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Editor's choice

This is a great pleasure to informing you that we are going to publish "The Beacon Medical Journal" first issue of volume-03 in January,2020.Next issue will be published in July 2020.The journal has published in 2 issues/year as regular basis. Ten thousand copies/issue has been distributed to graduate doctors throughout the country by our field colleagues. We have a strong advisory and review board to attract the attention of its authors and readers nationally and internationally.

Editorial of this issue is Depression: A neglected public health problem in Bangladesh. Depression is the leading cause of disability for both male and females. Lack of resources, lack of trained providers and social stigma associated with depression. Basic psychosocial support combined with antidepressant medication and psychotherapy can improve depression. Apart from that this issue also contains five original articles, one review article and three case reports.

Your opinion and suggestions are highly encouraged us for the development of this journal. The journal is freely available at www.beaconpharma.com.bd/-medical-journals for contributing the advancement of public health and medical research.

I do believe this journal will scientifically help doctors in their daily practice.

Dr. G.M. Raihanul Islam
Executive Editor
The Beacon Medical Journal

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3. Authors should keep one copy of their manuscript for reference & three hard copies along with soft copy should be sent to the Executive Editor, The Beacon Medical Journal.

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8. Each component of the manuscript should begin on a new page in the sequence of-

a. Title page

b. Abstract

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10. The title should be concise, informative & self explanatory.

11. The Abstract should be structured as-introduction with objectives, materials & methods, result, discussion with conclusion including key words number of figures, tables, reference & correspondence

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a. Reference should be numbered in order to which they appear in the text as superscript.

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Editorial

Depression: A Neglected Public Health Problem in Bangladesh

Depression is a common mental disorder that presents with depressed mood, loss of interest or pleasure, decreased energy, feelings of guilt or low self-worth, disturbed sleep or appetite, and poor concentration. Moreover, depression often comes with symptoms of anxiety. These problems can become chronic or recurrent and lead to substantial impairments in an individual's ability to take care of his or her everyday responsibilities. At its worst, depression can lead to suicide. Almost 1 million lives are lost yearly due to suicide, which translates to 3000 suicide deaths every day. For every person who completes a suicide, 20 or more may attempt to end his or her life[1] .

Depression is a significant contributor to the global burden of disease and affects people in all communities across the world. Today, depression is estimated to affect 350 million people. The World Mental Health Survey conducted in 17 countries found that on average about 1 in 20 people reported having an episode of depression in the previous year. Depressive disorders often start at a young age; they reduce people's functioning and often are recurring. For these reasons, depression is the leading cause of disability.

At a global level, over 300 million people are estimated to suffer from depression, equivalent to 4.4% of the world's population[2]. Depression, as stated by WHO, will be the leading cause of disease burden by 2030[3]. In Bangladesh, the prevalence of mental health disorders amongst the adult population since 1974 to 2005 declined significantly between 1974 (31.4%) and 2005 (16.1%), albeit alarmingly high in 2005[4]. The first national survey on mental health conducted in 2003-2005 revealed 16.1 % of the adult population had some form of mental disorder with a higher prevalence in women (19%) than in men (12.9%)[5]. Prevalence of mental disorders including depression amongst children in Bangladesh at 13.40% to 22.9% between 1998 to 2004[6,7]. The estimated prevalence of depressive disorders is 4.6%[8]. Unfortunately, mental health care is immensely inadequate due to a dearth of public mental health facilities, scarcity of skilled professionals, insufficient financial resource distribution and stigma.

There are multiple variations of depression that a person can suffer from, with the most general distinction being depression in people who have or do not have a history of manic episodes.

Depressive episode involves symptoms such as depressed mood, loss of interest and enjoyment, and increased fatigability. Depending on the number and severity of symptoms, a depressive episode can be categorized as mild, moderate, or severe. An individual with a mild depressive episode will have some difficulty in continuing with ordinary work and social activities, but will probably not cease to function completely. During a severe depressive episode, on the other hand, it is very unlikely that the sufferer will be able to continue with social, work, or domestic activities, except to a very limited extent.

Bipolar affective disorder typically consists of both manic and depressive episodes separated by periods of normal mood. Manic episodes involve elevated mood and increased energy, resulting in over-activity, pressure of speech and decreased need for sleep.

While depression is the leading cause of disability for both males and females, the burden of depression is 50% higher for females than males[9]. In fact, depression is the leading cause of disease burden for women in both high-income and low- and middle-income countries[9]. Research in developing countries suggests that maternal depression may be a risk factor for poor growth in young children[10]. This risk factor could mean that maternal mental health in low-income countries may have a substantial influence on growth during childhood, with the effects of depression affecting not only this generation but also the next.

Depression is a disorder that can be reliably diagnosed and treated in primary care. As outlined in the WHO mhGAP Intervention Guide, preferable treatment options consist of basic psychosocial support combined with antidepressant medication or psychotherapy, such as cognitive behavior therapy, interpersonal psychotherapy or problem-solving treatment. Antidepressant medications and brief, structured forms of psychotherapy are effective. Antidepressants can be a very effective form of treatment for moderate-severe depression but are not the first line of treatment for cases of mild or sub-threshold depression. As an adjunct to care by specialists or in primary health care, self-help is an important approach to help people with depression. Innovative approaches involving self-help books or internet-based self-help programs have been shown to help reduce or treat depression in numerous studies in Western countries Despite the known effectiveness of treatment for depression, the majority of people in need do not receive it. Where data is available, this is globally fewer than 50%, but fewer than 30% for most regions and even less than 10% in some countries. Barriers to effective care include the lack of resources, lack of trained providers, and the social stigma associated with mental disorders [11].

While the global burden of depression poses a substantial public health challenge, both at the social and economic levels as well as the clinical level, there are a number of well-defined and evidence based strategies that can effectively address or combat this burden. For common mental disorders such as depression being managed in primary care settings, the key interventions are treatment with generic antidepressant drugs and brief psychotherapy. Economic analysis has indicated that treating depression in primary care is feasible, affordable and cost-effective. The prevention of depression is an area that deserves attention. Many prevention programs implemented across the lifespan have provided evidence on the reduction of elevated levels

of depressive symptoms. Effective community approaches to prevent depression focus on several actions surrounding the strengthening of protective factors and the reduction of risk factors. Examples of strengthening protective factors include school-based programs targeting cognitive, problem-solving and social skills of children and adolescents as well as exercise programs for the elderly. Interventions for parents of children with conduct problems aimed at improving parental psychosocial well-being by information provision and by training in behavioral childrearing strategies may reduce parental depressive symptoms, with improvements in children's outcomes.

At present, there is only one national level specialized mental health facility in the country, the National Institute of Mental Health (NIMH) with limited human, research & logistical resources [13,14]. The country has long been in need of a new and comprehensive Mental Health Act, legislating established mental health care in the best interest of the Bangladeshi people, in relation to multidisciplinary action plans and care pathways. Bangladesh adopted a mental health policy, strategy and plan as part of its' effort in promoting surveillance and prevention of Non-Communicable Diseases (NCDs) in 2006 [15,16] and struggling to reap the best outcome from it.

Multiple challenges are responsible for this unfortunate scenario in depression and as a whole the mental health situation in Bangladesh, including dealing with old and inconsistent data related to mental health disorders. The estimated prevalence of depression is underestimated due to incomparable data between studies. Large-scale epidemiological studies are needed to update national statistics on depression, standardization of diagnostic tools, estimation of incidence rates closer in accuracy and the burden of disease as well as the quantification of its' impacts in the globalized language, such as DA. Efficacious and cost-effective treatments are available to improve the health and the lives of the millions of people around the world suffering from depression. On an individual, community, and national level, it is time to educate ourselves about depression and support those who are suffering from this mental disorder.

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Original Article

Characteristics of Hepatitis B Related Hepatocellular Carcinoma

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ABSTRACT

Background: *Hepatocellular carcinoma (HCC) is the fifth most common cancer and the third most common cause of cancer death worldwide. The etiology of HCC is known in more than 90% of cases, In South East Asia, hepatitis B is the most common cause. The highest incidence of HCC is in Asia, about 76% of all cases worldwide. In Bangladesh, HBsAg positivity in the healthy population is 5.4%. Evolution to HCC may be the direct effect of the virus itself, or it may be an indirect effect through the process of the inflammation, regeneration, and fibrosis associated with cirrhosis.*

Objective: *To find out the characteristics of hepatitis B related hepatocellular carcinoma.*

Method: *This observational study was carried out in the Department of Hepatology, BSMMU from January 2012 to December 2013. The study was approved by the Ethical Institutional Review Board (IRB) of BSMMU, Dhaka. The diagnosis of HCC was confirmed by pathological examination or AFP elevation (400ng/ml) combined imaging (CT/MRI) after exclusion of hepatitis C virus infection (Anti HCV+ve) and significant alcohol intake (>20 gm. /day). All patients were HBsAg positive done by ELISA test.*

Result: *A total 44 patients were included in this study. Among them, 91% were male (n=40) and mean age was 48.2 (±12.9) years with age range from 23 to 80. Mostly 93% were married and 38.6% were service holder. Abdominal pain (95.5%), weight loss (86.4%) & anorexia (97.7) were the cardinal presentation. Cirrhosis and Portal Vein Tumor Thrombosis were 79.5% and 41%. AFP level > 400ng/ml was 64 % and IL 28B Genotype showed Genotype (CC) & Allele (C) frequency of were 45.5% & 64.8% respectively.*

Conclusion: *Population-based vaccination programs against HBV and universal infant vaccination will have the potential to dramatically reduce the incidence of HCC in the future.*

Keywords: *Hepatitis B virus; Hepatocellular carcinoma.*

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Introduction:

HCC is the sixth most common malignant tumor and the third most common cause of cancer deaths worldwide [1]. The etiological agent of HCC is known in more than 90% of cases. In South East Asia, hepatitis B is the most common underlying cause. The highest incidence of HCC is in Asia, accounting for about 76% of all cases worldwide [2]. HBV infection is a serious global health problem. About 378 million people throughout the world are chronically infected with this virus [3]. Approximately15-40% of CHB patients will develop cirrhosis, liver failure and HCC [4]. Bangladesh is within the intermediate zone of prevalence of HBV infection. HBsAg positivity in healthy population is 5.4% [5].Evolution to HCC may be the direct effect of the virus itself, or it may be an indirect effect through the process of the inflammation, regeneration, and fibrosis associated with cirrhosis due to the HBV infection. HBV DNA has been shown to become integrated within the chromosomes of infected hepatocytes, the integration of viral genetic material occurring in a critical location within the cellular genome. The hepatitis Bx (HBx) gene product has been implicated in causing HCC because it is a transcriptional activator of various cellular genes associated with growth control. The HBx gene expression is also associated with activation of the Ras–Raf–mitogen-activated protein kinase pathway, an important cellular pathway that has been implicated in hepatocarcinogenesis.

In addition, HBx has been found to interact with p53, interfering with its function as a tumor suppressor. Another viral gene product that has been implicated in causing HCC is the truncated HBsAg gene product [6]. Based on this hypothesis, we find out the characteristics of hepatocellular carcinoma in hepatitis B infected individual.

Method:

This is a hospital based observational study of 44 HCC patients. Patients with HBsAg positive done by ELISA test and features suggestive of HCC attending at outpatient & inpatient department of Hepatology, Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka, Bangladesh from January 2012 to December 2013 were enrolled this study. Aims and objectives along with its procedure, risks and benefits of this study were explained to the patients and attendants in easily understandable local language (Bangla) and then informed written consent was taken from each patient. Prior to the commencement of the study, the research protocol was approved by the Institutional Review Board (IRB) of BSMMU.

The inclusion criteria were: HCC patients were recruited prospectively. The diagnosis of HCC was confirmed by α-fetoprotein elevation (>400 ng/ml) combined with computed tomography (CT) and/or magnetic resonance imaging (MRI) or Pathological examination (Biopsy/FNAC) [Figure 1] and exclusion criteria were alcohol abuse (>20g/day) and infection with HCV (anti-HCV positivity).

Procedure for fine needle aspiration (FNA) from liver space occupying lesions SOL(s)

After taking informed written consent, patients laid with empty bladder. The site was painted with iodine solution and draped. Skin and deeper tissue was infiltrated with local anesthesia (2% xylocaine) at the proposed puncture site using a 23 G needle. Under real-time USG guidance and using 22 G disposable spinal needles the cavity was entered and aspirated material was collected. The prepared glass slides ware fixed with 95% ethanol and kept in Kaplan's jar after labeling. Samples were sent for cytopathological examination to the Department of Pathology, BSMMU. Dressings were applied at the needle puncture sites and patients were followed up for next 6 hours.

Statistical Analysis:

All data was recorded systematically in a preformed data collection sheet and quantitative data expressed as mean ± SD. Qualitative data analyzed by chi square test and quantitative data by student's T test or Mann Whitney's U test. Differences in laboratory parameters compared using one-way ANOVA.P value of ≤ 0.05 was considered to be statistically significant. All statistical computations were performed by using SPSS version 20 (Statistical Package for Social Science).

