Increasing Trends of In Vitro Fertilization Worldwide

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Human reproduction has been redefined since the clinical introduction of In Vitro Fertilization (IVF) in 1978. Initially the only indication of IVF was to help the infertile couple to give a child. However, IVF has now been rapidly expanding its horizon including medical & genetic conditions, and fertility preservation. Infertility remains the main target for IVF utilization. Interestingly, the number of IVF babies born each year is increasing tremendously. This has been attributed to the increased number of IVF cycles throughout the world over the past decades.

Diversified social problems & changing demographics are the main parameters for increased IVF utilization. A better access of women, as well as effective contraception has contributed to progressively delayed child bearing & overall lower fertility rates worldwide. The average age at first birth now exceeds 30 years in most of the developed countries which was well beyond the peak fertility age in mid 20s. As a result, a large number of women is delaying childbearing to a point where age related fertility decline contributes to the prevalence of infertility & subsequently increasing the demand of IVF & oocyte cryopreservation.

Definitely the utilization of IVF is closely related to affordability & accessibility. Economic development in many of the developing countries has been tremendous over the last decade. This has helped many childless couple to afford and avail the opportunity of IVF. Increasing number of trained fertility specialists, embryologists and opening up of new IVF clinics have contributed significantly in increasing the number of IVF babies. Wide availability of ovulation induction drugs, gonadotropin injections, low cost ultrasound devices as well as different low cost protocols have encouraged the patients to go for IVF at a relatively cheaper cost than before.

Possibly technological development in the form of automation & miniaturization of the IVF laboratory has increased the IVF access to many[1]. The basic steps in the IVF laboratories include:

1. Identification & separation of sperm & oocytes.
2. Fertilization
3. Embryo culture.
4. Embryo selection for transfer.
5. Cryopreservation of surplus embryos & gamates.

Technical advancements including microfluids sperm sorting devices, advanced ICSI machines with precise micromanupulators, introduction of the time lapse incubators (Embryoscopes), liberal use of preimplantation genetic diagnosis (PGD) of trophoectoderm cells of blastocyst stage embryos as well as high class IVF labs equipped with HEPA filters & CODA filters are now being used in most of the developed IVF laboratories[2,3]. Cryopreservation of sperm, oocyte & embryos has become a standard practice providing opportunities to go for repeated frozen embryo transfer (FET cycles). It not only increases the the success rate of IVF cycles but also helps the patient to go for repeated trial at a low cost. Vitrification has become the dominant method for oocyte cryopreservation and is now being practised liberally worldwide.

Oocyte & ovarian tissue cryopreservation are now used in patients at risk to develop premature ovarian insufficiency (POI) due to gonadotoxic chemotherapy for cancer. Culture systems have advanced to a point where primordial follicles residing in ovarian cortical tissue can undergo activation, growth and in vitro maturation to produce Metaphase II (MII) oocytes[4].

The increasing trends of utilization of IVF will possibly play a significant role in a substantial proportion of human population worldwide in near future. There is a speculation that nearly 10% of all children will conceive through IVF in many countries

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in coming years. Many educated and professional women are deferring pregnancies. But the economic solvency of the couple as well as technical advancements in Assisted Reproductive Technology (ART) laboratories will possibly motivate & inspire more & more couple to avail the opportunity of IVF to complete their families. Male partner problem like azoospermia or severe oligoasthenospermia, female partner problems like bilateral tubal block or severe endometriosis now have a solution through IVF. Fertility preservation techniques for couple undergoing chemotherapy or who wish to defer pregnancies, IVF offers a new hope for them. The techniques involved sperm freezing, oocyte freezing, embryo freezing and ovarian tissue freezing has taken IVF to a new height beyond only reproduction.

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ORIGINAL ARTICLE

Clinical Spectrum and co morbidities of COVID 19 cases admitted at Anwer Khan Modern Medical College Hospital (AKMMCH): A Retrospective record review

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ABSTRACT

Background: Coronavirus diseases 2019 (COVID-19) caused by Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) has induced a sense of panic around the world and has been declared Pandemic by the World Health Organization (WHO) on the 11th March 2020. Bangladesh a country of 17 million people is not an exception regarding COVID-19. It has reported around five lacs COVID-19 cases with seven hundreds of deaths. In dealing those challenges AKMMCH has started opening a COVID-19 unit since July 2020 in order to render services for the admitted cases.

Objective: The objective of this study was to explore the clinical spectrum of COVID-19 admitted cases, co morbidities, in addition to selected socio-demographic characteristics under review.

Material and Methods: This descriptive type of retrospective record review was carried out among 1690 COVID-19 confirmed cases during the period of July-December 2020. Data were generated from hospital COVID unit admission records using a checklist. Data entry and statistical analysis were performed manually and by using computer.

Results: The study revealed that majority of the cases was found within age 31-70 years with mean age 52.58 and standard deviation ± 21.7. About 76% cases were male and 24% were female. It also revealed that the clinical spectrum of COVID-19, 63% & 23% cases were moderate and severe cases respectively and only 9% were critically severe. Majority of the cases had chronic illnesses and the most common co-morbidities were Hypertension (44%), Diabetes (26%) and Cardiac diseases (10%).

Conclusion: It may be stated that male persons with more than 52 years of age were mostly affected by COVID-19 diseases. Usually moderate to critically severe patient were admitted in hospital COVID-19 unit for better treatment. Hypertension, Diabetes, Asthma and Cardiac diseases were found as the most common co-morbidities. A comprehensive case management protocol involving allied disciplines (medicine, cardiology, and endocrinology) can be implemented towards improved services and better out come in particular.

Key Words: COVID-19, Pandemic, SARS-CoV-2

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Date of submission:06.08.2021, Date of acceptance: 17.09.2021

AKMMC J 2022; 13(1) : 03-07

Introduction

Coronavirus disease 2019 (COVID-19) is an acute infection of the respiratory tract that emerged in late 2019 in China and then progressed to different countries around the world and caused considerable morbidity and mortality.[1-2] These facts ultimately led WHO to declare COVID-19 a pandemic.[3] Although the etiological agent of COVID-19 is known, proper insights about its epidemiology, virology, pathogenesis and management strategy are yet to be developed; making it one of the most notorious public health problems in the world.

COVID-19 may exhibit a variety of clinical presentations. Some COVID-19 patients remain asymptomatic, but they are capable of transmitting the virus.[4] A second group of COVID-19 patients express mild symptoms, some of which are indistinguishable from normal flu and some of them develop moderate symptoms[5-6] of considerable concerns. Finally, some patients develop severe complications like respiratory distress and pneumonia resulting in death.[7–9] The severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) is primarily considered as a respiratory virus, emerging data indicate that COVID 19 involve several body tissues and organ and the virus of COVID 19 imparts its effect on many tissues, some are distal to the respiratory system and in divisive fashion. The symptoms of COVID-19 are induced by severe acute respiratory syndrome corona virus 2 (SARS-CoV-2), the pathological processes are possibly regulated by interactions of viruses with host immunity. The mechanisms underlying pathogenesis of COVID-19 are still elusive and more times will be required to get proper insights about major cellular and molecular events relating to diverse pathogenesis of COVID-19.[10–12] The disease usually starts with mild symptoms such as cough and fever with other allied symptoms of COVID-19. Some of the patients with mild symptoms experience a sudden deterioration of their condition either in the later stage of the disease or in the process of recovery. If the patient proceeds to acute respiratory distress syndrome (ARDS) and multiple-organ failure rapidly, death becomes the usual outcome. Host immunity to the virus seems to play a cardinal role with many other auxiliary factors. As the numbers of patients with COVID 19 has passed 80 million and numbers of death are over 8,00,000 in the world, strategies are needed to block further transmission of SARS-CoV-2 infection and management of COVID 19 patients. To achieve this goal to a suitable extent, the activities of the healthcare delivery system may be centered under T3: test, tracing and treatment as proposed by WHO.[13]

Bangladesh, a country of 170 million people, detected its first case of COVID-19 on 8th March 2020 and the first fatality was recorded on 18th March 2020. The numbers of patients with morbidity and fatality due to COVID-19 have been increasing since then and about 5–15% tested for SARS-CoV-2 are positive for the virus and many of these patients need hospitalization. The management of patients with COVID-19 remains a challenge for the entire world.[14]

The COVID-19 unit in this hospital was running since July 2020 that managing cases efficiently. Therefore, this record review of admitted cases was a modest attempt to explore /investigate some selected variables like; clinical spectrum of COVID-19 admitted cases, co morbidities, and some selected socio-demographic characteristics of the cases towards better & efficient case management in order to improve service delivery in future.

This study was conducted to classify the clinical spectrum of admitted cases of COVID19, to determine co-morbidities among the admitted cases and to find out the selected socio-demographic characteristics of the cases under record review.

Methodology

This was a descriptive type of retrospective record review among admitted cases in Anwer Khan Modern Medical College Hospital COVID Unit during the period from July to December, 2020. Data were generated from hospital admission records using a checklist. Only 1690 case records were reviewed out of 2817 laboratory confirmed admitted cases. The variables considered under review were selected socio-demographic characteristics, COVID-19 clinical spectrum, and related co-morbidities during

Approval of the study protocol, procedures and ethical clearance were obtained from the Institutional Ethical Review Board of AKMMC. The generated data were cross-checked and cleaned. Descriptive statistics including percentages, means and standard deviations were calculated. Data entry and statistical analysis were performed manually and by using computer.

Operational definition of clinical spectrum (SARS-CoV-2)[15]:

Based on the New Coronavirus Pneumonia Prevention and Control Program from the National Health Commission of China, patients with SARS CoV-2 infection were divided into asymptomatic carriers, mild patients, moderate patients, severe patients and critically severe patients. According to the guideline, asymptomatic carriers were not classified as confirmed cases. In our study, asymptomatic carriers were not included. In this study the criteria for different clinical spectrum of cases with SARS-CoV-2 infections considered are as follows:

Types	Characteristics
Asymptomatic carriers[1]	Laboratory confirmed SARS-CoV-2 infection without symptoms and imaging findings.
Mild	Mild clinical symptoms without imaging findings of pneumonia
Moderate	Fever or respiratory symptoms with imaging findings of pneumonia.
Severe	Meet any of the followings: 1. Respiratory distress with respiratory frequency ≥30 breaths/min. 2. Pulse oximeter oxygen saturation (SpO_2) ≤ 93% in resting state. 3. PaO_2/ FiO_2 ≤ 300mmHg (1mmHg = 0.133kPa) 4. Showing rapid progression (>50%) on CT imaging within 24-48h).
Critical severe	Meet any of the followings: 1. Respiratory failure in need of mechanical ventilation. 2. Shock 3. With other organ dysfunction

[1]Asymtomatic carriers were not classified as confirmed cases of COVID-19.

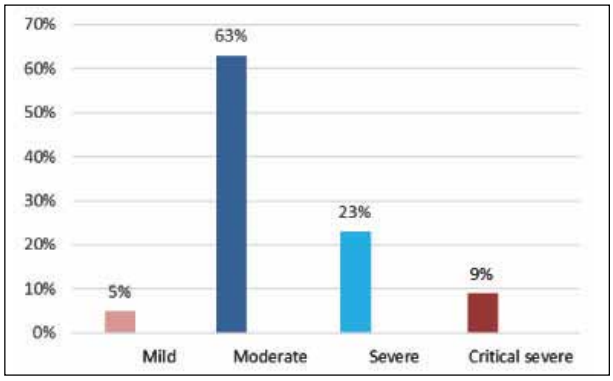
Results:

Table–I: Distribution of COVID-19 cases by socio-demographic characteristics n = 1690

Variables		Number of cases	Percentage (%)
Age	10-30	169	10
	31-50	625	37
	51-70	575	34
	71-90	321	17
Sex	Male	1284	76
	Female	406	24

About 71% cases were found within age of 31-70 years with mean age 52.85 and ± SD 21.7. Majority (76%) were male.

Figure-1: Bar diagram showing distribution of COVID-19cases by Clinical spectrum



Regarding clinical spectrum according to severity of disease, 63% were moderate, 23% were severe and 9% were critical severe.

Figure -2: Bar diagram showing distribution of cases by Comorbidities

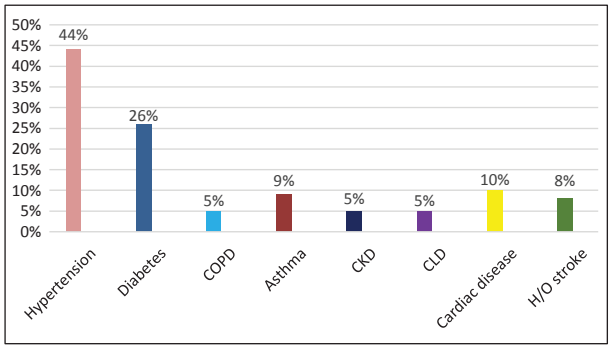


Figure shows that majority of cases had chronic medical illness and the most common comorbidities included were Hypertension (44%), Diabetes (26%) and Cardiac diseases (10%) and Asthma (9%).

A total 1690 cases were admitted cases were admitted between July to December, 2020. About 254 (15%) cases were expired and rest 1436 (85%) were discharged with treatment.

Discussion

It was a descriptive type of retrospective record review carried out on 1690 hospital admitted COVID-19 confirmed cases.

The study revealed that about 71% cases were found within the age 31-70 years with the mean age 52.85 and standard deviation ± 21.7. Recent data show that 27% of the young age group are mostly contracted with coronavirus.16 About 76% patients were male and 24% were female respectively. Some studies showed that an approximate 1:1 ratio of females to males such as 51.3% of female patients in Beiing8 and 51.3% in Jiangsu, China.

Regarding clinical spectrum of the cases during hospital admission, 63% were moderately severe, 23% were severe and 9% were critically severe. Moreover, the incidence of severe or critically severe illness was high in the elderly patient as nearly one third of elderly patients were severe or critically severe cases.

Co-morbidity or chronic illnesses were present on 139 (78.6%) patient and about 361 (21.4%) patient were free from any co-morbidity. Among the patient with co-morbid conditions, most common co-morbidities were Hypertension (44%), Diabetes (26%), Cardiac diseases (10%) and Asthma (9%) respectively. In addition, co-morbidities were mostly found in moderate and severe clinical cases that is about 52% & 17% respectively. Elderly patient with co-morbid conditions were more likely to progress to severe illness.6 Therefore, a comprehensive management protocol of chronic diseases was vital in elderly cases with COVID-19 those demands special attention on monitoring and controlling blood pressure and glucose.

This record review had an important limitation regarding record keeping by a well formulated data recording system and preservation. However, this review finding can be a basis to deal with the concern issues of limitations like; detailed medication & co-morbidities history, details of socio-demographic characteristics in addition to long term monitoring and follow up for early detection of pulmonary complications in deed.

The effective modalities of treatment of COVID-19 syndrome includes control of co-morbid conditions like Diabtetes, Hypertension etc, General management of upper respiratory tract infections, use antibiotics, antiviral (oral or parenteral) in mild to moderate cases. In severe cases, supplementation of oxygen, fluid, calorie and electrolyte balance, Injection low molecular weight heparin particularly in the elderly patient, steroid and in severe critically ill patient plasma therapy was given.[17]

Conclusion

COVID-19 mostly affects the people with age more than 52 years and males are more frequently affected than females. Usually, moderate to critically severe cases were admitted in hospital for better treatment. Comorbid conditions of the cases particularly Hypertension, Diabetes and Cardiac diseases demands comprehensive case management protocol towards better outcome and cost effective services in future in deed. A prospective follow up mechanism by e. mail/ telephone can also be considered for clinical evaluation and monitoring. Multicentric study can be conducted with COVID-19 syndrome.

The effective modality of treatment of COVID-19 syndrome include Paracetamol for fever, Supplementation of oxygen, Fluid, Calorie & electrolyte balance, Proning, Inj. Enoxaperin & Corticosteroid[17].

Acknowledgement

It is our pleasure to acknowledge Prof. Dr. Habibuzzaman Chowdhury, Vice –principal & Prof. Dr. Md. Mahfuzar Rahman, Visiting Professor, Department of Community Medicine of Anwer Khan Modern Medical College for their technical support.

Conflict of interest: There is no conflict of interest among the authors.

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ORIGINAL ARTICLE

Dyslipidaemia in Schizophrenia

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ABSTRACT

Background: Lipid neurochemistry is an important focus in schizophrenia research. Disorder of fatty acid metabolism within the brain tissue play an important role in the pathophysiology of schizophrenia.

Material & Methods: To evaluate the association of dyslipidaemia with Schizophrenia and compare the serum lipid profile with healthy individuals, a cross sectional analytical study was conducted between July 2011 and June 2012 in the Department of Biochemistry, Dhaka Medical College, following approval of a protocol. As per criteria, total 100 cases were included in this study and divided into two groups: Group-I (Diagnosed cases of schizophrenia) and Group-II (Healthy individuals). Written informed consent was taken from all cases. Serum lipid profile (Total Cholesterol, Triglycerides, HDL and LDL) was estimated from both groups by enzymatic determination.

Result: Fasting serum triglyceride ($p<0.03$), HDL cholesterol ($p<0.001$) and LDL cholesterol ($p<0.001$) between the groups are significantly related. In group-I mean serum HDL cholesterol is reduced, but LDL cholesterol and Triglyceride were elevated in comparison with group-II. No significant relationship was observed in fasting serum total cholesterol in between groups ($p>0.05$). Result indicates strong association between schizophrenia and dyslipidaemia. That association would increase the risk of developing coronary heart disease in those patients with schizophrenia compared with healthy individual.

Keywords: Dyslipidaemia, Schizophrenia, Risk factors

Introduction

Schizophrenia is a syndrome causing a major public health problem. The prevalence is similar worldwide at about 1% and the disorder is equally common in men and women. The children of one affected parent have approximately a 10% risk of developing the illness, but this rises to 50% if both parents are affected. Schizophrenia can present at any age but does so most commonly in young adults.[1]

Lipid neurochemistry is an important focus in schizophrenia research. Reports of abnormalities in brain lipids in schizophrenia appear widely in the medical and lay press. Disorder of fatty acid metabolism within the brain tissue play an important role in the pathophysiology of schizophrenia.[2] The increased rate of breakdown of phospholipids and the reduced rate of incorporation of highly unsaturated fatty acids into phospholipids are two abnormalities related to phospholipid metabolism in schizophrenia. Phospholipase A2 and fatty acid coenzyme A ligase-4 are two key enzymes involved in signal transduction processes following the activation of various receptors, including D2 and 5-HT2, which are involved in the pathophysiology and medical treatment of schizophrenia.[3]

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Date of submission: 11.08.2021, Date of acceptance: 15.09.2021

AKMMC J 2022; 13(1) : 08-13

Individuals with schizophrenia have a life expectancy which is approximately 20% shorter than that of the general population.[4] A meta-analysis concludes that 60% of the excess mortality in patients with schizophrenia is attributable to physical illness.[5] The causes of death comprise a broad range of conditions, similar to the general population, but schizophrenic patients die at a younger age. Mortality from cardiovascular disease is increased in both men and women with schizophrenia.[4]

The rates of cardiovascular events and new-onset diabetes are higher than expected in patients with schizophrenia and on antipsychotic medication.[6] The major risk factors for cardiovascular disease include obesity, dyslipidemia, hypertension and hyperglycemia.[7]

The previous studies of serum lipid profile have shown that schizophrenic patients have lower total cholesterol (TC) levels than healthy people.[8,9] However, another study conducted by Ryan et al. did not find significant difference in triglyceride (TG) levels between schizophrenic patients and normal control subjects.[9]

In patient with early onset schizophrenia have high serum TG levels in comparison with late on set disease.[10] Another study also showed that schizophrenic patients had lower serum low-density lipoprotein (LDL) cholesterol levels than normal control subjects; however, there were no differences in high-density lipoprotein (HDL) cholesterol levels in the two groups.[9]

The net impact on mortality in the schizophrenia population can be seen in the results of large epidemiologic studies, which have noted a standardized mortality ratio from cardiovascular disease two fold greater for schizophrenia patients than the general population.[11]

Therefore keeping all such important points and views in mind, the focus and aim of this study is to evaluate and assess the serum lipid profile in patient with schizophrenia. So far, no such study has been conducted on this topic in Bangladesh. As such this study will fill the gap, open new forum of discussion and will provide knowledge and information regarding the medical workup of patients with schizophrenia.

