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New normal adaptation- a revolutionary approach against COVID-19 pandemic and its successors

Yasmeen S

After 100 years of pandemic of Spanish flu (from 1918-1920), it is again COVID-19 which has devastated the whole world no matter how much developed they are. Rapid alteration of ecosystem and biodiversity is continuously yielding newly emerging and re-emerging biological, environmental and psychosocial health problems. So called social upliftment has been regarded as adverse reality of having high morbidity of non-communicable diseases and risk factors among human being. So we are now overwhelmed by double burden-communicable and non-communicable diseases. Most recent instance is COVID-19 pandemic, originating first in Wuhan, China in December, 2019 and later on declared as Pandemic on March 11, 2020.^{1,2} From the beginning of pandemic of COVID-19, none of the countries in the world could ready their health system as appropriate to combat this pandemic. As a consequence, we noticed high mortality and morbidity even in countries like USA, UK, Italy, France, Brazil, India etc.^{3,4} In course of time global scientists explored its epidemiological features, risk factors, high risk groups, course and gradient of infection, possible treatment modalities, post-infection complications, strategies for prevention. Recently invention of vaccines against COVID-19 within less than one-year time is the remarkable milestone in public health history.⁵ This spirit of innovation should be continued to prevent new addition and also for extinction/abolition of already existing diseases.

Now vaccination programme is running in every country, people are resuming regular activities phase by phase. After an observable decline in mortality and morbidity again in some countries like Russia, USA, Germany, India etc the epidemiological curve is rising even though the vaccination programme is running simultaneously.³ So even if we achieve herd immunity by vaccination that will not enough to save people and make the end to this pandemic. Undoubtedly, there are also other issues like life-style modification, inclusion of health etiquettes, transfer of technology, change in organizational behavior and norms based on scientifically sound evidence based public health practice should be regarded as additional herd structures. WHO, CDC and all international and national health authorities are already univocally echoing for solidarity toward heading to “New normal”- as an adjunct universal approach to have a control over this pandemic and there after.^{6,7}

Saying about New Normal- we must have a clear idea about its concept. The term ‘new normal’ first introduced as the dramatic economic, cultural and social transformations during the 2008 financial crisis. It caused precariousness

and social unrest, impacting collective perceptions and individual lifestyles.^{8,9} A **new normal** is a state to which life, economy, society etc. settles following a crisis, when this differs from the situation that prevailed prior to the start of the crisis. This term has been used again during the COVID-19 pandemic to point out how it has transformed essential aspects of human life.¹⁰ So we simply can say that new normal is a new way of living and leading our lives, work and interaction with other people. The whole world is now focusing on to save lives and managing livelihood side by side. It is clear that adjustment to “new normal” from present to future is very important to make a balance in every sphere of life. During pandemic the most familiar terms are-lock down, stay home, work from home, social distancing, wearing mask, cough etiquette, hand wash with sanitizer and soap, isolation, quarantine, COVID vaccine, telemedicine, online education, online shopping of grocery and other essential goods etc. People has been getting habituated with all these terms and techniques. We observed exploration and execution, innovation and invention, inculcation of humanity and unity. Enormous lessons learned which are to be applied for betterment and ease of life. New normal undoubtedly will supersede the old normal in a positive direction by the way of thinking, feeling and doing. Adaptation and resilience to challenges of prevailing pandemic and other survival issues, based on action oriented responses would greatly affect our personal and social life.⁸

The COVID-19 pandemic has severely disrupted the education systems in human history. It affected nearly 1.6 billion students in more than 200 countries. Closures of schools, institutions and other learning spaces have impacted more than 94% of the world's student population. The COVID-19 pandemic has provided us with an opportunity to pave the way for introducing digital learning worldwide. So new normal digital or online teaching-learning, professional communication has opened a new era of opportunities in the society.^{11,12} Already the Blended learning (BL), or the integration of face-to-face and online instruction has been widely adopted and being popularized in higher education more than a decade back.¹³ It is referred as “new traditional model”¹⁴ or the “new normal” in course delivery.¹⁵

New normal must go beyond clinical care and beyond direct face to face care. Increase focus to be given to preventive health care and public health. Remote health care to be powered and covered by digital health care. COVID-19 has encouraged a renewed interest from both patients and health-care providers for digital health solutions.¹⁶ It should be continued even after pandemic as a

part of new regular practice of health care as “new essential”.¹⁷

Practice of new normal at home, family and community level is very important for positive change of behavior. Prevention of health risk behavior, eating healthy diet, doing physical activities and many other healthy practices could be inculcated at home as new normal. Community engagement by the youth of the local community can change the scenario. This kind of voluntary involvement will refrain them from anti-social activities and encourage them to engage themselves to creative and social activities. Economic recession is existing due to pandemic. So cost containment with prioritization to a healthier living is important in new normal. Good health and wellbeing save life and money both. Quality family time increase bondage and improve mental health. Readiness to deal with complexity of life to be done unitedly and sharing responsibilities always ease and lighten our load.

It is almost a year and a half since emergence of COVID-19; people have started to restore health, economies and societies together despite the evolution of new coronavirus strains. WHO urged the governments to invest in health systems for the benefit of all populations beyond COVID-19, as well as to prepare for future public health emergencies.¹⁸ When the COVID-19 pandemic will be over, the best of our new normal will survive to enrich our lives and our work in the future.

Lastly we can say that to do list of new normal is unlimited. If we assume that COVID-19 pandemic will fly away soon forever and we can revert to our old normal- that will be a suicidal decision. We have to maintain and sustain new normal practice as a safeguard for prevention of disease and promotion of health physically, mentally and socially to lead a socially and economically productive life. So let's be patient, be strong in believing that we shall overcome someday.

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Clinicopathological evaluation of colorectal cancer in young adults in a tertiary care hospital in Dhaka city

Tabassum F^a, Hasan S K^b, Rahman S^c, Masud Z M^d, Haque A K M F^e

Abstract

Background: Colorectal cancer is generally a disease affecting individuals 50 years of age and older and is much less common in persons under 40 years of age. But currently young adults are being diagnosed with colorectal cancer which found to be associated with changes in dietary habits and lifestyle.

Objective: To evaluate the clinic-pathological finding of colorectal cancer cases with specific reference to young adults

Methods: The cross-sectional study was carried out in Bangladesh Medical College Hospital on colorectal carcinoma (CRC) patients who were diagnosed from the period of January 2015 to December 2017. The records were analyzed in detail for age, gender, site of primary tumor, clinical presentations, histopathological type, and pathologic stage, tumor marker, performance status, treatment and prognosis. Data were presented by tables in descriptive frequency and analyzed by SPSS version 20.

Results: Records of 120 patients up to 40 years of age who had colorectal cancer (CRC) were assessed. The median age at diagnosis was 27.5 years and age range was 15-40 years. Majority 74(46.6%) of tumors were detected in rectum. Histopathological examination showed majority of tumors were poorly differentiated mucin-secreting adenocarcinoma. Higher pathological T (T3 and T4 were 60%) stage was seen in 40 years or younger age group of CRC patients. CEA level was normal in 53.3% patients. Less than 10 gm/dl hemoglobin label was presented by 66.6% patients. Regarding performance status, 63.3% were in ECOG 1 and 10% were in ECOG 4. Most common presenting complain were per rectal bleeding 64.1% and abdominal pain 60.8%. Duration of symptoms at presentation were mostly less than 1 month 45.8%. About 57.5% patients under went curative surgery and 17% were in inoperable stage. Chemotherapy was received by 71% of the patients and 60.8% received radiotherapy. Our study showed poor prognosis of CRC in young age group. Survival rate was less than 2 years in 59% patients. Only 18.3 % patients had been surviving more than 24 months.

Conclusion: A lack of established screening programme to evaluate alarming bowel related symptoms in young people may be the cause of late detection and bad prognosis. Now, it is necessary to start a screening protocol particularly sigmoidoscopy among the target group with lowering the age limit.

Keywords: Colorectal cancer, Clinico-pathological evaluation, Young adults, Colonoscopy.

Introduction:

The estimated annual incidence of colorectal cancer (CRC)

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worldwide is 1.3 million, making it the third most common cancer in males and the second most common cancer in females.¹ There is wide geographic, racial, and ethnic variation in incidence and patterns, with 55% of cases occurring in high-resource nations. Higher proportions of colon cancers than rectal cancers (RC) and increased onset after age 50 are characteristics of CRC in high-income countries.²

The incidence in younger adults showed an increasing trend with a striking rectal preponderance. A previous analysis revealed that the incidence of RC increased 3.8% per year between 1984-2005 among people aged 40 and younger.³ Data from the United States suggest that approximately 11% of colon cancers and 18% of RCs occur in individuals younger than age 50.³ These cancers are more likely to be poorly differentiated, have mucinous and signet ring features. Men have proportionately higher incidence of rectal cancer than women and present at advanced stages. Familial syndromes account for approximately 20% of these cases. Possible reasons for this disturbing trend are speculated to be lack of screening in young adults and lifestyle factors, such as obesity, physical

inactivity, and a diet rich in processed foods and red meat with a low intake of fruits and vegetables.⁴

Low-resource countries such as India have reported CRC incidence rates of 4.2 and 3.2 per 100,000 in males and females, respectively.⁵ This is relatively low when compared with data from high-resource nations, where the incidence ranges from 25-44 per 100,000 populations. The traditional Indian diet, consisting predominantly of plant-based, fiber-rich foods and antioxidant-rich spices, has been postulated to be protective.⁶ Available data, however, indicate a steady rise in incidence, presumably a result of increasing urbanization and changing lifestyles and dietary patterns.⁷ However, these factors still do not sufficiently explain the striking differences that have been noted in the clinicopathologic profile of CRCs occurring in India when compared with their Western counterparts, with chief among these differences being a significantly lower median age of incidence and a rectal preponderance.^{8,9}

In recent years, we have observed an increased incidence of colorectal cancers in younger age group. Although exact incidence rate cannot be provided by a hospital-based study, the information would be useful in showing patterns of malignancies in our region. The present study was therefore designed to report age, gender, site of primary tumor, clinical features, histopathological type, and pathologic stage in patients with colorectal carcinomas (CRC) with special reference to young adults. The need for early detection is emphasized.

Material and Methods:

Materials and Methods: This cross-sectional study was conducted in the department of Oncology and department of Surgery, Bangladesh Medical College Hospital (BMCH). Histopathological records of all cases of malignant tumors which were received and diagnosed during last 2 years i.e. from January 2015 to December 2017 were studied. The records were analyzed in detail for age, gender, site of primary tumor, clinical features, histopathological type, and pathologic stage, tumor marker, performance status and treatment. Only carcinomas were included in the study. All young patients (defined as those 40 years old or younger) were studied separately. Cancer of the anus was not included.

Results:

A total of 120 cases were diagnosed to have CRC between January 2015 to December 2017 in BMCH.

Table 1: Age & Sex distribution of CRC patients (N=120)

Age in years	Number of patients	Percentage
15-19	10	8.3
20-24	19	15.8
25- 30	40	33.3
31-40	51	42.5
Total	120	100
Median age	27.5 years	
Age range	15-40 years	
Sex	Number of patients	Percentage
Male	64	53.3
Female	56	46.7

The median age at diagnosis was 27.5 years and age range was 15-40 years. Majority 51(42.5%) patients were between 31-40 years. Male predominance (53.3%) was found as shown in Table 1.

Table 2: Primary sites of CRC patients (N=120)

Primary Site	Number of patients	Percentage
Rectum	74	61.7
Colon	46	38.3
Total	120	100

Table 2 shows among 120 CRC patients, majority of tumors 74 (61.7%) occurred within the rectum and rest 46 (38.3%) occurred in colon.

Table 3: Histopathological findings on Grading and TNM stage (N=120)

Histological Grading	Number of patients	Percentage
Well differentiated	12	10.0
Moderately Differentiated	52	43.3
Poorly Differentiated	56	46.7
Total	120	100
T Stage	Number of patients	Percentage
T0-2	38	31.7
T3	58	48.3
T4	14	11.7
Not done	10	8.3
Total	120	100
N Stage	Number of patients	Percentage
N0	32	26.7
N1	50	41.7
N2	28	23.3
Not done	10	8.3
Total	120	100
Metastasis	Number of patients	Percentage
	14	11.7

Histopathological examination showed majority of tumors (46.7%) to be poorly differentiated mucin-secreting adenocarcinomas. Higher pathological T (T3 and T4 were around 60%) stage was seen in young age group. Also showed more advanced N stage (65% node positive). About 11.7% of the patients presented with metastasis.

Table 4: Tumor Marker (CEA level)

Tumor Marker (CEA)	Number of patients	Percentage
Normal range	64	53.3
Raised	36	30.0
Not done	20	16.7
Total	120	100

Table 4 shows that 53.3% patients had normal and 30% had raised CEA level.

Table 5: Hemoglobin level and Performance status (N=120)

Hemoglobin level	Number of patients	Percentage
<7 gm/dl	10	8.3
>7-10 gm/dl	70	58.3
>10 gm/dl	40	33.3
Performance status (ECOG)		
*0-1	76	63.3
2-3	32	26.6
04	12	10

*Eastern Cooperative Oncology Group Performance Status

About 66.6% patients presented with Hemoglobin level 10 gm/dl or less, regarding performance status: 63.3% were in ECOG 1 and 10% were in ECOG 4 (Table-5).

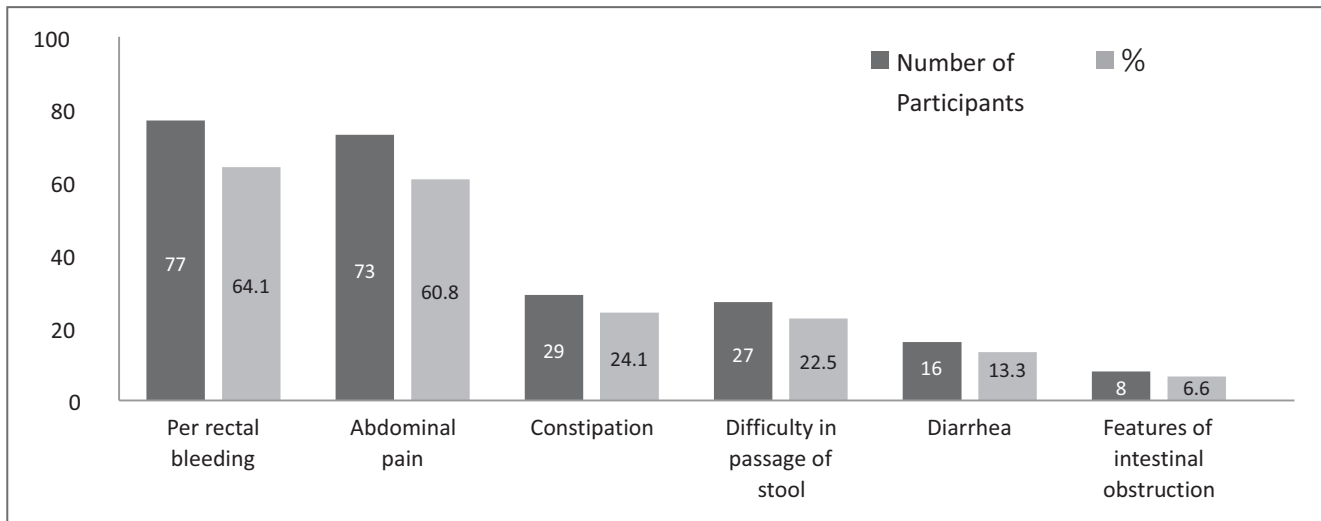


Figure 1: Clinical features of CRC patients

Most common presenting complains were rectal bleeding 64.1%, abdominal pain 60.8%, change of bowel habit (constipation and diarrhea) 37.4%, difficulty in passage of stool 22.5%, and features of intestinal obstruction 6.6% (Fig-1).

