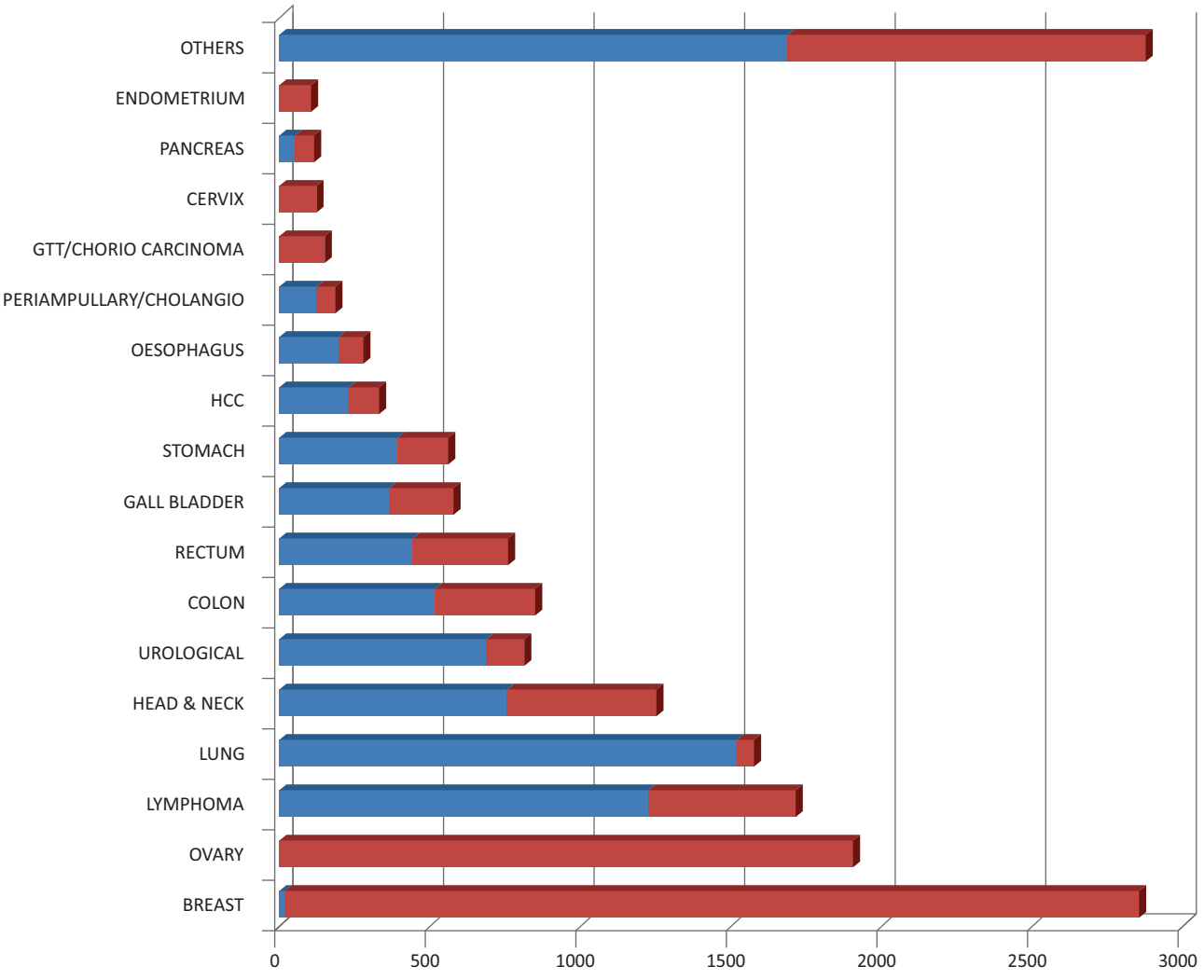
Table 3: Distribution of patients by top ten malignancies in female (n= 8767)

Cancer sites	Number	Percent
Breast	2848	31.3
Ovary	1901	21
Colorectal	643	7
Head & Neck	493	5.4
Lymphoma	479	5.3
Gall Bladder	213	2.3
Stomach	162	1.8
GTT/Choricarcinoma	150	1.6
Urological	124	1.4
Endometrium	106	1

Table 3 shows among female top was Breast cancer 31.3% followed by Ovary 21% and Colorectal 7% .

Table 4: Distribution of the patients by types of cancer and gender

Types of Malignancies	Male	Female	Total
	Frequency (%)	Frequency (%)	Frequency (100%)
Breast	18	2830	2848(16.5)
Ovary	0	1901	1901(11)
Lymphoma	1225	479	1704(10)
Lung	1516	53	1569(9.0)
Head & Neck	752	493	1245(7.22)
Urological	690	124	814(5.0)
Colon	520	328	848(4.91)
Rectum	442	315	757(4.39)
Gall Bladder	362	213	575(3.4)
Stomach	397	162	559(3.24)
HCC	230	97	327(2.0)
Oesophagus	196	86	282(1.63)
Periampullary/ Cholangio	119	66	185(1)
GTT/Chorio carcinoma		150	150(0.87)
Cervix		128	128 (0.74)
Pancreas	54	57	111(0.64)
Endometrium		106	106(0.6)
Others	1683	1179	2862(16.59)
Total	8204	8767	16971



	Breast	Ovary	Lymph oma	Lung	Head & Neck	Urological	Colon	Rectum	Gall Bladder	Stomach	HCC	Oesop hagus	Periam pullary /Chola ngio	GTT/ Chorio carcin oma	Cervix	Pancreas	Endom etrium	Others
Male	18	0	1225	1516	752	690	520	442	362	397	230	196	119			54		1683
Female	2830	1901	479	53	493	124	328	315	213	162	97	86	66	150	128	57	106	1179

Figure 3: Distribution of the patients by types of cancer and gender

Figure 3 shows predominant cancer in female were breast, ovary and colorectal cancer whether in male the predominant cancer were lung, lymphoma and urogenital cancer.

Breast Cancer were the most frequent malignancy (16.5 %) found in our study. Female had 99.4 %. Ovarian cancers are second common cancer (11%) found in our study. Gynecological cancer comprises 10% in our study. This group includes cervical cancer and ovarian cancer mostly.

Among Lymphoma c majority 72% were male. 96.6% lung cancer were male. Among colorectal cancer 60% were male.

Discussion:

The incidence and cancer profile varies in developed and developing countries. Incidence is high in developed countries because of the affluent society, diet and lifestyle.[2,11] Globally life expectancy at birth has increased from 45 years in 1950 to 66 in 2000 and is expected to reach about 77 years in 2050.[2]

This cross sectional retrospective descriptive study was conducted in 2020 at the Department of Oncology Bangladesh Medical College to find out the demographic distribution of the cancer patients from 2003 to 2019.

This current study revealed that among the total 16971 cancer patients 8204 (48.4%) were male and rest 8767 (51.6%) were female. Male: Female = 1:1.06 According to age of the patients' majority 9607 (56.6%) of the patients belonged to 40-59 years of age, followed by 3502(20.6%) between 20-39 years of age. More than half (60%) of the patients were literate. By economical distribution 90% of the patients belongs to middle to poor class, and only 10% belonged to well to do. According to tobacco consumption history (both smoke and smokeless form), 6789(40%) ever consume tobacco where 60% never consume. Among the tobacco consumer, majorities (80%) were male and 20% were female.

A Hospital based study on socio-demographic characteristics of cancer patients was conducted in India by Puri, Ashat and others and they found that 52.5% were female and most of the (32.3%) patients were in the age group 60- 69 years. Only 0.8% patients were aged <10 years, and 2.6% were of age 80 years or older. Majority (42.7%) of the patients were illiterate and only 4.5% were postgraduate. Out of 684 cancer patients, 33.4% belonged to the low socioeconomic status, while 6.6% belonged to the high socioeconomic status.[12]

Smoking in males was more as compared to that in females. Similar findings were evident in research done by Murthy.[13] Another study of Trivandrum too had emphasized that smoking increased the risk of oral cancer in men by as much as 90%.[14]

A similar study conducted by Kalyani, Bindra Singh and others in Kolar, India and they observed among 19,615 cases of histopathology and FNAC reported a total of 2744 (13.98%) were malignant, of which 1200 were males and 1544 females with male: female ratio of 0.7: 1, indicating female preponderance. Among all the cancers, cancer of the oral cavity was the leading cancer in both sexes (total n = 814 cases). In lymph node malignancies (n = 369 cases), metastatic cancers outnumbered (n = 292 cases), Hodgkin's disease and NHL (total n = 77) in both sexes. The top ten sites most frequently involved by cancer in males were oral cavity, stomach, esophagus, bone, NHL, prostate, liver, larynx, penis, and Hodgkin's disease / bladder cancer, whereas, the sites in females were oral cavity, cervix, breast, stomach, esophagus, thyroid, ovary, bone, rectum, and melanoma skin.[15]

In our study predominant cancer in female were breast, ovary and colorectal cancer whether in male the predominant cancer were lung, lymphoma and urogenital cancer.

Breast Cancer were the most frequent malignancy (16.5 %) found in our study. Female had 99.4 %. Ovarian cancers is second common cancer (11%) found in our study. Gynecological cancer comprises 10% in our study. This group includes cervical cancer and ovarian cancer mostly.

Among Lymphoma c majority 72% were male. Types of lymphoma could not be properly documented due inadequate information. Lung cancer comprises 9% of all cancer, 96.6% lung cancer were male and colorectal cancer were 9.3% with male predominance.

Head and Neck cancer comprises almost 7.2%% of all cancer. Female are approx 40% sufferer. Hepatobilliary cancer were 7% and 4.8% Urological cancer were found in our study.

In our study miscellaneous group comprises 16.8%. This large number is due to inadequate documentation, some are due to diagnostic dilemma. This group includes mostly Carcinoma of unknown origin, sarcomas, leukemia, brain tumor, skin cancers.

Conclusion:

Magnitude of cancer is increasing day by day as slow epidemic. Distribution in terms of population characteristics is variable due to the change of life style & behavior, dietary habit, eco-system etc. Mass awareness regarding primordial and primary prevention of cancer through lifestyle modification and behavioral change would play a very significant role. In addition, legislative measures are to be made more strengthened to order to have an effective control over the risk factors of cancers.

References:

1. Nanda Kumar A, Gupta PC, Gangadhar P, Visweshwara RN. Development of an atlas of cancer in India. First all India report: 2001-2002. National cancer registry program (ICMR) Bangalore, India. 2004.
2. Stewart SB, Kleihues P. World cancer report. IARC Press. Lyon 2003.
3. Gaur DS, Kishore S, Harsh M, Kusum A, Bansal R. Pattern of cancers amongst patients attending Himalayan Institute of Medical Sciences, Dehradun. Indian J Pathol Microbiol 2006; 49:193-8.
4. World Cancer Report 2014
5. De Martel C, Ferlay J, Franceschi S, et al. Global burden of cancers attributable to infections in 2008: a review and synthetic analysis. The Lancet Oncology 2012; 13: 607-615.
6. Margaret M, Robin P, et al. Comparative Effectiveness & Comparative Effectiveness & Medical Lead Asia Oncology
7. Jemal A, Center MM, De Santis C, Ward EM. Global patterns of cancer incidence and mortality rates and trends. Cancer Epidemiol Biomarkers Prev 2010; 19:1893-907.
8. Kalyani R, Das S, Bindra MS, Kumar H. Cancer profile in the Department of Pathology of Sri Devaraj Urs Medical College, Kolar: A ten years study. Indian J Cancer 2010; 47:160-5. [PUBMED]

9. Bleyer A, Barr R, Hayes-Lattin B, Thomas D, Ellis C, Anderson B; Biology and Clinical Trials Subgroups of the US National Cancer Institute Progress Review Group in Adolescent and Young Adult Oncology. The distinctive biology of cancer in adolescents and young adults. Nat Rev Cancer 2008; 8:288-98.

10. Cancer registry report 2008-2010, NICRH

11. www.indiastat.com [Accessed on 30.01.2008]

12. Puri S, Ashat M, Pandey A, Goel N K, Singh A, Kaushal V. Socio-demographic characteristics of cancer patients: Hospital based cancer registry in a tertiary care hospital of India. Indian J Cancer [serial online] 2014 [cited 2015 Sep 3]; 51:1-4. Available from: http://www.indianjcancer.com/text.asp?2014/51/1/1/134593

13. Murthy NS, Rajaram D, Gautham MS, Shivaraj NS, Nandakumar BS, Pruthvish S. Risk of cancer development in India. Asian Pac J Cancer Prev 2011; 12:387-91.

14. Muwonge R, Ramadas K, Sankila R, Thara S, Thomas G, Vinoda J, et al. Role of tobacco smoking, chewing and alcohol drinking in the risk of oral cancer in Trivandrum, India: A nested case-control design using incident cancer cases. Oral Oncol 2008; 44:446-54.

15. Kalyani R, Das S, Bindra Singh M S, Kumar H. Cancer profile in Kolar: A ten years' study. Indian J Cancer [serial online] 2010 [cited 2015 Sep 3]; 47:160-5. Available from: http://www.indianjcancer.com/text.asp?2010/47/2/160/63011

Original Article

Comparison of detection of carriage of Streptococcus pneumoniae directly from nasopharyngeal swabs by PCR and culture

Shormin M[a], Shamsuzzaman S M[b], Mondol M E A[c], Afroz S[d], Mostofa H A[e]

Abstract

Background: Studies of nasopharyngeal colonization of Streptococcus pneumoniae are hampered by the direct plaiting of the specimens at the site of sample collection/study fields; because S. pneumoniae (SPN) is a fastidious organism and there is chances of contamination during direct inoculation on routine laboratory media (Blood agar, Chocolate agar). Detection and monitoring of nasopharyngeal carriage of Streptococcus pneumonia is important to assess the impact and effectiveness of pneumococcal vaccine programs.

Objective: This study was undertaken to compare between the methods of detection of Streptococcus pneumonia by culture and directly from nasopharyngeal swabs by PCR.

Methods: The study was conducted in the department of microbiology of Dhaka Medical College Hospital (DMCH). Data were collected among 200 under five children from Pediatric OPD of Dhaka Medical College Hospital. S. pneumoniae were isolated and identified by culture, Gram staining and biochemical test and polymerase chain reaction (PCR). Sensitivity, specificity, accuracy and predictive value of PCR was calculated as comparison tool to culture method.

Results: Out of 200 nasopharyngeal swabs, 67 (33.50%) were positive by culture and 92 (46%) were positive by PCR for S. pneumoniae. Considering culture as gold standard, the sensitivity of PCR to identify Streptococcus pneumoniae was 100%, specificity was 81.2%, positive predictive value was 72.8%, negative predictive value was 100% and accuracy was 87.5%. Among culture negative samples, 25(18.80%) samples were positive for S. pneumoniae by PCR.

Conclusion: So in this study, PCR-based detection of S. pneumoniae from nasopharyngeal swabs was found to be a valuable tool to assess S. pneumoniae colonization and monitor trends in pneumococcal distribution without the requirement for culture and isolation of the organisms.

Keywords: Polymerase chain reaction, Culture Nasopharyngeal swab, Streptococcus pneumoniae, Sensitivity, Specificity, Accuracy.

Introduction:

streptococcus pneumoniae is a major cause of pneumonia, meningitis, and other invasive diseases resulting in high mortality and morbidity among children under the age of five, particularly in lower income countries. The World Health Organization estimated that there are nearly one million deaths each year in children younger than five years of age and one child under five years of age dies because of pneumococcal pneumonia in every 20 seconds.[1] S. pneumoniae is a bacterium that colonizes the nasopharynx of human and main source is person to person transmission.[2] S. pneumoniae colonization is often asymptomatic but may cause overt infections. Community-acquired pneumonia (CAP) and infections of normally sterile sites (pleural fluid, cerebrospinal fluid and blood) are the most common infections by S. pneumoniae which are collectively called invasive pneumococcal disease (IPD).[3] Pneumococcus is carried in the nasopharynx often with other bacteria, such as Haemophilus influenzae, Moraxella catarrhalis and Staphylococcus aureus. It is spread by respiratory droplets and children are the main source of transmission to adults. Universally, carriage rates are highest in young children (40- 60%), compared with older children (12%), adolescents (6 -10%) and adults (3-4%) pathogenesis of invasive pneumococcal disease (IPD) begins with nasopharyngeal (NP) colonization that proceeds, often

a. Dr. Moonmoon Shormin; M. Phil, MBBS
Assistant Professor, Department of Microbiology
Shaheed Monsur Ali Medical College, Dhaka.

b. Prof. S. M. Shamsuzzaman; M. Phil, Ph.D, MBBS
Professor and Head, Department of Microbiology
Dhaka Medical College, Dhaka

c. Prof. Md. Eunus Ali Mondol; FCPS, MBBS
Professor and Head, Department of Microbiology and
Principal, City Medical College, Gazipur

d. Dr. Samira Afroz; M Phil, MBBS
Assistant Professor, Department of Microbiology
Shahab Uddin Medical College, Dhaka

e. Dr. Hasbi Ara Mostofa; M. Phil, MBBS
Microbiologist, TB Hospital, Shyamoli, Dhaka

Correspondence to:
Dr. Moonmoon Shormin; M. Phil, MBBS
Assistant Professor, Department of Microbiology
Shaheed Monsur Ali Medical College, Dhaka.
Email: moonmoon.shormin@gmail.com.

through local infection, to blood stream invasion.[4] Although almost all children become colonized with Streptococcus pneumoniae repeatedly during the first few years of life, a very small fraction of these acquisitions results in invasive disease. Many studies of the dynamics and ecology of pneumococcal NP carriage, particularly in the setting of new conjugate pneumococcal vaccines, will be performed in setting where microbiologic facilities are not readily available.

Whilst vaccination has had success in reducing the burden of disease caused by vaccine-type S. pneumoniae, ongoing surveillance is important to monitor trends in pneumococcal carriage distribution as the benefits of vaccination could be offset by increased rates of pneumococcal disease.[5] Increasingly, molecular methods such as Polymerase chain reaction (PCR) are being used for the detection of S. pneumoniae as they are highly sensitive compared with culture and are not based on the growth of viable bacteria.[6] PCR for gene amplification has made it possible to detect low numbers of agents or even fragments of DNA from the agents.[7] So, PCR have been shown to be a more practical alternative for large epidemiological studies, and have been applied to nasopharyngeal swabs for continuous monitoring of S. pneumoniae carriage for future pneumococcal vaccination program to prevent pneumococcal diseases.

Materials and Methods:

Data collection

Nasopharyngeal swabs were collected from healthy children aged one month to less than five years who attended the outpatient department of DMCH for routine immunization, child growth monitoring and nutritional advice. Age group were selected from one month to 60 months' age group. Nasopharyngeal swabs were collected, labeled and placed immediately in one ml of skimmilktryptone-glucose-glycerol (STGG) medium and transported to the laboratory. After collection of the nasopharyngeal swabs, the swabs were inserted into the bottom of the screw-cap bottles containing STGG medium. The shaft portion of the swab sticks were cut at the top level of the bottles by a sterile scissor and tightened the cap carefully (Figure 1). Then the swab containing screw-cap bottles were vortexed on high speed for 10-20 seconds and placed at -70°C in upright position for culture.[8]

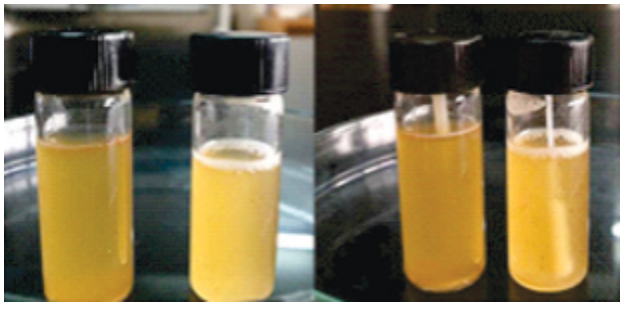


Figure 1: STGG media and STGG media with swab.