Result:

Table I: Demographic characteristics of the subjects in the study (n=44)

Characteristics	*Frequency*
Age	
Mean ± SD	48.20 ± 12.91 Years
Range	23 to 80 years
Gender (%)	
Female	09
Male	91
History of smoking (Yes) (%)	40.1
Marital Status (Yes)	93
Occupation (%)	
Housewife	09.1
Service	38.6
Farmer	27.3
Business	11.4
Others	13.6
Educational status (%)	
Illiterate	29.5
< SSC	27.3
< HSC	11.4
HSC & above	31.8
Monthly income (%)	
< 10,000 TK	34.0
10,000 – 20,000 TK	45.5
>20,000 TK	20.5
Family history of live disease (Y) (%)	27.3
History of known liver disease (Y) (%)	11.4
Known diabetes mellitus (Y) (%)	29.5
History of Blood transfusion(Y) (%)	09.1

Table I demonstrated the demographic parameters of the subjects, including age, gender, history of smoking, marital status, occupation, educational status, monthly income, family history of live disease, history of known liver disease, known diabetes mellitus & history of blood transfusion.

Table II: Presenting Clinical features of the subjects in the study (n=44)

Clinical Features	Percent
Upper abdominal pain (%)	95.5
Weight loss (%)	86.4
Anorexia(%)	97.7
Abdominal and/or legs swelling(%)	43.2
Bleeding per mouth (%)	04.5
Mass in the abdomen(%)	04.5
Itching(%)	04.5
Pallor (%)	34.1
Fever (%)	04.5
Stigmata of chronic liver disease (%)	
No stigmata	20.5
< 3 Signs	06.8
3 Signs	09.1
4 Signs	09.1
>4 Signs	54.5

Table II included abdominal pain, weight loss, anorexia, abdominal and/or legs swelling, bleeding per mouth , mass in the abdomen, itching, pallor ,fever & stigmata of chronic liver disease including jaundice, leukonychia, palmer erythema, gynecomastia, spider telangiectasia, edema, ascites, palpable spleen, testicular atropy .

Table III: Laboratory characteristics of the subjects in the study (n=44)

Parameter	*Mean ± SD*
Haemoglobin (g/dl)	11.43 ± 1.72
Platelet count (10^9/L)	227.2 ± 102.71
Prothombin time (Sec)	15.12 ± 2.20
INR	1.28 ± .19
Alanine aminotransferase (U/L)	76.52 ± 51
Aspartate aminotransferase (U/L)	82.52 ± 41
Serum bilirubin (µmol/L)	94.98 ± 115.06
Serum albumin (g/dl)	3.02 ± 0.55
Imaging study	
Multiple nodules (%)	43
Single nodule (%)	41
Diffuse HCC	16
Portal vein thrombus (PVT) (%)	41
Endoscopy of upper GIT	
Varices	46.5
Portal hypertensive gastropathy	02.3
Both	27.9
Normal	23.3
IL 28B Genotype (rs12979860) (%)	
Genotype CC	45.5
Genotype CT	38.6
Genotype TT	15.9
Allele T	35.2
Allele C	64.8

Table III includes the laboratory parameters including haemoglobin (Hb), platelet count(PLT), prothombin time (PT), alanine aminotransferase (ALT), aspartate aminotransferase(AST), serum bilirubin, serum albumin, α-fetoprotein (AFP), imaging study, endoscopy of upper GI study & IL 28B Genotype (rs12979860).

Table IV: Distribution of the study population by age range (n = 44)

Age range	Frequency	Percent	Cumulative Percent
< 20	01	02.3	02.3
21 -30	05	11.4	13 .7
31- 40	11	25.0	38.7
41- 50	11	25.0	63.7
51- 60	10	22.7	86.4
> 60	06	13.6	100.0
Total	44	100.0	100.0

Table IV shows distribution of the study population by age range. Maximum (50%) patients' ages were belonged to 35-55 years. The mean age was found 48.20 ±12.92 years with range from 18 to 80 years.

Gender distribution of the study population

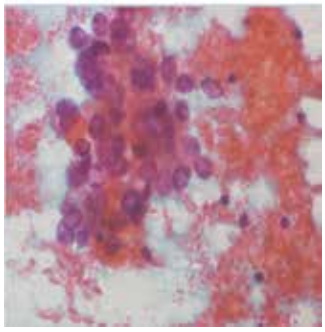

Figure1: Cytopathic features of HCC.H& E stain, (Courtesy: Department of Pathology, BSMMU). ID no:18

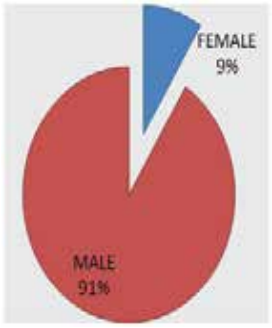

Figure 2. Gender distribution of the study population (n= 44).

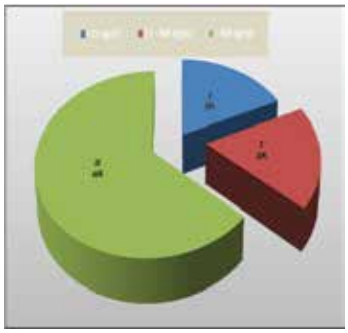

Figure 3. Distribution of the study patients according to serum AFP (n=44)

Figure 2 shows male gender was predominant 91% (40) of the study population. Male female ratio was 10:01. Distribution of the study population according to serum AFP

Figure 3 shows the serum AFP level > 400ng/ml, 15-400 ng/ml and < 15 ng/ml was 64 % (28), 18 % (8) and 18 % (8) respectively.

Discussion:

This is the study from Bangladesh in which the characteristics of HBV related HCC had been studied. HBV infection accounts for most primary HCC and treating HBV infection substantially reduces the risk of HCC development. Chronic HBV infection is recognized as the most important causal factor for HCC in humans.

The incidence of HCC increases with age. The development of HCC is uncommon before 40 years of age in western world. However, the pattern of HCC incidence by age is sometimes dependent on the geographic pattern or on etiologic factors .The age distribution of patients with HCC in the present study was similar to other studies in past. Studies from Bangladesh (M Khan et al & Gani ABMS et al), India (Sarma MP et al), China (Shan R et al) and Pakistan Abbas Z et al) have shown the maximum incidence of HCC in the fifth to sixth decade [7-11]. The male preponderance is similar to our previous Bangladeshi study and other studies

from India and Pakistan [7-9 & 11]. The population-based data show a male to female ratio of 3:1–2:1.1.22 However, high preponderance of HCC in males reported in hospital-based data could suggest a gender bias in seeking medical treatment.

This study revealed that proper screening of chronic hepatitis B infected individual is absent in Bangladesh. Most of the patients were unaware of their chronic infection before attending the tertiary hospital. All patients presented with complaints like abdominal pain, weight loss, anorexia, abdominal and/or legs swelling, bleeding per mouth, itching, pallor, fever and palpable mass in the abdomen. Only 11.4% patients know their liver disease previously and family history of live disease is known only 27.3%. The extend of liver cirrhosis was also in progressive state. Unfortunately, most of the patient attended the physician after development of HCC. American Association for the Study of Liver Diseases (AASLD) recommendations for HCC Surveillance

Among HBsAg carriers[12] - Asian males are over the age of 40 years, Asian females over the age of 50 years, All patients with cirrhosis who are seropositive for HBsAg, Those with a family history of HCC, those who were born in Africa and are over the age of 20 years & Patients with high serum levels of HBV DNA and ongoing hepatic injury.

Underlying cirrhosis was observed in almost 79.5% of our cases. HCC is accompanied by liver cirrhosis in 70–90% [13]. The cirrhosis along with HCC is reported in 70–86% of Indian autopsy studies. The present study is in conformity with the previous studies from Bangladesh [8] and India [9]. The strong association between cirrhosis and HCC is supported by the evidence of its intermediating role in the pathogenesis of HCC because of chronic viral hepatitis. The number of patients without cirrhosis (20.5%) in the present study and an increased risk was observed for HBV marker irrespective of the cirrhosis status of the HCC patients. This result confirms that HBV is the major etiological factor associated with HCC development. These findings are in agreement with biological data. HBV plays a direct role in liver cell transformation; thus, it can lead to HCC without the development of cirrhosis [6].

Alpha-fetoprotein (AFP) is a glycoprotein, belonging to the intriguing class of onco-development protein and generally designated as tumor marker such as HCC. Our study revealed 64 % positivity and similar which is 62.9% in Murugave KG et al. [14], 58.1% in Tangkijvanich P et al. [15], 54.6% Sarma MP et al. [9], 52% in Abbasi A et al [11]. These data suggest that in patients thought to have HCC on clinical grounds, AFP levels about 400 ng/ml should strongly confirm the presence of HCC by a tissue diagnosis. However, clinicians should remember that some patients with primary hepatic cancer will have normal AFP levels, and normal or moderately elevated levels should not be used to exclude the diagnosis of HCC.

Portal vein tumor thrombus (PVTT) is a crucial factor that can worsen the prognosis of HCC because it can lead to the wide dissemination of tumors throughout the liver and cause a marked deterioration of hepatic function. Despite this marked progress in medical science, the prognosis of advanced HCC remains poor, particularly in patients with tumor thrombus in the portal vein (PV). HCC has a high frequency of PV invasion, which is reportedly observed in 11% to 42% of patients with HCC [16-17]. PVTT was observed in almost 41 % of our cases. The present study is in similarity with the previous studies.

Several genome-wide association studies (GWAS) have identified a strong association between single nucleotide polymorphisms (SNPs) in and near IL28B (which encodes IFN- λ) and response to therapy [18]. As a therapeutic agent, IFN- λ might have longer and more potent effects than IFN-α. IFN- λ interacts with a trans membrane receptor to induce potent antiviral responses that are mediated through the activation of the JAK-STAT and MAPK pathways [19]. In vitro and in vivo models have shown the importance of IFN- λ in the immune response to several viral pathogens, including hepatitis C virus (HCV) and HBV [20].To our knowledge, this was the first time in Bangladesh to analyze the genetic polymorphism in IL28B rs12979860 in the hepatitis B related hepatocellular carcinoma and showed that the frequency of CC,CT, TT were 45.5%, 38.6%,15.9% respectively and Allele of C & T frequency were 64.85% & 35.2%. Shan R et al. (2012) pointed out that the IL28B rs12979860 C/T polymorphism might affect susceptibility to the chronic HBV infection and progression of HCC. Of note, the T allele and non-CC genotypes have strong predictive effect of increasing susceptibility of chronic HBV infection and HCC[10].

Conclusion:

HBV-related HCC is most common in developing countries like ours. Population-based vaccination programs against HBV and universal infant vaccination will have the potential to dramatically reduce the incidence of HCC in the future. Prolonged suppression of HBV replication with nucleoside or nucleotide analogs may reduce the risk of HCC in patients with chronic hepatitis B. The most important challenges are early detection and treatment. Currently, HBV related HCC is often detected late at a time when surgical interventions and liver transplantation are no longer feasible. Inexpensive, easily applied, and noninvasive biomarkers for HCC in high-risk patients would be helpful to identifying patients that can be resected or more successfully treated. Therapies for HCC are also critically needed. Standard cancer chemotherapy is largely ineffective against HCC and newer approaches are now becoming practical and have great promise.

Conflict of Interest Statement:

No potential conflicts of interest are disclosed.

