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Editorial

Dengue Vaccine: Past, Present and Future

BACKGROUND

Dengue infection, one of the most devastating mosquito-borne viral diseases in human, is now a significant problem in many countries like Bangladesh. It is estimated that some 500 000 people with dengue require hospitalization due to warning signs or severe dengue,[1] and causes about 20 000 deaths every year.[2] Considering fatal and non-fatal outcomes together, dengue was responsible for 114 million disability-adjusted life-years (DALYs).[2]

The causative dengue viruses are members of the genus Flavivirus, within the family Flaviviridae. There are four closely related serotypes, the dengue viruses (DENV) 1-4 and at least four genotypes within each serotype. Flaviviruses are lipid-enveloped, positive-strand RNA viruses, that encodes three structural proteins, namely capsid protein (C), precursor membrane/membrane protein (PrM/M) and envelope protein (E). Besides structural proteins, there are seven nonstructural proteins (NS) which are associated with viral replication and disease pathogenesis. The disease, caused by the four-dengue virus serotypes, ranges from asymptomatic infection to undifferentiated fever, dengue fever (DF), and severe dengue hemorrhagic fever (DHF). The primary vector, the urban-adapted Aedes aegypti, has become widely distributed across tropical and subtropical latitudes.

The 4 dengue serotypes are serologically and genetically distinct,[3] although they share several structural antigens. Following an infection with one DENV serotype, the antibodies induced are typespecific and also cross-reactive with other DENV serotypes. After human inoculation via the bite of an infected female mosquito, the virus replicates in local dendritic cells. Subsequent entry into macrophages and activation of lymphocytes is followed by entry into the bloodstream. Dengue viruses primarily infect cells of the myeloid lineage, including macrophages, monocytes, and dendritic cells. Haematogenous spread is the likely mechanism for infection of peripheral organs.

Prevention depends primarily on control of the mosquito vector which has achieved only limited success in reducing transmission of dengue. The primary vector, the urban-adapted Aedes aegypti, has become widely distributed across tropical and subtropical latitudes. It has spread globally with the advent of increased travel and trade in the past 50 years.

CURRENT DEVELOPMENT OF DENGUE VACCINES

The first dengue vaccines were evaluated in 1929.[4] Development of safe and effective dengue vaccines faces many challenges. Infection by one of the four dengue virus serotypes has been shown to confer lasting protection against homotypic reinfection, but only transient protection against a secondary heterotypic infection. Moreover, secondary heterotypic infection is associated with an increased risk of severe disease. Due to these dengue-specific complexities, vaccine development focuses on the generation of a tetravalent vaccine aimed at providing long-term protection against all virus serotypes. Despite those challenges, vaccine development has made remarkable progress in recent years, and the current dengue vaccine pipeline is advanced, diverse, and overall promising. At present, several dengue vaccines have been tested in human clinical trial, and a single candidate is now in phase III clinical trials. Different approaches in dengue vaccine development are discussed herein.

Live attenuated virus vaccine: The first major effort at live attenuated dengue vaccine development began at the University of Hawaii using the traditional method of serial passage of virus in a nonhuman host and then transferred to Mahidol University in Bangkok, Thailand for further passage and development of candidate vaccines and testing.[5,6] The candidate vaccine was used for phase I and II clinical trials in Thai adults and children. Not all of the volunteers seroconverted to all four dengue serotypes and some showed unacceptable reactogenicity, consequently further clinical testing was stopped.[7,8] Although the

development of this candidate vaccine was not successful, the initiative was responsible for the subsequent progress that has been made in developing a live attenuated tetravalent dengue vaccine.[9]

Chimeric virus vaccine: The US Centers for Disease Control and Prevention (CDC) developed a tetravalent chimeric dengue vaccine by inserting DENV-1, -3 and -4 prM and E genes into cDNA derived from the successfully attenuated DEN-2 component of the Mahidol University-Sanofi Pasteur live attenuated dengue virus vaccine (DEN-2, 16681 PDK-53). Dengue-dengue chimeras tetravalent vaccine candidate was then formulated and licensed to Inviragen, Inc. and Takeda respectively and has undergone clinical testing [10-13]

Inactivated virus vaccine: Inactivated whole virus vaccines have two advantages since they cannot revert to a more pathogenic phenotype, and they are unlikely to interfere with each other in combination. Moreover, induction of cell-mediated and humoral immune responses have been demonstrated with inactivated flavivirus vaccines.[14]

Subunit vaccines: Recombination subunit approaches offer advantages, including anticipated minimal reactogenicity and freedom from adventitious agents. However, incomplete post-translational processing of proteins can lead to proteins that differ from native proteins and antibody responses.[15] Production in mammalian cells may reduce some of these concerns.[16]

Dengue DNA vaccines: They offer a possible method to raise protective immunity, by passing the problem of interference seen with multivalent live virus vaccines. DNA vaccines are composed of a plasmid or plasmids containing dengue genes. Tetravalent DNA vaccine inoculated in mice and monkeys successfully raised neutralization antibodies. Monkeys resisted challenge with DEN-1 but not DEN-2.[17,18]

A DENV-1 DNA vaccine: It was evaluated in flavivirus-negative volunteers with the three-dose series at day 0, and at 1 and 5 months. None of the volunteers receiving a low dosage and half of those receiving a high dosage developed neutralizing antibodies.[19]

Vectored vaccines: Recombinant poxviruses and adenoviruses expressing foreign proteins have been demonstrated to induce strong humoral and cellular responses in humans against various pathogens. Several live virus vectors such as adenovirus, alphavirus, and vaccinia virus are designed for direct administration to the host and have been engineered to express DENV E protein for further evaluation as dengue vaccine candidates.[12,20]

CONCLUSION

Dengue virus is the causative agent of a wide spectrum of clinical manifestations, ranging from mild acute febrile illness to classical DF and DHF. DHF is caused by the potentially fatal forms of dengue virus infection, which has become an intractable global health problem. Vector control has achieved only limited success in reducing the transmission of dengue and there are currently no licensed antivirals to treat dengue. The most effective way to control dengue diseases in the future will include the use of a safe and effective vaccine. Dengue is a unique and complex disease; developing a dengue vaccine has proven equally complex. Although no licensed dengue vaccine is yet available, several vaccine candidates are under development, including live attenuated virus vaccines, live chimeric virus vaccines, inactivated virus vaccines, and live recombinant, DNA and subunit vaccines. The live chimeric virus vaccine is undergoing a phase III clinical trial. Other vaccine candidates have been evaluated in preclinical animal models or are being prepared for clinical trials.

For the first time in dengue-prone Bangladesh, researchers from International Centre for Diarrhoeal Disease Research, Bangladesh (ICDDR,B) and the Lerner College of Medicine at the University of Vermont in the United States have completed research on an encouraging tetravalent dengue vaccine, i.e., a vaccine that is effective against all four types of dengue virus. The study evaluated the single dose dengue vaccine TV-005 and found it to be safe for use in children, adults and able to induce immunity. The study results were recently published in the Lancet Infectious Diseases journal.[21]

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Original Article

Determinants of Type 2 Diabetes Mellitus among Children and Adolescents Attending A Tertiary Specialized Hospital in Bangladesh

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ABSTRACT

Background: *Type 2 diabetes in children and adolescents has increased in frequency around the world over the past two decades. The worldwide epidemic of childhood obesity has been accompanied by an increase in the incidence of type 2 diabetes in children and adolescents.*

Objective: *To observe the determinants of type 2 diabetes mellitus among children and adolescents attending a tertiary specialized hospital in Bangladesh.*

Methods: *This cross-sectional, descriptive study was done on a total of 151 children and adolescents attending the pediatric diabetic out-patient department (OPD) of Bangladesh Institute of Research and Rehabilitation in Diabetes, Endocrine and Metabolic Disorders (BIRDEM) Hospital, Dhaka, Bangladesh. The sampling technique was purposive. All patients who came to the hospital between July to December 2017 were included. Data was collected through a structured questionnaire.*

Results: *Among 151 respondents, 98 were in age group of 10-14 years (64.9%), female to male ratio of 1.22:1. The majority belonged to a high used to lead socio-economic class. Regarding food habit, 55.6% had history of taking fast food regularly used to lead sedentary lifestyle with lack of exercise. 43.7% children and adolescents were obese 76.8% had high cholesterol and 84.1% had high triglyceride levels. Most of the children had positive family history of type 2 diabetes mellitus (74.8%).*

Conclusion: *Our study reflects that determinants like obesity, physical inactivity, eating habit, family history are important factors of development of type 2 diabetes mellitus in children and adolescents.*

Keywords: *Bangladesh, children and adolescents, type 2 diabetes mellitus*

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INTRODUCTION

Type 1 diabetes is one of the most common chronic diseases among children and adolescents. Recently, type 2 diabetes has increasingly been reported in children and adolescents[1]. Type 2 diabetes has become increasingly common among children aged 6-11 years and adolescents aged 12-19 years[2-3]. A recent epidemiological review has led to the suggestion that as many as 8–45% of new-onset pediatric diabetes cases in the United States may be type 2[4-6]. Data from the Indian Health Service national outpatient database showed that the prevalence of diabetes in those aged 15-19 years increased by 68% between 1990 and 1998 (3.2 per 1000 to 5.4 per 1000). In all these children type 2 diabetes mellitus was

related to obesity and appeared at the time of puberty[7]. At present it has assumed epidemic proportions in Japan, Canada, and the United States.[8] Data from Libya, Bangladesh and aboriginal children in Australia and Canada indicate that childhood type 2 diabetes is occurring in these populations[9]. The prevalence of IGT in this group is reported to be 17.1% in a study done in Bangladesh;[10] and observed between 10% and 30% in various studies performed in different countries[11]. In a study done in school going children in India, the prevalence of pre-diabetes was 3.7%.[9] The prevalence of IFG (Impaired fasting glucose) was 3.4% & Type 2 diabetes was 1.8% in a study done in different schools in Bangladesh[12]. This study helped us to find out the magnitude of problems of Type 2 diabetes in children & adolescents, among obese adolescent population in our country. Hence, early diagnosis of risk factors, early interventions can be done to reduce mortality and morbidity. Type 2 diabetes happens when the body cannot effectively use the insulin it produces, due to both impairment of insulin secretion& resistance of insulin action. Type 2 diabetes depend on a combination of risk factors such as genes and lifestyle. The modifiable risk factors are eating habits, physical inactivity & weight gain. Although non-modifiable risk factors are family history, age, or ethnicity. The development of type 2 diabetes at an early age is likely to be associated with earlier development of complications[13-14]. Currently, more than 200 children and adolescents develop the disease everyday.[15]

To the best of our knowledge, there is hardly any specific study on clinical characteristics of type 2 diabetes in children and adolescents in our country. Our study aims to determine the baseline characteristics of type 2 diabetes in children and adolescents who were coming for follow-up in pediatric diabetic out-patient department (OPD) of Bangladesh Institute of Research and Rehabilitation in Diabetes, Endocrine and Metabolic Disorders (BIRDEM) Hospital, Dhaka, which is a tertiary specialized hospital in Bangladesh.

METHODS

This cross-sectional, descriptive study was conducted among a total of 151 children and adolescents attending the pediatric diabetic out-patient department (OPD) of Bangladesh Institute of Research and Rehabilitation in Diabetes, Endocrine and Metabolic Disorders (BIRDEM) Hospital, Dhaka, Bangladesh. A purposive sampling technique was adopted. All patients who came to the hospital between July and December of 2017 were included as study population. Data was collected through a structured questionnaire.

In a resource limited developing country like Bangladesh, C-peptide, antibody, or insulin level are not routinely done to classify the type of diabetes rather classify on clinical basis. Researchers do not fully understand why some children develop type 2 diabetes and others do not, even if they have similar risk factors. Type-2 diabetes occurs when insulin secretion is inadequate to meet the increased demand posed by insulin resistance, leading to relative insulin deficiency[16]and is generally associated with other metabolic abnormalities characteristic of insulin resistance (dyslipidaemia, hypertension, polycystic ovary syndrome, fatty liver etc.).

Informed consent was obtained from the parents to use the data of the children and adolescents and the family members for scientific purposes. Details of socieo-demographic and clinical history were recorded. Blood pressure was measured by auscultation after 5 minutes of rest and hypertension was diagnosed when blood pressure was e"95th percentile for age and sex[17]. Dietary habits were recorded. Healthy food habit contains all the components of food with exact proportions (carbohydrate, fat, proteins, and fibers), while fast food items are easily prepared and available yet are low on their nutritional values and contain extra fat and protein contents. The body mass index (BMI) was calculated as weight in kilogram divided by square of the height in meter. BMI was calculated and classified using the cutoff points (e"85th percentile overweight and e"95th percentile as obese) using the Center for Disease Control and Prevention growth chart[18]. Waist circumference was measured along with height and weight. A cutoff 0.5 was used to differentiate low waist to height ratio (WHtR) from high WHtR[19,20]. Regarding family history of first- and second-degree relatives of type 2 diabetes, had more chance of development of diabetes 74.8%. Investigations such as fasting blood glucose, glycated hemoglobin (HbA1c) and lipid profile were routinely done in all patients at diagnosis. Estimation of blood glucose and lipid profile was done by enzymatic colorimetric method using multichannel auto analyzer. Total cholesterol>200mg, triglyceride >150mg/dl, low-density lipoprotein cholesterol >130mg/dl and high-density lipoprotein <40mg/dl were designated abnormal.[21,22] HbA1c was assessed by Clover A1c using photoelectric method.

Data were processed using the Statistical Package for the Social Sciences (SPSS) (SPSS Inc, Chicago, IL., USA) version 20.0 for Windows. Continuous variables were

expressed as mean±SD and compared between groups by using unpaired student's t-test. Categorical variables were expressed as frequency and percentage and compared using the Chi-square test. The level of significance was at 95% confidence interval and a p-value <0.05 was considered as significant. The study was approved by the Institutional Review Board of Bangladesh Institute of Research and Rehabilitation in Diabetes, Endocrine and Metabolic Disorders (BIRDEM), Dhaka, Bangladesh.

RESULTS

Among 151 respondents, majority of determinants were in age group of 10-14years (64.9%) female predominance (54.9%) with female to male ratio of 1.22:1. Most of them were from urban areas (78.8%) and had a family history of DM (97.35%) (Table-I). The majority of them belonged to high socio-economic class (Fig. 1), history of eating fast food regularly, used to lead sedentary lifestyle with lack of exercise (Table-II, Fig. 2 & 3). Regarding family history of first and second-degree relatives of type 2 diabetes, had developed diabetes (74.8%). 43.7% of children and adolescents were obese,76.8% had high cholesterol and 84.1% had high Triglyceride. According to BMI, among 151 children and adolescents, 54(35.8%) had normal weight, 66(43.7%) were overweight, 31(21.5%) were obese, 73.5% of girls' hip circumference were >80cm and 14.7% of boys' hip circumference >90cm were considered to be in high-risk group. 7(4.6%) patients had hypertension. They were advised to follow up with weight-reducing dietary advice. 102 patients had their HbA1c >9.0%; hypertriglyceridemia was found in 15.9% and hypercholesterolemia in 23.2% patients (Table-III).

Table-I : *Demographic status among children and adolescents with type 2 diabetes (n=151)*

Characteristics	Frequency	Percentage
Age group		
7-9 years	9	5.96
10-14 years	98	64.9
15-19years	44	29.14
Gender		
Male	68	45.1
Female	83	54.9
Living Area		
Urban	119	78.8
Rural	32	21.2
Family history for DM		
Positive	147	97.35
Negative	4	2.65

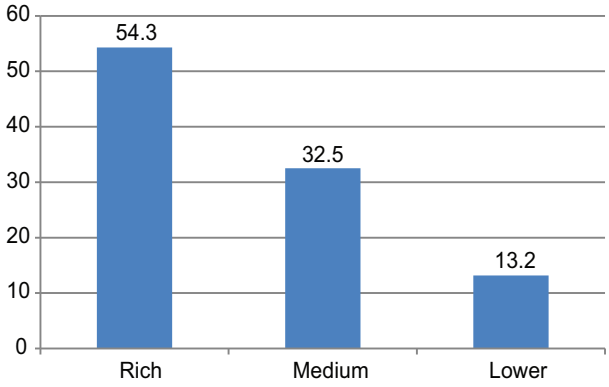

Figure 1: Socio-economic status of the children's family. (According to social welfare Department of BIRDEM Hospital, Lower income group BD Taka <10000/month, Medium income group BD Taka 20000-40000/month, Rich income group BD Taka >40000taka/month)[23]

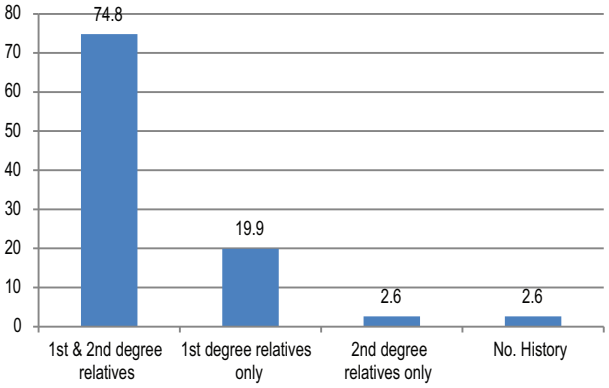

Figure 2: Distribution of family history of DM among participants (parents, siblings-first degree relatives by consanguinity, grandparents-second degree relatives)

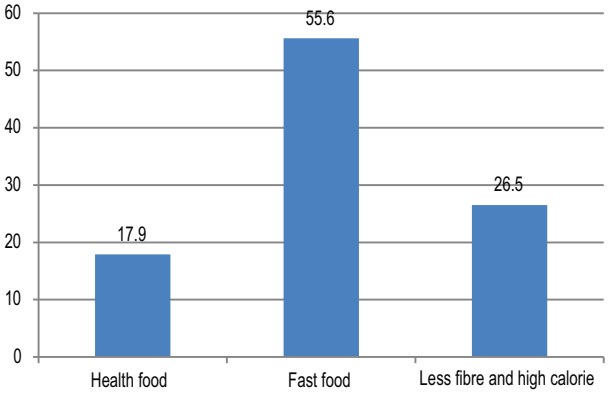

Figure 3: Dietary habits of the participants (n=151)

Table-II : *Association of Food habit and physical exercise and level of HbA1c (n=151)*

Characteristics	HbA1c level						P value
	<7.50		7.50 – 9.00		>9.00		
	Frequency	Percentage	Frequency	Percentage	Frequency	Percentage	
Food habit							
Healthy food habit	6	22.2	4	18.2	17	16.7	>0.05^{NS}
Unhealthy food habit	21	77.8	18	81.8	85	83.3	
Physical exercise							
Sedentary lifestyle	0	0.0	0	0.0	72	70.6	<0.001^{S}
Adequate	27	100.0	22	100.0	30	29.4	

S=significant; NS=not significant.