Methods:

This is a cross sectional analytical study and was conducted between July 2011 and June 2012 in the Department of Biochemistry, Dhaka Medical College. As per selection criteria, total 100 cases were included in this study and divided into two groups: Group-I (Diagnosed cases of schizophrenia) and Group-II (Healthy individuals). All the schizophrenic patients attending in Psychiatry ward of Dhaka Medical College Hospital & National Institute of Mental Health and Research, Dhaka are included in group-I and Group-II included healthy hospital stuff and attendance of the patients. Written informed consent was toke from all cases. Data was collected in a predesigned data collection sheet including particulars of the patients, history and relevant investigations. Complete physical and relevant clinical examination was performed. Diagnosis of schizophrenia was determined on the basis DSM-IV (Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition) diagnostic criteria for schizophrenia.

With all aseptic precaution, 5 ml of venous blood sample was collected from each study subject after 10-12 hours overnight fasting. Then blood sample was allowed to clot and then centrifuged at 2000 rpm for 20 minutes and the separated serum was aspirated for biochemical assay. The serum was assayed immediately or was stored at -70°C if the analysis is delayed, to avoid loss of bioactivity and contamination. A serum lipid profile (Total Cholesterol, Triglycerides, HDL & LDL) was estimated from both groups.

After meticulous checking & rechecking all data was compiled and expressed as mean ± SD (standard deviation). Data was analyzed using Statistical Package for Social Science (SPSS) version 17.0. The p value <0.05 was considered as statistically significant.

Results:

As per selection criteria, total 100 cases were included in this study and divided into two groups: Group-I (Diagnosed cases of schizophrenia) and Group-II (Healthy individuals).

Table-1: Distribution of the Study subjects by Age.

Age groups	Group- I	Group-II	Total	Percentage
20-30 years	12	7	19	19%
30-40 years	31	27	58	58%
40-50 years	7	16	23	23%
Total	**50**	**50**	**100**	**100%**

Mean age of Group – I = 31.90 ± 6.71 years and Mean age of Group – II = 28.12 ± 6.72 years. Most of the people (58%) participated in the study was from 30 to 40 years, 19% were between 20 to 30 years and 23% was above 40 years of age. Chi-square=5.113 with 2 degrees of freedom. (p = 0.078)

The proportions of observations in different columns of the contingency table do not vary from row to row. The two characteristics that define the contingency table are not significantly related. (p = 0.078)

Table-2: Distribution of the samples by sex.

Sex	Group – I	Group – II	Total	Percentage
Male	27	21	48	48%
Female	23	29	52	52%
Total	**50**	**50**	**100**	**100%**

48% of the study population was male and 52% was female. In Group – I, there was 27 (54%) male and 23 (46%) female. In Group – II, there was 21 (42%) male and 29 (58%) female.

Chi-square=1.002 with 1 degrees of freedom. (p= 0.317).

The proportions of observations in different columns of the contingency table do not vary from row to row. The two characteristics that define the contingency table are not significantly related. (p = 0.317).

Table-3: Educational status of the samples.

Educational status	Group-I	Group-II	Total	Percentage
Illiterate	1	2	3	3%
Primary	17	14	31	31%
Secondary	16	21	37	37%
Higher Secondary	9	7	16	16%
Graduate & Above	7	6	13	13%
Total	**50**	**50**	**100**	**100%**

In this study 3% patient were illiterate, 31% have primary level, 37% secondary level, 16% have higher secondary level and 13% have graduate and above level of education.

Table-4: Socioeconomic status of the samples

Socioeconomic Status*	Group – I	Group – II	Total	Percentage
Lower	29	16	45	45%
Middle	16	27	43	43%
Higher	5	7	12	12%
Total	**50**	**50**	**100**	**100%**

*Based on monthly income:

1. < 10000 taka = Lower class
2. 10000 -50000 taka = Middle class
3. >50000 taka = Higher class

45% of the subjects were from the lower, 43% were from middle and 12% were from higher socioeconomic group. Among the cases 29(58%) are from lower, 16(32%) are from middle and 5(10%) are from higher socioeconomic group.

Chi-square= 6.903 with 2 degrees of freedom. (p = 0.032)

The proportions of observations in different columns of the contingency table vary from row to row. The two characteristics that define the contingency table are significantly related. (p = 0.032).

Table-5: Serum lipid profile in Group-I and Group-II.

Lipid Profile	Group-I		Group-II	
	Mean ± SD	Range	Mean ± SD	Range
Total Cholesterol	212.14 ±51.17	138-292	222.60±45.14	157-305
Triglyceride	148.08±41.19	92-263	131.30±30.07	88-227
HDL Cholesterol	38.18±5.11	30-46	43.08±7.51	33-63
LDL Cholesterol	127.90±32.64	81-194	106.04±21.34	76-152

These are the lipid profile expressed in mg/dl found in group-I and group-II, showing as Mean ± SD and range of different parameter of lipid profile.

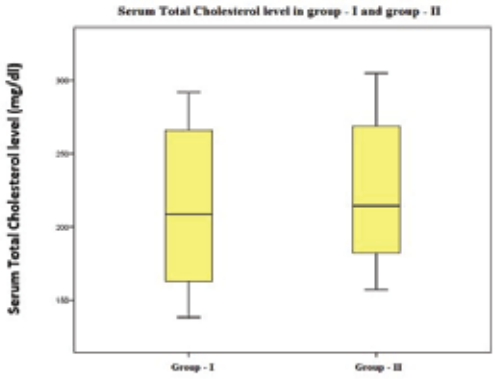

Figure-1: Serum Total Cholesterol level in group-I and group-II.

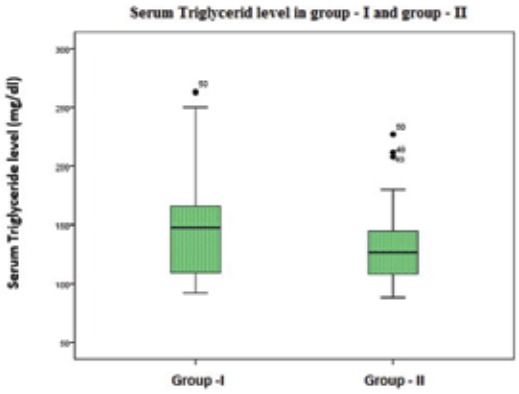

Figure 2: Serum Triglyceride level in group-I and group-II

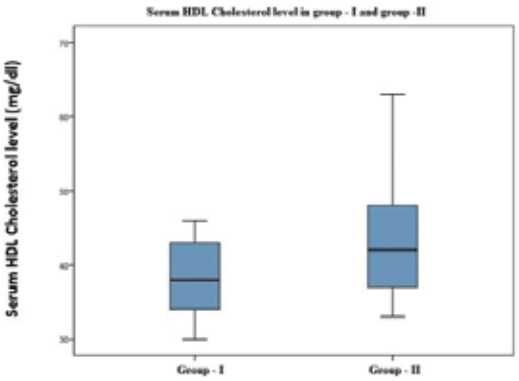

Figure 3: Serum HDL Cholesterol level in group-I and group-II

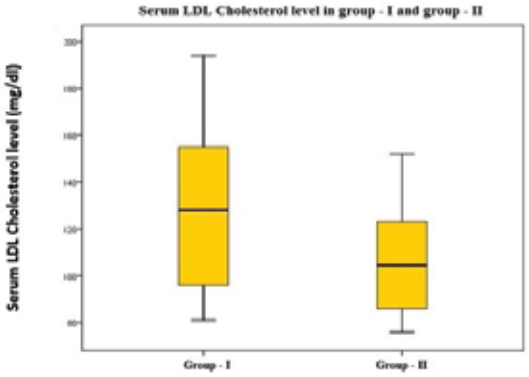

Figure 4: Serum LDL Cholesterol level in group-I and group-II

Table-6: Comparison of lipoid profile in between two groups.

Lipid Profile	Group-I (Mean ± SD)	Group-II (Mean ± SD)	Result of "t"test	*p* value
Total Cholesterol	212.14 ±51.17	222.60±45.14	-1.08	0.28
Triglyceride	148.08±41.19	131.30±30.07	2.33	0.02
HDL Cholesterol	38.18±5.11	43.08±7.51	-3.81	0.0002
LDL Cholesterol	127.90±32.64	106.04±21.34	3.96	0.0001

These results showed that, there were significant difference of serum triglyceride (t=2.33, p<0.03), HDL cholesterol (t=-3.81, p<0.001) and LDL cholesterol (t=3.96, p<0.001) in between groups but serum total cholesterol (t=-1.08, p>0.05) in between the groups was not significantly different.

In group-I, LDL cholesterol and Triglyceride were elevated and mean serum HDL cholesterol was reduced in comparison with group-II.

These findings indicate that dyslipidaemia present in group-I in comparison with group-II.

Discussion

Schizophrenia is a severe mental disorder that affects 0.5–1% of the population worldwide. It is also life-shortening illness with mortality rates twice as high as in general population. Patients with schizophrenia are at risk of developing hyperlipidaemia and its consequences due to unhealthy lifestyle and poor dietary habit. Thus hyperlipidaemia in these patients have a negative prognosis on somatic health.

Dyslipidaemia is a broad term that refers to a number of lipid disorders. Most (80%) lipid disorders are related to diet and lifestyle, although familial disorders (20%) are important as well. The basic categories of dyslipidemias include: elevated plasma triglyceride (≥150 mg/dl), and/or low high-density lipoprotein (HDL) cholesterol (< 40 mg/dl). Many studies have emphasized that, individuals most at risk to develop coronary heart disease (CHD) are those with combined dyslipidemia.12 Schizophrenic patients have abnormal fatty acid metabolism within the brain tissue, which play an important role in the pathophysiology of schizophrenia.

In the present study 52 were male and 48 were female among the total of 100 subjects. In group-I, 27 (54%) were male and 23 (46%) were female; in group-II, 21 (42%) were male and 29 (58%) were female. The mean age (Mean ± SD) of the group-I was 31.90 ± 6.71 years, ranging from 21-47 years and in group-II, it was 28.12 ± 6.72 years, ranging from 24-41 years. No statistically significant difference was found among the study subjects by age and sex. Regarding socioeconomic condition the subjects are significantly related, that indicate schizophrenia is more prevalence in lower socioeconomic group (p < 0.05).

This study found statistically significant difference of serum triglyceride in group-I and group-II. The serum mean triglyceride level in group-I was higher in comparison with group-II. This study found, serum triglyceride level in group-I was (Mean ± SD) 148.08 ± 41.1 mg/dl and group-II was (Mean ± SD) 131.3 ± 30.07 mg/dl. The result of the "t"- test shown t = 2.33, p<0.03. So the result of the "t" test showed that statistically significant difference in between groups. This result is consistent with studies other studies.[13,14] Triglycerides are the body's storage form of fat in the adipose tissue. The body uses triglycerides for energy supply when food intake is inadequate for the demand of the body. Raised triglyceride level indicates the breakdown or mobilization of stored fat.

The statistically insignificant difference of serum total cholesterol was found in between group-I and group-II, though the serum mean cholesterol level lower in group-I. The total cholesterol level in group-I was (Mean ±SD) 212.14 ± 51.17 mg/dl and in group-II was (Mean ± SD) 222.60 ± 45.14 mg/dl. The result of the "t"-test shown t=-1.08, p>0.05. So the result of the "t" test is statistically insignificant. This result is consistent with studies other studies.[8,15,16] Low cholesterol levels have been widely considered to increase the risk of depression because of neuronal dysfunction resulting from changes in the microviscosity of cell membranes or signal transduction dysfunction.[17,18]

The result has shown statistically significant difference of serum HDL cholesterol in between group-I and group-II. Here the serum HDL cholesterol level was lower in group-I in comparison with group-II. The HDL cholesterol level in group-I was (Mean ± SD) 38.18 ± 5.11 mg/dl and in group-II was (Mean ± SD) 43.08 ± 7.51 mg/dl. The result of the "t"- test shown t = -3.81, p<0.001. Therefore, the result of the "t" test is statistically significant. This result is consistent with studies other studies.[14,19] Low serum HDL cholesterol level is associated with increased risk of cardiovascular disease. It is considered to be beneficial because it removes excess cholesterol from the blood, prevent fatty build up and the formation of plaque in blood vessels.

This study has found statistically significant difference of serum LDL cholesterol between group-I and group-II. The serum LDL cholesterol was higher in group-I in comparison with group-II. The LDL cholesterol level in group-I was (Mean ± SD) 127.90 ± 32.64 mg/dl and in group-II was (Mean± SD) 106.04 ± 21.34 mg/dl. The result of the "t"- test shown t = 3.96, p<0.001. Therefore, the result of the t test is statistically significant. This result is consistent with other studies.[9,19] The high serum LDL cholesterol level is associated with increased risk of cardiovascular disease, because it can form plaque within the walls of arteries throughout the body. Such deposits can narrow arteries and limit blood flow.

The impact on mortality in the schizophrenia population can be seen in the results of large epidemiologic studies, which have noted a standardized mortality ratio from cardiovascular disease two fold greater for schizophrenia patients than the general population.[11] As the schizophrenia patient with dyslipidaemia and other metabolic syndrome are in greater risk of cardiac disease, so they should get extra care regarding cardiovascular disease.

From above discussion, it may be concluded that serum dyslipidaemia developed in group-I in comparison with group-II. This dyslipidaemia is related to increased risk of cardiovascular disease in those patients. Therefore, serum lipid profile should be investigated in all schizophrenia patients regardless of duration of illness to detect dyslipidaemia and should start lipid lowering agent.

Conclusion:

Schizophrenia a major psychiatric illness has strong association with dyslipidaemia. This association would increase the risk of developing diabetes and coronary heart disease in those patients and standardized mortality ratio from cardiovascular disease is two fold greater forschizophrenic than the general population. So, they should undergo regular screening with lipid profile for the early detection of dyslipidaemia and should be treated accordingly to prevent further complications and that would reduce their morbidity and mortality.

Conflict of interest: none.

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ORIGINAL ARTICLE

Early Metastasis in Different Types of Breast Carcinoma - A Personal Experience

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ABSTRACT

Background: Carcinoma breast is one of the leading causes of death in woman today and is the most common cancer among women. More than 2.3 million of women are diagnosed breast cancer each year world-wide. Carcinoma breast may present from an extent of non-palpable lump to a fixed mass with distal metastasis. As presentation is highly variable, management strategy varies even in same stage of disease.

Objective: To identify early metastasis of different types of breast carcinoma and its management.

Materials and methods: This is a prospective type of observational study in 100 cases done in the different surgical units of Dhaka Medical College Hospital (DMCH), Bangabandhu Sheikh Mujib Medical University (BSMMU) and Bashundhara Ad-din Medical College Hospital (BAMCH).Patients were selected clinically and by some standard investigation (FNAC and core biopsy) from January 2006 to December 2018.

Result: Patients at different age groups had suffered from different types of breast carcinoma. Early diagnosis by triple assessments and proper surgical and post-surgical managements reduced both loco- regional and distant metastasis and also reduced both morbidity as well as mortality. Results of treatment and histopathological reports were recorded. It was found that FNAC is cheap and minimally invasive diagnostic procedure with high sensitivity (100%) and specificity (95%).Core needle biopsy is more accurate tissue diagnostic in breast cancer. Down staging has profound symptomatic and cosmetic benefit. In renders inoperable tumors become operable and reduce morbidities.

Conclusion: Early diagnosis and treatment is the mainstay to achieve satisfactory outcome. Screening program especially Self-Breast Examination (SBE) is very much helpful in early diagnosis of disease in our social setting. Screening mammography has had the most substantial impact on the early diagnosis of, and subsequent decrease in mortality from breast carcinoma. Women of 20-40 years of age should have a breast examination every 2-3 yearly. Women of more than 40 years of age should have a breast examination every yearly.

Key Wards: Carcinoma breast,metastasis, FNAC, mammography, mastectomy, systemic therapy, neo adjuvant therapy.

Introduction

Breast cancer is the second leading cause of cancer deaths in women today (After lung cancer) and is the most common cancer among women, excluding non-melanoma of skin cancers. According to the World Health Organization (WHO) about 2.3 million women were diagnosed with breast cancer in 2020. The American cancer society estimates that 281,550 new cases of invasive breast cancer are expected to be diagnosed in women and about 2,650 in men in2021. About 43,600 women in the U.S. are expected to die in 2021. About 1 in 8 U.S.women (about 13%) will develop invasivebreast cancer in their lifetime. Any age may be affected but it is rare below the age of 30 years. One in 10 breast lumps referred to a breast clinic will prove to be malignant.2The above-mentioned information indicates the importance of early diagnosis and prompt adequate management in breast carcinoma. In Bangladesh breast cancer in not uncommon. Women at different age groups are presented commonly in advanced stage, with both

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Date of submission: 18.09.2021, Date of acceptance: 12.10.2021

AKMMC J 2022; 13(1) : 14-21

local and systemic manifestation, due to variety of causes like poverty, ignorance, shame, religion, poor health knowledge, lack of social awareness, reluctant to attend a male doctor, and blind dependency on indigenous and non-scientific measures compels our patients to present in a stage beyond cure.

Common formsof breast carcinoma-invasive ductal carcinoma (IDC), invasive lobular carcinoma (ILC), ductal carcinoma in situ (DCIS) and Lobular carcinoma in situ (LCIS). Less common forms of breast carcinoma: medullary carcinoma, tubular carcinoma, inflammatory carcinoma, Paget's disease of the nipple, malignant phylloides tumors, papillary carcinoma and metaplastic carcinoma.[1,2]

Metastasis of breast carcinoma commonly occurs through lymphatic and hematogenous routes. The main lymph channels pass directly to the axillary and internal mammary lymph nodes. Later spread occurs to the supraclavicular, abdominal, mediastinal, groin and opposite axillary lymph nodes.[1,2] Hematogenous metastasis is most commonly to bones (at the sites of red bone marrow i.e. vertebrae, skull, pelvis, ribs, sternum, upper end of femur, upper end of humerus), liver, lung andbrain. The ovaries and suprarenal glands are also frequent of deposits.[1-2]

To determine a cancer's histologic grade, examine the breast cancer cells and their patterns under a microscope. A sample of breast cells may be taken from a breast biopsy; lumpectomy or mastectomy.[1-2] Diagnosis depends on clinical breast examination, ultrasound,mammography,biopsy, cancer marker and certain imaging test such as chest X-ray, CT scan, MRI and bone scan. Blood tests are needed to evaluate a patient's overall health and detect whether cancer has spread to certain organs.[1-2]

Introduction of mammogram and other imaging techniques has tremendous impact in developed countries. Many patients were diagnosed carcinoma breast at a stage when they were clinically impalpable 5 to 10 years disease free survival has improved to very satisfactory level.

Treatment depends upon clinical stage of the disease at presentation and other tumor characteristics such as tumor grade. Treatment of early breast cancer will usually involve surgery with or without radiotherapy. Systemic therapy such as chemotherapy and hormone therapy are added if there are adverse prognostic factors such as lymph node invasion including metastatic relapse. Advanced or metastatic breast cancer is usually treated by systemic therapy to relieve symptoms and extend a women's life time. Fortunately, the mortality rate of breast cancer has reduced in recent years with an increased emphasis on early detection and more effective treatment.[3] It is observed that breast cancer survival rate has greatly increased over the past 20 years due to early detection and improved multidisciplinary approach in the form of neo-adjuvant therapy and per operative radiotherapy.[3] The cycle started with Beatson in 1896 and is currently resting with ATAC trial 2002.[5] Considering various case reports, Breast Conserving Surgery (BCS) is getting popular as 5 years survival rate is almost equal with mastectomy alone[1]. Additionally psychological trauma of losing breast will be reduced from BSC. Recent advances like BRCA-1, BRCA-2 and other (chromosomal) genetic factors, newer drugs and advances in targeted radiotherapy all added to hopes in successful management of breast cancer patient, only when disease is diagnosed early.

Materials and methods:

Type of study: Prospective study.

Study place: The study was conducted in the admitted patients of different surgical units ofDhaka Medical College Hospital (DMCH), Bangabandhu Sheikh Mujib Medical University (BSMMU) and Bashundhara Ad-din Medical College Hospital (BAMCH).

Study period: From January 2006 to December 2018.

Selection of cases: Patients presenting with clinical features of carcinoma breast and only who volunteered after proper explanation were selected finally for the study.

Inclusion criteria: All clinically diagnosed cases of carcinoma breast irrespective of age & sex.

Exclusion criteria:

1. Patients who had a history of mastectomy and recurrence.
2. Sarcoma and malignancies other than carcinoma.
3. Patients who willingly withdrawn themselves from the study.

Sample size: Total 100 patients.