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Original Article

Evaluation of Depression in Patients with Hypothyroidism

Bhattacharyya PM[1], Amin MR[2], Hussain AAM[3], Ekram ARMS[4], Islam MA[5]

Abstract

Introduction: *Hypothyroidism is a common endocrine disorder. Hypothyroidism decreases the production of both serotonin and dopamine in the brain which help regulate mood. The result is depressed mood, which manifests itself as persistent sadness, anxiety, irritability and disinterest in daily activities. There may be possibility of depression in patients with hypothyroidism and it needs to be treated.*

Objective: *To evaluate the relationship between hypothyroidism and depression.*

Method: *This cross-sectional observational study was carried out in the department of medicine, Rajshahi Medical College Hospital and in the Nuclear Medicine Centre, Rajshahi during the period of January 2009 to December 2010. Consecutive 72 patients with hypothyroidism and 30 clinically non- hypothyroid subjects were purposively selected for the study.*

Result: *Among the 72 hypothyroid patients 35(48.6%) were presented with depression and out of them mild, moderate and severe depression were present in 8(11.1%), 26(36.1%) and 1(1.4%) patients respectively. In non-hypothyroid (16.7%) subjects had mild degree of depression. The difference in depression between hypothyroid group and normal patients were highly significant (p=0.002). 94.4% (68/72) hypothyroid patients and16.7% (5/30) normal subjects had one or more 'ICD 10 group A' symptoms of depression and the difference between two groups was significant (p<0.001). 97.2 % (70/72) patients and 16.7% normal subjects had one or more 'ICD 10 group B' symptoms of depression and the difference between two groups was significant (p<0.001).*

Conclusion: *The prevalence of depression in hypothyroid patients was 48.6 % (35/72). Mild, moderate and severe depression was present in 11.1%, 36.1%, and 1.4% patients respectively. Among normal subjects 16.7% had mild depression. Hypothyroid patients suffer from depression significantly more than non-hypothyroid subjects.*

Key Words: *Hypothyroidism, Depression*

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Introduction:

Hypothyroidism is a common endocrine disorder. It is usually a primary process resulting from failure of the gland to produce adequate amount of hormone. Primary hypothyroidism is common. Population based surveys reveal that it is present in almost 5% of individuals. It is more commonly diagnosed in women and with advanced age, although it occurs in men and younger individuals. Secondary hypothyroidism is rare, representing less than1% of all cases [1]. Prevalence of primary hypothyroidism is 1:100 but may increase to 5:100 if patients with sub-clinical hypothyroidism [2]. According to study of thyroid clinic BSMMU 10-12% of the patients were presented with hypothyroidism[3]. At the 20 years follow-up of the Whickham cohort provided incident data and allowed the determination of risk factor for hypothyroidism in this period. The mean incidence of spontaneous hypothyroidism in the surviving women over the 20 years follow-up was 3.5 per 1000 per year, rising to 4.1 per 1000 per year and in men was 0.6 per 1000 per year. The prevalence of congenital hypothyroidism is approximately 1 in 3000-4000 live births [4,5,6]. 85% of cases of congenital hypothyroidism were due to thyroid dysgenesis and 15% have thyroid dyshormonogenic defects transmitted by an autosomal recessive mode of inheritance [7]. Clinical presentation of hypothyroidism is variable but well established. However, clinical features vary significantly among different populations owing to their climate, education status and awareness about the disease. Hypothyroidism commonly manifests as slowing in physical

and mental activity but may be asymptomatic. Classic signs and symptoms such as cold intolerance, puffiness, decreased sweating and coarse skin. Consequently, the diagnosis of hypothyroidism is based on clinical suspicion and confirmed by laboratory testing. There is a clear connection between the process of thyroid hormone regulation and depressive disorder. There has been much discussion in the literature regarding the factors that influence the development of depressive symptoms in patients with hypothyroidism. The reason hypothyroidism affects so many different aspects of the body is because the main thyroid hormones, T3 & T4, basically control the speed at which the body is running and utilizing resources. However, when thyroid function is decreased, all of these systems slow down including the productions of chemicals in the brain like serotonin. Serotonin is a neurotransmitter that is produced by the brain to help regulate mood along with dopamine, another mood elevating brain chemical. They are responsible for keeping individuals in a positive frame of mind and out of depression. However, hypothyroidism decreases the production of both serotonin and dopamine in the brain due to deficiency of key protein and amino acids. The result is depressed mood, which manifests itself as persistent sadness, anxiety, irritability and disinterest in daily activities.

Patients and Method:

A cross sectional observational study was conducted in the Department of Medicine (including indoor and outdoor) at Rajshahi Medical College Hospital and in the Nuclear Medicine Centre, Rajshahi, Bangladesh over a period of two years from January, 2009 to December 2010. Seventy-two patients having hypothyroidism were enrolled for the study. A written informed consent was taken from eligible patients. Inclusion criteria were male or female patients age more than 14 years to 60 years Recent clinically detected and biochemically confirmed hypothyroid cases having FT4 level are below normal reference range. Exclusion criteria were other chronic diseases or conditions that can produce depression like symptoms, Neoplastic diseases, Chronic renal failure, Chronic liver disease, Coronary artery diseases, Metabolic disorders, Age less than14 years or more than 60 years and Biochemically sub clinical hypothyroid patients.

Sample collection:

The patients who fulfilled the inclusion criteria were enrolled in this study. The sample was collected by the investigator himself. Blood sample was taken for FT3, FT4 and TSH and other relevant investigations.

Data collection: Complete history and physical examination were done and recorded in a case record form by the investigator himself. Diagnosis of hypothyroidism was based on clinical symptoms and bio¬chemical test. Diagnosis of depression was carried out by ICD- 10 criteria. Symptoms illustrated in ICD-10 were explained in Bengali by the investigator himself to the patients and diagnosis of depression was confirmed with the help of a psychiatrist who is also the co-guide of this study.

Statistical analysis:

Analysis was performed by using a computer based statistical program SPSS (Statistical Package for Social Sciences) version 12. Clinical and epidemiological data was analyzed to identify clinical characteristics. Comparison was done between hypothyroid patients and normal group. Pearson's chi-square (x2) (two tailed) test to compare categorical variables and Student's t test to compare means between groups were used. 95% confidence interval was calculated and p value of <0.05 was considered as significant.

Result and Observation:

To examine the relationship between hypothyroid and depressions we enrolled 72 hypothyroid patients and 30 clinically non hypothyroid subjects. We assessed the clinical and biochemical variables of the subjects and compared between the hypothyroid patients and non hypothyroid subjects. The results were expressed as mean ± SD, frequency and percentage. Comparison was done by student's t test for continuous variables and by chi-square test between categorical variables. 95% confidence interval was calculated. P value <0.05 was considered significant.

Table- 1: Mean ± SD age between two groups.

Parameters	Hypothyroid group (n=72)	Normal group (n=30)	*p* value	95% CI
Age (years)	32.64 ± 11.96	34.97 ± 12.94	0.384(ns)	-7.609 to 2.954

*ns = non significant (p > 0.05), n= number of subjects.

The mean ± SD age of the hypothyroid patients was 32.64 ±11.96 years and of the normal subjects was 34.97± 12.94 years. The difference between mean age of the groups were not statistically significant (p=0.384, 95% CI= -7.609 to 2.954).

Table-2: Distribution of subjects by sex.

Sex	Hypothyroid group	Normal group	*p* value
Male	15(20.8%)	8(26.7%)	0.521
Female	57(79.2%)	22(73.3%)	
Total	72(100%)	30(100%)	

Among the 72 patients of hypothyroid groups 15(20.8%) were male and 57 (79.2%) patients were female. Among 30 normal subjects 8(26.7%) subjects were male and 22(73.3%) subjects were female. The difference of sex between two groups were not significant (p=0.521). So the hypothyroid group and normal group were age and sex matched.

Table-3: Distribution of subjects by symptoms.

Symptoms	Hypothyroid group	Normal group	*p* value
Tiredness	53(73.6%)	7(23.3%)	<0.001
Weight gain	52(72.2%)	6(20.0%)	<0.001
Cold intolerance	41(56.9%)	3(10.0%)	<0.001
Somnolence	55(76.4%)	2(6.7%)	<0.001
Hoarseness of voice	27(37.5%)	2(6.7%	<0.001
Goiter	23(31.9%)	0(0%)	<0.001
Constipation	43(59.7%)	8(26.7%)	0.002
Dry skin and hair	14(19.4%)	2(6.7%)	0.09
Alopecia	2(2.8%)	0(0%)	0.50
Leg swelling	14(19.4%)	1(3.3%)	0.03
Menorrhagia	21(29.2%)	1(3.3%)	0.002
Psychosis	3(4.2%)	0(0%)	0.35
Aches and pain	47(65.3%)	3(10.0%)	<0.001
Vitiligo	4(5.6%)	0(0%)	0.24
Infertility	4(5.6%)	1(3.3%)	0.54
Ascites	5(6.9%)	0(0%)	0.17
Proximal myopathy	12(16.7%)	2(6.7%)	0.15
Difficulty in hearing	19(26.4%)	1(3.3%)	0.005
Total	72(100%)	30(100%)	

Among the hypothyroid patients presenting symptoms were tiredness (73.6%), weight gain (72.2%), cold intolerance(56.9%), somnolence(76.4%) , hoarseness of voice(37.5%), goiter(31.9%), constipation(59.7%), dry skin and hair(19.4%), alopecia (2.8%), leg swelling (19.4%), menorrhagia (29.2%), psychosis (4.2%), aches and pain (65.3%), vitiligo (5.6%), infertility (5.6%), Ascites (6.9%), proximal myopathy (16.7%) and difficulty in hearing (26.4%).

Among the normal control some of the features of hypothyroidism like tiredness (23.36%), weight gain (20.0%), cold intolerance (10.0%), somnolence (6.7%) , hoarseness of voice (6.7%), constipation (26.7%), dry skin and hair (6.7%), leg swelling (3.3%), menorrhagia (3.3%), aches and pain (10.0%), infertility (3.3%), proximal myopathy (6.7%) and difficulty in hearing (3.3%).

The symptoms that were significantly more in hypothyroid patients than normal control were tiredness (p<0.001), weight gain (p<0.001), cold intolerance (p<0.001), somnolence (p<0.001), hoarseness of voice((p=0.001), goiter (p<0.001), constipation (p=0.002), leg swelling (p=.029), menorrhagia (p=0.002), aches and pain (p<0.001) and difficulty in hearing (p=.005).

Table-4: Distribution of subjects by condition of the thyroid gland.

Thyroid gland	Hypothyroid Group	Normal group	*p* value
Diffuse and firm swelling	25(34.7%)	0(0%)	0.002
Diffuse and hard swelling	1(1.4%)	0(0%)	
Nodular swelling	1(1.4%)	0(0%)	
Normal	45(62.5%)	30(100%)	
Total	72(100%)	30(100%)	

In hypothyroid group diffuse and firm swelling was present in 25(34.7%) patients, diffuse and hard swelling in 1(1.4%) patients, Nodular swelling was found in 1(1.4%) patients and normal thyroid gland was seen in 45(62.5%) patients. In normal groups all 30 (100%) subjects had normal thyroid gland. The hypothyroid group had significantly higher pathological conditions of thyroid gland than the normal group (p<0.05).

Table-5: Distribution of subjects by physical findings.

Physical findings	Hypothyroid group	Normal group	*p* value
Ankle edema	11(15.3%)	1(3.3%)	0.078
Dry skin	11(15.3%)	4(13.3%)	0.534
Xanthelasma	7(9.7%)	1(3.3%)	0.256

Ankle edema was present in 11(15.3%) patients of hypothyroid group and in 1(3.3%) subject in normal group, dry skin was present in 11(15.3%) patients of hypothyroid group and in 4(13.3%) subject in normal group, xanthelasma was present in 7(9.7%) patients of hypothyroid group and in 1(3.3%) subject in normal group. The difference in ankle edema, dry skin and xanthelasma between two groups were not significant (p>0.05).

Table 6: Cardiodynamic status of the patients.

Cardiodynamic variables	Hypothyroid group (n=72)	Normal group (n=30)	*p* value	95% CI
Pulse (beat/min)	66.03±9.7	74.5±4.7	<0.001	-12.131to -4.746
Systolic blood pressure (mmHg)	126.3±14.3	115.7±8.2	<0.001	5.058 to 16.108
Diastolic blood pressure (mmHg)	81.5±11.3	74.7±6.7	0.003	2.402 to 11.181

n= number of subjects.

The mean ± SD pulse of the hypothyroid patients was 66.03±9.7 beat/min and of the normal subjects was 74.5± 4.7 beat/min. The mean pulse of the hypothyroid group was significantly less than the normal group (p<0.001, 95% CI, -12.131to -4.746).

The mean ± SD systolic blood pressure of the hypothyroid patients was 126.3±14.3 mmHg and of the normal subjects was115.7±8.2 mmHg. The mean systolic blood pressure of the hypothyroid group was significantly higher than the normal group (p<0.001, 95% CI, 5.058 to 16.108).

The mean ± SD diastolic blood pressure of the hypothyroid patients was 81.5±11.3 mmHg and of the normal subjects was 74.7±6.7 mmHg. The mean diastolic blood pressure of the hypothyroid group was significantly higher than the normal group (p=.003, 95% CI, 2.402 to 11.181).

Table-7: Distribution of subjects by criteria for 'depressive episode' in ICD 10 .