Culture and isolation

The NPS-STGG specimens were thawed at room temperature (25°C) and vortexed for 10-20 seconds. Then specimens were inoculated on blood agar using one loop (10µl) of sample. The plates were streaked into four quadrants and incubated at 37°C for 24 hours with CO_2 atmosphere inside a candle jar.[8]

Identification of Streptococcus pneumoniae

Small, smooth and transparent colonies were seen on blood agar plate. Colonies were low convex, tiny and they became flattened centrally showing the 'draughtsman form'. A narrow zone of ∝ hemolysis (Figure 2) was seen around the colonies. Gram positive diplococci were seen which were ovoid or lanceolate in shape and Catalase negative. The isolates with presumptive identification were confirmed by optochin sensitivity test, bile solubility test and PCR (Figure 3).

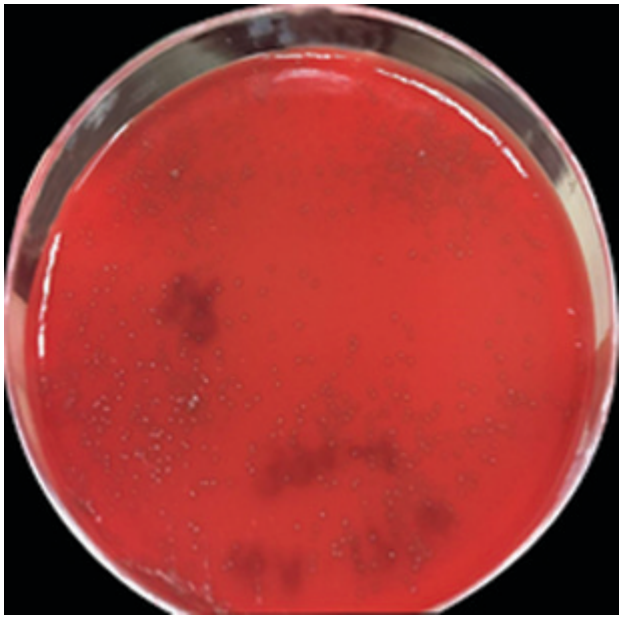


Figure 2: Culture in blood agar media showing α hemolytic colonies of S. pneumoniae.

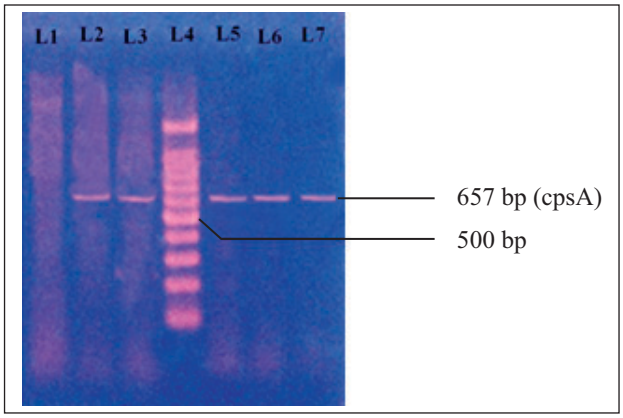


Figure 3: Photograph of PCR amplified cpsA gene of Streptococcus pneumoniae

- Lane 1: negative control with DNA of Staphylococcus aureus ATCC25923,
- Lane 2, 3, 5, 6, 7: amplified DNA of 657 bp of cpsA gene.
- Lane 4: hundred bp DNA ladder

Procedure of polymerase chain reaction (PCR):

- **Bacterial pellet formation**

(A) From preserved nasopharyngeal samples: Samples preserved in STGG medium were brought out from freeze and kept them at room temperature to demoisture and samples were vortexed to make a homogenous suspension. Then the swab sticks were removed and the vortexed specimens were taken into two micro centrifuge tubes, labeled proper centrifuged at 10,000 X g for 10 minutes and the supernatant was discarded. The deposit was used as pellet for PCR. The micro centrifuge tubes containing pellet were kept at -20°C until DNA extraction.

(B) From culture colonies: The colonies (about 5 to 6) of specific bacteria were subcultured on blood agar media at 37°C for 24 hours in a candle jar. After overnight incubation, scraped all the growth by a sterile cotton tipped swab. Then the swab was kept into a cryotube, containing one ml of STGG media and vortexed on high speed for 10-20 seconds. Then the swab stick was removed and the vortexed material were taken into two micro centrifuge tubes, labeled properly, centrifuged at 10,000 X g for 10 minutes and the supernatant was discarded. The deposit was used as bacterial pellet for PCR. The micro centrifuge tubes containing pellet were kept at -20°C until DNA extraction.

- **DNA Extraction**

A) From bacterial culture: Two hundred micro litter of sterile distilled water was added into micro centrifuge tubes having bacterial pellet and vortexed until mixed. Mixture was heated at 100°C for 10 minutes in heat block. After that the tubes were immediately kept on ice for 5 minutes. Then the tubes were centrifuged at 4ºC at 14000 X g for 10 minutes. Then the supernatant was taken into another micro centrifuge tube using micropipette and was used as template DNA for PCR and kept at -20ºC for future use.

B) From specimens: Two hundred micro litter of lytic buffer was mixed with the sample pellets and vortexed until mixed well. Then the tubes were incubated at 60°C for 3 hours. After incubation, tubes were kept in heat block at 100°C for 10 minutes for boiling. Then the tubes were immediately placed on ice for 5 minutes. After that the tubes were centrifuged at 4°C at 14000 X g for 10 minutes. Finally, supernatant was taken using micropipette and used as template DNA for PCR. This DNA was kept at -20°C for future use.[9] The primer cpsA were used for targeted highly conserved gene that exists in all capsular loci thus far characterized.[10]

Results:

Table 1: Demographic characteristics of the study participants (n=200)

Age groups	Number (%)
1 month-12 months	40 (20.00)
13 months-36 months	65(32.50)
37 months-60 months	95 (47.50)
Total	**200 (100.00)**
Socio-economic groups	**Number (%)**
Low income	63 (31.50)
Middle income	129 (64.50)
High income	8 (4.00)
Total	**200 (100.00)**

Table 1 shows out of 200 children majority 95(45.5%) children were in 37- ≤ 60 months' age group, followed by 65(32.5%) children in 13-36 months' age group. Among socioeconomic classes most of them 129 (64.5%) were from middle income class.

Table 2: Identification of S. pneumoniae & its difference to Viridans streptococcus

Characteristics	S. pneumoniae	Viridans streptococcus
Colonies	Flattened, draughtsman	Convex
Effect on BA	Narrow zone of α-haemolysis	Narrow zone of α-haemolysis
Optochin sensitivity	+ve	-ve
Bile solubility	+ve	-ve

Table 2 shows presumptive identification of S. pneumoniae by colony morphology, as flattened, draughtsman, blood agar culture shows narrow zone of α-haemolysis and optochin sensitivity test and bile solubility test both resulted positive.

Table 3: Results of culture and PCR for *S. pneumoniae* from nasopharyngeal swabs (n=200)

Methods	Nasopharyngeal swab Number (%)
Culture positive	67 (33.5)
PCR positive	92 (46.00)

Total 200 under five children were tested, among them, 67(33.50%) were positive for *S. pneumoniae* by culture and 92 (46%) were positive by PCR (Table 3).

Table 4: Comparison of PCR for detection of S. pneumoniae from nasopharyngeal swabs with culture (n=200)

PCR	Culture		Total
	Positive (No.)	Negative (No.)	No.(%)
Positive	67	25	92(46%)
Negative	00	108	108(54%)
Total	**67**	**133**	**200 (100%)**
Sensitivity, Specificity, Accuracy, and Positive Predictive value & Negative Predictive value of PCR			
Sensitivity	67*100/67=100%		
Specificity	108*100/133= 81.2%		
Accuracy	(67+108)*100/200=87.5%		
Positive Predictive Value	67*100/92=72.8%		
Negative Predictive Value	108*100/108=100%		

Table 4 shows the comparison of results of PCR for detection of S. pneumoniae from nasopharyngeal swabs with culture. Among 200 samples, 67 were positive by both PCR and culture, whereas 108 were negative by both methods. Of the remaining cases, 25 were positive by PCR but negative by culture. Considering culture as gold standard, the sensitivity of PCR was 100%, specificity was 81.2%, accuracy was 87.5%, positive predictive value was 72.8%, and negative predictive value was 100%.

Discussion:

S. pneumoniae is a common cause of respiratory infections requiring hospitalization in young children worldwide with increasing rates of antibiotic resistance.[11] Generally, detection of S. pneumoniae is performed by culture of the organism followed by optochin sensitivity test and bile solubility test. These methods of detection are hampered by the direct plaiting of the specimens at the site of sample collection/Study fields; because S. pneumoniae (SPN) is a fastidious organism and there is chances of contamination during direct inoculation on routine laboratory media (Blood agar, Chocolate agar). The development of PCR-based detection has the potential to overcome some of the difficulties associated with the conventional methods.

In the present study, a total of 200 nasopharyngeal swabs were processed for culture. Out of 200 nasopharyngeal swabs, 67 (33.50%) were culture positive for S. pneumoniae. In two different studies in Bangladesh[12,13] reported that nasopharyngeal carriage rate among under five children were 47% and 59% respectively by culture. Another study in Ethiopia showed carriage rate of 43.8% by culture.[14] All the results of these previous studies showed higher carriage rate in contrast to the present study by culture. In comparison, low carriage rate (6.5% to 24%) was reported in New Delhi, India, in Italy and in Kenya by culture.[15,16,17] The differences in the proportion of nasopharyngeal carriage of S. pneumoniae might be due to different age groups, geographical area, crowding status, rural area, and concomitant respiratory tract illness or HIV infection, nutritional status, co-carriage with other pathogens, seasonal variation and sampling technique[18]. In the present study detected carriage was lower than that reported in previous study of Bangladesh. The reasons might be due to the fact that in the previous study data were collected from only lower socioeconomic population and from a single community in a government housing area of urban Dhaka. But in the present study data were collected from different socio-economic groups and from the children who attended DMCH from different section of society and some children were vaccinated. Besides, S. pneumoniae isolation from nasopharyngeal swab by culture was less sensitive which might be due to the fastidious nature of the organism and low load of the organism with cocolonization that can result in false negative results.[19] In the present study, 92 (46%) nasopharyngeal carriage of S. pneumoniae was detected by PCR (Table-3). A study in Switzerland reported that carriage rate was 51.6% by PCR[20]. Another study reported 69% carriage rate in Netherland by PCR[21]. All the results of the previous studies showed higher carriage rate in contrast to the present study. The reasons might be due to different geography. Besides in the present study data were enrolled from healthy, urban children. In the present study, PCR base detection of carriage was higher than culture (46% vs 33.50%). Some previous studies [20,21] reported that PCR significantly increased the detection of carriage of S. pneumoniae compared to culture. The results of the previous studies and the results of the present study showed that PCR based detection is higher in comparison to culture. S. pneumoniae isolation from nasopharyngeal swab by culture was less sensitive which might be due to the fastidious nature of the organism and low load of the organism with co-colonization that can result in false negative results. PCR can detect bacterial DNA even if the numbers of organism are too low to grow in culture[22] and can detect from non-viable organisms after treatment with antibiotics.[23] Considering culture as gold standard, the sensitivity of PCR to identify S. pneumoniae from nasopharyngeal swabs was 100%, specificity was 81.2%, positive predictive value was 72.8%, negative predictive value was 100% and accuracy was 87.5% (Table-4). Sensitivity of PCR were reported as 100%, 95% and 92% [24, 25, 26] which are almost similar to the present study. A study reported that PCR is highly sensitive for detection of nonviable organisms.[6] The findings of the present study coincide with the findings of previous studies that PCR is better than culture for detection of pneumococcal carriage.

Conclusion:

Detection rate of nasopharyngeal carriage of S. pneumoniae was relatively more using PCR than culture. So, PCR can be used directly on sample, improving the ability to diagnose invasive Pneumococcal disease burden and implications for vaccine policy.

Recommendation:

PCR may enhance the diagnostic accuracy of traditional techniques, especially when Gram stain and culture are negative or inconclusive even if PCR tests are a bit expensive currently.

References:

1. World Pneumonia Day. Universal Access for Pneumonia Prevention and Care, 2014.
2. Gray BM, Converse GM, Dillon HC. Epidemiologic studies of Streptococcus pneumoniae in infants: acquisition, carriage, and infection during the first 24 months of life. J Infect Dis 1980; 142: 923-933.
3. Lang ALS, McNeil SA, Hatchette TF, Elsherif M, Martin I, Jason J, et al. Detection and prediction of Streptococcus pneumoniae serotypes directly from nasopharyngeal swabs using PCR. J Med Microbiol 2015; 64: 836-844
4. Yildirim I, Hanage WP, Lipsitch M, Shea KM, Stevenson A, Huang S, et al. Serotype specific invasion capacity and persistent reduction in invasive pneumococcal disease. Vaccine 2010; 29: 283-288.
5. Huss A, Scott P, Stuck AE, Trotter C, Egger M. Efficacy of pneumococcal vaccination in adults: a meta-analysis. CMAJ 2009; 180: 48-58.
6. Shakrin N, Balasubramaniam SD, Yusof HA, Mastuki MF, Masri, SN, Taib NM, et al. Evaluation of PCR-based approach for serotype determination of Streptococcus pneumoniae. Trop Biomed 2013; 30: 338-344.
7. Gillespie SH. The diagnosis of Streptococcus pneumoniae infections. Rev Med Microbiol 1994; 5: 224-232.
8. Saha SK, Baqui AH, Darmstadt GL, Ruhulamin M, Hanif M, Arifeen SE, et al. Comparison of Antibiotic Resistance and Serotype Composition of Carriage and Invasive Pneumococci among Bangladeshi Children: Implications for Treatment Policy and Vaccine Formulation. J Clin Microbiol 2003; 41: 5582-5587.
9. Rubin GR, Rizvi A, Baer A. Effect of swab composition and use of swabs versus swab-containing skimmilk- Tryptone- Glucose- Glycerol(STGG) on culture or PCR-based detection of Streptococcus pneumoniae in simulated and clinical respiratory specimens in STGG transport medium. J Clin Microbiol 2008; 46: 2635-2640.
10. Morona JK, Morona R, Paton JC. Analysis of the 5'portion of the 19A capsule locus identified two classes of cpsC, cpsD and cpsE genes in Streptococcus pneumoniae. J Bacteriol 1999; 181: 3599-3605.
11. Resti M, Moriondo M, Cortimiglia M, Indolfi G, Canessa C, Becciolini L, et al. Community acquired bacteremic pneumococcal pneumonia in children: diagnosis and serotyping by real time polymerase chain reaction using blood samples. Clin Infect Dis 2010; 51: 1042-1049.
12. Saha S, Modak JK, Naziat H, Al-Emran HM, Chowdury M, Islam M, et al. Detection of co-colonization with Streptococcus pneumoniae by algorithmic use of conventional and molecular methods. Vaccine 2014; 11: 713-718.
13. Saha SK, Baqui AH, Darmstadt GL, Ruhulamin M, Hanif M, Arifeen SE, et al. Comparison of Antibiotic Resistance and Serotype Composition of Carriage and Invasive Pneumococci among Bangladeshi Children: Implications for Treatment Policy and Vaccine Formulation. J Clin Microbiol 2003; 41: 5582-5587.
14. Assefa, A, Gelaw B, Shiferaw Y, Tigabu Z. Nasopharyngeal carriage and antimicrobial susceptibility pattern of Streptococcus Pneumoniae among pediatric outpatients at Gondar University Hospital, North West Ethiopia. Pediatr Neonatal 2013; 54: 315-321.
15. Wattal C, Oberoi JK, P.K. Pruthi PK, Gupta S. Nasopharyngeal carriage of Streptococcus pneumoniae. Ind Pediatr J 2007; 74: 905-907.
16. Marchisio P, Esposito S, Schito GC, Maechese A, Cavagna R, Principi N, et al. Nasopharyngeal carriage of Streptococcus pneumoniae in healthy children: implications for the use of heptavalent pneumococcal conjugate vaccine. Emer Infect Dis 2002; 8: 479-484.
17. Githii S, Revathi G, Muigai A, Kariuki S. Carriage rate and serotypes of Streptococcus pneumonia amongst children in Thika Hospital, Kenya. Afr J Lab Med 2013; 2: 1-5.
18. Richard AA, DeAntonio R, Hill PC, Roca A, Usuf E, Hoet B, et al. Carriage of Streptococcus pneumoniae and other respiratory bacterial pathogens in low and lower-middle income countries: A systemic review and meta-analysis. PLoS One 2014; 9: e103293.
19. Pasinato A, Indolfi G, Marchisio P, Valleriani C, Cortimiglia M, Spanevello V, et al. Nasopharyngeal carriage in children pneumococcal serotype distribution in 1315 nasopharyngeal swabs from a highly vaccinated cohort of Italian children as detected by RTPCR. Vaccine 2014; 32: 1375-1381.

20. Brugger SD, Hathaway LJ, Muhlemenn K. Detection of Streptococcus pneumoniae strain colonization in the nasopharynx. J Clin Microbiol 2009; 47: 1750-1756.

21. Wyllie AL, Wijmenga AJ, Marlies A, Groot JA. Molecular surveillance of nasopharyngeal carriage of Streptococcus pneumoniae in children vaccinated with conjugated polysaccharide pneumococcal vaccines. Sci Rep 2016; 6: 238-242.

22. Rudolph KM, Parkinson AJ, Black CM, Mayer LW. Evaluation of polymerase chain reaction for diagnosis of pneumococcal pneumonia. J Clin Microbiol 1993; 31: 2661-2666.

23. Wheeler J, Murphy OM, Freeman R, Kearns AM, Steward M, Lee MJ. PCR can add to detection of pneumococcal disease in pneumonic patients receiving antibiotics at admission. J Clin Microbiol 2000; 38: 3907-3911.

24. Greiner O, Philip JR, Philipp P, Imeri F, Altwegg M. Quantitative detection of Streptococcus pneumoniae in nasopharyngeal secretion by Real-Time PCR. J Clin Microbiol 2001; 39: 3129-3134

25. Abdeldaim MK, Stralin K, Korsgaard J, Blomberg J, Welinder-Olsson C, Herrmann B. Multiplex quantitative PCR for detection of lower respiratory tract infection caused by Streptococcus pneumonia, Haemophilus influenzae. BMC Microbiol 2010; 10: 310-315.

26. Stralin K, Backman H, Holmberg H, Fredlund H, Olcen P. Design of a multiplex PCR for Streptococcus pneumonia, Haemophilus influenza, Mycoplasma pneumonia and Chlamydia pneumonia to be used on sputum samples. J Clin Microbiol 2005; 113: 99-111.

Original Article

Comparative evaluation of low dose Fentanyl and Lignocaine in attenuating hemodynamic response to laryngoscopy and tracheal intubation

Khalilullah I[a], Akter K[b], Hasnain K M S[c], Akter F[d], Khan R H[e], Ibrahim K[f]

Abstract

Background: Hemodynamic stability is an integral and essential part of any anesthetic management plan. Laryngoscopy and tracheal intubation is almost invariably associated with a reflex sympathetic pressor response resulting in elevated heart rate & blood pressure due to release of catecholamine in circulation. This may prove detrimental in high risk patients.

Objective: The objective of this study is to compare the effects of low dose fentanyl and lignocaine in attenuation of pressor response to laryngoscopy and tracheal intubation.