Management:

Breast carcinoma should be managed by multidisciplinary approach of general surgeon and reconstructive surgeon.[1] Great dispute is present regarding the management of carcinoma breast since the history of treatment available. To reach a consensus is very difficult as the management depends upon the patient status, modalities available and other different factors. Two methods of treatment are accepted till date. One is systemic therapy in the form of chemotherapy and hormone therapy. Another is local therapy, which includes surgery and radiotherapy.[1]

Early breast cancers are managed by surgery and radiotherapy. On the other hand, locally advanced or metastatic cases are usually treated by systemic therapy to palliate symptoms and surgery playing a much smaller role. Treatment of breast carcinoma is highly variable in different centers. Roughly stage I and stage II diseases are managed by curative surgery. Patients in stage I and II can be managed by breast conserving surgery followed by local radiotherapy to the breast. Intra operative radiotherapy may help. Axillary sampling can be done by separate incision in the axilla. Sentinel lymph node biopsy can help in the management of axilla in negative cases. If properly evaluated it can avoid extensive axillary dissection and reduce ultimate morbidity. Stage II cases can be managed by Patey's mastectomy effectively. In stage III disease down staging may avoid radical surgery and breast conserving surgery still might be possible in those cases after appropriate neo-adjuvant therapy. In stage IV diseases there is no scope of curative surgery. Various palliative measures may help. Patients with fungating or necrosed lesions are managed by toilet mastectomy. Pre-menopausal women respond to chemotherapy and post-menopausal women respond to hormone therapy significantly.[9] Irrespective of age estrogen receptor positive cases respond well to hormone therapy.[9]

Observations & Results:

After data collection, individual cases were analyzed and the presented in this section by tables and pictures.

Table-01: Age distribution of patients

Age	Number	Percentage (%)
20-29	04	04
30-39	10	10
40-49	14	14
50-59	22	22
60-69	42	42
70-79	06	06
80-89	02	02
Total	100	100

The above table shows distribution of patients according to age group. It shows majority of patients 42 (42%) were between the ages of 60-69 years. Next highest percentage of patients 22 (22%) were in the age range of 50-59 years and a quiet number of patients 14 (14%) were below 40 years; among them maximum 10 (10%) were between 30-39 years. Mean age is 46.19 years and age range from 25-80 years. It indicates that younger age group is not escaped from developing malignancy.

Table-02: Side of breast involvement

Side	Number	Percentage (%)
Right	64	64
Left	34	34
Both	02	02
Total	100	100

The above table shows right breast was mostly involved in 64 (64%) cases. Both breasts were involved only in 02 (04%) cases. Left sided breast was involved in 34(34%) cases.

Table-03: Area of breast involved in malignancy

Quadrant	Number	Percentage
Upper outer	40	40
Upper inner	32	32
Central	08	08
Lower outer	12	12
Lower inner	04	04
Multiple	04	04
Total	100	100

This table summarizes the area of involvement. It shows that in majority of patients, 40 (40%) there was involvement of upper outer quadrant. This indicates maximum patients presented in early stage. Upper inner quadrant was involved in 32 (32%) cases. 12 (12%) patients were presented with lower outer quadrant lump. Eight (08%) patients had involvement of the central part and lower inner part was involved in four (04%) cases.

Table-04: Associated signs found during examination

Sign	Number	Total
Peau-d-orange	04	
Oedema	00	
Skin infiltration	10	
Ulcer	02	
Nipple retraction	08	44
Puckering	04	
Satellite nodules	16	

Skin infiltration was involved in 10 (10%) of which 02 (02%) had ulceration of different sizes. Nipple retraction was found in eight (08%) patients. Sixteen (16%) had satellite nodule away from the tumour site. All these figures are tabulated in table 04. Clinical features documented above were present singly or in combination. So the incidence of symptoms does not correlate with total numbers of patients.

Table-05: Lymph node status (Axillary)

Clinical Examination			Classification based on preoperative findings					
Trait	Number	(%)	N_0		N_1		N_2	
			Number	(%)	Number	(%)	Number	(%)
N_0	42	42	22	22	20	20	00	00
N_1	18	18	00	00	10	10	08	08
N_2	40	40	00	00	06	06	34	34
Total	100	100	22	22	36	36	42	42

The above table (table-05) indicates lymph node status and accuracy of clinical examination. Clinically forty-two (42%) cases were in N0. Among them per operative N0 was only 22 (22%) and rest of the twenty (20%) cases had N1. It indicates though axillary lymph nodes were assumed clinically impalpable, per operatively they were found enlarged. In the same way 18 (18%) patients had mobile axillary lymph nodes clinically i.e. N1. Among them 10(10%) were mobile and 08 cases (08%) had fixed lymph nodes (N2)per operatively. Again 40 patients (40%) showed fixed lymph nodes (N2)clinically. Six (06%) of them were mobile (N1) per operatively and 34 (34%) cases had fixed lymph nodes actually. Sensitivity of clinical examination was calculated as 42%. This table also unfolds the inaccuracy rate of clinical examination.

Table-06: Types of breast carcinoma (invasive)

Types of breast carcinoma (Invasive)	Number	Percentage (%)
Invasive ductal Ca	80	80
Invasive lobular Ca	16	16
Medullary Ca	02	02
Mucinous Ca	02	02
Others	00	00
Total	100	100

This table was shown 80 patients (80%), most of the patients suffered frominvasive ductalCa, 16 patients (16%), suffered from invasive ductal lobular Ca. Only 02patients (02%) suffered from both medullary and mucinous Ca of breast. Others type not found.

Table-07: Grading of breast carcinoma

Grade		Differentiation		Total	Percentage
Grade-I	00	Well	00	00	00
Grade-II	28	Moderate	28	28	28
Grade-III	72	Undifferentiated	72	72	72
Total				100	100

This table was showed all patients presented at Grade-II and Grade-III, on patient at Grade-I. There were 72% at grade-III and 24% at grade-II.

Table-08: Metastasis

Status	Number	Percentage (%)
M_0	86	86
M_1	14	14
Total	100	100

Above table indicates that only fourteen patients (14%) presented with metastasis at the time of diagnosis and 86 patients (86%) had no distal metastasis.

Table-09: Duration of distant metastasis in relation to histopathological types of breast Ca

Types of breast carcinoma	Duration of distant metastasis (from history)	Site of metastasis
Invasive ductal carcinoma	1 month	Bone
	1 ½ months	Liver
	6 months	Bone
	4 months	Bone
Invasive lobular carcinoma	3 months	Lung
	2 ½ months	Lung
	6 months	Liver

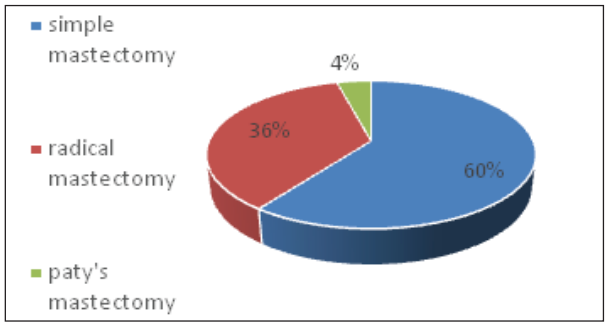
This table showed more aggressiveness of breast carcinoma to the distant metastasis like bones, lungs and liver within 6 months.

Table-10: Comparison between FNAC and histopathology report

Report	FNAC		Positive for malignancy	
	Number	(%)	Number	(%)
Benign	06	06	00	00
Malignant	94	94	100	100
Total	100	100	100	100

Out of 100 patients six (06%) patients were reported benign and 94 (94%) patients were diagnosed as malignant by FNAC. In histopathology report all patients were diagnosed as malignant and no case as benign. Three cases were therefore false negative. Specificity of FNAC was calculated to be 100% and sensitivity was 96%.

Pie chart-1: Surgical treatment



This pie chart shows the spectrum of surgical procedures 60 (60%) patients were managed by simple mastectomy with axillary dissection; 36 (36%) patients by radical mastectomy and only 04 (04%) patient by Patey's mastectomy.

Table-11: Site of distal metastasis

Site	Number	Percentage (%)
Bone	06	42.86%
Lung	04	28.58%
Liver	04	28.58%
Brain	00	00
Total	14	100

This table shows the site of distal metastasis with their frequency. In six (42.86%) i.e. most of the cases, bones were the site of involvement. In four (28.58%) cases, it involved lungs, and in only in four (28.58%) cases, liver was involved. These were documented from bone scan, Chest CT scan and Ultra sonogram of whole abdomen.

Discussion:

Breast cancer is nota disease of modern society; the ancient Egyptians recognized it as long as ago 1600 BC. However, breast cancer has become a major health problem over the last 50 years, affecting as many as one in twelve women during their lifetime.[1,2] The burden of breast cancer worldwide in both developed and developing countries are increasing and evidence suggests that unless action is taken it will continue to grow for the foreseeable future.

Breast cancer is a significant health problem in the industrialized western world, where it is the most common form of cancer among women in North America and almost all of Europe. It is estimated that

each year the disease is diagnosed in over 2.3 million women in worldwide and is the cause of death in over 400000 women.[16] The incidence and prevalence of breast cancer increases with increasing age. It is known that incidence rates for breast cancer is rare below the age of 20 years and then steadily rises so that by the age 90, 20% women are affected.1 In our study it shows that majority if patients i.e. 42 (42%) were between the age of 60-69 years. Next highest percentage of patients i.e. 22 (22%) as in the age range of 50-59 years. Median age for carcinoma of breast is 60 years.[10] In our study median age was 46.19 years. This is alarming that earlier age groups are affected in comparison to western world in our country. In the USA, 75% of new diagnosed cases are women aged 50 years or older, and the lifetime risk of a diagnosis of breast cancer is approximately 12.5%.[1,2]

Breast cancer presents with various features extending from non-palpable mass to invasive lesions. About 70% patients of breast cancer present with lump.[9] Our observation was 100%. Though there is no predilection to the right or left breast, in our study it revealed 64% in the right and 34% in left breast was involved. Less than 01% percent patient presents with bilateral breast involvement.[9] Our study shows it as 02%. This is not far from standard results. 60% of the lesions arise in the upper and outer quadrant.1In our study it was 40%. Most of the lesion occupied upper quadrants of the breast. This was due to the advanced stage of disease Males are affected 0.5% by carcinoma breast1 but in our study we got no male patients. Family history of breast cancer may be present in 5% cases. 65 None of our patients had positive family history.

Although benign breast lump are six times more common than malignant. The persistence of any mass in the breast raises the suspicion of carcinoma, which are the most malignant lesion of breast and leading cause of death from cancer in women. Therefore, no mass is trivial to be investigated. There are various diagnostic tools among them FNAC is the cheapest and easiest to perform. False positive result of FNAC is extremely low (<1%) and false negative result is albeit higher (10%).[9]

In our study, FNAC gives sensitivity to 96% and specificity of 100%. Amin el Tahir et al13 showed predictive values of 97.3% with sensitivity of 93.5% and specificity of 98.1%. our result is not far from others. So FNAC is an extremely reliable diagnostic tool. It appears that clinical examination of axilla remains incomplete so significant number of cases remains under staged pre operatively. One reason may be that patients are conservative in exposure and examination cannot be done freely specially in outpatient department and ward. All patients should be examined in a room with special arrangements for privacy and comfort. So that, patients can relax. Using examination gloves will also help examination in a clinical setup. There is 30% error rate in clinical evaluation of axillary lymph nodes and tumour size.[12] Physical examination is notoriously in accurate in lymph node assessment having false positive result in 25-31% cases and false negative result in 27-33% cases.[11] Another finding has quoted that clinical examination has 86% sensitivity and 90% specificity.[8] Sensitivity of clinical examination in our study in lymph node assessment was 55.75%. Lesions assuming malignant clinically proved benign in biopsy were 60% and 30% lesions assuming benign clinically proved malignant in biopsy.[9]

5% patients in UK present as locally advanced disease and 20% in developing countries. In 1980 American College of Surgeons showed that 85% first seen with stage-I or Stage-II disease. Positive lymph node was 40%. Average size presenting to doctor was less than 2cm.7 In our study 40% patients were in Stage-III and 14% patients were in stage-IV at presentation. About 8% patients had distal metastasis at their first presetation.[10] Lack of awareness and aversion to male surgeon was the leading cause of this advanced presentation. Neo adjuvant therapy is an important modality of management which simultaneously down stage the disease and combats systemic disease. 70% cases responded to neo adjuvant therapy by tumor shrinkage.[8] Significant clinical response was observedin about 70-90% cases after neo adjuvant therapy but complete pathological response was observer in less than 15% cases.[6] In our study about 50% patients showed significant clinical improvement after neo adjuvant therapy and more cosmetic result was achieved. Cancer WG et al demonstrated 84% patients had significant clinical response to neo adjuvant therapy.[13] This difference might be due to inadequate use of chemotherapy agents.

Lymph node response after neo adjuvant therapy was 33% in our set up. Lisa A Newman MD et al showed the response as 33%.[14] In my study both tumor and lymph node responders were 12%. Lisa A Newman M D et al showed the response was 21%.[14] Our result is consistent with others observations. Neo adjuvant therapy has no role in long term survival of patients after management rather it aids in down staging with a view to make fit for breast conserving surgery and in advanced cases to make the dissection easy and limited.[7] So that primary closure after mastectomy would be possible avoiding skin grafting. Ideally stage-III patients are eligible for neo adjuvant therapy but in our study stage-IV patients were also included only to ease closure after toilet mastectomy or to control aggressive features like bleeding from lesion. Management of axillary lymph nodes became easier after neo adjuvant therapy.Newman M D et al shows that after completion of neo adjuvant therapy 59% patients were eligible for breast conserving surgery. Before completion it was 39%.14In our set up breast conserving surgery was not performed but surgery became easier and less invasive after completion of neo adjuvant therapy.

Local recurrence and distal metastasis are major problem in the management of carcinoma of breast. Dital metastasis will be found at local relapse in about 20% cases.[10] In our study distal metastasis was observed in 23.26% patients. Whereas Cance W G et al observed 31% in their study.[13] Our study reveals that distant is more in patients with advanced stage if disease and patients who didn't use adjuvant chemotherapy adequately.

Local recurrence after complete treatment is the main barrier of management outcome. Systemic micro metastasis causes it. Recurrence in breast, chest wall, axilla clinically found 80% cases within 2 years. So, in our study local recurrence occurred in 36.84% patient. Cancer W G et al showed in their study it was 14% only.[13] In the study by Scholl by et al the rate if local recurrence by neo adjuvant chemotherapy users group was 27%.6 It was greater in our setup as majority of patients could not avail chemotherapeutic agents regularly and presented in advanced stage of disease and who didn't use adjuvant therapy regularly as per schedule.

Multidisciplinary approach with neo adjuvant therapy followed by local surgery and radiation therapy and chemotherapy has resulted on rates of local control that exceeds 80% and 5 years survival rates exceeding 50% are not ususal.[15] Although clinically worth while the benefit of adjuvant systemic therapy for operable carcinoma breast are modest and in range of 20-30% reduction in the odds of recurrence or death.[7]

Management strategy depends upon stage of disease and modalities available. 75% treated with mastectomy and 25% with breast conserving surgery.[9] Despite an increasing trend toward breast conserving surgery up to 50% of women still require mastectomy.[1] Breast conserving surgery was not possible at all in our setup as about 93% patients were in stage-III and stage-IV. Other patients were not convinced for breast conserving surgery. So, it's outcome could not be assessed in my study. So, surgical management was Paty's mastectomy in 04 % of the cases.

Carcinoma of breast is more aggressive in younger than elderly. Local recurrence happened in the form of nodule, ulceration, local pain and swelling. Systemic spread may involve bones, lungs, brain, liver, spinal cord etc. Metastasis to bone observed in 49-60% cases, 15-20% cases in lungs, 10-15% to pleura, 7-15% to soft tissue and 5-15% to liver.[12] In our limited observation we found 42.86% bony metastasis, 28.58% pulmonary metastasis and 28.58% in hepatic metastasis. The low percentage of this prospective study is not very far from others. The low accuracy rate can be improved by increasing practice and number of cases.

Conclusion:

Breast cancer is an extremely emotional topic by virtue of its anatomical location and the importance of female breast in today's society. Breast is a common site of cancer in women and carcinoma breast is the leading cause of death among middle aged women in western countries.[1] Although it is common in western and affluent populations but it is not uncommon in our country. Early age groups are not escaped rather suffer more aggressive form of disease. Twelve years study was performed to observe early metastasis of different types of breast carcinoma. The aims of this study to identify different histopathological types of breast carcinoma in our country were more common, early diagnosis of metastasis and different modalities of treatment according to patient's condition. 100 diagnosed case of carcinoma breast were studied.

Preventive measures are not satisfactory except prophylactic mastectomy in high-risk cases, which is not feasible in all cases. Features are variable before the disease is advanced. So, it should not be missed clinically. Early staging showed better outcome after proper management. If adjuvant therapy is used adequately, local recurrence and distal metastasis is delayed. Chemotherapeutic agents should be cheap and easily available. Counselling should be performed to use full course of adjuvant therapy. Self-breast examination is a very effective tool of breast cancer screening. Vulnerable group should be encouraged to perform it as per schedule. Though it may raise anxious group, it will obviously reduce the burden of advanced disease. Man is not immortal. If horrors of carcinoma breast are hastened by modifiable factors that will be distressing and not acceptable. So, proper steps should be taken to raise awareness among the vulnerable group. Breast cancer awareness program should be taken at various levels to ensure early diagnosis and treatment with an aim to prevent metastasis and achieve good prognosis.

Conflict of interest: none.

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ORIGINAL ARTICLE

Periodontal Diseases and Associated Factors among Type 1 Diabetes Mellitus Patients from Selected Clinics in Dhaka, Bangladesh

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ABSTRACT

Introduction: Periodontal disease and diabetes mellitus are the two most prevalent chronic diseases and global burdens in the world. Periodontal disease comprises gingivitis and periodontitis. An increasing trend of periodontal disease is reported among diabetic patients in Bangladesh. Limited studies have investigated the association between type 1 diabetes mellitus and periodontal disease in Bangladesh. This study, therefore, aims to investigate the association of demographic characteristics, lifestyle factors, diabetic-related factors, and oral hygiene practice with periodontal disease among type 1 diabetes mellitus in Dhaka, Bangladesh.

Methods: Survey and clinical examination of this cross-sectional study were conducted in three well-known clinics in Dhaka. A total of 182 participants were clinically examined based on inclusion and exclusion criteria.

Results: A higher prevalence of periodontitis was found compared to gingivitis among type 1 diabetes mellitus. About 30.2% of the respondents had moderate periodontitis, followed by mild periodontitis 28.6%. The majority of respondents (30.8%) had mild gingivitis and only 14.8% had moderate gingivitis. Furthermore, proportions of periodontitis and gingivitis were positively associated with age [(aOR1.12 (95%cis=1.07, 1.17)] and lower education. A significant association of periodontitis was found with the duration of diabetes [(aOR) 0.95 (95%cis=0.90, 0.99)] and frequency of toothbrushes (42-fold greater).

Conclusions: The findings of this study imply that dentists should emphasize on patients for well metabolic control to prevent the progression of periodontal disease.

Keywords: Periodontal disease; Diabetes mellitus; Associated factors.

Introduction

Periodontal disease is one of the most prevalent chronic non-communicable oral inflammatory diseases in the world which leads to the gradual destruction of connective tissue that supports and helps to hold the tooth in its position. If it is left in untreatable condition, the periodontal disease eventually primes to tooth loss in the severe stage. Important for a person's periodontal health is to equilibrium between bacterial plaque challenges and body immune-inflammatory response. Under the specific influence of multiple behavioural, environmental, and genetic factors of host responses can determine the general susceptibility of the host or the local susceptibility of progression of periodontal disease. In this regard, it is common in severe forms of periodontal disease in individuals with compromised immune systems, e.g., those with Diabetes Mellitus, HIV infection, leukaemia, and Down syndrome.[1]

Periodontal disease principally consists of gingivitis and periodontitis. Pocket measurement and Papillary bleeding index are conducted in the clinical site to determine the stages of gingivitis and periodontitis. Gingivitis is characterized by redness of the gum margins, swelling, and bleeding on brushing.[1] Periodontitis is a chronic low-grade infection, results in tissue destruction and alveolar bone resorption.[2]

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Date of submission: 16.06.2021, Date of acceptance: 13.10.2021

Periodontitis is considered as one of the main causes of tooth loss generally noticed among adult people compare to young people.