Criteria for 'depressive episode'Tiredness	Hypothyroid group	Normal group	*p* value
Group A symptoms			
No symptoms	4(5.6%)	25(83.3%)	<.001
Depressed mood	5(6.9%)	0(0.0%)	<.001
Loss of interest and enjoyment	13(18.1%)	0(0.0%)	<.001
Reduced energy and decreased activity	9(12.56%)	0(0.0%)	<.001
Depressed mood& loss of interest and enjoyment	11(15.3%)	2(6.7%)	<.001
Depressed mood & reduced energy and decreased activity	14(19.4%)	2(6.7%)	<.001
Loss of interest and enjoyment & reduced energy and decreased activity	5(6.9%)	1(3.3%)	<.001
Depressed mood & loss of interest and enjoyment & reduced energy and deceased activity	11(15.3%)	0(0.0%)	<.001
Group B symptoms			
No symptoms	2(2.8%)	25(83.3%)	<.001
Reduced concentration	1(1.4%)	0(0.0%)	<.001
Reduced self-esteem and confidence	1(1.4%)	0(0.0%)	<.001
Disturbed sleep	5(6.9%)	0(0.0%)	<.001
Diminished appetite	2(2.8%)	0(0.0%)	<.001
Reduced concentration & reduced self-esteem and confidence	2(2.8%)	0(0.0%)	<.001
Reduced concentration & disturbed sleep	4(5.6%)	0(0.0%)	<.001
Reduced self-esteem and confidence & Ideas of self harm	0(0.0%)	1(1.4%)	<.001
Reduced self-esteem and confidence & disturbed sleep	9(12.5%)	2(6.7%)	<.001
Reduced self-esteem and confidence & diminished appetite	1(1.4%)	0(0.0%)	<.001
Ideas of guilt and unworthiness & pessimistic thoughts	0(0.0%)	2(6.7%)	<.001
Ideas of self harm & disturbed sleep	1(1.4%)	0(0.0%)	<.001
disturbed sleep & diminished appetite	5(6.9%)	0(0.0%)	<.001
Reduced concentration & reduced self-esteem and confidence & disturbed sleep	15(20.8%)	0(0.0%)	<.001
Reduced concentration & reduced self-esteem and confidence & diminished appetite	4(5.6%)	0(0.0%)	<.001
Reduced concentration & Ideas of self harm & diminished appetite	1(1.4%)	0(0.0%)	<.001
Reduced concentration & disturbed sleep & diminished appetite	4(5.6%)	0(0.0%)	<.001
Reduced self-esteem and confidence & ideas of guilt and unworthiness & diminished appetite	1(1.4%)	0(0.0%)	<.001
Reduced self-esteem and confidence & Ideas of self harm & diminished appetite	1(1.4%)	0(0.0%)	<.001
reduced self-esteem and confidence& disturbed sleep & diminished appetite	4(5.6%)	0(0.0%)	<.001
Reduced concentration & reduced self-esteem and confidence & Ideas of self harm & disturbed sleep	1(1.4%)	0(0.0%)	<.001
Reduced concentration & reduced self-esteem and confidence& disturbed sleep & diminished appetite	2(2.8%)	0(0.0%)	<.001
Reduced self-esteem and confidence & Ideas of self harm & disturbed sleep	2(2.8%)	0(0.0%)	<.001
Reduced concentration& ideas of guilt and unworthiness& disturbed sleep& diminished appetite	3(4.2%)	0(0.0%)	<.001
Reduced self-esteem and confidence & Ideas of self harm & disturbed sleep& diminished appetite	1(1.4%)	0(0.0%)	<.001

According to criteria for "depressive episode" in ICD 10 group A symptoms 68 (94.4%) hypothyroid patients and 5 (16.7%) subjects had one or more symptoms of depression. Single symptoms like depressed mood, loss of interest and enjoyment, and reduced energy and decreased activity were present in 5(6.9%), 13(18.1%) and 9(12.56%) patients in hypothyroid patients. A combination of symptoms like depressed mood and loss of interest and enjoyment were present in 11(15.3%) in hypothyroid patients and 2(6.7%) in normal controls, depressed mood+ reduced energy and decreased activity in 14(19.4%) hypothyroid patients and 2(6.7%) in normal controls, loss of interest and enjoyment and reduced energy and decreased activity in 5(6.9%) hypothyroid patients and 1(3.3%) in normal controls and depressed mood and loss of interest and enjoyment and reduced energy and deceased activity in 11(15.3%) hypothyroid patients. The difference between two groups for ICD 10 criteria group A symptoms was significant (p<0.001).

According to criteria for "depressive episode" in ICD 10 group B symptoms 70 (97.2%) patients and 5 (16.7%) subjects had one or more symptoms of depression. The difference between two groups for ICD 10 criteria group B symptoms was significant (p<0.001).

Table-8: Distribution of subjects by severity of depression

Severity of depression	Hypothyroid Group	Normal group	*p* value
Few or no symptoms	37(51.4%)	25(83.35%)	0.002
Mild	8(11.1%)	5(16.7%)	
Moderate	26(36.1%)	0(0.0%)	
Severe	1(1.4%)	0(0.0%)	
Total	72(100%)	30(100%)	

Among the 72 hypothyroid patients 37(51.4%) patients had few or no symptoms of depression and 35 (48.6%) patients had some degree of depression. Among them mild, moderate and severe depression were present in 8(11.1%), 26(36.1%) and 1(1.4%) patients respectively. In normal group 5 (16.7%) subjects had mild degree of depression. The difference in depression between hypothyroid and non-hypothyroid group were highly significant (<0.002).

Discussion:

We studied 72 hypothyroid patients and 30 non-hypothyroid subjects to evaluate the relationship between hypothyroid and depressions. The clinical and biochemical variables of the hypothyroid patients and non hypothyroid subjects were assessed and compared. The mean ± SD age of the hypothyroid patients was 32.64 ±11.96 years.

Among the 72 patients of hypothyroid groups 15(20.8%) were male and 57 (79.2%) patients were female. Hypothyroidism is more common in female. Sapini, Rokiah, Nor Zuraida (2008) stated that among the functional disorder of the thyroid, hypothyroidism is the most common with

prevalence ranged from 1.0% - 11.7% in female and 0.9%-5.14% in male.

The present study found that the symptoms of hypothyroidism were tiredness (73.6%), weight gain (72.2%), cold intolerance(56.9%), somnolence(76.4%) , hoarseness of voice(37.5%), goiter(31.9%), constipation(59.7%), dry skin and hair(19.4%), alopecia (2.8%), leg swelling (19.4%), menorrhagia (29.2%), psychosis (4.2%), aches and pain (65.3%), vitiligo (5.6%), infertility (5.6%), ascites (6.9%), proximal myopathy (16.7%) and difficulty in hearing (26.4%).

Our findings are similar to the findings of McDermoitt and Ridhway (2001). They stated that mild thyroid failure is often asymptomatic; however, nearly 30% of patients with this condition may have symptoms that are suggestive of thyroid hormone deficiency. The symptoms of thyroid hormone deficiency studied in 2,336 subjects were dry skin (28%), poor memory (24%), slow thinking (22%), muscle weakness (22%), fatigue (18%), muscle cramps (17%), cold intolerance (15%), puffy eyes (12%), constipation (8%), and hoarseness (7%)[13].

The mean ± SD pulse of the hypothyroid patients was 66.03±9.7 beat/min, the mean ± SD systolic and diastolic blood pressure of the hypothyroid patients was 126.3±14.3 and 81.5±11.3 mmHg. Increased total peripheral resistance causes increased blood pressure. Constant et al (2001) found a low cardiac output per square meter of body surface with a normal or elevated mean arterial pressure in hypothyroidism, indicating that the total vascular resistance of the body was increased in hypothyroidism[31].

The study considered ICD 10 criteria for 'depressive episode' which have two groups of symptoms. Group A includes the symptoms like 'depressed mood', 'loss of interest and enjoyment' and 'reduced energy and deceased activity'. Group B symptoms consist of reduced concentration, reduced self-esteem and confidence, ideas of self harm, ideas of guilt and unworthiness, pessimistic thoughts, disturbed sleep and diminished appetite. To classy as having mild depression patients should have at least two of the symptoms of group and two of the symptom of group B.

Some of our patients had one symptom of group A and one or more than one symptoms of group B and some of our patients had one symptom of group B and one or more than one symptoms of group A. None of them could be classified as patients suffering from depression, at least mild depression, in spite of having some of the features of depression.

According to criteria for "depressive episode" in ICD 10 group A symptoms 68 (94.4%) hypothyroid patients and 5 (16.7%) subjects had one or more symptoms of depression. Single symptoms like depressed mood, loss of interest and enjoyment, and reduced energy and decreased activity were present in 5(6.9%), 13(18.1%) and 9(12.56%) patients in hypothyroid patients. They were not classified as patients of depression.

According to criteria for "depressive episode" in ICD 10 group B symptoms 68 (97.2%) hypothyroid patients and 5 (16.7%) normal subjects had one or more symptoms of depression. Single symptoms like reduced concentration, reduced self-esteem and confidence, disturbed sleep, diminished appetite were present in 1(1.4%), 5(6.9%), and 2(2.8%) patients in hypothyroid patients. However they could not be classified as patients suffering from depression.

The present study revealed that the prevalence of depression in hypothyroid patients is 48.6 %(35/72) and in normal subjects 16.7 %(5/30). Among the hypothyroid patients mild, moderate and severe depression were present in 11.1%, 36.1% and 1.4% patients respectively and in normal group all 16.7% subjects had mild degree of depression. The findings of present study are consistent with the findings of with the findings of the studies done by Haggerty and co-workers (1993); Constant et al (2005); Constant et al (2001);

Sapini, Rokiah, Nor Zuraida (2008); Gold, Pottash and Extein (1981); Carta et al (2004).

Haggerty et al (1993) described that a high incidence of co-morbidity exists between depression and both clinical and sub-clinical hypothyroidism. A small study of 31 subjects highlighted that the lifetime frequency of depression was significantly higher in those who met the criteria for sub-clinical hypothyroidism (56%) than in those who did not (20%).

Constant et al (2005) verified the presence of anxiety and depressive symptoms in hypothyroidism. The authors found that in hypothyroidism, the participants were more anxious and depressed than the controls[16].

Constant et al (2001) stated that adult onset hypothyroidism may have a variety of somatic, neuropsychological and psychiatric symptoms such as inattentiveness, inability to concentrate, deficits in memory, psychomotor slowing, depressive mood state, anxiety, and sometimes persecutive delusions[31].

Sapini, Rokiah, Nor Zuraida (2008) described that depression and anxiety are the most common psychiatric presentation in thyroid disorders. Both subclinical and overt thyroid disorder have been associated with mood disorders[11].

Gold, Pottash and Extein (1981) evaluated the relationship between hypothyroidism and depression in 250 patients referred to a psychiatric hospital for treatment of depression. They found that less than 1% had overt hypothyroidism; 3.6% had mild and 4% had subclinical hypothyroidism. They suggested that a significant proportion of patients with depression may have early hypothyroidism.

Bahlsa and Carvalhob (2004) stated that thyroid hormones regulate the neuronal cytoarchitecture, the normal neuronal growth and the synaptogenesis, and their receptors are widely distributed in the central nervous system. In patients with endocrine diseases there has been commonly found a high prevalence of mood disorders in general and particularly of major depression. Specifically regarding thyroid diseases, the prevalence of depressive symptoms in hypothyroidism is near to 50% whereas in hyperthyroidism it reaches up to 28% of the cases. Clinical depression occurs in more than 40% of people suffering from hypothyroidism[10].

Kierkegaard and Faber (1998) explained the pathogenesis of endogenous depression. They described that a lack of serotonin in the brain has a central role in the development of

depression. Acute as well as chronic T3 treatment has been shown to increase the serotonin levels in the cerebral cortex and plasma serotonin levels correlate positively with T3 concentrations. Brain serotonin synthesis is reduced in hypothyroidism and increased in hyperthyroidism[21].

Constant et al (2001) described that T4 and T3 hormones regulate the cellular function in most organs including the brain. High concentrations of T3 nuclear receptors are found in the amygdala and hippocampus of brain. It could be thus predicted that in hypothyroidism there might be a decreased regional cerebral metabolism in the amygdala and hippocampus causing depression[31].

Conclusion:

The present study concludes that the magnitude of depression in hypothyroid patients was 48.6 % (35/72). Among the depressed patients of hypothyroid group mild, moderate and severe depression was present in 11.1%, 36.1%, and 1.4% patients respectively. In normal subjects 16.7 %(5/30) had mild depression. Hypothyroid patients suffer from depression significantly more than non-hypothyroid subjects.

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Original Article

Emergency Tracheostomy at a Tertiary Level Hospital.

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ABSTRACT

Background: Tracheostomy remains a very important life saving surgical procedure worldwide and particularly in our environment where patients present late in upper airway obstruction. Little work has been done on this subject in our environment and therefore it was necessary to conduct this study to describe our own experiences with tracheostomy

Objective: To study various indications, socio-demographic profile, difficulties and complications of emergency tracheostomy.

Method: This cross sectional study was conducted at the department of ENT & Head Neck Surgery of Dhaka Medical College Hospital, Dhaka from December 2015 to May 2016. All patients admitted as emergency basis, having a compromised upper airway developing an upper respiratory tract obstruction/respiratory insufficiency were selected for this study. A quick assessment of the degree of upper airway obstruction was made from the patient's dyspnea, stridor, cyanosis & suprasternal and intercostal recession and patients were selected for emergency tracheostomy. All tracheostomies were done by open surgical technique under local anaesthesia.

Result: Out of 50 patients, 39(78.0%) were male and 11(22.0%) were female. Mean age was 54.6 years and Std. deviation ±18.59, ranging from 04 to 80 years. Majority of people were from rural areas (52.0%) bearing poor socio-economic status (78.0%). The most common indication for emergency tracheostomy was found carcinoma larynx (52.0%) which was significantly high in elderly male patients. About 76.0% of the patients were smoker either singly or in combination with betel nut or alcohol. In this study other indications were advanced hypopharyngeal carcinoma (12.0%), cut throat injury (10.0%), multiple papilloma of larynx (8.0%), neck space infection causing stridor (6.0%), blunt injury neck with stridor with surgical emphysema (4.0%), laryngeal edema due to radiotherapy (4.0%), carcinoma of thyroid gland (2.0%) and failed intubation (2.0%). Hemorrhage (12.0%) is the most common complication observed followed by surgical emphysema (10.0%), tube blockage (8.0%) etc

Conclusion: *Upper airway obstruction due to carcinoma of larynx was the most common indication for emergency tracheostomy. Carcinoma of larynx was significantly high in smoker elderly male patients. Tracheostomy is still a life saving procedure. However, despite being a safe procedure, tracheostomy can be associated with complication. But most of the complications are preventable and should be avoided by careful operative technique and meticulous post operative management.*

Key words: Emergency tracheostomy, Indications, Complications, Carcinoma Larynx, Hypopharyngeal carcinoma, Haemorrhage.