Method: This was a double blinded, randomized cross sectional clinical study. A total number of 60 adult patients with ASA physical status I & II scheduled for various elective surgical procedures under general anesthesia were enrolled in this study. Patients randomly allocated equally, 30 in each group, into two groups, F and L. Patients of Group F (n=30) got intravenous Fentanyl 2mcg/Kg (diluted in 10ml of volume) 5 minutes before laryngoscopy and patients who were enrolled in Group L (n=30) received intravenous Lignocaine 1.5 mg/kg (diluted in 10 ml of volume) 3 minutes before laryngoscopy.

Results: Patients belonging to Fentanyl (2mcg/Kg) group showed rise in heart rate just after intubation, 3 minutes & 5 minutes after tracheal intubation were significantly lower (p value <0.05) compared to Lignocaine (1.5mg/Kg) group. Rise in Systolic Blood Pressure, Diastolic Blood Pressure and Mean Blood Pressure just after intubation, at 3 minutes & 5 minutes after tracheal intubation were also lower which was statistically significant in Fentanyl group (p value <0.05) compared to Lignocaine group.

Conclusion: Our study showed that, fentanyl attenuated hemodynamic stress response to laryngoscopy and tracheal intubation more effectively than lignocaine.

Keywords: Laryngoscopy, Attenuate Intubation response, Fentanyl, Lignocaine.

Introduction:

Stress response is a state of alarm of the body. Through a combination of nerve and hormonal signals, this system prompts adrenal glands, to release a surge of hormones e.g. adrenaline and cortisol. Cardiovascular response to laryngoscopy and tracheal intubation has been extensively studied during past several decades. Direct laryngoscopy and passage of a tracheal tube are noxious stimuli that can provoke adverse responses in the cardiovascular, respiratory, and other physiologic systems. The procedure increases blood pressure and heart rate.[1,2] Mechanism of cardiovascular response to intubation is assumed to be a reflex sympathetic response to the mechanical stimulation of larynx and trachea. Reflex changes in the cardiovascular system after laryngoscopy and intubation lead to an average increase in blood pressure by 40 – 50% and 20% increase in heart rate.[3-4] Significant elevations in serum levels of norepinephrine and epinephrine following laryngoscopy, with or without tracheal intubation, have been demonstrated.[2] The response of direct laryngoscopy and endotracheal intubation is transient, occurring 30 seconds after intubation and lasting for less than 10 minutes.[1] It may be well tolerated in healthy people, but may be hazardous in patients with hypertension, coronary artery disease, cerebrovascular disease, myocardial infarction and thyrotoxicosis.[5]

a. Dr. Ibrahim Khalilullah; DA, FCPS
Assistant Professor & Associate Consultant, Cardiac Anesthesiology
Ibrahim Cardiac Hospital & Research Institute, Dhaka

b. Dr. Khaleda Akter. MD (Biochemistry)
Specialist, Diagnostic Laboratory Services, Ibrahim Cardiac Hospital & Research Institute, Dhaka

c. Dr. Khan Mahmud Shamim-Ul- Hasnain; DA, FCPS
Jr. Consultant, Cardiac Anesthesiology, National Heart Foundation Hospital & Research Institute, Dhaka

d. Dr. Fardushy Akter; MD
Specialist, Department of Anesthesiology, Asgar Ali Hospital, Dhaka

e. Dr. Rafiqul Hasan Khan; MCPS, FCPS
Associate Professor, Department of Anesthesiology
Bangladesh Medical College Hospital

f. Prof. Kamal Ibrahim; FCPS, FICS
Professor & Head, Department of Anesthesiology, Bangladesh Medical College Hospital

Correspondence to:
Dr. Ibrahim Khalilullah; DA, FCPS
Assistant Professor & Associate Consultant, Cardiac Anesthesiology
Ibrahim Cardiac Hospital & Research Institute, Dhaka
Email: ibrahimbgd@yahoo.com

Materials and Methods:

This was a cross sectional, randomized, double-blinded clinical trial to compare the effectiveness of low dose Fentanyl and Lignocaine in attenuating hemodynamic response to Laryngoscopy and tracheal intubation among adult patients undergoing general anaesthesia for elective surgery carried out during the period of July 2015 to December 2015. Ethical clearance was taken from the concerned authority. A total number of 60 patients were included in this study. Inclusion criteria's were all surgical patients of both sexes who are calm & quiet, hemodynamically stable before the procedure, age between 18-60 years, ASA grading I & II, mallampati grading I & II, elective surgical procedures involving GA with IPPV.Exclusion criteria's were patients unable to understand normal command/suggestion, patient refusal, having unstable hemodynamics (Hypertension or hypotension, Tachycardia or Bradycardia or any other dysrhythmias) before the procedure, known allergy to Fentanyl or Lignocaine, long standing Diabetic patients, patients with hepatic or renal impairment. Main outcome variables were Heart Rate (HR), Systolic BP (SBP), Diastolic BP (DBP), Mean Arterial Pressure (MAP) and SpO_2. Variables are recorded at pre-anesthetic period, just after laryngoscopy and Intubation, at 3 minutes, 5 minutes and 10 minutes after intubation. The value, just after intubation was taken after confirmation of endotracheal tube position by hand ventilation and chest auscultation and other values taken subsequently.

After pre-oxygenation for 5 minutes, calculated doses of Fentanyl & Lignocaine was given slowly in group F and L respectively. Patients were induced with intravenous injection of thiopental sodium (5mg/kg), this was followed by intravenous Succinylcholine (1.5mg/kg) to facilitate intubation. Laryngoscopy was done 3 mins after receiving Lignocaine and 5 mins after Fentanyl. Total duration of laryngoscopy was noted. Patients, whose total duration of laryngoscopy was more than 20 seconds were excluded.
Anesthesia was maintained with 60% nitrous oxide in 40% Oxygen and halothane at a value of 0.5%. Vecuronium bromide (0.1mg/kg) was given for maintenance of muscle relaxation. At the end of surgery, all patients were reversed with intravenous injection of Neostigmine (0.05mg/kg) and atropine (0.02mg/kg). Parameters like heart rate, systolic and diastolic blood pressure were recorded just after intubation, 3 minutes, 5 minutes and 10 minutes after intubation.

Statistical Analysis

All data presented as mean (standard deviation) unless otherwise indicated. Analysis of variance (ANOVA) and chi-square test used to detect the demographic data among the two groups. Independent sample t-test done to analyze the collected data. A *p* value <0.05 accepted as statistically significant. Statistical analysis carried out using Statistical Package for Social Science (SPSS) for Windows version 20.0.

Results:

Table 1: Demographic data and baseline hemodynamic parameters

	Group F (Mean ± SD)	**Group L** (Mean ± SD)
Age	34.40 ± 11.06	37.37 ± 12.62
Gender (Male/Female)	14/16	14/16
Weight (Kg)	57.23 ± 7.42	56.60 ± 9.51
Baseline hemodynamic parameters		
SBP	115.13 ±11.46	112.67 ± 10.06
DBP	69.03 ± 8.50	67.33 ± 7.40
MAP	84.30 ± 8.73	82.33 ± 7.80
HR	80.3 ± 7.8	80.4 ± 9.9

Patient characteristics, baseline hemodynamic variables (SBP, DBP, MAP & HR) were similar between groups. Mean age of the patients of group F and group L were 34.40±11.06 and 37.37±12.62 years respectively. In both groups 46.66% patients were male and 53.33% were female. Mean weights of the patients of group F was 57.23±7.42 and group L was 56.60±9.51 respectively as shown in Table 1.

Table 2: *p* values of different haemodynamic parameters at different time period

SBP	Baseline (Before Intubation)	Just after intubation	3mins after intubation	5mins after intubation	10mins after intubation
DBP	0.379	0.000**	0.025**	0.101	0.492
MAP	0.412	0.001**	0.027**	0.018**	0.760
HR	0.361	0.000**	0.014**	0.030**	0.987
	0.425	0.001**	0.000**	0.000**	0.114

Table 2 shows significant differences ($p<0.05$) among groups in terms of heart rate, diastolic pressure and mean blood pressure respectively at just after intubation, 3 minutes and 5 minutes after intubation, compared with baseline values. At 10 minutes after intubation, there was no significant difference in terms of these values. There was significant difference between groups ($p<0.05$) compared to baseline values, in terms of systolic blood pressure at just after intubation and 3 minutes after intubation. There were no significant differences on the subsequent time readings for SBP. It was observed that at 10 minutes after intubation all values (SBP, DBP, MAP & HR) were reduced than preoperative values.

Table 3: Haemodynamic parameters at different time period of endotracheal intubation

	Baseline (Before Intubation)	Just after intubation	3mins after intubation	5mins after intubation	10mins after intubation
SBP	115.13±11.46	133.23±9.58	123.50 ±8.25	116.90±10.22	103.40 ±9.73
DBP	69.03 ±8.50	84.13±5.73	76.57 ±4.92	70.50 ±6.46	63.87 ±7.38
MAP	84.30± 8.73	100.46±6.42	92.10±5.27	85.93±7.55	77.07±7.26
HR	80.3 ± 7.8	102.7±8.3	91.3±9.0	83.0±9.2	74.9±6.2
Lignocaine Group					
SBP	112.67±10.06	142.06±8.58	128.53 ±8.63	121.07 ±9.13	105.17 ±10.04
DBP	67.33 ±7.40	90.30±7.98	80.00 ±6.70	74.73 ±7.00	63.23 ±8.54
MAP	82.33±7.80	107.42±7.73	96.00±6.62	90.13±7.09	77.10±8.49
HR	80.4 ± 9.9	110.6±8.8	100.8±8.9	92.4±9.1	78.4±10.2

Table 3 shows that rise of HR, SBP, DBP, and MAP in groups F were lower compared with group L at just after intubation, 3 and 5 minutes after intubation.

Discussion:

The aim of our study was to compare the effect of lignocaine (1.5 mg/kg) to fentanyl (2mcg/Kg) in attenuation of cardiovascular stress response during laryngoscopy and endotracheal intubation. Lignocaine[6-7] & also Fentanyl,[8-9] advocated widely and were standard agents for attenuation of the pressor response. Both the drugs individually have been shown to attenuate the increase in heart rate, Blood pressure and intra-cranial pressure associated with laryngoscopy and intubation.

Stress may be reduced by modifying or controlling the response to stress.[10] Premedication is used to provide sedation, anxiolysis and to enhance quality of induction, maintenance and recovery from anesthesia. Many attempts have been made in modifying these hemodynamic responses e.g. premedication, deep anesthesia by additional use of inhalational agent with IV agents,[11] topical anesthesia,[12] use of ganglion blockers,[13] beta blockers,[14] calcium channel blocker,[15-16] antihypertensive agents like phentolamine,[17] magnesium[18] etc. Vasodilators like sodium nitroprusside[19] and nitroglycerine[20] are effective but require continuous infusion through pump.

The optimal time of injection of I/V lignocaine for the maximal attenuation of circulatory response was studied by Cambel JM et al.[21] They concluded that a dose of 1.5 mg/kg offered complete attenuation against post intubation increases in heart rate and arterial blood pressure when given 3 minutes prior to intubation and partial attenuation when given 2 minutes prior to intubation. And the optimal time of injection of I/V Fentanyl for the maximal attenuation of circulatory response was studied by He-Sun Song et al[22]. They concluded that the most effective time to administer fentanyl to protect circulatory responses to Laryngoscopy and tracheal intubation is 5mins before intubation.

Yushi U et al[9] studied over one hundred surgical patients showed that, a significant reduction in hemodynamic response in the group treated with fentanyl and intubated using the fiberoptic technique. They concluded that there was no significant difference in the hemodynamic responses to orotracheal intubation by fiberscopy and laryngoscopy without fentanyl pretreatment, whereas 2mcg/kg fentanyl significantly reduced the hemodynamic responses in the group intubated by fiberscopy.

Gurulingappa et al[23] studied over seventy-five ASA I and II status normotensive patients, divided into three groups, received fentanyl 4micrograms/kg IV bolus, lignocaine 1.5mg IV bolus and placebo (normal saline) respectively, 5 minutes before laryngoscopy and intubation. HR, systolic, diastolic blood pressure were recorded noninvasively before induction 0, post induction, 1,2,3,4 and 5 minutes from the onset of laryngoscopy. After intubation incidence of tachycardia (HR>100/min) and rise in both systolic and diastolic blood pressure were significantly greater in placebo and lignocaine group than in fentanyl group ($p<0.05$). They concluded that attenuation of pressor response is seen both with lignocaine and fentanyl. Of the two drugs fentanyl 4mgicrogram IV bolus provides a consistent, reliable and effective attenuation as compared to lignocaine 1.5mg/kg IV bolus.

Woon-Young Kim et al[24] investigated the effect of IV lidocaine on the hemodynamic and Bispectral Index responses to induction of general anesthesia and endotracheal intubation. Systolic blood pressure increased significantly at 1 and 2 min after intubation in the control group compared with baseline value ($p<0.05$) but did not increased significantly in the lignocaine group. Heart rate increased at I and 3 min in both groups ($p<0.05$), but there was no significant difference between the two groups.

In contrast Miller CD and Warren SJ[25] showed that I/V lignocaine fails to attenuate the cardiovascular response to laryngoscopy and tracheal intubation. Laurio CE, et al[26]

gave nebulized lignocaine 4 mg/kg over 15 minutes and Chara-Emmer Jorgensen B, et al [27] gave IV lignocaine 1.5 mg/kg beginning 2 min before laryngoscopy, both these studies showed that lignocaine had no significant effect in the cardiovascular effects of intubation and laryngoscopy.

In this study, Just after intubation, the hemodynamic parameters were significantly raised ($p<0.05$) in all groups. The findings of our study are comparable to those of Bakiye et al[28] who found a rise in HR and MAP, just after intubation, and comparable to those of King et al[3] who found a rise of HR, SBP, DBP, and MAP 1 min after intubation. They also found gradual return of these parameters to baseline as anaesthesia deepened.Our study demonstrated that rise of HR, SBP, DBP, and MAP in groups F were significantly lower compared with group L at just after intubation, 3 and 5 minutes after intubation.

Conclusion:

There are a lot of options to attenuate the stress response to Laryngoscopy and Tracheal intubation. But we need to find out most cost effective and easily available option as we are the people of a developing country. Both Fentanyl and Lignocaine are cost effective and easily available in our country at present. So we tried to find out more effective one between these two drugs. Our study showed that, with fentanyl (2 mcg/kg), the rise in heart rate, systolic blood pressure, diastolic blood pressure and mean arterial pressure were significantly lower compared to lignocaine (1.5mg/Kg) at Just after intubation, 3 minutes and 5 minutes after intubation. The difference of hemodynamic variables between two groups at 10 minutes was not statistically significant. We concluded that fentanyl attenuated hemodynamic stress response to laryngoscopy and tracheal intubation more effectively than lignocaine.

References:

1. Russell WJ, Morris RG, Frewin DB, Drew SE: Changes in plasma catecholamine concentration during endotracheal intubation. Br J Anaesth 1981; 53:837-9
2. Shribman AJ, Smith G, Achola KJ: Cardiovascular and catecholamine response to laryngoscopy with and without endotracheal intubation. Br J Anaesth 1987; 59:295-9
3. King B D, Harris L C, Griefeinstein F E, Elder J D and Dripps R D. Reflex circulatory response during anaesthesia. Anesthesilogy 1951;12: 556
4. Derbyshire DC, Chmielewski A, Fell D, Vater M, Achola K, Smith G: Plasma cathecolamine response to tracheal intubation. Br J Anaesth 1983; 55:855-60
5. Fox EJ, Sklar GS, Hill CH, Villanueva R, King BD: Complications related to the pressor response to endotracheal intubation. Anesthesiology 1977; 47:524-5
6. Stoelting RK. Circulatory changes during direct laryngoscopy and tracheal intubation: influence of duration of laryngoscopy with or without lignocaine. Anaesthesiology 1977; 47:381-84
7. Abou-Madi MN, Kieszler Hand Yacoub JM. Cardiovascular reaction to laryngoscopy and endotracheal intubation following small and large intravenous doses of lignocaine**.** Canadian Journal Of Anaesthesia 1977; 24: 12-19
8. Donald E, Martin, Henry R, et al. Low dose fentanyl blunts circulatory response to tracheal intubation**.** Anaesthesia Analgesia 1982; 61: 680-4
9. Yushi U. Adachi, Maiko S, Hideyuki H and Kazuhiko W. Fentanyl Attenuates the Hemodynamic Response to Endotracheal Intubation More Than the Response to laryngoscopy. Anesth Analg 2002; 95:233–7
10. Wylie and Churchill Davidson, Stress Mangement, A Practce of Aaesthesia, 7th edition,1997; 1326
11. Shiro T, Tetsuya H, Hiroaki M, Osamu S and Koji S. Hemodynamic and Catecholamine Responses to Tracheal Intubation during Inhalation of Isoflurane or Sevoflurane. Acta Med. Nagasaki 1994; 41:76-79
12. Qureshi FM, Padmanabha S, Rahaman, H, Imran S, Mohan PR. Efficacy and Optimal Time of Oropharyngeal Topical 10**%** Lignocaine Spray Before Induction of Anaesthesia in Attenuating the Pressor Response to Direct Laryngoscopy and Endotracheal Intubation**.** IOSR Journal of Dental and Medical Sciences 2013; 9*(6):*57-63
13. Sakshi A, Anita K, Ajay Kumar B**.** Attenuation of hemodynamic response to laryngoscopy and orotracheal intubation using intravenous clonidine**.** Journal of Anaesthesiology Clinical Pharmacology 2015; 31(1):110-114
14. Coleman AJ, Jordan C. Cardiovascular response to anaesthesia. Influence of beta-adrcnoceptor blockade with metoprolol. Anaesthesia 1980; 35:972-8
15. Pun GD, Batra YK. Effect of nifidepine on cardiovascular response to laryngoscopy and intubation. Br J Anaesth 1988; 60:579-81.
16. Nishikawa T, Namiki A. Attenuation of the pressure response to laryngoscopy and tracheal intubation with intravenous verapamil. Act. Anaestheologica Scandinavica 1989; 33:232-5
17. Devault M, Griefenstein FE, Harris IC Jr. Circulatory response to endotracheal intubation in light general anaesthesia, effect of atropine and phentolamine. Anaesthesiology 1960; 21:360.
18. G.D. Puri, K. S. Marudhachalam, Pramila Chari and R. K. Suri. The effect of Magnesium Sulphate on hemodynamics and its efficacy in attenuating the response to endotracheal intubation in patients with Coronary artery disease. Anesth Analg 1998; 87:808-11

19. Stoelting RK. Attenuation of blood pressure response to laryngoscopy and tracheal intubation with sodium nitroptusside. Anesth Analg. 1979; 58:116-9

20. Grover VK, Sharma S, Mahajan RP, Singh H. Intranasal Nitroglycerine attenuate pressure response to tracheal intubation in beta blocker treated hypertensive patients. Anaesthesia 1987; 42:884-87

21. Cambel JM, Tames, Chung F. Attenuation of circulatory responses to endotracheal intubation using intravenous lignocaine, a determination of the optimal time of injection**.** Canadian Journal of anaesthesia 1985:32: 565

22. He-Sun Song, Seong-Hoon Ko, Dong-Chan Kim and Young-Jin Han. Small dose fentanyl: Optimal time of injection for blunting circulatory responses to tracheal intubation. Anesth Analg 1998; 86:658-61

23. Gurulingappa, Md Asif Aleem, M.N. Awati, Adarsh S. Attenuation of Cardiovascular Responses to Direct Laryngoscopy and Intubation-A Comparative Study Between iv Bolus Fentanyl, Lignocaine and Placebo(NS). Journal of Clinical and Diagnostic Research 2012; 6(10): 1749-1752

24. Woon-Young Kim, Yoon-Sook Lee, Se Jim Ok, Jac-Hwan Kim, Young-Cheol Park, Hye-Ja Lim. Lidocaine does not prevent bispectral index increases in response to endotracheal intubation. Anaesth analg 2006; 102: 156-159

25. Miller CD and Warren SJ. I. V lignocaine fails to attenuate the cardiovascular response to laryngoscopy and tracheal intubation**.** Br J A 1990; 65: 216-219

26. Laurio CE, et al. Effect of aerosolized lignocaine. A Haemodynamic response to laryngoscopy and intubation**.** Anaesth analg 1988; 67: 389-392

27. Chara-Emmer Jorgensen B, et al. Lack of effects of intravenous lignocaine on haemodynamic response to rapid sequence induction of general anaesthesia**.** Anaesth Analg 1986; 65

28. Bakiye Ugur, Mustafa Ugurlu, Erdal Gezer, Osman Nurim Aydin and Feray Gursoy; Effects of Esmolol, Lidocaine and Fentanyl on Haemodynamic responses to Endotracheal Intubation- A comparative study. Clinical drug investiation 2007; 27(4): 269-27

Original Article

Malocclusion on the normal oral function and psychosocial state in females: an experience of 100 cases

Quasem S I[a], Mohammadullah[b], Zaman T[c], Farook T H[d]

Abstract

Background: Malocclusion is the improper relationship of maxilla and mandibular dentition often leading to occlusal disharmony and associated oral and temporomandibular dysfunctions.