Several studies have shown that periodontal disease is highly prevalent in both developing and developed countries.[2-4] The World Health Organization (WHO) reported that the worldwide prevalence of deep periodontal pockets (≥6 mm) among adults was 10% to 15%.[5] Consequently, along with the growing ageing population, the burden of periodontitis will increase globally for tooth retention loss.[6-8] Periodontal disease progression is much faster among the poor population because of social differences.[6,9]

Periodontal diseases are more common among men than women in the world. According to Ahmed et al.[10] from Update Dental College Hospital in Bangladesh stated that about 56 % of males and 43.6 % of females are suffering from gingivitis, 48.6% males and 51.4% females were diagnosed as suffering from chronic periodontitis. Periodontal disease diagnosed was increased by age as follows; 0 to 20 years (11% gingivitis, 1.5%(periodontitis), in 21 to 40 years (64% gingivitis, 30.7% gingivitis), in (41-60) years of age (25% gingivitis, 67.8% periodontitis).[10]

On the Other hand, Diabetes Mellitus is the most common metabolic syndrome in the human body. In this metabolic disorder, the body unable to produce adequate or act in response to insulin from the pancreas causes a rise of sugar level in the bloodstream abnormally. Diabetes Mellitus is classified into three major categories: Type 1(Insulin Dependent Diabetes Mellitus), Type 2 (Non-Insulin Dependent Diabetes Mellitus), and Gestational Diabetes Mellitus (GDM). Type 1 diabetes mellitus is caused by a deficiency of insulin secretion due to autoimmune destruction of insulin-secreting beta cells of the islets of Langerhans in the pancreas,11 as well as association with periodontal diseases has been recognized.[12] Children and people who have aged below thirty years commonly suffering from type 1 diabetes mellitus.[13] Older people are also affected with Insulin Dependent Diabetes Mellitus.[14] Therefore, Insulin Replacement Therapy is the main treatment for type 1 diabetes mellitus.

Diabetes mellitus is considered a major public health problem and 245 million people have this disorder. In 2030, the projected number of diabetes mellitus patients is 366 million people in the world.[15] The increasing prevalence and number of diabetes mellitus patients in Bangladesh have been reported that from 1995 to 2000 was 4% and 5% in 2001 to 2005, whereas 9% was accounted for in 2006 to 2010.[12] The International Diabetes Federation (IDF) projected the expected prevalence of diabetes mellitus in Bangladesh will be 13% by 2030.[15]

Previous studies have shown that diabetes mellitus is a risk factor for the progression of periodontal disease.[16] It is well established in theoretical and practical that diabetes mellitus and periodontal disease are linked.[17] Diabetes mellitus enhances inflammation and apoptosis specifically that mainly affects on periodontal tissues of patients with a poor periodontal health condition. Moreover, the increasing severity of periodontal disease among diabetes mellitus patients may reflect an alteration in the pathogenic process of bacteria and enhancing the breakdown of periodontal tissues, results in more frequent and severe periodontal tissue destruction.[18]

In Bangladesh, incidence rate of type 1 diabetes mellitus for <25 years was 1.24/100 000 per years (males 0.92, females 1.71) and 0.96/100 000 for <15years (males 0.63, females 1.55).19 Type 1 diabetes mellitus patients were facing many social challenges in Bangladesh. Economically, the majority of type 1 diabetic patients are in poor status in Bangladesh. Hence, low afford or little access for buying/getting insulin from public hospitals or other private institutes. In addition, lack of knowledge about good oral hygiene maintenance with poor metabolic control can assist in the development of periodontal disease among type 1 diabetes mellitus patients. Many studies have been conducted in Bangladesh to determine the relationship between type 2 diabetes mellitus and periodontal disease. According to the researcher's knowledge, there is limited, or no study had been conducted in Bangladesh to determine the association with the associated factors between type1 diabetes mellitus and periodontal disease.

More importantly, the public healthcare system in Bangladesh offers limited access to dental services, especially for individuals with diabetes mellitus who are not given treatment priority. Therefore, the findings of this study about the association between type 1 diabetic-related factors and periodontal diseases can assist to improve oral health behaviours and prevent the progression of periodontal disease.

Method and Materials

This study was a cross-sectional study that was conducted in three well-known clinics at Bhasantek Bazar in Dhaka Cantonment, Dhaka, Bangladesh. All the consecutive type 1 diabetes mellitus patients were attending these three clinics which had been selected for this study based on exclusion and inclusion criteria. 306 sample size was estimated for the finite population by using Open Epi info v.3, and the confidence level was taken as 95%. Descriptive analyses were calculated as the proportion (%), mean, SD and/or median and IQR for qualitative and quantitative variables respectively. In multivariate analysis, calculated adjusted odds ratio and 95% CI by binary logistic regression. A P-value of< 0.05 was considered statistically significant.

Inclusion criteria

- Patients with type 1 diabetes mellitus diagnosed for at least last year or more and registered by the medical practitioner.
- Willingness to participate in the study during the study period.
- 18 years and above as well as giving written consent to participate in the study.

Exclusion criteria

- Pregnancy and lactation.
- Inflammatory disease, chronic liver disease, or patients receiving any treatment that could modify the study parameters, such as, antibiotics, immune suppressants, antiepileptic treatment.

Study instruments

The study instrument consisted of two parts: A survey questionnaire and clinical parameters

Survey questionnaire

The survey questionnaire included of total 42 items including socio-demographic factors and diabetic history was adapted from Izuora et al.[20]. Management of diabetic self-compliance items was adapted from Kim et al.[21]. Oral health-related items were adapted from Quisumbing et al.[22] Kojima et al. [23] and Izuora et al.[20].

Clinical parameters

A careful oral examination was carried out with the help of a dental mirror, tweezer, surgical gauge, and caries explorer. For determined periodontal health, papillary bleeding index and Community Periodontal Index (CPI) were measured by using WHO-probe (Hu-Freidy, Chicago, IL, USA). Community periodontal index; considers the worst condition encountered in six sites evaluated and used the following four codes:0 = healthy; 1 = absence of pockets, bacterial plaque retention factors, or bleeding following probing; 2 = depth as much as 3 mm and presence of bacterial plaque retention factors; 3 = pockets with probing depth between 4 and 5 mm; 4 = probing depth $\geq$6 mm. Papillary bleeding index; the interdental sites were probed in order from the right maxillary second molar to the left maxillary second molar [17, 16, 11, 26 & 27] and from the left mandibular second molar to the right mandibular second molar [37, 36, 31, 46 & 47]. The stratification of the papillary bleeding index was following; Score 0-no bleeding; Score 1- A single discreet bleeding point; Score 2- Several isolated bleeding points or a single line of blood appears; Score 3- The interdental triangle fills with blood shortly after probing; Score 4- Profuse bleeding occurs after probing; blood flows immediately into the marginal sulcus.

Diabetic-related factors such as duration and compliance to self-management of diabetes were obtained by questionnaire. Each question of self-compliance management was rated on a 4-point Likert scale (1 = always and 5 = never). Respondents who were unable to answer these diabetic-related questions, the researcher helped them to get the answer to these questions. Detailed information of HbA1c was collected as the percentage of haemoglobin (glycosylated) from the medical records of participants in the particular clinic.

Result

Table 1. Factors associated with gingivitis by multivariate analysis

Factors	Adjusted odds ratio (95%CI)	P-value
Sociodemographic and lifestyle factors		
Age (18 years and above)	1.12 (1.07,1.17)	0.000
Gender		
Female	1	0.211
Male	2.204 (0.64 ,7.59)	
Income		
31000 to 40000 Taka	1	0.214
21000 to 30000 Taka	0.315 (0.07, 1.35)	0.119
Less than 20000 Taka	0.412 (0.13, 1.36)	0.146
Education		
Masters or Higher	1	0.079
Bachelor	4.118 (0.75, 22.57)	0.103
Secondary (lower & higher)	4.248 (1.2, 15.07)	0.025
Tobacco smoking		
No	1	0.804
Yes	0.871 (0.29, 2.61)	
Tobacco chewing		
No	1	0.182
Yes	0.418 (0.12, 1.51)	
Diabetes-related factors		
Duration of diabetes	0.969 (0.93, 1.01)	0.136
Hba1c	1.046 (0.88, 1.25)	0.620
Self-compliance score	1.232 (1.03, 1.47)	0.020
Oral hygiene practice		
Frequency of toothbrush		
Twice	1	0.001
Once	22.611 (3.39,151.03)	
Clean by doctor		
Yes	1	0.002
No	92.222 (5.41, 1573.13)	
Use of Mouthwash		
Yes	1	0.897
No	0.924 (0.28, 3.04)	

Results in table 1 had shown that respondents' age was positively associated with the proportion of gingivitis adjusted odds ratio [(aOR) 1.12 (95%CIs=1.07, 1.17)]. The odds of being having gingivitis were 4-fold higher among the patients who were less educated compared to patients who had higher education. Patients who had higher compliance scores had higher odds of having gingivitis [(aOR)1.232 (95%CI=1.03,1.47)]. The odds of having gingivitis were 23-fold higher among the patients who brushed their teeth once a day compared to patients who brushed their teeth two times a day. Patients who did not undergo dental cleaning had higher odds of having gingivitis 92-fold (CI=5.41, 1573.13) than patients who were cleaned by the doctor regularly.

Table 2. Factors associated with periodontitis by multivariate analysis

Factors	Adjusted odds Ratio (95%CI)	P-value
Sociodemographic and lifestyle factors		
Age	1.080 (1.02, 1.15)	0.010
Gender		
Female	1	0.178
Male	3.103 (0.6, 16.09)	
Income		
31000 to 40000 Taka	1	0.061
21000 to 30000 Taka	0.434 (0.09, 2.02)	0.287
Less than 20000 Taka	2.754 (0.57, 13.4)	0.209
Education		
Masters or Higher	1	0.120
Bachelor	8.577 (0.74, 99.66)	0.086
Secondary (lower & higher)	14.451 (1.14, 183.36)	0.039
Tobacco smoking		
No	1	
Yes	2.066 (0.41, 10.54)	0.383
Tobacco chewing		
No	1	0.003
Yes	41.46 (6.66, 258.25)	
Diabetic history		
Duration of diabetes	0.948 (0.90, 0.1)	0.044
Hba1c	1.318 (0.99, 1.76)	0.060
Self-compliance management	1.217 (0.92, 1.60)	0.162
Oral hygiene practice		
Frequency of toothbrush		
Twice	1	0.000
Once	42.713 (5.71, 319.81)	
Clean by doctor		
Yes	1	0.094
No	9.635 (0. 68, 136.52)	

Table 2 had shown that respondents' age was positively associated with the proportion of periodontitis adjusted odds ratio [(aOR)1.08 (95%CIs=1.02, 1.15)]. The odds of being having periodontitis were 14-fold higher among the patients who had less educated compared to patients who were higher education. Patients whose tobacco chewed had higher odds of having periodontitis [(aOR) 41.48 (95%CIs=6.66, 258.25)] than patients who did not take tobacco. Patients who had a longer duration of diabetes had higher odds of having periodontitis [(aOR) 0.95 (95%CIs=0.90, 0.99)]. The odds of being having periodontitis were 42-fold greater among the patients who brushed their teeth once a day compared to patients who habited to brush their teeth two times a day.

Discussion:

Age was significantly associated with both periodontitis and gingivitis suggesting greater susceptibility for periodontal disease. It has been confirmed from previous studies that increasing age was one of the predictors of the severity of periodontitis and gingivitis. In concurrence with a previous study both periodontitis and gingivitis were increasing in prevalence with age.[24]

The finding of this study was also following another study Rajhans et al.[25] which reported that the age of the diabetic patients has increased, the prevalence and severity of periodontal disease have increased. A study conducted by Ababneh[26] in Jordan found that 40 to 49 years old patients had only 21.2%, whereas, 53% reported periodontitis over 50 years. Our study has confirmed that type 1 diabetic patients' lower education level was significantly associated with periodontal disease. Patients who were less educated had a higher risk of periodontitis and gingivitis than those with higher educated. The present finding was similar to previous studies, a low level of education had an excess risk of gingivitis and periodontitis when compared with a higher level of education.[27,28] Low education level is likely to lead to low prestige and low pay occupations, and residing in a deprived area, therefore, resulting in the lack of adequate oral health knowledge, insufficient preventive behaviours, and low use of oral health services. The impact of environmental conditions on periodontal health has been widely described such that individuals living in a neighbourhood in the most socially marginalized areas has experienced twice the risk of periodontitis relative to those in the most affluent.[28,29] Smokeless tobacco was significantly associated with periodontitis. The finding of this study was consistent with the previous finding by Kamath et al.[30] that the habit of tobacco chewing among Asians was associated with high scores and risk of periodontal disease. A similar association was also found in developed countries such as the US, Sweden.[31,32] In the current study, smokeless tobacco users were at greater risk of developing periodontal pockets than non-users of smokeless tobacco. We categorized smokeless tobacco users into four groups and concluded that previous to current users play a corresponding role in the disappearance of the periodontal disease once the smokeless tobacco use was stopped. These findings are similar to previous studies that report a significant association between periodontal disease and smokeless tobacco use.[33,34] In contrast, some studies failed to show the association between smokeless tobacco and periodontitis.[35,36] For instance, a study conducted in Saudi Arabia revealed that SLT was not a significant risk indicator in the development of periodontal disease.[37] Such contradictory observations may be attributed to several factors, such as differences in the trends of oral SLT practices and the type of SLT products and duration of diabetes used by the sample of patient's studies. On the other hand, periodontitis and gingivitis were not significant with other lifestyle factors such as smoking and betel nut in this study. When compared with the previous study, smokers were three times more likely to have a severe form of periodontal disease than non-smokers.[38] Some studies had shown that betel nut biting increases the prevalence of gingival inflammation.[39-42] Duration of diabetes and periodontitis are positively associated. This finding is similar to the previous finding, the correlation between the duration of diabetes and the severity of periodontitis has been reported.[43] The longer duration of the disease can affect the probing pocket depth, bleeding on probing, and clinical attachment level.[42] Cerda et al.[44] stated that the duration of diabetes was a significant factor in the severity of the periodontal disease. Firatli et al.[45]

observed a clear relationship between the years of evolution of diabetes mellitus and clinical attachment loss of periodontal tissue. In contrast, patients with a shorter duration of diabetes had less periodontal disease, while those with a longer duration had a higher prevalence and severity of periodontal disease.[46] Moreover, type 1 diabetes is onset at a younger age; hence the longer duration of diabetes implies that the patient is older. There was no significant association between periodontal disease and glycemic control (Hba1c) in our study. The finding of the current study was similar to a previous study.[47] In contrast, most previous studies agreed that HbA1c was associated with the severity of periodontitis.[48-49] Although Jindal et al.[50] showed that patients with poor glycemic control had more severe gingival inflammation as evident by the higher scores of Gingival Index (GI). Lalla et al.[51] found greater gingival inflammation in a large cohort of type 1 diabetics patients as compared to non-diabetic controllers. Gingivitis was significantly associated with the management of diabetic self-compliance in the present study. Knecht et al.[52] reported that participants who have good compliance to self-management of diabetes tend to have higher dental self-efficacy which is related to good periodontal health. In our study reported that patients who manage their diabetes such as regular hospital visits as per doctor's recommendation, maintain optimal blood sugar levels, taking insulin regularly had a risk of developing gingivitis.

A recent study reported a significant association between periodontal diseases and the frequency of tooth brushing. Consistent with other studies, a majority of respondents reported brushing their teeth once daily.[53-56] However, a previous study of the Chinese population showed that, in general, a high percentage of the 2105 respondents reported inadequate oral hygiene practices such as 66.7% as well as 1402 of respondents brushed their teeth once a day or less reported that 15.1% had periodontitis.[57] The current study showed, that for patients who did not undergo dental clinic, gingivitis was higher than patients who cleaned their teeth by the dentist. Good oral hygiene and regular dental cleaning are recommended to prevent and manage oral health problems.[58] A survey conducted in Malaysia revealed that half (51%) of the people with diabetes believed teeth problems were not serious and this belief was one of the main reasons behind refusing a dental referral.[59] Unpleasant dental visits, doctor anxiety, the scare of sound and vibration from handpieces during a surgical procedure, extraction, and difficulty in scheduling appointments were found to discourage people from seeking dental care.[60,61] The results of this study have several implications for oral health professionals, policymakers, and diabetes care providers. Oral health professionals, diabetes care providers should play a more active role in promoting oral health programs among their patients. They should educate patients about their increased risk for oral health complications and advise them to have regular dental check-ups. Oral health professionals should inform diabetes mellitus patients about good oral health behaviours and emphasize the importance of good diabetes control in minimizing oral health risks. Diabetes care providers may also need to improve their knowledge in this area to incorporate oral health promotion into their practice. Besides, policymakers need to develop and implement standardized oral health care guidelines and oral health promotional resources for diabetes care settings as well as create appropriate referral pathways to increase uptake of dental services for this at-risk population. The findings of our study should be interpreted and considering the limitation described that the sample was studied from a clinic that would not be representative of type1 diabetic patients in the community, therefore, results might not apply to all type 1 diabetic patients. This study did not use a standard questionnaire to obtain information about lifestyle factors such as (smoking, tobacco, betel nut). Hence, these could be misclassification bias, leading to a lack of association of smoking with periodontitis. In our study examined the smaller sample than the minimum sample size we calculated for this study due to higher non-response. Hence, the present study did not have sufficient power for the association as indicated by wide CI for the adjusted odds ratio

Conclusion

The present study aims at signifying the relationship between type 1 diabetes mellitus and periodontal disease and to analyze how diabetes metabolic control, diabetes complications, and diabetes duration would be related to periodontal parameters. A link between diabetes and periodontitis in adults has been confirmed. Periodontitis has been considered the sixth complication of diabetes mellitus. It is well established that diabetes increases the prevalence, severity, and progression of periodontal disease. In our study periodontal disease was associated with age, education, duration of diabetes, frequency of toothbrush. These findings imply that dentists should emphasize well diabetes control for prevention and slowing the progression of periodontal disease. Furthermore, a physician treating diabetic patients should advise on the importance of oral health care and refer the opportunity to dentists for preventive oral health.

Ethical Approval:

The standard protocols, data collection tools and procedures for demographic and clinical examinations were reviewed by the Joint committee (JC) of research and ethics of the International Medical University (IMU). During the survey, interviewers informed that participation in the survey was voluntary. They were also assured about the confidentiality of the information to be provided and could opt not to answer any of the questions during the interview. Informed consent was obtained from each survey participant. The data collection was conducted from September 2017 to November 2017. The intended period for data collection was two weeks. Difficulty in getting a response from the participants conferring to exclusion or inclusion criteria, the data collection time was longer than planned.

Conflict of Interest: No conflict of interest.

Acknowledgements:

First of all, thank Almighty Allah SWT for sparing my life, sustaining me and enabling me to realize my MSc in Public Health dream and ongoing support during the process.

During this journey, I have been blessed with honourable supervisors' Associate Professor Dr. Chandrashekhar Thummala Hally Sreerama Reddy, Dr. Pulikkotil Shaju Jacob whose guidance, insights, feedback and gentleness have been very precious and invaluable in putting the pieces of my dissertation together. Their constructive criticisms and diligence in reading and commenting on the numerous drafts have improved the clarity and quality of the dissertation.

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ORIGINAL ARTICLE

Relationship of the antibody level between male and female SARS-CoV-2 infected patients in Dhaka city

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ABSTRACT

Background: The Coronavirus disease 2019 (COVID-19) caused by SARS-CoV-2 (Severe Acute Respiratory Syndrome Coronavirus 2) created an emergency situation experienced by the world.

Objective: To compare the antibody status after SARS-CoV-2 infection in male and female patients.

Methods: This cross-sectional study was conducted in the Department of Biochemistry and Molecular Biology, BIRDEM General Hospital, from July, 2020 to June, 2021. A total of 154 patients (age 18 – 70 years) infected by SARS-CoV-2 were enrolled for this study. Among them, 78 were male and 76 were female. The study subjects were non-vaccinated. For this study, serum IgG level was measured by the automated analyser. For statistical analysis, the Mann Whitney U test was done.

Results: the age distribution of male and female patients. The age group of 50-59 years comprised most of the male patients in comparison to the female study group. Patients with hypertension, diabetes mellitus were more prone to SARS-CoV-2 infection in both groups. Here male patients had more positive history of comorbidities than female patients. Mann-Whitney U test was done to analyze the data which revealed presence of significantly higher IgG in female patients. Here, $p < 0.02$ which was fairly statistically significant.

Conclusion: The antibody level of female patients was significantly higher than that of male patients after SARS-CoV-2 infection.