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Introduction:

Tracheostomy is one of the oldest medical procedures known[1]. The word tracheostomy is derived from two Greek words meaning 'I cut trachea'[2]. It is a life-saving procedure involving incision on trachea followed by insertion of a tube which maintains the patency of the opening in trachea either temporarily or permanently and is very ancient surgical procedure described in first century BC[3]. The early history of tracheostomy started with Galen & Aretaeus. Galen approved the operation & successfully opened the wind pipe of a goat[4]. Many authors recognized Asclepiades of Bittynia (Second century AD) as the first to perform the operation[5]. In the fourth century BC, Alexander the Great "punctured the trachea of a soldier with the point of his sword when he saw a man choking from a bone lodged in his throat"[6]. This life saving procedure is performed by a standard technique

ideally in the operating room as described by Jackson in 19097,[8]; and is the procedure which deals with airway so the operation theatre is considered as the ideal place[9].The evolution of tracheostomy transude various stages at different periods. Period of 'legend' (2000 B.C. to A.D. 1546); Period of 'fear' (154 6 to 1833) only brave few performs the procedure , Period of 'drama' (1833 to 1932) procedure done only as emergency, Period of 'enthusiasm' (1932 to 1965) 'if you think of tracheostomy do it' that was the popular adage; and Period of 'rationalization' (1965 to date)[6].Tracheostomy is one of the three methods of airway intervention, others being endotracheal intubations, cricothyroidotomy and in recent times Percutaneous Dilatational Tracheostomy (PDT), but the last one is not yet routinely practiced in our country. So surgical tracheostomy are practiced here in vast majority of cases to manage airway problems. There are several indications for performing tracheostomy: to relieve upper airway obstruction, to facilitate prolonged intubation, to allow staged extubation by reducing the anatomical dead space, and to protect and give access to the tracheobronchial tree[10], Orotracheal or nasotracheal intubation and cricothyrotomy may be alternatives to or precede tracheostomy[11]. It has been argued that these alternative procedures may be associated with fewer complications than a standard tracheostomy[12].Head and neck region is a frequent site of malignancy. Many of these malignancies arise in and around the upper aerodigestive tract. They often present at advanced stages with respiratory distress. Main indication of tracheostomy in our country particularly in adult is upper airway obstruction due to head and neck malignancy[13].Tracheostomy in the pediatric age group has been reported to be different from that in adults because in pediatric patients this procedure is challenging and technically more demanding and carries higher degree of morbidity and mortality when compared to the adult population[14]. Over the past two decades, there has been a change in the indications for pediatric tracheostomy. Previously the procedure was performed mainly for the relief of upper airway obstruction secondary to infectious disorders like epiglottitis and croup. With the introduction of immunization against common infectious diseases, development of better anesthetic techniques and safer endotracheal intubations, the management of these conditions no longer required tracheostomy[15].However, despite being a safe procedure, tracheostomy can be associated with complications[14]. Complications of tracheostomy quoted in the literature ranges 6 to 66 percent for surgical tracheostomy[16]. The complications could be either early or late. The early complications include hemorrhage, wound infection, pneumomediastinum, and pneumothorax while late complications include tracheal stenosis, laryngeal stenosis, and failed reinsertion of cannula[17]. The mortality of tracheostomy is reported to be less than 2%[18]. In the recent years more and more airway problems are managed with either endotracheal intubation or percutaneous endoscopically guided tracheostomy[13]. But in our country percutaneous endoscopi- cally guided tracheostomy is not yet routinely practiced, conventional tracheostomy is practiced in vast majority of cases to manage airway problems. A conventional subhyoid tracheostomy is performed[19]. Very few studies have been carried out regarding emergency tracheostomy. I have undertaken this study was to see the various indications, demographic profile of patients, and pattern of complications in emergency tracheostomy to enrich the ideas regarding further management.

Method:

A Cross-sectional observational study was conducted in the department of ENT and Head- Neck surgery, Casualty, Neurosurgery, Burn & Plastic Surgery & relevant OPD in Dhaka Medical College Hospital over a period of six months 6th December 2015 to 5th May 2016. Fifty patients having tracheostomy were enrolled for the study. A written informed consent was taken from eligible patients. Inclusion criteria were male or female patients age 04 years to 80 years. Patients diagnosed as severe stridor & acute upper airway compromised cases due to any causes. Patients' willing to be included in this study. Exclusion criteria was Patient age less than o4 years to more than 80 years. Patients undergoing elective tracheostomy for any surgical cases, ICU patients with prolonged ventilation requiring tracheostomy and patient who does not wish to be included in the study was excluded.

Sample collection:

This is a prospective study, conducted in the department of ENT and Head Neck surgery, Casualty, Neurosurgery, Burn & Plastic Surgery & relevant OPD in Dhaka Medical College Hospital, Dhaka. Total 50 cases were enrolled from 6th December'2015 onwards according to inclusion, exclusion criteria.

Statistical analysis:

Data for socio- demographic and clinical variables were obtained from all participants by the use of a pre- designed and easily understandable questionnaire. The socio-demographic variables studied- age, sex, place of residence and occupation. Socioeconomic levels were determined by occupation, household's income and expenditure. After collection of all information, these data were checked, verified for consistency and edited. After editing and coding, the coded data directly entered into the computer by using SPSS version 6. Data cleaning validation and analysis was performed using the SPSS/PC software, Graph and chart are by MS excel.

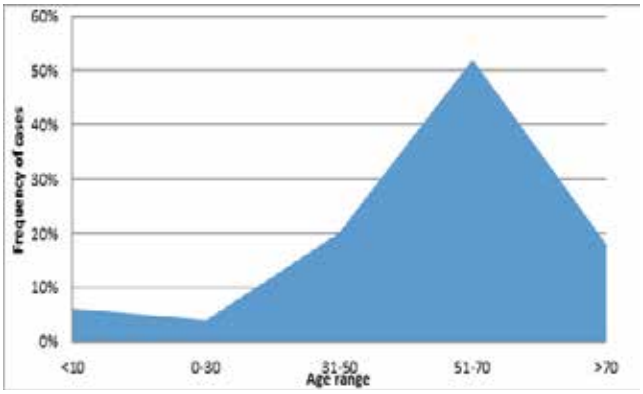
Result:

Table 1 Age distribution of the subjects (n=50)

Age in Years	Number	Percentage	Mean ± SD
< 10	03	06	
10-30	02	04	
31-50	10	20	54.6 ± 18.59
51-70	26	52	
> 70	09	18	

Table shows, in this series, out of 50 subjects the maximum numbers of patients (52%) were between 51-70 years age groups, next (20%) were 31-50 years. Mean age was 54.6 ± 18.59 years

Figure- 1: Area chart showing the frequency of tracheostomy with age variation (n=50)



Area chart shows that, frequency of etiology for emergency tracheostomy gradually increases with elderly and 51-70 years were more prevalent for any causes of emergency tracheostomy, observed in (52%) cases.

Figure- 2: Pie chart showing sex distribution of the patients (n=50)

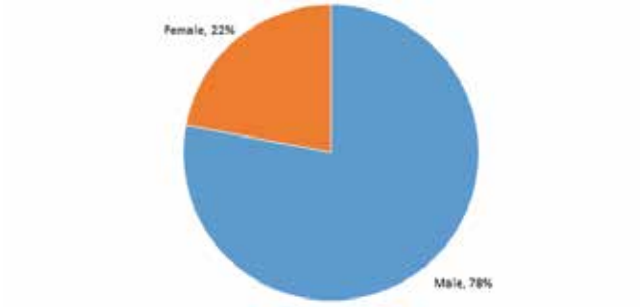


Figure show, out of 50 cases 78% was male and 22% were female. Male – female ratio was 3.54:1.

Table-2: Socioeconomic status (SES) of study population (n=50)

Income classes	Frequency	Percentage
Poor	37	74.0
Middle class	11	22.0
Higher middle class	2	04.0
Total	50	100.0

Table show, among the patients the poor class (74%) comprising the major percentage of the patients, followed by middle class (22%) and remaining are upper class (04%).

Figure- 3: Doughnut showing distribution of participants in urban and rural area (n=50)

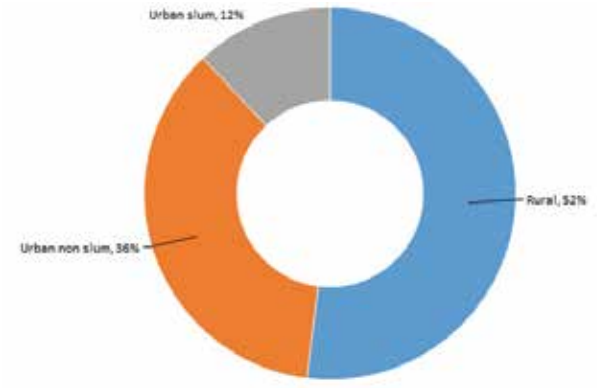


Figure shows (52%) patients came from rural, (36%) from urban non slum and (12%) from urban slum areas.

Table- 3: Distribution of patients according to occupation (n=50)

Occupation	Number of patients	Percentage
Business	11	22.0
Farmer	8	16.0
Driver	3	6.0
Laborer	7	14.0
Sailor	3	6.0
House wife	9	18.0
Rickshaw puller	5	10.0
Others	4	8.0
Total	50	100.0

Table show, highest percentage of patient comprised of business (22%), farmer (16%) and laborer (14%).

Table- 4: Distribution of personal habit of the patients (n=50)

Personal habit	Number of patients	Percentage
Smoking	23	46.0
Chewing pan & betel nut	6	12.0
Alcohol intake	0	0.0
Smoking & alcohol	5	10.0
Smoking & betel nut	10	20.0
None	6	12.0
Total	50	100.0

Table show, highest percentage of patient had history of smoking (46%), smoking & betel nut (20%) and chewing pan & betel nut (12%).

Table- 5: Distribution of patients with level of education (n=50)

Occupation	Number of patients	Percentage
Illiterate	21	42.0
Primary	16	32.0
Secondary	5	10.0
Total	50	100.0

Table show, the highest percentage of patients is illiterate (42%) and then primary (32%), secondary (10%).

Table- 6: Indications for emergency tracheostomy (n=50)

Indication	Number of patients		Total
	Male	Female	
Carcinoma Larynx	24(48.0%)	2(4.0%)	26
Carcinoma of hypopharynx	2(4.0%)	4(8.0%)	6
Multiple papilloma of larynx	3(6.0%)	1(2.0%)	4
Cut throat injury	3(6.0%)	2(4.0%)	5
Carcinoma of thyroid gland	0	1(2.0%)	1
Blunt injury neck with stridor with surgical emphysema	2(4.0%)	0	2
Neck space abscess causing stridor	2(4.0%)	1(2.0%)	3
Laryngeal edema due to radiotherapy	2(4.0%)	0	2
Failed intubation	1(2.0%)	0	1
Total	39(78.0%)	11(22.0%)	50

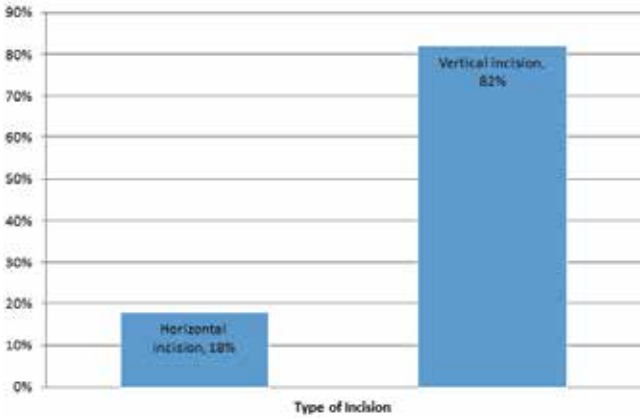
Table gives impression that carcinoma larynx (52%) and carcinoma of hypopharynx (12%) was the most common etiology for emergency tracheostomy.

Table- 7: Relationship of carcinoma larynx and others causes of emergency tracheostomy with age variation (n=50)

Variable (Age)	Carcinoma Larynx	Others	total
< 60 yrs	7(14.0%)	14(28.0%)	21
≥ 60 yrs	19(38.0%)	10(20.0%)	29
Total	26(52.0%)	24(48.0%)	50

Table show, carcinoma larynx as an etiological factor of emergency tracheostomy is significantly higher in older age group. Out of 26(52.0%) patients of carcinoma larynx, 19(38.0%) patients had age ≥ 60 years.