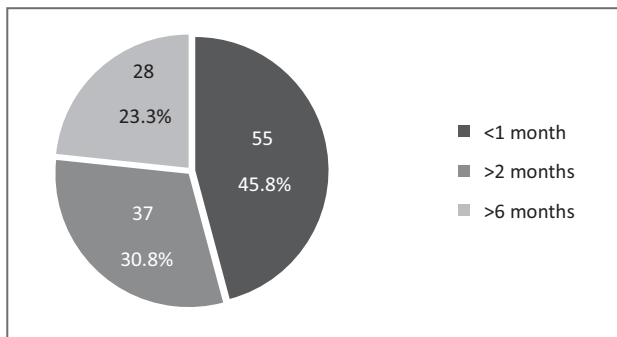


Figure 2: Duration of symptoms

Figure 2 shows duration of symptoms were mostly <1 month in 55 (45.8%), >2 months in 37(30.8%) and >6months in 28(23.3%) cases.

Table 6: Colonoscopic and Ultrasonogram findings

Colonoscopic findings	Number of patients	Percentage
Big lceroproferative growth, scope could not pass beyond lesion	75	62.5
Nodular growth, scope passed	45	37.5
USG finding	Number of patients	Percentage
Ascites present	14	11.7
Ascites absent	106	88.3

Table 6 shows 62.5% patients had big ulceroproliferative growth and scope could not pass beyond lesion in colonoscopy and 11.7 % presented with ascites in ultrasonography.

Table 7: Treatment profile of CRC patients by Surgery, Chemotherapy and Radiotherapy (N=120)

Surgery	Number of patients	Percentage
Curative	69	57.5
Palliative	31	25.8
Inoperable	20	16.7
Chemotherapy	Number of patients	Percentage
Received	85	70.8
Not received	35	29.2
Radiotherapy	Number of patients	Percentage
Received	73	60.8
Not received	47	39.2

Table 7 shows 57.5 % of the patients under went curative surgery and 16.7 % were in inoperable stage. About 70.8% of the patients received Chemotherapy and 60.8 % received Radiotherapy.

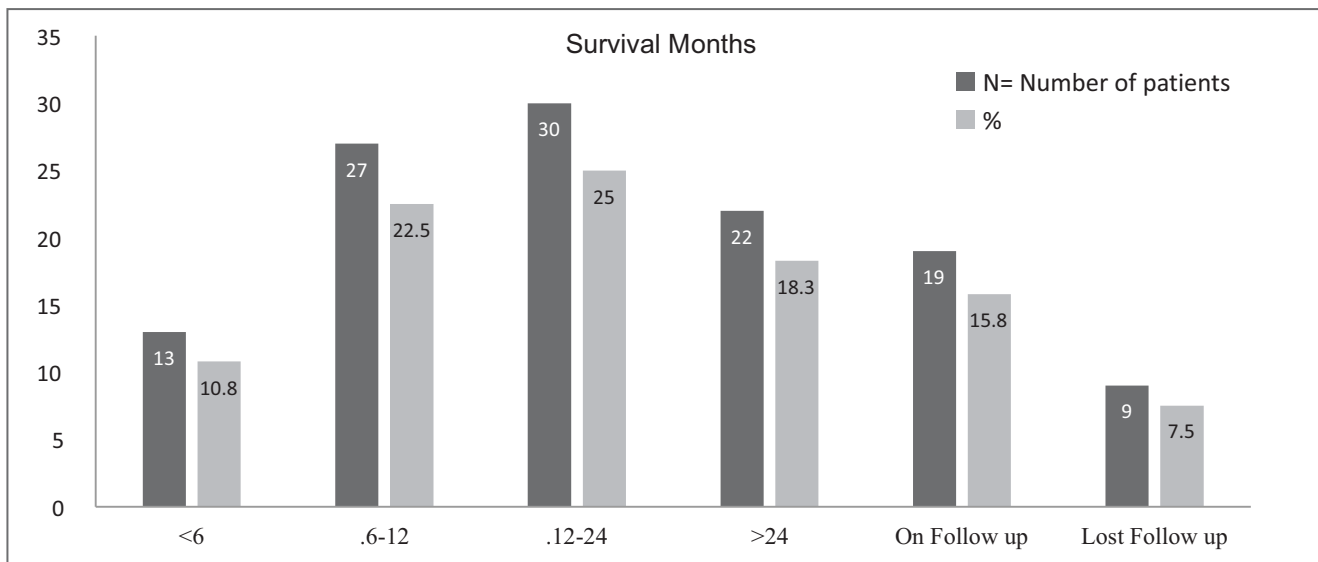


Figure 3: Prognosis in terms of months of survival among CRC patients (N=120)

Figure 3 shows poor prognosis of CRC in young age group. Survival rate was ≤ 2 years in 58.3% patients. Only 18.3 % patients are surviving more than 24 months, 15.8% were on follow up and 7.5% were lost to follow up.

Discussion:

This study illustrates higher occurrence of CRC (42.5%) among the age group 31-40 years (Table 1). These findings are generally consistent with two previous studies that analyzed CRC trends using SEER databases.^{9,10,11} Genetic and familial etiologies account for less than 20% of colorectal cancers in the US. The remaining 80% of cases are random, with dietary factors affecting the risk significantly.¹⁰ O'Connell et al. reported an increase in incidence rates in ages 20 to 39 years for both colon and rectal cancers during 1973 to 1999.¹¹ Obesity is a major risk factor for CRC in men and, to a lesser extent, for colon

cancer in women.¹² Consumption of red and processed meat has been shown to increase risk of cancers of the distal colon and rectum,¹³ whereas milk and calcium consumption have shown a protective effect against these sub sites.¹⁴ Recently fast-food consumption in the Bangladesh increased markedly among children and adults. A diet high in fast food is associated with both greater meat consumption and reduced milk consumption. It is plausible that the emergence of unfavorable dietary patterns in children and young adults over the past one decade may have contributed to the increase in CRC among young adults observed in our study. The median age in

our series was 27.5. The youngest patient in our series was a 15 year old male. It is apparent from the present study that colorectal cancer majority (42.5%) at the age group 31-40 years in our institute. In this series, the male to female ratio was 8:7. Rectal tumors accounted for 61.7 % and colonic tumors for 38.3% (Table 2). Similar rectal predominance has been reported by others.^{15,16}

Minardi et al. found a large proportion of Dukes' stage C (37%) in young patients with colorectal cancer.¹⁷ In our study among those younger than 40 years, majority i.e., 46.7 % cases were poorly differentiated mucin-secreting adenocarcinomas and 60% cases presented at advanced pathologic stage (T3 and T4) as shown in Table 3. The reason for this is not clear. A genetic basis for tumorigenesis has been implicated in early onset CRC among young patients. The increase in incidence in rectal cancer in this region may not, however, be related to familial adenomatous polyposis (FAP) as none of our cases showed adenomatous polyposis coli. However, there is a high possibility of genetic background to at least some young rectal cancers in India. Microsatellite instability has been identified in most of the patients with early onset of CRC, suggesting genetic etiology.¹⁸

In our study, we found that 53.3% patients had normal and 30% was raised CEA level (Table 4) with 66.6 % patients presented with Hemoglobin level 10 gm/dl or less (Table 5). Baqar AR et al. has found CEA levels were higher for higher T stages and in undifferentiated, poorly differentiated tumours and higher nodal disease.¹⁹ In CRC hemoglobin level is usually found lower in right sided tumor. Sadahiro et al. shows similar findings where carcinoma of the cecum, ascending colon, and transverse colon; large-size carcinoma, invasion beyond the proper muscle layer; positive lymph node metastasis; and clinical stage (Dukes' B, C, and D) were factors associated with high incidence of anemia.²⁰ Our study shows that, most common presenting complain were rectal bleeding 64.1% and abdominal pain 60.8%, change of bowel habit 37.4%, difficulty in passage of stool 22.5% and features of intestinal obstruction 6.6% (Figure 1). This is similar to a study done by Agyemang-Yeboah F et al.²¹

The data of our study shows that duration at presentation of symptoms were mostly less than 1 month 55 (45.8%) (Figure 2). But another study reported that the median duration of symptoms (from onset to diagnosis) was 14 weeks.²² Table 6 shows 62.5 % of patient had big ulceroproliferative growth and scope could not pass beyond lesion in lower gastro intestinal endoscopy and 11.7 % presented with ascites in ultrasonography. Ayantunde et al. reported about 3.7% patients were detected ascites with CRC.²³ Here, curative surgery was done in 57.5% of patients and 16.7 % were in inoperable stage. Chemotherapy was received by 70.8% of total patients while 60.8 % received Radiotherapy (Table 7).

The concern for colorectal cancer affecting young population below 40 years old was due to the poor

prognosis attached to it. Our study shows poor prognosis of CRC in young age group. Less than 2 years survival rate was seen in 58.3% patients. Only 18.3% patients are surviving more than 24 months (Figure 3). There are several studies in the literature that report a more advanced stage and a poorer prognosis in patients younger than 40 years.²⁴

Conclusion:

A lack of established screening programme to evaluate alarming bowel related symptoms in young people may be the cause of late detection and bad prognosis. Now, it is necessary to start a screening protocol particularly sigmoidoscopy among the target group with lowering the age limit. CRC in early age may be correlated with modern dietary habit and obesity. Appropriate dietary changes, regular physical activity, and maintenance of healthy weight could substantially reduce the morbidity and mortality associated with colorectal cancer.

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A retrospective analysis of rape victims in Comilla Medical College: Experience of 282 cases

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Abstract

Background: Rape is considered as an extreme form of unlawful sexual offence against women and children. It has physical, psychological, and social impact on the victim. Sexual assault destroys the morality, hope and creates disappointment and anger in the minds of the victim. Victims lack self-confidence, drown in frustrations and may commit suicide. Thus this crime is considered as a form of violation of human rights.

Objectives: This study was carried out to find out the pattern of reported rape cases in a rural district of Bangladesh, in order to create nationwide awareness against this heinous crime.

Methods: It was a retrospective cross-sectional study conducted in the department of Forensic Medicine and Toxicology, Comilla Medical College during January 2020 to December 2020 on 282 rape victims. Data were collected on the pertinent variables from the case reports and medico-legal examination records. Data were presented by frequency distribution tables and diagram. Data analysis was done by SPSS version 12.

Results: It was revealed from the findings that among 282 sexually assaulted victims, 18.09% of rape cases were reported in the month of October 2020, 27.30% were in 16-20 years' age group and 24.11% in 10-15 years of age group. About 83.68% of the victims were Muslims, 56.03% victims were unmarried, 43% victims were students, 39.71% were illiterate and 65.60% were from poor socio-economic background. About 33% of assailants were acquaintance of the victim. Majority (30.14%) of the incidence of sexual abuse occurred in victim's own house. Regarding injury pattern of victim, 39.72% had genital injuries; negative spermatozoa were found among all respondents. All victims in our study were found as anxious and depressed.

Keywords: Rape, Unlawful, Sexual offence, Violation of human rights.

Introduction:

The prevalence of sexual violence is quite high in Bangladesh. The rate is much higher in the rural areas compared to the urban areas. Even in the pandemic of COVID-19 we are observing higher occurrence of rape and other sexual assaults in our society. Rape is a crime or sexual offence. It is not a medical diagnosis rather it is a legal term. The word 'rape' is derived from Latin term 'rapio' which means 'to seize'. Thus rape literally implies forcible seizure.¹ Rape is defined as physically forced or otherwise coerced penetration— even if slight— of the vulva or anus, using a penis, other body parts or an object. The attempt to do so is known as attempted rape.² There is no age limit either for the victims or for the accused.³ It is the duty of the court to take appropriate decision as whether a young accused can be considered as sexually potent or

capable or not.⁴ Regardless of the age of the victim, sexual assault should be investigated as soon as possible after the heinous act. The need for promptness is obvious from a legal standpoint, but it is equally important medically to document injuries that could be diagnostic of sexual assault like fondling/digital penetration, simulated intercourse, vaginal penetration, penetration etc. Clinical documentation is essential because ejaculation may not have occurred.⁵ Rape can be committed even when there is inability to produce a penile erection.⁶ There are many well-documented cases of genital trauma in absence of ejaculation, and increasing numbers of perpetrators are using condoms both to protect themselves from venereal disease and to avoid leaving damaging evidence.⁷

There is an alarming rise in the incidence of rape amid the Covid-19 pandemic across Bangladesh. According to the Bangladesh Mahila Parishad (BMP), a survey revealed the figures that some 1,093 children and women have been raped from January to October of 2020 in the country. Out of the total victims, 205 women were gang-raped.⁸ According to statistics compiled by human rights organization Ain o Salish Kendra, a total of 632 rape incidents took place between April and August 2020. It means on average, four women have been raped every day in the mentioned period. People have been confined to their homes for a long time due to the Corona virus pandemic and many have lost their jobs. Such crimes are on the rise

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due to familial, social, political and moral degradation.⁹ This study reflected the sociodemographic and other key factors related to the heinous act with an aim to address attention for creating social awareness.

Material and Methods:

The study was conducted in the department of Forensic Medicine & Toxicology at Comilla Medical College from January 2020 to December 2020 on 282 sexually assaulted victims. They hailed from 18 different upazilas of Comilla district and were reported to the Forensic Medicine department of Comilla Medical College for medico-legal examination. Examination of all victims was carried out by doctors of the said department. Detail information regarding age, literacy, income, pattern of relationship with the assailant, physical examination including genital and extra genital injuries, status of victim's vaginal swab test and victims state of mental condition were noted. Data were collected in a structured sheet from the record book of the department of Forensic Medicine, CMC. Prior to medico-legal examination, informed written consent were taken from the victims. Collected data were compiled and presented in tables. Data analysis was done by statistical software SPSS version 12.

Results:

Table 1: Age group of rape victims (n=282)

Age in years	Frequency	Percentage
4-9	24	8.51
10-15	68	24.11
16-20	77	27.30
21-25	61	21.63
26-30	28	9.93
31-40	14	4.96
41 -60	10	3.55
Total	282	100

Table 1 shows that 27.30% of the victims belong to 16-20 years of age group, 24.11% of victims belong to 10-15 years and 21.63% of victims to 21-25yrs age group.

Table 2: Distribution of rape victims according to religion (n=282)

Religion	Frequency	Percentage
Muslim	236	83.68
Hindu	34	12.06
Christian	12	4.26
Total	282	100

Table 2 shows that 83.68% rape victims were Muslims, 12.06 % were Hindu's and 4.26 % were Christians.

Table 3: Marital status of rape victims (n=282)

Marital status	Frequency	Percentage
Married	84	29.79
Unmarried	158	56.03
Divorced	22	7.80
Widow	18	6.38
Total	282	100

Table 3 shows that 56.03% of the rape victims were unmarried, 29.79% were married, 7.80% were divorced and 6.38% of victims were widows.

Table 4: Frequency distribution of rape cases considering victim's occupation (n=282)

Profession category	Frequency	Percentage
Student	123	43.46
Housewife	106	37.58
Unemployed	28	9.93
Employed	25	8.87
Total	282	100

Table 4 shows that 43.46% of rape victims were students, 37.58% of victims were housewives, 9.93% were unemployed and remaining 8.87% of victims were employed.

Table 5: Distribution of education status of rape victims (n=282)

Level of education	Frequency	Percentage
Illiterate	112	39.71
Upto class 5	80	28.36
Class 6 to 9	70	24.82
Class 10 to 12	20	7.09
Total	282	100

Table 5 shows that 39.71 % of rape victims are completely illiterate, 28.36 % of victims have the knowledge of primary education and remaining 24.82 % have knowledge of secondary education and remaining 7.09% of these victims have education of higher secondary level.