Table-III : *Clinical characteristics of type 2 diabetes mellitus among participants (n=151)*

Characteristics	Frequency	Percentage
BMI		
Normal weight	54	35.8
Overweight	66	43.7
Obese	31	21.5
Mean hip circumference (cm)	91.75±10.57	
Mean waist circumference (cm)	90.75±8.93	
Blood Pressure		
Mean systolic BP (mm of Hg)	112±11.5	
Mean diastolic BP (mm of Hg)	71.8±7.6	
Glycated hemoglobin (HbA1c)		
>9%	102	67.5
7.5-9%	22	14.6
<7.5%	27	17.9
Lipid profile		
Mean cholesterol (mg/dl)	175.47±49.54	
Mean triglycerides (mg/dl)	107.43±96.11	

DISCUSSION

The present study was undertaken to assess the determinants of type 2 diabetes among 151 children and adolescents attending the pediatric diabetic outpatient department of a tertiary specialized hospital. Most of our participants were from urban areas. Rapid urbanization has become a risk factor for type 2 diabetes. In one study, found that 86% of cases were from urban area, which is similar to some other studies.[23-25]

The American Academy of Diabetes recommends for screening overweight in children aged 10 years or more with a family history of diabetes and or signs of insulin resistance for diabetes[5]. Another study looked at familial history and other factors in weight management strategies to prevent further metabolic diseases.[26] In our study, 6% were diagnosed at 7-9 years of age, which was similar to a recent report[27]. The worldwide epidemic of childhood obesity has been accompanied by an increase in the incidence of type 2 diabetes in youth. Obesity was present in more than half of my patient, which was consistent in a study done in Asian-Indian children.[28] In the present study, the majority of the children and adolescents (54.3%) belonged from higher socio-economic class. This finding was surprising to us; it was previously well accepted that obesity was prevalent among affluent society.[29]

Along with family history, obesity stands out as a prominent risk factor for the development of type 2 diabetes. In our study, 83.3% of the children and adolescents with type2 diabetes had a history of taking fast food or rich food intake. Moreover, 70.6% of children and adolescents with type 2 diabetes had sedentary lifestyle. When compared blood sugar level (HbA1c) with physical inactivity, it was significantly ($p<0.001$) related to the development of type 2 diabetes. Hyperlipidemia is a well-known co-morbidity in children and adolescents with type 2 diabetes. Isolated hypertriglyceridemia (15.9%) and hypercholesterolemia (23.2%) were found in our patients. Hypercholesterolemia in one third and hypertriglyceridemia in more than half patients were found in a study done in Australian youth with type 2 diabetes.[30]

CONCLUSION

Our data revealed that certain determinants like obesity, physical inactivity, eating habits, family history are important factors of development of type 2 diabetes in children and adolescents. Association of different risk factors with type 2 diabetes were analyzed and physical inactivity was significantly related to development of type 2 diabetes. Family history of first- and second-degree relatives of type 2 diabetes also increases chance to develop diabetes at later age. In this study, triglyceride and cholesterol levels were significantly higher among children and adolescents having type2 diabetes. Fasting blood glucose, 2 hours after breakfast and glycated hemoglobin (HbA1c) need to be routinely done in all children having those factors present in their medical history.

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Original Article

Association between Serum Ferritin and Insulin Resistance Markers with Distinct Glycemic Profiles in an Adult Bangladeshi Population

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ABSTRACT

Background: *Type 2 diabetes mellitus (T2DM) is a global health concern. Around 56% of subjects in Bangladesh go undiagnosed, increasing the risk of stroke and cardiovascular issues. Iron stores impact on diabetes is gaining attention, with ferritin as a key biomarker. Hyperferritinemia probably contributes to insulin resistance and subsequently to decreased insulin secretion, causing the development of insulin resistance. The link between ferritin and insulin resistance (IR) varies based on ethnicity, gender, and glycemic state.*

Objectives: *This study investigates serum ferritin levels in different glycemic stages and explores potential correlations between ferritin and insulin resistance markers (blood glucose, serum insulin and HOMA-IR)*

Methods*: The study was conducted at the Department of Biochemistry, Sir Salimullah Medical College, Dhaka, Bangladesh, from March 2018 to February 2019. A total of 140 subjects were included to conduct this study. Participants were categorized into three groups: those with normal fasting glucose (NFG group), impaired fasting glucose (IFG group), and newly diagnosed type 2 diabetes mellitus (Diabetic group) according to WHO (2006) criteria. A purposive convenient sampling method was used, focusing on adults aged 25 to 55 years. Exclusion criteria were applied to eliminate individuals with inflammatory diseases, chronic conditions, major cardiovascular events, anemia, or specific medications that could affect ferritin levels.*

Results: *The study found that serum ferritin levels significantly differed among three glycemic groups (NFG, IFG, and T2DM) with higher levels in T2DM. IFG and T2DM groups also had elevated serum insulin and HOMA-IR. Serum ferritin correlated strongly with fasting blood glucose, serum insulin, HOMA-IR, and BMI . The highest tertile of ferritin levels were associated with IFG & diabetic group.*

Conclusion. *Elevated serum ferritin levels in IFG and type 2 diabetes may significantly impact on glucose regulation. Compared to NFG, there are high insulin resistance markers (fasting insulin, glucose, HOMA-IR) in T2DM and IFG. They have crucial implications for both therapy and prognosis in these conditions.*

Keywords*: S.Ferritin, IR Markers, Glycemic state.*

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INTRODUCTION

As a predominant public and medical issue, the emergence of T2DM has increased dramatically in recent years and put a tremendous burden on medical, economic and social infrastructure. The International Diabetes Federation (IDF) estimates that in 2015, there were 415 million people with diabetes worldwide and indicates that the absolute number will reach 642 million by 2040[1]. For every diagnosed diabetic case, another one is undiagnosed; overall, undetected people are at significantly higher risk for stroke, coronary artery disease, and peripheral vascular disease. The proportion of undiagnosed DM

in Bangladesh is about 56.0 %[1]. While obesity and diabetes are reaching epidemic proportions in the developed world, the role of insulin resistance and its sequelae is gaining prominence[2]. Genetic and environmental factors cause IR & lead to impaired glucose tolerance, and play a crucial patho-physiological role in the development of diabetes[3]. Insulin resistance occurs before the development of T2DM and might be the best indicator for it[4]. Recent studies have shown Insulin resistance syndrome (IRS) correlated with increased serum ferritin, suggesting the pathophysiological link between the severity of IRS and serum ferritin levels[5].

There is an increasing interest in the adverse health outcomes associated with elevated body iron stores[6]. Through its oxidative properties, iron has also been suggested to play a role in IR and beta cell dysfunction, which are cardinal features of altered glucose homeostasis[7] Iron is the body's most abundant metal and an essential human nutrient. It is a cofactor for several enzymes involved in oxidation-reduction reactions due to its ability to exist in two ionic forms-ferrous and ferric[8]. Elevated iron stores may induce diabetes through various mechanisms, including oxidative damage to pancreatic beta cells, impairment of hepatic insulin extraction by the liver and interference with insulin's ability to supress hepatic glucose production. Long-term microvascular and macrovascular complications of diabetes may be due to raised serum ferritin[9-11]. Body iron stores are commonly assessed by serum ferritin, a widely available clinical biomarker to evaluate iron status[8,12]. Cross-sectional studies indicate an independent link between high iron stores and T2DM occurrence[13,14]. And found Ferritin, a reliable marker, has been linked to glycemic status and complications of Diabetes Mellitus, including Retinopathy, Nephropathy, Neuropathy, and Vascular dysfunction[15].

A few studies have demonstrated an association between markers of insulin resistance (fasting insulin, glucose and HOMA-IR) and ferritin[16,17]. They found that plasma ferritin concentrations positively correlate with fasting insulin and fasting glucose. Some observational studies have shown that elevated serum ferritin is associated with IR when assessed by HOMA-IR[18,19]. Another survey by Suarez-Ortegan[19] showed that serum ferritin did not significantly predict HOMA-IR in the healthy Colombian population. A study on the Finnish population suggests that the strength and direction of the association between serum ferritin and HOMA-IR depend on the population's glycemic state[7].

In diabetes mellitus, increased glycation of transferrin decreases its ability to bind ferrous iron. Hence, there is an increased pool of free iron, which stimulates increased ferritin synthesis[20]. An increase in Ferritin synthesis is believed to result in the internalization of Insulin receptors, which contributes to Insulin resistance[11]. Thus, glucose metabolism is found to be interlinked with iron metabolism and measuring serum ferritin levels as part of diabetic management could aid in predicting the outcomes. Higher ferritin concentrations are observed in Asian populations, and even moderately increased iron stores are associated with diabetes[12,21]

A previous study observed positive correlation between serum ferritin concentration and HbA1c in T2DM patients in our country[22] But association of body iron stores and glucose homeostasis at different glycemic states were unclear.

Hence, We proposed this study to assess the association of serum ferritin to insulin resistance markers (fasting insulin, glucose and HOMA-IR) in three different glycemic states and tried to establish its role in glucose homeostasis.

METHODS

It was a cross-sectional, observational study conducted at the Department of Biochemistry of Sir Salimullah Medical College, Dhaka, Bangladesh, between March 2018 and February 2019. A total of 140 subjects were included to conduct this study divided into three groups: Group A having individuals with normal fasting glucose (NFG group) and Group B having individuals with impaired fasting glucose (IFG group), and Group C having individuals with newly diagnosed type 2 diabetes mellitus (Diabetic group). Adult people aged 25 to 55 years were included. Participants with acute or chronic inflammatory diseases, chronic liver diseases, major cardiovascular events, chronic alcoholism, and anaemia were excluded by history taking and clinical examinations. Conditions that altered ferritin level, e.g. Hemochromatosis, history of blood transfusion or iron therapy in the previous year and subjects with very high serum ferritin level (>800 ng/ml) were excluded. History of taking antidiabetic, lipid-lowering agents, or other medication that affect

carbohydrate, lipid or insulin metabolism were also excluded. Those with malignancy and pregnancy were excluded. All surveys were conducted after obtaining written informed consent. Anthropometric variables were measured accordingly, and a blood sample was collected to measure biochemical variables.

Subjects were selected from the outpatient department (OPD) of Medicine and Endocrinology of Sir Salimullah Medical College and Mitford Hospital, Dhaka, and National Academy for Educational Management (NAEM), Dhaka, as a part of their routine examination. Before collecting specimens, each eligible person was firmly approached and proper counselling about aims, objectives, and risks. benefit and procedure of the study were done. Only voluntary candidates were recruited as participants. Then they were interviewed, and relevant information was recorded systematically in a pre-designed standard datasheet, including general information and history of chronic diseases, and family history of diabetes. Data were checked and edited. All surveys were conducted after obtaining written informed consent. Anthropometric variables were measured accordingly, and a blood sample was collected to measure biochemical variables.

Diabetes was defined according to the WHO 2006 guidelines as having fasting blood glucose measurement e"7.0 mmol/L. Normal fasting glucose (NFG) indicates a healthy state where the blood glucose level is below 6.1 (mmol/L) after fasting. In impaired fasting glucose (IFG) signifies a condition in which the fasting plasma glucose falls between 6.1 and 6.9 mmol/L, suggesting a potential risk for diabetes. or having been diagnosed by a physician. Markers of insulin resistance as assessed by Fasting insulin, glucose and HOMA-IR[23]. BMI was calculated as weight in kilograms divided by the square of height in meters.

All statistical analyses were performed using SPSS (statistical package for social science) for Windows 22.0 version. The mean with standard deviation was determined to compare continuous variables. ANOVA test was done to compare continuous variables. Bonferonni test was performed for the comparison of groups. Serum ferritin concentrations were divided into tertiles to observe the trend of the related variables. The statistical significance, direction and strength of linear correlation between two quantitative variables were measured using Pearson's correlation coefficient test. $p<0.05$ was considered a test of significance in all statistical tests. Sample size was determined by applying the formula for a comparison of two means. Using IR values from Kim et al.[24]

The study was approved by the Ethical Review Committee of Sir Salimullah Medical College, Dhaka, Bangladesh.

RESULTS

The study is basically targeted to analyze the serum ferritin behaviour in the three groups representing different stages of glycemia. Table-I meticulously compiles mean values and standard deviations (SD) of baseline and biochemical parameters across three distinct glycemic groups. Notably, parameters such as age, BMI, SBP, DBP, WC, WHR, fasting plasma glucose, serum insulin, HOMA-IR, and serum ferritin exhibited significant differences among these groups ($p<0.001$), as validated by the ANOVA test.

Upon applying the Bonferroni test for intergroup comparisons, it emerged that serum ferritin levels were notably higher ($p<0.001$) in individuals with Type 2 Diabetes (T2DM) compared to those in the Impaired Fasting Glucose (IFG) group. Furthermore, subjects with IFG and T2DM displayed significantly elevated ($p<0.001$) serum insulin and HOMA-IR levels compared to the Normal Fasting Glucose (NFG) group. Specifically, the mean ferritin concentration was markedly higher in subjects with IFG (84.04±80.79) and newly diagnosed T2DM (158.1± 44.9) in comparison to those with NFG (40.50±28.512) (Fig. 1).

Table-II shows insightful correlations between serum ferritin and key variables—fasting blood glucose, serum insulin, HOMA-IR—across the studied groups. Notably, strong correlations existed between serum ferritin and fasting blood glucose, serum insulin, and HOMA-IR levels. Furthermore, a significant correlation was found between serum ferritin and participants' Body Mass Index (BMI). These correlations were consistent across groups, lacking significant differences.The normal reference interval of serum ferritin has a wide range because of age and gender variations9 The reference range for adult male is between 20-270 µg/L and that of adult female is 10-120 µg/L. In the current study, we also observed that ferritin distribution was positively skewed. Higher tertiles of serum ferritin were notably (Â0.01) associated with Type 2 Diabetes (T2DM) Illustrated in Figure 2.

Table-I: *Characteristics of the studied population (n=140)*

Variables	Group A (NFG) (n=60)	Group B (IFG) (n=50)	Group C (T2DM) (n=30)	p-value
Age (years)	35.60±8.77	42.64±8.54	49.73±5.13	<0.001
BMI (kg/m^2)	23.25±2.18	27.74±2.29	27.75±2.29	<0.001
SBP (mmHg)	113.88±10.65	115.20±7.57	118.9±10.7	<0.001
DBP (mmHg)	75.50±8.61	83.60±5.69	87.7±4.17	<0.001
WC (inch)	85.05±7.77	97.56±7.31	94.4±9.0	<0.001
WHR	0.83±0.10	0.95±0.10	0.95±0.08	<0.001
FPG (mmol/L)	5.14±0.40	6.26±0.17	9.69±2.41	<0.001
Serum Insulin (µU/ml)	5.98±1.90	11.64±2.62	12.67±4.27	<0.001
HOMA -IR.	0.78±0.25	1.60±0.31	1.89±0.64	<0.001
Serum ferritin (ng/mL)	40.50±28.51	84.04±80.79	158.1±44.9	<0.001

	Age	BMI	Serum Insulin (µU/ml)	HOMA -IR.	Serum ferritin (ng/mL)
Group A vs B	0.002	<0.001	<0.001	<0.001	<0.05
Group A vs C	<0.001	<0.001	<0.001	<0.001	<0.001
Group B vs C	<0.05	1.000	0.758	0.067	<0.001

Data were expressed as mean±SD; ANOVA test was performed to compare the three groups.

Table-II : *Correlation of serum ferritin with BMI, FPG, serum insulin and HOMA IR*

Name	Overall		Group A (NFG) (n=60)		Group B (IFG) (n=50)		Group C (T2DM) (n=30)	
Variables	r	p-value	r	p-value	r	p-value	r	p-value
BMI	0.297	0.007	0.384	0.515	0.185	0.376	0.383	0.159
FPG	0.520	<0.001	0.448	0.554	0.303	0.141	0.243	0.382
S.insulin	0.461	<0.001	0.191	0.238	0.156	0.456	0.129	0.648
HOMA -IR	0.504	<0.001	0.156	0.336	0.181	0.387	0.191	0.495

Correlation is significant at the 0.05 level (2-tailed); Pearson correlation coefficient test was performed.

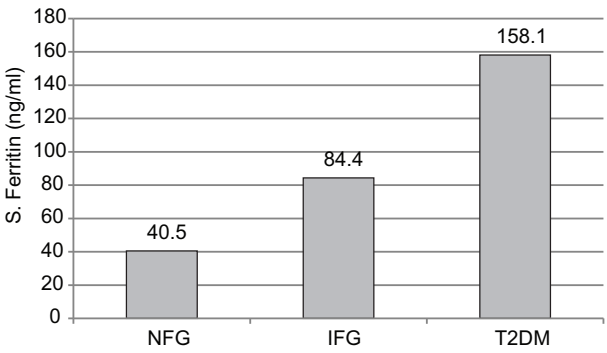

Figure 1: *Bar diagram showing mean ferritin concentration between three groups, showing increased serum ferritin levels in type 2 DM compared to the NFG and IFG groups.*

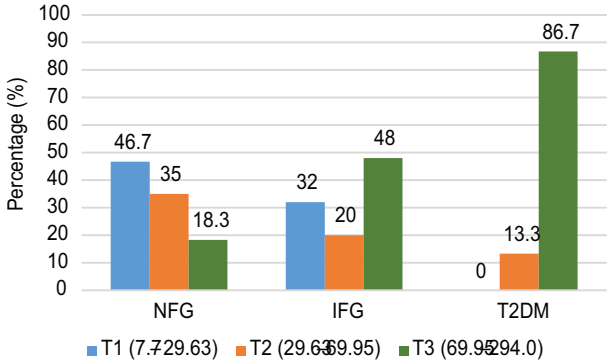

Figure 2: *Showing serum ferritin tertile with the association of glycemic status, where 86.7% of T2DM patients belonged to the highest tertile, which is statistically significant.*

DISCUSSION

The impact of type 2 diabetes mellitus (T2DM) on Bangladesh's economic and social well-being is significant, with macrovascular complications appearing before the disease manifests. Screening for T2DM is crucial for surveillance and identifying individuals with prediabetes for timely interventions[25]. Body iron stores are commonly assessed by serum ferritin, a key protein that regulates iron homeostasis, a widely available clinical biomarker to evaluate iron status[12]. The study analyzed serum ferritin due to its interconnection with iron and glucose metabolism[13]. A total of 140 subjects were included in this study based on predefined enrollment criteria. The subjects comprised 60 normoglycaemic, 50 with impaired fasting glucose and 30 newly diagnosed type 2 diabetes mellitus. Therefore, this cross-sectional study evaluated the association between serum ferritin concentration and IR markers (fasting insulin, glucose and HOMA-IR) in Bangladeshi adult subjects of different glycemic states.

Serum ferritin levels were significantly higher in IFG and diabetics compared to the NFG group, consistent with previous research findings[11,23]. In the present study, subjects with impaired fasting glucose (IFG) and type 2 diabetes mellitus (T2DM) exhibited a notable rise in serum insulin and HOMA-IR levels when compared to the normal fasting glucose (NFG) group, as indicated in Table I. This finding aligns with the results reported by a previous study conducted over six years in France. The French study demonstrated that individuals with elevated serum ferritin levels faced an increased risk of hyperinsulinemia and high HOMA-IR values in both genders [26].

The exact mechanism linking elevated serum ferritin with insulin resistance IR is not fully understood, but several theories have been proposed. Iron's pro-oxidant nature can induce oxidative stress, disrupting insulin signaling at the cellular level[13]. Secondly, ferritin can increase pro-inflammatory cytokines, potentially mediating its association with IR[27]. Thirdly, iron accumulation in the liver may interfere with insulin extraction, impairing glucose tolerance[27] Lastly, iron might hinder insulin action and glucose utilization in adipocytes, contributing to IR. According to Pramiladevi et al.[9]elevated serum ferritin levels might contribute to insulin resistance (IR) even before the onset of diabetes. A prospective study by Jung et al.[28] demonstrated that the risk of IR increased proportionately to serum ferritin levels, independent of metabolic factors, suggesting the predictive value of serum ferritin in IR. Frequent blood donation and phlebotomy therapy have been linked to improved insulin sensitivity, as reported in studies[13]. In this study, higher serum ferritin tertile levels were significantly associated with impaired glycemic states (IFG and T2DM) (Fig II), aligning with findings from a survey by Koo et al. [29,] which suggested that hyperferritinemia might increase the risk of diabetes mellitus through heightened insulin resistance rather than dysfunctional beta cells. In a prospective study, Nakamura et al.[30] observed that clinically high-normal and mildly elevated iron storage in the body may cause diabetes, mainly by inducing insulin resistance, regardless of race. This influence is likely independent of the potential pathway between obesity and insulin resistance.

It was evident from the study that high serum ferritin, serum insulin and HOMA-IR were observed in IFG and type 2 diabetic subjects, and hyperferritinemia was significantly associated with insulin resistance markers like fasting insulin, glucose and HOMA-IR.

We found a positive association between ferritin and BMI and showed that higher serum ferritin is associated with increased BMI. However, we did not consider obesity status, which is positively correlated with the degree of insulin resistance.