Figure- 4: Distribution of cases according to the type of incision during emergency tracheostomy (n=50)



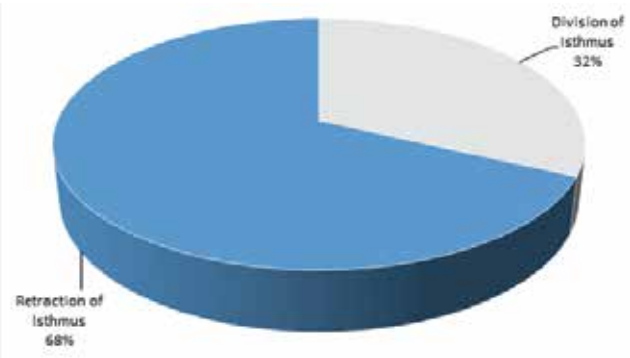
Column chart shows that, during procedure of emergency tracheostomy, out of 50 patients, vertical incision was made in 41(82.0%) patients and horizontal incision was made in 9(18.0%) patients.

Table- 8: Distribution of difficulties of emergency tracheostomy(n=50)

Difficulties	Number of patients	Percentage
Delay in presentation	14	28.0
Associated Co^{morbidities}	11	22.0
Lack of qualified assistant	7	14.0
Inappropriate illumination	2	4.0
Inadequate sucker facilities	1	2.0
Lack of proper instruments	3	6.0

During emergency tracheostomy very often surgeons have to face many difficulties. In my study the highest percentage of difficulties during emergency tracheostomy is delay in presentation (28%), then presence of associated co-morbidities (22%) and lack of qualified assistant (14%).

Figure- 5: Distribution of cases according to division and retraction of thyroid isthmus during emergency tracheostomy (n=50)



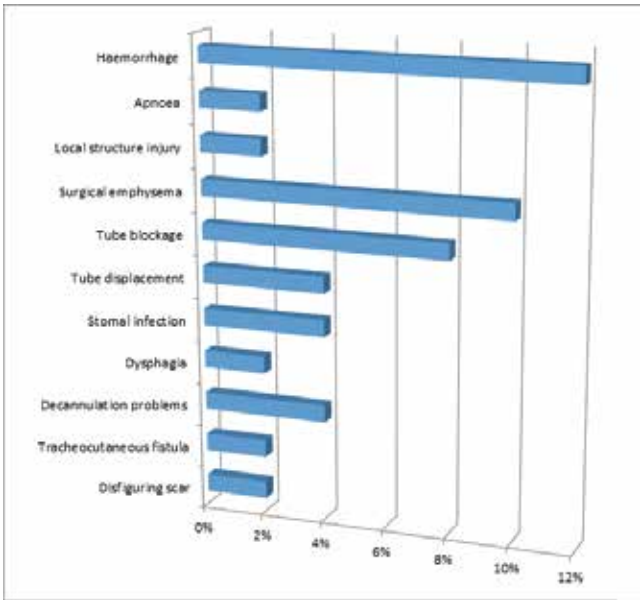
Pie chart shows that, during procedure of emergency tracheostomy, retraction of thyroid isthmus was done in 34(68.0%) patients and division of thyroid isthmus was done in 16(32.0%) patients.

Table- 9: Complications of emergency tracheostomy(n=50)

Complications	Frequency	Percentage
Intra-operative		
Haemorrhage	6	12. 0
Apnoea	1	2.0
Local structure injury	1	2.0
Intermediate		
Surgical emphysema	5	10.0
Tube obstruction/blockage	4	8.0
Tube displacement	2	4.0
Stomal Infection	2	4.0
Dysphagia	1	2.0
Late		
Decannulation problems	2	4.0
Tracheocutaneous fistula	1	2.0
Disfiguring scar	1	2.0

Table shows complications of emergency tracheostomy. Out of 50 cases 26 cases had various types of complications. Haemorrhage (12%) was the most common Intra operative complication. Surgical emphysema (10%), tube obstruction (8%) were the common intermediate complications. Decannulation problems (4%), disfiguring scar and tracheocutaneous fistula were the late complications.

Figure- 6: Bar chart showing distribution of as a whole complications of emergency tracheostomy(n=50)



Bar chart show out of 50 cases overall complications was 52.0% and the most common complication was hemorrhage (12.0%). The other significant complications include surgical emphysema (10.0%), tube blockage (8.0%), and tube displacement (4.0%).

Table- 10: Distribution of co-morbidities of the subjects.

Co-morbidities	Frequency	Percentage
Heart disease (HTN, Angina, H/OMI)	3	6.0
History of cerebrovascular disease	1	2.0
Chronic Obstructive Pulmonary Disease / Bronchial Asthma	2	4.0
Diabetes Mellitus	5	10.0
Kidney disease	1	2.0

Table show, out of 50 patients 12 patients had co-morbidities associated with the primary disease. Among the co-morbidities diabetes mellitus (10%) and heart diseases (6%) were the common complications.

Table- 11: Distribution of the experience of the surgeons.

Experience of the surgeons	Numbers	Percentage
Senior Surgeons	3	6.0
Junior Surgeons	10	20.0
Trainee Doctors	37	74.0
Total	50	100.0

Table show, out of 50 cases most of the emergency tracheostomy was performed by trainee doctors (74%). Senior surgeons experienced surgeons with more than 10 years of experience in the field of ENT & Head Neck Surgery. Junior surgeons experienced with 3 to 5 years of training. Trainee doctors worked in ENT & Head Neck Surgery but with less than 3 years of training.

Discussion:

Life is very prestigious and it is a gift of God but critical airway is a life-threatening condition, from hypoxemia to become hypoxia followed by failure or inadequate ventilation. The two classical indications for emergency tracheostomy, i.e. laryngeal pathologies and failure to pass the endotracheal tube for ventilate the patient to relieve the respiratory distress[50,51]. Tracheostomy remains a very important life-saving surgical procedure worldwide and particularly in our environment where patients presented with upper airway obstruction either due to severe trauma of head and neck region or advanced laryngeal and hypopharyngeal malignancies [52].

In this study mean age of emergency tracheostomy was 54.60 years and Std. deviation ± 18.59, ranging from 04 to 80, where it was 50.50 years in Allam Choudhury et al study[19]. The age of those with malignant condition is significantly higher than those of non malignant condition in emergency tracheostomy. In a previous study highest frequency of tracheostomy for malignant condition[53], the age group was 45-60 years, in this study it was age group of 51-70 years. Figure 3.1 shows that, 51-70 years were more prevalent for any malignant causes of emergency tracheostomy, observed in (52.0%) cases.

Here, it is found that male preponderance of 78.0% as compared to female 22.0% with a ratio of 3.54:1. While this is consistent finding in Shaikh et al54 study, where male to female ration was 3:1 but in Amarnath et al[21] study, it was 2:1. In Allam Choudhury et al[19] study male predominance was also observed (9:1).

In emergency tracheostomy, majority people were from poor socio economic conditions[53,55]. Present study shows that socioeconomically majority of patients were from poor class (78.0%).

Tracheostomy for malignant condition was significantly more common in those with lower levels of education. It is observed that in this group of patients presented in a more advanced stages of disease.

In this study 52.0% patients came from rural, 36.0% from urban non slum and 12.0% form urban slum areas. Higher percentage of patients from rural area may be due to low cost treatment in a government medical college and high intensity referral to DMCH from various parts of this country.

The study revealed that most common occupational group was businessman (22.0%), which was followed by farmers (16.0%) & day laborer (14.0%). Less common occupational groups were drivers, sailors & rickshaw pullers. In a previous study it was found to be cultivators (32.0%), businessman (23.0%), service holders (17.0%), day laborer (13.0%) and housewife (8.0%)[56].

In the study of the distribution of personal habits of the subjects, it showed that 46.0% of the study subjects were smoker, 20.0% cases were habituated in both smoking & betel nut, 12.0% were habituated with chewing pan and betel nut only, 10.0% were habituated in smoking & alcohol and 6% were habituated with nothing. In the Bhuiyan et al[56] study, carried out in our country, it was found to be 71.0% smoker, 21.0% betel nut & betel leaf chewer, 2.0% alcoholic and 6% taking nothig which is not so similar to this study.

In consideration of the level of education, in this study among the 50 cases 21 patients were illiterate, 15 patients were educated up to primary level and only 5 patients were educated up to secondary level. Higher percentage of patients were illiterate in this study signifies that due to lack of education patients were least acquainted with their disease process and they initially got treated inappropriately by village quack. Finally when the disease process becomes very critical some of them can access to tertiary level hospital.

The study revealed that malignancy of the upper airway tract as the most common indication of emergency tracheostomy which comprises of 66.0% of total cases. Among the malignant cases, carcinoma larynx (52.0%) was the commonest one followed by carcinoma hypopharynx (12.0%) and less commonly carcinoma of thyroid gland (2.0%). In a previous study carried out in this country it was found to be carcinoma larynx 53.33% followed by advanced hypopharyngeal carcinoma 13.33% and carcinoma of thyroid gland 6.67% which was almost similar to this study[19]. After tracheostomy all the malignant cases were biopsied by direct laryngoscopy under local anesthesia or general anesthesia and sent for histopathological examination. Later they were confirmed as carcinoma of squamous cell variety with HPE reports. Apart from malignancy there were some other indications of emergency tracheostomy which incduded cut throat injury (10.0%), multiple papilloma of larynx (8.0%), neck space abscess causing stridor (6.0%), blunt injury neck with stridor with surgical emphysema (4.0%), laryngeal edema due to radiotherapy (4.0%), and failed intubation (2.0%).

Carcinoma of larynx was the commonest indication because the incidence of carcinoma of larynx is high in this country due to high use of smoking, tobacco chewing & tobacco taking with betel nuts and betel leafs, lack of consciousness about the effect of tobacco on health.

Most of the operations were done by vertical incision (82.0%) and some of the operations were done by horizontal incision (18.0%). Vertical incision is the most favoured incision used in emergency procedures, because it gives rapid access with minimum bleeding and minimum tissue dissection. Transverse incisions are mainly used in elective procedures and have the advantage of cosmetically better scar.

During emergency tracheostomy very often surgeons had to face many difficulties. In this study, the highest percentage of difficulties during emergency tracheostomy was delay in presentation (28.0%) followed by presence of associated co-morbidities (22.0%), lack of qualified assistant (14.0%), lack of proper instruments (6.0%), inappropriate illumination (4.0%) and inappropriate sucker facilities (2.0%).

During open surgical tracheostomy, the isthmus is sometimes retracted rather than divided but this practice is potentially hazardous as the tube may subsequently become displaced and reintubation could be hampered by the isthmus springing back into position. But in this study, during procedure of emergency tracheostomy, retraction of thyroid isthmus was done in 34(68.0%) patients and division of thyroid isthmus was done in 16(32.0%) patients.

Complications were divided into peroperative, intermediate postoperative and late postoperative. There were no deaths due to airway obstruction or to the tracheostomy. This study revealed, early complications were observed in 8, among these 6 were haemorrhage, 1 was apnoea and 1 was local structure injury. Intermediate complications were observed in 14 cases, 5 were due to surgical emphysema, 4 were tube blockage and remaining 5 cases were tube displacement, stomal infection & dysphagia. Finally, late complications were observed in 4 cases, two were difficult decannulation & others were tracheocutaneous fistula & disfiguring scar,.

Total complication rate that was observed in the study conducted by Mehta et al[57] was (48.4%) and 44.0% in the study of Abdul Aziz Hamid et al[58]. However it was significantly higher than those studies of Choudhury et al[19] (33.35%), Manzoor et al[59] (27.2%), Amarnath et al[21] (24.0%) & Zaitouni et al[49] (24.0%). In this study the rate of total complication was 54.0% which is not similar to the studies mentioned above.

Haemorrhage was the most common complication in this study constituting 12.0% of total complications while it is 6% in Abdul Aziz Hamid et al[58], 6.67% in Allam Choudary et al[19]. Haemorrhage is most commonly arising from anterior jugular veins and thyroid gland. In one study the authors described haemorrhage as the most common fatal complication; out of 36 deaths due to direct complications of tracheostomy 10 deaths were due to haemorrhage[60]. But in this study no death was caused by haemorrhage. In some other studies death rate were found to be 1.00%, 0.49% and 1.78%[53,61,62].

In our study incidence of haemorrhage was more as the patients were in respiratory distress and prime air was the establishment of an airway. Although we used vertical incisions in majority of cases to trachea, bleeding was due to injury to the anterior jugular vein and vessels in the strap muscles. Another cause of haemorrhage was injury to thyroid isthmus. Major haemorrhage during the procedure is rare but even minor bleeding can be life threatening if it interferes with identification of trachea or gaining access to airway. Haemorrhage from brachiocephalic trunk during tracheostomy is rare and could be fatal. A case report regarding this, a patient had experience bleeding after brachiocephalic trunk dissection accidentally[30]. The cause of massive haemorrhage is usually related to erosion of innominate artery although of right carotid artery has also been reported[63].