Table 6: Distribution of socio-economic status of the rape victims (n=282)

Income aka/month	Status	No. of victims	Percentage
Up to 5000 Tk	Low socioeconomic class	185	65.60
5001-15000 Tk	Middle class	85	30.14
More than 15000 Tk	Upper class	12	4.26
Total		282	100

Table 6 shows that 65.60% of rape victims were from low socio-economic status and 30.14% were from middle class and 4.26% were from upper class families.

Table 7: Pattern of relationship between victim and assailants (n=282)

Pattern of relationship	Frequency	Percentage
Acquaintance	93	32.97
Strangers	46	16.31
Close friends	58	20.56
Neighbours	46	16.31
Students of same school/ college	05	1.77
Master and servant	22	7.80
Teacher and student	12	4.26
Total	282	10

Table 7 shows that 32.97% of assailants were acquaintance, 20.56% were close friends, 16.31% were strangers and neighbour's of the victim.

Table 8: Place of incidence of the offence (n=282)

Place of incidence	Frequency	Percentage
Victim's house	85	30.14
Boy's hostel	15	5.32
Assailant's house	28	9.93
Relatives house	52	18.44
Road side/isolated place	30	10.63
Park/jungle	32	11.35
Guest house/hotels	25	8.87
Institution/private tutor's house	15	5.32%
Total	282	100

Table 8 shows that 30.14% of the incidence of sexual abuse occurred inside victim's own house, 18.44% in relative's houses and 10.63% on roadside /isolated places.

Table 9: Pattern of Injury on medico-legal examination of victims (n=282)

Pattern of injury	Frequency	Percentage
Genital injuries	112	39.72
Extra-genital injuries	66	23.40
Combined genital & extra genital injuries	46	16.31
Abrasions, bruise	58	20.57
Total	282	100

Table 9 shows injury pattern in victims consisting of genital injuries (39.72%), extra genital injuries (23.40%), Abrasions and bruise (20.57%)

Discussion:

It is estimated that approximately 35% of women worldwide have experienced sexual harassment in their life.¹⁰ According to a survey conducted by the South African Medical Research Council, South Africa has the highest incidence of rape in the world followed by Botswana, Lesotho, Swaziland, Bermuda, Sweden, Suriname, Costa Rica, Nicaragua and Grenada.¹⁰ According to World Population review data of 'Rape statistics by reported Country 2020', India recorded an average of 87% rape cases daily in 2019.¹⁰ The magnitude of rape or sexual harassment is high all over the world. But negligible number is. In the majority of countries with available data; less than 40% of the women who experience violence seek help of any sort.¹¹ The under reporting of cases of sexual assaults are mainly due to social stigma; prejudice with regard to the chances of marriage, publicity in press, embarrassment in court, doubt in local law enforcement, risk of losing the love and respect of society.¹²

Out of 282 cases studied in this paper, 27.30% victims were aged between 16-20 years' age group (Table-1). Similar findings were observed with the study of Al-Azad MAS et al¹³, Ali N et al¹⁴, Sarkar et al¹⁵, Saha et al¹⁶ where they found that most of the victims were young, below the age of 20 years. In our study, majority of the victims (83.68%) were Muslims (Table-2). This result is similar with study of Al-Azad MAS et al¹³ and Ali N et al¹⁴. It differs with study of Sarkar et al¹⁵ where majority of the victims were Hindus. This is consistent with the population majority of both the countries. Our study revealed 56.03% of victims were unmarried (Table-3). These results are in agreement with the study of Al-Azad MAS et al¹³, Ali N et al¹⁴, Sarkar et al¹⁵, Ferdous NF¹⁷ and Islam MN et al¹⁸. In this study we found that majority (43%) of these victims' occupation were students (Table-4). This finding is in agreement with the study of Ferdous NF et al¹⁷ where 78% victim were students and garment workers. In our study, the majority of the victims (39.71%) were illiterate (Table-5). This finding is similar with Al-Azad MAS et al¹³ and Sarkar et al.¹⁵ Saha et al¹⁶ in a study observed it to be a bit higher (85%). About 65.60% victims in our study were from a low socio-economic background (Table-6). These findings are consistent with findings by Al-Azad MAS et al¹³ and Sarkar et al.¹⁵ In our study, 32.97% of assailants were acquaintance of the victim (Table-7). This finding is similar with the study of Al-Azad MAS et al¹³, Ali N et al¹⁴, Sarkar et al¹⁵ and Islam MN et al¹⁸. In our study, majority (30.14%) of the incidence of sexual abuse occurred in victim's own house (Table-8). This finding is in agreement with the study of Al-Azad MAS et al¹³, Ali N et al¹⁴ and Sarkar et al¹⁵ where it was 36.95%, 64.20% and 41.1% respectively.

In this study, genital findings in the victim included genital injuries 39.72% and extra genital injuries 23.40% (Table-9). These findings are consistent with Al-Azad MAS et al¹³ where genital injuries were 39.57% and but extra genital injuries were about 36.09%. Islam MN et al¹⁸ in a study

reported genital injuries 32.3% and extra genital injuries in 21.5% cases. The high vaginal swab (HVS), which was collected for detection of spermatozoa from 282 victims and were found to be negative due to victims' delayed arrival for medico-legal examination, washing of private parts etc. This finding is similar with Al-Azad MAS et al¹³, Ali N et al¹⁴, Ferdous NF et al¹⁷ and Islam MN et al¹⁸ and Hossain MN et al.²⁰ This finding differed with the study of Sarkar et al¹⁵ where spermatozoa were positive in 5.55% cases and Riggs et al¹⁹ reported spermatozoa in 48% cases. In our study all respondents were found to be anxious and depressed, which is similar with study by Ferdous NF et al.¹⁷

Conclusion:

Sexual violence is an unceasing major public health problem for the social, legal, medical and mental health services. Government should recognize the scale of the problem & create stronger laws to protect the rights of our children and women of Bangladesh. Death sentence should be implemented so that accused is duly punished. The study findings demand a growing need of focus on incidences of rape in the district levels and would be helpful to the policymakers by adopting strategies for adequate coverage of incidences, prompt legal support, post rape health care and social services to the distressed victims of sexual assaults in Bangladesh. .8 % received Radiotherapy.

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Incidental diagnosis of hypothyroidism in patients attending the OPD of tertiary medical college hospital in Dhaka city

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Abstract

Background: Thyroid hormone is a key substance in normal homeostasis, having variable influence on cell metabolism on different organs. Hypothyroidism is a common functional disorder of the thyroid gland.

Objective: The study was conducted to determine the rate of incidental diagnosis of hypothyroidism in patients attending outpatient departments (OPD) of two tertiary care hospitals in Dhaka city.

Methods: This cross sectional study was conducted on 265 patients attending OPD at Bangladesh Medical College Hospital (BMCH) and International Medical College Hospital for incidental diagnosis of hypothyroidism. They were included in the study upon fulfilling the inclusion and exclusion criteria and giving informed consent. Fasting TSH, T3, FT4 were measured along with other routine laboratory investigations. TSH, T3, FT4 were estimated by the enzyme-linked immunosorbent assay (ELISA) method. Data were presented in frequency tables and diagram and analyzed by SPSS v 16.0.

Results: Out of 265 patients studied, 104 were incidentally diagnosed with hypothyroidism which constitutes 39.25% of the study population. Majority of the patients (37.50%) belonged to the age group of 31–40 years with female predominance 87.50%. Among the newly diagnosed hypothyroid cases, 45.19% were overweight and 44.23% had positive family history. No significant relationships were found between hypothyroidism, being overweight and having a positive family history. Main clinical presentations found in our hypothyroid cases were muscle weakness (98%) and lethargy (97%). Most of the patients (55.77%) came from urban areas.

Conclusion: Hypothyroidism is no longer a rarity. Our study demonstrates that incidental diagnosis of subclinical hypothyroidism was higher in females with age group of 31–40 years and there is a significant prevalence of it in the study population.

Keywords: Hypothyroidism, ELISA method, Fasting TSH, T3, FT4.

Introduction:

Among various endocrine problems, thyroid disorders are the second most common worldwide and one-third of the

world's population lives in iodine deficient areas.^{1,2} At the beginning of the twenty first century hypothyroidism, Graves' disease, postpartum thyroiditis and thyroid malignancies are common thyroid disorders in Bangladesh while iodine deficiency disorders are still persisting in low prevalence. It is believed that around 10% of the Bangladeshi people suffer from clinically evident thyroid disorders.³ Actual prevalence of subclinical hypothyroidism in general population of Bangladesh is not known but it is not negligible. It is estimated that about 3% to 8% of the population without known thyroid status are affected with subclinical hypothyroidism.^{4,5,6} Thyroid hormones (TH) regulate the basal metabolic rate and renal hemodynamics of most cells. The thyroid gland synthesizes and releases triiodothyronine (T3) and thyroxine (T4), which represent the only iodine containing hormones in the vertebrates. T3 is the biologically active thyroid hormone.⁷ These hormones are required for the normal growth, development and function of nearly all tissues, with major effects on oxygen consumption and metabolic rate.⁸ TH synthesis and secretion is regulated by a negative feedback system that involves the hypothalamus, pituitary and the thyroid gland.⁹ THs regulate the basal metabolic rate of all cells including hepatocytes and hence, modulate hepatic function; the liver in turn metabolizes the thyroid hormones and regulates

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their systemic endocrine effects.¹⁰ Normal circulating levels of thyroid hormone are required for both normal hepatic circulation and normal bilirubin metabolism.¹¹

Clinically, hypothyroidism is a syndrome manifested by a collection of symptoms and signs. They are influenced by the age of the patient, the rate at which the hypothyroidism develops and the presence of other disorders. In very young infants, hypothyroidism can result in irreversible mental and physical retardation, unless treatment is initiated within weeks after birth, whereas, in children and adults, the effects of hypofunction of thyroid though profound are reversible.¹²

Hypothyroidism may be primary and subclinical. Primary hypothyroidism is defined as high serum TSH concentrations and low serum free T4 concentrations. Subclinical hypothyroidism is defined as high serum TSH (usually < 10 mU/L) and normal free T4 concentrations.¹² The prevalence of hypothyroidism increases with age and is nearly 10 times more common in females than in males. The risk of hypothyroidism is higher in people with a family history of thyroid disease and those over 60 years. The prevalence and incidence of hypothyroidism are variable because existing studies have differed significantly in regard to population age range, geographic location, environmental factors such as dietary iodine and goitrogen intake, genetic characteristics of study population, and criteria used to define presence and degree of thyroid failure. Among the general population in Europe, the prevalence of hypothyroidism varies between 0.2 and 5.3%, while in the USA between 0.3 and 3.7%, this variation probably being due to different iodine intake in diverse areas.^{13,14,15}

Subclinical hypothyroidism is more prevalent having been found in 4%–10% in multiple populations. The prevalence of subclinical hypothyroidism is variable, depending on the cohort considered and going from 7.5%, as shown in the Wickham study to around 21% in women and 16% in men as shown in the Colorado study.¹³⁻¹⁷

Serum TSH measurement is the most convenient and sensitive method for screening of hypothyroidism because there is a linear relationship with serum TSH and circulating thyroid hormone level. Hypothyroidism can occur if the thyroid gland fails to work properly or if the thyroid gland is not stimulated properly by the hypothalamus or pituitary gland.¹⁸⁻²¹

There are no nationwide studies on the prevalence of hypothyroidism from Bangladesh either in the pre or post iodization periods. Hence a large cross-sectional, comprehensive and prospective study is required to provide a clear picture of the evolving profile of thyroid disorders across the whole country, especially as the country is in the post iodization era.²² The main aim of this study was to find out the incidental diagnosis of hypothyroidism among the patients attending OPD of two tertiary care hospitals in Dhaka city and to create awareness among the population about the disorder so that adequate management is possible for prevention of developing further systemic complications related to abnormal thyroid status.

Material and Methods:

Participants

This hospital-based cross-sectional study was conducted at the outpatient department of Bangladesh Medical College Hospital and International Medical College Hospital, Dhaka city. It was carried out from July 2019 to June 2020. It was approved by the institutional ethical committee. Inclusion criteria were- Patients attending OPD of the Bangladesh Medical College Hospital and International Medical College Hospital, age is 18 years and above. Exclusion Criteria included pregnant women, long term user of estrogen or contraceptive drugs, already diagnosed cases of hypothyroidism, patients who were receiving drugs that could interfere with the thyroid function tests, patients who underwent thyroid surgery, radio-iodine and other ablation exposure in head and neck region, patients not willing to participate in the study and critically ill patients.

Finally, out of 265 patients 104 patients were selected to participate in the study by fulfilling all the inclusion and exclusion criteria.

Study Procedure

All the subjects underwent medical history assessment, general clinical examination, before enrollment including examination of thyroid glands. Patients gave informed consent before they participated in the study. All the participants then were asked to complete a questionnaire to collect basic demographic information such as age, gender, place of living, clinical features and family history of thyroid disease. Then anthropometric measurements height and weight were measured. According to WHO, subjects were classified as BMI ≤ 25 kg/m² (normal), BMI 25-29.9 kg/m² (overweight), and BMI ≥ 30 kg/m² (obesity).

With full aseptic precautions 5 ml of venous blood was collected to estimate TSH, T3, FT4 by the enzyme-linked immunosorbent assay (ELISA) method.

Diagnostic Criteria

The reference normal range using this method was:

TSH: 0.40-4.0 uIU/ml

T3: 0.81-1.79 ng/ml

Free T4 (FT4): 0.89-1.76 ng/dl

- Subclinical Hypothyroidism: Serum TSH is raised and serum T3 and T4 concentrations are at the lower end of the reference range. Presentations of these patients are usually non-specific.
- Primary Hypothyroidism: Serum TSH level should be > 20 mIU/L to confirm the diagnosis.

Data Analysis

Data were recorded into semi-structured pre-tested proforma. It was entered into Microsoft Excel and analyzed using SPSS v 16.0. Summarization of data was done according to data types and appropriate statistical

tests were done. Data were presented by descriptive frequency. p-value of <0.05 was considered to be statistically significant.

Results:

Among 265 patients, 104 cases were diagnosed as hypothyroid patients.

Table 1: Age distribution of hypothyroid and non-hypothyroid patients

Age group in years	Hypothyroid cases No. (%)	Non-hypothyroid cases No. (%)	Total cases No. (%)
18-30	27 (25.96%)	24 (14.91%)	51 (19.25%)
31-40	39 (37.50%)	36(22.37%)	75 (28.30%)
41-50	19 (18.27%)	34(21.11%)	53 (20.00%)
51-60	12 (11.53%)	40(24.85%)	52 (19.62%)
> 60	7 (6.73%)	27(16.77%)	34 (12.83%)
Total	104 (100%)	161(100%)	265 (100%)

Majority of the diagnosed hypothyroid patients were in 31-40 years of age group 39(37.5%), followed by 18-30 years of age group 27(25.96%). Only 7 (6.73%) were >60 years of age as shown in Table-1. In comparison, the highest frequency of nonhypothyroid cases were from the 51-60 years' age group 40 (24.85%)

Table 2: Gender Distribution of patients (n=265)
Among hypothyroid cases 91(87.5%) were female and 13(12.5%) were male (Table 2).

Gender	Hypothyroid Cases No. (%)	Non-hypothyroid Cases No. (%)	Total Cases No. (%)	p-value
Female	91 (87.5%)	77 (47.83%)	168 (63.40%)	0.035
Male	13 (12.5%)	84 (52.17%)	97 (36.60%)	
Total	104 (100%)	161 (100%)	265 (100%)	

Chi-square test demonstrated a statistically significant (p<0.05) relation between gender and hypothyroidism.