CONCLUSION

To conclude, our data reveals a positive correlation between serum ferritin levels and glycemic status, particularly in IFG and diabetes mellitus type 2, compared to normoglycaemic subjects., IFG and type 2 diabetic subjects had higher insulin resistance markers (fasting insulin, glucose and HOMA-IR) levels than the NFG group, which presents significant opportunities in diagnosing and managing diabetes. This finding holds promise for predicting an individual's tendency to develop diabetes and related complications. Integrating serum ferritin assessments into screening programs could identify high-risk individuals, enabling targeted preventive measures. Lowering elevated serum ferritin levels through interventions offers a potential avenue for reducing

the morbidity and mortality associated with type 2 diabetes mellitus.

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Original Article

Comparison of the Effects of Nitroglycerin, Labetalol and Lidocaine in Hypertensive Patients in Attenuation of the Endotracheal Intubation Reflex

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ABSTRACT

Background: *Laryngoscopy and tracheal intubation integral parts of general anesthesia which may cause acute haemodynamic instability. Hypertensive patients are more prone of developing cardiovascular complications such as pulmonary oedema, cardiac failure and cerebrovascular haemorrhage. To attenuate such intubation reflex, some drugs are used, e.g., opioids. lidocaine sodium nitroprusside, nitroglycerin, beta blockers, calcium channel blockers etc.*

Objective: *The purpose of the study is to see the effectiveness of nitroglycerin, labetalol and lidocaine in attenuation of intubation reflex and their anesthetic outcome in hypertensive patients.*

Methods: *This randomized controlled study was carried out in the Department of Anesthesia, Pain, Palliative and Intensive care Medicine, Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka, Bangladesh, between March and September of 2021. A total of 90 patients were included: 30 in each group as per inclusion and exclusion criteria. Group A patients received inj. nitroglycerin 2 minutes before intubation, while group B patients received inj. labetalol 0.25mg/kg 5 minutes before intubation, and group C was given 2% lidocaine 1.5mg/kg 2 minutes before intubation. Haemodynamic status of all patients was checked before and after intubation.*

Results: *Mean age of the patients was 44.4±10.9 years in group A, 47.6±9.4 years in group B and 46.4±10.6 years in group C. Heart rate after intubation was low and statistically significant in groups-B after 1.2 and 5 minutes. Regarding mean arterial pressure (MAP), group A patients had significantly low blood pressure. Rate pressure product (RRP) of the patients was significantly low in group B at 1 minute, 2 minutes and 5 minutes. Regarding ECG changes sinus tachycardia was observed in 26.6%, 86.6% and 20% in group A, group B and group C immediately after intubation. Groups B patients showed lower incidence of sinus tachycardia than that of two other groups and showed no premature ventricular contractions, whereas group A (6.7%) and group C (3.3%) showed premature ventricular contractions.*

Conclusion: *Labetalol showed better rhythm control, mean arterial pressure and less incidence of tachycardia. To summarize, labetalol is safer and more effective than nitroglycerin and lidocaine to attenuate the endotracheal intubation reflex in hypertensive patients.*

Keywords: *Endotracheal intubation reflex, hypertensive patient, nitroglycerin, labetalol, lidocaine*

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INTRODUCTION

Tracheal intubation is an important part of general anaesthesia where muscle relaxation and controlled ventilation is needed. The most important response of laryngoscopy and intubation often results in hypertension and tachycardia.[1,2] These responses are mediated by the cardioaccelerator nerves and sympathetic chain ganglia with widespread release of norepinephrine and epinephrine.[2] The degree of reflex response to laryngeal stimulation appears to vary with the depth of anaesthesia, the duration as well as on patient-dependent variables including age and cardiovascular disease.[3] These effects are generally well tolerated by overall healthy patients but can be lethal to patients with preexisting conditions such as hypertension, coronary artery disease, recent myocardial infarction, geriatric population, pre- eclampsia, and cerebrovascular pathology such as tumours, aneurysms or increased intracranial pressure etc. and are at increased risk of morbidity and mortality.[4]

Hypertension is a common comorbid condition among Bangladeshi adults which is increasing every year.[5] During laryngoscopy and endotracheal intubation hypertensive patients more frequently develop various cardiovascular events such as pulmonary oedema, cardiac failure, and cerebrovascular haemorrhage than that of normotensive patients.[6] Endotracheal intubation induces increased plasma concentration of catecholamines and there may be associated myocardial ischaemia and cerebral haemorrhage. There have been various attempts were taken to attenuate this sudden response. However, no specific regimen or drug combination has demonstrated effectiveness in the attenuation of this response in patients requiring endotracheal intubation.[6,7] Methods like smooth and gentle intubation, blocking the glossopharyngeal nerve and superior laryngeal nerve have been used but none of these approaches have been proved entirely satisfactory.[6] Increasing the depth of anaesthesia often results in haemodynamic compromise. A wide variety of pharmacological agents were also tried to attenuate the hemodynamic responses to laryngoscopy and endotracheal intubation like lidocaine, opioids, sodium nitroprusside, nitroglycerin, beta blockers, calcium channel blockers with varying results.[7]

Nitroglycerin, a direct acting vascular smooth muscle relaxant intravenous or sublingually has been used for attenuating hypertensive response during laryngoscopy, tracheal intubation and for controlling hypertension during intubation.[8] Nitroglycerin generates nitric oxide in vascular smooth muscle which produces vasodilation leading to decrease in blood pressure; however, it increases blood flow to the myocardium.[9] Intravenous bolus dose of nitroglycerin as 1-2 ìg/kg administered at the start of laryngoscopy and intubation was found to be effective in attenuating the hypertensive response.[8]

Labetalol is an antihypertensive drug which is selective alpha-1 and nonselective beta-1 and beta-2 adrenergic antagonist. It decreases the systemic vascular resistance by alpha-1 blockade and thereby lowers the blood pressure. It also causes simultaneous beta blockade which attenuates the reflex tachycardia occurring because of vasodilatation.[10,11] It was found that inj. labetalol as administered 0.15-0.3 mg/kg body weight has effectively attenuates the sympathoadrenal response to laryngoscopy and intubation.[11]

Lidocaine was used initially in the management of arrhythmias. It subsequently was found to be effective as a topical anesthetic and in the administration of regional and neuraxial anesthesia. Intravenous lidocaine has anti-inflammatory, analgesic, anti-hyperalgesic properties and is used for attenuating stress response to laryngoscopy and intubation.[10,12] Lidocaine (1.5mg/kg) blunts the sympathetic response during intubation, extubation and surgical stimulation.[12]

The purpose of our study is to see the effects of these three drugs in attenuation of the endotracheal intubation reflex. The result of the study is expected to help aneasthesia physicians to effectively manage hypertensive patients by reducing those cardiovascular complications due to endotracheal intubation reflex, and provide good anesthetic outcome, less hospital stays and reduced treatment cost by using those common drugs.

METHODS

This randomized controlled study was carried out in the Department of Anaesthesia, Analgesia and Intensive care Medicine, Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka, Bangladesh, between March and September of 2021. The patients included in the study were 18 between 70 years with previously diagnosed hypertension (became normotensive under antihypertensive drug while

participating in the study). However, patients receiving â-blockers or nitrates and had history of myocardial ischemia or infarction, cerebrovascular stroke, pulmonary, hepatic, and renal diseases were excluded. We used a convenient sampling technique. Finally, a total of 90 patients were included in the study based on our inclusion and exclusion criteria. The patients were randomly and equally allocated into three groups by computer generated random numbers, i.e., 30 in each group. Group A received inj. nitroglycerin 2 ìg/kg (diluted up to 5 ml in distilled water) 2 minutes before intubation, while group B received inj. labetalol 0.25 mg/kg (diluted up to 5 ml in distilled water) 5 minutes before intubation, and group C was the control group and received inj. 2% lidocaine 1.5 mg/kg (diluted up to 5 ml in distilled water) 2 minutes before intubation. Pre-anesthetic check-up was done in all the patients on the day before surgery. Patients on regular antihypertensive medication whose arterial blood pressure was d"140/90 during the preoperative anesthetic visit before surgery. On arrival of the patient in the operating room ASA standards monitoring system were attached with the patients and baseline parameters such as heart rate (HR), ECG, blood pressure (BP), respiratory rate, and oxygen saturation (SpO_2) were observed and recorded. Intravenous (IV) access was established with 18G cannula on non-dominant upper arm. All patients were pre-hydrated with 500 ml of Ringer's lactate solution. The Patients were pre-oxygenated with 100% oxygen for three minutes. Then the study drug was given as mentioned above. After that the patients were induced with Fentanyl 1.5 ìg/kg, 2.5% thiopental sodium 5mg/kg till the eyelash reflex was lost, followed by succinylcholine 1.5mg/kg IV to facilitate tracheal intubation. After the disappearance of fasciculation, laryngoscopy and intubation was done using standard Macintosh laryngoscope. The Patients were ventilated with 50% N_20 in 50% 02. Immediately after tracheal intubation, ECG, heart rate, systolic, diastolic, and mean arterial blood pressure (MAP), rate pressure product (RPP) was recorded as 0 minute. After 5 min, administration of volatile inhalational agent was started. The Patients were maintained on inhalational agent and a non-depolarizing muscle relaxant as per the need of the surgical procedure. At the end of surgery residual neuromuscular block was antagonized with intravenous inj. neostigmine 50ìg/kg and inj. atropine 20ìg/kg. Patients were observed for any side effects like hypotension, bradycardia, arrhythmias, and bronchospasm during the intraoperative period. If the patient developed hypotension, then treated with inj. Ephedrine and if the patient developed bradycardia, then he/she was treated with inj. atropine. Evaluation of the response to intervention: All haemodynamic parameters were recorded during the basal period, immediately after intubation (0 min), 1 minute, 2 minutes, and 5 minutes after intubation.

After multiple checks, data was recorded in a predesigned data collection sheet. Continuous variables were expressed as mean±SD and compared between groups by using unpaired student's t-test. Categorical variables were expressed as frequency and percentage and compared using the Chi-square test. The level of significance was at 95% confidence interval and a P-value <0.05 was considered as significant. Data were analyzed using SPSS (Statistical package for Social Sciences) version 22.0. The study was approved by the Institutional Review Board of Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka, Bangladesh.

RESULTS

Patients were randomly divided into three groups having 30 patients in each group. We observed the haemodynamic response before and after laryngoscopy and tracheal intubation after intravenous administration of nitroglycerin and labetalol. We considered group C as the control group who received standard lidocaine injection. The mean age of the patients was 44.4±10.9 years in group A, 47.6±9.4 years in group B and 46.4±10.6 years in group C. On consideration of weight, the patients had 61.2±7.3 kg, 62.5±6.7 kg and 63.6±5.4 kg respectively. No significant differences were observed in age, weight, sex and duration of laryngoscopy among those groups (P<0.05) (Table-I). There were no significant differences in heart rates (HR) among those groups before induction; however, in group B heart rate became lower than the other groups which was statistically significant at 0-minute, 1 minute, 2 minutes and 5 minutes (P<0.05). Heart rates were well maintained in all three groups; however, it was lowest in group B that received inj. labetalol (Table-II). Regarding the mean arterial pressure (MAP) between three groups which was significantly decreased in group A than group B and C at 0 minute (P<0.05). However, there was no significant difference (P>0.05) in case of MAP in other recordings at different time

intervals (Table-III). The rate pressure product (RPP) of the patients was significantly lower in group B at 1 minute, 2 minutes and 5 minutes except 0 minute than that of other two groups. RPP was also significantly lower in group A than that of group C at 0 minute (Table-IV). Regarding ECG changes at different times, sinus tachycardia was observed in 13.3%, 16.7% and 10% in group A, group B and group C respectively before induction. However, no other types of rhythm abnormalities were obserbved in any of the groups before induction. 26.7% of the patients in group A, 6.7% in group B and 20% in group C developed sinus tachycardia immediately after intubation; group B shows lower incidence of sinus tachycardia. In Group B, 10% after 1 minute, 13.3% patient after 2 minutes and 20% patient after 5 minutes developed sinus bradycardia, whereas it was 3.3%, 10% and 6.7% respectively in group C. No patient in group A had sinus bradycardia. 6.7% and 3.3% of the patients developed premature ventricular contractions after 1 minute of intubation in group A and group C respectively, while no patient in group B was found with premature ventricular contraction (Table-V).

Table-I: *Demographic characteristics of the patients and duration of laryngoscopy (n=90)*

Characteristics		Group A (n=30)	Group B (n=30)	Group C(n=30)	P value
Age (in years)		44.4±10.9	47.6±9.4	46.4±10.6	0.72
Weight (kg)		61.2±7.3	62.5±6.7	63.6±5.4	0.57
Gender	Male	18(60%)	16(53.4%)	20(66.67%)	0.69
	Female	12(40%)	14(47.6%)	10(33.33%)	0.65
Duration of Laryngoscopy (in seconds)		22.8±4.6	21.4±4.9	22.1±4.2	0.67

Table-II: *Comparison of heart rates of the patients (n=90)*

Heart rate (beat/min)	Group-A (n=30)	Group-B (n=30)	Group C (n=30)	P value A vs B	P value B vs C	P value C vs A
Before Induction	76.6±7.6	79.2±6.8	78.3±6.5	0.262	0.342	0.423
0 minute	79.7±7.3	69.3±5.5	80.8±6.7	0.005[s]	0.003[s]	0.321
1 minute	76.2±5.5	70.4±5.3	75.3±6.3	0.021[s]	0.028[s]	0.357
2 minutes	75.3±6.2	70.5±5.9	74.2±6.2	0.029[s]	0.029[s]	0.369
5 minutes	76.4±6.8	71.1±5.7	75.8±6.1	0.034[s]	0.037[s]	0.321

Table-III: *Comparison of mean arterial pressure (MAP) of the patients (n=90)*

Mean arterial pressure (mmHg)	Group A (n=30)	Group B (n=30)	Group C (n=30)	P value A vs B	P value B vs C	P value C vs A
Before Induction	94.6±6.3	97.2±5.4	96.2±5.8	0.64	0.57	0.63
0 minute	86.3±7.1	92.6±5.5	90.8±4.8	0.014[s]	0.64	0.042[s]
1 minute	90.2±5.5	90.4±5.3	90.9±5.7	0.52	0.74	0.72
2 minutes	93.3±6.2	89.5±5.9	94.4±5.9	0.43	0.36	0.63
5 minutes	93.8±6.7	90.1±5.7	94.9±6.4	0.48	0.43	0.58

Table-IV: *Comparison of rate pressure product (RRP) of the patients (n=90)*

Rate pressure product	Group A (n=30)	Group B (n=30)	Group C (n=30)	P value A vs B	P value B vs C	P value C vs A
Before Induction	11095.8±863	10970.2±880	11734.51±=882	0.43	0.53	0.61
0 minute	8889.6±931	8553.1±758	9934.6±834	0.36	0.023[s]	0.027[s]
1 minute	8983.7±859	7535.4±832	8625.6±925	0.018[s]	0.037[s]	0.34
2 minutes	9456.3±932	7342.5±892	8621.8±921	0.002[s]	0.019[s]	0.49
5 minutes	9763.5±976	7658.4±927	9261.3±989	0.004[s]	0.013[s]	0.53

S = statistically significant

Table- V: *ECG rhythm changes at various intervals (n=90)*

ECG Rhythm	Group A(n=30)			Group B(n=30)			Group C(n=30)			
	WNL	ST	PVC	WNL	ST	SB	WNL	ST	SB	PVC
Before induction	26(86.7%)	4(13.3%)	-	25(83.3%)	5(16.7%)	-	27(90%)	3(10%)		-
Just after ETI (0 minute)	20(66.6%)	8(26.7%)	2 (6.7%)	28(93.3%)	2(6.7%)	-	23(76.7%)	6(20%)		1(3.3%)
1 minute after ETI	22(73.3%)	8(26.7%)	-	26(86.7%)	1(3.3%)	3(10%)	26(86.7%)	3(10%)	1(3.3%)	-
2 minutes after ETI	24(80%)	6(20%)	-	25(83.3%)	1(3.3%)	4(13.3%)	24(80%)	3(10%)	3(10%)	-
5 minutes after ETI	29(96.7%)	1(3.3%)	-	24(80%)	-	6(20%)	25(83.3%)	3(10%)	2(6.7%)	-

Data was expressed as frequency and percentage. ETI: Endotracheal intubation; WNL: Within normal limit; ST: Sinus tachycardia; SB: Sinus bradycardia; PVC: Premature ventricular contraction

DISCUSSION

Endotracheal intubation reflex ensued by direct laryngoscopy technique results in transient changes mainly of cardiovascular, respiratory and central nervous physiology by reflex sympathetic stimulation and catecholamine discharge.[1,2] Hypertensive patients remain a concern for the anesthesia physician, as they are more prone to greater cardiovascular responses resulting more complications.[1,5] Hemodynamic response to laryngoscopy and intubation begins immediately after tracheal intubation and reaches maximum value within one minute. Therefore, timing of drug administration and their peak effect, used for attenuation of hemodynamic response, should correspond to those of hemodynamic response.[11]

The three groups of our study were comparable. The patients from labetalol group (group B) showed significantly lower heart rate in comparison to nitroglycerin and lidocaine at every interval after intubation. In the other two groups, there was no significant rise or fall of heart rate after intubation compared to baseline value. In our study, labetalol corroborates well with the findings of Kim et al. who reported that a single dose of labetalol of dosage 0.25 mg/kg given preoperatively 5 minutes before intubation decreases heart rate significantly after intubation up to 10 minutes.[13] Roelofse et al. found that labetalol of dosage 1 mg/kg given as i.v. bolus dose 1 min before laryngoscopy was not effective in the attenuation of heart rate.[14] This finding of that study can be explained by the different time of administration of the study drug because labetalol IV has onset of action at 2-3 min and has peak effect after 5 min.

However, the finding of heart rate in group B and group C of our study did not match with some previous studies as we observe no significant rise or fall of heart rate after intubation. They had documented that nitroglycerine does not attenuate the rise in heart rate after intubation which can be attributed to reflex tachycardia produced by vasodilation.[15,16] Regmi & Singh observed that nitroglycerine significantly decreases blood pressure, prevents rise in RPP but does not attenuate heart rate after endotracheal intubation.[17] These can be explained by difference in induction drugs, e.g., Mikawa et al. used IM atropine 0.01 mg/kg as premedication which could induce tachycardia,[15] while Grover et al. used glycopyrrolate 0.2 mg in all patient which could slightly rise the heart rate.[16] Both the studies used vecuronium to facilitate tracheal intubation, whereas in our study, we used succinylcholine 1.5 mg/kg which is a known drug that can cause bradycardia. The difference might be the cause of no significant rise in heart rate.

In our study, systolic blood pressure (SBP) was well controlled in all three groups; however, group B (labetalol) showed more sustained control than group C (lidocaine) and group A (nitroglycerin) group at all the time intervals after intubation. group B showed lower value of systolic blood pressure at 2 minutes and 5 minutes interval. The mean arterial pressure (MAP) was significantly decreased in group A at 0-minute but there was no significant difference in case of MAP at other time intervals. For systolic and mean arterial pressure the result of labetalol and lidocaine group corroborates with other recent studies. Jaiswal et al. showed that both lidocaine (1.5 mg/kg) and labetalol (0.25 mg/kg) effectively blunt the hemodynamic pressor response to endotracheal intubation and definitely have cardio protective action,[18] while Ratnani et al. reported that labetalol works better.[19] In our study systolic blood pressure was significantly lower in group A at 0 minute and 1

minute than two other group this can be explained by relative early onset of action and shorter duration of action of nitroglycerin. This finding is similar with the result of recent studies, Mikawa et al. reported single IV dose of nitroglycerin is a practical, effective, and safe method for attenuating the intubation induced hypertension.[15] Regmi & Singh showed nitroglycerin significantly decreases blood pressure, prevents rise of rate pressure product (RPP), but does not attenuate heart rate after endotracheal intubation.[17] Singh et al. reported that i.v. lidocaine 1.5 mg/kg is also an effective agent in suppressing hemodynamic response to laryngoscopy and intubation without any deleterious effect.[20]

In our study, RPP always remained below 12,000 in all three groups after intubation. In group B, RPP was the lowest throughout the post-intubation period. Nitroglycerin and lidocaine group also showed good control over rate pressure product throughout the study period. This finding confirms the cardio-protective effect of study drugs during laryngoscopy and intubation. It was showed that labetalol had more cardio-protective effect than nitroglycerin and lidocaine as the RPP was lower in labetalol group than two other groups. Swami et al. also found RPP in labetalol group was lower than that of other group at intubation, 1 min post intubation and onwards.[21] In another study done by Ratnani et al. showed mean RPP was most effectively attenuated by labetalol, whereas lignocaine showed least attenuation effect among their three study drugs.[19] It may be worth mentioning that nitroglycerine also showed similar response while used through sublingual route.[22]

In our study, among the three study drugs labetalol group showed better rhythm control in ECG as there was less incidence of tachycardia, rhythm abnormality like premature ventricular contraction was noted in group A (nitroglycerin) and group C (lidocaine). Incidence of tachycardia was highest in nitroglycerin group. Control of ECG rhythm in lidocaine group was better than nitroglycerin group as there was less incidence of tachycardia and premature ventricular contraction. This finding corroborates with other previous studies.[23,24] Besides, no cardiac dysrhythmias were noted in the study with labetalol.