The second commonest complication was surgical emphysema for emergency tracheotomy (10.0%). In a previous study surgical emphysema was the commonest complication (9.47%)[55]. Subcutaneous emphysema can be alarming, but is seldom fatal. It is mostly confined to the neck but can extend to the face and chest wall. It usually presents within the first day and is self-limiting by the seventh day, unless the precipitating factors persist. To tight closure of the skin or subcutaneous tissue, too large incision in the trachea, improperly fitting tracheotomy tube and excessive coughing are the causative factors6. The risk of tracheotomy tube displacement is increased in cases of marked surgical emphysema due to increase in neck swelling.

Apnoea was observed in 2% of cases which was due to sudden reversal of respiratory acidosis. Tube blockage was found in 8.0% in cases of emergency tracheotomy. In some other studies it was found to be in 2.7%, 2% and 3.5% cases respectively [6,53,55]. Tracheotomy alters the basic physiology of the inspired air from filtered, warm and humidified to dry cold air coming into direct contact with the trachea. This alteration dry up the tracheal and pulmonary secretions and interferes with ciliary capacity to move the mucous blankets, and thus causes production of thick, tenacious mucuous scabs & crusts. If the situation is not controlled the scab will increase in size with the result that they are difficult or impossible to cough out or even removed by suction6. Tube blockage was typically manifested by either high airway pressure or inability to pass a suctioning catheter. At DMCH during study period, there were no facilities for humidification of air, so there was crusting and subsequently tube blockage results.

Tube displacement was 2% in Abdul Aziz Hamid et al[58], 3.33 % in Allam choudhury et al[19] which was 4.0% in this study. Length of the tube and thickness of the neck are clearly the most important factors; postoperative edema, hematoma and emphysema will cause a broadening of the distance between the skin surface and the anterior wall of the trachea[6]. Overweight patient or patient with full neck or when the patient coughs excessively or moves the head tube can easily slips out of the trachea and into the interstitial tissues of the neck[64].

Stomal infection (12.0%) which was the most common complication in Abdul Aziz Hamid et al[58] study, occurred in only 4.0% cases in this study due to advance developed Regarding our knowledge in wound infection and sterilization. Fortunately infection in the neck in tracheostomy is local, indolent and produces local cellulitis with some granulation tissues. Antibiotics are seldom necessary as the wound is open and drainage is adequate[6].

Dysphagia, decannulation problems, tracheocutaneous fistula and disfiguring scar were found less commonly in this study. Other studies also showed a few or no incidence of these types of complications. Although different studies showed incidence of stomal recurrence, stomal stenosis, pneumothorax, aspiration, trachea-oesophageal fistula and cardiac arrest, we found no such complication. In this study no fatality was found. The fatality was due to cardiac arrest during tracheostomy, the rate varied from 0% to 5% in different studies65. Patients having cardiac arrest following tracheostomy may need immediate cardiac massage with close monitoring even may need ICU support.

Study revealed that there were some co-morbidities present in patients undergoing emergency tracheostomy such as diabetes mellitus (10.0%), heart disease (6.0%), history of cerebrovascular disease (2.0%), pulmonary disease (4.0%) and kidney disease (2.0%).

Most of the operations were done by trainee doctors (74.0%) because DMCH is one of the largest tertiary hospital of our country and in this hospital patients are referred from different parts of the country, so numbers of trainee doctors are more for their learning purpose. Besides patients are admitted although there is no vacant bed and may get admission with accommodation in the floor.

Emergency tracheostomy remains a very important life-saving surgical procedure worldwide and particularly in our environment where patients present late in upper airway obstruction. Little work has been done on this subject in our environment and therefore it was necessary to conduct this study to describe our own experiences with tracheostomy, outlining the common indications, difficulties and complications in our setting and compare our results with those from other centers in the world.

Conclusion:

Emergency tracheostomy are practiced in majority of cases to manage airway problems. Upper airway obstruction due to carcinoma of larynx was the most common indication for emergency tracheostomy. Carcinoma of larynx was significantly high in smoker elderly male patients. Tracheostomy is still a life saving procedure. However, despite being a safe procedure, tracheostomy can be associated with complication. But most of the complications are preventable and should be avoided by careful operative technique and meticulous post operative management.

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Original Article

Depression Among Undergraduate Medical Students of Pabna Medical College

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ABSTRACT

Background: *Depressive disorder is a common mental disorder. Psychological stress is very common among students of medical college and it is associated with depression. Medical students are increasing day by day but only few studies are done concerning mental health of medical students in Bangladesh.*

Objective: *A cross-sectional study with a convenience sample conducted in Pabna medical college. Survey was carried out among the undergraduate medical students of Pabna medical college. 140 undergraduate students were enrolled in the study conducted between October 2018 to June 2019. The depression levels were assessed using Zung depression scale. Students were asked to complete the questionnaire and then the depression levels calculated. The stress inducing factors during their course of medical education were also assessed.*

Results: *The overall prevalence of depression among the students was 5 percent.The prevalence of depression was 3.57 percent among female students versus 1.43 percent in male students. Academic stress is the main factor.*

Conclusion: *The prevalence of depression is seen among medical students more among females. So, attempts should be made to alleviate the stressors . Academic stress proved to be the most important factor . So measures should be taken regarding academic curriculum and more student friendly environment.*

KEY WORDS

Depression, medical students, zung depression scale

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Introduction:

Approximately 300 million people worldwide are suffering from depression, and women are affected more than men. Disability and impairment of a person's ability to function normally at work, home, or taking part in community activities appear to be some of the symptoms of depression. The personal and social sacrifice by the medical students in order to maintain a good academic result in a highly competitive environment puts them under a lot of stress. Previous studies have shown fairly high levels of distress, such as symptoms of depression among medical undergraduates. Medical students are known to experience stress during their 6 years of medical education, and stress was shown to decrease the quality of life and academic achievement. The stress that the medical students experience was determined to be associated with depressive symptoms, and 30% of the students reported depressive symptoms. It is important for medical educators to know the magnitude of depression in students and factors causing them, which not only affect their health and academic achievement but also has serious consequences as suicide.

Method:

The Study was a descriptive cross sectional study conducted at Pabna Medical College,Pabna, bangladesh during the period of October 2018 to January 2019. 140 students were included in the study after randomized sampling. The recruited students were informed about the purpose of study and explained about the general instructions. Informed consent was taken prior to the study. The students were allowed to respond in their own time and privacy. The participation was entirely voluntary. Then they were given the questionnaires which comprised of personal data, Zung Depression Inventory & stress inducing factors.

• Personal Data: This included age, sex, batch, religion and home country.

• Zung Depression Scale: It is a 20 itemed self rated questionnaire which assess the level of depression symptoms. It has already been used in primary care and community settings and as a screen for depression. Answers thus obtained are scored between one to four for each question with a total score ranging from 20 to 80. A score less than 50 were considered to represent a case with no depression while a score ≥50 was considered to represent a case with depression.

• Stress inducing factors: After in-depth literature review and peer consultation, five most important stress inducing factors were selected. The students were asked to strike the factors they thought to be important from the following. a) Academic stress b) Home sickness c) Relationships d) Hectic lifestyle e) Future concerns.

Data were entered into Microsoft excel and analyzed using SPSS 16 statistical software.

Result:

Out of the 150 questionnaires distributed to the medical students, 140 were returned completed, giving a response rate of 93.3 %. Out of the 140 respondents, 50 were males and 70 females. 26 students were enrolled in First year of study and 23 students were from final year of medical college. The mean age of study subjects was 21 years with a standard deviation of 2 years and a range of 18 to 24 years. It was noteworthy that the overall prevalence of depression in medical students was found to be 5 %. The prevalence of depression in first and fourth year of medical college is shown in table 2. Interestingly, it was found to be more among the first year students than the fourth year students. The incidence of depression was found to be more among female students which is shown in table 3.

Table 1: Socio demographic Characteristics

Socio demographic characteristics	n (%)
Gender	140
Male	50(35.71%)
Female	70(64.28%)
Age,Years(± SD)	21 ± 2
College year	
Year 1	26(18.57%)
Year2	29(20.71%)
Year3	39(27.85%)
Year4	23(16.42%)
Year5	23(16.42%)
Living Condition	
Hostel	131(93.57%)
With Family	09(9.14%)
Smoking Habit	
Smoker	07(5%)
Non smoker	133(95%)

Table 2: Prevalence of depression:First year versus fourth Year

N=49	No of depressed students	Percentage
Year1	3	3.49%
Year4	2	2.49%

Table 3: Prevalence of depression:Male versus Female students

Prevalence of depression	Number of depressed students	Percentage
Depressed females	05	3.57%
Depressed males	02	2.14%

Table 4: Stress inducing Factors

Factors	Students	Percentage
Acedemic stress	07	100%
Home sickness	03	42.85%
Future Concerns	05	71.42%
Relationship	02	28.57%
Hectic Lifestyle	04	57.14%

Discussion:

Our aim was to determine the prevalence of depression among undergraduate medical students in Pabna Medical College . The prevalence of depression in our sample was not so high. The high frequency of mild–moderate depression (55.9%) was not similar to that of other studies among medical students. Also, in Oman, the severe level of depression in medical students was 13.8%, whereas it was 5% in our study. We find difference in depression severity among male and female medical students, which is a similar in comparison to other studies that found that female students are more vulnerable to depressive symptoms.

The frequency of reporting depressive symptoms gradually decreased with advancing toward the final year . Another study carried out in India showed the same pattern as found in our study in decreasing depressive symptoms from first year to the fifth year. This could be explained by confidence in the level of knowledge or even by the fact that they are in their final years of medicine, in comparison with those who

just started college especially when a high grade point average is a major goal.

There was no significant difference between the students of smoker and non smoker group.

Conclusion:

Depression symptoms were found among female medical students (5%) in Pabna medical college. Students in the first year of college should be screened for depression, Academic stress is the most important factor for depression. So, measures should be taken regarding academic curriculum, more student friendly environment and psychotherapy can improve the situation.

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Original Article

Efficacy and Safety of Apremilast in Moderate to Severe Plaque Psoriasis: An Open Label Single Arm Study:

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ABSTRACT

Background: Psoriasis is a chronic, inflammatory, autoimmune skin disease characterized by a wide range of symptoms including scaling, itching, redness, and burning. It affects men and women of all ages, regardless of ethnic origin, in all countries. Disfiguration, disability, depression and marked loss of productivity are common challenges for people with psoriasis. Topical corticosteroids have become the mainstay of treatment of various dermatoses including psoriasis. But long-term effects of corticosteroids use include skin atrophy, striae, telangiectasia, purpura, Cushing syndrome, Hypothalamic-pituitary-adrenal (HPA) axis suppression. Oral methotrexate is an effective treatment for psoriasis being initially used more than 50 years ago. The major toxicities that are of greatest concern in patients treated with methotrexate are myelo suppression, hepatotoxicity and pulmonary fibrosis. In recent years, biologics are used for the treatment of psoriasis. But biologics therapies are costly and not affordable by most of the patient. Treatment of psoriasis should be affordable, effective and safe in the long term use. Apremilast is a phosphodiesterase 4 inhibitor that regulates the immune response associated with psoriasis. Oral apremilast was approved by the US-FDA for the treatment of adult patients with moderate-to-severe plaque psoriasis. Apremilast demonstrates an acceptable safety profile, and no new significant adverse effects. So, Apremilast considered as a good alternative for the treatment of moderate to severe plaque psoriasis.

Objective: To evaluate the efficacy and safety of Apremilast in moderate to severe plaque psoriasis.

Method: An open label single arm study was conducted in the Kabir National Skin Centre, Dhaka, Bangladesh over a period of nine months from November,2016 to July 2017. Eighty six patients who had come for the treatment of moderate to severe plaque psoriasis were enrolled for the study. Each patient was treated with Apremilast 30 mg b.i.d for 24 weeks. Outcome measures such as PASI score at 8th,16th and 24th weeks as well as adverse effects were all documented.

Result: This study had shown that Apremilast is very effective and safe drug for the treatment of moderate to severe plaque psoriasis. After 8 weeks of treatment PASI-50 achieved in 74.4% patients, PASI-75 achieved in 59.45% patients and PASI-90 achieved in 41.8% patients. At week 16, PASI-50 achieved in 94.1% patients, PASI-75 achieved in 80.25% patients, PASI-90 achieved in 59.3% patients and PASI-100 achieved in 4.6% patients. At week 24, PASI-50 achieved 97.6% patients; PASI-75 achieved in96.5% patients, PASI-90 achieved in 79.0% patients and PASI-100 in 25.5% patients. Few adverse effects were observed like nausea, vomiting, headache and vertigo which were not statistically significant.

Conclusion: Apremilast appears to be a safe, effective and new oral drug in the treatment of moderate to severe plaque psoriasis after 24 weeks of treatment.

Key Words: Plaque psoriasis, Apremilast, Phosphodiesterase 4 inhibitor.

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Introduction:

Psoriasis is a chronic inflammatory disease of the skin resulting from an immune response, which leads to a chronic imbalance in the production of pro and anti-inflammatory cytokines. It is estimated that psoriasis affects 2% of the population, with 85% of cases falling into the plaque psoriasis category [1].The reported prevalence of psoriasis in countries ranges between 0.09% and 11.4%, making psoriasis a serious global problem [2, 3]. Psoriasis involves the skin, nails and is associated with a number of co morbidities. Skin lesions are localized or generalized, mostly symmetrical, sharply demarcated, red papules and plaques, and usually covered with white or silver scales. Between 1.3% and 34.7% of individuals with psoriasis develop chronic, inflammatory arthritis (psoriatic arthritis) that leads to joint deformations and disability [4,5]. Between 4.2% and 69% of all patients suffering from psoriasis develop nail changes [6, 7, 8].