Table 3: Thyroid function status of the hypothyroid patients (n=104)

Thyroid function status	Subtype	No. of patients	Percentage
Hypothyroid	Subclinical	87	83.7
	Primary	17	16.3
Total		104	100

Table 3 shows majority of the hypothyroid patients were found to have subclinical hypothyroidism 87(83.65%) and 16.34% were primary hypothyroidism.

Table 4: Distribution of patients according to their BMI

BMI (Kg/m ²)	Hypothyroid cases No. (%)	Non-hypothyroid cases No. (%)	Total cases No. (%)	p value
<25 (Normal)	39 (37.50%)	76 (47.21%)	115 (43.40%)	0.614
25-30 (overweight)	47 (45.20%)	59 (36.64%)	106 (40.00%)	
> 30 (obese)	18 (17.30%)	26 (16.15%)	44 (16.60%)	
Total	104 (100%)	161 (100%)	265 (100%)	

Among the 104 hypothyroidism patients, 47 (45.19%) were overweight. Among the non-hypothyroid patients 59 (36.64%) were overweight and 26 (16.15%) were obese. However, in this study BMI was not significantly found associated with hypothyroidism as shown in Table 4.

Table 5: Family history of thyroid diseases among study population

Family History of Thyroid Diseases	Hypothyroid Cases No. (%)	Non-hypothyroid Cases No. (%)	p-value
Yes	46 (44.23%)	64 (39.75%)	0.795
No	58 (55.77%)	97 (60.25%)	
Total	104 (100%)	161 (100%)	

Table 5 shows, family history of thyroid diseases were found among 46 (44.23%) of hypothyroid patients. However, family history was not found significantly associated in this study with hypothyroidism (p=0.795).

Table 6: Clinical symptoms in patients with hypothyroidism

Symptoms	No. of cases (%)
Muscle weakness	102 (98%)
Lethargy	101 (97%)
Dry, coarse skin	42 (40%)
Bodyache	68 (65%)
Facial puffiness	37 (35%)
Constipation	73 (70%)
Somnolence	73 (70%)
Cold intolerance	38 (36%)
Weight gain	49 (47%)
Leg edema	25 (24%)
Menstrual abnormalities	45 (43%)
Paresthesia	46 (44%)

Multiple response

Table 6 shows, majority of the hypothyroid patients presented with muscle weakness (98%) and lethargy (97%). Cold intolerance (36%) and leg edema (24%) were observed in a minority of the study population.

Discussion:

In our study the majority of hypothyroid patients were at the age group of 31-40 years (37.50%) and minimum was noted in the age group of >60 years (6.73%) as shown in Table 1. Unnikrishnan et al²³ reported that the prevalence of overt hypothyroidism was highest in the age group of 46-54 years and lowest in the age-group of 18-24 years whereas subclinical hypothyroidism was most prevalent in the age group of >55 years and least prevalent in the age-group of 18-24 years.

In this study, out of 265 cases incidental hypothyroidism was detected in 104 cases where 83.65% and 16.34% patients were subclinical and primary hypothyroid respectively (Table 3). A population-based study done in Cochin²⁶ on 971 adult subjects estimated the prevalence of hypothyroidism to be 3.9% and that of subclinical hypothyroidism to be 9.4%. In an epidemiological study conducted in eight cities of India, Unnikrishnan et al²³ reported the overall prevalence of hypothyroidism to be 10.95%, which included 7.48% self-reported hypothyroidism and that of subclinical hypothyroidism to be 8.02%. Self-reported hypothyroidism has not been included as a separate entity in the present study. A study conducted in Mumbai by Deshmukh et al.²⁵ found the prevalence of subclinical hypothyroidism to be 11.3%.

We did not find a significant correlation between hypothyroidism and BMI (Table 4). Recently, a study from China showed that TSH levels were positively correlated with BMI.²⁷ Cooper also reported that a higher BMI was associated with a higher frequency of hypothyroidism.¹⁵ Furthermore, we found that people who had a family history of thyroid disease were not significantly related with their development of hypothyroidism (Table 5). The absence of specific symptoms of hypothyroidism and low awareness for hypothyroidism result in the low diagnosis rate may account for the phenomenon.^{28,29}

The most common presenting clinical features of hypothyroidism in the present study are weakness (98%) and lethargy (97%) as shown in Table 6. Table 7 shows the common presenting clinical features of early and recent studies.

Table 7: Comparison of clinical symptoms of hypothyroidism in different studies

	Symptoms	Percentage of cases
Early studies (1930s)	Weakness	99
	Dry skin	97
	Lethargy	91
	Slow speech	91
	Cold intolerance	89
	Facial edema	79
	Constipation	61
	Weight gain	59
	Menorrhagia	32
	Recent study (1990)	Dry skin
Cold intolerance		60
Periorbital puffiness		54
Weight gain		52
Paresthesia		52
Constipation		48

Source of table: Medical management of thyroid disease. 2nd ed. p. 146. Edited by David S Cooper. Published by Informa Healthcare, USA. (Early studies, 1930 and Recent study 1990)

Conclusion:

The present study was carried out to find the incidental diagnosis of hypothyroidism in patients attending OPD, in a tertiary care hospital, Dhaka city. Our study suggests that subclinical hypothyroidism is the most prevalent disease in the urban females of study population with maximum age group of 31-40 years. In view of the findings of the present study and keeping in mind its limitations, a long-term population-based follow-up study of thyroid disorders in Bangladesh is the need of the hour. Prompt detection and corrective treatment with thyroxine can prevent many complications. Therefore, routine testing with serum TSH is a sufficient and cost-effective screening tool and should be applied.

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Comparison of Mantoux test with quantiFERON-TB gold plus assay for detection of tuberculosis infection among chronic kidney disease patients in a tertiary care hospital in Dhaka city

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Abstract

Background: Tuberculosis is one of the communicable diseases in Bangladesh. Highest prevalence is seen in immunocompromised patients with chronic kidney diseases (CKD). In CKD, tuberculosis stays as latent infection and develops in active cases on a later date. Early detection of tuberculosis infection among CKD patients could lead to a better therapeutic outcome.

Objective: This study aims to compare Mantoux test with QFT-Plus assay and check its sensitivity and specificity against QFT-Plus for detecting tuberculosis infection, latent and active, both, among CKD patients.

Methods: This was a cross-sectional type of descriptive study conducted in the department of Nephrology, Bangabandhu Sheikh Mujib Medical University (BSMMU) among 103 adult patients with CKD during the period of January 2019 to December 2019. Patients with past history of Tuberculosis were excluded from the study. QuantiFERON-TB gold plus assay was done for each patient along with Mantoux test. QuantiFERON-TB gold plus assay was done for each patient from the Department of Microbiology and Immunology, Bangabandhu Sheikh Mujib Medical University. Sensitivity analysis of Mantoux test was done among the study population using QuantiFERON-TB gold plus assay as standard test for detection tuberculosis infection in both latent and active cases, as per WHO recommendation. Sensitivity analysis was done using a 2x2 table. Accuracy of the test was measured along with predictive values and likelihood ratios. Predictive ratio was used to estimate trust ability of the test.

Results: Study population were predominantly male (68.9%) and for the age group 45 to 59 years (33%). QuantiFERON-TB gold plus assay was conducted among the study population and 47.6% were found positive. Mantoux test was also performed and 18.4% were found positive. For Mantoux test, sensitivity, specificity, accuracy, positive predictive value, negative predictive value, positive predictive ratio, negative predictive ratio, positive likelihood ratio and negative likelihood ratio were found to be 34.7%, 96.3%, 67%, 89.5%, 61.9%, 2.35, 0.17, 9.4 and 0.68 respectively.

Conclusion: Mantoux test showed low sensitivity for detecting tuberculosis infection among CKD patients & should be avoided as screening test for Tuberculosis among CKD patients. QuantiFERON-TB gold plus assay should be done in CKD patients as it shows better sensitivity and specificity than Mantoux test.

Keywords: Chronic Kidney Disease (CKD), Mantoux Test, QuantiFERON-TB gold plus assay, Sensitivity, Specificity.

Introduction:

Tuberculosis (TB) is one of the greatest public health problems and leading cause of mortality and morbidity in

the world.¹ Significant amount of cases still being unaccounted for due to incorrect diagnosis and underreporting. Based on the Global Tuberculosis Report 2020, most cases of tuberculosis were found in Asia (44%) on 2019, with 3.6% of global total TB cases found in Bangladesh. Bangladesh is one of the top eight countries with highest number of TB patients worldwide.² Effort are being focused on not only treatment but also on prevention by conducting screening for tuberculosis infection especially latent infection.²⁻⁴ Latent infection doesn't produce any clinical symptoms, radiological abnormality, or microbiological evidence of infection or may present with active infection.^{5,6} Currently more than one third of the world population is at risk for tuberculosis infection.⁷ Screening for Tuberculosis is one of the top priority in World Health Organization's (WHO) End TB Strategy.²

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Immunocompromised adult patients like chronic kidney disease (CKD) are at a higher risk of acquiring tuberculosis, with a risk between 6.9 to 52.5 times greater than the general population.⁸ Early screening methods to detect tuberculosis infection are highly recommended.^{1,9,10} It has been reported that 5-10% of the immunocompromised patients with latent Tuberculosis develops active tuberculosis infection.^{11,12} The World Health Organization guidelines recommend the use of Mantoux test or interferon- γ release assay (IGRA) for detection of latent tuberculosis infection.¹³ In that context, Mantoux test has been done for some time for detection of tuberculosis infection. This test also comes with low sensitivity and a high rate of false-negative results among immunocompromised patients like CKD. Diagnostic method like interferon-gamma release assays (IGRAs) replaces older tests like Mantoux test for better screening and detection.^{10,14-17}

QuantiFERON-TB gold plus (QFT-Plus) is the latest generation of IGRAs, launched in 2015. The QFT-Plus kit contains two tubes with two specific antigens (TB antigen 1 and TB antigen 2).^{14,15} TB antigen 1 stimulates immune response from CD4+ T cells and TB antigen 2 stimulates response from both CD4+ and CD8+ T cells.^{18,19} This response from CD8+ T cells makes QFT-Plus particularly useful for detecting tuberculosis in CKD patients where CD4 count is low due to immunocompromised state of the patients.¹⁶ In Bangladesh, low cost Mantoux test has been in regular use to detect tuberculosis infection among CKD patients, but QFT-Plus shows better sensitivity and specificity than Mantoux test. So, QFT-Plus should be used as a routine screening test among CKD patients. This study aims to compare Mantoux test with QFT-Plus assay and check its sensitivity and specificity against QFT-Plus for detecting tuberculosis infection, latent and active, both, among CKD patients.

Material and Methods:

This was a cross-sectional type of descriptive study conducted in the Department of Nephrology, Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka, Bangladesh among adult patient with CKD during the period of January 2019 to December 2019. As per selection criteria, 103 patients were enrolled for the study patients with past history of Tuberculosis were excluded from the study. Patients were fully briefed regarding the study before the enrollment and written consent were collected from every participant during enrollment. QuantiFERON-TB gold plus assay was done for each patient from the Department of Microbiology and Immunology, BSMMU. For Mantoux test, intradermal injection of 0.1 ml of purified protein derivative (PPD) into the flexor surface of the forearm was given. Reaction was measured in millimeters of the induration (palpable, raised, hardened area or swelling). All relevant data were collected using research instruments through face-to-face interview and checking the laboratory test results. All data were compiled and processed with the help of statistician and were analyzed using windows-based computer software with

Statistical Packages for Social Sciences (SPSS-25) (SPSS Inc, Chicago, IL, USA). Ethical approval was taken from the Institutional Review Board (IRB) of BSMMU. Necessary precautions were taken to protect privacy, anonymity and confidentiality of the information given by the respondents. Participants enjoyed the right to withdraw themselves from the study at any time. An informed written consent was obtained from the respondents during enrollment.

Sensitivity analysis of Mantoux test was done among the study population using QuantiFERON-TB Gold Plus Assay as gold standard test for detection tuberculosis infection in both latent and active cases, as per WHO recommendation. Sensitivity analysis was done using a 2x2 Table-A. Accuracy of the test was measured along with predictive values and likelihood ratios.^{20,21} Predictive ratio were used to estimate trust ability of the test.²²

Table A: For sensitivity analysis

		Disease status according to a predefined gold standard	
		Present	Absent
Test status	Negative	a	b
	Positive	c	d

Sensitivity and Specificity

Sensitivity is the proportion of people with a condition who are correctly identified by a screening test as indeed having that condition and specificity is the proportion of people without a condition who are correctly identified by a screening test as indeed not having the condition.²⁰

$$\text{Sensitivity} = a/(a+c)$$

$$\text{Specificity} = d/(d+b)$$

Accuracy

Accuracy of a test is its ability to differentiate the patient and healthy cases correctly. It is the proportion of true positive and true negative in all evaluated cases.²³

$$\text{Accuracy} = (a+d)/(a+b+c+d)$$

Predictive Values

Positive predictive value (PPV) is the probability that people with a positive screening test result indeed do have the condition of interest and negative predictive value (NPV) is the probability that people with a negative screening test result indeed do not have the condition of interest.²⁰

$$\text{Positive predictive value (PPV)} = a/(a+b)$$

$$\text{Negative predictive value (NPV)} = d/(c+d)$$

Likelihood Ratios

Positive likelihood ratio (PLR) is the ratio of sensitivity to the false positive fraction. $PLR = 1$ means a test equally detects correctly among persons with the disease and without the disease. $PLR > 1$ means a test more effectively detects correctly persons with the disease and is less likely to wrongly identify a healthy person as a person with the disease. $PLR < 1$ means a test detects correctly persons with the disease less frequently than it incorrectly identifies a healthy person as a person with a disease.^{20,21} Similarly, the negative likelihood ratio (NLR) = 1 means a test equally not detect the disease incorrectly among persons with the disease and without the disease. $NLR < 1$ means a test more effectively identifies correctly healthy persons more frequently than it detects incorrectly persons with a disease as being without it. $NLR > 1$ means a test is more misleading than helpful in detecting the absence of a disease.²²

Positive likelihood ratio (PLR) = $\text{Sensitivity} / (1 - \text{Specificity})$

Negative likelihood ratio (NLR) = $(1 - \text{Sensitivity}) / \text{Specificity}$

Predictive Ratio

Positive predictive ratio (PPR) and negative predictive ratio (NPR) were estimated. PPR is the ratio of the PPV to the False Negative Fraction in the patient population. $PPR = 1$ means a test will equally “diagnose correctly” and “fail to diagnose” persons with the disease. $PPR > 1$ means a test more effectively “diagnose correctly” persons with the disease relative to “fail to diagnose” persons with the disease. $PPR < 1$ mean a test is misleading and It diagnoses unhealthy persons as not having a disease more frequently than it diagnoses correctly a person with a disease. NPR is the ratio of the False Positive Fraction in the patient population to the NPV. $NPR = 1$ means a test equally “diagnoses correctly” persons without the disease and “fail to diagnose” persons without the disease. $NPR > 1$ means the test is misleading. It diagnoses healthy persons as having a disease more frequently than it diagnoses correctly persons without a disease. $NPR < 1$ means a test correctly diagnoses healthy persons as persons without a disease more frequently than it diagnoses incorrectly a person without a disease as having the disease. The lower the value of NPR, the more effective is the test.²⁰

Positive predictive ratio (PPR) = $PPV / (1 - NPV)$

Negative predictive ratio (NPR) = $(1 - PPV) / NPV$

Results:

A total 103 adult patients were enrolled in this study.