In this study, we observed some of the haemodynamic variables (heart rate, blood pressure and rate pressure product) and electrocardiographic rhythm changes in hypertensive patients treated with study drugs. However, respiratory, hormonal, and central nervous system changes were not measured. With both intra and inter-group comparison all three drugs were effective for the attenuation of heart rate, systolic blood pressure, mean arterial pressure and rate pressure product after endotracheal intubation through direct laryngoscopy.

CONCLUSION

All three medications were effective in attenuation of direct laryngoscopic intubation reflex. The hemodynamic parameters such as heart rate, blood pressure, rate pressure product and elertrocardiographic rhythm changes were relatively more stable in labetolol group as compared to nitroglycerin and lidocaine. To summarize, labetalol is safer and more effective than nitroglycerin and lidocaine to attenuate the endotracheal intubation reflex in hypertensive patients.

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Original Article

Bacteriological Study and Antibacterial Susceptibility in Ludwig's Angina in a Tertiary Level Hospital in Dhaka, Bangladesh

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ABSTRACT

Background: *The knowledge of the local pattern of infection and antibacterial sensitivity in Ludwig's angina is essential to enable efficacious treatment for it.*

Objective: *To find out the pattern of bacteria responsible for developing Ludwig's angina and their antibacterial susceptibility.*

Methods: *It is a prospective, observational type of study carried out in the Department of Otolaryngology & Head-Neck Surgery, Dhaka Medical College Hospital, Dhaka and Department of Clinical Microbiology, ICDDR,B, Dhaka, Bangladesh, between April and September of 2016. A total of 100 patients were included in this study.*

Results: *This study was done among 100 patients. In this study 42 cases (42%) were in the 31-45 years age group. The male patients were 60 (60%) and female were 40 (40%). Majority of patients 70(70%) came from poor class family with educational level up to HSC (75%), maximum 35(35%) patients use meswak to clean teeth, 70 (70%) patients came from rural area, 70 (70%) patients had dental infection, 25 (25%) patients had diabetes mellitus, all the cases (100%) presented with swelling in the floor of the mouth and neck, pain and tenderness and fever. The major complication was necrotizing fasciitis 8 (8%), 36 (36%) patients were discharged within 1-2 weeks after treatment, Streptococcus 40 (40%) was the most common organism and most effective antibiotic was Ceftriaxone (65%).*

Conclusion: *The most frequently isolated organism in Ludwig's angina is Streptococcus and sensitivity results showed majority of isolates is susceptible to Ceftriaxone.*

Keywords: *Ludwig's angina, microorganism, antibiogram, antibiotics.*

Mugda Med Coll J. 2023; 6(2): 71-76

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INTRODUCTION

Ludwig's angina is a rapidly progressive, potentially fulminant cellulitis of the submandibular space. It is named after the German physician Willhem Frederick von Ludwig, who first described the condition in 1836. The word 'angina' comes from the Greek *ankhon* meaning 'strangling'.[1] It is manifested by swelling of the floor of the mouth, tense edema and induration of submental soft tissues and elevation and posterior displacement of tongue. The pain and trismus, along with swelling of the oral and cervical tissues and tongue displacement, create a severely compromised airway.[2] Grodinsky developed strict criteria for the diagnosis of Ludwig's angina. According to him the disease can be recognized by five identifying characteristics: (1) the infection is a cellulitis of the submandibular space, not an abscess; (2) it never involves only one space, and it is usually bilateral;

(3) the cellulitis causes gangrene with sero-sanguineous infiltration and very little or no frank pus; (4) the cellulitis attacks the connective tissue, fascia, and muscles, but not the glandular structures; and (5) the cellulitis spreads by tissue continuity, not by the lymphatics.[3] Over 80 percent of patients have a dental infection and the rest usually have an upper respiratory tract infection.[1]The most common predisposing factors for the development of Ludwig's angina are carious and abscessed teeth, periodontal disease and extractions of the lower molars. Other etiology includes floor of the mouth trauma, mandibular fractures, peritonsillar abscess and sialdadenitis.[4] The second and third mandibular molars have roots which lie at the level of the mylohyoid muscle either adjacent to or below the submandibular space. Abscesses of these lower molar may perforate the mandible and spread into the submandibular and submental spaces, leading to Ludwig's angina.[5]Mixed infections involving both aerobes and anaerobes are common. Streptococcus viridans is the most common pathogen followed by Staphylococcus epidermidis, Staphylococcus aureus and Escherichia coli.[1] Pseudomonas spp,Bacteroides spp.,Fusobacterium spp., Actinomyces spp. and Haemophilus influenzae are also identified.[3] A study identified Sterptococcus (40.62 %), Staphylococcus (18.75 %), E.Coli (12.5 %), Pseudomonus (9.37%), Proteus (2%), Klebsiella (1%) among the 12 most common pathogens.[6] All age groups may be affected. Patients are often elderly and young. There is trismus and excessive salivation. The swelling is diffuse, and there is erythema and cellulitis of the skin. The floor of the mouth appears oedematous, brown in colour with the tongue pushed upwards and back which can cause a potential airway obstruction.[1] Patients have neck swelling, pain, and elevation of the tongue, malaise, fever, dysphagia and stridor. The submandibular area can be indurated, sometimes with palpable crepitus.[7,8] The diagnosis and treatment of deep neck space infections have challenged physicians and surgeons. The complexity and the deep location of this region make diagnosis and treatment of infections in this area difficult. The diagnosis is based on the history and examination and made on clinical grounds. The white cell counts and the inflammatory markers, such as ESR and CRP, are usually raised. The ultrasound or CT scan will delineate the abscess and confirm diagnosis, although abscess formation is rare if initial antibiotic therapy is targeted at gram-positive, gram negative organisms and oral cavity anaerobes. Empirical therapy with IV penicillin G, clindamycin or metronidazole is recommended before culture report is available. Antibiotic treatment before hospital admission often results in sterile cultures. Intravenous steroids can be given for 48 hours & it can decrease edema and cellulitis and thus help maintain the integrity of the airway and enhance antibiotic penetration.[8] Usually this illness is associated with other comorbid conditions. It is very important to identify and address these comorbidities. Diabetes mellitus is an important comorbid condition which should be checked for. Proper handling of diabetes is also an important part of comprehensive treatment. Complications includes airway obstruction due to laryngeal edema or swelling or pushing back of tongue, extension to mediastinum causing mediastinitis, sepsis and septicemia, pleural empyema, pericarditis, and pericardial tamponade and even may result in the death of the patient.[4]

This study will predict the microorganisms responsible for Ludwig's angina and their antibacterial susceptibility and help the ENT and Head Neck surgeon to diagnose and manage patients of Ludwig's angina in Bangladesh thereby decreasing mortality and morbidity of the patient.

METHODS

This prospective, observational type of descriptive study was conducted in the Department of Otolaryngology & Head-Neck Surgery of Dhaka Medical College Hospital, Dhaka and Department of Clinical Microbiology of International Centre for Diarrheal Disease Research, Bangladesh, (ICDDR,B), Dhaka, Bangladesh, between April and September of 2016. Our study population included all the patients of different age, sex admitted into the Department of Otolaryngology & Head-Neck Surgery with Ludwig's angina. However, a total of 100 patients were finally included in the study based on our inclusion and exclusion criteria. We adopted a nonrandom, convenient, purposive sampling technique.

Inclusion criteria:

1. All the diagnosed cases of Ludwig's angina in whom incision and drainage were done to obtain pus which was sent for culture and sensitivity
2. All the diagnosed case of Ludwig's angina who gave consent willingly to take part in the study.

Exclusion criteria:

1. All cases of Ludwig's angina treated conservatively.
2. All the diagnosed cases of Ludwig's angina who will not give consent willingly to take part in the study.

Informed written consent was taken from the patient or the legal guardian of the patient. Patient personal history, medical history and records, clinical examination findings, culture and sensitivity report of the pus collected were recorded in a structured questionnaire data sheet. Thus, our data sheet was prepared including patient questionnaire, examination findings and investigation results. Wound swab or pus was collected by dry swab stick according to standard method and the sample was sent to the designated lab immediately for culture and antibiotic sensitivity. The culture and sensitivity tests were done in the Department of Clinical Microbiology of ICDDR,B, Dhaka. The swab was first moistened by sterile normal saline and then inoculated on blood agar, MacConkey agar and chocolate agar media. The plates were incubated aerobically at 37^0C for 18-24 hours. Antibiotic sensitivity testing was done by Kirby Bauer disc diffusion method. Susceptibility to antibiotic reports were reported as per CLSI (Clinical and Laboratory Standards Institute) guidelines of 2020. Following antibiotics were considered for sensitivity testing:

Amikacin, Amoxiclav, Ampicillin, Azithromycin, Cefixime, Ceftazidime, Ceftriaxone, Ciprofloxacin, Cloxacillin, Cotrimoxazole, Doxycycline, Gentamicin, Levofloxacin, Penicillin G &Vancomycin.

The sensitivity patterns of the isolates were categorized as 'Sensitive' and 'Resistant'.

Collected data were coded, kept confidential and processed and analyzed using computer software SPSS (Statistical Package for Social Sciences) version 20.0. The test statistics used for analysis of data were t-test (for comparison of data presented in quantitative scale). For any analytical test the level of significance was 0.05 and $p<0.05$ was considered statistically significant.

The study was approved by the Ethical Review Committee of Bangladesh College of Physicians and Surgeons (BCPS), Dhaka, Bangladesh.

RESULTS

Most of the patients (42%) were in the 31-45 years age group (Table-I). Among the participants, 60% was male and 40% was female. Male-female ratio was 1.5:1. Most of the patients (35%) used meswak to clean their teeth (Fig.1). 70% of the cases presented with dental infection followed by history of tooth extraction (10%) (Fig. 2). 25% of the cases presented with diabetes mellitus, while 15% presented with isolated diabetes mellitus (Table-II). Table-III shows that all of the cases (100%) presented symptoms of swelling in the floor of the mouth and neck, pain and tenderness and fever followed by dysphagia (80%) and dental infection (70%). However, more than one symptom was present in all patients. Major complications observed among the patients were necrotizing fasciitis and septicemia (30.8%) followed by mediastinitis (23.1%) (Fig. 3). Most of the patients (36%) were discharged from hospital within 1-2 weeks (Fig. 4). Table-IV shows that Streptococcus (40%) was the most common organism followed by Staphylococcus aureus (23%). However, no organism was found in 5% cases. Mixed organisms were responsible for most of the infections in 30% cases (Table-V). Table-VI shows that most effective antibiotic was Ceftriaxone (65%), followed by Ceftazidime (58%).

Table-I: *Age distribution of patients (n=100)*

Age group (in years)	No. of cases	Percentages
1-15	5	5
16-30	15	15
31-45	42	42
46-60	34	34
>60	4	4
Total	100	100

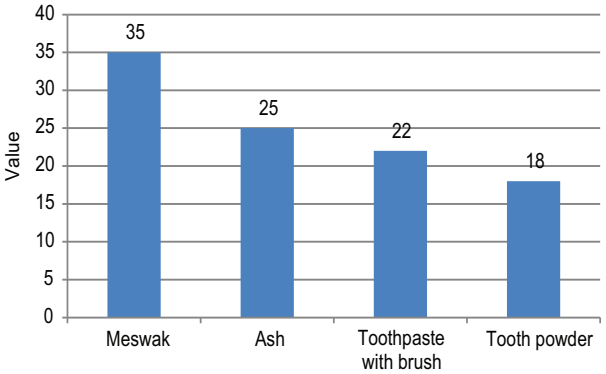

Fig. 1: *Distributions of patients by personal tooth cleaning habits (n=100)*

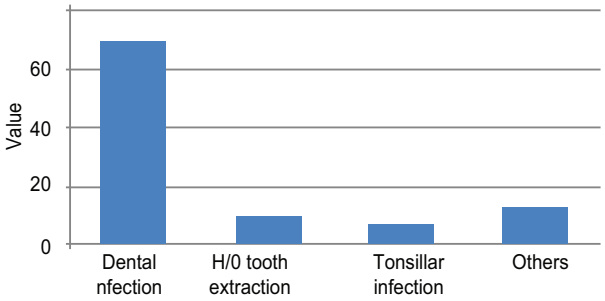

Fig. 2: *Distribution of the patients based on aetiological factors (n=100)*

Table- II : *Comorbidities among patients (n=100)*

Aetiological factors	Number of cases	Percentages
Isolated Diabetes mellitus	15	15
Diabetes mellitus with aetiological factors	10	10
No Diabetes Mellitus	75	75
Total	100	100

Table- III : *Distribution of the patients by clinical presentation (n=100)*

Symptoms	Number of cases	Percentages
Swelling in the floor of the mouth and neck	100	100
Pain and tenderness	100	100
Fever	100	100
Dysphagia	80	80
Dental infection	70	70
Trismus	15	15
Foul smell	24	24
Respiratory distress	3	3
Muffled voice	10	10

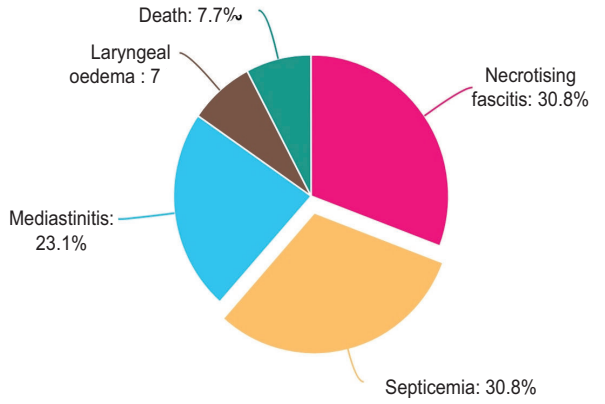

Fig. 3: *Complications observed among the patients (n=100)*

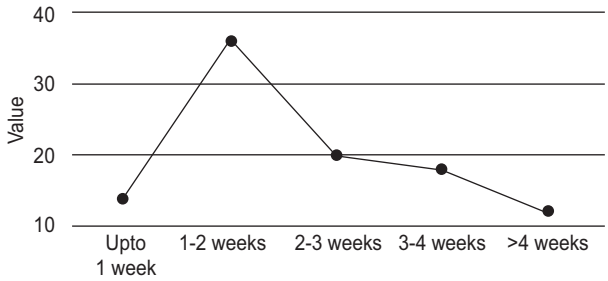

Fig. 4: *Duration of hospital stay among the patients (n=100)*

Table-IV : *Identification of causative microorganisms in the pus of Ludwig's (n=100)*

Strains	Number of cases	Percentages
Streptococcus viridans	40	40
Staphylococcus aureus	23	23
Coagulase negative staphylococcus	20	20
Escherichia coli	13	13
Pseudomonas	12	12
Proteus	11	11
Klebseilla	16	16
No organism	5	5

Table-V: *Identification of causative microorganisms in the pus of Ludwig's angina: Isolated and mixed microorganism (n=100)*

Strains	Name of organism	Number of cases	Percentages
Isolated	Streptococcus viridans	25	25
	Staphylococcus aureus	15	15
	Coagulase negative staphylococcus	10	10
	E coli	10	5
	Pseudomonas	5	3
	Proteus	3	5
	Klebsiella	2	2
Mixed		30	30
No organism		5	5
Total	100	100	

Table-VI: *Identification of isolated microorganism and their antibiotic sensitivity (n=95)*

	Antibiotics								
	Strep (25)	Staph (15)	CNS(10)	E. coli(5)	Pseud(3)	Prot(2)	Kleb(5)	Mixed(30)	Total(95)
Amikacin	9	5	5	4	2	2	4	11	42
Amoxiclav	18	12	8	2	1	1	2	6	50
Ampicillin	18	10	5	2	0	0	1	5	41
Azithromycin	20	8	2	2	1	2	5	0	40
Cefixime	15	8	7	3	1	1	4	11	50
Ceftazidime	17	10	9	4	2	2	4	10	58
Ceftriaxone	19	11	8	4	3	2	4	14	65
Ciprofloxacin	16	10	8	4	2	2	4	10	56
Cloxacillin	20	12	8	1	0	1	2	0	44
Cotrimoxazole	13	9	7	3	1	1	3	5	42
Doxycycline	8	7	5	4	2	2	4	8	40
Gentamicin	7	5	5	5	2	2	4	11	41
Levofloxacin	15	7	6	2	1	1	2	6	40
Penicillin G	18	8	6	2	0	0	1	6	41
Vancomycin	21	13	8	2	1	1	2	4	50

DISCUSSION

Ludwig's angina is an infection of the submandibular region, manifested by swelling of the floor of the mouth and elevation and posterior displacement of the tongue.[6] In the pre-antibiotic era, Ludwig's angina was frequently fatal, antibiotics and aggressive surgical intervention have frequently reduced mortality.[17] Regarding age distribution our study showed maximum cases were in the 35-45 years age group (42%) followed by 46-60 years age group (34%). In this study, males were affected more than female. The male and female ratio was 1.5:1. De Best et al. also found male female ratio in their study 2:1.[9] In this study, most of the cases used meswak to clean their teeth (35%) followed by ash (25%). This poor tooth cleansing habit might explain their susceptibility to dental infection and subsequent development of Ludwig's angina. Another study done by Fakir et al. they found 41% patients used meswak and 20% used ash to clean their teeth.[6]

In this study, most of the clinical presentation of the patients were dental infection (70%) followed by a history of tooth extraction (in 10% patients). Lemonick et al. showed in their study dental infection was the prime cause in Ludwig's angina (63%).[14]

In comorbidity association we found in this study 25 % cases presented with diabetes mellitus, whereas Sakarya EU et al studied diabetic mellitus as comorbidity in ludwig's angina of 21%.[10]

In all the cases 100 (100%) presenting symptoms were swelling in the floor of the mouth and neck, pain and tenderness and fever. More than one symptom was present in all patients. Mahmud et al. and Fakir et al. showed in their study 90% and 87% cases clinical presentation were more than two feature respectively.[6,16]

In this study, most of the complications of Ludwig's angina were necrotizing fasciitis (8%) followed by septicemia (7%) and mediastinitis (6%). Two patients were died due to mediastinitis. Christian et al. found septicemia, necrotizing fascitis, mediastinitis as in 10%, 7% and 5% of the patients respectively.[11]

In the opresent study, most of the patients were discharged from hospital after adequate treatment within 1-2 weeks (36%). In this study, Streptococcus viridans 40 (40%) was the most common organism followed by staphylococcus aureus (23%), Coagulase negative staphylococcus (20%), Klebseilla (16%), Escherichia coli (13%), Pseudomonas (12%), Proteus (11%) cases. Mixed infection was found (30%) of cases. Maran et al. identified Streptococcus viridans (39%) was the most common pathogen followed by

Staphylococcus epidermidis (22%), Staphylococcus aureus (22%) and Escherichia coli.[1]Fakir AY et al. identified 50 Sterptococcus (40.62 %), Staphylococcus (18.75 %), E. Coli (12.5 %) were most common pathogen.[6] Another study in Bangladesh by Mahmud et al. identified. Klebsiella and pseudomonas were the most common pathogen.[16] Yang et al. identified the predominant aerobes were viridans streptococci, Klebsiella pneumoniae, and Staphylococcus aureus. The predominant anaerobes included species of Prevotella, Peptostreptococcus, and Bacteroides.[19]

Initial antibiotic therapy is targeted at gram-positive organisms and oral cavity anaerobes. Empiric therapy with IV penicillin G, clindamycin or metronidazole is recommended before culture report is available.[8] Alternative choices include Cefoxitin sodium or combination drugs such as Ticarcillin-Clavulanate, Piperacillin, Tazobactam or Amoxicillin-Clavulanate or Ceftriaxone and Metronidazole.[12,13] In this study, after incision and drainage pus was sent for culture and sensitivity. Empirical therapy was started with parental Ceftriaxone, Flucloxacillin and Metronidazole. When culture and sensitivity reports were available antibiotics were changed accordingly. In this study, most effective antibiotic was Ceftriaxone (65%) followed by Cetazidime (58%). Winters et al. and Rao et al. found ceftriaxone 55% and 62% effective, while, ceftazidime 60% and 59%, and Metronidazole 51% and 48% effective antibiotic respectively.[15,18]

Since the facility to culture and sensitivity test for anaerobic bacteria is not available in ICDDR,B and Dhaka Medical College, Dhaka, the possibility of Ludwig's angina due to anaerobic microorganisms could not be evaluated.