Objective: To evaluate the effects of malocclusion on the normal oral function and psychosocial state of females.

Method: This cross sectional study was done on 100 female subjects in an area within Mohammadpur of Dhaka City in June 2017. The subjects were selected using non probability convenient sampling. The subjects were studied using a structured questionnaire. The questionnaire contained information pertaining to demographics, subject's satisfaction with their teeth in respect to aesthetics and function. For the patients dissatisfied, they were questioned regarding the functional difficulties and the social stigma faced by the subjects regarding their malocclusion.

Results: Seventy-two percent of the female subjects expressed dissatisfaction with their occlusal status. Social stigma faced included a variety of situations with 36.11% of subjects being embarrassed having their pictures taken, 36.11% being embarrassed to smile in public and 27.28% having low self-esteem in general. About 8.33% complained of myofacial pain dysfunction, 16.67% complained of masticatory pain, 27.78% complained of difficulties during speaking and 13.89% complained of cheek biting.

Conclusion: Malocclusion has varying etiology but eventually lead to the same outcome; emotional distress and low self-esteem caused by a strong social stigma, and a more silent functional impairment which progressively worsens if proper treatment is not availed.

Keywords: Malocclusion, normal oral function, self-esteem, psychology, social stigma

Introduction:

Malocclusion, also known as improper occlusion between the maxilla and mandible often lead to poor or misplaced occlusal contacts and thus lead to occlusal disharmony.[1] If left untreated, this state of occlusion progresses to temporomandibular joint dysfunctions and impede normal functions of life.[2]

The effects of malocclusion on emotional health of patients often go unnoticed[3]. This survey was carried out to assess the female population's satisfaction with their current occlusion as well as note the functional and emotional difficulties that they faced as a result.

a. Dr. Sheepar Ibnul Quasem; BDS, MS (Prosthodontics)
Associate Professor, Department of Prosthodontics
Bangladesh Dental College, Dhaka

b. Dr. Mohammadullah; BDS, MS (Prosthodontics)
Medical Officer, Department of Prosthodontics, Faculty of Dentistry
Bangabhandhu Sheikh Mujib Medical University, Shahbag, Dhaka

c. Dr. Tamanna Zaman; BDS, M. Phil
Associate Professor & Head, Department of Dental Public Health
Bangladesh Dental College

d. Dr. Taseef Hasan Farook; BDS
Ex-Intern Doctor, Bangladesh Dental College Hospital, Dhaka

Correspondence to:
Dr. Sheepar Ibnul Quasem; BDS, MS (Prosthodontics)
Associate Professor, Department of Prosthodontics
Bangladesh Dental College
Email: sheepards@yahoo.com

Materials and Methods:

A cross sectional study was done on 100 female subjects age ranging from 19-35 years old in an area within Mohammadpur of Dhaka City in June 2017. The sample was obtained by non-probability convenient sampling. Inclusion criteria of samples mandated all female subjects had minimum academic qualification of S.S.C completion or equivalent and were moderately conscious regarding their oral health. Subjects who had previously received any orthodontic or prosthodontic treatment were not included. An ultra-structured questionnaire was prepared in English and Bangla. The questionnaire contained information pertaining to demographics, subject's satisfaction with their teeth in respect to aesthetics and function. For the patients dissatisfied, they were questioned regarding the social stigma faced by the subjects regarding their malocclusion. The subjects were also asked regarding any functional difficulties that they faced which could be associated with occlusal disharmony

The data were then analyzed, the results were tabulated and interpretations were made

Results:

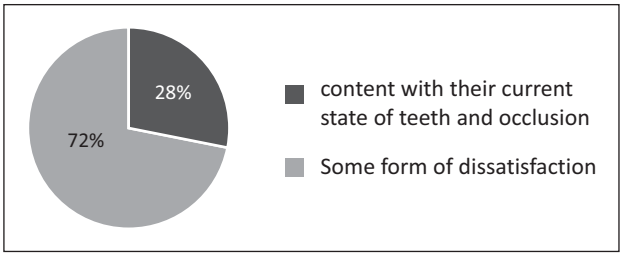


Fig 1: Distribution of subjects according to their satisfaction with their current occlusion (n=100)

Twenty-eight percent of the subjects were content with the current state of their teeth and occlusion whereas 72% of the subjects showed some form of dissatisfaction.

Table 1: Social Stigma faced by dissatisfied female subjects due to their occlusion (n=72)

Stigma	Frequency	Percent
Embarrassment in public gatherings	14	19.44
Hesitation while taking photographs	26	36.11
Hesitation during smiling	26	36.11
Negative comments from peers and family	12	16.67
Low self-esteem in general	20	27.28

About 36.11% (26) of the subjects felt a sense of hesitation during smiling as well as hesitation while having their photographs taken, 19.44% (14) felt embarrassed in public gatherings while 16.67% (12) received some form of criticism from their peers and family and 27.28% had low self-esteem in general.

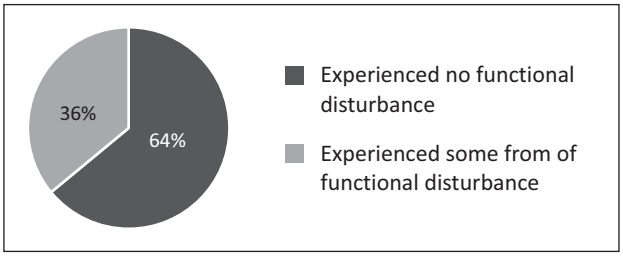


Fig 2: Distribution of subjects claiming to have experienced functional disturbances caused by their occlusion (n=100)

Sixty-four percent of the subjects experienced no functional disturbances whereas 36% experienced some form of functional disturbance.

Table 2: Distribution of subjects according to the types of functional disturbances experienced (n=36)

Physiological disturbances	Frequency	Percent
Cheek bite	10	13.89
Difficulties during speaking	20	27.78
Myofascial pain dysfunction	6	8.33%
Masticatory pain	12	16.67%

Of the subjects 8.33% (6) complained of myofascial pain dysfunction, 16.67% (12) complained of pain during mastication, 27.78% (20) complained of speech difficulties and 13.89% (10) complained of cheek bite

Discussion:

Malocclusion has a widely varying etiology but eventually leads to the same outcome; emotional distress and low self esteem[4,5] caused by a strong social stigma, and a more silent functional impairment[6] which progressively worsens if proper treatment is not availed.[7] Malocclusion is an epidemic found also amongst the Bangladeshi population.[8] From this study, it was found that most subjects felt a sense of embarrassment because of the current state of their occlusion. This can be attributed to the fact that social norms play an important role in deciding what is acceptable and what is not. (Matilda, 2008) Apart from the aesthetic and psychological aspect, the daily functions suffer from improper occlusion as well, as also seen in the survey. Although the most common functional complaint was difficulties during speaking, this can be attributed to a multitude of factors: Stuttering and speech impairment are very rare occurrences in malocclusion cases[9] however lip bite and lip incompetency can also lead to speech difficulties. Another factor associated with speech difficulties is the position of the anterior teeth as occlusal disharmony in the anterior segment often lead to poor pronunciation of certain alphabets.[10] Other disorders associated with the TMJ and muscles of mastication have also been seen in other parts of the world as common functional disturbances caused by improper occlusion (Manfredini, 2015). Emotional distress like anxiety and depression founded upon dental problems are in fact issues of concern and should not be ignored, rather acted upon promptly[11, 12] as there might be underlying functional abnormalities as well. The dental practitioner is also recommended to observe signs of depression and anxiety among their patients and counsel them appropriately during treatment.

Conclusion:

Occlusal disharmony has varying etiology but eventually lead to the same outcome; emotional distress and low self-esteem caused by a strong social stigma, and a more silent functional impairment which progressively worsens if proper treatment is not availed. Emotional distress like

anxiety and depression are in fact issues that should not be ignored and acted upon appropriately. The dental practitioner should also provide psychological counseling to their patients as well as provide appropriate treatment for the patients' functional disturbances.

References:

1. Redzepagic Vrazalica Lejla, Ilic Zlatko, Laganin Slaven , Dzemidzic Vildana , Tiro Alisa. An epidemiological study of malocclusion and occlusal traits related to different stages of dental development: South Eur J Orthod Dentofac Res; 2017; 4 (1), 9-13
2. Manfredini D, Perinetti G, Stellini E, Di Leonardo B, Guarda-Nardini L. Prevalence of static and dynamic dental malocclusion features in subgroups of temporomandibular disorder patients: Implications for the epidemiology of the TMD-occlusion association. Quintessence Int. 2015;46(4):341-9.
3. Matilda Mtaya, Anne N Astrom, Pongsri Brudvik. Malocclusion, psycho-social impacts and treatment need: A cross-sectional study of Tanzanian primary school-children. Published online 2008 May 6. doi: 10.1186/1472-6831-8-14
4. Onyeaso CO, Sanu OO. Psychosocial implications of malocclusion among 12-18-year-old secondary school children in Ibadan, Nigeria. Odontostomatol Trop. 2005; 28:39–48. [PubMed]
5. Bernabé E, Flores-Mir C, Sheiham A. Prevalence, intensity and extent of Oral Impacts on Daily Performances associated with self-perceived malocclusion in 11-12-year-old children. BMC Oral Health. 2007; 7:6.
6. Kovalenko A1, Slabkovskaya A, Drobysheva N, Persin L, Drobyshev A, Maddalone M. The association between the psychological status and the severity of facial deformity in Orthognathic patients. Angle Orthod. 2012 May; 82(3):396-402. doi: 10.2319/060211-363.1. Epub 2011 Oct 18
7. Eugene Twigge, Rachel M. Roberts, Lisa Jamieson, Craig W. Dreyer, Wayne J. Sampson. The psycho-social impact of malocclusions and treatment expectations of adolescent orthodontic patients. European Journal of Orthodontics, December 2016; 38(6):593-601. https://doi.org/ 10.1093/ejo/cjv093
8. Shamim Jubayer, Md Abdul Kader, Salma Sharmin, Nasrin Sultana, Mohammad Shamim Al Mamun. Prevalence of malocclusion among the age group of 15-25 years in Bangladeshi population. Bangladesh Journal of Orthodontics and Dentofacial Orthopedics 2014; 4. (1-2)
9. Craig A, Blumgart E, Tran Y. The impact of stuttering on the quality of life in adults who stutter. Journal of Fluency Disorders; 1990. 34, 61-71
10. Giovannetti Martina, Casucci Alessio, Casucci Daniele, Mazzitelli Claudia, Borracchini Andrea. (2018). Phonetic analysis and maxillary anterior tooth position: a pilot study on preliminary outcomes. International Dentistry SA; 11(5): 32-39
11. Seema G, Somesh G, Deepak A. Psychological Aspects to orthodontic treatment. J Ind Orthod Soc 2001; 34: 92-94
12. Peñaranda P. Importance of psychology in dentistry. Acta Odontol Venez. 1990 May-Dec;28(2-3):39-48.

Haematuria in Children- An Overview

Arefin KE [a], Lucky MA [b], Bhuiyan M E [c]

Introduction:

EHaematuria is one of the most common urinary findings in the children.[1] Generally, haematuria is defined as the presence of 5 or more red blood cells (RBCs) per high-power field in 3 of 3 consecutive centrifuged specimens obtained at least 1 week apart.[1] For screening purpose a urine dipstick test is quite useful. The strips can detect 5 to 10 intact RBC per mm^3, which roughly corresponds to 2 to 5 RBC per HPF.[2]

Haematuria can be classified in various ways. It may be gross (The presence of RBC which can be visible to the naked eye) or microscopic (The presence RBC that can be visible only under microscope), symptomatic (Haematuria plus lower or upper urinary tract symptoms) or asymptomatic (Incidental detection of non-visible haematuria in the absence of upper or lower urinary tract symptoms), transient (It is proven haematuria that is non repetitive and does not lead to a diagnosis) or persistent (It refers to six months of observation with at least one proven haematuric episode per month), glomerular or non-glomerular, and either isolated or associated with proteinuria and other urinary abnormalities.[3]

Gross haematuria is suspected when red or brown urine is present.[4] The prevalence of gross haematuria in children is estimated to be 0.13%.[1] and asymptomatic microscopic haematuria in school-aged children has been estimated at 0.5% to 2.0%.[5,6] In United States the prevalence of gross haematuria in children is estimated to be 1.3 per 1000.[7] For the family, gross haematuria is an alarming occurrence which usually leads the parents to seek medical help fast, irrespective of whether the child has other symptoms.[3] More than 50% of children presenting with gross haematuria have a readily apparent cause.[8] However, red or brown urine can be due to causes other than blood. Thus, the initial step in the evaluation of patients with red urine is to establish whether or not the urine discoloration is due to blood or another substance.[4]

a. Dr. Khondoker Ehsanul Arefin; MD, MPH, MBBS
Associate Professor (CC), Department of Paediatrics
Bangladesh Medical College

b. Dr. Mohsina Akter Lucky; MD, MPH, MBBS
Jr. Consultant of Paediatrics
Sheikh Fazilatunnessa Mujib Memorial KPJ Specialized Hospital and Nursing College.

c. Dr. Md. Elias Bhuiyan; FCPS, MRCP, MBBS
Assistant Professor (CC), Department of Medicine
Bangladesh Medical College

Correspondence to:
Dr. Khondoker Ehsanul Arefin; MD, MPH, MBBS
Associate Professor (CC)
Dept. of Paediatrics
Bangladesh Medical College
Email: drarefin@yahoo.com

Microscopic haematuria is a common finding in children.[9,10] Asymptomatic microscopic haematuria is, on the average, 10-fold as prevalent as gross haematuria.[1] Increased use of multiple dipstick test for routine examination of urine together with the increased sensitivity of the hemastix portion of the test has led to many more children with microscopic haematuria coming to light (Postlethwaite 1994).[3]

In Japan the prevalence of isolated persistent microscopic haematuria in school children was approximately 0.05%. Prevalence of microscopic haematuria with associated proteinuria was 0.08% of primary school children and 0.4% of junior high school children.[11] In Shanghai, urine screening was done in more than 40,000 school children between 2003 and 2005. The prevalence of microscopic haematuria was found to be more than 5%.[12] One of the largest screening done in Helsinki using Ames hemastix test and prevalence of microscopic haematuria was found 3.4%.[3]

There is a long list of causes of microscopic haematuria, most of which are benign, especially in children with isolated asymptomatic microscopic haematuria. The dilemma that faces the clinician is to identify the child in whom haematuria caused by significant underlying disease.[9,10] Child with persistent microscopic haematuria is facilitated with the determination of whether the blood originates from the glomeruli or whether it comes from elsewhere in the urinary tract. Clues to a glomerular origin include the presence of other manifestations of glomerular disease such as significant proteinuria, RBC casts, and dysmorphic erythrocytes in the urinary sediment, hypertension, and renal insufficiency.[11] Clues to the blood originating from the lower urinary tract include blood clots in the urine, normal erythrocyte morphology, and a pertinent history pointing to the lower tract such as that of trauma, urolithiasis, urological or vascular abnormality, or symptoms of bladder inflammation .[13,14]

The role of the primary care physician in the management of a child with haematuria includes recognizing and confirming the finding of haematuria, identify common etiologies and selecting patients who have significant urinary system disease that might require further expertise in either diagnosis or management and referral.[15,16]

Re-orientation of haematuria in children is very much essential for clinical practice to suggest a practical approach in management of a case with haematuria. So the objective of this review was planned to update the current knowledge about haematuria in children for correct diagnosis and management and also appropriate referral to a specialist.

Pathophysiology of Haematuria:

The pathophysiology of hematuria depends on the anatomic site in the urinary tract from which blood loss occurs. A distinction has conventionally been drawn between glomerular and extraglomerular bleeding, separating nephrologic and urologic disease.[17]

Blood originating from the nephron is termed glomerular or nephronal hematuria. RBCs can enter the urinary space from the glomerulus or rarely, from the renal tubule. Disruption of the filtration barrier in the glomerulus may result from inherited or acquired abnormalities in the structure and integrity of the glomerular capillary wall. These RBCs can be trapped in Tamm-Horsfall mucoprotein and will be manifest in the urine by RBC casts. Finding casts in the urine represents significant disease at the glomerular level.[17,18] However, in disease of the nephron, casts can be absent and isolated RBCs may be the only finding. The presence of proteinuria helps support a glomerular source of blood loss. Hematuria without proteinuria or casts is termed isolated hematuria. Although a few glomerular diseases may produce isolated hematuria, this finding is more consistent with extraglomerular bleeding. Anything that disrupts the uroepithelium, such as irritation, inflammation, or invasion, can result in normal-appearing RBCs in the urine. Such insults may include malignancy, renal stones, trauma, infection, and medications. Also, nonglomerular renal causes of blood loss, such as tumors of the kidney, renal cysts, infarction, and arteriovenous malformations, can cause blood loss into the urine .[18]

Haematuria can be classified in various ways [3]

As per visibility

a) ***Gross haematuria****:* The presence of blood in the urine in sufficient quantity to be visible to the naked eye.

b) ***Microscopic haematuria:*** The presence of blood in the urine is too low to change the color of the urine and that can be visible only under microscope.

As per Symptoms

a) ***Symptomatic:*** Haematuria plus lower urinary tract symptoms (hesitancy, frequency, urgency, dysuria) or upper urinary tract symptoms (anorexia, fever, abdominal pain).

b) ***Asymptomatic:*** Incidental detection of non-visible haematuria in the absence of upper or lower urinary tract symptoms.

As per duration of illness

a) ***Transient:*** It is proven haematuria (present at >5 RBC/HPF), that is non repetitive and does not lead to a diagnosis.

b) ***Persistent*****:** It refers to six months of observation with at least one proven haematuric episode per month.

With Association

a) ***Isolated:*** A condition characterized by an "abnormal" number of red blood cells in the urine in the absence of proteinuria and normal renal function.

b) With proteinuria

As per Site

a) ***Glomerular:*** Inflammation of the renal glomeruli causes leukocyte infiltration and cellular proliferation of the glomeruli. These structural and functional abnormalities usually lead to haematuria. Hallmarks of glomerular bleeding are discolored urine, RBC casts, and distorted RBC (such as budding or blebs) morphology.

b) ***Non glomerular:*** The presence of blood clots and isomorphic RBC in urine are indicative of extra glomerular bleeding.