Table 1: Sociodemographic status of the study population (N=103)

Criteria	Frequency	Percentage
Age in years		
18-29	22	21.4
30-44	33	32
45-59	34	33
≥ 60	14	13.6
Total	103	100
Sex		
Male	71	68.9
Female	32	31.1
Total	103	100
Education		
SSC or below	38	36.9
HSC	46	44.7
Graduate or above	19	18.4
Total	103	100

Among the study population, 33% were from age group 45-59 years followed by 32% from 30-44 years. Study population was predominantly male 68.9% and completed HSC 44.7% as shown in Table 1.

Table 2: Results of QuantiFERON-TB gold plus assay and Mantoux test (N=103)

Tests	Frequency	Percentage
QuantiFERON-TB gold plus assay		
Positive	49	47.6
Negative	54	52.4
Total	103	100
Mantoux Test		
Positive	19	18.4
Negative	84	81.6
Total	103	100

QuantiFERON-TB gold plus assay was conducted among the study population and 47.6% were found to have been positive for tuberculosis. Mantoux test was also performed on study population and 18.4% were found positive for tuberculosis by Mantoux test (Table 2)

Table 3: Sensitivity Analysis of Mantoux Test compared to QuantiFERON-TB gold plus assay

		Tuberculosis status according to QuantiFERON-TB gold plus assay	
		Present	Absent
Results of Mantoux Test	Negative	17	2
	Positive	32	52

Table 3 shows sensitivity analysis of Mantoux test in comparison to QuantiFERON-TB gold plus assay. Out of the 103 samples, 17 were true positive and 52 were true negative for Mantoux test.

Table 4: Estimated values of Mantoux test parameters

Test parameters	Values
Sensitivity	34.7%
Specificity	96.3%
Accuracy	67%
Positive predictive value (PPV)	89.5%
Negative predictive value (NPV)	61.9%
Positive predictive ratio (PPR)	2.35
Negative predictive ratio (NPR)	0.17
Positive likelihood ratio (PLR)	9.4
Negative likelihood ratio (NLR)	0.68

Sensitivity was found to be 34.7% and specificity was found to be 96.3% for Mantoux test. Accuracy of Mantoux test was found to be 67%. Positive predictive value (PPV) and Negative predictive value (NPV) were found to be 89.5% and 61.9% respectively. Positive predictive ratio (PPR) and negative predictive ratio (NPR) were found to be 2.35 and 0.17 respectively. Positive likelihood ratio (PLR) and negative likelihood ratio (NLR) were found to be 9.4 and 0.68 respectively (Table 4).

Discussion:

The pathophysiology of CKD related immunodeficiency suggests that CKD could be a risk factor for TB.³⁴ Immunodeficiency associated with CKD appears to be multifactorial in etiology.²⁵ Advanced CKD is associated with oxidative stress and inflammation, 25-hydroxyvitamin D deficiency and malnutrition with evidence of functional abnormalities in a variety of immune cells including B and T cells, neutrophils, monocytes and natural killer cells. Changes in immunity begin as early as stage 3 CKD (defined as a glomerular filtration rate <60 ml/min) and worsen in later stages as kidney function deteriorates and waste products accumulate.²⁶

In present study, QuantiFERON-TB gold plus assay was conducted among the study population and 47.6% were found to have been positive for tuberculosis (Table 2). Mantoux test was also performed on study population and

18.4% were found positive for tuberculosis by Mantoux test. Sensitivity analysis was done for Mantoux test compared to QuantiFERON-TB gold plus assay where out of the 103 samples, 17 were true positive and 52 were true negative for Mantoux test (Table 3). Sensitivity was found to be 34.7% and specificity was found to be 96.3% for Mantoux test (Table 4). Accuracy of Mantoux test was found to be 67% means Mantoux test could correctly identify 34.7% of the latent tuberculosis positive cases and 96.3% of the latent tuberculosis negative cases (Table 4). In a 2019 study, sensitivity for Mantoux test was found to be 93% and specificity was found to be 57% among health care workers, whereas our study samples were all chronic kidney disease patients.²⁷ This difference in results between these two studies indicates that Mantoux test could be less sensitive for detecting tuberculosis infection among immunocompromised patients like CKD.

In our study, Mantoux test showed higher sensitivity and lower specificity in comparison to a study where sensitivity shows 50% and specificity 52% among immunocompromised patients.²⁸ Using abnormal chest x-ray as gold standard for detecting TB, sensitivity and specificity of Mantoux test was found to be 14% and 88% respectively, both are lower than present study findings.²⁹ Among CKD patients, Mantoux test showed 21.2% sensitivity which is lower than our study finding.³⁰ Sensitivity in present study is also higher than 12.3% found in another study among CKD patients, indicating an overall poor sensitivity of Mantoux test for detecting tuberculosis among CKD patients.³¹ Studies among general population showed a relatively high sensitivity and specificity for Mantoux test, 94% and 88% respectively, showing substantial difference in sensitivity compared to present study.³² This finding indicates that Mantoux test has lower usability for detecting tuberculosis among CKD patients.

Positive predictive value for Mantoux test was found to be 99% and negative predictive value was up to 66% in a study, compared to 89.5% and 61.9% from our study respectively (Table 4).²⁷ Both studies showed high predictive values, meaning Mantoux test could detect positive TB cases with high accuracy, 67% to be precise among this study samples. Positive predictive value and negative predictive values of Mantoux test in presenting study is lower than the 100% and 95% found respectively in a study among patients with kidney disease.³³ Study among general population showed positive predictive value of Mantoux test between 75-95, close to our study finding, but negative predictive value was 86%, higher than our study finding.^{32,34}

In present study, PPR was found to be 2.35 (> 1), which means among the patients with tuberculosis, Mantoux test could correctly detect more cases than it failed to detect. NPR was found to be 0.17 (<1), meaning among the patients without tuberculosis, Mantoux test could correctly detect more cases as healthy than it didn't.³⁰ PLR was found to be 9.4 (> 1), meaning Mantoux test could detect correctly more persons with disease than incorrectly detecting a health person as one with the disease. NLR was found to be 0.68 (<1), meaning Mantoux test could detect correctly less

persons with disease than incorrectly detecting a healthy person as one with disease.²⁰⁻²²

The use of the Mantoux test remains controversial in patients with renal disease due to its high rate of false negative results.³⁵ Currently, IGRA is used as a diagnostic tool for latent Tuberculosis infection.³⁶ IGRA has several advantages, including convenience and application in an immuno-compromised population, BCG-vaccinated population and high non-tuberculous mycobacteria (NTM) prevalent area.^{37,38}

Conclusion:

Mantoux test showed low sensitivity for detecting tuberculosis infection among CKD patients & should be avoided as screening test for Tuberculosis among CKD patients. QuantiFERON-TB gold plus assay should be done in CKD patients as it shows better sensitivity and specificity than Mantoux test.

Limitations

A small sample size of 103 from one hospital was used for the study; a bigger sample size from multiple hospitals would have generated more accurate results.

Conflict of Interest

Authors declare that there is no conflict of interest.

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Gallstones among dyspeptic patients: An experience of 308 cases

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Abstract

Background: Gallstone is one of the most common gastrointestinal disease in general practice. Most patient with cholelithiasis are asymptomatic and gallstones are incidentally found during clinical evaluation of dyspepsia by routine ultrasonography of abdomen.

Objective: The aim of this study is to assess the clinical status of dyspeptic patients and to explore the frequency of gallstone in patients presenting with dyspeptic symptoms.

Methods: This cross-sectional study was conducted on 308 patients of dyspepsia attending Popular Medical Centre, Sylhet, Bangladesh from July 2018 to December 2018. Data were collected by purposive sampling. Informed consent was taken from the participants (patients). Epidemiological data, clinical findings and reports of relevant investigations including abdominal ultrasonogram and flexible upper gastrointestinal endoscopy were documented. Data were presented by descriptive frequency and in tables and diagram. Statistical analysis was done using SPSS version 20.

Results: Among total of 308 patients, age-range varied from 20 to 70 years with mean age 40.85 ± 13.01 years. Majority 216 (70.1%) were male and 96 (29.9%) were female. Common presenting symptoms were pain in abdomen-150(48.7%), flatulence-123(39.9%), heart burn-113(36.7%) and fullness of abdomen-112(36.4%). Ultrasound findings revealed gall stone in 46(14.9%) and fatty change in liver in 44(14.3%) cases of dyspepsia. The common endoscopic findings among the patients with dyspepsia were nonerosive gastritis - 48(15.6%), erosive gastritis -34(11.0%) and duodenal ulcer -20(6.5%). Among 46 gall stone cases of dyspeptic patients, 56.5% showed no abnormality in upper endoscopic examination but among rest 45.5% cases, majority showed non-erosive gastritis (6, 13%) and erosive gastritis (5, 10.9%).

Conclusion: Gall stone disease and hepatic fatty change are common in patients presenting for dyspepsia. So clinical evaluation is meticulously to be done to ensure proper management without delay.

Keywords: Dyspepsia, Gall stone disease, Ultrasonogram, Upper endoscopy.

Introduction:

The term dyspepsia includes epigastric pain and burning (60 to 70%), feeling bloated after a meal (80%), early satiation (60 to 70%), distension in the epigastric region (80%), nausea (60%), and vomiting (40%). The symptoms of dyspepsia may be acute or chronic. Acute state appears from gastroenteritis; for chronic case, underlying organic

(e.g., ulcer, reflux, pancreatic disease, heart and muscle disease) or functional factors may be responsible.¹

Prevalence of dyspepsia ranges between 10-45% in general population.^{2,3} Nevertheless, dyspepsia remains a common issue with annual incidence rates estimated between 1-6%.² On diagnostic work-up, 20 to 30% of patients with dyspepsia are found to have organic diseases that account for their symptoms.^{4,5}

The majority of these symptoms, however appear to be dysmotility-like or reflux-like and are preferably to the upper gastrointestinal tract and the stomach in particular. Hence, it is reasonable to assume that the presence of gallstones may in some way be influencing gastric motility, thus causing dyspeptic symptoms.⁶

Gall stones are extremely common in worldwide. The prevalence of asymptomatic gallstone was reported between 10%-15%.^{7,8} The average risk of developing symptomatic disease were estimated 2-2.6% annually. Approximately 10% and 20% of asymptomatic patients became symptomatic within 5 and 20 years of diagnosis, respectively.⁹ Gall stones associated symptoms may be non-specific, it could be difficult to distinguish between symptomatic disease and functional dyspepsia. On the

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other hands, most gall stones are incidentally found during clinical evaluation of dyspepsia or routine ultrasonography.¹⁰ Studies suggested Trans-abdominal ultrasonography as a gold standard test for the diagnosis of gall stone disease with more than 95% sensitivity and specificity.¹¹ Some patients with dyspepsia unfortunately sometimes remain treated symptomatically for years without exploring the associated pathological conditions among which gall stone disease is most common. This lingers patients' sufferings and also increase treatment cost. So assessment of the clinical status of dyspeptic patients and also to explore its correlation to gallstone disease is important in terms of appropriate management of patients with symptoms of dyspepsia at the right time.

Material and Methods:

This cross-sectional study was carried out on patients with dyspepsia attending for consultation with gastroenterologist at a selected private institution, Popular Medical Centre, Sylhet, Bangladesh from July 2018 to December 2018. Patients with chronic or recurrent pain or discomfort centered in the upper abdomen with or without heartburn, vomiting or nausea for at least 3 months were included. Patients with any evidence of organic disease on the upper endoscopy examination or clinical assessment, prior history of cholecystectomy or gastric surgery, history of peptic ulcer disease and any evidence that dyspepsia related to irritable bowel syndrome (IBS) were excluded. Patients unwilling to take part in the study were also excluded.

All participants were requested to come in the next afternoon after a fast of ≥ 8 h for ultrasonography. Upper gastrointestinal endoscopy (Olympus CV170, Japan) of all patients were performed. Then upper abdominal ultrasonography was done by an expert radiologist in order to find gallstone disease including wall thickness (>3 mm), evidence of fatty liver and others. Abdominal ultrasonography was done using a scanner equipped with a 2.0-5.0-MHz transducer (Philips Affiniti 30 USA). The sonologists were unaware of the patients' endoscopic findings. All subjects were interviewed by using a questionnaire that covered the demographic features, clinical manifestations and investigation findings. Data were presented as absolute frequencies and percentages in tables and diagrams. Statistical analysis was carried out with the SPSS version 20.0.

Results:

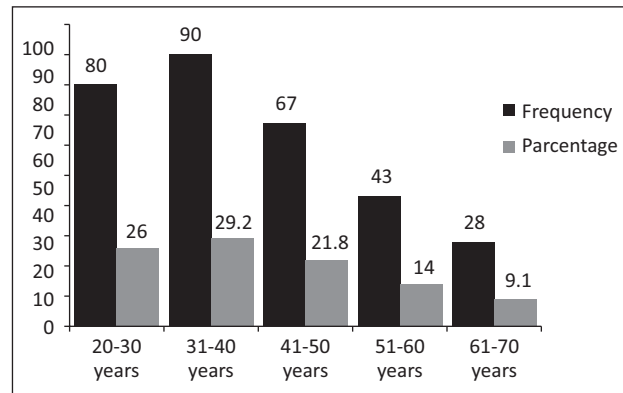


Figure 1: Age-group distribution of dyspepsia patients (n=308)

Figure-1 shows that out of 308 patients, age range varied from 20 to 70 years with mean age of 40.85 ± 13.01 years. Majority of the patients 90 (29.2%) were in age group of 31-40 years, followed by 80 (26%) patients in 20-30 years, 67 (21.8%) patients in 41-50 years, 43 (14%) patients in 51-60 years and 28 (9.1%) patients in 61-70 years' age group.

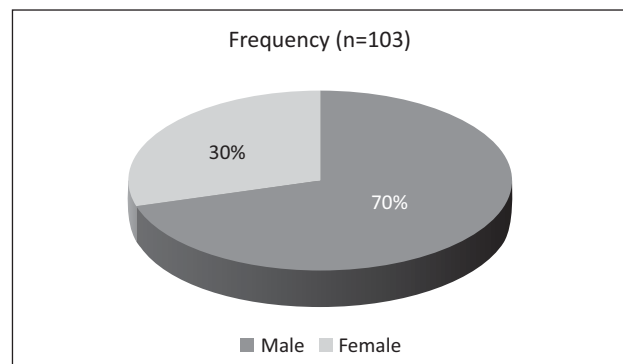


Figure 2: Gender distribution of dyspepsia patients (n=308)

Among 308 dyspeptic patients, males were 216 (70.1%) and females were 92 (29.9%) with male and female ratio 2.35:1 as shown in Figure-2.

Table 1: Distribution of the respondents by presenting symptoms (n=308)

Symptoms	Frequency	Percentage
Pain abdomen	150	48.7
Heart burn	113	36.7
Fullness of abdomen	112	36.4
Flatulence	123	39.9
Nausea and Vomiting	58	18.8

*Multiple response

The most common presenting symptoms was pain abdomen (48.7%), followed by flatulence (39.9%), heart burn (36.7%) and fullness of abdomen (36.4%) as shown in Table 1.

Table 2: Distribution of the respondents by ultrasound findings (n=308)

Ultrasound findings	Frequency	Percentage
Gall stone	46	14.9
Fatty liver	44	14.3
No abnormality	218	70.8
Total	308	100.0

In Table 2, ultrasound findings revealed gall stone in 46 (14.9%) and fatty change in liver in 44 (14.3%) patients presenting with symptoms of dyspepsia. Majority (218, 70.8%) showed no abnormality.