Key words: SARS-CoV-2, Antibody, Comparison

Introduction

The Coronavirus disease 2019 (COVID-19) is a pandemic situation experienced by the world. It is caused by Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) which is an enveloped single stranded RNA virus of Coronaviridae family and Orthocoronaviridae sub family.[1] It has four structural proteins: spike (S), envelope (E), membrane (M) and nucleocapsid (N) proteins. The spike protein facilitates viral entry into host cells by binding to a host receptor through the RBD in the S1 subunit. Afterwards, viral and host membranes fuse through the S2 subunit.[2] Body immune system responses to a pathogen with both innate and adaptive immunity. One aspect of the adaptive immunity is humoral response that features the production of antibodies recognizing specific antigens.[3] S1 and S2 subunits of the viral spike protein act as antigen. After immunological reaction anti-S1, anti-S2 IgG are produced within the body.[4] People in Central Europe were much more affected than people in East Asia in

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Date of submission: 13.10.2021, Date of acceptance: 09.12.2021

AKMMC J 2022; 13(1) : 32-36

comparison to the numbers of cases and deaths due to SARS-CoV-2.5 The idea about serological findings after 30 days in non-severe disease remain limited and conflicting. Several follow-up studies of hospitalized patients in Sweden had reported about the development of IgG in majority of patients.[6] An experimental study in Italy noticed non-hospitalized subjects developed lower antibody titer compared to patients in Intensive Care Units (ICU). The highest levels of IgG antibody was associated with severe disease. The persistence period of IgG antibodies in circulation was not well defined but within a month after being COVID-19 negative, antibody titer was half then before.[7] A case control study investigated that the concentration of IgG was lowest in early disease stages but raised at 15 days of post illness. Moreover the IgG concentration reached peak during 21-25 days after illness as 16.5 μg/mL, and stayed at a comparatively high concentration 11.4 μg/mL until 31-41 days in hospital admitted patients.[8] A single center study in Iran reported majority of cases were in the age group of 50 to 60 years of old. The male-to-female ratio was 1.93:1. Male gender, older age, history of comorbidities like hypertension, diabetes mellitus were the important risk factors. Male patients within age group 50 to 60 year and with comorbidities are in vulnerable condition in case of SARS-CoV-2 infection.[9] SARS-CoV-2 infected male patients aged 50 years or more were associated with 15.4-folds significantly increased risk of mortality.[10] A Retrospective observational study in India reported that patients with T2DMwere more likely to be negative for anti-SARS-CoV-2 antibodies than those without DM. Impaired sero conversion could theoretically increase the risk of re infections in patients with DM.[11] The noticed expanded seriousness and mortality of COVID-19 pneumonia with hyperglycaemia was not the aftereffect of a hindered humoral reaction against SARS-CoV-2. Produced IgG was related with a noteworthy defensive impact with diabetes.[12] Increasing age, male gender, hypertension, diabetes, and cardiovascular diseases adversely affect viral clearance.13 Another study reported that COVID-19 positive hypertensive patients deteriorated more rapidly than non-hypertensive group.[14] However there are limited idea about the duration of persistence of antibody after infection, IgG level in patients with co-morbidities like hypertension, diabetes etc and is there any re-infection within the interval. So far literature review reveals scarce of relevant co-relational study in Bangladesh. We need to know about the quantitative antibody status of male and female patients after SARS-CoV-2 infection .

The study of antibody level after SARS-CoV-2 infection may give idea about any difference of immunological protection between male and female patients.

Methods

This cross-sectional study was conducted at Department of Biochemistry and Molecular Biology, BIRDEM General Hospital, Shahbag, Dhaka from July, 2020 to June, 2021. A total of 154 study subjects, who had confirmed COVID-19 and recovered (78 male patients were taken as group I and another 76 female patients were taken as group II). In this study, 84 patients were treated in hospital and 70 patients were treated at home. Inclusion criteria for both group I and II were RT-PCR positive for SARS-CoV-2 within last 3 to 6 months, age 18 to 70 years. Vaccinated patients against SARS-CoV-2 virus, pregnancy, lactation, chronic liver and renal disease, history of heart failure, any malignancy, any immunosuppressive disorders and radiation therapy were the exclusion criteria for both groups. Institutional Review Board (IRB) of BIRDEM Academy, Shahbag, Dhaka approved the research protocol. A structured questionnaire and data sheet were prepared for this research including all the variables of interest. Blood sample was collected by maintaining all aseptic precautions. The serum was separated from individual sample and stored at -56ºC. Estimation of serum IgG was performed at the Department of Biochemistry and Molecular Biology, BSMMU and assessed by Chemiluminescent Microparticle Immunoassay (CMIA) using Abbott Allinity i Autoanalyzer (USA).

Collected data were entered, checked and edited (to remove the outliers) with the help of the Statistical

Package for Social Sciences (SPSS) software, version 26 and analysed. The data were expressed as frequency and percentage, mean ± SD for normally distributed data or median (inter-quartile range) for data not normally distributed. The Mann-Whitney U test was done to compare IgG status between male and female SARS-CoV-2 infected patients. p value ≤ 0.05 was considered statistically significant.

Results

A total of 154 study subjects, who were infected 3 to 6 months ago, were enrolled for this study. The mean ± SD age of male patients was 45.98±13.05 and female patients was 46.36±13.22 years. It was observed that males needed hospital support in comparison to the females (Table-I).

Table I: Grouping of the SARS-CoV-2 infected study subjects on the basis of Home and hospital treatment (n=154)

	Male	**Female**
Hospital treated	64(82.10%)	20(26.30%)
Home treated	14(17.90%)	56(73.70%)
Total	78	76

Table-II showed age, gender and habitats of the study subjects. Many of the SARS-CoV-2 infected patients were distributed in the age group 50-59. In this study, except 18 study subjects, all were from suburban area.

Table-II: Demographic characteristics of the study population (n=154)

Variables	**No. of patients (n)**	**Percentage (%)**
Age group (years)		
20-29	26	16.90
30-39	25	16.20
40-49	29	18.80
50-59	50	32.50
60-70	24	15.60
Gender		
Male	78	50.60
Female	76	49.40
Habitat		
Urban	136	87.7
Suburban	18	11.7

Results are expressed as frequency (n) and percentage (%)

Table-III showed the age distribution of male and female patients. The age group of 50-59 years comprised most of the male patients in comparison to the female study group.

Table-III: Age distribution of the study population (n=154)

Age group (years)	Male (n=78)	Female (n=76)
20-29	12 (15.40%)	16 (21.10%)
30-39	13 (16.70%)	19 (25.00%)
40-49	17 (21.80%)	15 (19.70%)
50-59	28 (35.90%)*	09 (11.80%)
60-70	08 (10.30%)	17 (22.80%)
Total	78 (100.0%)	76 (100.0%)

Table-IV showed distribution of comorbidity among the study population. Patients with hypertension, diabetes mellitus were more prone to SARS-CoV-2 infection in both groups. Here male patients had more positive history of comorbidities than female patients.

Table-IV: Distribution of the respondents by comorbidity (n=154)

Specific of comorbidity of the patients	**Male (n=78)**	**Female (n=76)**
HTN, DM	18(23.10%)	15(19.70%)
DM	31(39.7%)	14(18.40%)
HTN	18(23.1%)	21(27.60%)
None	11(14.10%)	26(34.20%)
Total	78(100.0%)	76(100.0%)

Mann-Whitney U test was done to analyze the data which revealed presence of significantly higher IgG in female patients. Here, p <0.02 which was fairly statistically significant (Table-V).

Table V: Distribution of the respondents according to IgG (AU/ml) status (n=154)

	Male (n=78)	Female (n=76)	p-value
Median with range of IgG (AU/ml)	720.90 (314.0-2620.50)	1858.00 (484.20-5046.60)	**<0.02***

Data were expressed as median (Inter Quartile Range, IQR).

Discussion

This cross-sectional study reported that male patients needed hospital support after SARS-CoV-2 infection. There was difference between the number of home and hospital treated patients regarding gender. Gomez et al. observed that rate of hospital admission after SARS-CoV-2 infectio was higher in male patients.[15] This finding was also in aggrement with a recent study in Italy done by Vahidy et al. The study reported 17% males needed hospital support and as compared to females were 14.6%.[16]

In this current study, the participants within age group 50-59 years were more infected. This result was consistent with Nikpouraghdam et al. a recent study in Iran. The study reported that the majority COVID-19 infected patients were in the age group of 50 to 60 years old.[17]

It was observed that most of the male patients had previous history of comorbidity. On the other hand female patients showed less history of comorbidity. A retrospective cohort study in Peru mentioned that 65.31% were male in the study. More frequency of diabetes mellitus (21.95%) and hypertension (21.68%) were recorded among the patients.[18] A systemic review and meta analysis reported that male patients, age more then 50 years, or had history of comorbidities were significantly associated with increased risk of mortality after SARS-CoV-2 infection.[19]

This cross-sectional study identified a discrepancy in SARS-CoV-2 IgG status in male and female patients. The amount of antibody produced by female patients reported fairly significant difference than that of male patients. In a study Zeng et al. observed that female patients had high concentration of serum SARS-CoV-2 IgG antibody in comparison to male patients. It was also reported that in early phase of infection the generation of IgG was stronger in female patients.[20]

Conclusion

The antibody level of female patients was significantly higher than that of male patients after SARS-CoV-2 infection.

Conflicts of interest: None.

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ORIGINAL ARTICLE

Lung Cancer Scenario of NICRH: A Cross Sectional View

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ABSTRACT

Introduction: Lung cancer alone and in coalition can deactivate life-wheel. But a very little attention had been paid to address the riddle. This effort is to candle the light on the lung cancer disease.

Objective: This study was conducted to delineate the sociodemographic factors and clinical conditions of lung cancer patients. To determine some associations of SD variables and clinical conditions.

Methods & Materials: This cross sectional study was conducted in NICRH from July 2017 to June 2018 among 167 LC patients. Data were collected by interview using semi-structured questionnaire and reviewing of check list. Data were checked thoroughly, edited, coded, categorized, cleaned and analyzed using software (SPSS version 23).

Results: This study revealed that mean age of the patients was 56.16 ± SD 9.88. Among which 80.2% were male and 19.8% female. Majority had primary 51.1% education, Secondary were 26.4%. Regarding occupation, farmer were 37.1%, businessmen were 20.4% and homemaker were 15.6. The mean income was Tk. 17163 ± SD Tk. 10587. Most had nuclear family 89.2%. Rural inhabitants were 61.1%. In describing cancer type, 81.5% had NSCC and 16.8% had SCC. Regarding clinical condition, 70% had poor, 7.8% had average and 22.2% had severe clinical condition. The residential areas are significantly ($\chi 2$, $p < .05$) associated with clinical conditions. Staging of lung cancer is significantly ($\chi 2$, $p < .05$) associated with clinical conditions.

Conclusion: Socioeconomic factors like age, family income, education, residential condition may affect clinical condition.

Keywords: Lung cancer, Socioeconomic factors.

Introduction

Cancer is a leading cause of death worldwide, accounting for 8.8 million deaths globally in 2015, nearly 1 in 6 deaths is due to cancer. The most common cause of cancer death is lung cancer (1.69 million deaths). Approximately 70% of deaths from cancer occur in low- and middle-income countries[1].

Fatigue is one of the most prevalent symptoms experienced by cancer patients. CRF has been accepted as a diagnosis in the International Classification of Diseases, Tenth Revision and clinical practice guidelines for its management have been formulated by the Institutes of Health and the National Comprehensive Cancer Network[2].

There are 13 to 15 lakh cancer patients in Bangladesh, with about 2 lakh patients newly diagnosed with cancer each year[3]. Policy interventions that target additional resources to improving access to the poor would be more affordable in the short term than solving the overall problem of high out-of-pocket spending[4].

According to the latest WHO data published in April Lung Cancers Deaths in Bangladesh reached 18,124 or 1.89% of total deaths. The age adjusted death rate is 20.29 per 100,000 of population ranks Bangladesh # 59 in the world[5].

According National Institute of Cancer Research & Hospital, Dhaka, Bangladesh, the occurrence of lung

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Date of submission: 12.11.2021, Date of acceptance: 15.12.2021

cancer is 16.7% of all cancers and the most common cancer (25%) among the male cancer patients,[6]. 1:1 male female ratio. Approximately 95 percent of all lung cancers are classified as either small cell lung cancer (SCLC) or non-small cell lung cancer (NSCLC). This distinction is essential for staging, treatment, and prognosis.

Cancer and its treatment results in the loss of resources and opportunities for patients, families, employers, and society overall. Death from cancer worldwide are projected to continue a rise to over 13.1 million by 20306.

About 70% of all cancer death occurs in low and middle income countries. 1.37 million Death annually, which comprises 17% of total new cancer cases and 23% of total cancer death. Bangladesh harbours 162 million people, is the 9th most populous country in the world[7].

There are 13 to 15 lakh cancer patients in Bangladesh, with about 2 lakh patients newly diagnosed with cancer each year[8].

OBJECTIVES

General Objective:

To find out the sociodemographic and clinical conditions of lung cancer patients

Specific Objectives:

a. To see the age, gender, education, occupation, residential distribution of LC patients.

b. To find out the lung involved, type and staging of LC.

METHODS AND MATERIALS

This cross sectional study was conducted to find out the sociodemographic and clinical conditions of lung cancer patients, study was conducted in National Institute of Cancer Research and Hospital to see the age, gender, education, occupation, residential distribution of LC patients and to find out the lung involved, type and staging of LC. The duration of study period was from July 2017 to June 2018. Initially research protocol was developed and approved by local ethical committee of NIPSOM, Mohakhali, Dhaka, pre testing in DMCH and data were collected from 1st February to 30 April in NICRH.

RESULTS

Table-1: Sociodemographic characteristics of patients (n=167)

Among the respondents, 71.9% had age more than 50 yrs. Male predominant,80.2%. 51.1% were primary educated, 37.1% were in the occupation of farming, 53.1% had income ≤ 10,000, 89% had nuclear family and 38.9% were living in semi-pucca house.

Variables		Frequency f (%)
Age(Years)	≤ 50	**47(28.1)**
	51 – 65	**93(55.7)**
	≥ 66	**27(16.2)**
	Mean ± SD Age	**56.16 ± 09.88**
Sex	Male	**134(80.2)**
	Female	**33(19.8)**
Education	Primary	**87(51.1)**
	Up to SSC	**44(26.4)**
	HSC and above	**14(8.4)**
	Illiterate	**22(13.2)**
Occupation	Service Holder	**15(9.0)**
	Retired	**11(6.6)**
	Business	**34(20.4)**
	Farming	**62(37.1)**
	Homemaker	**26(15.6)**
	Others	**19(11.4)**
Monthly	≤ 10,000	**90(53.9)**
Family	10,001 - 30,000	**67(40.1)**
Income	30,00 and above	**10(406)**
(Taka)	Mean ± SD Income	
Residential	Urban	**25(15**.0)
Area	Rural	**102(61.1)**
	Sub-Urban	**40(24.0)**
Family Type	Nuclear	**149(89.2)**
	Joint	**27(10.8)**
Type of House	Pucca	**32(19.2)**
	Semi-pucca	**65(38.9)**
	Kancha	**70(41.9)**

Fig-1: Distribution of respondents by Lung Involved (n=167)

Among the respondents 102(61.1%) had been suffering from right lung and rest 65(38.9%) had been suffering from left lung.

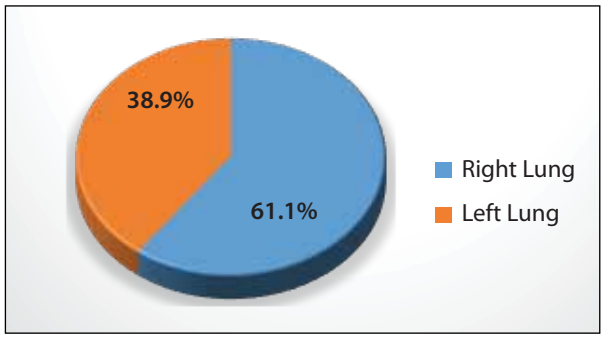

Fig- 2: Distribution of respondents by type of Lung Cancer (n= 167)

Among the respondents 136(81.5%) had been suffering from NSCS, 28(16.8%) had been suffering from SCC and 3(1.8%) from carcinoid tumour.

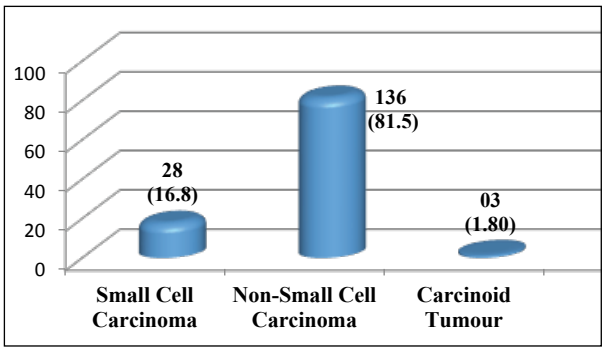

Fig-3: Distribution of respondents by Staging of LC (n=167)

Among the respondents 01(.06%) had been diagnosed in Stage-1, 11(6.6%) had been diagnosed in Stage-2, 94(55.7%) had been diagnosed in Stage-3and rest

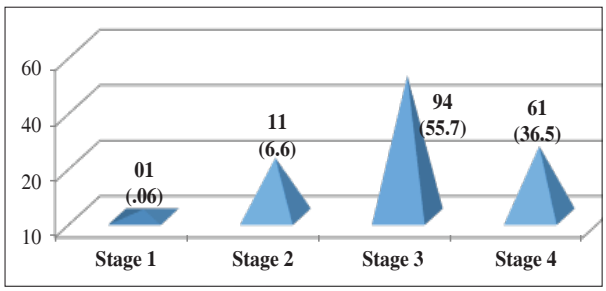

Fig- 4: Distribution of respondents by clinical conditions (n=167)

Among the respondents 13(7.8%) had been diagnosed as average clinical condition, 117(70%) had been diagnosed in poor clinical condition, 37(22.2%) had been diagnosed in severe clinical condition.

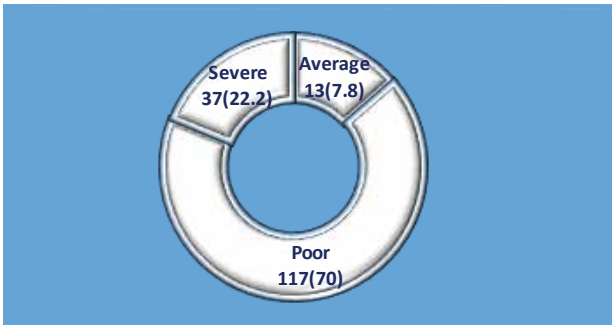

Table- 2: Association of staging by clinical conditions (n=167)

Staging of Lung Cancer	Clinical condition of lung cancer			Total
	Average	Poor	Severe	
Up to stage 2	2(16.66)	8(66.68)	2(16.66)	12(100)
Stage 3	7(7.44)	72(76.59)	15(15.95)	94(100)
Stage 4	4(6.55)	37(60.65)	20(32.78)	61(100)
Total	13(7.78)	117(70.05)	37(22.15)	167(100)

In consideration of staging up to Stage-2, 02(16.66) had average clinical condition, 08(68.66) had poor and 02(16.66) had severe condition. In Stage-3, 07(7.44) had average clinical condition, 72(76.59) had poor and 15(15.95) had severe clinical condition. Among Stage-4, 04(6.55) had average, 37(60.65) had poor and 20(32.78) had severe clinical condition. Chi-squire test done but difference was not statistically significant. ($\chi 2$= 8.66; df = 4; p < .06).

Table- 3: Association of residential area by clinical conditions (n=167)

Residential Area	Clinical condition of lung cancer			Total
	Average	Poor	Severe	
Urban	1(4)	22(88)	2(8)	25(100)
Rural	11(10.8)	69(67.6)	22(21.6)	102(100)
Sub-Urban	1(2.5)	26(65.0)	13(32.5)	40(100)
Total	13(7.78)	117(70.05)	37(22.15)	167(100)

In consideration of residential area, from Urban, 1(04) had average clinical condition, 22(88) had poor and 02(08) had severe condition. Among Rural, 11(10.8) had average, 69(67.6) had poor and 22(21.6) had severe clinical condition. Among Sub-Urban, 01(2.5) had average, 26(65.0) had poor and 13(32.5) had severe clinical condition. Chi-squire test done but difference was not statistically significant. ($\chi 2$= 8.66; df = 4; p < .06).

DISCUSSION

This cross-sectional study was carried out on lung cancer patients at NICRH Dhaka to find out the sociodemographic characteristics and clinical conditions.

The mean age of the lung cancer patients were 56.16 ± SD 9.88, in this study aged people are the victim of lung cancer. Another study where mean age was 62 years, age range was 25 years to 95 years, which is near to similar to this study findings9 .A further study conducted in Bangladesh, showed the mean age of the patients was 56.99 years, which is almost similar to present study[10].