CONCLUSION

In Ludwig's Angina, Streptococcus viridans is the commonest pathogen and Ceftriaxone is the most sensitive antibiotic. Though some factors may vary in different situations, from this study it can be concluded that early diagnosis and immediate treatment is the key for successful management of Ludwig's angina which need to be evaluated for better management.

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Original Article

Demographic Characteristics and Clinical Factors of the Patients Suffering from Osteoarthritis of Hand – A Study Done in A Tertiary Specialized Hospital in Bangladesh

Sultan MZ[1], Sharmin S[2], Sultana R[3], Tanzil M[4]

ABSTRACT

Background: *Osteoarthritis (OA) is one of the most common forms of arthritis. Hand OA is a heterogeneous, age and gender-dependent disorder, occurring more frequently in postmenopausal women over 50 years of age.*

Objective: *This study aims to identify demographic pattern and factors associated with osteoarthritis of hand among patients attending a tertiary level hospital in Bangladesh.*

Methods: *This cross-sectional study was done in Department of Orthopedics, Shaheed Ziaur Rahman Medical College Hospital, Bogura, Bangladesh, between January and December of 2021. A total of 90 patients with OA of hands were included in this study. All patients were selected conveniently, and informed written consent of the patients was taken. Participant data were collected through face-to-face interview using semi-structured questionnaire. Statistical analyses were done with Statistical Package for Social Science (SPSS) version 25.0. Quantitative variables were analyzed by mean and standard deviation while qualitative variables were summarized by percentage.*

Results: *In this study, the age distribution of the patients ranges from e"40 years to d"75 years irrespective of sex. The mean age of the patients of both sexes was 56.6±8.72 years. Among those 90 patients, 35 persons (38.9%) were male and 55 (61.1%) were female. Most of the patients are housewives 38 (42.22%). Most of the women (87.27%) are menopausal among the total 55 female patients. Only 13 (14.45%) persons had previous history of hand injury, 20 (22.22%) persons had habit of smoking or previously smoker. Most of the subjects 78 (86.67%) were right hand dominant and maximum 67 (74.45%) persons enrolled in this study showed priority affected CMC1 OA to the dominant hand. Most of them (75.55%) took medications for treatment for arthritis.*

Conclusion: *Our study revealed that osteoarthritis of hands is predominant in females and affects mostly right hand. Further high-quality studies examining the risk factors for hand osteoarthritis are needed to replicate these findings and determine modifiable factors in symptomatic patients.*

Keywords: *Hand osteoarthritis, clinical factors, demographic characteristics*

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INTRODUCTION

Osteoarthritis (OA) is one of the commonest forms of arthritis; prevalence rises progressively with age i.e., by 65 years; clinically, 80% of the patients have radiographic evidence of OA, where only 25-30% of them may have symptoms like pain and disability.[1] Hand OA is a disorder which is heterogeneous, age and gender-dependent, occurring more frequently in postmenopausal women over 50 years of age,[2] but can be started relatively earlier in life.[3] Thumb OA is typically bilateral both clinically and

radiographically featuring tenderness, stiffness, crepitus, swelling, and pain on writing movements or other motions that cause abduction of the thumb.[4,5] In Bangladesh, prevalence of hand pain related with musculo-cutaneous disorder is ranged from 5.8 to 6.4% but individual study on OA thumb is not available.[6] A study done in Iran reported that the first carpometacarpal (CMC1) was found the third most common site (34%) of OA hand after the distal interphalangeal (DIP) (79%) and proximal interphalangeal (PIP) joint groups (41%).[7] In Sweden, the prevalence of CMC1 OA estimated at 1.4% in a mean (SD) age 67.7 years of which women were (78.5%) three to four times higher than men.[8] Some undisputable risk factors have been discussed in several studies, e.g., older age seems to be the strongest risk factors for symptomatic and radiographically proven hand OA,[9,10] while body mass index is also positively associated with hand OA.[11-13] Other risk factors include female sex, family history, menopausal status, parity, obesity, higher bone density, greater forearm muscle strength, and joint laxity, heavy work causing pressure on the hands or occupations involving repetitive thumb use or recreation-related usage.[9-16] Prior hand injury, smoking, bone and cartilage mineralization factors, grip strength, and handedness may also play roles.[2,14-16] In a developing country like Bangladesh, poor working conditions involving heavy manual labor and occupational injuries probably contribute to the high prevalence of OA in people living in slum communities.[6] There are also highly increasing professional female groups, mobile users, computing indicates in increasing prevalence of thumb OA patients in upcoming decades. Increased incidence of hand OA will ultimately create higher clinical and socioeconomic burdens to the population and national economy in the long run. This scenario is not only true for our country, but also evident in the western countries.[17] Hence, we proposed this study to identify demographic pattern and factors associated with hand osteoarthritis (OA) in a selected tertiary specialized hospital in Bangladesh.

METHODS

This cross-sectional study was done in the outdoor of Department of Orthopaedics, Shaheed Ziaur Rahman Medical College & Hospital, Bogura, Bangladesh, between January and December of 2021. A total of 90 patients with thumb OA were selected who fulfilled inclusion and exclusion criteria, which was based on a convenient sampling technique. Patients at age e"40 years and both sexes who meet the diagnostic criteria of OA hand, thumb pain due to chronic non inflammatory causes and pain duration >1month, stable level of activities of daily living (ADL) with no history of light sensitivity or skin lesion were included in this study. Patients were excluded from the study if they had a neurologic disorder or known debilitating diseases, had received previous treatment for their hand problem in the last six months, including an intraarticular joint injection; had fractures or a significant hand injury or previous surgery to thumb, pregnant women, and had history of light sensitivity or skin lesion.

Informed written consent of the patients was taken. Participant data were collected through face-to-face interview using semi-structured questionnaire. Data was checked and verified manually. Data analysis was done by using Statistical Package for Social Science (SPSS) version 25.0. Quantitative variables were analyzed by mean and standard deviation while qualitative variables were summarized by percentage. The study was approved by the Ethical Review Committee of Shaheed Ziaur Rahman Medical College, Bogura, Bangladesh.

RESULTS

In our study, a total of 90 patients were enrolled. The age distribution of the patients ranged from ≥40 years to ≤75 years irrespective of sex. The mean age of the patients of both sexes was 56.6±8.72 years. Most of them (45.56%) belonged to the 51-60 years age-group. In this study, 35 persons (38.9%) were male and 55 (61.1%) were female. Male to female ratio was 1:1.57. In the present study, most of the patients were housewives (42.22%). Out of 90 patients, 18 of the patients (20%) belong to manual workers group and 15(16.66%) are related with services or managerial activities (Table-I). Most (64.44%) of the study subjects were from middle class families followed by poor socioeconomic status 20 (22.22%) according to monthly income. (Fig. 1). In the present study, most of the women (87.27%) are menopausal among the total 55 female patients. 13(14.45%) persons had previous history of hand injury. 20 (22.22%) persons had habit of smoking or previously smoker. Most of the subjects 78 (86.67%) were right hand dominant and 67 (74.45%) persons enrolled in this study showed priority affected CMC1 OA to the dominant hand. Most of them (75.55%) took medications for treatment for arthritis.

Baseline characteristics in patients with CMC1 OA are shown in Table-II. Out of the 90 patients of the study irrespective of sex, it was observed that in 65 (72.22%) patients' symptoms were exacerbated mostly by activities followed by 15 (16.66%) patients who are almost severely affected even had persistent symptoms. On the other hand, most of the patients (75.55%) mentioned their getting relief following NSAIDs uses, while 15.56% had some relief from rest/ inactivity, 6.67% patients were benefited by heat and rest 2.22% by splinting. However, none of them got benefits from by active joint movement (Table-III)

Table-I: *Demographic characteristics of the study participants (n=90)*

Variables	Frequency	Percentage
Age in years		
41-50	18	20%
51-60	41	45.56%
61-70	20	22.22%
>70	11	12.22%
Gender		
Male	35	38.9%
Female	55	61.1%
Occupation		
Housewife	38	42.22%
Service/Managerial/Desk work		15
16.66%		
Manual worker	18	20%
Farmer	4	4.44%
Business	3	2.7%
Retired	9	3.33%
Recreational job	3	3.33%
Total	90	100.0%

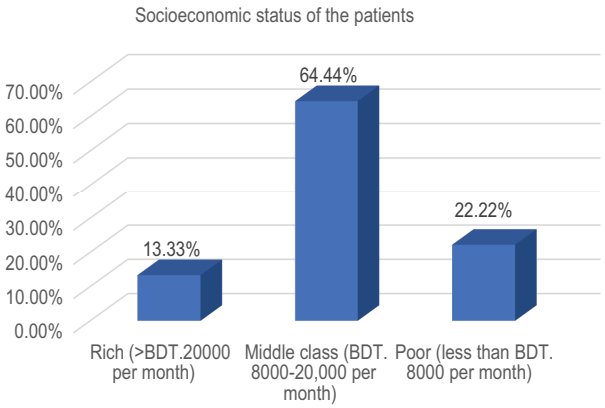

Fig. 1: *Bar diagram of the socioeconomic status of the patients (n=90)*

Table-II: *Baseline characteristics of the study population for CMC1 OA (n=90)*

Characteristic		Frequency	Percentage
H/O hand injury		13	14.45%
Smoker/Previously smoker		20	22.22%
Dominant hand	Right	78	86.67%
	Left	12	13.33%
Affected hand	Right	52	57.78%
	Left	16	17.78%
	Both	22	24.44%
Take medication for	Yes	68	75.55%
arthritis	No	22	24.44%
Menopausal women among total female (n=55)		48	87.27%

Table-III : *Aggravating and Relieving factors for the CMC1 OA patients*

Variables	Frequency	Percentage
Aggravating factors		
Activities	65	72.22%
Rest	3	3.33%
Persistent	12	13.33%
Relieving factors		
Rest	14	15.56%
Heat	6	6.67%
NSAIDs	68	75.55%
Splint	2	2.22%
Total	90	100%

DISCUSSION

In this study, out of 90 patients, most (45.56%) of the patients belong to age group 51-60 years, 20% from 41-50 years group, 22.22% from 61-70 years group and other 12.22% from >70 years age group. Interestingly, a total of 72 patients (80%) were above 51 years. The mean age of the patients of both sexes was 56.6±8.72 years. To date, only few studies specific to hand OA are available in Bangladesh; however, none of them dealt with clinical factors or demographics of the patients. Bani et al.[18] found the mean age was 56.6 years in their study. Roux et al.[19] got 42 patients of CMC1 OA during their study in a mean age of 64.8±8.0. Several studies support the high

prevalence of CMC1 OA in the age group with 51 and above.[20-23] Contrary to the common belief, it is not necessarily a disease of older people, but can occur relatively earlier in life, impairing the patient's capacity to work.[3] In our study, among total 90 subjects completed the study, 38.9% were male and 61.1% were female. Male to female ratio was 1:1.5. In terms of the expected and proved predominance in prevalence of symptomatic hand OA; CMC1 OA is ought to be occurred predominantly in female group, which is supported by many studies including meta-analysis and systemic reviews.[18-21,24-27] In Bangladesh, the point prevalence estimates of musculoskeletal pain in rural, urban slum, and affluent urban communities were 26.2% (women 31.3%, men 21.1%), 24.9% (women 27.5%, men 22.6%), and 27.9% (women 35.5%, men 18.6%), respectively.[6] Hence, these findings regarding gender distribution are consistent with relative studies. In the present study, most of the patients of CMC1 OA are female and housewives 38 (42.22%) among the total participants. Two other different studies done in Bangladesh showed that patients are predominantly female and mostly housewives are more affected.[28,29] Out of 90 patients, 18 of the patients (20%) belong to manual workers group and 15(16.66%) are related with services or managerial activities. Roux et al.[19] found that 14.3% of subjects in managerial job, 14.3% in liberal profession and larger part which is more than 50% of study population as retired. According to social trends and socioeconomic condition in Bangladesh along with higher female subjects, the lion's share of study subjects was within housewife group. Most (64.44%) of the study subjects were from middle class families followed by poor socioeconomic status 20(22.22%). A person belongs to the middle-class category when his/her income ranges between BDT. 8000-20000 per month according to Bangladesh Bureau of Statistics (BBS).[30] Most of the subjects came from Dhaka metropolitan city and urban areas. In studies, they found most of the osteoarthritis patients are from middle class group followed by poor people which represents a common scenario.[28,29] In the present study, the mean age of the patients of both sexes was 56.6±8.72 years. Most of the women (87.27%) are menopausal among the total 55 female patients. Age seems to be the strongest risk factors for radiographic and symptomatic hand osteoarthritis.[9,10] The present study found that 18 subjects were engaged with manual activities (20%), while 13 patients (14.45%) had history of previous hand injuries. Among total patients, 22.22% had habit of smoking or previously smoker. Several studies mentioned about potential risk factors for OA of CMC joint of thumb include female sex, increasing age over 40, family history, age of menarche, menopausal status, obesity, heavy work causing pressure on the hands or occupations involving repetitive thumb use or recreation-related usage; prior hand injury, smoking, bone and cartilage mineralization factors, grip strength, and handedness also played roles.[2,14-16] Most of the subjects (86.67%) are right hand dominant and 57.78% enrolled in this study showed priority affected CMC1 to the right hand, which was very similar to the findings of two other studies.[24,31] 65(72.22%) patients showed that symptoms get exacerbated mostly by activities, followed by 15(16.66%) patients who are almost severely affected even had persistent symptoms in most of the day. On the other hand, most of the patients (75.55%) mentioned their getting relief of pain by taking NSAIDs, while 15.56% had some relief from rest/inactivity, 6.67% patients by heat and 2.22% by splinting. However, none of them got benefits from active joint movement. Sillem et al.[24] and Brosseau et al.[31] mentioned that a larger group who used to take medications got relieved of symptoms.

CONCLUSION

From the results of the present study, it may be concluded that there are various risk factors for hand OA, which might have strong influence over the hand finger joints for prolonged period which might predispose for the development of hand OA. Housewives (homework activities), post-menopausal female gender age more than 51 years, smoking, ageing, low educational level, and previous hand trauma are also considered risk factors for the development of hand osteoarthritis. Further high-quality studies examining the risk factors for hand osteoarthritis are needed to replicate these findings and determine modifiable factors in symptomatic patients.

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Original Article

Bacteriological Trends of Chronic Mucosal Otitis Media in a Tertiary Care Hospital in the Northern Region of Bangladesh

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ABSTRACT

Background: *Chronic otitis media (COM) is a disease of multiple etiology caused by bacteria and its importance lies in its chronicity and awful complications. The microbiological study shows the growth of a lot of organisms, frequently multiple and those differ based on geographical variation, patient population, climate and many other factors.*

Objective: *To evaluate current bacteriological trends of ear infections in patients with chronic otitis media which will be beneficial for appropriate treatment as well as for reducing complications. The study also focuses on rapid diagnosis through exploring the other factors like, age and sex wise distribution, socioeconomic status, distribution of patients according to type of dwelling, bathing habit of patients.*

Methods: *This cross-sectional, observational study was conducted in the Department of ENT and Head-Neck Surgery, Rangpur Medical College Hospital in Rangpur, a northern district of Bangladesh, over a period of 6 months on a total of 80 patients who had attended outpatient and inpatient department. Aural swab was taken from the discharging ears which were inoculated on blood agar and MacConkey's agar media. Organism pattern was then tabled based on the culture reports.*

Results: *The most common bacteria causing COM was Pseudomonas aeruginosa in (45.0%) followed by Staph. aureus (27.5%), mixed isolates in 8.75%, E. coli in 5%, Proteus in 3.75%, S. pneumoniae in 2.5% and Klebsiella in 1.25%.*

Conclusion: *The study proved to be useful for clinicians in management of COM and its complications. Early and effective microbiological diagnosis and intervention is the best solution. From this study, it is observed that Pseudomonas aeruginosa is the commonest pathogen for bacterial ear disease followed by S. Aureus.*

Keywords: *Chronic otitis media, ear infection, aerobic bacteria, bacteriological trends*

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INTRODUCTION

Chronic otitis media (COM) is a chronic inflammation of the middle ear cavity with recurrent discharge through tympanic membrane perforation for a period of 3 months or more irrespective of the etiology or pathogenesis.[1] The causes and pathogenesis of COM are multifactorial.[2] The disease usually begins in childhood as an acute infection of the middle ear.[3] It is much prevalent in low socioeconomic societies of developing countries because of poor hygiene, recurrent upper respiratory tract infection, overcrowding, malnutrition and inadequate health care,[4] where poorer rural community has a significantly higher prevalence rate than the urban.[5] According to World Health Organization (WHO), COM is the neglected tropical diseases due to its

higher prevalence in developing countries. Approximately 31 million people developed COM around the world every year.[6] Globally, 21 000 individuals succumb yearly to COM complications. The average global incidence rate of COM is estimated at 4.76/1000 individuals, totaling 31 million cases (all ages) per year; among the patients, 22.6% are below 5 years of age.[7] The persistence of low grade infections and antibiotic resistance are caused by widespread haphazard, half-hearted and indiscriminate use of antibiotics and poor follow up. that makes obligatory periodic surveillance of microbiological profile of COM.[8,9]

To prescribe appropriate antibiotics for treatment and to prevent complications, it is mandatory to know the types of bacteria responsible for the event of suppuration.[10] The most common bacterias found in COM are Escherichia coli, Pseudomonas aeruginosa, Staphylococcus aureus, Proteus spp. and Klebsiella spp., with methicillin-resistant Staphylococcus aureus (MRSA) isolated in some cases. However, depending on the geographical area and other factors, the type of bacteria associated with COM alters.[11] Various complications associated with the disease are irreversible local destruction of middle ear structures, facial palsy, serious intracranial and extracranial complications.[12] The assay of the local pattern of infection is essential to establish efficient treatment as the untreated cases can lead to these wide range of complications.[5] This study was undertaken to isolate the present bacteriological trends in the patients suffering from COM.

METHODS

This cross-sectional, observational study was conducted at the Department of ENT and Head-Neck Surgery, Rangpur Medical College Hospital in Rangpur, a northern district of Bangladesh, from January to June of 2019. The study was conducted upon a total of 80 patients who had attended outpatient and indoor department of ENT and Head-Neck Surgery, Rangpur Medical College Hospital having chronic mucosal otitis media. They aged between 6 to 55 years.

Inclusion criteria:

1. Chronic mucosal otitis media (active variety)
2. Patient not receiving systemic and topical antibiotics at least for last 7 days.
3. Both male and female patients are included.
4. Age between 6 years to 55 years.
5. Willing to participate in the study & have given written consent.