Table 3: Distribution of the respondents by endoscopic findings (n=308)

Endoscopic findings	Frequency	Percentage
Non erosive gastritis	48	15.6
Erosive gastritis	34	11.0
Duodenal ulcer	20	6.5
Antral gastric ulcer	10	3.2
Duodenal ulcer remission	11	3.6
Oesophagitis	4	1.3
Others	6	1.9
No abnormality	175	56.8
Total	308	100.0

Table 3 shows that common endoscopic findings were non-erosive gastritis 48(15.6%), erosive gastritis 34(11.0%) and duodenal ulcer 20(6.5%). Most of the patients 175(56.8%) did not show any abnormality.

Table-4: Endoscopic finding of the gall stone patients (n=46)

Endoscopic findings	Frequency	Percentage
Non erosive gastritis	06	13.0
Erosive gastritis	05	10.9
Duodenal ulcer	04	8.7
Antral gastric ulcer	01	2.2
Duodenal ulcer remission	03	6.5
Oesophagitis	01	2.2
No abnormality	26	56.5
Total	46	100.0

Among 46 gall stone cases of dyspeptic patients, 56.5%

showed no abnormality in endoscopic examination but 45.5% cases constituted majority with non-erosive gastritis (6, 13%) and erosive gastritis (5, 10.9%).

Discussion:

This study reported the frequency of gall stones founded by ultrasonography in patients with dyspepsia. In this study the mean age of the dyspeptic patients was 40.85 ± 13.01 years, which higher than that in Japan (31.5 ± 16.3 years)¹² and Singapore (29.7 years),¹³ but lower than that in Iran (48 ± 11.4 years).¹⁴ This may be due to differences in socio cultural, environmental and dietary habits. This study also revealed that the age group of 20-40 years constituted the highest proportion of dyspepsia (Figure-1) which is consistent with another report from our country.¹⁵

In our study dyspepsia is more prevalent among males which is 70.1% (Figure-2). It is consistent with report from India,¹⁶ Japan^{12,17} and Saudi Arab.¹⁸

Common presenting symptoms in this study were pain abdomen (48.7%), followed by flatulence (39.9%), heart burn (36.7%) and fullness of abdomen (36.4%) as presented in Table-1. Report from Iran showed that abdominal pain and excess flatus are common symptoms in dyspeptic patients.¹⁴ Studies from USA¹⁹ and India²⁰ reported upper abdominal pain, postprandial abdominal fullness, upper abdominal discomfort, upper abdominal bloating, belching, nausea and vomiting as common symptoms of dyspepsia.

Dyspeptic patient with gall stones may experience symptoms such as abdominal pain, nausea and upper abdominal discomfort.¹⁴ Studies explored associations between prevalent gallstones and abdominal symptoms. Meta-analyses identified abdominal pain localized in the upper abdomen, epigastrium, or upper right abdominal quadrant, with radiation to the back or right side of constant nature, causing use of pain medication to be associated with prevalent gallstones.^{21,22} One study included participants aware of gallstone status identified pain in the right hypochondrium and epigastrium as predictive factors for incident gallstones or cholecystectomy.²³ The results from these previous studies are somehow supported by findings of this study, except for the pain localization in the right side of the abdomen or the use of analgesics. The mechanisms involved in pain symptoms caused by gallstones are not completely identified but are suggested to be caused by the migration of a gallstone in the cystic or common bile duct. Gallbladder dysmotility and decreased gallbladder emptying are generally risk factors for gallstone formation.²⁴ A muscular component has been suggested to explain pain in a study correlating pain index and in vitro gallbladder smooth muscle contractility in patients undergoing cholecystectomy for uncomplicated disease.²⁵ An association of dyspepsia with nausea and vomiting has also been identified in previous studies.²¹ Experimental studies have found low esophageal pH values in subjects with gallstones compared to controls as well as a low vagal tone and large antral volumes in the

Conclusion:

Gallstone is common among dyspeptic patients. So physicians should consider upper abdominal ultrasonography in the work up of patients with dyspepsia for screening and early detection of gall stones.

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Long COVID as a new burden in iceberg of disease: A review

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Abstract

Background: COVID-19 is a new rapid spreading, extremely contagious infectious disease. The duration and the long-term consequences and pathogenesis of long COVID, are still is not understood. Its existence in the tip and hidden part of iceberg of disease will increase the disease burden as direct and indirect consequences of long COVID.

Aim: Aim of this review is to highlight multisystem involvement of long COVID with some essential needful holistic approach of management.

Methods: Electronic databases (PubMed, google scholar, MEDLINE) were searched. Original articles, review articles, editorials, committee opinions, WHO guidelines and book chapters were included. Forty seven (47) literatures after primary screening were retrieved and reviewed for this manuscript writing.

Findings: Patients with long COVID experience a wide range of physical and mental/psychological symptoms. After the onset of COVID-19, evidence of cardiac, respiratory, neuropsychiatric, renal and endocrine disorders were detected among patients with long COVID. Management of long COVID is variable as there is wide spectrum of clinical manifestations and in many cases multi-systems are involved. It needs a multidisciplinary team consisting of physicians, nurses, paramedics and other supporting staffs for better management of patients. Among the treatment modules one of the most important components is physical rehabilitation which prevents disability and enhances the quality of life.

Conclusion: Duration and existence of COVID-19 and long COVID is still unknown and newer variants are still emerging with high transmissibility. So effective treatment, vaccination and other preventive measures like hand washing, mask wearing, social distancing, cough etiquette etc. are the essentials of now normal era for control and prevention of long COVID.

Keywords: Long COVID, COVID-19, Multisystem involvement, Physical rehabilitation. Iceberg of disease.

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Introduction:

COVID-19 is a new rapid spreading, extremely contagious infectious disease. It was first identified in Wuhan, Hubei province, China in December 2019, from where it has spread all over the world. In March 2020, World Health Organization (WHO) has officially declared the outbreak as pandemic.¹ Globally by 28th June 2021, over 182,314,068 confirmed cases of COVID-19, including 3,970,701 deaths have been reported to WHO and whereas in Bangladesh 896770 confirmed cases of COVID-19, including 14,388 deaths.² The clinical course and consequences of this new disease are still not explored completely. COVID-19 infected people and fraction of people with long COVID are variable in regard to manifestations and management. The duration and the long-term consequences and pathogenesis of Long COVID, are still is not understood and there is also lack of satisfactory treatment as well.³

The increasing concern is now long COVID because some people who contract Coronavirus Disease 2019 (COVID-19) does not make a rapid or full recovery.^{4,5,6} Recently, the term “post-acute sequelae of SARS-CoV-2 infection” (PASC), “long-COVID-19”, and “post-acute COVID-19”, “long-haulers” has been utilized.^{7,8} Here in this article we are using the term “long-COVID” as it seems more self-

explanatory in relation to the definition. Long COVID defined as the presence of signs and symptoms that develop during or following an infection consistent with COVID-19 which continue for 12-weeks or more and are not explained by an alternative diagnosis. This includes both ongoing symptomatic COVID-19 (from 4 to 12 weeks) and "Post-COVID Syndrome" (12-weeks or more).⁹

Clinically COVID-19 presentation ranges from asymptomatic, mild symptomatic to fulminant and fatal cases. Serious complications including pneumonia, acute respiratory distress syndrome (ARDS), sepsis, blood clotting, acute kidney injury, myocarditis, acute myocardial infarction, multiple organ failure, and other viral and bacterial infections can occur in severe cases of infection.^{10,11} Death due to COVID-19 is possibly a result of pneumonia and hyperinflammation associated with cytokine storm syndrome.¹²

Its existence in the tip and hidden part of iceberg of disease will increase the morbidity and mortality of NCDs and other diseases as direct and indirect consequences of long COVID. Aim of this review is to highlight multisystem involvement of long COVID with some essential needful holistic approach of management in this context.

Incidence of long COVID:

Most of the patients who suffer from COVID-19 return to normal after acute infection, few portion report ongoing health issues. People who are affected with longer term sequelae after acute COVID-19 remains unknown, but approximately 10–20% of COVID-19 patients experience lingering symptoms for weeks to months following acute SARS-CoV-2 infection.¹³ In Bangladesh a study found 60% long COVID patients were aged <40 years and only 8% patients were >60 years and the proportion of men with COVID-19 was higher than that of women with ratio of 1.4:1.¹⁴ In a study from the USA, 31% patients were aged >65 years.¹⁵ The reason may be the proportion of the elderly population (5%) is lower in our country than that in Western world (North America, 16%; Europe, 21%).¹⁶ It is also related to under reporting and negligence about the care of the elderly citizens in our society. Most of the elderly patients do not come for follow up after recovery from COVID-19. Their post-covid symptoms are considered usually as features of common cold and flu.

Risk factors:

Specific risk factors for long COVID are yet to be identified.^{17,18,19} It has not yet been established how ethnicity, sex, age, gender, underlying health conditions, viral dose, or progression of COVID-19 significantly affect the risk of developing long-term effects of COVID-19.²⁰ A latest study identified some risk factors for post COVID symptoms like female sex, respiratory distress, lethargy, long duration of illness, and moderate severity of the disease. They found a significant association between post-

COVID-19 syndrome and female sex, prolonged recovery, persistent positivity on RT-PCR after day 14 of the initial test. All age groups had a similar susceptibility to develop post-COVID symptoms. An overlap of fatigue, cough, dyspnea, chest pain, headache, anosmia, and body ache was also found.¹⁴ Another study found that during the post-COVID-19 follow-up most COVID-19 symptoms persisted.¹⁷ Attention should be given to identify diverse new symptoms like adjustment disorder, memory disturbances, sleep disorder and restless leg syndrome which develop in post COVID-19.

Symptoms of long COVID:

Patients with long COVID experience a wide range of physical and mental/psychological symptoms. Long COVID-19 complications varied significantly ($p < 0.05$) between symptomatic and asymptomatic COVID-19 patients in Bangladesh.²¹ Interestingly, tiredness (12.45%) and weight loss (9.18%) were more frequent in symptomatic groups than in asymptomatic groups. ACE-2 receptor present in muscle that helps entry of virus might explain these effects.²²

Cardiovascular abnormalities

Abnormal findings of cardiovascular abnormalities were 78% 2–3 months after the onset of COVID-19 and 60% had evidence of myocardial inflammation independent of the severity of their acute illness.²³ Another study reported that up to 40% of COVID-19 patients presented with pericarditis or myocarditis > 70 days after infection.²⁴ Hypertension ranks the second most newly observed post-COVID-19 complication in COVID-19 patients. COVID-19 symptomatic (2.45%) patients were more experienced with new-onset hypertension than asymptomatic (1.41%) patients.²¹

Pulmonary abnormalities

Patients after discharge for acute COVID-19 and reported a decrease in lung diffusion capacity for carbon monoxide (DLCO) in 53% and decrease respiratory muscle strength in 49% of patients.²⁵ Lung function abnormalities were also reduced in a quarter of patients (14/55) at three months after hospital discharge. The commonest lung function abnormality (16.36%) was DLCO. At admission, a higher level of D-dimer was significantly associated with DLCO% <80% suggesting that D-dimer might be a potential biomarker for the prediction of DLCO decline patients with COVID-19. Evidence of lung fibrosis and persistence of symptoms 64% were also reported.²⁶ The most common high-resolution computed tomography pattern observed in a study was ground glass opacity.²⁷ Recent studies reported that, many patients experienced persistent respiratory complications like cough, fibrotic lung disease, bronchiectasis, and pulmonary vascular disease after recovering from COVID-19.^{28,29}

Neuropsychiatric abnormalities

After COVID-19 infection, cognitive symptoms were observed in some cases. Surveillance and investigation will have sought out the problem for better treatment management. The occurrence of encephalitis, seizures and other conditions such as major mood swings and cognitive impairment (brain fog) have been reported in patients up to two to three months after the onset of acute illness.³⁰ Magnetic resonance imaging scanning of previously hospitalized patients with COVID-19 suggested possible disruption to micro-structural and functional brain integrity at three months of follow-up,³¹ thus signifying the neuro-invasive capabilities of the SARS-CoV-2 virus and the potential for long-term consequences of the infection.

Neuropsychiatric symptoms like headache (44%), attention disorder (27%), and anosmia (21%) have been reported. Other symptoms including brain fog and neuropathy were also reported.^{32,33} The etiology of neuropsychiatric symptoms in COVID-19 patients is complex and multifactorial, and could be related to the direct effect of the infection, cerebrovascular disease (including hypercoagulation), physiological compromise (hypoxia), side effects of medications, and social aspects of having a potentially fatal illness. Adults have a double risk of being newly diagnosed with a psychiatric disorder after the COVID-19 diagnosis, and the most common psychiatric conditions presented were anxiety disorders, insomnia, and dementia.^{34,35} Another study showed 23% of previously hospitalized patients suffered from anxiety or depression with women having higher odds than men.²⁷

Occurrence of post-traumatic stress disorder (PTSD) was significantly higher and more severe in women with long COVID. However, a significant proportion of patients with moderate-to-severe PTSD symptoms had a past psychiatric diagnosis. Inadequate social support was linked to the occurrence and severity of PTSD symptoms.³⁶ Sleep disturbances might contribute to the presentation of psychiatric disorders.³⁷ Prompt diagnosis and intervention of any neuropsychiatric care is recommended for all patients recovering from COVID-19. A significant proportion of patients had sleep disturbances, including insomnia and circadian rhythm sleep disturbances was detected in a study done in Bangladesh.¹⁴ Involvement of hypothalamus was previously seen in other SARS-CoV infections, so these symptoms might be due to involvement of hypothalamus might be the reason for these symptoms.²⁴ A large number of patients with adjustment disorders was identified which may develop due to mental stress caused by COVID-19.¹⁴ No visual anomaly was reported in asymptomatic patients, but 1.42% of the symptomatic individuals developed a visual problem.²¹

Renal disorder

Acute kidney injury (AKI) is a common complication in COVID-19 patients with worst outcomes. A study showed approximately one-third of previously hospitalized

patients, who had AKI during the acute phase of COVID-19, did not fully regain renal function at discharge or post-hospitalization follow-up.³⁸

Endocrine disorders

Two studies reported newly diagnosed diabetes mellitus (DM) in patients after hospitalization.³⁹ However, more research is required to fully understand the aetiology. DM as Post-COVID-19 complication is now observed in different studies. A credible reason could be due to an imbalance of ACE-2 receptor activation in the pancreas which would lead to acute β -cells dysfunction and ultimately resulting in a hyperglycemic state.⁴⁰ Since SARS-CoV-2 uses the ACE-2 receptor as a cellular entry point, it could be possible that entry of the virus in β -cells impair pancreatic insulin secretion and thereby either aggravating DM or triggering new-onset DM.^{41,42} Some author observed that around 2.24% of symptomatic patients were newly experienced with diabetes mellitus, where 0.7% was asymptomatic.²¹

Risk of readmission:

The incidence of readmission of previously hospitalized patients with long COVID ranging from 1.4% to 15%.^{27,43} So patients who are released from hospital need supervised follow up to prevent future readmission and also to minimize the features of long COVID.