Causes of haematuria in children could be glomerular haematuria and non-glomerular/extra glomerular haematuria. Glomerular haematuria in children includes IgA nephropathy (Berger disease), Alport syndrome (hereditary nephritis), Thin glomerular basement membrane nephropathy, Post-infectious glomerulonephritis, Membranous nephropathy, Membranoproliferative glomerulonephritis, Focal segmental glomerulosclerosis, Anti glomerular basement membrane disease. Some multisystem disease causes glomerular haematuria like Lupus nephritis, Anaphylactoid purpura (Henoch-Schönlein purpura), Wegener granulomatosis, Polyarterirtis nodosa, Goodpasture syndrome, Hemolytic uremic syndrome, Sickle cell glomerulopathy, HIV nephropathy. Extraglomerular/Nonglomerular haematuria includes Pyelonephritis, Interstitial nephritis, Acute tubular necrosis, Papillary necrosis, Nephrocalcinosis, Arterial venous thrombosis, Malformations, Nutcracker syndrome. Crystalurea (Calcium, Oxalate, Uric acid), Anatomic (Hydronephrosis, Cystic kidney disease, Tumour. Trauma), Hemoglobinopathy.[1,16]

Some drugs are responsible for haematuria like Captopril, Cephalosporins, Chlorothiazide, Ciprofloxacin, Furosemide, NSAIDs, Omeprazole, Penicillins, Silversulfadiazine, Trimethoprim-sulfamethoxazole, Cyclophosphamide (Cytoxan).

Other causes of red urine include foods (Particularly beetroot and berries (anthocyanins) and confectionery containing vegetable dyes. Drugs (Pyridium (phenazopyridine), phenindione, Phenothiazines, Rifampicin, Despherrioxamine, phenolphthalein and anthraquinone laxatives (e.g. Dorbanex, danthron), Metals: (Copper sulphate, Lead, Gold, Phosphorus), Haemoglobinuria, Myoglobinuria, Urates, which in high concentration may produce a pinkish tinge.[20]

Diagnostic Approach to a Case with Haematuria in Children:

History

Haematuria-Timing, dysuria, urgency, frequency, enuresis, abdominal pain, renal angle pain, trauma, hearing loss, frequency and intake of medications, exercise, sore throat, skin infection, viral infection.

Family history

Haematuria, deafness, hypertension, coagulopathy, haemoglobinopathy, calculi, renal failure, dialysis or transplant.

Physical Examination

Fever, arthritis, rash, blood pressure, oedema, nephromegaly, renal angle tenderness. Presence of abdominal mass should be looked for and blood pressure accurately measured. Several malformation syndromes are associated with renal disease including VATER (vertebral body anomalies, anal atresia, trachea-esophageal fistula and renal dysplasia). Hematuria seen in patients with neurologic or cutaneous abnormalities may be the result of renal cystic disease or tumour associated with several syndrome including Tuberous Sclerosis, Von Hippel Lindau syndrome and Zellweger syndrome. Ophthalmic examination should be done.[2]

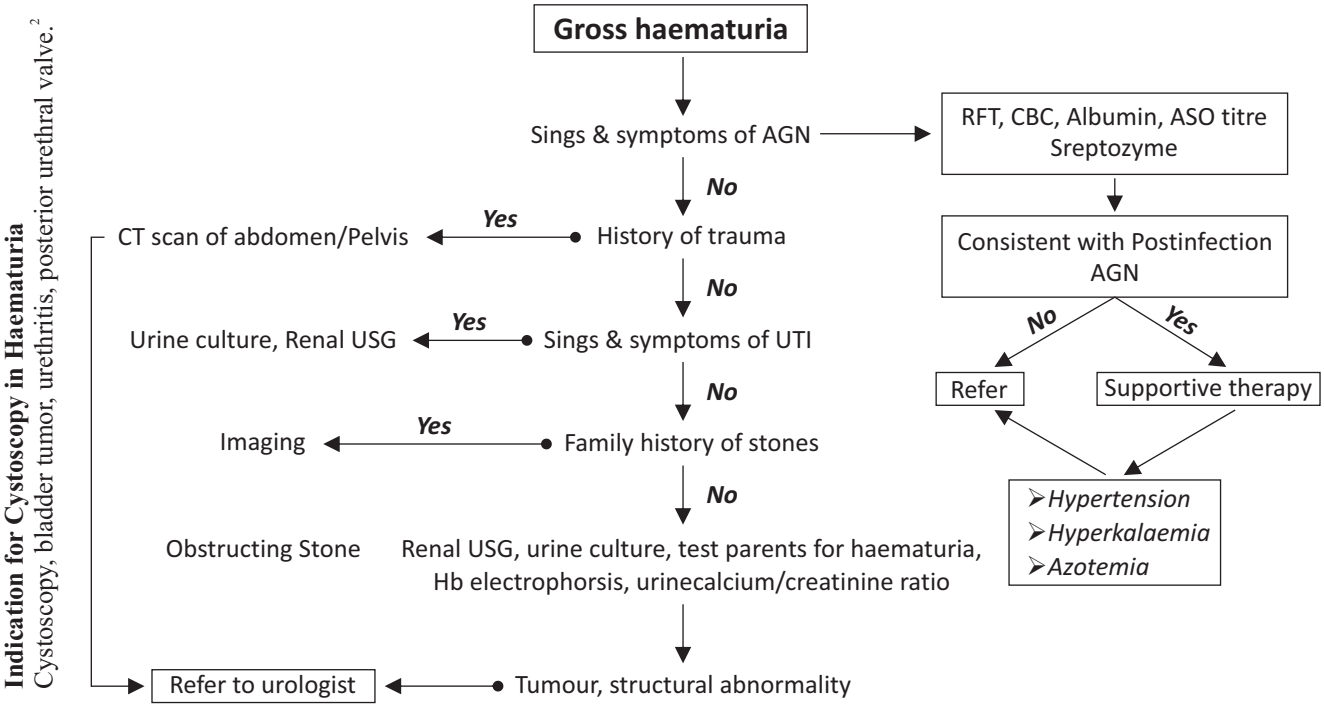
Investigation

The laboratory tests ordered for the evaluation of haematuria must be based on the clinical history and the physical examination. The physician should ensure that serious conditions are not overlooked, avoid unnecessary laboratory studies, reassure the family, and provide guidelines for additional studies. The Investigations are Urinalysis (Dip strip analysis, Urine microscopy, Phase contrast microscopy), 24 hours urinary total protein, urine calcium, serum creatinine, blood urea nitrogen, serum electrolytes, hematologic and coagulation studies. Serologic tests include serum complement levels, ASO titer, Anti-dnase B, ANA titers and double-stranded DNA (dsdna) levels. Some imaging studies are done in haematuria- Ultrasound, plain AXR, imaging, MCUG, IVP, CT scan, MRI.

Indication for renal biopsy in haematuria

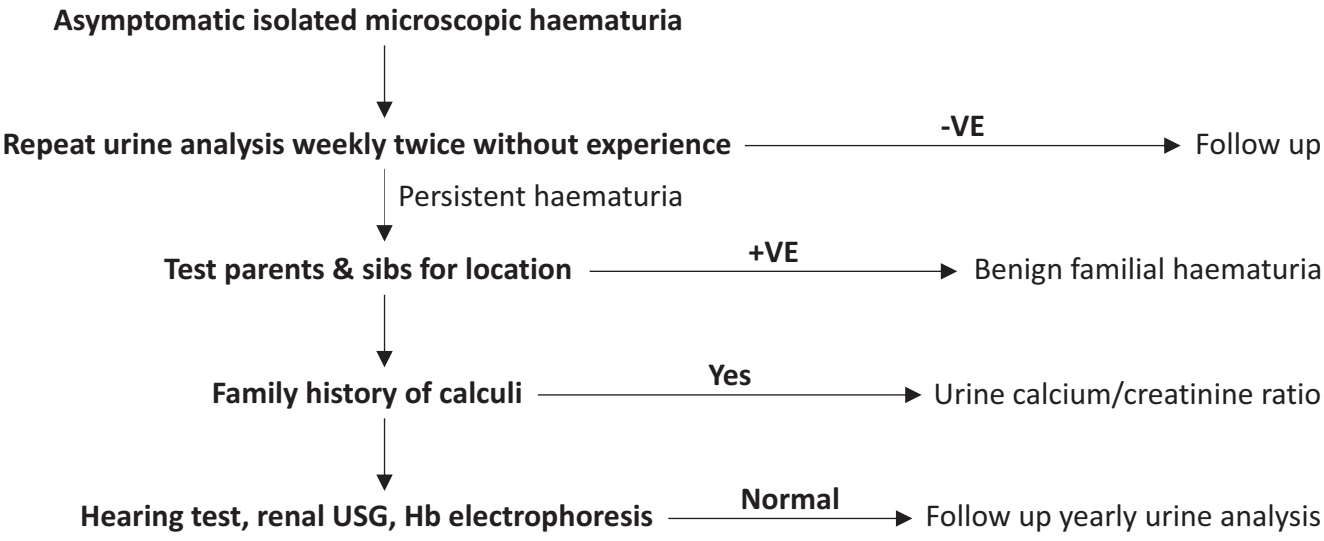
Biopsy rarely indicated. Relative indications are significant proteinuria, abnormal renal function, recurrent persistent haematuria. serological abnormalities (abnormal complement, ANA or Anti ds DNA). recurrent gross haematuria, family history of ESRD. [19]

Evaluation of a child with gross haematuria[21]

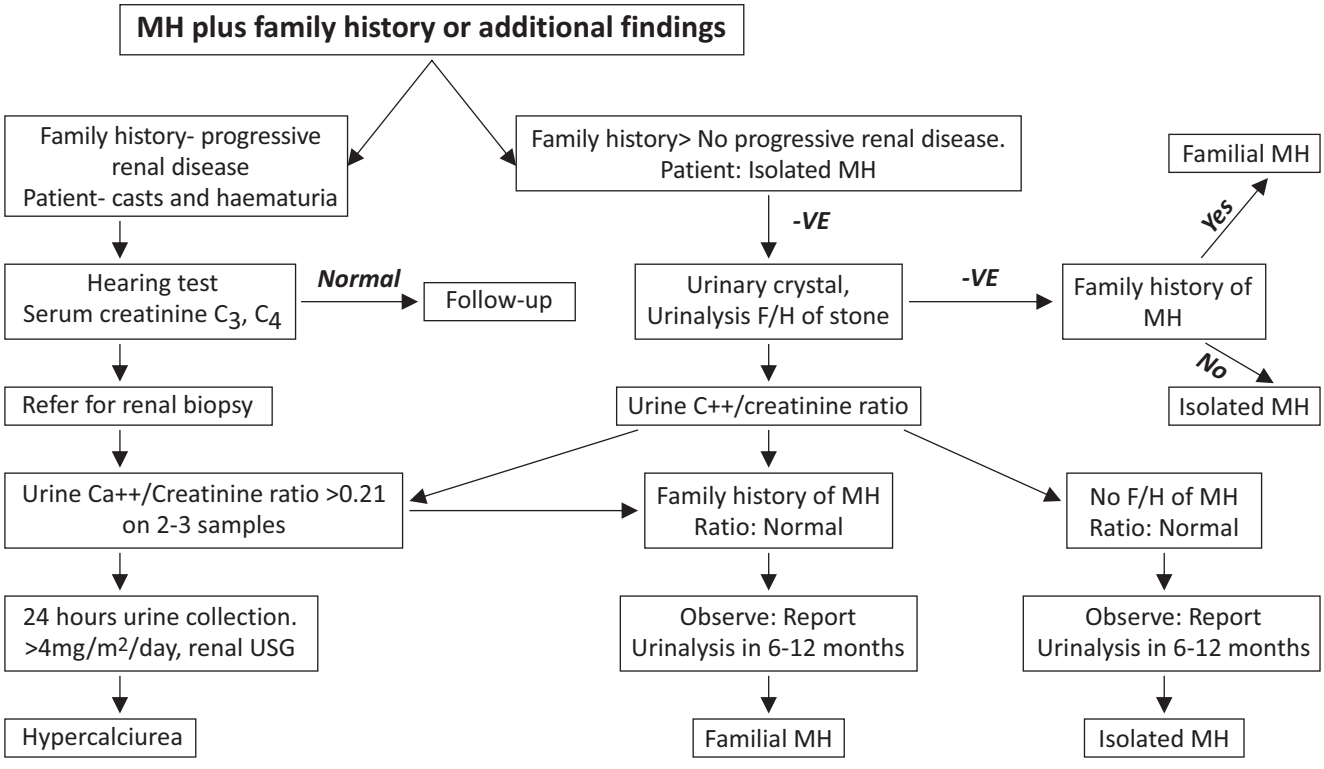


RFT- **Renal test;** CBC- **complete blood count;** AGN- **acute glomerulonephritis;** USG- **ultrasonography;** UTI- **urinary tract infection;** ISO- **antistreptolysin o;** CT- c**omputed tomography;** Hb- **haemoglobin**

Evaluation of a child with asymptomatic microscopic haematuria[21]



Evaluation of a child with symptomatic microscopic haematuria[21]



MH- **Microscopic haematuria**

Treatment: Treatment is based on a combined approach of multidisciplinary team. Here pediatrician plays the central role. Treatment depends upon the primary etiology. Appropriate referral is very important to treat some cases.

Role of Primary Care Physician in The Management of Haematuria

- Recognize and confirm the findings of haematuria.
- Identify common etiologies.
- Selection of patients for early referral.

Conditions Need Referral of a Child with Haematuria to specialist [16]

Nephrologist: APSGN with hypertension, azotemia or hyperkalaemia, hypertension, Persistent hypocomplementemia, Other GN with proteinurea.

Urologist: Anatomical abnormality, trauma, stones, tumour, nonglomerular gross haematuria.

Counseling: Counseling depends on the nature and course of the primary disease. It is very essential to discuss the problem with the anxious parents of the child and to be optimistic since much haematuria is relatively transient. It is best to impress on them the rarity of renal failure and the fact that the child is healthy and has kidneys which work well and then to follow-up the child during the next few months with the parents testing the urine occasionally and a record being kept of the occurrence of any haematuria.[3] If the haematuria persists either macroscopically or microscopically for at least a year, then it is probably worth investigating further.[22]

Follow up: The follow up for the various conditions associated with haematuria is dependent on the primary medical condition that caused the haematuria.

Conclusions:

Haematuria is a common clinical condition for referral from general practitioner. Some cases require sophisticated investigation including renal biopsy for confirmation of diagnosis.

References:

1. Gulati S & Pena D. Haematuria, E Medicine Specialties. Retrieved June, 2010 from http:// emedicine. medscape.com/article/981898-overview.
2. Srivastava RN, Bagga A. Pediatrics Nephrology. 4th ed. Jaypee Brothers medical publishers (Pvt) LTD. New Delhi 2005;203-06.
3. Postlethwaite RJ. Clinical Paediatric Nephrology.2nd ed. Butterworth-heinemann LTD 1994.
4. Gagnadoux MF. Evaluation of gross haematuria in children, retrieved May, 2008 from www.uptodate. com.
5. Bergstein J, Leiser J & Andreoli S. The Clinical significance of asymptomatic gross and microscopic haematuria in Children'. Arch Pediatr Adolesc Med 2005; 159:353-355.
6. Greenfield SP, Williot P, Kaplan D. Gross hematuria in children: a ten-year review. Urology 2007; 2:159-166.
7. Meyers KEC. Evaluation of hematuria in children. Urol Clin N Am 2004; 31:559-573.
8. Ingelfinger JR, Davis AE & Grupe WE. Frequency and etiology of gross haematuria in a general pediatric setting. PEDIATRICS 1977; 59:557-62.
9. Dodge WF, West EF & Smith EH. Proteinuria and haematuria in school children: epidemiology and early natural history. J Pediatr 1976; 88:327.
10. Vehaskari VM, Rapola J & Koskimies O. Microscopic haematuria in school children: epidemiology and clinicopathologic evaluation. J Pediatr 1979; 95: 676.
11. Kitagawa T. Screening for renal disease in school children: experience in Japan. Indian Journal of Pediatrics 1988;55: 481-494.
12. Hui ZY, Xu H & Hua ZG. Efficacy of urine screening at school: experience in Shanghai, China. Pediatric Nephrology 2007; 22: 2073-79.
13. Lieu TA, Grasmeder M & Kaplan BS. An approach to the evaluation and treatment of microscopic hematuria. Pediatr Clin North Am 1991; 38:579-92.
14. Yadin O. Haematuria in children. J Pediatr 1994; 23:474-8.
15. Diven SC. Travis LB. A practical primary care approach to haematuria in children. Pediatr Nephrol 2000;14;65-72.
16. Behrman RE, Kleigman RM, Jenson HB & Santon BF. Nelson Textbook of Pediatrics.18th ed 2008; 2:186.
17. Wellsphere. Pathophysiology of Hematuria. Retrieved August 2010 from http://www.wellsphere.com/ wellpage/pathophysiology-of-hematuria.
18. Fauci AS, Braunwald E, Kasper DL, Hauser SL, Longo DL, Jameson JL et al. Alterations in Urinary Function and Electrolytes. Harrison's Principles of Internal Medicine, 17th ed.2008;209-10.
19. Feld LG, Stapleton FB & Duffy L. Renal biopsy in children with asymptomatic haematuria or proteinuria: survey of pediatric nephrologists. Pediatr Nephrol 1993;7: 441-3.
20. Free A & Free H. Urinalycis in Clinical Laboratory Practice. Cleveland, CRC Press 1976:1090-91.
21. Rahman MH. An approach to management of haematuria in children.10th International Scientific Conference. Paediatric Nephrology Society of Bangladesh 2007.
22. Garg AX, Suri RS & Barrowman N. Long-term renal prognosis of diarrhea-associated hemolytic uremic syndrome'. JAMA 2003; 290:1360-1370.

Case Report

Bowen's disease of nipple and ductal carcinoma in situ of breast: A rare presentation

Nafisa A[a], Ahmed S K F[b], Mostafa G[c], Alam M A[d], Murad S S[e], Ahmed S[f], Priam S M[g], Ferdous H[h]

Abstract

The clinical and morphological features of Bowen's disease (Squamous cell carcinoma in situ) of the nipple have been reported here as a rare case in Bangladesh. The 48-year-old patient had an eczema type change in the left nipple with minor ulceration and nipple discharge for over 1 month. The microscopic evaluation of the extensive segmental resection showed Bowen's disease of the nipple. Paget's disease was excluded with certainty. The treatment of choice was extended segmental resection. She also had an area of lumpiness in left breast. Her mammogram was normal and ultrasonogram showed small anechoic lesion, possibly fibrocystic change. Her FNAC showed atypia with ductal proliferation. This was removed and surprisingly showed a completely excised intermediate grade, 1 cm area of ductal carcinoma in situ (DCIS). Epidermal Bowen's disease of breast is an uncommon entity but with similar clinical signs as in other anatomical areas and has prognostically favorable outcome.

Keywords: Bowen's disease, Squamous cell carcinoma, Ductal carcinoma in situ breast.