Exclusion criteria:

1. Chronic mucosal otitis media (inactive)
2. Chronic squamous otitis media
3. Otomycosis
4. Otitis externa
5. Immunocompromised patient-DM, CKD

We developed structured questionnaire, a preformed data sheet was used to collect data. After taking a meticulous history about discharge, duration, site, socioeconomic condition, general and systemic examination was done. Thorough examination of ear, nose and throat was done in all cases. Aural swab was taken from the discharging ear on the first day of attending, by using sterile swab stick and aural speculum. All care was taken to avoid surface contamination. Collected swabs were inoculated on blood agar and MacConkey's agar media. The culture plates were incubated aerobically at 37^0C up to 48 hours.[8]

After incubation, the plates were examined for growth of any suspicious organism. The isolated organisms were stained by gram stain and morphological study was done. Then the organism was identified by observation of pattern of hemolysis on blood agar media, motility test and standard biochemical test. The organism pattern was then tabled on the basis of the culture reports. All information was endorsed in the data sheet.

Collected data were coded, kept confidential and processed and analyzed using computer software SPSS (Statistical Package for Social Sciences) for Windows (version 20.0). The test statistics used for analysis of data were t-test (for comparison of data presented in quantitative scale). For any analytical test the level of significance was 0.05 and $p<0.05$ was considered statistically significant. The study was approved by the Ethical Review Committee of Bangladesh College of Physicians and Surgeons (BCPS), Dhaka, Bangladesh.

RESULTS

Among the 80 patients, the age distribution shows that most of them were in the 16-25 years age group (36.25%) and minimum cases were in the 46-55 years age group (5%) (Table-I). The study included 80 diagnosed cases of COM comprising of 45(56.25%) were male and 35(43.75%) were female; male-female ratio was 1.4:1. Regarding Socioeconomic status, maximum 41(51.25%) patients came from lower class, 34(42.5%) from middle class and 5(6.25%) from higher class. 51(63.75%) patients came from rural areas and the rest 29(36.25%) from urban areas (Fig. 1). Out of 80 patients, 60(75.0%) patients used to take bath in pond and river and 3(3.75%) by supply water (Fig. 2). Among 80 bacterial isolates, Pseudomonas aeruginosa was the predominant bacterium in 36(45.0%) followed by Staphylococcus aureus in 22(27.5%), mixed isolates in 7(8.75%), E. coli in 4(5%), Proteus in 3(3.75%), Streptococcus pneumoniae in 2(2.5%) and Klebsiella in 1(1.25%) (Table-II).

Table-I : *Age distribution of the patients (n=80)*

Age group (in years)	No. of cases	Percentages
6-15	22	27.5
16-25	29	36.25
26-35	13	16.25
36-45	12	15.0
46-55	04	5.0
Total	80	100

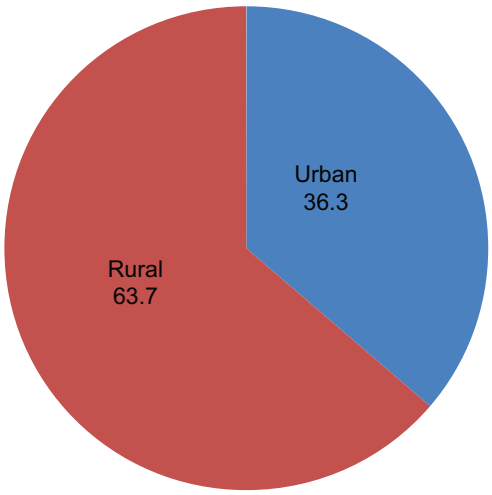

Fig. 1: *Dwelling status of the patients (n=80)*

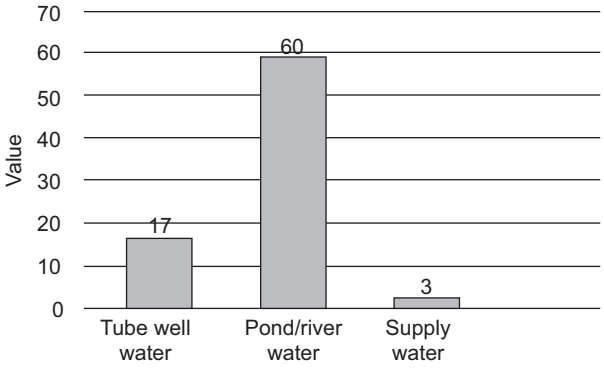

Fig. 2: *Pattern of bathing habit of the patients (n=80)*

Table-II : *Identification of microorganisms in the pus of COM (n=80)*

Name of organism	No. of isolates	Percentages
Pseudomonas	36	45.0
Staph. Aureus	22	27.5
Proteus	03	3.75
E. Coli	04	5.0
Strept. Pneumoniae	02	2.5
Klebsiella	01	1.25
Mixed growth	07	8.75
No growth	05	6.25
Total	80	100

DISCUSSION

COM and its associated complications are the most common conditions seen by the pediatrician, otologist, and the general practitioners now-a-days. It is a condition of the middle ear that is characterized by diligent or intermittent release through an endless aperture of the tympanic layer. Due to puncturing of the tympanic membrane, microorganisms may pick up passage to the center ear by means of the outer ear.[2] The removed muco-pus from ears with active COM is rarely sterile; therefore a priori and quick microbiological diagnosis ensures effective and prompt treatment to avoid complications. Microbiology cultures yield many organisms and these vary depending on climate, patient population, whether antibiotics have or have not been recently used and so many other conditions.[8] Due to changing trends of bacteriological profile of otitis media, it has become very imperative to find out the organism causing the disease. As the strains of bacterial isolates responsible for COM are still found to be responsive

to first line drugs, the treatment of COM should be given according to the pattern in the microbiological flora of each discharging ear.[13,14]

Our study primly focuses on rapid diagnosis through exploring the factors like, age and sex wise distribution, socioeconomic status, distribution of patients according to type of dwelling, bathing habit of patients and major bacteriological growth patterns responsible for COM in the study area.

Usually, the disease was more common in first and second decades of life. Current study revealed that the major disease burden is before the age of 25 years, a maximum 29 cases (36.25%) were in the (16-25) years age group. These findings are in correlation with that of various studies which were carried out in developing countries.[2,7,9,11-17]

Young children may develop COM due to unhygienic condition and over gathering in school premises.[9] In contrast, maximum number of patients in the age group of 6-10 years (41%) were observed by Sharma et al.[5]

COM generally affects both sexes. In our study, males (56.25%) were more commonly affected than females (43.75%) that reflects slight male predominance (1.4:1) which was in accordance with Shrestha et al.[12] and Kazeem et al.,[17] but differs from that of Shrestha et al.,[18] where females (55.2%) are more than males (44.8%). Male predominance may be due to their more exposed way of life, or it might be simple reflection of overall high male attendance in hospital outpatient department or may be due to increased vulnerability of the male child to organisms and apparently decreased attention to personal hygiene compared to the female counterparts in this environment.

The prevalence of COM is greater in lower socioeconomic groups due to poor hygiene and nutritional status as well as lack of health education. In present study, 51.25% of samples were in lower socioeconomic condition. This finding was similar to the study conducted by Hiremath et al.[13] Generally, poor housing and sanitation are prevalent in rural areas the urban. This study showed 63.75% of patients came from rural areas; this finding was supported by many studies which were carried out in the Southeast Asia region. Study conducted by Biswas et al.[19] also reported the similar results.

Water of the ponds, river or canals is usually polluted which infects the middle ear cleft frequently and also interrupts to heal the pre-existing tympanic membrane perforation and pathology within the middle ear. About 75% of the individuals, revealed in this study, used to take bath in pond and river, which are in correlation with that of study carried out by Shaheen et al.[20]

In the present study, of 80 bacterial isolates, Pseudomonas aeruginosa was the predominant bacterium in 36(45.0%) followed by Staphylococcus aureus in 22(27.5%), mixed isolates in 7(8.75%), E. coli in 4(5%), Proteus in 3(3.75%), Streptococcus pneumoniae in 2(2.5%) and Klebsiella in 1(1.25%). Kumar et al.,[2] Pavani et al.,[3] Shilpa et al.,[8] Hiremath et al.[13] and Govindaraj et al.[14] found that Pseudomonas is the predominant organism (i.e., 54.43%, 34%, 49%, 38.79% and 38%, respectively), in their studies. On the other hand, Neha et al.,[1] Shrestha et al.,[12] Ahmed et al.,[15] and Samanth et al.[21] observed that S. aureus is commonest isolate in (i.e., 39.82%, 44.8%56.7%, and 35.0% respectively) in their studies.

The observations made from different studies indicate that there can be variation in causative organism based on ethnic, geographic factors. Overall, our study showed significant difference in isolates trends in COM patients compared to previous studies conducted. The variation may be related to differences in geography and local antimicrobial prescribing practices. The limitation of our study is that we did not study the anaerobic bacterial profile in chronic otitis media.

CONCLUSION

Predominantly, COM is a disease of childhood to early adulthood with ear discharge as an early and frequent symptom along with deafness. Early and effective microbiological diagnosis and intervention can decrease the chronicity of COM and prevent long-term complications. From this study, it is observed that Pseudomonas aeruginosa is the commonest pathogen for bacterial ear disease followed by S. Aureus. The study also showed that chronic mucosal otitis media is associated with many social, economic, and environmental factors. This study was carried over in short period of time and in small number of patients. Therefore, further study with a larger number of samples and longer period is recommended to get a more accurate result.

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Original Article

Growth Status and Glycemic Control of Diabetic Children in a Tertiary Care Hospital in Dhaka City

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ABSTRACT

Childhood growth is a critical indicator of the health status of a child which also determines the overall developmental potential in adult life.Along with increased risk of developing various co-morbidities, diabetic children remain susceptible to growth delay in terms of height and weight. Thus it is necessary to evaluate their growth status in relation to their glycemic control. This cross sectional study observed 148 sequentially selected diabetic children aged 9 to 15 years, with 5 years diabetes duration attending a tertiary level hospital. Data regarding their anthropometric measurements including height and weight, HbA1c status, diabetic history has been collected. HbA1c level is a significant determinant of height, weight, BMI of the study subjects ($p<0.05$). The age at diagnosis of diabetes found to have significant impact on the height of the girls and weight of the both boys and girls and also on their HbA1c level, where, in all groups, the age at diagnosis at 5 to 9 years found to have highest proportion of children whose growth was less than the reference range. The duration of diabetes in this study was not related to the anthropometric measurement of the children ($p>0.05$) although it was significantly associated with the HbA1c level of them ($p<0.05$).This study results observed growth alteration among children with diabetes in association to their HbA1c level and age at diagnosis, which suggests that, diabetic children should be undertaken for routine monitoring of growth and glycemic control to provide with timely and adequate interventions to prevent growth delay among them.

***Keywords**: Diabetic children, HbA1c level, Anthropometric measurements, Growth alteration*

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INTRODUCTION

The increasing incidence of diabetes among children is a growing public health concern.[1]Type 1 diabetes is highly prevalent type of diabetes among children and adolescent diabetic patients and recent study in Bangladesh showed that, out of 100 diabetic individuals (under 22 years), 84 respondents had type 1 diabetes. [2] Per year, the national incidence rate of type 1 diabetes among children (0 to 19 years) has been reported to be at 8 out of 10000. [3]Longitudinal study results observed that, children who developed diabetes earlier the age of 10 years, live nearly 18 years shorter in case of female and nearly 15 years shorter in case of male in comparison to the non-diabetic people. [4] Which emphasizes the necessity of the constancy of management of these patients. Treatment of diabetic children is complicated as it requires lifelong care along with close monitoring of glycemic level and strict adherence to the prescribed management.[5]Marinating the body insulin level through exogenous administration to keep the blood sugar level in control is the mainstream treatment strategy for these patients. [6]It is recommended to keep their HbA1C level lesser than 7.5%.[7] One of the focus treating these diabetic children are to maintain the normal physical development. [8]Research estimation suggests that, poor glycemic control can impact the normal growth of a child in negative way. [9] Growth retardation have been found to be prevalent among 11–14% of diabetic children.[10]Appropriate childhood

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growth is essential to reach the full development potential in later life. [11]The absolute mechanism of growth retardation in children with Type I diabetes has not been established yet, although, among these children, IGFs (insulin like growth factors) and IGFBPs (IGF binding proteins) have been found to be notably reduced [12], whereas, IGFs and IGFBPs are important factors for the linear growth.[13]

As childhood is the most vital developing period, thus, rigorous analysis of the overall diabetic status as well as growth competence is very essential to reduce the morbidity and mortality associated with this disorder. Therefore, the present study assessed the height and weight of diabetic children in association to their diabetic status which might aid in understanding the current situation of this disease impact on growth of children in Bangladesh, as, data on this prospect is scarce in our country.

METHODS

Study methods and selection of study subjects: This research work was carried out with a cross sectional study design. 148 Study participants were selected sequentially from the diagnosed cases of type 1 diabetes (age: 9-15 years) with 5yrs diabetes duration, attending the outpatient department of a selected tertiary care level diabetes specialized hospital, who met the selection criteria of the study.

Data collection and analysis: Face to face interview was conducted with a semi-structured questionnaire to collect data. Data regarding the age at diagnosis, duration of diabetes and glycemic control in terms of glycosylated hemoglobin (HbA1C) level has been checked and recorded from the medical records. Anthropometric measurements in terms of standing height and weight was measured with standardized technique and BMI of the participants was calculated and recorded. With the recorded measurements, participants were categorized according to the reference growth chart. [14]The collected data were analyzed by IBM SPSS (statistical package for social science) software, version 22. Necessary tabulations, charts and diagrams were drawn for summarizing and easy visual presentation of data.

Ethical considerations: Ethical approval from the respective authority before conducting the study has been taken.After selecting the study participants according to the selection criteria of the study, guardians were approached and their informed written consent has been gathered before collection of data.

RESULTS

Table I: *Height and Weight of the Children (n=148) in Relation to their HbA1c level*

			HbA1c level						
			≤7.50 n=2		7.50to9.00 n=24		≥9.00 n=121		p value
		Total	N	%	N	%	N	%	
Height	Less than reference value	96	2	2.08	11	11.46	83	86.46	0.003
	Normal range	39	0	0.00	6	15.38	33	84.62	
	Greater than reference value	13	0	0.00	7	53.85	6	46.15	
Weight	Less than reference value	92	0	0.00	8	8.70	84	91.30	0.000
	Normal range	36	2	5.56	7	13.00	27	75.00	
	Greater than reference value	20	0	0.00	9	45.00	11	55.00	
BMI	≤24.99	141	2	1.4	19	13.5	120	85.11	0.000
	25.00-29.99	6	0	0	5	83.3	1	16.67	
	≥30.00	1	0	0	0	0	1	100	
Duration of diabetes (years)	≤5	18	2	11.1	4	22.2	12	66.67	0.000
	6-7	67	0	0	4	5.97	63	94.03	
	≥8	63	0	0	16	25.4	47	74.6	
Age at diagnosis (years)	≤4	40	0	0	14	35.00	26	65.00	0.000
	5-9	93	2	2.2	4	4.3	87	93.55	
	≥10	15	0	0	6	40.00	9	60	

Chi-square test was done after adjusting with Fishers exact to reach the value

This study has observed that, the fraction of diabetic boys and girls was 76 (51.4%) and 72 (48.6%) respectively. The HbA1c level among them was below 7.50% for 2 (1.35%), 7.5 to 9% for 24 (16.22%) and above 9% for 121 (81.76%) of them. The height of the children was less than reference value for 96 (64.86%), within normal range for 39 (26.35%) and greater than reference range for 13 (8.78%) of them. Among the children with height less than reference range, 86.46% of them had the HbA1c level 9.0% or more than that. Among the children with height greater than the reference range, 46.15% of them had HbA1c level 9.0% or above. The weight of the children was less than reference value for 92 (62.16%), within normal range for 36 (24.32%) and greater than reference range for 20 (13.51%) of them. Children with HbA1c level of 9.0% or more had 91.3% of the children whose weight was less than the reference range. Observation of the BMI of the children showed that, 85.11% of the children with BMI less than 25 kg/m^2 had the HbA1c level of 9.0% or more. Children who had diabetes for less than 6 years, among them 66.67% had HbA1c level 9.0% or more, children with diabetes duration 6 to 7 years among them 94.03% had HbA1c level 9.0% or more. Among the children who has been diagnosed with diabetes before the age of 5 years, 65.0% of them had, who had been diagnosed between 5 to 9 years, 93.55% of them and who had been diagnosed at 10 years or later, 60.0% of them had HbA1c level of 9.0% or more. According this study findings, HbA1c status was in significant association with the height, weight and BMI; it was also dependent on the duration of the diabetes as well as the age at diagnosis of diabetes ($p<0.05$) (Table I).

On evaluation of the growth of the children in relation to their age at diagnosis of diabetes has showed that, the height of the children was significantly associated with the age at diagnosis in case of girl diabetic children. The weight of the children was significantly associated with the age at diagnosis both in case of girls and boys ($p<0.05$) (Table II).

Table II : *Height and Weight of the Boys (n=76) and Girls (n=72) in Relation to Their Age at Diagnosis of Diabetes*

	Age at Diagnosis			Less than referencevalue		Normal Range		Greater than referencevalue		p value
	Years		Total	N	%	N	%	N	%	
Height	Girls	≤4	18	6	33.3	11	61.1	1	5.56	0.006
		5-9	41	26	63.4	14	34.1	1	2.44	
		≥10	13	9	69.2	1	7.7	3	23.08	
	Boys	≤4	22	16	72.7	2	9.1	4	18.18	0.445
		5-9	52	37	71.2	11	21.2	4	7.69	
		≥10	2	2	100	0	0	0	0	
Weight	Girls	≤4	18	9	50	9	50	0	0	0.011
		5-9	41	22	53.7	13	31.7	6	14.63	
		≥10	13	3	23.1	4	30.8	6	46.15	
	Boys	≤4	22	14	63.6	3	13.6	5	22.73	0.012
		5-9	52	44	84.6	6	11.5	2	3.85	
		≥10	2	0	0	1	50	1	50	

Chi-square test was done after adjusting with Fishers exact to reach the value

Table III: *Height and Weight of the Boys (n=76) and Girls (n=72) in Relation to The Duration of Diabetes*

	Duration			Less than reference value		Normal Range		Greater than reference value		p value
		Years	Total	N	%	N	%	N	%	
Height	Girls	≤5	8	8	100	0	0	0	0	0.059
		6-7	33	20	60.6	11	33.3	2	6.06	
		≥8	31	13	41.9	15	48.4	3	9.68	
	Boys	≤5	10	7	70.0	3	30.0	0	0.00	0.251
		6-7	34	27	79.4	5	14.7	2	5.88	
		≥8	32	21	65.6	5	15.6	6	18.75	
Weight	Girls	≤5	8	4	50	1	12.5	3	37.5	0.166
		6-7	33	15	45.5	11	33.3	7	21.21	
		≥8	31	15	48.4	14	45.2	2	6.45	
	Boys	≤5	10	7	70	3	30	0	0	0.299
		6-7	34	28	82.4	3	8.8	3	8.82	
		≥8	32	23	71.9	4	12.5	5	15.63	

Chi-square test was done after adjusting with Fishers exact to reach the value

The impact of duration of diabetes on the anthropometric measurements have been tried to observed. It has been seen that, the duration of diabetes was not in statistically notable in regard of height or weight among diabetic boys or girls ($p>0.05$) (Table III).