Management and control of long COVID:

Management of long COVID is variable as there is wide spectrum of clinical manifestations and in many cases multi-systems are involved. It needs a multidisciplinary team consisting of physicians, nurses, paramedics and other supporting staffs for better management of patients. Among the treatment modules one of the most important component is rehabilitation which prevents disability and enhance the quality of life. Non-hospitalized patients with long COVID require physical rehabilitation.⁴⁴ Pulmonary rehabilitations improve patients' breathing, lung capacity, muscle tone and ultimately improve the quality of life.⁴⁵ Cardiopulmonary problems also need rehabilitation to improve their daily activities.⁴⁴ Neurological rehabilitation improves mobility and coordination of the patients having neurological disorders in long COVID patients like stroke, hemiplegia etc. Occupational therapy improves motor function. Patients who have experienced severe acute COVID-19 having underlying co-morbidities, adequate management is essential to avoid clinical deterioration and further readmission. Psychological as well as mental health support is another important issue which supports the patients according to their need.¹⁹ Long-term follow up cares of the patients with long COVID are necessary to monitor their symptoms and assess the treatment outcome including the impact on quality of life. Application of digital health care service can supplement the health care service as well. Collection of patient-reported outcomes

can help to identify patients with ongoing symptoms and also patients who were not previously hospitalized.⁴⁶ To reduce the cost of care educating the patients and care givers can play a vital role. A significant number of patients with long COVID are unable to do work due to persistent symptoms. They may require financial support by the government and social services support.^{44,47} For control of long COVID, vaccination of the people is mandatory. So a combined and coordinated measures are to be adopted for effective management and control of long COVID.

Conclusion:

In some cases, long COVID symptoms have a devastating effect on the patient and family members. Recurrent or persistent physical and mental symptoms should be taken into consideration seriously. Timely effective and targeted treatment and availability, affordability and accessibility of various types of physical rehabilitation is very vital to ensure. Attention to be given also for screening and identification of risk factors to reduce the size of iceberg of disease in the community. However, it is well understood that COVID-19 and long COVID would not go away shortly and newer variants are still emerging with high transmissibility. This pandemic state might be ended up to endemic and epidemic form in various parts of the world. So vaccination and other preventive measures like hand washing, mask wearing, social distancing, cough etiquette etc. are the essentials of now normal era. Continuous collaboration should be continued nationally, internationally and globally for innovation and invention through research.

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Rhino-orbital mucormycosis in end stage renal disease patient: A case report

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Abstract

Mucormycosis, a severe and often fatal angioinvasive fungal infection, has entered public consciousness in response to an outbreak of cases in India specially during second wave of COVID-19. We present a 36 years' old lady with chronic kidney disease on maintenance hemodialysis with rhino-orbital mucormycosis without prior history of diabetes mellitus, COVID-19 pneumonia or prior use of high dose steroid. Patient presented with pain and swelling of left side of her face along with periorbital swelling and history of blackish nasal discharge. Examination of nasal cavity revealed black necrotic tissue and examination of oral cavity also revealed black discoloration of gum. All laboratory parameters were apparently normal, CT scan of nose and paranasal sinuses revealed diffuse, extensive, marked mucosal thickening with almost total soft tissue opacification of the left sided sinuses and endoscopic evaluation from maxillary antrum revealed extensive necrosis and exophytic growth inside the left maxillary antrum with purulent discharge, Histology from exophytic growth revealed necrotic tissue containing few broad non septate fungal hyphae which was morphologically suggestive of mucor species. After diagnosis liposomal amphotericin B was started and without further surgical debridement patient improved completely. Despite having high mortality, early diagnosis and initiation of treatment resulted very rewarding outcome.

Keywords: Chronic kidney disease (CKD), End stage renal disease (ESRD), Maintenance Haemodialysis, Rhino-orbital mucormycosis, Diabetes Mellitus (DM).

Introduction:

Mucormycosis is rare and emerging fungal infection which usually occurs in a patient with impaired host defense and has been increasingly recognized as a cause of high morbidity and mortality. It is the third invasive mycosis in order of importance after candidiasis and aspergillosis and represents 8.3%–13% of all fungal infections encountered in such patients.¹ Mucormycosis caused by the Zygomycetes fungi belonging to the order Mucorales. Eleven (11) genus and 27 species belonging to the order Mucorales are known to cause mucormycosis.^{2,3} *Rhizopus arrhizus* is the most common agent causing mucormycosis worldwide, followed by *Lichtheimia*, *Apophysomyces*, *Rhizomucor*, *Mucor* and *Cunninghamella* species.^{2,3}

Depending on organ involved, mucormycosis is classified into rhinocerebral, pulmonary, cutaneous, gastrointestinal or disseminated, and rhinocerebral (39%) being the most common.² Predisposing factors are poorly controlled diabetes mellitus, ketoacidosis, neutropenia, corticosteroid use or iron overload, malnutrition and skin macerations. There has been an alarming rise of mucormycosis in patient with COVID-19 during second wave of pandemic in India. Uncontrolled diabetes and use of prolonged and high doses corticosteroid are two well-known causes of mucormycosis in COVID-19.

Mortality among patients with mucormycosis is significant. which was as high as 84% in the on 1950s and then decreased to approximately 40% in the 2000s, the drop in mortality attributed to due to early diagnosis and the widespread use of amphotericin B in the 1960s.²

The early diagnosis and treatment of mucormycosis is very important in terms of prognosis. We have presented a case of a patient with ESRD on maintenance haemodialysis with rhino-orbital mucormycosis without prior history of diabetes and other immunocompromised state. Here we described a very good outcome by only medical management.

Case Presentation:

A 36 years old lady, presented to Bangladesh Medical College Hospital on 20-06-2021 with 10 days' history of pain and swelling left side of face associated numbness over her mandible. Her pain was so severe in nature which hampered her sleep and was very difficult to subside with any medication. Gradually she developed pain and swelling at left periorbital region (Figure 1). She also gave

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history of one episode of profuse thick blackish nasal discharge. Patient had 4 years' history of hypertension and chronic kidney disease (CKD); she was on maintenance haemodialysis for last 3 years. She also received intravenous iron therapy three times over the last two months. Patient denied any history of COVID-19 pneumonia or any history of high dose steroid intake. Just before endoscopic examination through nasal cavity she was tested with RT PCR for COVID-19 and it was negative. Her HRCT chest also revealed no evidence of ground glass opacity.

Examination of nasal cavity revealed black necrotic tissue. Examination of oral cavity revealed that there was swelling of gum and associated blackish discolouration of left side of gum and her hard palate was red and inflamed.

CT scan of nose and paranasal sinuses showed diffuse, extensive, marked mucosal thickening with almost total soft tissue opacification of the left sided sphenoid, frontal, maxillary antrum as well as ethmoidal sinuses that merge the nasal turbinate and partially obliterating the nasal cavity (Figure 2a,2b).

Endoscopic examination from maxillary antrum found extensive necrosis of left inferior turbinate, medial wall of maxilla. There was exophytic growth inside the left maxillary antrum with purulent discharge coming from antrum (Figure 3).

Histology from exophytic growth of left maxillary antrum revealed pieces of necrotic tissue containing few broad non septate fungal hyphae branching at right angle which morphologically suggestive of mucor species.

After histological evidence, treatment with Amphotericin B as 3mg/kg was started immediately on 17th day of symptoms and patients pain and swelling subsided gradually and patient received total 3 doses of liposomal amphotericin B after each haemodialysis session.



Figure 1: Showing swelling of left side of face

CT scan figure



Figure 2a: Shows diffuse, extensive, marked mucosal thickening with almost total soft tissue opacification of the left sided sphenoid, maxillary antrum as well as ethmoidal sinuses.



Figure 2b: Shows diffuse, extensive, marked mucosal thickening with almost total soft tissue opacification of the left frontal sinus.



Figure 3: Endoscopic feature of maxillary antrum showing necrotic tissue.

Discussion:

The incidence of mucormycosis is increasing worldwide, but the rise is very high in India and China among patients with poorly controlled diabetes mellitus.^{4,5,6} The incidence of mucormycosis is approximately 1.7 cases per 1000,000 inhabitants per year. Its prevalence in India is estimated to be 0.14 per 1,000 populations.⁴ The recent increase in the reported case of mucormycosis has been suspected to increased longevity of patients with immunodeficiency states, particularly because of frequent use of potent antineoplastic drugs in patients with malignant diseases and because of availability of chronic maintenance haemodialysis for ESRD patients^{7,8} and also increased diagnostic facilities. India also is one of the worst affected countries by the COVID-19 pandemic.

Humans acquire infection predominantly by inhalation of fungal sporangiospores that have been released in the air or from direct inoculation of organisms into disrupted skin or gastrointestinal tract mucosa. In immunocompromised host, factors predisposing for mucormycosis include uncontrolled diabetes with or without diabetic ketoacidosis, malignant hematological disease, prolonged and severe neutropenia, iron overload, major trauma, prolonged use of corticosteroids, intravenous drug abuse, neonatal prematurity and malnourishment, and chronic renal insufficiency.¹ However, mucormycosis has been described in previously healthy individuals as well.^{9,10}

COVID-19-associated rhino-orbital-cerebral mucormycosis (ROCM) has reached epidemic proportion during India's second wave of COVID-19 pandemic, with several risk factors being implicated in its pathogenesis. COVID-19 produces a hypoxic environment with high glucose levels, high levels of ferritin, and attenuated phagocytic activity of leukocytes due to immunosuppression by the

virus itself and the corticosteroids used in the management. This setting is highly conducive for the fungal spores to germinate and proliferate.¹¹ A retrospective study conducted in India among 2826 with COVID-19-associated ROCM where 87% of the patients were treated with corticosteroids, (21% for >10 days), Diabetes mellitus (DM) was present in 78% of all patients, 57% of the patients needed oxygen support for COVID-19 infection.¹²

A recent study from India reported CKD (8.9%) as emerging risk factors of mucormycosis.⁴ As patients with CKD become vulnerable to invasion by opportunistic infection a variety of renal diseases including chronic glomerulonephritis and acute and chronic renal failure are associated with systemic mucormycosis.^{13,14,15}

Impaired cell-mediated immunity and neutrophil function including chemotaxis and phagocytosis have been documented as mechanism of immunodeficient state in renal failure,¹ other mechanism metabolic acidosis and malnutrition, all play a role in the pathogenesis. In metabolic acidosis when blood pH drops, iron required for hyphal growth released from transferrin, makes more susceptible for fungal growth.¹⁶

Our patient has CKD for 4 years and on maintenance haemodialysis for 3 years and patient received 3 doses of iron therapy over last 2 months.

Based on clinical presentation and anatomic site, invasive mucormycosis is classified as one of the following 6 major clinical forms: (1) rhinocerebral, (2) pulmonary, (3) cutaneous, (4) gastrointestinal, (5) disseminated, and (6) uncommon rare forms, such as endocarditis, osteomyelitis, peritonitis, and renal infection.^{17,18} the most common form is rhinocerebral (39%).¹ This form may be divided into subtypes based on which tissues are affected: rhino-nasal, rhino-orbital or rhino-orbitocerebral. our patient presented with features of rhino-orbital mucormycosis.

Yohai et al reviewed 145 case reports of ROCM, 60% of them had diabetes,¹⁹ Our patient, despite of being non diabetic and any other risk factors, presented with features of Rhino-orbital mucormycosis.

The initial symptoms of Rhino-orbital mucormycosis are consistent with those of sinusitis and periorbital cellulitis which include eye and/or facial pain and facial numbness followed by blurry vision, multiple cranial nerve palsies, unilateral periorbital facial pain, orbital inflammation eyelid edema, blepharoptosis, proptosis, internal or external ophthalmoplegia, headache, and acute vision loss.²⁰

Nevertheless, there are some features which should be considered to be "red flags" includes a cranial nerve palsy, diplopia, sinus pain, proptosis, periorbital swelling, orbital apex syndrome, and ulcers of the palate.²¹

Our patient presented with pain and swelling along with numbness of left side of face. She also had periorbital swelling but no features of ophthalmoplegia, diplopia, proptosis or features like any other cranial nerve palsy. Computed tomography or magnetic resonance imaging are useful modalities to assess the extent of the disease. In our case paranasal sinuses were involved, while Ferry et al and Yohai et al reported sinuses involvement in 69% and 79% respectively.^{19,22}

Immunocompromised host, after infected by Mucorales, invade and kill the living tissue. The most striking pathological feature is extensive angioinvasion with thrombosis, resulting infarction and necrosis in the affected organ being a hallmark of mucormycosis.²³ In our patient extensive necrotic tissue found during endoscopic evaluation of maxillary antrum along with discharge of necrotic tissue.

Definite diagnosis of mucormycosis requires a histologic demonstration of hyphal invasion. Hyphae of Mucorales are nonseptate or pauci-septate,²⁴ have a variable width (6 to 25 μm), and show an irregular, ribbon-like appearance. The angle of branching is variable and includes wide-angle bifurcations. However, when fungal hyphae are seen in histopathologic analysis, fungal cultures are only positive in 50% of cases.²⁵ Species identification is of interest for a better epidemiological understanding of mucormycosis. In our study typical Hyphae of Mucorales was found.

In most cases, rapidly progressing infection which results in death unless underlying risk factors (i.e. metabolic acidosis) are corrected, early and aggressive treatment with antifungal agent instituted and surgical excision is done. One study showed that patients who begin treatment within 6 days have a survival rate of 76-81%, while a treatment delay of more than 12 days reduces this rate to 36-42%.^{26,27}

Factors associated with poor survival in ROCM include (i) delay in diagnosis and treatment, (ii) hemiparesis, (iii) bilateral sinus involvement, and (iv) facial necrosis.¹⁹ Yohai et al reported survival of 63% of patients with a lag time from 7 to 12 days and 44% in those with a lag time of 13 to 30 days.¹⁹

In our case The lag time between onset of symptoms suggestive to mucormycosis and the start of amphotericin B was only 17 days which also helped for rewarding outcome.

Roden et al reviewed 929 cases, among which 64% were treated with some form of antifungal chemotherapy including liposomal amphotericin B. Survival in this group was 62%. Survival was 57% for those treated with surgery alone; survival increased to 70% for those treated with a combination of surgery and antifungal chemotherapy. A total 26% received no treatment for their infection. Within this subgroup, the survival rate was 3%.²

our patient after, 3rd dose of liposomal amphotericin B,

symptoms gradually improved after 3rd dose of liposomal amphotericin B and due to financial issues and as improving symptoms she refused for further surgical debridement and after 15 days she arrived with complete resolution of her facial pain and swelling.

Conclusion:

Rhino-orbital-cerebral mucormycosis (ROCM) is a rare life-threatening disease mostly affecting immunocompromised patients. Despite advances in medical therapy and laboratory procedures, mucormycosis remains associated with high mortality and morbidity, even after diagnosis is made, management is challenging. Being a very fatal disease with high mortality, early diagnosis is very important for good outcome. High index of suspicion, recognition of host factors, and prompt assessment of clinical manifestations, identifying red flag signs remain prerequisite of management.

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Torsion of the pregnant uterus: An uncommon obstetric complication to encounter

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Abstract

Torsion of the uterus is defined as a rotation greater than 45 degrees around the longitudinal axis of the uterus. It is a very rare complication of pregnancy and a rare event in obstetric practice. We are reporting a case of 180° uterine torsion at 37⁺ weeks of gestation in a multiparous woman with previous four normal vaginal deliveries who underwent an emergency caesarean section due to non-reassuring fetal status: Biophysical Profile (BPP) score 4/10. Following delivery of the baby and placenta it was realized that incision had been made on the posterior wall of the uterus. Torsion of uterus was discovered during operation and managed. Intra-uterine contraceptive device Cu-T was introduced according to the couple's prior informed consent after correction of retroversion followed by repair of the posterior hysterotomy incision. She had a normal post-operative convalescence.

Keywords: Torsion, Pregnant uterus, Biophysical Profile, Obstetric complication.