Introduction:

Squamous cell carcinoma in situ (Bowen's disease) is a common skin condition but has only rarely been described on the nipple.[1] Bowen's disease is a very early form of skin cancer that's easily treatable and all reported cases have been treated with wide local excision. The main feature is a patch; the patch may be red or pink, scaly or crusty, flat or raised, up to a few centimeters across, itchy- but isn't always on the skin. It affects the squamous cells- which are in the outermost layer of skin- and is sometimes referred to as squamous cell carcinoma in situ.[2] The patch is usually very slow growing, but there's a small chance that it could turn into a more serious type of skin cancer if left untreated. The patch can appear anywhere on the skin but is especially common on exposed areas like the lower legs, neck and head. Sometimes they can affect the groin area and, in men, the penis. If the patch bleeds, starts to turn into an open sore (ulcer) or develops a lump, it could be a sign that it has turned into squamous cell skin cancer. Bowen's disease can look like other conditions, such as psoriasis or eczema.[3] Differential diagnoses for Bowen's disease of the nipple include Paget's disease of the breast, which is more common in this site and the less prevalent superficial spreading melanoma. It is challenging to macroscopically and/or histologically differentiate Bowen's disease from Paget's disease or melanoma. For definitive diagnosis immunohistochemical approach is needed. Tissue from patients with Bowen's disease exhibits positivity for low- and high-molecular-weight cytokeratins and/or epithelial membrane antigen and melanoma tissue shows strong positivity for S-100.[4]

a. Dr. Ali Nafisa; FCPS, MBBS
Associate Professor, Department of Surgery
Anwer Khan Modern Medical College, Dhaka

b. Dr. SK Farid Ahmed; FRCS, MBBS
Breast & Oncoplastic Breast Surgeon, Wycombe Hospital
Buckinghamshire Healthcare NHS Trust, UK,
Visiting Consultant and Advisor, Anwer Khan Modern Breast Care Unit and Research Centre, Dhaka

c. Prof. Dr. Golam Mostafa; M. Phil, MBBS
Professor, Department of Histopathology, National Institute of Cancer Research and Hospital, Mohakhali, Dhaka

d. Dr. Md. Ahasanul Alam; MBBS
Assistant Registrar, Department of Vascular Surgery,
National Institute of Cardiovascular Disease, Dhaka

e. Dr. Shoeb Sarwar Murad; MS, MBBS
Assistant Professor, Department of Orthopedic surgery,
Anwer Khan Modern Medical College, Dhaka

f. Dr. Salma Ahmed; MBBS
Medical Officer of Surgery, Anwer Khan Modern Medical College, Dhaka

g. Dr. Samanta Meharin Priam; MBBS
Medical Officer of Surgery, Anwer Khan Modern Medical College, Dhaka

h. Dr. Hasnatul Ferdous; MBBS
Medical Officer of Surgery, Anwer Khan Modern Medical College, Dhaka

Correspondence to:
Dr. Ali Nafisa
Associate Professor, Department of Surgery
Anwer Khan Modern Medical College, Dhaka, Bangladesh.
Email: alinafisadr@gmail.com

Case Presentation:

A 48-year-old patient presented with one-month history of nipple change in Anwer Khan Modern Medical College Hospital. Clinically, she had small red, superficial ulceration in (Fig-1) left nipple with no obvious palpable suspicious mass. There was no history of breast disease or family history of breast or ovarian cancer. She was hypertensive. She was investigated with normal mammogram. USG showed anechoic lesion, possible

fibrocystic disease. She had US guided FNAC, discharge cytology. FNAC showed atypia ductal proliferative lesion. Wedge excision of nipple confirmed the diagnosis of Bowen's disease (Fig-2). Histopathology shows focal epidermal hyperplasia with hyperkeratosis and parakeratosis with keratinolytic crowding & pleomorphism. Mitotic figures were seen within the keratinocytes (Fig-3). The whole lesion was confined within the epidermis. The basement membrane was intact. She was also found to have a lumpy area of abnormality, FNAC showing of ductal proliferation with atypia.

Surgical plan was to resect nipple and peroperative ultrasonogram guided wide local excision (Fig- 4) under general anesthesia. A horizontal margin was established beginning at the nipple, which was resected down to the level of the areolar subcutaneous fat proximal to the lactiferous duct (Fig- 5 & 6). Frozen section biopsy confirmed margin clear. Histopathological analysis of the resected rest of nipple showed no residual tumor in nipple. Histologically breast lump showed as completely excised 1 cm area of high-grade DCIS, all margins were clear with ER 5/8, PR 0/8.

Postoperatively, we advised adjuvant radiotherapy to breast but patient refused to radiotherapy as patient had second opinion elsewhere. That is why patient chose to have completion mastectomy and SNB (Sentinel Node Biopsy). Histopathology showed no residual tumor and SNB negative.

The patient refused radiation therapy of the left residual breast because of treatment-related anxiety. The regular follow up at 6 months interval and contralateral annual mammogram, the patient remained symptom free. After two and half years, the patient showed no signs of recurrence and was undergoing follow-up on an outpatient basis.

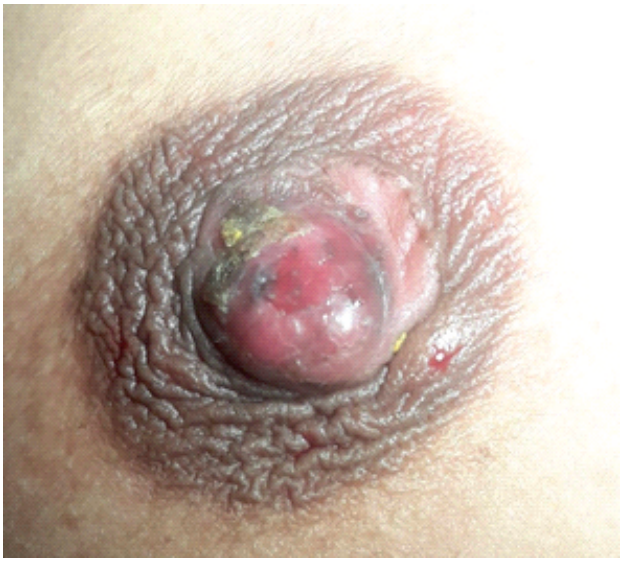


Figure 1: The epidermis of the right nipple was inflamed and swollen

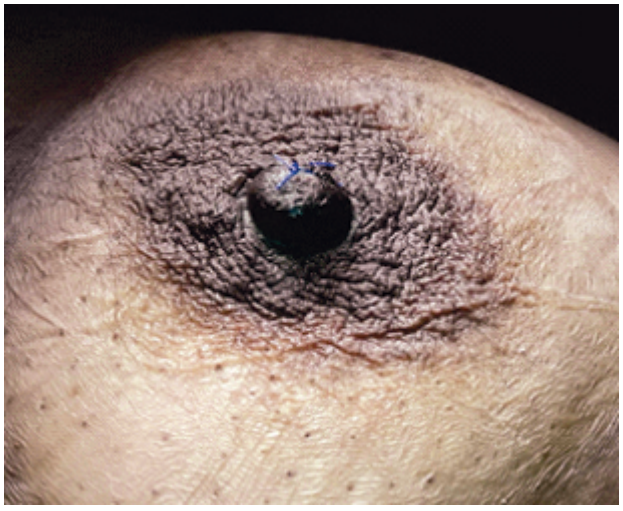


Figure 2: Post wedge biopsy of lesion

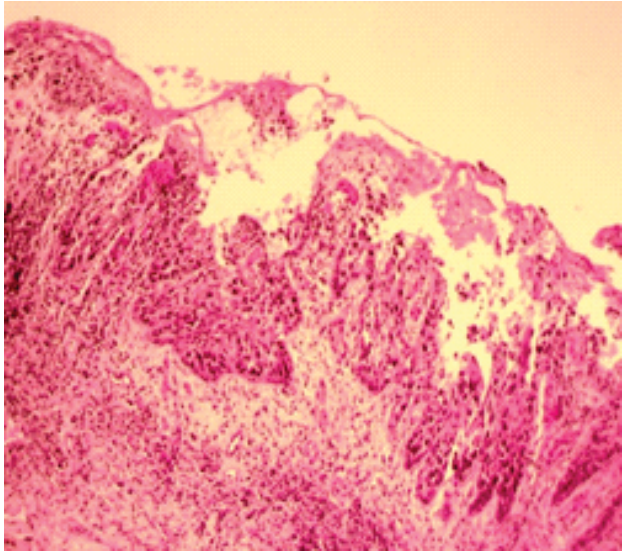


Figure 3: Histopathological image showing Bowen's disease

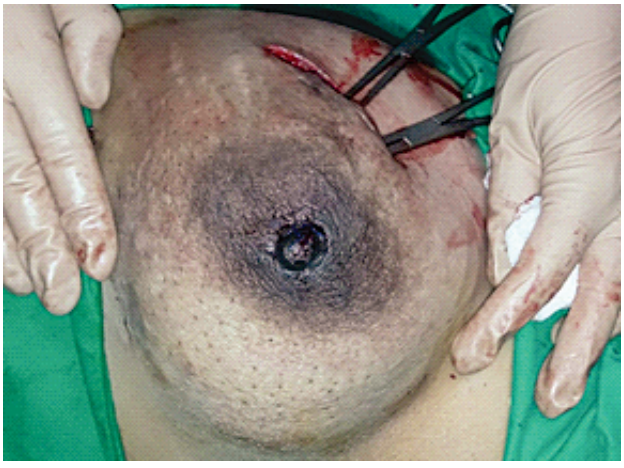


Figure 4: Per operative excision of small non palpable lump with help USG guided localization

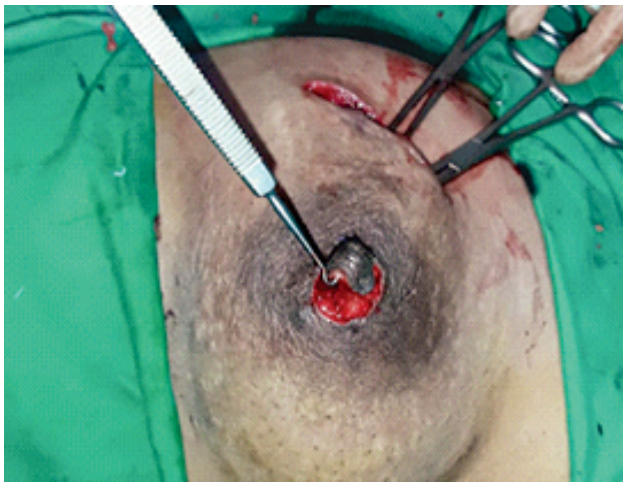


Figure 5: Wide local Excision of Nipple

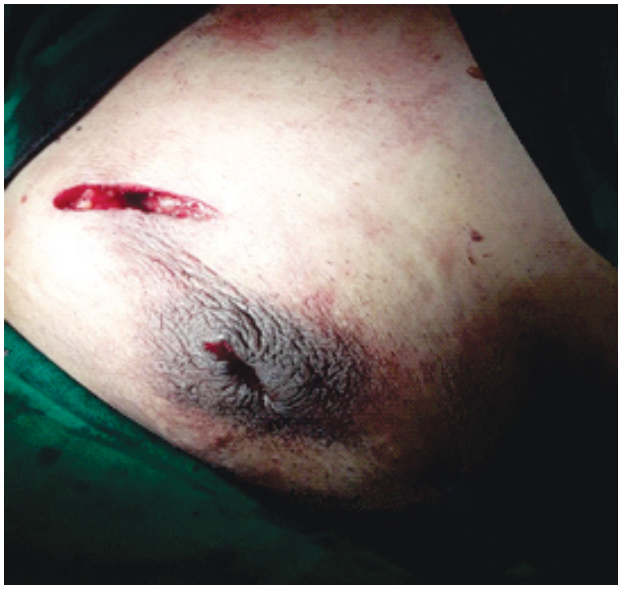


Figure 6: Wide local Excision of nipple and 1cm non palpable lump.

Discussion:

Bowen's disease of nipple is very rare case. It may confuse with Paget's disease of nipple and eczema. Bowen's disease was first described in the medical literature by a physician named JT Bowen in 1912.[5]

Bowen's disease usually affects older people in their 60s and 70s.[6] The exact cause is unclear, but it has been closely linked with: long-term exposure to the sun or use of sunbeds- especially in people with fair skin. Having a weak immune system like - taking medication to suppress their immune system after an organ transplant, or those with AIDS, previously having radiotherapy treatment, the human papillomavirus (HPV).[7] Three percent of cases can progress to invasive form.[8] Bowen's disease is an intraepidermal SCC in situ. Punch biopsy/ Wedge biopsy of nipple and histopathology and immunohistochemistry can confirm the diagnosis to rule out dermal invasion and mammogram and ultrasonogram to find out other pathology in breast. Beside variety of treatment options, wide local excision of nipple with clear margin is safe treatment for Bowen's disease. Treatment options for Bowen's disease includes topical chemotherapy, cryotherapy, curettage, photodynamic therapy and wide local excision.[1] The response may vary from person to person. It is recognized that one patient was treated successfully with a combination of photodynamic therapy and cryotherapy.[5] Treatment plan for Bowen's disease should be individualized.

Statement of Ethics:

Written informed consent was obtained from the patient for publication of this case re-port and accompanying images.

References:

1. Brookes PT, Jhawar S, Hinton CP, Murdoch S, Usman T. Bowen's disease of the nipple-a new method of treatment. Breast. 2005 Feb;14(1):65-7.
2. Miyuki Kitaharaa M, Hozumia Y, Watanabea A Iijimab T. Report on Bowen's Disease of the Nipple. Case Rep Oncol 2018; 11:609-614.
3. Shah KD, Tabibzadeh SS, Gerber MA. Immunohistochemical distinction of Paget's disease from Bowen's disease and superficial spreading melanoma with the use of monoclonal cytokeratin antibodies. Am J Clin Pathol. 1987 Dec;88(6):689-95.
4. Vanstapel MJ, Gatter KC, De Wolf-Peeters C, Millard PR, Desmet VJ, Mason DY. Immunohistochemical study of mammary and extra-mammary Paget's disease. Histopathology. 1984 Nov;8(6):1013-23.
5. Yazicioglu MB, Tokyol C, Turel KS, Keskin AI, Aktepe F. A rare disease of the breast: Bowen's disease. Natl J Med Res 2014; 4:168-9.
6. Hosaka N, Uesaka K, Takaki T, Zhang Y, Takasu K, Ikehara S. Poorly differentiated squamous cell carcinoma of the nipple: a unique case for marked exophytic growth, but little invasion with neuroendocrine differentiation. Med Mol Morphol. 2011 Sep;44(3):174-8.
7. Arlette JP, Trotter MJ. Squamous cell carcinoma in situ of the skin: history, presentation, biology and treatment. Australas J Dermatol. 2004 Feb;45(1):1-9.
8. Kao GF. Carcinoma arising in Bowen's disease. Arch Dermatol 1986; 122:1124-6

Case Report

Vaginal angiomyxoma: An uncommon clinical entity

Habib A[a], Begum S F[b], Ghosh P K[c], Khanam R[d], Jahan F[e], Kabir S T[f]

Abstract

Aggressive angiomyxoma (AA) is an uncommon mesenchymal tumor that is mostly derived from the female pelvic and perineal regions. Painless swelling located around the genitofemoral region is the common symptom and is commonly diagnosed on histology. Oestrogen and progesterone receptors are commonly found in AA. It is thus likely to grow during pregnancy and respond to hormonal manipulation. The term "aggressive" denotes its propensity for local aggression and recurrences after excision. Usually, this tumor is non-metastasizing, but there are reports of multiple metastases in women treated initially by excision and who later succumbed to metastatic disease. Here we report a case of vaginal angiomyxoma presenting as a vaginal anterior wall mass in a 32-year old hypertensive woman, which she noticed 6 months following her delivery mimicking a cystocele/anterior vaginal wall descent.

Keywords: Angiomyxoma, Aggressive, Mesenchymal tumor, Cystocele .

Introduction:

Aggressive angiomyxoma (AA) is a slow-growing vulvovaginal mesenchymal neoplasm with a marked tendency for local recurrence, but with a low tendency to metastasize. AA was first described by Steeper and Rosai in 1983.[1] It usually presents as a vulval polyp clinically and is diagnosed on histology. Estrogen and progesterone receptors are commonly found in AA.[2] It is thus likely to grow during pregnancy and respond to hormonal manipulation. It involves mainly the pelvis, vulva, perineum, vagina and urinary bladder in adult women in the reproductive age. Considering its locally aggressive nature, appropriate management with wide local excision and long-term follow-up is necessary. Many options for the treatment of recurrences have been tried with varying success, but no single modality is clearly beneficial over others. Here we report a case of vaginal angiomyxoma presenting as a vaginal anterior wall mass in a 32-year old hypertensive woman, which she noticed 6 months following her delivery mimicking a moderate cystocele/ anterior vaginal wall descent.

Case Presentation:

A 32-year old woman, para 1 (LUCS), presented with something protruding through vaginal canal for 8 years. According to the patient's statement, 6 months after the caesarean birth she noticed something protruding through vaginal canal, which was gradually increasing in size and painless. She has no menstrual abnormality or associated urinary complaints. She is non diabetic, non-asthmatic, but hypertensive for 2 years controlled by a combination of Tab.Amlodipine 5 mg and Atenolol 25mg. Her bladder and bowel habit was normal. Her general examination findings were unremarkable. On internal examination, a big cystic ovoid mass approximately 12 cm x 6 cm is protruding through the introitus which could be partly repositioned. The mass apparently was seen to arise from the anterior vaginal wall sub-urethrally. The cough impulse was negative. On bimanual examination: Cervix: normal, Uterus: normal in size and there was no descent of the cervix. The mass is felt through the anterior vaginal wall and upper limit can be reached just 1cm beneath the external urethral meatus. All other systemic examination revealed no abnormality. The provisional diagnosis was Gartner's duct cyst or Cystocele. The patient was counselled about her condition & informed about the management plan. We planned for resection of the mass with anterior colporrhaphy and did the routine pre-anaesthetic investigations. The operative findings were as follows;

A large mass was found protruding through introitus. Bladder was evacuated by metallic catheter. The catheter didn't protrude inside the mass. A longitudinal incision was made over the mass and vaginal wall was separated. There

a. Dr. Asma Habib; FCPS, MBBS
Assistant Professor, Department of Gynae & Obstetrics
Bangladesh Medical College

b. Prof. Syeda Farida Begum; FCPS, MBBS
Professor, Department of Gynae & Obstetrics
Bangladesh Medical College

c. Prof. Paritosh Kumar Ghosh; M. Phil, MBBS
Professor and Head, Department of Pathology
Bangladesh Medical College

d. Dr. Rehana Khanam; M. Phil, MBBS
Associate Professor, Department of Pathology
Bangladesh Medical College

e. Dr. Fauzia Jahan; M. Phil, MBBS
Associate Professor, Department of Pathology
Bangladesh Medical College

f. Dr. Shahanje Tasneem Kabir
Intern, Department of Gynae & Obstetrics
Bangladesh Medical College Hospital

Correspondence to:
Dr. Asma Habib; FCPS, MBBS
Assistant Professor, Department of Gynae & Obstetrics
Bangladesh Medical College
Email: asma.imam2003@yahoo.com

was difficulty in identification of the structure because of the large volume of the dissected mass, so urologist was consulted who identified it not to be the bladder. The mass was carefully dissected from the anterior vaginal wall and its thick base was identified just 2 cm away from the urethral meatus, therefore almost complete resection of mass was done keeping a 1cm circumferential tissue sub-urethrally. Anterior colporrhaphy was performed (Fig 1 & 2). Bleeding was average. A catheter was kept in situ. Vaginal pack was given. Specimen sent for histopathology. Gross Appearance on histopathology revealed two collapsed cystic structures, the larger one measures 11x6 cm. The wall is about 0.6 cm thick (Fig:3). Microscopic appearance showed a benign mesenchymal lesion composed of spindly mesenchymal cells disposed in a loose myxoid background. Proliferation of many blood vessels with variable wall thickness were seen, some of which were filled with blood. Mitotic figures were not seen. Focal areas showed cystic degeneration. The diagnosis was - Features compatible with Angiomyxoma with cystic change (Fig: 4). The patient had an uneventful post-operative recovery. She was advised to come for a follow-up evaluation. After the confirmation of the histopathology, the nature of the lesion was delicately disclosed. The risk of local recurrence was informed and the necessity of long -term follow-up was described.