DISCUSSION

Childhood is the important developmental period where proper growth is attributed by adequacy of endocrine function, as well as nutrition obtainability. [15] Being the most common endocrine disorder among children, type 1 diabetes itself interferes with nutrient metabolism, thus increases the probability of growth impediment among them. [16] It has been observed that, the diabetic children under this study were in poor control of glycemic status in most instances ((81.76%), which also found to be a significant determinant of short stature (86.46%), poor weight (91.30%), poor BMI (85.11%) among the children ($p<0.05$). Comparable to this finding, another study found that, among the diabetic children, poor HbA1c level group of children gained less height than the children with fair metabolic control. [17] Likewise weight also found to be affected in case of diabetic children compared to that of the non-diabetic children in other study. [18]Also, poor metabolic control observed to be concomitant with poor BMI in a long term retrospective study on 5 to 17 years old diabetic children. [19]

In this study, the age at diagnosis found to be in significant association with the height and weight of the girls and with the weight of the boys ($p<0.05$). Previous study results showed that, diabetic children with prepubertal onset of diabetes had lower final height than the diabetic children who had the diabetic onset at the puberty or after that. [17]Lower weight for age of the children was not found to be significantly affected by age at diagnosis of diabetes in other studies, although younger age of onset observed to be prevalent with lower weight for age z score in comparison to their control ($p>0.05$). [20]In our study, age at onset also was significantly associated with the glycemic control which is similar to other study observation, where it was concluded that, younger age at onset of diabetes found to be a predictor of poor growth and poor glycemic control. [21]In this study, the duration of diabetes was not in significant relation to the anthropometric findings of the children, which was parallel with the findings of another study. [22]

CONCLUSION

Glycemic control as well as age at diagnosis found to be important factor to impact the growth among the children with type 1 diabetes. It is recommended to conduct large scale follow up study to assess the growth among the children, who have the onset of diabetes during their pre-pubetrtal to pubertal period. These children also require to be under strict

supervision so as to avoid growth retardation among them and also to prevent poor glycemic control associated acute and long term complications.

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Review Article

Ethical Issues in Rehabilitation Medicine

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ABSTRACT

Within the past few decades there has been a tremendous increase in the knowledge and awareness of ethical issues and dilemmas within the medical profession. However, until more recently, the problems of chronic illness, and more specifically of rehabilitation-related issues, have received relatively little attention. We reviewed a large amount of literature concerning various ethical dilemmas that occur specifically within the context of chronic care and rehabilitation medicine. The review was done through extensive searching of databases between January and June of 2018. The search was confined to Google Scholar, HINARI and PubMed published articles. Besides, some institutional guidelines were taken into consideration. Keywords used for searching were 'rehabilitation', 'rehabilitation medicine', 'chronic disease', 'chronic illness', 'disability', 'ethics', 'ethical issues' and 'ethical dilemma'. After meticulous scrutiny, a total of 21 journal articles and 3 guidelines were selected for this review. The goal of this review is to provide a brief overview of the major ethical principles as well as some specific examples of ethical issues that might be encountered on a day-to-day basis by the rehabilitation practitioners.

Keywords: *Ethical issue, ethical principles, rehabilitation medicine, chronic illness, disability*

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INTRODUCTION

Within the past few decades there has been a tremendous increase in the knowledge and awareness of ethical issues and dilemmas within the medical profession.[1] However, until more recently, the problems of chronic illness, and more specifically of rehabilitation-related issues, have received relatively little attention.[1,2] Physical medicine and rehabilitation physicians need to master a complex body of knowledge and skill and use that responsibly in rehabilitative care settings.[3] Rehabilitation physicians are trained to care for patients with several complex medical conditions, e.g., brain injury, neuromuscular disorders, spinal cord injury, musculoskeletal injuries, pain syndromes and cardiopulmonary disorders.[2-6] As a leader of an interdisciplinary team or sometimes as a member of the team, physicians related to rehabilitation medicine should be accustomed to actively engaging in decision making as well as facilitating and empowering patients in the decision-making processes.[2-5] Since this unique paradigm is not typically employed in many other areas of medicine, it is imperative that rehabilitation physicians must have firm understanding of the possible ethical issues or dilemmas they may come across in their professional practice.[1-3,6] In recent times, there has been a tremendous increase in the amount of literature concerning various ethical dilemmas that occur specifically within the context of rehabilitation medicine. However, there is a scarcity of literature, discussion paper, or guidelines on ethical dilemmas in clinical practice of physical medicine and rehabilitation (PM&R) in Bangladesh. Moreover, there is no formal bioethics education and training available in the country. Hence, we proposed to do a

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review on ethical issues in rehabilitation medicine based on available literature. The goal of this review paper is to provide a brief overview of the major ethical principles as well as some specific examples of ethical issues that might be encountered on a day-to-day basis by the rehabilitation practitioners in the country.

METHODS

We reviewed a large amount of literature concerning various ethical dilemmas that occur specifically within the context of chronic care and rehabilitation medicine. The review was done through extensive searching of databases between January and June of 2018. The search was confined to Google Scholar, HINARI and PubMed published articles. Besides, some institutional guidelines were taken into consideration. Key words used for searching were 'rehabilitation', 'rehabilitation medicine', 'chronic disease', 'chronic illness', 'disability', 'ethics', 'ethical issues' and 'ethical dilemma'. We selected the articles and guidelines through the following inclusion criteria:

1. Literature published in English language;
2. Literature published between 1991 and 2018;
3. Articles that discussed ethical issues on rehabilitation medicine (having narratives, or qualitative components and discussion rather than having only quantitative opinions); and
4. Ethical issues not conflicting to the cultural norms and values relevant to diverse communities of Bangladesh (e.g., medical assistance in dying to minimize suffering in longstanding incurable disease is not legal in Bangladesh, and communities are resistant to it due to socio-cultural norms and religious beliefs).

This review of literature included both original research and review articles, book chapters and some western professional association's guidelines. Only relevant documents were downloaded after going through the abstracts and we did an extensive review of the downloaded papers and documents. After meticulous scrutiny, a total of 21 journal articles and 3 guidelines were selected for writing this review paper.

RESULTS

In a dynamic and growing field like physical medicine and rehabilitation (PM&R) in the country, it is relevant and important to examine the ethical challenges faced by the practitioners in the specialty. Our literature review has identified "four specific areas" of PM&R practice that are inevitably associated with ethical principles and considerations. These are: 1) ensuring informed consent and determining decisional capacity, 2) addressing patients who refuse or discontinue the treatment or procedures, 3) providing patient centered care and justice, and 4) rehabilitation research and education. These points are not always separated, rather there are much overlapping when we elaborate along with specific scenarios in PM&R practice.

DISCUSSION

Informed consent and decisional capacity are very much inseparable and together they constitute the foundation for ethical clinical practice in all disciplines. Informed consent represents crucial interactive relationship between the patient and his/her attending physician performing the any examination or intervention.[8] This process provides patients with information regarding the purpose of treatment, treatment options, risks and benefits of the procedure, and the opportunity for them to indicate their understanding prior to giving or withholding consent.[2-5,8,9] Once consent is provided, a document reflecting this discussion is signed by both patient/surrogate decision maker and physician and is included in the medical record.[7] Now the other aspect of consent is consent for research, which is necessarily obtained to carry out research studies in a clinical setting. Research consent should be an informed one, which means description of the investigational study, possible risks and benefits, contact information for study staff, and approval by an institutional review board are presented in front of the study participants (patients), and written consent is sought.[10-12] It is important to note that both informed and research consent are for ensuring patient safety and allows the patient or healthcare proxy to partake in the decision-making process in modern healthcare.[10,11]

Competence and capacity are often used interchangeably in clinical practice, but we feel an importance to distinguish them in our review. Competence is obviously a legal concept which can be determined formally through legal proceedings. In contrast, capacity is determined by a physician and, of course, is an essential element in the informed consent process for medical treatment.[13] In some cases, e.g., elderly people with gross cognitive

impairment (dementia), mentally ill patients, and/or mentally disabled adults; patients with head injuries; and patients who object to a recommended treatment, etc. individual's capacity to make medical decisions is commonly questioned and falls under scrutiny.[13-15] Hence, competence is said to refer to legal judgments whereas capacity is said to refer to clinical judgments, which is more in our concern as physicians.[15] We must admit that a patient is not necessarily globally incapable for all treatment or interventions. Sometimes an individual may be capable of consenting to some treatments and not others. However, it is the physician's responsibility to thoroughly assess capacity when the patient's condition is serious, and treatment options are relatively dangerous. In day-to-day practice, physicians may also experience that in some cases the patient's capacity may fluctuate and require repeat assessments. A person is capable of consenting to treatment if the person is able to: "understand" the information that is relevant to making a decision about treatment, and "appreciate" the reasonably foreseeable consequences of a decision or lack of a decision.[13] Generally speaking, a person is presumed to be capable with respect to treatment unless reasonable grounds to suspect incapacity exist.[13,16] Some of these patients require alternative communication and interpretive strategies, while others simply cannot adequately participate.[17] In patients without decisional capacity, a surrogate decision maker is utilized based on either patient's previous wish/direction or as directed by legal authorities (country's rules or regulations). Practitioners usually follow that; however, they should not hesitate to consult legal representatives or a bioethics team of the hospital when conflicts and contradictions ensue in shared decision making.[16-18] Another ethically problematic conflict is raised by the patients with stroke who refuse nutritional treatment or severely injured patient asks for withdrawal of life-saving therapies like ventilators; these patients' autonomy should be respected, while also considering beneficence, i.e., prognosis, options for maintaining fluid and food intake or life expectency and quality of life and act on the best interest of the patient.[19-21]

Another important issue is maldistribution of health resources and the divide between the rich and poor which seems a major ethical and political issue when considering rehabilitative treatment for severe accidental injuries like brain or spinal cord injuries. Those treatments are expensive and time consuming, which their livelihoods. In the western countries, compensation given by the insurance company may facilitate them by having access to home modifications, equipment, care, and support and have greater social and financial security for the rest of their lives. However, in low-income countries like Bangladesh, those facilities are almost absent, and most the treatment expenses are made out-of-pocket.[22,23] Hence, physicians sometimes need to deal with justice issues regarding bed occupancy, advanced therapy options, hospital stay, and rehabilitative support from the hospital for those patients, etc.[21-25] This is clearly inequitable and deprives the society of the valuable contribution that the poorly supported patient might make with more support.[22,23]

In such conditions, physical medicine and rehabilitation practitioners also need to develop and maintain knowledge, personal awareness, sensitivity, and skills and demonstrate a disposition reflective of a culturally competent professional while working with diverse client populations.[26,27]

In 1978, the Belmont Report[10] was published which outlined three main bioethical principles which ultimately became accepted by all medical fields to ensure quality and safety in healthcare as well as in research involving patients: i) respect for persons (autonomy for those with decisional capacity and protection for those who lack that capacity), ii) benevolence and non-maleficence (doing good, doing no harm), and iii) justice (equal treatment regardless of social status, financial ability, sexual orientation, or cultural factors). These are crucial and need to be followed by one who is in PM&R practice. Similarly, few years later, Beauchamp and Childress[28] came up with the '*Principlism*', consisting of four principles of biomedical ethics in which different approaches could generate and sustain a common set of ethical principles for bioethical discourse and practice in the field of medical science. Those principles are: patients' autonomy, beneficence, non-maleficence and justice. However, the authors tried to fulfil the need for an approach that recognized the value of ethical theory for practical judgments; they did not impose a single type of theory or promote a single principle over all others. There is a known obligation to follow all four principles, *prima facie*, unless principles conflict. Conflict of principles is common particularly between beneficence and autonomy and in those situations

finding common ground leads to beneficence encompassing autonomy, where the patient's best interest is inherently linked to their preferences.[10,26,29] We all know that ethical and moral decisions are made in our day-to-day practice in the field of rehabilitation medicine. Many of these are minor, such as the decision to explain the risks and obtain consent for a joint injection or electrodiagnostic procedure, while many others, however, are more complex and difficult in nature, and may involve the participation of several different people. Some issues are very specific to the specialty, while some need interdisciplinary intervention.[30] From above discussion, we have seen that the principles of autonomy, beneficence, non-maleficence, and justice must be considered in PM&R practice, and as applicable in different situation, an attempt to strike a balance among those principles must be made.[26,29]

Physicians face ethical dilemmas every day in deciding about choice of treatment, continuation of treatments, events near the end of life, conflicts of interest, and risk management.[26] Recently, Atanelov et al. specified "five ethical considerations for practicing in the field of rehabilitation", as per endorsement of American Medical Association (AMA):[4]

1) Scarce resource allocation and the potential for discrimination against disabled people;
2) The ethics of accommodating people with disability and chronic neuromuscular disorders, including medical settings;
3) Identifying optimally inclusive nomenclature and terminology (e.g., using the word "physical diversity" rather than "disability");
4) Conflict between the goals of promoting acceptance and accommodation for persons with disability on one hand and securing resources for restoration of functional efficiency and meaningful mission on the other hand; and
5) The ethics of rehabilitating persons with neurological and behavioral disorders e.g., anosognosia (deficits of awareness), in which maximizing rehabilitation may mean abandoning or overriding patient autonomy.

In modern medicine, patient-centred care is a philosophy for organising and delivering healthcare based on patients' needs, preferences and experiences,[30,31] which is very crucial in rehabilitation medicine, as rehabilitation occurs across the care continuum (e.g., in inpatient, outpatient and community settings) and over a long period of time, where patient's needs may change along the way and require changes in how practitioners and services work, for instance, moving from reducing impairment to compensating for a loss of function or even for the development of any new capacity or function, beyond those actually lost.[30,31] Hunt and Ells[32] developed the Patient-Centered Care Ethics Analysis Model for Rehabilitation (PCEAM-R) in 2013 to guide ethical rehabilitative care given the complexity of the care team, patient's degree of impairment/disability and a variety of possible interventions. The six steps of the PCEAM-R are:

1) *Identify the ethical issue(s) to address:* What is at stake and for whom?
2) *Collect information:* What do we need to know to be able to evaluate the issue(s)?
3) *Review and analyze:* Do we need to reformulate the issue(s) and what can help us better understand it?
4) *Identify and weigh options:* What are our options and what rationales support them?
5) *Make decision(s):* What is the best option and how should we implement it?
6) *Evaluate and follow-up:* What was the outcome and how can we learn from it?

This six-step process for ethical decision making is theoretically grounded in the International Classification of Functioning Disability and Health (ICF)[33] and has a sufficiently detailed list of questions to provide a comprehensive and balanced assessment of each patient's situation.[32] This may be one of the best methods for the practice of physiatry to ensure justice for all patients of differing abilities.

To our knowledge and understanding, all those ethical considerations as we discussed are important to address as they help to ensure highest standard of care and foster patient and public trust in physicians and the profession as well as in health system of the country. Besides, they construct part of our public health policies promoting greater diversity, tolerability, and functionally appropriate environments for patients who are often poor, underserved, marginalized, and physically disabled.

Finally, we would like to remind all current and future practitioners that the physician owes a duty of loyalty to protect and act on the patient's best interests and goals of care by using his/her expertise, knowledge, and prudent clinical judgment.

CONCLUSION

Rehabilitation professionals must establish and maintain ethical standards consistent with the specialty and national standards. Professional ethics and patient safety are intertwined fundamental concepts in all fields of medicine. The code of ethics and duty of service to patients, that are very foundational, must be followed by all physicians and medical students. It actually falls upon the senior faculty members and largely on the institution to teach these attributes to the trainees/residents. Teaching through ethical grand rounds, case discussion, role play, workshop and mentoring as well as role modelling can help trainees learn ethical principles, how to handle ethical dilemmas, ensuring empathetic care and meet the expectations set up for their practice in rehabilitation medicine. Besides, online resources for ethics education and discussion may be warranted.

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Review Article

Understanding Burnout in Surgeons: How to Avoid Burnout?

Alam MS

SUMMARY:

Although surgeons work in more stressful medical fields, surgeons are generally considered to offer some of the best lifestyles among physicians. Burnout among surgeons is increasing at an alarming rate. The goals of this review are to increase awareness of the symptoms, causes, and consequences of surgeons' burnout and how to avoid burnout? Surgeons' burnout is largely attributed to work-related factors and personal -related factors. Burnout has many potential adverse consequences including professional consequences and personal consequences. The recovery from surgeon's burnout can take months or longer, therefore it's important to try to avoid it in the first place through preventative strategies.

Key words: *Surgeons' burnout, Adverse consequences, Preventative strategies.*

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INTRODUCTION

Medicines can cure diseases, but only doctors can cure patients. Doctors have the ability to apply their knowledge through a holistic approach, doctors can treat their patients with a comprehensive understanding of medicine. Doctors not only save lives but also prevent them from getting worse. Nobody entered the medical profession thinking it would be an easy job! Most people would have been aware of the shift work and long hours required.

Depression is as common among the medical profession as the general population. Lifetime rates of depression in women physicians were 39% compared to 30% the General Population.[1] Common symptoms of depression are loss of interest in the things that were previously pleasurable, depressed and sadness, hopelessness, anxiety, increased feeling of guilt, irritability, impatience, sleep disturbances, tearfulness, difficulty concentrating etc. Symptoms of anxiety and depression are prevalent among healthcare workers (HCWs) during the COVID-19 pandemic in Bangladesh.[2]

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Training for and practicing surgery are stressful endeavors.[3] Do you feel that the majority of your day is spent on tasks you find either dull or overwhelming. Stress among surgeons can have serious manifestations, including anxiety, depression, divorce or broken relationships, alcoholism, substance abuse, and suicide. Although most surgeons are aware of major depression and anxiety disorders, they may be less familiar with the specific symptoms associated with burnout or the consequences of those symptoms.[4]

The term "burnout" is commonly used in the medical literature, although definitions vary.[5] Burnout is an emotional exhaustion caused by mental breakdown, physical fatigue, and long-term uncontrollable and unresolved work stress, personal stress, and environmental stress such as major illness, family difficulties, workplace bullying, or other persistent adversity.[6,7,8]

According to the WHO, Burnout is a syndrome conceptualized as resulting from chronic workplace stress that has not been successfully managed. It is characterized by three dimensions: feelings of energy depletion or exhaustion, increased mental distance from one's job, or feelings of negativism or cynicism related to one's job; and reduced professional efficacy.[9,10] Thus, burnout is not considered a medical condition but is entirely an occupational phenomenon.[10]

Work burnout is a type of strain resulting from prolonged exposure to chronic, job-related stressors.[11] Although surgeons work in more stressful medical fields, surgeons are generally considered to offer some of the best lifestyles among physicians. Still have questions? Are they working too many hours, or taking stress/tension home with them? Yes, Surgeons work hard, work long hours, deal regularly with life-and-death situations with their patients, and make substantial personal sacrifices to practice in their field.[4] Accordingly, Burnout among surgeons is increasing at an alarming rate. Surgical burnout is a serious condition, which affects many surgeons across the country. The effects of burnout have untold consequences, and could significantly shorten the careers of surgeons if untreated.

The goals of this review are to (1) increase awareness of the symptoms, causes, and consequences of surgeon distress and burnout, (2) encourage surgeons to be proactive in their personal health habits, (3) how to avoid burnout?

Methods (Evidence Review):

An electronic search encompassing MEDLINE, Hinari, PsycInfo, and EMBASE was completed using the following MeSH search terms: *Surgeons' burnout, adverse consequences, and preventative strategies*. The search criteria incorporated relevant full articles published in English from January 1, 1990, to December 31, 2022 that evaluated surgical specialists were included. Review articles and evaluations that included medical students or nonsurgical health care professionals were excluded. Of 41 titles, 26 articles met these criteria. The standardized methodological principles for reporting reviews guided were analyzed. Primary end points are causes of surgeons' burnout, adverse consequences, and preventative strategies. Secondary outcomes included recommended number of tools that are available to both decrease and reverse surgeons' burnout data are reported.

INCIDENCE OF BURNOUT AMONG SURGEONS:

As the prevalence of burnout has increased, most surgeons now report some degree of burnout and the problem cuts across all demographic lines within the profession. In a large General Surgeons study, 582 surgeons who trained at the University of Michigan–Ann Arbor, 32% showed high levels of emotional exhaustion, 13% showed high levels of depersonalization, and 4% showed evidence of a low sense of personal accomplishment. Notably, younger surgeons were more susceptible to burnout than their older colleagues ($P < .01$).[12]

An Australian study of 126 surgeons indicated that burnout levels were significantly higher for surgeons than for the normative population, with 47.6% of the sample reporting high burnout levels. Younger surgeons reported significantly higher burnout levels, regardless of career stage.[13] In the published survey of 549 members of the Society of Surgical Oncology, 28% of respondents met the criteria for burnout.[14] In addition, Bertges and colleagues conducted a survey of 209 actively practicing transplantation surgeons. Burnout was present in 38% of respondents.[15]

Johnson and colleagues (1993) conducted a survey of 395 members of the American Society of Head and Neck Surgery and the Society of Head and Neck Surgeons. A total of 34% who responded believed they were burned out.[16] Another study of 501 colorectal and vascular surgeons in the United Kingdom showed that 32% had high burnout on at least 1 subscale of the Maslach Burnout Inventory.[17]

DEMOGRAPHIC PREDICTORS OF BURNOUT

- Younger age (under 50 y)
- Hours worked per week
- Female gender 60% more likely than men to report burnout
- Higher emotional exhaustion, lower depersonalization
- Odds increased 12-15% for each additional 5 hours worked over 40 hrs./wk.