Introduction:

Torsion of uterus is an uncommon occurrence during pregnancy. It has been observed in all trimesters. No known connection exists between torsion and maternal age or parity. It ranges from 45° to 180° but in some cases up to 720° torsion has also been reported.¹ Dextrorotation is found in two thirds of cases and levo-rotation occurs in the rest. Exact etiology of uterine torsion occurs is not clear but numerous abnormalities have been documented with uterine torsion. These include fibroid uterus, uterine malformations and abnormal fetal presentation. The recorded fetal and maternal mortality rate since 1976 are 12% and 0% respectively.² Non-specific clinical features and rarity of this condition make it more difficult to diagnose before surgery and therefore cases of lower degrees of torsion are likely to go unnoticed in vaginal delivery without having any obstetric consequence. Our case describes 180-degree levorotation at 37⁺ weeks of gestation in a multiparous woman with previous four normal vaginal deliveries who underwent an emergency caesarean section due to non-reassuring fetal status: Biophysical Profile (BPP) score 4/10.

Case Presentation:

A 34-years-old woman G: 5, P: 4, presented at 29 weeks of

pregnancy with the complaints of less fetal movement. Her prior obstetrical history included four vaginal deliveries. The outcome of the pregnancies revealed: the first pregnancy ended as term intrauterine death, 2nd issue was alive, 3rd and 4th issue were term deliveries but succumbed to early neonatal death. Upon admission, the foetal condition was comprehensively evaluated with Pregnancy profile and Doppler flow velocimetry of the Uterine and Umbilical artery. Her pregnancy profile was 28 weeks of pregnancy with mild utero-placental insufficiency and breech presentation with no evidence of IUGR or altered AFI (Amniotic Fluid Index). She was found to be hypertensive with mild proteinuria, categorizing her as pre-eclampsia without severe features. She gave history of Gestational Diabetes Mellitus in her prior pregnancies. On investigation, HbA_{1c} was found to be 6.8% and Fasting Blood Sugar was 10.4 mmol/l. Insulin was instituted with Regular acting formulation s.c.(Subcutaneous) 100 IU, 12+12+8. She was diagnosed as hypothyroid 2 years back and was on replacement Levothyroxine therapy (50 micro-gram) which was continuing in the same dose throughout her pregnancy. She was discharged with advice to carefully monitor fetal movement and to comply with the ongoing medicine. On 35th week of gestation, she again presented with the same complaint of less fetal movement. The fetal heart rate was difficult to locate/auscult on doptone and Cardiotocography tracing (CTG) could not be done because of large pendulous abdomen. Then ultrasonography was repeated. As the ultrasonography report and fetal movements were satisfactory, she was discharged after 24 hours of observation. Finally, on 37⁺³ weeks on antenatal check-up, repeat ultrasonography with BPP (Biophysical profile) score revealed a poor fetal tone and reduced breathing movement (BPP score of 4/10) with cephalic presentation. She was advised for admission for an emergency caesarean section. On C-section, pfannenstiell incision was made to enter the peritoneal cavity, Doyen's retractor was placed and left ovary was found anteriorly misplaced and visible in the uterovesical pouch. A suspicion aroused regarding the possible torsion of the

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gravid uterus. The bladder base vessels were found to be much engorged and tortuous. A transverse incision was made on the apparent anterior wall of the lower segment of uterus and a healthy 2.47 kg male baby was delivered by cephalic presentation. The head was found floating. Following delivery of the fetus and placenta, the uterus was exteriorized (Figure-1). Then it was discovered that the whole uterus had undergone 180° levo-rotation. So, uterus was untwisted. It became clear that a posterior lower transverse incision had been made. No uterine anomalies or fibroids were seen. The incision was closed in layers after placement of an Intra-uterine contraceptive Cu-T device (according to the patient's choice and consent). After closure of the posterior uterine incision, the anterior wall of the uterus and bladder surface was rechecked. Engorged vessels were found to have resolved spontaneously upon untwisting of the uterus. She had an uneventful recovery and was discharged on the 4th post-operative day. Her post-natal visit also revealed unremarkable findings.



Figure 1: The uterus is exteriorized after delivery of the fetus and the fundus is directed towards the patient's leg end to reveal the posterior surface.



Figure 2: Postpartum view

Discussion:

Rotation of the gravid uterus in third trimester is usually common. But a rotation of greater than 45 degrees around the longitudinal axis of the uterus is rarely encountered in obstetrical practice. Torsion from 60° to 720° has been also described. Few cases have been documented with a variant of clinical presentations at a range of gestational periods. A case of 180 degrees of torsion of a myomatous uterus has been reported in which the foetus was in breech presentation, that particular case was managed by a deliberate posterior hysterotomy incision; as in our case. The concluding statement was that when de-rotation of the uterus is not possible prior to delivery of the foetus, a transverse incision in the lower posterior uterine segment, if feasible, is a safe choice.³ Another case presenting at 19 weeks of gestation in a 33-year-old primi-parous lady with acute appendicitis was diagnosed upon laparotomy to incidentally reveal levorotation of the uterus by about 100 degrees. As signs of ischemia were absent, the uterus was returned into its normal position. Intraoperative and postoperative period were uncomplicated as in our case. Later the patient underwent cesarean section at 36 weeks due to PROM (Premature rupture of the membrane) and failure to progress during first stage of labour.⁴

Another case of torsion uterus at 22 weeks' gestation has been reported, the patient presented with severe abdominal pain and features of shock. An emergency laparotomy was performed for suspected abruptio placenta. Perioperatively, torsion of the uterus (about 180°) was diagnosed with features of ischemia/congestion. In this her case posterior hysterotomy was performed to deliver the foetus. The patient was kept under follow-up; she had a normal pregnancy outcome, being delivered at term by cesarean section one year later.⁵

Advanced maternal age, obesity, lax musculature and multi-parity, fetal distress/abnormal CTG have been found to be commonly associated with significant degrees of uterine torsion.⁶ Our case has similar clinical correlates: 5th gravida, 34 year of age, P:4 with multiple co-morbidities with a BMI of 34 with a hugely pendulous abdomen, having undergone LUCS for foetal compromise. She was suffering from gestational diabetic mellitus and hypothyroidism contributing to her obesity and abdominal laxity. Another risk factor is repeated vaginal deliveries with consequent cervical elongation. Cervical elongation as a consequence of previous vaginal deliveries may act as an apex of torsion of the uterus in subsequent pregnancies.⁷

Conclusion:

Though uterine torsion is nearly always an unexpected diagnosis, this complication needs to be considered while dealing with a multiparous woman with abnormal presentation of the foetus, uterine myoma and/or uterine anomalies. In our case, she had four previous vaginal deliveries which raise the possibility of ligamentous laxity and cervical elongation as a retrospective cause of 180° of

levo-rotation. The diagnosis was made during C-section by noticing the unexpected anterior position of the left ovary instead of its usual anatomic position posterior to the fallopian tube. Lower posterior transverse incision was made to deliver the foetus followed by de-rotation of the uterus. The patient had an uneventful post-operative recovery. This report describes that intra-operative alertness can achieve a successful maternal and foetal outcome.

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Diabetic ketoacidosis with lateral medullary syndrome- A case report

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Abstract

Neurological complication owing to diabetic ketoacidosis is scarce in clinical practice but not unusual. Careful evaluation and management are mandated for getting the best outcome in patient with features of the ischaemic stroke with diabetic ketoacidosis. Although the outcome depends on largely site of the lesion, extension and time of starting treatment. Recently, a case of diabetic ketoacidosis associated with the right lateral medullary syndrome was managed successfully in a tertiary care hospital. At the beginning, this 57-year-old right handed man with a history of uncontrolled diabetes mellitus presented with vertigo, difficulty swallowing and tingling, numbness on right side of face. Clinical examination revealed features suggestive of right lateral medullary syndrome and diabetic ketoacidosis supported by brain imaging and laboratory investigations. Early diagnosis and appropriate treatment of both DKA as well as medullary stroke leads to recovery of the patient with minimum disability.

Keywords: Diabetic ketoacidosis, lateral medullary syndrome

Introduction:

Diabetic ketoacidosis (DKA), one of the acute complications of diabetes mellitus (DM) is characterized by hyperglycemia, metabolic acidosis and increased circulating total body ketone concentration. If not effectively handled at an appropriate time, it can result in morbidity as well as 2-5% mortality, what rarely springs from it, instead due to its underlying precipitating cause or its complications.¹ DKA is not just an extreme of glucose metabolism disturbance but also-

1. A systemic inflammation characterized by vascular endothelial injury which leads to a state of increased C-reactive protein, cytokines, TNF (Tumor Necrosis Factor) and complement activations.
2. A procoagulant state resulting from vascular endothelial injury, abnormal levels and activities of several coagulation factors as well as increased platelet numbers and activities
3. A state of disturbance in blood volume, flow and vascular reactivity, resulting in disturbance of cerebral autoregulation, and systemic hypoperfusion

4. A state, may be complicated by cerebral oedema, disseminated intravascular coagulation.²

All these contributes to oxidative stress and leading to tissue ischemia.²

Neurological complications associated with diabetic ketoacidosis (DKA) such as cerebral edema, cerebral arterial infarction, venous sinus thrombosis and central nervous system infection accounting for 31 % DKA associated death and 21% of all diabetic death.³ Stroke is the one of the life-threatening neurological complications of DKA though it is reported that stroke and DKA can act as a risk factor for the development of each other in a patient with DM.⁴ Recently, a case of DKA with right lateral medullary syndrome was encountered in a tertiary care hospital, Bangladesh. Though ischaemic stroke is a delayed diagnosis, it was handled sensibly to get the best outcome.

Case Presentation:

A 57 years old right-handed man, by profession a businessman, hailing from Chandpur, Bangladesh, having diabetes mellitus for quite a long time, around 17 years, not controlled adequately with insulin, admitted with the complaints of sudden onset of vertigo followed by difficulty in swallowing, numbness & tingling sensation on the right side of the face for two days. The onset was sudden and gradually progressive. He also had severe vertigo, for what he could not stand. It was associated with a tendency to fall on the right side. At the same time, he felt difficulty in swallowing, both solid and liquid food. Nonetheless, there was no weakness of the limbs, headache, blurred vision, and convulsion or unconsciousness. He was a smoker and used to smoke 20 packs year. There was no family history of stroke, diabetes mellitus, hypertension. On query, he pointed out respiratory difficulties for last one day, that was gradually increasing in time. On the day of presentation, he

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was conscious and orientated to time, place and person, Glasgow coma scale 15/15. However, poor concentration was noticed during the examination. There was moderate dehydration, 130/80 mm Hg blood pressure, 124/min pulse, 28 breaths/min respiratory rate. Neurological examination revealed signs of right sided lateral medullary lesion – Horner syndrome (partial ptosis, miosis and anhidrosis), normal fundus, ipsilateral 9th, 10th cranial nerve palsy, ipsilateral impaired pain and temperature sensation of face, contralateral impaired pain and temperature sensation of body, ipsilateral cerebellar signs-ataxia, dysmetria and dysdiadochokinesia. Investigations revealed hemoglobin 12.8 gm/dl, white blood cell-15.2 x 10⁹/L, with 86% neutrophils, 11% lymphocytes, normal platelet count, random blood sugar - 18.9 mmol/L, HbA1c-9.9%, urine for ketone body - present (+++), urea 13 mmol/L, blood p^H 7.30. Serum electrolytes were normal and serum osmolality was 266mOsmol/kg. Doppler Echocardiography displayed LVEF 67% with no regional wall motion abnormality. At the early of disease, CT scan of the brain showed no significant abnormality. After admission, he was treated as diabetic ketoacidosis (DKA) and supervised according to the protocol with intravenous 0.9% normal saline, intravenous insulin and potassium supplementation. As his preliminary CT scan of the brain was normal, he underwent for MRI of the brain, which revealed brain stem infarct in the posterior aspect of the right side of the medulla oblongata. MRA of brain revealed no significant abnormality. With appropriate treatment of both Ischaemic stroke and DKA as well as proper nutritional management through nasogastric feeding the patient recovered within three weeks, Follow-up visit after 2 months showed recovery of vertigo and dysphagia with minimum disability.

Discussion:

Diabetic ketoacidosis is characterized by hyperglycaemia (>250 mg/dl), metabolic acidosis (pH<7.3) and ketonuria.⁵ Cerebrovascular disorder can be associated with diabetic ketoacidosis (DKA) in adult due to prothrombotic tendency as a result of endothelial injury, activation of platelets and relative hypofibrinolysis.⁶ Few cases were reported regarding DKA with ischaemic stroke in adult, among the neurological complications, stroke only contributes approximately 10%.⁷ A population-based, propensity score-matched, longitudinal follow-up study of long term risk of stroke in type II diabetes patients with diabetic ketoacidosis revealed that patients with DKA were 1.55 times more likely to have a stroke than those without DKA.⁸

A cerebral hypo-perfusion in untreated DKA may lead to cerebral injury, arterial ischemic stroke, cerebral venous thrombosis, and hemorrhagic stroke.⁶ In this case, though initial CT was found normal even with clinical features of lateral medullary syndrome, magnetic resonance imaging

(MRI) detected the lesion in the posterior aspect of right side of the medulla oblongata. As very few cases of stroke with diabetic ketoacidosis are observed, a careful evaluation is prerequisite to all suspected cases of acute stroke with hyperglycaemia. Both biochemical tests as well as advanced neuroimaging is needed for appropriate and timely management of such cases. Here for timely diagnosis and management the patient recovered completely with minimum disability.

Conclusion:

Control of DM is the first approach to prevent DKA leading to its complications including neurogenic events. The outcome of the DKA with ischaemic stroke may vary depending on the site of the lesion, its extension and time of onset of treatment. So readiness with clinico-diagnostic tools have a pivotal role to deal with the patients of DKA with its multimodal complications.

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College Events:

- International Mother Language Day was observed in Bangladesh Medical College and Hospital on 21st February 2021 at the local premises.
- Bangladesh Medical College and Hospital celebrated 101st birth anniversary of Father of the Nation, Bangabandhu Sheikh Mujibur Rahman on 17th March, 2021. In the 3 days' events there were- complete recitation of the Holy Quran followed by dua mahfil and special prayers, national flag hoisting and remembrance speech by Hon'ble Minister of Agriculture, the Government of Peoples' Republic of Bangladesh Dr. Muhammad Abdur Razzaque MP, Chairman, E.C, BMSRI, wreath laying in the mural of Bangabandhu, cutting of cake and delivery of free medical care for poor patients in the campus.
- National Independence Day was observed on 26th March, 2021 in Bangladesh Medical College and Hospital at the local premises.

Book published:

- A book titled as “Imaging in Otolaryngology–Head & Neck Surgery” was published by Prof. Dr. Md. Ashraful Islam, Professor and Head of the Dept. of ENT, BMC. The purpose of the book is to provide a quick understanding on basic knowledge of imaging in Otolaryngology-Head & Neck surgery for otolaryngological trainees, otolaryngologists and other related fraternities. The author also published previously ENT book in Bangla and Manual on Temporal Bone Dissection.

- A training program on “Strengthening the function of Infection Prevention & Control (IPC) and Antimicrobial Stewardship (ASP) Committees in Tertiary Care Hospitals in Bangladesh” was organized by Infection Prevention & Control Committee of Bangladesh Medical College & Hospital with collaboration of icddr,b and CDC Bangladesh from 24.4.2021 to 6.5.2021. Teachers, doctors, interns, nurses, cleaners, watchman and other supporting staffs of health care facilities of Bangladesh Medical College & Hospital participated on that event and participants were 318.

New appointment of teachers in BMC:

- Dr. Tarannum Morshed, Assistant Professor, Dept. of Radiology & Imaging
- Dr. Sonia Mahjabin, Assistant Professor, Dept. of Nephrology
- Dr. Muhtamim Chowdhury Zubin, Assistant Professor, Dept. of Neurosurgery
- Dr. Shanjida Munmun, Lecturer, Dept. of Forensic Medicine

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