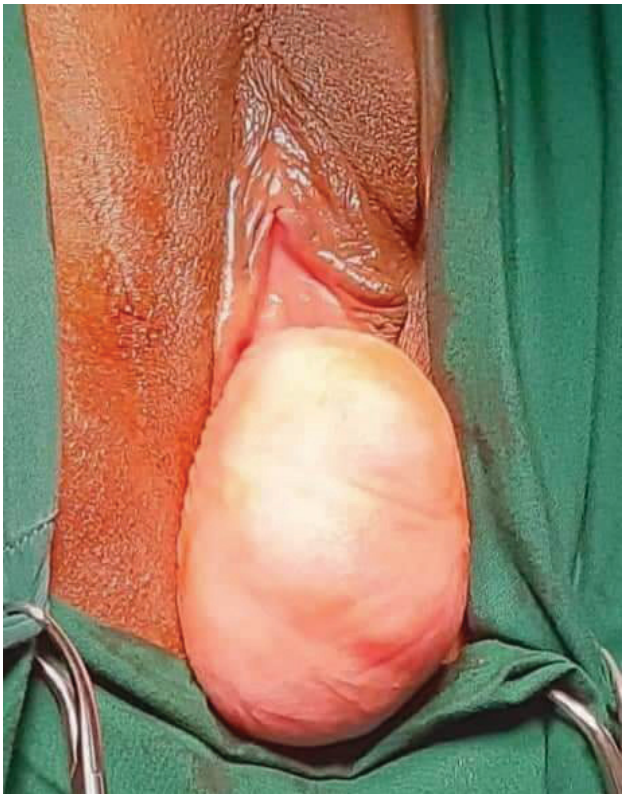


Figure 1: The vaginal cyst-like mass (intact)

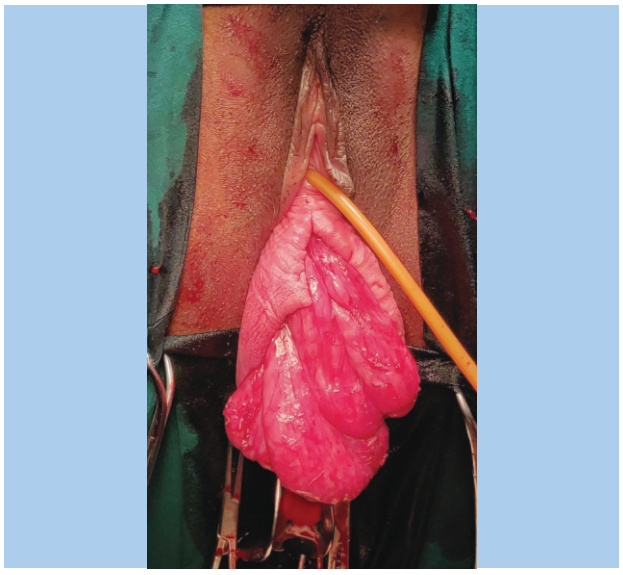


Figure 2: The vaginal wall lesion exposed after a longitudinal incision

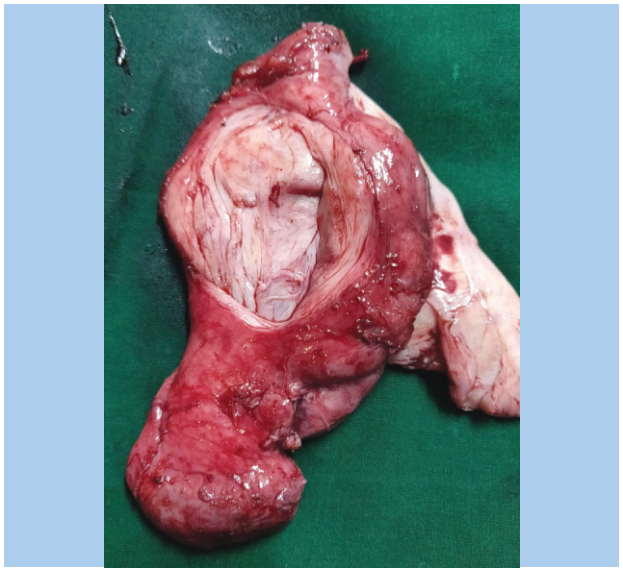


Figure 3: Gross appearances and cut section of the lesion revealing its thick glistening wall with 'layered' structure

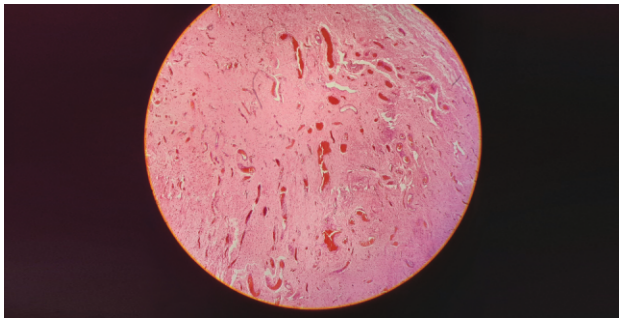


Figure 4: Features compatible with Angiomyxoma with cystic change.

Discussion:

The incidence of Angiomyxoma in females is significantly higher than in males (female-to-male ratio of 6:1).[1,2] The main site of disease is the perineum, followed by the pelvic cavity and vagina. In 1863, Virchow first classified myxomata as a distinct type of soft tissue tumors, whose tissues were similar to the normal human umbilical cord tissues with considerable variation in the organization of the tumor stroma. In 1983, after reviewing the cases reported over a hundred years, based on the clinical and pathological features of 9 patients, Steeper and Rosai [3] named this tumor "aggressive angiomyxoma" for the first time. The 2003 third edition and 2013 fourth edition of the World Health Organization Classification of Bone and Soft Tissue tumors, classified it as a tumor of uncertain differentiation, and named as deep (aggressive) angiomyxoma.[1] Clinically, AA may be misdiagnosed as Bartholin cyst, lipoma, labial cyst, Gartner duct cyst, levator hernia or sarcoma. CT scan and MRI may show specific changes but is actually diagnosed on histology. Our case was suspected to be an anterior vaginal wall descent or cystocele because of its location.

Five cases of AA with mean age of 42 have been reviewed by Hong Chen et al.[4] The patients mainly presented as slow-growing mass in the abdomen and perineum (3 cases in the pelvis, 1 in the vulva, and 1 in the buttock). Color Doppler flow imaging revealed blood flow for the 3 pelvic lesions. Enhanced computed tomography (CT) and magnetic resonance imaging(MRI) of the other 2 cases showed the typical "swirled" or "layered" structure characteristic. Through the pathological examination, its positivity to estrogen and progesterone receptors can justify enlargement and recurrence, confirming the tumor is AAM. All 5 patients underwent local tumor resection. Two patients recurred 8 and 15 months after surgery, respectively. The longest follow-up was 42 months. Our patient was not evaluated pre-operatively by Color Doppler flow imaging or CT /MRI scan or Immunohistochemistry after surgery.

On gross morphology, aggressive angiomyxomas are usually soft, fleshy tumors, similar in consistency as lipomas. On cut section, they are tan to white and glistening. It is an infiltrative tumor. The Microscopic key features: Abundant myxoid stroma with hypocellular background, cells loosely scattered in a myxoid stroma, Scattered spindle cells with bipolar cytoplasmic processes and bland stellate cells with an ill-defined cytoplasm, Fusiform to oval nuclei with bland chromatin pattern, no evidence of nuclear atypia and mitosis and numerous, thin-to-thick wall vessels of different sizes.

Also, it has thick-walled vessels, which are less numerous than the thin-walled vessels in angiomyofibroblastoma. [5,6]

On computed tomography (CT) scan, these tumors have a well-defined margin with attenuation less than that of the muscle. On MRI, these tumors show high signal intensity on T2-weighted images. The attenuation on CT and high signal intensity on MRI are likely to be related to the loose myxoid matrix and high water content of angiomyxoma.[7] Our patient was not subjected to radiological investigation as its clinical appearance at presentation was consistent of Gartner's cyst/Cystocele.

The tumors reviewed by Hong Chen et al [4] were gray, lobular, poorly encapsulated masses, measuring from 7×4.4×3 to 36×7.5×5cm, for an average diameter of 18cm; the description of which matches our case. The cut surface was glistening, myxedematous or gelatinous, and gray reddish-brown similar to ours. Immunohistochemistry using antibodies against vimentin, desmin, smooth muscle actin (SMA), actin, estrogen receptor (ER), progesterone receptor revealed strong expression of vimentin, desmin, ER and PR, partial or weak expression was observed for SMA (Smooth Muscle Actin), CD34, and S-100. Immunohistochemistry was not done in our case.

The results of the report by Jingping and Chunfu[8] study showed that the average positive rates were 100% for vimentin, desmin, and SMA, whereas it was 60% for CD34, 100% for ER, 100% for PR, 20% for S-100, and 3% for Ki-67. The immunohistochemistry results supported that the tumor cells may originate from mesenchymal cells with the characteristics of fibroblasts and myofibroblasts. The 3% positive rate of Ki67 was in agreement with the tumor features such as slow growth and inactive cell proliferation. The low positivity of Ki67 may therefore be a good prognostic marker, supplementing the poor metastasizing propensity of the AA.

Treatment:

The current treatment of AA is complete surgical excision with tumor-free margins. Long-term follow-up and careful monitoring are essential due to its high tendency of local recurrence in spite of wide excision of the tumor. Recurrences may occur from months to several years after excision (2 months to 15 years).[8] AA, despite the name, is not that aggressive, with only a 30% chance of recurrence, which is eminently treatable by excision with a 1 cm margin. Hormonal manipulation with tamoxifen, raloxifene and gonadotropin-releasing hormone analogues has been shown to reduce the tumor size rendering feasibility of complete excision of large tumorous mass avoiding gross disfigurement. This modality may also be used in the treatment of recurrence and as an adjuvant antihormonal therapy for preventing recurrence in case of suboptimal resection.[9] However, long-term use of these drugs is still controversial because of their adverse effects. Radiation therapy and chemotherapy are considered less-suitable options due to low mitotic activity. Angiographic embolization may also help. Embolization of the tumor has been reported as an alternative approach in subsequent resection by shrinking the tumor as well as making it easier to identify it from surrounding normal tissues; however, it remains insufficient due to the extensive vascular network of the tumor.[10] As late recurrences are known, all patients need to be counselled about the need for long-term follow-up.

Some studies speculate that since the tumor immunohistochemistry shows positive ER and PR in most patients, and since the tumor is likely to grow during and after pregnancy, the tumor may be considered as a hormone-dependent tumor.[10] Therefore, gonadotropin-releasing hormone agonist (GnRH-α), aromatase inhibitors, and estrogen and PR blocker therapy can be considered. GnRH-α is a commonly used drug for postmenopausal women; however, aromatase inhibitors have also been reported to be effective.[11] Some studies demonstrated that the GnRH-α and other antiestrogen drugs can shrink or abolish the tumor.[12] Nevertheless, it is not yet elucidated whether long-term use of the GnRH-α drug can cure the disease or whether recurrence will appear when the drug is discontinued.[13] It has been reported that with the use of radiation therapy on recurrent patients, the recurrence was not observed for 2 to 3 years.[12] Our patient has been informed and will be reviewed at least annually for any evidence of local or distant recurrence.

Prognosis:

Although it is a benign tumour and does not invade the neighboring tissue, it has a tendency to recur after surgical excision so it is termed as aggressive. The recurrence can be as close as six months from initial resection. It will not be surprising to find cases coming to tertiary medical centers with history of having a labial mass (sometimes misdiagnosed as Gartner's cyst) and have multiple surgical excisions from various doctors. There is no proven medical therapy and physicians have tried various sorts of chemotherapy like Tamoxifen, GnRH agonist Leuprolide and even full-blown chemotherapy. Multiple local recurrences and relapses in adjacent organs and tissues may occur, but pulmonary and mediastinal metastases been reported resulting in death. These cases may expand the current concepts of potential behavior of aggressive angiomyxoma.[10-13]

Conclusion:

Since AA was first described in 1983 by Steeper and Rosai, approximately 200 cases have been reported in medical literature up to date. Because of its rarity, the clinical presentation and the treatment modality of the tumor have been described mostly based on individual case presentations. It is noteworthy that there is still a lack of knowledge about the clinical presentation, the management options, and the follow-up results of AA in the current literature. The recent report of mediastinal and pulmonary parenchymal spread in a case has put a red alert on the long-term clinical surveillance of these patients.

References:

1. Mahendra M Kura, Saurabh R Jindal, and Usha N Khemani. Aggressive angiomyxoma of the vulva: An uncommon entity. Indian Dermatol Online J. 2012 May-Aug; 3(2): 128-130.
2. Alper Sozutek, Oktay Irkorucu, Enver Reyhan, Kemal Yener, Ali Ayberk Besen, Kivilcim Eren Erdogan, Gulfiliz Gonlusen, and Figen Doran. A Giant Aggressive Angiomyxoma of the Pelvis Misdiagnosed as Incarcerated Femoral Hernia: A Case Report and Review of the Literature. Case Reports in Surgery. 2016(2016):1-6 http://dx.doi.org/10.1155/2016/9256749
3. Steeper TA, Rosai J. Aggressive angiomyxoma of the female pelvis and perineum. Report of nine cases a distinctive type of gynecologic soft-tissue neoplasm. Am J Surg Pathol. 1983; 7:463-75.
4. Hong Chen, Hongyan Zhao, Yan Xie, Mulan Jin. Clinicopathological features and differential diagnosis of aggressive angiomyxoma of the female pelvis:5 case reports and literature review. Medicine (Baltimore) 2017 May; 96(20): e6820
5. Nucci MR, Fletchr CD. Vulvovaginal soft tissue tumors: Update and review. Histopathology. 2000; 36:97-108.
6. Han-Geurts IJ, van Geel AN, van Doorn L, den Bakker M, Eggermont AM, Verhoef C. Aggressive angiomyxoma: Multimodality treatments can avoid mutilating surgery. Eur J Surg Oncol. 2006; 32:1217-21.
7. Alameda F, Munne A, Baro T, Iglesias M, Condom E, Lloreta-Trull J, et al. Vulvar angiomyxoma, aggressive angiomyxoma and angiomyofibroblastoma: An immunohistochemical and ultrastructural study. Ultrastruct Pathol. 2006; 30:193-205.
8. Jingping Z, Chunfu Z. Clinical experiences on aggressive angiomyxoma in China (Report of 93 cases). Int J Gynecol Cancer 2010; 20:303-7 [PubMed] [Google Scholar].
9. Outwater EK, Marchetto BE, Wagner BJ, Siegelman ES. Aggressive angiomyxoma: Findings on CT and MR imaging. AJR Am J Roentgenol. 1999; 172:435-8.
10. Behranwala KA, Thomas JM. Aggressive angiomyxoma: A distinct clinical entity. Eur J Surg Oncol. 2003; 29:559-63.
11. McCluggage WG, Jamieson T, Dobbs SP, Grey A. Aggressive angiomyxoma of the vulva: Dramatic response to gonadotropin-releasing hormone agonist therapy. Gynecol Oncol. 2006; 100:623-5.
12. Magtibay PM, Salmon Z, Keeney GL, Podratz KC. Aggressive angiomyxoma of the female pelvis and perineum: A case series. Int J Gynecol Cancer. 2006;16:396-401.
13. Blandamura S, Cruz J, Faure-Vergara L, Machado-Puerto I, Ninfo V. Aggressive angiomyxoma: A second case of metastasis with patient's death. Hum Pathol. 2003; 34:1072-4.

Case Report

A Case of Wilson Disease

Purba S C[a], Rana M A[b]

Abstract

Wilson disease, a genetic disease having predominantly hepatic and neurological manifestation, is not uncommon in our country. Here we present a case of cirrhosis of liver due to Wilson disease. A 12-year-old girl presented with progressive abdominal distension and edema with jaundice. Physical examination revealed mild icterus, moderate edema and huge ascites. Neurological examination findings were normal. Examination of the eye revealed presence of K-F ring (Kayser-Fleisher ring). Laboratory examination revealed deranged liver function with low albumin, raised prothombin time along with raised bilirubin and transaminases. All viral markers were negative. Serum ceruloplasmin was low and 24-hour urinary copper was high. Ultrasonography of liver showed cirrhosis as evidenced by coarse echo texture of liver. She was started on penicillamine and zinc and her condition started improving.

Wilson disease has a good prognosis if diagnosed early and treatment could be continued consistently. A high index of suspicion is needed so that the diagnosis is not missed.

Keywords: Wilson disease, Cirrhosis of liver, K-F ring, Hepatic presentation.

Introduction:

Initially described by Kinnear Wilson[1] in 1912, Wilson's disease (WD, or Wilson disease) is the clinical condition resulting from mutations in the chromosome 13q14 in the region coding for the protein product *ATP7B*, and occurs in a sporadic fashion as well as inherited as an autosomal recessive disease.[1] Homozygous, or, more commonly, compound heterozygous mutations lead to defective incorporation of copper into apo-ceruloplasmin and the subsequent formation of holoceruloplasmin, hampering the normal excretion of copper into bile. With a shorter half-life than that of holoceruloplasmin, circulating apoceruloplasmin (ceruloplasmin) are abnormally low, albeit the gene responsible for this protein, localized on chromosome 3, is intact, providing one of the most important clinical diagnostic tools for WD.[2]

The clinical manifestations of WD are extraordinarily diverse. In the first decade of life, WD presents more often with hepatic manifestations. After the age of 20 years,75% of cases present with neurological manifestations and 25% with both hepatic and neuropsychiatric manifestations.[3] WD patients with neurological manifestations have a poorer outcome than do patients with hepatic manifestations.[4]

a. Dr. Shudeshna Chakraborttye Purba; MBBS
Assistant Registrar, Department of Gastroenterology
Bangladesh Medical College and Hospital.
b. Dr. Mushtaque Ahmad Rana; FCPS,MD,MBBS
Associate Professor & Head, Department of Gastroenterology
Bangladesh Medical College and Hospital

Correspondence to:
Dr. Mushtaque Ahmad Rana; FCPS, MD, MBBS
Associate Professor & Head,
Department of Gastroenterology
Bangladesh Medical College and Hospital
Email: ranamushtaque2@yahoo.com

The prevalence of WD, a rare disease, is similar in most world regions, corresponding to approximately 0.5 cases per 100000 inhabitants or the most common figure 30 cases per million, with a gene frequency of 0.56% and a carrier frequency of 1 in 90.[5,6,7] Nevertheless, the disease is much less uncommon in certain areas/countries, with certain mutations being described more frequently in specific populations. Over 500 mutations have been found so far, and the lower number of actual clinically manifest cases with respect to the frequency of allele carriers in the population, probably reflect the reduced penetrance of mutations.[8]

Although the form of the disease initially described was predominantly neurological, the disease manifestations can be pleomorphic, and although the correlation mutation-predominant manifestation has been elusive, clinical forms of the disease tend to cluster and wide geographical differences exist. [9,10, 11] Thus, WD may be predominantly hepatic, neurological or psychiatric, and manifestations of disease may range from an asymptomatic state to life-threatening fulminant hepatic failure.[12-16] Liver involvement spans from asymptomatic disease with transaminase elevation, to acute hepatitis, acute-on-chronic liver failure, and cirrhosis. Liberation of copper into the bloodstream causes Coomb's negative hemolytic anemia, with transient episodes of low-grade hemolysis and jaundice.[17,18] Neurological manifestations can be categorized as: (1) an akinetic-rigid syndrome similar to Parkinson's disease; (2) pseudosclerosis dominated by tremor; (3) ataxia; and (4) a dystonic syndrome, which often leads to severe contractures.[19,20] Neuropsychiatric symptoms and signs, including decrease in scholastic performance, hand-eye discoordination, and behavioral changes may foretell a more florid neurological presentation.[21]

Treatment is based on the removal of copper excess by chelating agents such as penicillamine, trientine or tetrathiomolybdate or by blocking the intestinal copper absorption with zinc salts[25] , with the ultimate goal of normalizing free plasmatic copper. [22,23,24,25] Initially its chloride salt, followed by its sulfate salt, zinc was first used in the early 1960s to treat WD but was kept unrecognized until 1978.[26] Zinc acetate is regarded to have a better gastric tolerance. However, in terms of efficacy, there is no difference between zinc salts.[27] Its mechanism of action is different from the above-mentioned agents, in that it induces enterocyte metallothionein, an endogenous chelator of metals, thus favoring copper entrapment into enterocytes and its elimination in the feces with the normal shedding of intestinal cells.[28] Liver transplantation is the recommended therapy for patients with fulminant hepatitis, or in those with relentless progression of hepatic dysfunction despite drug therapy, and survival rates are only very slightly inferior to those after transplant for other indications. Liver transplantation corrects the underlying hepatic metabolic defect in WD.[29]

Case Presentation:

A 12 years old female, 2nd child of 1st degree consanguity, from Savar, Dhaka, presented with mild right upper quadrant abdominal pain with nausea. On 3rd day, mother noticed gradual distension of her abdomen and swelling both lower limb with increasing yellowish discoloration of eyes and hands and feet. Her urine was also dark. She had no itching. She felt feverish but temperature was not recorded. She did not get any blood/blood products as transfusion. Her family live in a clean well-ventilated house and drink boiled water. She does not take outdoor foods. She gives no history of similar illness in the past. Her siblings are relatively healthy. Her physical and mental growth has followed the developmental milestone. Her school performance is good.