PHYSIOLOGY OF BURNOUT:

Persistent clinical burnout is associated with a reduction in the volume of gray matter of the anterior cingulate cortex and dorsolateral prefrontal cortex as well as in the volume of the caudate and putamen structures, with reduced dendritic arborization and number of dendritic spines and reduced synaptic density.

TYPES OF BURNOUTS

Gillespie distinguished two types of Burn out

Active Burn out

- Characterized by the maintenance of assertive behaviour
- It relates to the factor's organizations or external elements to the profession

Passive Burn out

- Dominated by feelings of withdrawal and apathy.
- It has to do with internal psychosocial factors.

DEGREES OF BURNOUT:

1. First degree - failure to keep up and gradual loss of reality.
2. Second degree - accelerated physical and emotional deterioration.
3. Third degree - major physical and psychological breakdown.

3 STAGE TRANSACTIONAL MODEL OF BURNOUT:

STAGE 1: demands exceeding emotional resources.

STAGE 2: attempts to balance between demands and resources.

STAGE 3: maladaptive coping mechanisms develop.

- Maladaptive coping mechanisms: Responses - 1) Physical, & 2) Emotional
- Adaptive coping mechanisms: - 1) balance restored, 2) responses resolved.

WHAT CAUSES SURGEONS' BURNOUT?

Surgeons' burnout is largely attributed to organizational / work and personal and family-related factors.

Work-related factors

1. **Extensive** length of training and delayed gratification increases burnout.
2. **Long working hours and enormous workload-** Are you working too many hours? Working too many hours increases the chances that you burn out.
3. **Taking night or weekend call** increases your odds of burnout by 3 to 9 percent for each additional night or weekend you spend on call.
4. Inefficient & / or **hostile workplace environment**.
5. Are you taking work home with you? **Performing work-related tasks at home** increases your odds of burning out by 2 percent for each additional hour you work at home per week.
6. **Having a work-home conflict** increases burnout odds by 200 to 250 percent.
7. **Organizational issues** like excessive bureaucracy, poor communication among healthcare professionals, and limited control over the hospital medical services increase burnout.
8. Practicing in certain specialties, such as orthopedics, general surgery, neurosurgery, Urology, obstetrics and gynecology increases odds of becoming burned out.
9. **Unrealistic expectations of patients** increase burned out.
10. **Working in a private practice increases** your odds of burnout by about 20 percent no matter what your specialty or work hours.
11. **Financial issues** (salary, budgets, mode of payments etc.) - Receiving FFS or incentive pay increases your burnout odds by 130 percent when compared to surgeons who are paid under other salary models.
12. Being a midcareer surgeon an **ongoing pressure on continuous learning** increases your burnout odds, with burnout 25 percent more likely among these surgeons than those early or late in their career.[18]
13. **Imbalance between career and family**- having a career that doesn't fit what you find most personally meaningful increases the odds of your becoming burned out.
14. Grief and guilt feeling about patient death or unsatisfactory outcome increases burnout odds.
15. **Using computerized physician order entry or enduring** other clerical burdens drives burnout.
16. **Insufficient protected research time and funding** increases burnout odds.

Personal and Family-related factors

1. Age- younger age more vulnerable.
2. Sex - Female > Male.
3. Sleep habits changed.
4. Using food, drugs or alcohol to feel better or to simply not feel.
5. Feeling isolated or loss of time to connect with family members, colleagues, and friends.
6. Setting unrealistic goals or having them imposed on self.
7. Become cynical or critical.
8. Troubled by unexplained headaches, depression, bipolar disorder, stomach or bowel problems, cardiac problems, or other physical complaints.
9. Become irritable or impatient with family members, co-workers, patients or clients

10. Lack of satisfaction from achievements.
11. Lack of control- an inability to influence decisions that affect your job — such as your schedule, assignments or workload — could lead to job burnout.
12. Surgeons continued to have a higher **divorce** rate (relative risk of 1.7 compared with internal medicine physicians) on multivariate analysis controlling for other factors.[19]

SYMPTOMS & SIGNS OF BURNOUT

Physical Exhaustion/Fatigue

Emotional Exhaustion/Fatigue

Headaches

GI Disturbances

Weight Loss

Sleeplessness

Frequent Illness

Boredom

Frustration

Depression

General Lack of Interest & Commitment to Work

Irritability With Coworkers, Friends and Family

Low Morale

Impaired Job Performance

Decreased Empathy

Psychologically detaching from work and becoming apathetic, cynical, and rigid.[20]

CONSEQUENCES OF SURGEON BURNOUT

Burnout has many potential adverse consequences including 1) professional consequences and 2) personal consequences. [21]

1) Professional Consequences - Burnout can adversely affect-

- Job dissatisfaction - affect surgeons' satisfaction with their work.
- Adversely affect the quality of surgical care they provide.[22]
- Affect patient safety and quality of patient care,
- Increased medical errors
- Decreased patient satisfaction with medical care.[23]
- Surgeons who are less satisfied tend to be less productive, and
- Eventually may decide to quit for a different practice opportunity or take early retirement.[12]
- Increase the threat of malpractice litigation.
- Poses substantial risk to the economic well-being of health care organizations.[24]

2) Personal Consequences - Surgeons' Burnout can spill over into personal life -

- Increased rates of depression.
- Broken relationships.
- Disengaged from co-workers and others.
- Excessive stress
- Headaches
- Anxiety
- Sleep disturbances
- Hypertension
- Alcoholism or Increased rates of substance abuse.
- High blood pressure
- Myocardial infarction or heart diseases
- Type 2 diabetes
- Vulnerability to illnesses, and
- Absenteeism – Abuse of sick-leave.
- Increased rates of early retirement.

TREATMENT AND PREVENTION

Management Approaches for Burnout

A) Psychotherapy

B) Pharmacotherapy + Psychotherapy

A) Psychotherapy

1) Person or Organisational Approaches

1.1) Person Directed,

1.2) Organisational Approaches

2) Psychotherapeutic Approaches

2.1) Etiological Interventions

2.2) Symptomatic Interventions

3) Coping Strategies

1. Active Cognitive Coping
2. Active Behavioural Coping
3. Coping by Avoidance Psychotherapy

The personal and organizational costs of burnout have led to proposals for various intervention strategies. Some try to treat burnout after it has occurred. Intervention may occur on the level of the individual, workgroup, or an entire organization.

1) Person or Organizational Approaches

1.1) Person Directed,
1.2) Organizational Approaches
1.3) Combined

1.1) Person Directed

- Psychotherapy
- Counselling
- Adaptive Skill Training
- Communicative Skill Training
- Social Support
- Exercises for Relaxation

1.2) Organisational Approaches

- Training Supervisors and Managers
- Changing Organisational Practices
- Training For Better Coping and Stress Management Techniques
- Change Shift Work System and Introducing Vacations
- Counselling And Exercises

2) Psychotherapeutic Approaches

- Experimental group therapy
- Group analytic therapy

2.1) Etiological Interventions

- Cognitive restructuring
- Self-control training
- Training of active coping
- Rational training for frustration

2.2) Symptomatic Interventions

- Proper medications
- Physical relaxation techniques for fatigue
- Behavioral training for frustration
- Social support
- Identifying interesting areas and motivating

3) Coping Strategies

Objectives

- Coping oriented to problem
- Coping oriented to emotion

1. Active Cognitive Coping
(Management by assessing potential stressful events)

2. Active Behavioural Coping
(Observable efforts managing stressful conditions)

3. Coping by Avoidance Psychotherapy
(Avoiding stressful conditions and problematic situations)

B) Pharmacotherapy (+ Psychotherapy):

1. FDA Approves Drug to Treat Medical Burnout

   — Idongivafumab (Peaceaudi)- targets and inhibits C-suite peptides- for the treatment of medical burnout.

2. Support your mood and energy levels with a healthy diet

a. **Minimize sugar and refined carbs** - High-carbohydrate foods quickly lead to a crash in mood and energy.

b. Eat more **Omega-3 fatty acids** to give your mood a boost.

c. **Avoid Smoking** (nicotine), Alcohol, caffeine, unhealthy fats, and foods with chemical preservatives or hormones.

DISCUSSION

Burnout defines as an erosion of the soul caused by deterioration of one's values, dignity, and spirit. For many years, burnout has been recognized as an occupational hazard for various people oriented professions, such as human services, education, and health care.[8] Clinical burnout was originally defined by three pillars of symptomatology: emotional exhaustion, depersonalization, and low sense of personal accomplishment. This study reviewed the prevalence, causes, and consequences of reported burnout in surgeons.

The experience of burnout has been the focus of much research during the past few decades. Burnout also occurs in depression. These include extreme exhaustion, feeling low, and reduced performance. Some characteristics of burnout are very different from those of depression. These include alienation, especially from work. In depression, negative thoughts and feelings are not only about work, but about all areas of life. Other typical symptoms of depression are-lack of self-esteem, hopelessness, and suicidal tendencies. These are not regarded as typical symptoms of burnout. So not every case of burnout will have depression at its root. But burnout symptoms may increase the risk of someone getting depression.

Burnout among surgeons remain unclear on the development, consequences, and interventions for burnout in surgeons. The implications of burnout go beyond the individual. Risk factors associated with increased reporting of surgeon's burnout include female gender, community affiliated teaching

hospitals, and increased work hours.[7] Although surgeons are often better compensated than non-surgical physicians, the drawback is that surgical specialties undoubtedly also work longer hours or perform more stressful or taxing tasks. Female and younger surgeons are at higher risk of burnout. Burnout is manifest in many ways. Suicide rates of surgeons aged above 45 were 1.5–3.0 times more likely than the age matched population. [7] Those experiencing burnout can also present with alcohol or substance abuse. Surgeons also face the most conflict at home with high divorce rates (33%).[21] Increased incidence of medical errors and sub-optimal care were reported to be associated with longer work hours and burnout.[25 , 26]

Burnout crisis threatens surgical profession. The recovery from surgeon's burnout can take months or longer, therefore it's important to try to avoid it in the first place through preventative strategies. Prevention is always better than cure so we focus on how to prevent burnout by promoting engagement.

HOW TO AVOID BURNOUT AS A SURGEON

Although recovery from burnout is possible, prevention is a better strategy. Surgeons who actively nurture and protect their personal and professional well-being on all levels—physical, emotional, psychological, and spiritual—are more likely to prevent burnout.

1. Surgeon's well-being, such as

a) Notice self-burnout and realistic recognition
b) Providing healthy snack options in break rooms.
c) Ensure adequate sleep, exercise, and nutrition
d) Strive to achieve balance between personal and professional life

2. Professional well-being, including

a) Identify professional values and priorities
b) Supportive help and talking with others about issues and stressors
c) Professional resources
d) Forming firm Boundaries so to avoid increased stress and problems
e) Using Humor and Laughter
f) Mentoring programs, leadership opportunities
g) Identify areas of work that are most meaningful to surgeons (patient care, patient education, medical education, participation in clinical trials, research)

3. Social well-being, including

a) Nurture religion and spirituality practices
b) Develop hobbies and use vacations to pursue nonmedical interests
c) Based on priorities, determine how conflicts should be managed

4. Psychological well-being, such as

a) Providing free-time activities like hiking, movies, restaurants, pubs, and museums.
b) Using Humor and Laughter
c) Forming firm Boundaries so to avoid increased stress and problems
d) Group counseling sessions with psychologists.

In fact, burnout is a reversible condition and a number of tools are available to both decrease and reverse burnout:

1) Promoting a culture of remedy that values work-life balance,
2) Surgeons having access to online self-assessment tools to identify levels of stress and burnout,
3) Promote the "just culture" paradigm during training and not tolerating shaming and humiliation,
4) Defining our psycho-social-spiritual support system and accessing it readily and frequently,
5) Identify our power vs. powerlessness over people, places, things and situations,
6) Identify connection vs. disconnection,
7) Identify self-knowledge vs. self-awareness,
8) Developing educational programs that promote supportive environments,
9) Most importantly, give ourselves permission to be sick and to accept good surgical care.

CONCLUSION:

Burnout among surgeons is associated with work-to-family conflict, unrealistic expectations of patients, an ongoing pressure on continuous learning, long working hours, excessive bureaucracy, organizational issues, poor communication among healthcare professionals, and personal issues. Surgeons are at high risk for burnout with resulting slow destruction, depression, and suicidal ideation. The solution to

burnout must be addressed at individual, institutional, and national levels. Further research into the factors leading to surgeon burnout and enactment of effective strategies to mitigate burnout must be pursued. Finally, effective research on preventing and alleviating aspects of Burnout among Surgeons requires giving the issue a high priority within the profession.

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Case Report

Hypertensive Disorder of Pregnancy with Vertebral Artery Aneurysm and Vasospasm Led to Vertebral Artery Dissection – A Case Report

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ABSTRACT

Hypertensive disorder of pregnancy (HDP) can lead to various complications affecting maternal and fetal health. In this case report, we present the rare occurrence of vertebral artery aneurysm leading to vasospasm with vertebral artery dissection (VAD) in a woman having pregnancy-induced hypertensive disorder. Her clinical presentation, diagnostic evaluation, and management are discussed, highlighting the importance of early recognition and appropriate intervention. This case highlights the potential link between pregnancy-induced hypertensive disorders and a rare vascular complication like vertebral artery aneurysm which may lead to vertebral artery dissection. Current literature consists of a few incidences documenting adverse outcomes and management. The incidence of recurrence of such events (arterial aneurism and dissection) in subsequent pregnancies is unknown. Timely recognition, appropriate diagnostic evaluation, and multidisciplinary collaboration are essential for optimal management and patient outcomes.

Keywords: *Hypertensive disorder of pregnancy, vertebral artery aneurysm, vertebral artery dissection*

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INTRODUCTION

Hypertensive disorder of pregnancy (HPD), including preeclampsia and eclampsia, are well-known complications during pregnancy that can result in significant maternal and fetal morbidity.[1] However, existing texts and literature hardly covers the links between pregnancy-induced hypertensive disorders and vascular complications like aneurysm of arteries which sometimes needs immediate arterial dissection. Current evidence is limited to case reports and case series.[2] Moreover, some reports have shown that pregnancy-related strokes may result from vasculopathy and hypercoagulability; the exact mechanisms remain unclear though.[3,4] Arterial dissection is a rare complication of pregnancy and puerperium. There have been reports of aortic, coronary and cervical artery dissection in association with pre-eclampsia; however, vertebral artery dissection (VAD) in course of hypertensive disorder of pregnancy and related vertebral artery aneurism is very rare. Here, we present a rare occurrence of vertebral artery aneurysms leading to vasospasm that led to vertebral artery dissection in a woman with eclampsia in an antenatal setting.

CASE SUMMARY

A 45-year-old lady working as a religious teacher in a school presented herself to the Emergency Department of Raja Isteri Pengiran Anak Saleha (RIPAS) Hospital, Bandar Seri Begawan, Brunei

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Darussalam, with pregnancy (third trimester), complaining of headache and drowsiness along with altered sensorium off and on. She had a history of gestational hypertension that she developed around the 24th week of pregnancy. She was taking routine tab. labetalol 100 mg thrice daily. Her obstetric history was G10 P7+2. She was found hypertensive at AE, and her BP was 165/115 mm of mercury. Her GCS was GCS E3V4M5, and with brisk pupils. No focal neurological deficit was noted. Her protein creatinine ratio was 23.2 (WNL), while her haemoglobin was 9.7 g/dL, WBC was 22.8, and platelet count 322. Serum Electrolyte, LFT, PT/APTT and INR were in acceptable range. Her Serum creatinine 57.9 mmol/L was and urea 3.8 mmol/L. She was diagnosed with eclampsia based on ACOG Diagnostic Criteria.

The Patient was closely monitored, and her blood pressure was managed with i.v. infusion of labetalol. She was scheduled for an emergency Cesarean section operation due to the severity of her preeclampsia. Postoperatively, the patient was transferred to HDU for monitoring. In the postoperative period, her GCS fluctuated, and she developed bilateral lateral rectus palsy (affecting the 6th cranial nerve). The neurosurgical team and intensive care unit were involved. Urgent CT scan of brain done that revealed supra and infratentorial acute subarachnoid haemorrhage with intraventricular extension, resulting in moderate communicating hydrocephalus. Cerebral angiogram showed bilateral ACA, while MCA and PCA are normal. Bilateral ICA and Basilar artery were also normal. No stenosis or aneurysm was seen.

The neurosurgical team inserted an EVD promptly, and the patient was kept in the ICU. She remained intubated. The neurosurgical team decided to do a DSA scan, which showed severe vasospasm in the vertebrobasilar arterial system, with possible dissection of the left vertebral artery. A suspected aneurysm was also identified. The patient was managed conservatively. Aspirin and heparin were given immediately. Nimodipine with anticonvulsants was also continued as per suggestion of neurosurgical consultants. Besides, i.v. infusion of labetalol was used for controlling hypertension.

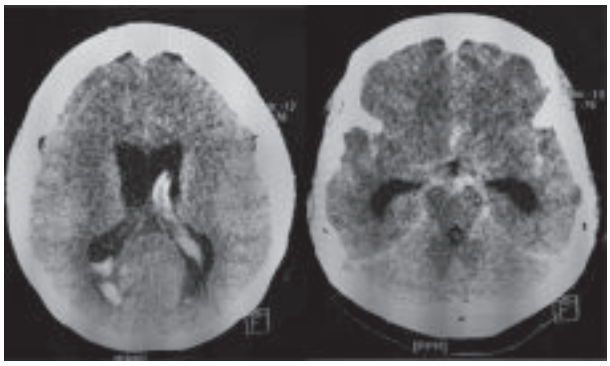

Fig. 1: *CT scan of brain shows bilateral ACA.*

She was gradually weaned from the 4th ICU day and extubated on the 6th ICU day. Her EVD was also removed on the 7th ICU day. Her GCS improved to E4V4M6, and she was found to be moving all four limbs, but muscle power was weak UL 3/5 and LL 3/5. She was transferred to the neurosurgical ward and referred to the physiotherapy department. She was discharged after one month with neurosurgical and occupational therapy follow-up. Her DSA scan was repeated after 2 months and found a left vertebral artery V4 Segment wide neck aneurysm. She was planning for endovascular stenting later.

DISCUSSION

Pregnancy-induced hypertensive disorders can have systemic effects on blood vessels, leading to several vascular complications.[1] The actual mechanism of VAD in association with HDP is still unknown. There is a paucity of population-based data to establish the association between HDP and arterial aneurisms and the sequelae of events.[5] Hypertensive surge is possibly a risk factor as the vertebral artery is prone to mechanical damage of hypertensive surge. Maternal endothelial dysfunction in HDP and the endothelial damaging effect of hypertensive surge potentially increases the risk of dissection.[6,7] Incidence of recurrence of such event (arterial aneurism) in subsequent pregnancies is unknown.[7] Evidence showed that the association between preeclampsia and vertebral artery aneurysm is rare but underscores the importance of vigilance in managing hypertensive disorders during pregnancy.[8] Similar patient profiles, presentation and outcomes were reported by several researchers.[6,9-11] Given the presence of collateral circulation, unilateral vertebral artery dissections may go unrecognized and may be more common than suspected. VAD is an important differential diagnosis, if women present with headache and neck pain, particularly in HDP.[12]

CONCLUSION

This case highlights the potential link between pregnancy-induced hypertensive disorders and a rare vascular complication like vertebral artery aneurysm which may lead to dissection of the vertebral artery. Current literature consists of a few incidences documenting adverse outcomes and management. Timely recognition, appropriate diagnostic evaluation, and multidisciplinary collaboration are essential for optimal management and patient outcomes. Healthcare providers should be aware of those potential complications when managing pregnant women with hypertensive disorders.

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