In present study most of the lung cancer patients i.e. 80.2% were male and 19.8% were female. The findings were similar with the study conducted by NICR&H where feature like 80% were male and 20% were female. It coincides with a study where 81% were male and 19% were female[9]. Due to more exposure in risk factors of lung cancer, male patients were more in number. But now a days increase more number of female patients due to more exposure in risk factors of lung cancer. American Cancer Society said that culminated by mid-century lung cancer becoming the leading cause of cancer death among men.

In this study, majority of lung cancer patients i.e. 51.1% had primary education while 26.4% passed SSC, 8.4% had HSC and above and illiterate were 13.2%. In respect of occupation, the present study findings are, 37.1% having farming occupation while 20.1% are businessman, retired persons are 6.6%, homemaker are 15.6% and 9% are service holder. This study findings are almost similar with the study conducted in Bangladesh where, farmers were 25.0%, businessmen were 34.30%, service holder were 10.60 %[9].

It is seen that average monthly income of the lung cancer patients TK. 17163 ± SD 10587 with minimum, TK. 5000 and maximum TK. 100000. Among the respondents 53.9% had income TK. 5000-10000, 40.1% had income Tk. 10001-30000, and 6% had income Tk. (30001-50000.

The present study reveals that, 89.2% belongs to nuclear family and 10.8% belongs to joint family.

In the present study, 61% are rural inhabitants, 24% are sub-urban and 15% are urban. According to demographic profile, the percentage of urban population is 35.811.

Among the respondents 38.9% are living in semi pucca houses, 19.2% are living in pucca houses and 41.9% are living in kancha houses. The first epidemiologic study of lung cancer in Nepal on "socio-economic status and lung cancer in Nepal reveals 84.1% rural and 15.9% urban population , this is due to different sociodemographic and cultural trends of the neighboring state[12].

Among the respondents 38.9% are living in semi pucca houses, 19.2% are living in pucca houses and 41.9% are living in kancha houses.

Among the respondents 16.8% had small cell carcinoma, 81.5% had non-small cell carcinoma and 1.8% had carcinoid tumour.

Among the respondents 6.6% are diagnosed as stage Ⅱ cases, 55.7% are diagnosed as stage cases and 36.5% are diagnosed as stage cases.

Among the respondents 7.8% had average lineal condition, 70% were in poor clinical condition and 22.2% were in severe clinical condition.

Conclusion

End of life is the most deleterious outcome of lung cancer but a little attention had been paid to alleviate the problem in context of the burden. This cross sectional study was conducted to find out the sociodemographic characteristics and clinical outcome of lung cancer patients. In this study, aged people were the main victim, male predominance, majority had primary education, and farming was the top of the list as occupation. More than four-fifth of

the patients had nuclear family, near to half of the patients were rural inhabitants. More than four-fifth cases were non-small cell carcinoma. Most of the cases were diagnosed in late stage with poor and severe clinical condition, this study revealed, clinical condition had significant relationship with residential area and staging. Effective interventions to improve QOL and was to relieve some of the inimical burden that a diagnosis of a cancer can bring.

Recommendations

- On the basis of study findings, following recommendations are put forward for consideration of policy makers, health administrators, public health specialists and future researchers:
- To attend socio-demographic status: To improve socio-demographic status, Political, bureaucratic, professionals have to work hand in hand and the nation is well advance in this way.
- To improve clinical condition: Best possible treatment has to be ensured within the capacity of both end because clinical improvement improves fatigue level and QOL bilaterally.
- To attend personality traits: Lung cancer is an old age, gender inclined disease so, character traits and risk factors of lung cancer has to be attended in well advance to reduce the disease incidence.
- To halt the disease process: Early diagnosis of lung cancer should be ensured by screening program at primary level of health system focusing on cause and remedy so, early diagnosis and prompt treatment and proper rehabilitation is required.
- To develop community awareness: About possible risk factors responsible for development and consequence of lung cancer. Awareness programme should be initiated using mass media and social network to create nationwide cognizance amid the population.
- To enhance professional excellency: Comprehensive wide scale research work should be carried out to focus on pragmatic scenario of lung cancer and to undertake doable and effectual ascendency accordingly.

Conflict of interest: None.

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ORIGINAL ARTICLE

Residual astigmatism following cataract surgery

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ABSTRACT

Objective: To determine the amount of residual astigmatism following cataract surgery.

Materials and methods: A hospital based observational study was conducted in a tertiary eye hospital, Bangladesh during the period of July, 2013 to June, 2014. Patients was selected for the study who diagnosed as ARC with variable amount of astigmatism (1.5 to 3.5D), and excluded any other ocular pathology or history of previous ocular surgery. Phacoemulsification with PC Toric IOL implantation in all cases. Auto refracto-keratometer was done Preoperative and postoperatively for assessing the astigmatism. Main outcome measured were included preoperative uncorrected visual acuity, postoperative uncorrected visual acuity on 1stPOD, after 1 week and 1month, Preoperative keratometry, Preoperative astigmatism, Postoperative uncorrected keratometry on 1stPOD, after 1 week and 1month, Postoperative uncorrected astigmatism on 1stPOD, after 1 week and 1month

Results: 30 eyes of 28 patients were assessed in this study. Due to clear corneal incision during phacoemulsification, the steep meridian became flat significantly from pre-operative keratometry 44.329±1.473D (mean±SD) to 30thpost operative keratometry 43.971±1.431D (mean±SD) having $p<0.001$. On the other-hand the flat meridian became steeper from pre-operative keratometry 42.225±1.471D (mean±SD) to 30thpost operative keratometry 42.421±1.501D (mean±SD) having $p<0.001$. Preoperative mean astigmatism [Mean±SD] was 2.104±0.319D, after the first postoperative day, mean astigmatism decreased to 0.954±0.494D with $p<0.01$, and finally after 1 Month there was significant reduction of pre-operative astigmatism to 0.583±0.413D with $p<0.0001$. So, the mean pre-operative astigmatism decreased significantly in the successive post-operative days.

Conclusion: Toric Intraocular lens implantation in phacoemulsification surgery can correct pre-existing corneal astigmatism significantly after one month of surgery.

Keywords: Toric, Intraocular lens, Phacoimulsification, Cornea, Astigmatism

Abbreviation: D-Diopter, PC-Posterior chamber, IOL- Intraocular lens, ARC-Age related cataract, SD-Standard deviation, K1-Flat keratometry, K2-Steep keratometry

Introduction

Cataract is the leading cause of visual impairment and blindness in the world. There is various method of cataract extraction such as, Intracapsular cataract extraction (ICCE), extracapsular cataract extraction (ECCE), small incision cataract surgery (SICS) and Phacoemulsification cataract surgery.[1]

Currently, phacoemulsification with posterior chamber intraocular lens (PCIOL) implantation is the most popular treatment modality for cataract. In recent years, phacoemulsification through a clear corneal tunnel tunnel incision has become increasingly popular due to ease of the technique, reduced length

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Date of submission: 15.11.2021 Date of acceptance: 20.12.2021

AKMMC J 2022; 13(1) : 42-46

of the surgery, little or no trauma to the conjunctiva, quick rehabilitation of vision and the reduced risk of wound leakage and endophthalmitis.[2]

Astigmatism occurs when the patient's cornea is steeper in the vertical axis (with-the-rule astigmatism) or in the horizontal axis (against-the-rule astigmatism)[3] when the principal meridians are perpendicular. A third type of regular astigmatism, oblique astigmatism, occurs when the steepest curve lies between 120–150° and 30–60°. When replacing a lens during cataract surgery, astigmatism can either be corrected by prescription glasses, contact lenses, corneal relaxing incisions, astigmatic keratotomies, limbal relaxing incisions, excimer laser ablation, and toric IOL implantation. Toric intraocular lens provide a safe and predictable alternative to reduce or eliminate refractive astigmatism with a cylindrical correction, offering patients with preexisting corneal astigmatism optimal distance visual acuity without the use of spectacles or contact lenses.[4]

A toric lens is one whose two surfaces differ, with one being spherical in shape and the other being toroidal. Such a shape may allow for the correction of both with-the-rule (WTR) and ATR astigmatism depending on placement of the toroidal axis.[5]

Visual rehabilitation after phacoemulsification largely depends on corneal astigmatism.[6] So it should be addressed properly. Around 50% of people have astigmatism of about 0.25D to 0.50D. Astigmatism can be classified into regular and irregular astigmatism.[7] Besides pre-existing astigmatism, surgically induced astigmatism is also a subject of concern which largely depends on the type, site and length of incision and suture closure technique.[8]

The smaller the incision, the less is the corneal astigmatism. With the shortening of corneal tunnel incisions from 5.5 mm to 3.2 mm, 2.8 mm, 2.4 mm and 2.2 mm visual function postoperatively has steadily increased.[9] Smaller incisions provide less astigmatism as well as better self-sealing of wound.[10]

Most of patients come to our hospital with the complaints of dimness of vision. Among them cataract with astigmatism is one of the important causes for this. For the correction of astigmatism during cataract surgery toric IOL implantation offers a predictable, stable and safer way to reduce pre-existing astigmatism. Here we adopted phacoemulsification and PCIOL implantation with the 2.4 mm on axis clear corneal incision. Multiple factors may influence the final outcome and the degree of residual astigmatism if any. While our incisions for phacoemulsification is thought to cause a predictable degree of flattening, patient's age, pachymetry, corneal diameter, tilted IOL, wound healing and other factors can cause astigmatism to vary significantly. A large degree of IOL optic tilt is seen typically in cases with a compromised capsular bag or in asymmetric IOL placement with one haptic in the bag with the other in the sulcus. But even in a perfectly done cataract surgery, the patient's healing response, scarring and fibrosis can cause an IOL to tilt enough to induce some astigmatism. The aim of this study is to determine the amount of postoperative residual astigmatism and visual outcome with Toric IOL implantation during phacoemulsification.

Materials and methods:

A hospital based prospective observational study was conducted at the department of Cataract in the National Institute of Ophthalmology and Hospital, Sher-e-Bangla Nagar, Dhaka, and the duration of study was from July, 2013 to June, 2014. Among 30 eyes of 28 patients who came with the complaints of dimness of vision due to cataract with variable amount of astigmatism (range 1.5 to 3.5D). Those who came with any other ocular pathology or history of previous ocular surgery were not included in this study. Cataract extraction were done by phacoemulsification surgery with implantation of Toric IOL. All the surgeries were done with INTREPID Micro-Coaxial system using the INFINITY Vision system by the same surgeon under local & topical anaesthesia. The cornea was marked with a marker pen at 12 O'clock position (90 degree) for each eye before anaesthesia was given to avoid anaesthesia related cyclotorsion. Peroperatively, the orientation of axis is determined in left eye; temporal 0,

superiorly 90 nasal 180 and right eye; nasal o, superiorly 90 and temporal 180. The clear corneal tunnel incision was performed with the side-port 70 degree apart and to the left side of main incision. The tunnel incision was done in all patients with a 2.4mm Webal Edge knife and side-port with 1.2mm Webal Edge knife. After phacoemulsification Toric IOL was implanted in the capsular bag. All incision was left suture less and were sealed by corneal stromal hydration. Patients follow up was done on 1st POD, 1st week and 1st month after surgery for all cases. Preoperative and postoperative keratometry readings were made by autorefractokeratometer. Analysis of the astigmatism was restricted to the keratometric readings. The change in the keratometric cylinder was examined by simple subtraction method of calculating cylinders without regards to axis.

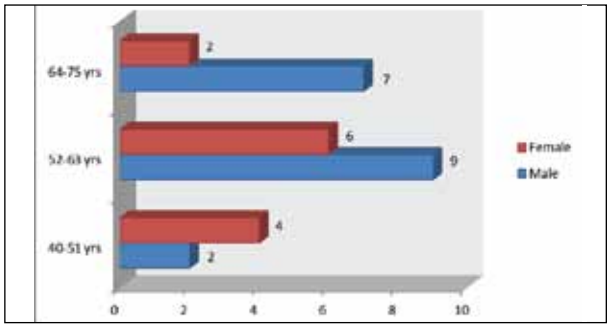
Main outcome measures were assessed by preoperative uncorrected visual acuity, postoperative uncorrected visual acuity on 1st POD, after 1 week and 1-month, preoperative keratometry, preoperative astigmatism, postoperative uncorrected keratometry on 1stPOD, after 1 week and 1month, postoperative uncorrected astigmatism on 1stPOD, after 1 week and 1month. Data was collected in a predesigned data collection sheet and then compiled accordingly. Appropriate statistical analysis was done using computer-based software SPSS program 13.0 version.

Ethical measures: Patients were informed about the study purposes and how they have to participate for the study and the possible complications related with the surgical procedure. They were assured and confirmed that no way their normal treatment would be hampered for this study. And at any time, they could withdraw themselves for any reason without explanation. And any private information gathered for this study will be kept confidential. Informed written consent has been taken from patient's legal guardian prior to data collection.

Results

We assessed 30 eyes of 28 patients in this study. The age range was from 40 years to 75 years. The most of the cases was above 50 years of age. The male was 60% and female was 40% [Figure-1].

Figure-1: Bar diagram showing distribution of demographic profile of the study patients



Due to clear corneal incision during cataract surgery, the steep meridian pre-operative mean keratometry was 44.329D (P value<0.01). Postoperative mean keratometry readings were 44.196D at 1st POD, and 43.97D at 1 month of surgery (P value <0.001) [Table-1].

Table-1: Pre-operative and Post-operative keratometry of steep axis with comparison

Pre operative(D) Mean±SD	Post operative(D), mean ±SD			Paired-t test
	1st POD	7thPOD	30th POD	P Value
44.329±1.473	44.196±1.419			*p*=0.001
		44.033±1.404		*p*<0.001
			43.971±1.431	*p*<0.001

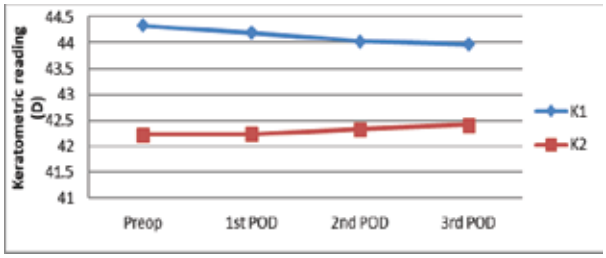
Due to clear corneal incision during phacoemulsification surgery, the steep meridian became flat significantly from pre-operative keratometry to post operative keratometry. On the other-hand the flat meridian became steeper from pre-operative keratometry to 30thpost operative keratometry. [Table-2].

Table-2: Pre-operative and Post-operative keratometry of flat axis with comparison

Pre operative(D) Mean±SD	Post operative(D), mean ±SD			Paired t-test
	1st POD	2ndPOD	3rdPOD	P Value
42.225±1.471	42.233±1.515			*p*=0.742
		42.333±1.492		*P*=0.001
			42.421±1.501	*p*<0.001

The preoperative visual status was Hand Movement (HM) to 1/60 in 10.7% of patients, 2/60 to 6/60 was in 60 % of patients; 6/36 to 6/24 was in 23.3% of patients. Visual acuity in the 1stpost operative day were 6/6 in 6 (20%) cases, 6/9 in 13 (43.3%) cases, 6/12 in 8 (26.7%) cases, 6/18 in 2(06.7%) and 6/24 in 1 (03.3%) case. The visual acuity in the 7th post operative day were 6/6 in 14 cases (46.7%), 6/9 in 9 cases (30%), 6/12 in 6 cases (20%) and 6/18 in 1 (03.3%) case (Table 3.3). The final visual outcome in the 30th post operative day were 6/6 in 21 cases (70%), 6/9 in 7 cases (23.3%) and 6/12 in 2 (06.7%) cases.

Figure-2: Pre-operative and post operative keratometric (K1 and K2) reading changes



The flat axis become steeper from preoperative readings to final postoperative readings, whereas the steeper meridian became flat [Figure-2].

Preoperative mean astigmatism was 2.104D. After 1 Month, there was significant reduction of pre-operative astigmatism to 0.583D with P value <0.0001. So, the mean astigmatism was decreased significantly in the successive post-operative days [Table-3].

Table-3: Pre-operative and Post-operative astigmatism with comparison

Pre operative(D) Mean±SD	Post operative(D), mean ±SD			**Paired t-test**
	1st POD	7thPOD	30th POD	**P Value**
2.104±0.319	0.954±0.494			*P*<0.001
		0.608±0.407		*p*<0.001
			0.583±0.413	*p*<0.0001

Discussion

Cataract surgery is one of the types of refractive surgery. But the corneal astigmatism plays an important role in ultimate post-operative visual status of the patient. The visual status of an individual depends not only on the visual acuity, but also on field of vision, colour vision, contrast sensitivity, glare sensitivity and binocularity. The clarity of image in astigmatism is never as good as those having no astigmatism. Astigmatism significantly affects patient's independence, quality of life and well-being. Considering these facts, many studies are going on in recent time to minimize the pre-existing corneal astigmatism by adopting different procedures during cataract surgery.

In this study the effect on pre-existing corneal astigmatism by implantation of Toric intraocular lens during cataract surgery and residual astigmatism after surgery is assessed. The toric IOL was devised by Shimizu et al. in 1994 and has been used clinically since then.[11]

In this study, the age range was from 40 years to 75 years. The peak incidence of cataract was among 52- 63 years. The age-related cataract is common as early as the fifth decade of life, with 11.5% of people aged 43–54 years having some evidence of cortical opacity.[12] Our study also more or less corresponds with it.

Female were more affected by age related cataract, about 60.1%[13] whereas in our study we found an opposite scenario, male were 18 (60%) and female were 12 (40%). This difference may be due to female patients in our country deprived of proper treatment and approach to a tertiary hospital is difficult.

The decreased visual acuity in early post operative day may be due to residual corneal astigmatism as wound was not healed. Visual acuity is improved after 1 month may be due to correction of residual astigmatism as wound was healed. This study was compatible with the result of another study on cataract patients with high degree of astigmatism.[14] They showed uncorrected distant VA of 20/40 or better in 83% of eyes and 20/30 or better in 50% of eyes.

Due to clear corneal incision, the steep meridian became flat significantly from pre-operative keratometry 44.329±1.473D (mean±SD) to 30thpost operative keratometry 43.971±1.431 D (mean±SD) having p<0.001. On the other hand, the flat meridian became steeper from pre-operative keratometry 42.225±1.471 D (mean±SD) to 30thpost operative keratometry 42.421±1.501 D (mean±SD) having p<0.001 (Table -3.6). So, the pre-existing astigmatism reduced gradually. The test of significance was done by Paired- Sample T Test. This study was compatible with Beltrame et al. in 2001, who showed significant wound related flattening and non-orthogonal steepening at 2 opposite radial sectors induced by different oblique cataract incision.[15]

Preoperative mean astigmatism [Mean±SD] was 2.104±0.319 diopter (D), after the first postoperative day, mean astigmatism decreased to 0.954±0.494 D with p<0.01, after 1 week mean astigmatism reduced to 0.608±0.407 D with p<0.001 and finally after 1 Month there was significant reduction of pre-operative astigmatism to 0.583±0.413 D with p<0.0001 (Table -3.7). So, the mean pre-operative astigmatism decreased significantly in the successive post-operative days (Fig 3.4). This study was compatible to other study14 who showed after implantation of Toric

IOL, residual refractive cylinder was less than 0.75 D in 62% of eyes and less than 1.00 D in 81% of eyes.

The limitations of the study included small sample size, single center study, short follow up times, absence of control group and long-term results couldn't be assessed. Epidemiological studies should be carried out to define the prevalence of the problem in Bangladesh. This will help in subsequent management plans.

Cataract surgery as a form of refractive surgery demands uncorrected quality vision postoperatively. Ophthalmologists planning to bring quality vision for the patient after cataract surgery by phacoemulsification would be prudent to adopt the best suited procedure to minimize the pre-existing astigmatism for the individual patient. Even if patients have residual astigmatism after cataract surgery Ophthalmologists have to treat accordingly.

Conclusion:

The Toric IOL implantation during cataract surgery can be a good option for correction of pre-existing corneal astigmatism significantly in phacoemulsification surgery. However, the complete and perfect correction of astigmatism is not yet obtained in all cases. To minimize postoperative residual astigmatism, we have to evaluate preoperative and per operative risk factors carefully and correct postoperative residual astigmatism. But a study comprising larger study population of longer duration is necessary to draw a better inference.

Conflict of interest: none.