On examination, she was ill-looking and mildly icteric. Edema was mild. Vitals were found normal. Abdomen was distended, flanks were full, umbilicus centrally placed and everted. Shifting dullness was absent but fluid thrill was present. Liver and spleen were not palpable. Upper border of liver dullness started from 5th right intercostal space.

Higher psychic Function was intact, no scanning or slurring of speech and hand writing was average. Muscle power- 5/5. Tone- normal, no cog-wheel rigidity. Intention and Flapping tremor were absent. No inappropriate and in-co-ordinate movement was present. Ophthalmologist confirmed presence of "Kayser Fleischer Ring" (Fig 1), no sun-flower cataract in both eyes.

On investigation, hemoglobin was 10.70g/dl, prothrombin time was 19 second, total bilirubin-1.0mg/dl, ALT-86 IU, AST-104 IU, Hepatotrophic viral markers were all negative, urine R/M/E showed 8-10 pus cell/HPF. Serum Albumin- 21gm/dl, serum ceruloplasmin was 5mg/dl, 24hours urinary copper- 292 +/-29 mgm/L.

USG of abdomen showed moderate to marked ascites in abdomen and pelvic region, mild pleural effusion in both hemithorax and coarse hepatic parenchyma with heterogenous echotexture.

According to the scoring system proposed by the 8th International meeting on Wilson disease and Menke disease[30], our patient had a score of 4 (2 for K-F ring ang 2 for low ceruloplasmin) and a diagnosis of Wilson disease was made. Due to financial constraint we could not do other investigations like MRI of brain to see any asymptomatic neurological involvement.

Ascites and edema were managed with fresh frozen plasma with frusemide and spironolactone. She was started on Pencillamine and zinc acetate. Her condition improved with decrease in ascites, disappearance of edema. She was discharged with advice to follow a diet low in copper. She came for follow up after one month and her LFT improved with normalization of ALT, AST with improvement in serum albumin level.

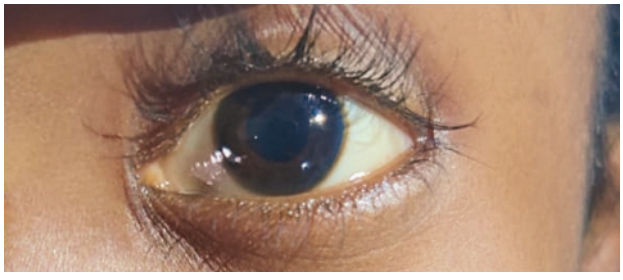


Fig 1: Kayser Fleischer Ring in eye

Discussion:

Wilson disease is not uncommon in our country. In a cross-sectional study, Das et al. showed that 3.64% cirrhotic patients in Bangladesh has Wilson disease.[31] So, a high index of suspicion should be maintained so that this diagnosis is not missed. In a study on 100 cases of Wilson disease carried out in Bangabandhu Sheikh Mujib Medical University, consanguinity of marriage was seen in 30% cases.[32] In our case it was also seen. The parents were first degree cousins.

Children with WD are usually normal at birth and may remain healthy for a variable period of time; most cases present in the second and third decade of life.[33] Our patient also presented at age 12 with no prior signs or symptoms of illness.

Hepatic presentation is more common in younger patients than in older patients. In our case, the 12-year-old patient presented with ascites with pleural effusion with hypoalbuminemia, prolonged prothombin time and evidence of course hepatic echotexture in ultrasonogram. She had no neuropsychiatric manifestations.

Our patient has not yet developed neurological features

which usually manifest later than hepatic presentations. Moreover, K-F ring is usually associated with neurological manifestations. So, a close follow up is necessary to see any development of neurological features. The parents were adequately educated regarding this.

As there is first degree consanguinity among parents in this case other siblings are also at risk of Wilson disease. Screening tests for Wilson disease were advised for the siblings and the parents agreed to do the same.

The long-term treatment of symptomatic cases of WD entails the chronic use of copper chelators and zinc, while liver transplantation provides a cure. The copper chelators commonly used for WD are penicillamine and trientine hydrochloride. In our case we used penicillamine was used as copper chelator along with zinc acetate to prevent absorption of copper.

In Wilson disease, severe neurological disease may not resolve entirely on treatment, but patients with early hepatic disease have a generally favorable prognosis as long as treatment is consistent. In our case, the parents were requested to ensure strict compliance of their child with the medications and for regular follow up in case any deterioration of the disease occurs or any adverse effect of the medications occur.

Conclusion:

Wilson disease is not uncommon cause of cirrhosis or acute hepatic failure in our country. If diagnosed timely and treatment started early, this disease has a good prognosis. Here we presented a case of Wilson disease where a high index of suspicion led to the diagnosis and prompt initiation of treatment. All these might confer a good long-term prognosis for this patient.

References:

1. Wilson S. Progressive lenticular degeneration: A familial nervous disease associated with cirrhosis of the liver. Brain. 1912:295–509.
2. Yang FM, Friedrichs WE, Cupples RL, Bonifacio MJ, Sanford JA, Horton WA, Bowman BH. Human ceruloplasmin. Tissue-specific expression of transcripts produced by alternative splicing. J Biol Chem. 1990; 265:10780–10785.
3. Riordan SM, Williams R. The Wilson's disease gene and phenotypic diversity. J Hepatol 2001; 34:165–171.
4. Merle U, Schaefer M, Ferenci P, *et al*. Clinical presentation, diagnosis and long-term outcome of Wilson disease: a cohort study. Gut 2007; 56:115–120.
5. Ala A, Walker AP, Ashkan K, Dooley JS, Schilsky ML. Wilson's disease. Lancet. 2007; 369:397–408.
6. Scheinberg IH, Sternlieb I. Wilson's disease. In: Smith JL, editor. Major problems in internal medicine. Philadelphia: WB Saunders; 1984. pp. 25–35.
7. Scheinberg I, Sternlieb I. Wilson Disease. In: Lloyd H, Smith J, editors. Major Problems in Internal Medicine. Saunders: Philadelphia; 1984. p. 23.
8. Available from: http://www.wilsondisease.med.ualberta.ca/database.
9. Vrabelova S, Letocha O, Borsky M, Kozak L. Mutation analysis of the ATP7B gene and genotype/phenotype correlation in 227 patients with Wilson disease. Mol Genet Metab. 2005; 86:277–285.
10. Nicastro E, Loudianos G, Zancan L, D'Antiga L, Maggiore G, Marcellini M, Barbera C, Marazzi MG, Francavilla R, Pastore M, et al. Genotype-phenotype correlation in Italian children with Wilson's disease. J Hepatol. 2009; 50:555–561.
11. Lee BH, Kim JH, Lee SY, Jin HY, Kim KJ, Lee JJ, Park JY, Kim GH, Choi JH, Kim KM, et al. Distinct clinical courses according to presenting phenotypes and their correlations to ATP7B mutations in a large Wilson's disease cohort. Liver Int. 2011; 31:831–839.
12. Ferenci P, Caca K, Loudianos G, Mieli-Vergani G, Tanner S, Sternlieb I, Schilsky M, Cox D, Berr F. Diagnosis and phenotypic classification of Wilson disease. Liver Int. 2003; 23:139–142.
13. Schilsky ML, Scheinberg IH, Sternlieb I. Liver transplantation for Wilson's disease: indications and outcome. Hepatology. 1994; 19:583–587.
14. Walshe JM. Wilson's disease presenting with features of hepatic dysfunction: a clinical analysis of eighty-seven patients. Q J Med. 1989; 70:253–263.
15. Scott J, Gollan JL, Samourian S, Sherlock S. Wilson's disease, presenting as chronic active hepatitis. Gastroenterology. 1978; 74:645–651.
16. Stremmel W, Meyerrose KW, Niederau C, Hefter H, Kreuzpaintner G, Strohmeyer G. Wilson disease: clinical presentation, treatment, and survival. Ann Intern Med. 1991; 115:720–726.
17. Saito T. Presenting symptoms and natural history of Wilson disease. Eur J Pediatr. 1987; 146:261–265.
18. Roberts EA, Schilsky ML. Diagnosis and treatment of Wilson disease: an update. Hepatology. 2008; 47:2089–2111.
19. Svetel M, Potrebić A, Pekmezović T, Tomić A, Kresojević N, Jesić R, Dragasević N, Kostić VS. Neuropsychiatric aspects of treated Wilson's disease. Parkinsonism Relat Disord. 2009; 15:772–775.
20. Svetel M, Kozić D, Stefanova E, Semnic R, Dragasevic N, Kostic VS. Dystonia in Wilson's disease. Mov Disord. 2001; 16:719–723.
21. Taly AB, Meenakshi-Sundaram S, Sinha S, Swamy

HS, Arunodaya GR. Wilson disease: description of 282 patients evaluated over 3 decades. Medicine (Baltimore) 2007; 86:112-121

22. Scheinberg IH, Jaffe ME, Sternlieb I. The use of trientine in preventing the effects of interrupting penicillamine therapy in Wilson's disease. N Engl J Med. 1987; 317:209-213
23. Walshe JM. Tetrathiomolybdate as an anticopper agent in man. Orphan disease and orphan drugs. Sheinberg. Manchester University Press: 1986. pp. 76-85.
24. Brewer GJ, Dick RD, Johnson V, Wang Y, Yuzbasiyan-Gurkan V, Kluin K, Fink JK, Aisen A. Treatment of Wilson's disease with ammonium tetrathiomolybdate. I. Initial therapy in 17 neurologically affected patients. Arch Neurol. 1994; 51:545-554.
25. Hoogenraad TU, Van den Hamer CJ. 3 years of continuous oral zinc therapy in 4 patients with Wilson's disease. Acta Neurol Scand. 1983; 67:356-364.
26. Hoogenraad TU, Van den Hamer CJ, Koevoet R, Korver EG. Oral zinc in Wilson's disease. Lancet. 1978; 2:1262.
27. Brewer GJ. Zinc acetate for the treatment of Wilson's disease. Expert Opin Pharmacother. 2001; 2:1473-1477.
28. Sturniolo GC, Mestriner C, Irato P, Albergoni V, Longo G, D'Incà R. Zinc therapy increases duodenal concentrations of metallothionein and iron in Wilson's disease patients. Am J Gastroenterol. 1999; 94:334-337
29. Groth CG, Dubois RS, Corman J, Gustafsson A, Iwatsuki S, Rodgerson DO, Halgrimson CG, Starzl TE. Metabolic effects of hepatic replacement in Wilson's disease. Transplant Proc. 1973; 5:829-833
30. Ferenci P, Caca K, Loudanios G, Mieli-Vergani G, Tanner S, Sternlieb I et al: Diagnosis and phenotypic classification of Wilson disease, Liver Int. 2003; 23(3):129-130
31. Das DC, Mahbub MA, Rahim MA, Malakar D, Kabir A, Rahman S. Hepatitis B remains the leading cause of cirrhosis of liver in Bangladesh. Bangladesh Med J. 2016 sept; 45(3)
32. Rokunuzzaman M. Wilson's Disease in Bangladeshi Children: Analysis of 100 cases. Pediatr Gastroenterol Hepatol Nutr 2015 June; 18(2):121-127
33. Saito T: Presenting symptoms and natural history of Wilson disease. Eur J Pediatr. 1987; 146 (3): 261-265.

College News

College Events:

- The National Mourning Day was observed in Bangladesh Medical College and Hospital on 15th August 2019, the 44th death anniversary of Father of Nation Bangabandhu Sheikh Mujibur Rahman. Teachers, doctors, nurses, students of BMCH and officials & staffs of BMSRI participated with full enthusiasm in that event.

- The 49th "Victory Day" of Bangladesh was celebrated in Bangladesh Medical College and Hospital premises on 16th December 2019. Teachers, doctors, nurses, students of BMCH and officials & staffs of BMSRI participated with full enthusiasm in that event.

- The commencement ceremony of BM-34 was held on 12th January 2020 in the campus of Bangladesh Medical College.

Seminars:

- Seminar on "True breakthrough in the management of heart failure" was held on 29th August 2019 in BMC. The speaker was Dr. Muhammed Akhtaruzzaman, Assistant Professor of Cardiology, BMC.

- Seminar on "Radiology & Imaging: Updates with application" was held on 3rd October, 2019 in BMC. The speaker was Dr. Kamrun Nahar, Associate Professor of Radiology & Imaging, BMC.

- An integrated seminar on "Breast cancer awareness" was held in BMC on 24th October, 2019. The speakers were: Prof. Sharmeen Yasmeen, Head of the dept. of Community Medicine, BMC, Prof. Nazmun Nahar, Head of the dept. of Radiology & Imaging, BMC, Prof. Riaz Ahmed Chowdhury, Head of the dept. of Surgery, BMC, Prof. Zafor Md. Masud, Head of the dept. of Oncology, BMC, Dr. Saidur Rahman, Associate Professor of Pathology, BMC and Head of Clinical Pathology, BMCH and Dr. Sultana Jebunnaher, Associate Professor of Gynae & Obstetrics, BMC.

- An integrated seminar on "Overview on AIDS" was held on 19th December, 2019 in BMC. The speakers were: Dr. Asma Habib, Assistant Professor of Gynae & Obstetrics, BMC, Dr. Sharmila Huda, Associate Professor (CC) of Pharmacology, BMC and Dr. Abdul Basit Ibne Momen, Registrar (CC) of Medicine, BMC.

Participation in the International Conferences/Seminars/Workshop/ Congress/Meetings:

- Prof. Dr. Zafor Md. Masud, Head of the dept. of Oncology, BMC, attended the conference of European Society for Medical Oncology (ESMO) held in Barcelona, Spain from 27th September to 1st October, 2019.

- Prof. Dr. Md. Sarwar Fardaus, Head of the dept. of Paediatrics, BMC, attended the 94th Nestle Nutrition Institute Workshop Program held in Switzerland from 23rd to 25th September, 2019.

- Dr. Kamruzzaman, Associate Professor & Head of the dept. of Orthopaedics, BMC, attended the SIGN Conference 2019 held in USA from 11th to 14th September, 2019.

- Dr. Azizun Nahar, Associate Professor, dept. of Microbiology, BMC, attended the 16th Annual Conference of the Hospital Infection Society of India (HISICON 2019) held in India from 12th to 15th September, 2019.

- Dr. Mushtaque Ahmad Rana, Associate Professor & Head, dept. of Gastroenterology, BMC, attended the World Congress of Gastroenterology held in Istanbul, Turkey from 21st to 24th September, 2019.

- Prof. Md. Ashraful Islam, Head of the dept. of ENT, BMC, attended the 3rd Annual Conference–GN Hear More 2019 held at Kuala Lumpur, Malaysia from 26th to 29th September 2019.

- Prof. Dr. Md. Zahid Hasan Bhuiyan, dept. of Urology, BMC attended the 39th Congress of the Society International d'Urology held in Greece from 17th to 20th October, 2019.

- Prof. Dr. Md. Ashraful Islam, Head of the dept. of ENT, BMC, attended the Convocation Ceremony' 2019 and also attend the 105th Annual Clinical Congress held at San Francisco, USA from 27th to 31st October 2019.

- Prof. Dr. Md. Tarek Alam, Professor (C.C) & Head, dept. of Medicine, BMC, attended the 24th Congress of the Asian Pacific Society of Respirology (APSR 2019) held in Viet Nam from 14th to 17th November, 2019.

- Dr. Kamrun Nahar, Associate Professor, dept. of Radiology and Imaging, BMC, attended the Workshop on Abdominal Oncoradiology (ESOR 2019) organized by Indian Radiological & Imaging Association held at Kolkata, India from 15th to 16th November, 2019.

- Dr. Syed Khalid Hasan, Associate Professor, dept. of Surgery, BMC attended the Sing Health's General Surgery Quality Initiative cum International Conference on Humanitarian Medical Missions (ICHMM) held in Singapore from 21st to 23rd November, 2019.

- Prof. Dr. Md. Mizanur Rahman, Head of the dept. of Ophthalmology, BMC, attended the Comprehensive Cataract Conference-2019 and the 3rd Biennial World Conference on MSICS held at India from 29th November to 1st December, 2019.

- Prof. Dr. Raihana Begum, Dept. of Community Medicine, BMC, attended the Workshop on policies to control non-communicable diseases (NCDs) and options for moving towards evidence–informed policies held in Doha, Qatar from 13th to 14th December, 2019.

- Dr. Mushtaque Ahmad Rana, Associate Professor & Head, dept. of Gastroenterology, BMC, attended the Asian Pacific Digestive Week (APDW 2019) held at Kolkata, India from 11th to 15th December, 2019.

- Dr. Muhammed Akhtaruzzaman, Assistant Professor, dept. of Cardiology, BMC, attended the 2019 Heart Failure Preceptorship Program held in South Korea from 1st to 2nd November, 2019.

- Prof.Dr. Sharmeen Yasmeen, Head of the dept. of Community Medicine, BMC, attended the 9th WHO's Biennial Meeting of South East Asia Public Health Education Institutions Network (SEAPHEIN) held at Jaipur, India from 13th to 15th November 2019. She was elected as the member of Executive Committee of SEAPHEIN.

New Appointment:

Prof. Dr. Paritosh Kumar Ghosh,Head of the dept. of Pathology, BMC appointed as Principal in-Charge of Bangladesh Medical College from 25th July 2019.

Prepared by:
Shahana Akter Dalia
Sr. Admin. Assistant
Bangladesh Medical College