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REVIEW ARTICLE

Outcome of Different Treatment Modalities in Non-caseating Granulomatous Mastitis: A Narrative Review

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ABSTRACT

Granulomatous mastitis (GM) is a benign inflammatory condition of breast disease that affects women of childbearing age with a history of breastfeeding. The rarity and complex pathophysiology make the diagnosis and management quite dilemmatic for clinicians. This review explored the available treatment options for the disease condition in light of the recent literature. Surgery alone, intervention with or without steroids, antibiotic therapy, abscess drainage, methotrexate therapy, and antibiotics are widely used in different settings. However, surgery (with or without steroids) showed a higher recovery rate along with a lower recurrence rate. Steroid therapy is promising, but its use is limited due to the higher number of recurrences. In addition, the use of methotrexate showed an increased remission rate, but the toxicity profile was still high. However, treatment outcome mostly depends on the severity of the disease and individual physical status, and therefore, a comprehensive evaluation of the patients is crucial. This review recommended the formulation of a standard guideline for uniform management of granulomatous mastitis conditions in our country.

Key words: Granulomatous mastitis, non-caseating,

Introduction

Granulomatous mastitis (GM) is a rare disease condition with complex pathophysiology that was first described by Kessler and Wolloch in 1972.[1] It is a chronic inflammatory pseudotumor characterized by noncaseating chronic granulomatous inflammation in breast lobules.[2,3] The etiology of GM is quite variable, and the pathophysiology is still hypothetical. The identified risk factors for GM include a history of pregnancy, breastfeeding, autoimmunity, tuberculosis, oral contraceptives, smoking, alpha-1 anti-trypsin deficiency, sarcoidosis, etc.[4,5] Diagnosis of the disease condition is quite challenging, as it mimics several types of mastitis.[4] Patients are often diagnosed with a late presentation, which makes management more difficult.[4] Moreover, consensus on standard treatment options for disease management is rarely available and impedes finding suitable treatment options.[6]

Available treatment options for granulomatous mastitis are surgical excision, curettage and drainage, use of corticosteroids, and earlier administration of antibiotics. The use of methotrexate (MTX) is also practiced in several centers. Additionally, close observation with symptomatic treatment and a combination of any of these were also chosen by the attending physicians.2,[7–9] However, the optimal treatment is variable and still contradictory10. Pandey et al. and Aghazandadeh et al. reported over two-thirds recovery by administration of steroids. The use of steroids can provide more than 70% recovery.[7,11] In patients with early detection of GM presenting mild symptoms, only observation with symptomatic medication showed excellent recovery rates.[12,13] A meta-analysis by Lei et al. observed that surgical management with and without steroid therapy was associated with a higher incidence of

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Date of submission: 05.01.2022, Date of acceptance: 12.01.2022

AKMMC J 2022; 13(1) : 47-51

complete recovery of GM14, which was also supported by another review that emphasized surgical management only.[15] Risngsted and Friedmen also highlighted that due to the high frequency of systemic inflammation, patients with GM often need to be treated with methotrexate (MTX), and a multidisciplinary approach may require early and complete recovery.

GM mainly occurs in women of childbearing age, and mostly a history of breastfeeding was reported.[16] The disease usually develops approximately two years after breastfeeding, and the average age is 30 years[17]. Most patients with GM are diagnosed after progression of the disease process.16 The protracted course of the disease itself, along with the diagnostic dilemma and the complex treatment process, significantly affect the quality of life of the patients.[16] The present review was planned to summarize the current available treatment options for this chronic disabling disease with their alternatives.

Clinical presentation and diagnostic approach:

The disease most frequently appears in the 3rd or 4th decade of life, and reports have shown that the variable age of presentations ranged from 11 to 83 years. The main symptom of granulomatous mastitis (GM) is the presence of a tender and painful mass in the breast. It is primarily unilateral, but bilateral presentations are not rare. The most common quadrant in the posterior areola.[16] Almost half of the patients present with erythema and swelling along with redness, areola strictures, fistulas, and ulcers. One-third of the patients typically consult with physicians with an abscess at their first presentation.[6] Lymphadenopathy is variable and is not the only presenting feature of this patient group.[18] Signs of systemic inflammation, including erythema nodosum and arthritis, have also been reported at multiple frequencies.[10] A recent estimate suggests a lag period of months from the onset of symptoms and final diagnosis.[19]

Histopathology is the cornerstone step for the diagnosis of GM. The disease is characterized by a nonnecrotizing granuloma accompanied by limited infiltration of multinucleated giant cells, epithelioid histiocytes, lymphocytes, and plasma cells. With neutrophilic infiltrates, organized sterile microabscesses may form in fewer instances. In a severe form of the disease, inflammation may extend into adjacent lobules. Loss of acinar structures and damaged ducts are also observed in the parenchyma under the microscope.[20]

Although GM is a noninfectious disease, a study by Taylor et al. mentioned the presence of corynebacteria in the granuloma.[21] Studies by Emre et al. and Dobinson et al. also observed the presence of species of cornybacterium.[22,23] These cases also present granulomatous and neutrophilic inflammation along with cystic spaces in histopathology, which were defined as 'cystic neutrophilic granulomatous mastitis' in a study by Al-Mansara et al. [24] In contrast, some authors stated that the presence of corynebacteria in GM lesions is a contaminant from normal skin flora.[18]

The radiological evaluation of GM lesions showed nonspecific features that coincided with the characteristics of inflammatory carcinoma of the breast.[25] Multiple contiguous hypoechoic masses with posterior acoustic shadowing or enhancement are found on ultrasonography. The majority of cases have hypervascularity, which may be diagnosed by Doppler imaging.[26] The most common pattern on mammography is unilateral focal or regional asymmetry.[21] Depending on the intensity of the inflammation, MRI (magnetic resonance imaging) indicates heterogeneous ill-defined masses along with nonmass enhancement.[16]

Hence, the confirmatory diagnostic tool for GM is core needle biopsy, and correct diagnosis depends on the quality of biopsy tissue.[13] Laboratory findings of GM patients usually showed inconclusive results for rheumatoid factors, serum complements, c-reactive protein, carcinoembryonic antigen, and cancer antigen[20,21]

Management options of granulomatous mastitis:

For early diagnosed patients with granulomatous mastitis (GM), only observation was enough, as GM is sometimes a self-limiting condition.16 Pandey et al. and Buton et al. observed 100% complete remission among early diagnosed GM patients only after close

follow-up.[27,7] Hur et al. observed 87.5% complete remission following observation.[12] However, both conservative therapy and surgical management of GM are suggested in the literature.

Conservative management:

Conservative management mostly focused on symptomatic management of the patients and medical therapy. Each treatment option has its own merits and demerits.

Steroid therapy:

Steroid therapy is a widely practiced norm in chronic granulomatous mastitis patients. Initially, high-dose steroid therapy was proposed. DeHerthogh et al. first recommended corticosteroid therapy with prednisolone 30 mg/day for at least two months.[28] In general, this leads to a decrease in the diameter of the lesion but also to a variety of side effects, such as weight gain, hyperglycemia, and the risk of Cushing's syndrome. In recent years, a lower-dose regimen of steroids followed by slow tapering administration described by Freeman et al. has become more popular for the treatment of GM.[6] The recovery rate after steroid therapy varied greatly in different trials, ranging from 31% as described by Hur et al.[12] to 86% as described by Yabanglu et al., Neel et al.[29,30] The use of topical corticosteroids to minimize systematic adverse events was also under investigation.

Role of methotrexate:

Methotrexate (MTX) is a folate antagonist used as a disease-modifying agent in several rheumatologic diseases. However, the role of GM has also been tested and found to be promising. Ringsted and Friedmen, in their review, conclude with a stronger connection between inflammatory arthritis, erythema nodosum, and patients with GM.[10] Therefore, the drug was hypothesized to potentiate the action. They also observed a higher rate of relapse-free remission of GM following administration of methotrexate (MTX) in comparison to high steroid treatment and low steroid treatment. Sheybani et al. and Aghajanzadeh et al. also observed a higher remission rate from methotrexate.[8,11] Based on the supporting evidence, methotrexate is considered a treatment option for patients who have relapsed or who do not tolerate high-dose corticosteroid therapy or steroid-sparing agents.

Empirical antibiotics therapy:

Multiple infective and inflammatory conditions have been recognized, but recently, attention has been drawn to corynebacterial species as specific pathogens in this disease. However, in reality, most patients with granulomatous mastitis are prescribed blind antibiotic therapy without enough microbiological evidence due to the similarity of the presentation with bacteriological mastitis.[16] Even if microbiological evidence is sought, diagnosis can be challenging due to their particular growth requirements and prolonged incubation time. Consequently, current knowledge about antimicrobial options to treat Corynebacterium mastitis is still lacking. GM, as per definition, is a sterile inflammatory disease; therefore, blind antibiotic therapy usually fails in most cases.[31]

Surgical approach:

The choice of surgical management of GM varies depending on the progress of the disease and associated clinical presentations. Approximately one-third of GM patients present with abscesses. Therefore, abscess drainage has been considered a management option of GM for those patients. The decision of abscess puncture and drainage depends on the features of the presenting mass. However, the presenting mass might have necrotic tissue in the center, making the procedure difficult to conduct. The outcome is also often unsatisfactory due to the absence of bacterial causative agents.[16]

Surgical excision showed a satisfactory outcome in the management of GM. The success rate of surgical excision ranges from 61 to 100%, as reported in various trials. The inclusion of steroid therapy with surgery was described by some previous studies. The meta-analysis by Lei et al. described a 94.5% pooled incidence of complete recovery by the combination of oral steroids and surgical management. Surgical management showed 90.6%, and oral steroids showed a 71.8% complete remission rate14. A systematic review and meta-analysis by Ma et al. also showed that surgery significantly improved the rate of complete recovery (RR 1.22, 95% CI 1.10-1.36) compared to steroid-only therapy, whereas no difference was observed between only surgery and the combination of surgery and steroids (RR 0.78, 95%

CI 0.55-1.11). Steroid therapy requires a long time to achieve recovery. Surgery (with and without steroids) requires a relatively shorter period for recovery, which offers quicker rehabilitation to normal life. Other than a shorter recovery period, surgical management offered the highest incidence of recovery 7,11,21–23,25,26. A lower recurrence rate was observed with surgical management compared to oral steroids and other treatment options 29,30. Therefore, surgical management is the most effective management approach for GM.

However, steroid therapy was also observed as a recommendable therapy. Therefore, patients who are not comfortable with surgery and surgical scars and have any contraindication for surgery could be approached for steroid therapy. However, it requires a more extended period to achieve recovery and is associated with a high frequency of steroid side effects.[29,12] Moreover, a higher recurrence rate was also observed in steroid-only therapy.[29,30]

The available literature indicates variable findings regarding the therapeutic outcome and recurrence rate of GM. However, the overall results indicate the superiority of surgical management regarding a higher recovery rate, quicker recovery, and lower recurrence rate. Antibiotics and abscess drainage offer very low efficacy. However, early diagnosed cases showed a very good recovery only after observation. For patients with relapse who are not fit enough for high doses, steroids could be recommended as an additional methotrexate therapy, according to some studies.[10]

To measure the outcome of GM, no scale or scores have been established yet. Different trials have been conducted in different countries of the world, but a standard guideline has yet to be formed. The associated adverse effects due to the surgical approach and steroid therapy should be considered when recommending a complete treatment guideline for GM.

Conclusion:

Surgical procedures along with or without additional steroids seem to be the most efficient and recommended treatment option for patients with granulomatous mastitis. Steroid therapy in a dose-tapering manner has also shown a good recovery rate. Hence, the efficiency of certain management strategies varies from patient to patient due to their immunological status and associated comorbidities. Extensive trials should be conducted before concluding the best treatment approach, although the rarity of the disease is a significant obstacle to conducting a trial with a larger sample size.

Conflict of interest: none,

Acknowledgment: The authors must thank the entire team of the Pi Research Consultancy Center (www.pircc.org) for their constant support throughout the research work.

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CASE REPORT

Progressive pseudo-rheumatoid dysplasia -a rare genetic disorder: Case Report

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ABSTRACT

Progressive pseudorheumatoid dysplasia (PPRD), also known as spondyloepiphyseal dysplasia tarda with progressive arthropathy (SEDT-PA), is an autosomal recessive disorder, resulting from mutations in the WNT1-inducible signaling pathway protein 3 (WISP3) gene involving the axial skeleton as well as small peripheral joints. Because of rarity here we present a case of 14-year-old boy, 1st issue of consanguineous parents who was presented with pain & gradual development of contracture in 3rd distal interphalangeal joint of right hand when he was 4-year-old, then gradual involvement of other interphalangeal joints of hands, bilateral wrists, elbows, shoulder, knees &ankles occurred over years with the development of contractures and restricted movement. For last few years, he developed difficulty in walking. Clinically spinal scoliosis and coxa vara was present. Mobility of spines and multiple joints including proximal & distal interphalangeal joints of hands, wrists, elbows, shoulders, knees, ankles were restricted with flexion contractures. The gait of the patient was limping. Radiological evaluation showed osteopenia in X-ray of pelvis with both hip joints and both knee joints. Generalized osteopenia, fusiform swelling in distal interphalangeal joint, flexion deformity in distal interphalangeal joint of middle and ring fingers of both hand was shown in X-ray of both hands. MRI of lumbosacral spine showed dorso-lumbar vertebral bodies dysplastic with anterior wedging producing bullet nose. Superior epiphyseal deformity was also noted in lower dorsal bodies suggestive of spondyloepiphyseal dysplasia of dorso-lumbar spine. Genetic study showed homozygous nonsense variation in exon 5 of the WISP3 gene suggestive pathogenic variant. Finally, he was diagnosed as a case of PPRD and treated with physiotherapy, family counseling, and anti-inflammatory medications.

Key words: Progressive pseudorheumatoid dysplasia (PPRD), Spondyloepiphyseal dysplasia tarda with progressive arthropathy (SEDT-PA), WNT1-inducible signaling pathway protein 3 (WISP3) gene.

Introduction

Progressive pseudorheumatoid dysplasia (PPRD), also known as spondyloepiphyseal dysplasia tarda with progressive arthropathy (SEDT-PA), is an autosomal recessive disorder, resulting from mutations in the WNT1-inducible signaling pathway protein 3 (WISP3) gene, located on chromosome 6q22[1,2]. WISP3 is a member of the CCN family of genes, which encode growth factors in connective tissue, responsible for the regulation of cell proliferation, differentiation and migration1.This rare disorder with a global prevalence of only 1/1 000 000 with two-thirds of reported cases from arabic countries[3]. This skeletal dysplasia typically presents with progressive involvement of the metacarpophalangeal (MCP), proximal (PIP) and distal interphalangeal (DIP) joints, wrists, elbows, knees, shoulders and ankle joints associated with contractures, fatigability and gait anomalies[4,5]. Usually signs of joint inflammation are absent. The disease is usually manifests between the ages of 3 and 6years 5 and boys are affected more[6,7].

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Date of submission :07.12.2021, Date of acceptance:25.12.2021

AKMMC J 2022; 13(1) : 52-55

Case Report

A 14-year-old-boy, 1st issue of consanguineous parents, hailing from Sylhet, Bangladesh, presented with pain & gradual development of contracture in 3rd distal interphalangeal joint of right hand when he was 4-year-old-boy, then gradual involvement of other interphalangeal joints of hands, bilateral wrists, elbows, shoulder, knees & ankles occured over years with development of contractures and restricted movement. For last few years, he developed difficulty in walking. His birth history & milestones of development were normal. There was no family history of such type of problem. Clinically spinal scoliosis and coxa vara was present. Mobility of spines and multiple joints including proximal & distal interphalangeal joints of hands, wrists, elbows, shoulders, knees, ankles were restricted with flexion contractures (Fig.1). The gait of the patient was limping. Other systemic examination revealed nothing abnormality.

Radiological evaluation showed osteopenia in X-ray of pelvis with both hip joints and both knee joints (Fig.2& Fig.3). Generalized osteopenia, fusiform swelling in distal interphalangeal joint, flexion deformity in distal interphalangeal joint of middle and ring fingers of both hand (Fig.4) was shown in X-ray of both hands. MRI of lumbosacral spine showed dorso-lumbar vertebral bodies dysplastic with anterior wedging producing bullet nose. Superior epiphyseal deformity was also noted in lower dorsal bodies suggestive of spondyloepiphyseal dysplasia of dorso-lumbar spine. (Fig.5)

Fig.1: Flexion contractures of fingers in both hand

Hematological investigations including serum calcium. phosphate, full blood count, vitamin D, C reactive protein (CRP), erythrocyte sedimentation rate (ESR), rheumatoid factor, anti-CCP, HLA-B27 were all normal.

Genetic study showed homozygous nonsense variation in exon 5 of the WISP3 gene (chr6:g.112390563C.T; Depth :65x) suggestive pathogenic variant (Fig.6).

He was treated with physiotherapy and non-steroidal anti-inflammatory medications was prescribed to take when needed for joint pains. Genetic counseling to family was done and patient was referred to the orthopedic surgeon for assessment and follow-up as he would need corrective surgery in future.

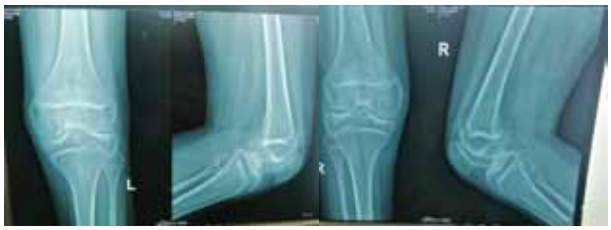

Fig.2: Osteopenia in both knee joints

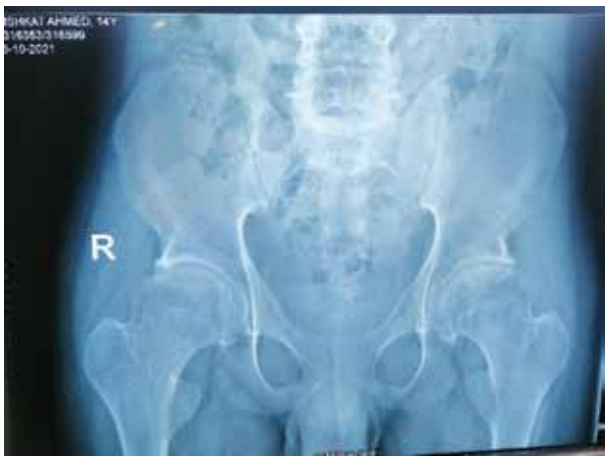

Fig.3: Osteopenia in pelvis with both hip joints

Fig.4: Generalized osteopenia, fusiform swelling in distal interphalangeal joint, flexion deformity in distal interphalangeal joint of middle and ring fingers of both hands.

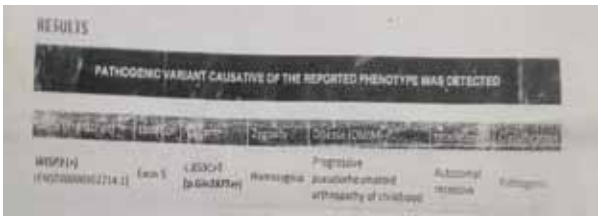

Fig.6: Genetic test report

Discussion

PPRD is a rare epiphyseal dysplasia generally begins between the ages of 2 and 8 years[8]. Here age of presentation was at 4 years. The disease is characterized by progressive joint stiffness, deformity, and limited mobility and is often clinically misdiagnosed as juvenile idiopathic arthritis. Our patient also presented with similar features. In some cases, corneal changes and osteoporosis is reported [9,10]. But in our patient, there was no evidence of corneal change. Characteristic imaging findings will be generalized platyspondyly and epiphyseal involvement, with enlargement of both ends of the short tubular bones of the hands[11]. In present case generalized osteopenia, fusiform swelling in distal interphalangeal joint, flexion deformity in distal interphalangeal joint of middle and ring fingers of both hand and spondyloepiphyseal dysplasia of dorso-lumbar spine was noted in imaging studies. The differentiation between juvenile idiopathic arthritis (JIA) and PPRD is challenging and most cases are misdiagnosed in the beginning as JIA. These two diseases can be differentiated by presence of joint inflammation, morning stiffness, joint destruction and elevated ESR and CRP in JIA. Moreover, dysplastic vertebrae are not a feature of JIA[12]. On the other hand, absence of laboratory changes indicating systemic or synovial inflammation, no joint erosions and the presence of characteristic X-ray changes of spondyloepiphyseal dysplasia help in the differential diagnosis of PPRD from JIA[13].

The definitive diagnosis of PPRD is established with identification of the characteristic radiological findings and biallelic pathogenic variants in WISP3 on molecular genetic testing [14]. In the present case genetic study showed homozygous nonsense variation in exon 5 of the WISP3 gene (chr6:g.112390563C.T; Depth :65x) suggestive of pathogenic variant. Treatment is mainly conservative. Pain relief, rehabilitation, and surgical interventions such as osteotomy and arthroplasty for secondary degenerative changes may be required[13,15]. Genetic studies need to be done for family counseling. Immobilization (e.g., casting) should be avoided. In present case patient was treated with physiotherapy and non-steroidal anti-inflammatory medications was prescribed to take when needed for joint pains. Genetic counseling to family was done and patient was referred to the orthopedic surgeon for assessment and follow-up as he would need corrective surgery in future.

Conclusion

Progressive pseudorheumatoid dysplasia (PPRD), though a rare disease, should be kept in mind as a differential diagnosis of JIA to prevent delayed diagnosis and to begin early rehabilitation thus avoiding potentially serious late morbidity. The combination of non-inflammatory joint disease with radiological abnormalities of the spine is the clue to the diagnosis of underlying PPRD.

Conflict of interest: None

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CASE REPORT

Primary Distal renal tubular acidosis: case series

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ABSTRACT

Primary Distal renal tubular acidosis is an infrequent tubular disorder with complex pathophysiology that present with poor growth, skeletal changes and sometimes life-threatening hypokalemia. Here we present two siblings one girl and one boy with a consanguineous parents presented with polyuria, polydipsia, failure to thrive and skeletal deformity. Both cases showed non-anion gap metabolic acidosis with alkaline urine and the younger brother had periodic paralysis due to hypokalemia. After diagnosis and treatment they showed good response with alkali therapy.

Key words: Renal tubular acidosis, autosomal recessive, failure to thrive, alkali therapy.

Introduction

Kidney contribute to acid-base balance by reabsorption of filtered bicarbonate (HCO3-) and excretion of hydrogen ion (H+). All filtered HCO3- should absorbed before dietary H+ can be excreted. About 90% HCO3- absorbed in the proximal tubule and 10% in the distal tubule. 1 Renal tubular acidosis is a condition that causes accumulation of acid in the body due to failure of the kidneys to appropriately acidify the urine and characterized by normal anion gap metabolic acidosis and normal or near-normal glomerular filtration rate. [1,2]

RTA occur due to impairment of bicarbonate reabsorption or excretion of H+ ions or a combination of both. In children distal RTA (type 1) and proximal RTA (type II) are common and third form (type IV) characterized by hypoaldosteronism and hyperkalemia which is very rare.[1,3] This tubular defect may be hereditary/primary originating from genetic defect or acqutrait whereas pRTA occurs as AR ired (secondary) due to systemic disease or adverse drug reactions.[4,5,6] Inherited form of dRTA may be autosomal dominant and autosomal recessive with or without deafness. Dominant disease usually presents in late childhood but recessive variant presents in infancy /early childhood.[1,4,7]

In dRTA there is failure of H+ secretion into the lumen by alpha intercalated cells of the collecting duct and distal nephron leads to inability to acidify urine and consequently develop academia. Loss of sodium bicarbonate distally, due to lack of H+ to bind to in the tubular lumen results increase chloride reabsorption and hyperchloremia. As H+ not excreted K+ cannot reclaimed by cells and produce hypokalemia. In acidosis urinary citrate excretion increase. Both hypocitraturia and alkaline urine aggravates deposition of calcium phosphate and form nephrocalcinosis.[1,2,3]

Distal RTA shares features with pRTA including non-anion gap metabolic acidosis and growth failure. During infancy and early childhood the clinical features include failure to thrive, polyuria, polydipsia, muscle weakness due to hypokalemia and sometimes severe rachitic deformities.[1,3] Growth failure is due to chronic acidosis itself and bony changes due to acidosis induced loss of bone minerals.[1]

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Date of submission: 13.12.2021, Date of acceptance: 26.12.2021

The diagnosis can be made by presence of alkaline urine with normal anion gap systemic academia. In case of incomplete dRTA ammonium chloride loading test shows failure to acidify urine. The treatment is straightforward that the correction of academia with oral sodium bicarbonate, sodium citrate, or potassium citrate.[1,3]

Case 1

The index case a 13-year-old girl was born to healthy consanguineous parents was first hospitalized at the age of 4 years of her age with the complaints of bowing of legs and failure to thrive since her early infancy. She had history of polyuria and polydipsia for 9 months. Initially she was treated as nutritional rickets with vitamin D (stoss therapy) supplementation for 3 times without any significant improvement. There was no history of any fever, head trauma, urinary urgency, hematuria, or taking any offending drugs. Physical examination revealed she was fatigue but alert, afebrile, mildly pale, tachypnoeic, tachycardic, normotensive, severely stunted and moderately wasted. She had mild motor delay with reduced tone and power in lower limbs and normal tendon reflexes. No abnormalities of the heart, lungs or abdomen was found. The laboratory findings are shown in Table 1. These values were consistent with non-anion gap hyperchloremic metabolic acidosis with hypokalemia and hypocalcemia. Urinalysis showed alkaline PH with positive urinary anion gap. X-ray lower limb showed features of rickets. X-ray and ultrasonography of KUB showed normal findings. The patient was treated with oral shohl's solution three times a day along with sodibicarb 1 tab three times daily and oral potassium supplements two times daily. Calcium and vitamin D supplementation were also given. Up to now, she has been followed for last 9 years and dosage were adjusted and her rachitic changes resolved, achieved all age appropriate gross motor milestone and has had normal puberty. She has had quite good academic performance.

Case 2

A 7.5-year-old male the younger brother of 1st case and 2nd issue of her parents presented with paralysis of both lower limb following a history of vomiting for several times. He also had polyuria, polydipsia failure to thrive since his 2 years of age. He had same type of illness like generalized weakness, transient lower limp paralysis about 4-5 times for last 2 years. But parents did not seck any medical help as he had no apparent bony deformity. As the child condition was gradually worsening the hospitalized him. Like his sister he had no history of any fever, head trauma, convulsion, dribbling of urine, hematuria, or taking any offending drugs. On physical examination he was lethargic, afebrile, some signs of dehydration, tachypnoic, tachycardic, normotensive, severely stunted and wasted. Neurological examination revealed muscle power 4/5 in upper limb and 2/5 in lower limb with no signs of meningeal irritation. Other systemic examination revealed no abnormality. The laboratory findings shown in Table 1. Blood and urine examination consistent with dRTA with severe hypokalemia and x-ray lower limb shows early features of rickets without any evidence of nephrocalcinosis. His general condition also improved after one month of treatment.

Table 1: Laboratory findings of two cases.

Investigations		1st case	2nd case
S. potasium		2.3 mmol/L	1.8 mmol/L
S. chloride		12o mmol/L	115 mmol/L
	PH	7.19	7.22
ABG	PCO2	16 mmHg	19.5 mmHg
	HCO3	9 mmol/L	9 mmol/L
S. anion gap		10	13
Urine anion gap		36	35

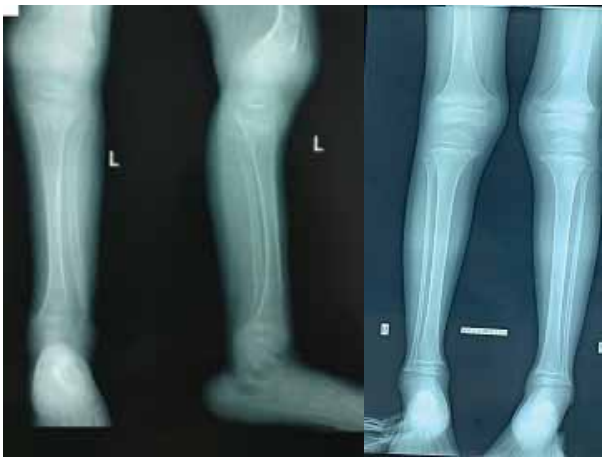

Fig 1. Bone radiographs of the patients, 1st one was elder sister showed rachitic changes in the lower extremities and 2nd one was her brother shower early changes of rickets.

Discussion:

Some characteristics of the clinical picture presented in the two patients of same family draw attention and deserve to be analyzed. The two siblings presented with different symptoms like elder sister mainly presented with rickets but younger brother presented with muscle weakness and paralysis. The other manifestations of the both siblings like polyuria, polydipsia and growth failure, which is frequently reported in dRTA.[8,9] Hypokalemic paralysis and progressive weakness are rare manifestations reported in children but common in adult.[10] However, rickets is common in untreated dRTA because of bone resorption to buffer chronic metabolic acidosis.[11]These cases also coincided with that is reported in the literature regarding clinical presentation at a very young age is almost always primary[12,13] and we did not get other possible clue for secondary dRTA although genetic studies were not carried out. The majority of patients with autosomal recessive distal RTA have sensorineural deafness but none of our patients had hearing impairment, which is compatible with dRTA type 1c.[14]

Both of our patients had typical findings of RTA, including metabolic acidosis with a normal anion gap and hypokalemia. Additional findings of alkaline urine, positive urine anion gap and rickets suggested that both of them had dRTA. These findings are consistent with other literature.

Distal RTA is often associated with nephrocalcinosis and progression of nephrocalcinosis may lead to development of CKD.[15] Fortunately none of our patients had nephrocalcinosis. Literature showed that proper diagnosis early therapy usually leads to an excellent prognosis.[16,17] Similarly both of our patients showed complete symptomatic recovery and achieved catch-up growth.

To best of our knowledge this is one of the first family cases with dRTA reports in our country. In Colombia there was a reported case series where 3 siblings presented dRTA in early infancy and identified as autosomal recessive presentation.[18]

Conclusion

Distal RTA in children is a controllable disease with favorable long-term prognosis. Early detection and accurate characterization of this condition is pivotal to uncover an underlying disease, tailor a specific therapy, and prevent further renal function decline. Treatment during the early stages in infant with dRTA is of great importance for patient prognosis.

Conflict of interest: none.

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CASE REPORT

Goldenhar syndrome

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ABSTRACT

Goldenhar Syndrome or Oculoauriculovertebral Syndrome is a complex syndrome characterized by an association of maxillomandibular hypoplasia, deformity of the ear, ocular dermoid and vertebral anomalies and the most severe form of hemifacial microsomia. Here we describe a 12 years female patient with Goldenhar Syndrome came to Ophthalmology department at Anwer Khan Modern Medical College & Hospital.

Key Words: Goldenhar Syndrome, Oculoauriculovertebral Syndrome, Oculoauriculovertebral Dysplasia, Hemifacial Microsomia, Limbal Dermoid.

Introduction

Goldenhar syndrome is a congenital defect characterized by asymmetrical malformations classically involving face, eyes and ears. Goldenhar syndrome was first observed and recorded by Carl Ferdinand von Arlt.[1,2] Maurice Goldenhar was the first to describe the syndrome in detail and thus the condition was called Goldenhar Syndrome.[3] The vertebral anomalies were included by Gorlin Et Al. in 1963 and then the name Oculo-auriculo-vertebral (OAV) dysplasia was suggested.[4,5] It is also associated with anomalies of CNS, cardiac and renal anomalies. The precise incidence of Goldenhar syndrome is unknown but estimated from 1 in 35,000 to 1 in 56,000 live births.[6] The male-female ratio is 3:2. Sporadic in nature occurring randomly with no apparent cause. Positive family history have been described that have suggested autosomal dominant in nature but rarely it may present as autosomal recessive and multifactorial inheritance.[6,7] Drugs like thalidomide, tamoxifen, retinoic acid and cocaine by pregnant mothers may be implicated. Heavy alcohol consumption during pregnancy and maternal infection and maternal diabetes have also been suggested as etiological factors.[8,9] The diagnosis of this syndrome is mainly based on clinical aspects. Most consider presence of ear anomalies are essential for diagnosis.

CASE REPORT

A 12 years old female came to Ophthalmology department of Anwer Khan Modern Medical College & Hospital with the complaints of Swelling over the left eye and Swelling in front of the left ear since birth. Decreased vision & hearing impairment since childhood. Initially the swelling was small and yellow-grayish in color but gradually increased in size for last 12 years. She comes from a lower socio-economic family and all her family members are in good health. According to mothers statement her maternal period was uneventful. No history of taking teratogenic drugs, pre-eclampsia, GDM, maternal infection, preterm labour or preterm birth. There is no history of neonatal infection and low birth weight of the baby.

On general examination anaemia, jaundice, cyanosis, oedema, dehydration, clubbing, koilonychia, leukonychia all are absent. Her pulse: 84 b/m, BP: 100/60 mmHg and temperature: 98^{o}F. On nervous

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Date of submission: 20.12.2021, Date of acceptance:28.12.2021

system examination she was well oriented and no abnormalities were found. On Ocular examination following findings were found:

Table-1: Ocular examination findings.

	Right eye	**Left eye**
Characteristic features of swelling	No abnormality	A painless dome shaped swelling, soft in consistency, size 1/1.5cm with hair follicles over the smooth surface, immobile and adherent to the anterior & lower temporal surface of left eye touching the eyelid, conjunctiva and cornea which resembles a limbal dermoid [Fig-1].
Visual acuity	6/6	3ft finger count
Nystagmus	Absent	Absent
Ocular motility	Full in all cardinal gaze	Lateral gaze movement is restricted
Eyelid	Normal	Swelling adherent with the lower eyelid margin and at lateral canthus.
Conjunctiva	Normal	Adherent with the swelling
Cornea	Normal	Yellow-grayish swelling with hair is adherent with the temporal limbus & infero-temporal quadrant of the cornea.
Pupil	Round, regular and reacting to light	Round, regular and reacting to light
Fundus	Normal	Normal

Fig-1: Limbal Dermoid on left eye

Fig-2: Prominent hemifacial microsomia on left side of the face

On Musculoskeletal Examination, Hemifacial Microsomia is prominent on left side of the face [Fig-2]. On Otolaryngorhinological examination, preauricular skin tag of the left ear with microtia [Fig-3] and conductive type of hearing deafness evaluated by Waber and Rinne test. On cardiorespiratory, abdominal and renal system examination no abnormality were found.

Fig-3: Preauricular skin tag with microtia of left ear

We have done some investigations and they are CBC, RBS, SGPT, BT, CT, Serum Creatinine, Urine R/M/E, ECG, X-ray chest PA view and Covid 19 RT PCR test. All the test report findings are in normal range except for X-ray chest which shows scoliosis with hemivertebrae [Fig-4]. Though the patient has scoliosis we did not find any visible abnormality of her posture, gait and body movements. She also did not have any complaints of back pain or walking difficulties.

Fig-4: X-ray chest PA view showing scoliosis with hemivertebrae

Depending upon patients history, clinical examination and investigation findings our diagnosis is Goldenhar Syndrome. Diagnosis is made due to the presence of classical presentation like hemifacial microsomia, limbal dermoid, preauricular skin tag and scoliosis with hemivertebrae. After diagnosis from the Ophthalmology department we have provided surgical treatment as Excision of limbal dermoid & Biopsy for histopathological examination. On histopathological examination lipodermoid was found as the sample contains fibrous tissue, hair follicles and fat cells. Depending upon histopathological report our final diagnosis is Goldenhar Syndrome.

After 1 month patient came to us for follow up and she was doing well. Her cosmetic appearance has improved. There is no swelling over her left eye but scar mark can be seen on infero-temporal part of left side of cornea [Fig-6]. Her vision has improved to 5ft finger count and with spectacle correction it has improved to 6/60 on left eye. Her ocular motility in left eye is full in all cardinal gazes [Fig-6].

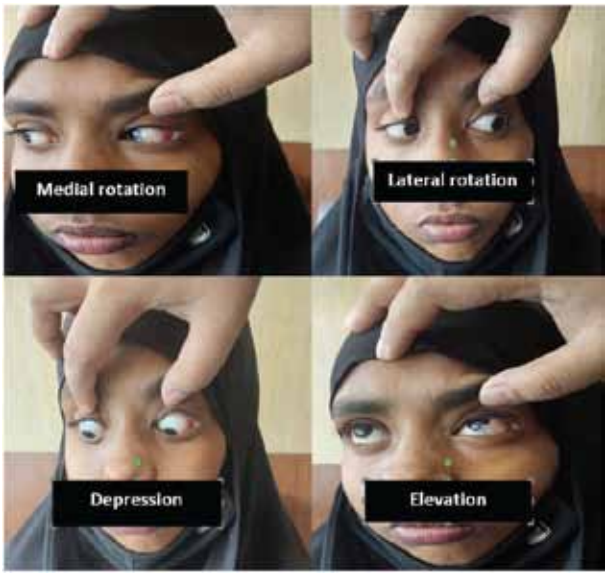

Fig-6: Ocular motility full in all cardinal gazes on left eye

DISCUSSION

The classic features of Goldenhar syndrome include ocular anomalies like epibulbar or limbaldermoids, microphthalmia and coloboma of eye lid and optic disc, ENT features such as preauricular skin tag, hearing loss, low implantation of the auricular pavilion, microtia, micrognathia, facial asymmetry like hemifacial microsomia where hypoplasia of the mandible is most common and vertebral anomalies such as scoliosis or hemivertebrae. The abnormalities are unilateral in most of the cases. Incidence of association with other body systems are cardiac (tetralogy of Fallot, ventricular septal defects and transposition of the great vessels), renal (ectopic or fused kidneys, renal agenesis, vesicoureteral reflux, ureteropelvic junction obstruction, ureteral duplication and polycystic kidney and CNS (microcephaly, encephalocele, hydrocephaly and hypoplasia of the corpus callosum).[10,11,12,13]

Goldenhar syndrome is also called 1st and 2nd Branchial Arch Syndrome (BAS) as it involves the first and second branchial arches 1st and 2nd branchial arch abnormalities manifests as combined

tissue deficiencies and hypoplasias of the face, external ear, middle ear and maxillary and mandibular arches.[14] They represent the second most common craniofacial malformation after cleft lip and palate. Hemifacial microsomia arise from branchial arch defect where preauricular skin tags are ramnents of branchial cleft.[14]

The etiopathogenesis of this Goldenhar syndrome is multifactorial, not yet fully established and involves genetic and environmental factors that cause disturbances in neural crest division, abnormal development of the first and second branchial arches during embryogenesis as well as occlusion of placental vessels.1[1,15,16]

In terms of genetic association 5p deletions, 14q23.1 duplications, or abnormalities of chromosomes 18 and 22 were observed. Families with autosomal dominant inheritance (1-2%) have shown segregation of chromosome 14q23.1 duplication inclusive of the OTX2 gene.[11,16,17]

Drugs like thalidomide, tamoxifen, retinoic acid, vasoactive (pseudoephedrine, aspirin, ibuprofen)and cocaine by pregnant mothers may be implicated. Heavy alcohol consumption during pregnancy, 5 maternal infection, maternal second trimester bleeding, gestational diabetes mellitus, multiple gestation and maternal use of assisted reproductive technology are the most common external factors involved in the occurrence of Goldenhar syndrome.[11,12]

The diagnosis of Goldenhar syndrome is clinical, however, there are some diagnostic tests that can be helpful. Prenatal ultrasonic diagnosis may theoretically be done at the 11th–15th week in utero.[18] Newer imaging modalities such as three-dimensional ultrasound may help in detection of microtia, preauricular skin tags, and asymmetry of the mandible even in mild forms. Most cases of Goldenhar syndrome occur de novo, but an autosomal dominant or recessive inheritance has also been noted. A three-generation family history has to be determined looking for cases as mild as ear tags or ear pits. Although there is not yet a specific genetic test to detect Goldenhar syndrome, array comparative genomic hybridization should be considered while testing for a possibility of recurrence.

The treatment of the patient depends on the age and systemic condition. Management is usually cosmetic. In our case we have diagnosed Goldenhar syndrome by patients history (maternal, birth and postnatal), clinical examination which shows classical presentations of Goldenhar syndrome and related investigations. Treatment was given and suggested according to patients condition.

Conclusion

Goldenhar syndrome is a rare disease and a congenital one meaning it is present at birth and it causes certain abnormalities especially craniofacial part with systemic associations. A multidisciplinary approach is necessary for the overall well-being of the patient and the treatment protocol should be determined as early in the life as possible to avoid physical difficulty and psychological stigma to the growing child. Pediatric specialists along with ophthalmologists, ENT specialists, orthopedic surgeons, neurosurgeons, orthodontists, cardiologists, urologists and maxillofacial surgeons to decide on the most appropriate treatment plan, which varies with age and systemic associations. Goldenhar Syndrome can affect the routine and social life of the patient. Early detection can help avoid complications at a later stage of life.

The prognosis for this condition is good in patients with no systemic complications.[19] They can live relatively normal lives and have a normal life span. They can get married, have children and enjoy work and recreational pursuits. Management of Goldenhar Syndrome requires long term commitment with treatment from birth to the period of growth and development.

Declaration of patient consent

We have obtained informed written consent from the patient. All the images and other clinical information to be reported in the journal with the patients consent. The patient understand that her name and initials will not be published and due efforts will be made to conceal her identity and gave her consent.

Interest of conflict: None

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