Various types of drugs are used for the treatment of Psoriasis. But treatment should be affordable, effective and safe in the long term use. Topical corticosteroids have become the mainstay of treatment of psoriasis, but in long-term effects of corticosteroids use cause skin atrophy, striae, telangiectasia, purpura, iatrogenic Cushing syndrome, hypothalamic-pituitary-adrenal (HPA) axis suppression and other potential systemic adverse events [10].

Cyclosporine provides rapid alleviation of symptoms, but cyclosporine is not approved for use in children. Acitretin is an oral retinoid with a slow onset of approx¬imately three to six months.

Acitretin is teratogenic, and adverse effects include mucocutaneous lesions, hyper¬lipidemia, and elevated liver enzyme levels [11].

Methotrexate competitively inhibits the enzyme dihydrofolate reductase, thus decreasing the synthesis of folate cofactors needed to produce nuclei acids. Because the effects of methotrexate are most dramatic on rapidly dividing cells, it was originally thought that its beneficial effects in psoriasis were a result of the inhibition of epidermal proliferation [12]. However, it is now known that there is little effect on epidermal cells [13]. The major toxicities that are of greatest concern in patients treated with methotrexate are myelosuppression, hepatotoxicity and pulmonary fibrosis [14, 15]. Hepatitis, reactivation of tuberculosis (TB), and lymphoma, especially the B-cell type that is commonly associated with Epstein-Barr virus infection, have all been reported in patients being treated with methotrexate [16,17].

In recent years, biologics have changed the treatment of psoriasis, giving us additional therapeutic options that are potentially less toxic to the liver, kidneys, bone marrow and are not teratogenic. But biologics therapies are costly and not affordable by most of the patient [18].

Apremilast is a novel oral agent of the phosphodiesterase type 4 (PDE4) inhibitor for the treatment of moderate to severe plaque psoriasis in patients who are candidates for phototherapy or systemic therapy. The drug's mechanism of action is inhibition of PDE4 results in increased intracellular cyclicadenosine monophosphate (cAMP) and reduced symptoms of psoriasis [19]. By inhibiting PDE4, apremilast prevents the degradation of cyclic adenosine monophosphate (cAMP). The subsequent increased level of cAMP results in an antagonistic effect on the production of pro inflammatory cytokines such as TNF, IL-23, and interferon (IFN), and an increase in anti-inflammatory mediators (e.g., IL-10).Thus, apremilast works intracellularly to interrupt the inflammatory cascade at an early point, unlike biologic agents that target single pro-inflammatory markers (e.g., TNF) [19]. A lot of studies have been published in international journals regarding the efficacy and safety of Apremilast. Based on these data oral apremilast provides a new therapeutic option for the treatment of patients with moderate-to-severe plaque psoriasis and may help address unmet patient needs. We had conducted this clinical study to evaluate the efficacy and safety of appremilast in Bangladeshi population.

Method:

An open label single arm study was conducted in the Kabir National Skin Centre, Dhaka, Bangladesh over a period of nine months from November, 2016 to July 2017. Eighty six patients with moderate to severe plaque psoriasis were enrolled for the study. Each patient was treated with Apremilast 30 mg b.i.d. for 24 weeks. A written informed consent was taken from eligible patients.

Inclusion criteria were male or female patients over 18 years old with moderate to severe plaque psoriasis suffering for more than 6 months with 15% affected total body surface area, and who had not received any prior local or systemic treatment within two months.

Exclusion criteria were serious medical condition, laboratory abnormality , or psychiatric illness,pregnant or lactating females,current erythrodermic, guttate, or pustular psoriasis,history of clinically significant cardiac, endocrinologic, pulmonary, neurologic, psychiatric, hepatic, renal, hematologic diseases or other major diseases like Hepatitis B or Hepatitis C, history of malignancy within previous five years and patients with psoriatic arthritis were excluded. Outcome measures such as PASI score at 8^{th},16^{th} and 24^{th} weeks as well as adverse effects were all documented.

Statistical analysis:

Analysis was performed by using a computer based statistical program SPSS (Statistical Package for Social Sciences) version 16. Quantitative data were expressed as means ±SD. 95% confidence interval was calculated and p value of <0.05 was considered as significance.

Result:

A total of 100 patients were initially recruited for inclusion in this study. 14 cases were excluded (4 had poor improvement,4 were self-discontinued,2 had severe nausea,2 had adverse reaction,1 had severe vomiting and 1 had erythroderma) from the study. Thus 86 patients formed the final study group and were included in the final analysis. Mean age of study population were 36.8 ± 1.1(Table I). Among the study patients 67.4% (58) were male and 32.6% (28) were female (Table 2).Each patient obtained 30 mg of apremilast b.i.d.orally. After 8 weeks of treatment PASI-50 achieved in 74.4% patients, PASI-75 achieved in 59.45

patients and PASI-90 achieved in 41.8% patients(Table 3). At week 16 PASI-50 achieved in 94.1% patients,PASI-75 achieved in 80.25 patients,PASI-90 achieved in 59.3% and PASI-100 achieved in 4.6% patients(Table 4).And at week 24 PASI-50 achieved 97.6%,PASI-75 in 96.5%,PASI-90 in 79.0% and PASI-100 in 25.5% patients(Table 5).Few adverse effects were observed like nausea, vomiting, headache and vertigo which were not statistically significant.

Table-1. Age of study patients (n=86)

Age	Frequency
Mean Age	36.8 ± 1.1
Minimum age	18
Maximum age	77

Data were presented as mean ±SD. Minimum age were 18 years and Maximum age were 77

Table - 2 .Sex of the study patients (n=86)

Sex	Number	Percentage
Male	58	67.4%
Female	28	32.6%

Total numbers of Male patients were 67.7% (58) and Female patients were 32.6% (28)

Table –3 .Outcome of the patient at week-8: Psoriasis area and severity index (PASI) score (n = 86)

PASI	Number of patients	Percentage
PASI-50	64	74.4%
PASI-75	51	59.4%
PASI-90	36	41.8%

PASI-50 achieved 62.8% (64) patients, PASI-75 achieved 59.4% (51) patients and PASI-90 achieved 41.8% (36) patients.

Table –4 .Outcome of the patient at week-16: Psoriasis area and severity index (PASI) score (n = 86)

PASI	Number of patients	Percentage
PASI-50	81	94.1%
PASI-75	69	80.2%
PASI-90	51	59.3%
PASI-100	4	4.6%

PASI-50 achieved 94.1% (81) patients, PASI-75 achieved 80.2% (69) patients PASI-90 achieved 59.3% (51) patients and PASI-100 achieved 4.6% (4) patients.

Table –5 .Outcome of the patient at week-24: Psoriasis area and severity index (PASI) score (n = 86)

PASI	Number of patients	Percentage
PASI-50	84	97.6%
PASI-75	83	96.5%
PASI-90	68	79.0%
PASI-100	22	25.5%

PASI-50 achieved 97.6% (84) patients, PASI-75 achieved 96.5% (83) patients PASI-90 achieved 79.0% (68) patients and PASI-100 achieved 25.5% (22) patients.

Table – 6 Adverse effects (n = 86)

Side effects	Present (n= 86) n (%)	Absent (n=86) n (%)	Pvalue
Nausea	1.2%(1)	98.8%%(85)	0.425
Vomiting	1.2% (1)	98.8% (85)	0.425
Vertigo	2.3%(2)	97.7%(84)	0.420
Diarrhea	0(0.0)	00%(0)	0.50
RTI	0(0.0)	00%(0)	0.50
Headache	1.2%(1)	98.8%(85)	0.425

There were no major adverse effects observed in the study population. The differences were not statistically significant (P>0.05).

Discussion:

Our results had shown that apremilast 30 mg b.i.d was very effective and safe for the treatment of moderate to severe plaque psoriasis over 24 weeks of treatment . Outcome measures such as PASI-50,PASI-75,PASI-90 and PASI-100 at 8 weeks,16 weeks and 24 weeks as well as adverse effects were documented.

Paul C., Cather J. and Gooderham et al[19] performed a prospective randomized controlled trial in patients with moderate to severe plaque psoriasis where the mean age group of study patient were 45.3 years and among these patients 64.2% were male and 35.8% were female.In our study mean age group of the patients were 36.8 years and among these patients 67.4% were male and 32.6% were female.

Paul C, Cather J and Gooderham et al[19] also showed that at 16 weeks,55.5% patients achieved PASI-50.In our study after 16 weeks of treatment; 94.1% patients achieved PASI-50.

Paul C, Cather J. and Gooderham et al[19]also showed that after 16 weeks ,28.8% patients achieved PASI-75.Reich k, Gooderham M and Green L et al20 showed that 39.8% patients achieved PASI-75 at 16 weeks.In our study after 16 weeks of treatment; PASI-75 achieved in 80.2% patients.Moreover we found PASI-90 in 59.3% patients and PASI-100 achieved in 4.6% patients.

In this study it was observed after 8 weeks of treatment that PASI-50 achieved in 74.4% patients,PASI-75 achieved in 59.45% patients and PASI-90 achieved in 41.8% patients. At week 24 PASI-50 achieved in 97.6% patients,PASI-75 in 96.5% patients,PASI-90 in 79.0% patients and PASI100 in 25.5% patients.

Gottlieb AB and Matheson RT et al [21] showed in their study that most adverse effect of apremilast were mild. Papp KA and Kaufmann R et al [22] showed the majority of adverse effects were mild.The most common reported side effects were diarrhea, nausea and headache.In our study there were no major adverse effects observed in the study population.The most common side effects were vertigo, nausea,vomiting and headache which were not statistically significant.

Psoriasis has a profound impact on patient's everyday life. The burden of the disease extends beyond physical

manifestations and includes significant physical, social and psychological impairment.[23] Furthermore, as a chronic disease, psoriasis affectsthe quality of life of both patients and their close relatives in a cumulative way.[24] To treat the psoriatic disease we need an effective drug which is affordable,safe and cost effective for the patients.

So the promising findings suggested that apremilast appears to be an effective new drug which is safe and affordable for the treatment of moderate to severe plaque psoriasis.

Conclusion:

Apremilast appears to be a safe, effective and new oral drug in the treatment of moderate to severe plaque psoriasis after 24 weeks of treatment.

Acknowledgments:

This study was conducted in the Kabir National Skin Centre, Dhaka. The preparation of Apremilast was “Arsenor” manufactured by Beacon Pharmaceuticals Limited, Bangladesh. The research team would like to thank all doctors, health staff and patients for participating in the clinical trial.

Conflict of interest:

The authors declare that there is no conflict of interests regarding the clinical trial.

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Review Article

Deflazacort – A Safer Corticosteroid

Islam GMR[1], Mahbuba MS[2], Faruquee M.H[3], Showkat T[4], Mozumdar SH[5], Zaman M[6], Das BK[7], Islam SU[8], Uddin MS[9]

ABSTRACT

Glucocorticoids are one of the most frequently used drugs in the current day-to-day practice. They have wide range of applications from simple allergic disorder to the most complex immune disorders. Long-term use of these drugs could result in weight gain, growth retardation, abnormal fat distribution, hyperglycaemia and osteoporosis. Many diseases like nephrotic syndrome and autoimmune diseases require long-term corticosteroid therapy. In this situation the threat of other adverse events is more alarming. To overcome the situation, we need a promising corticosteroid with strong immunosuppressive and potent anti-inflammatory action with lesser adverse effect and have long-term safety profile. Deflazacort is a glucocorticoid and an oxazoline derivative of prednisolone. In both short-term and long-term use, conventional oral steroids like prednisolone have various adverse effects. Deflazacort may be a step as an alternative oral steroid with fewer side-effects. Hence, in this review we discuss the advantages of deflazacort over conventional steroid therapy is discussed.

Key Words: Deflazacort, Corticosteroid, Prednisolon

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Introduction:

Glucocorticoids are one of the most frequently used drugs in our daily practice. They have been used in a variety of life-threatening and disabling conditions and have saved or improved many lives.These classes of drugs are also the most commonly misused drugs. The currently available corticosteroids are nonselective, as a result of this they pose a significant problem of adverse effects on many healthy anabolic processes in the body. Long-term use of these drugs could result in weight gain, abnormal fat distribution, hyperglycaemia and osteoporosis. Many diseases like nephritic syndrome and autoimmune diseases require long-term corticosteroid therapy. In this situation the threat of other adverse events is more alarming. The current article focuses on pharmacological profile of deflazacort, a new glucocorticoid. Also focussed on comparison of deflazacort with other corticosteroids.

Pharmacological Profile of Deflazacort:

Pharmacodynamics:

In vitro studies have reported that deflazacort significantly inhibits proliferation of human peripheral blood mononuclear cells and also inhibits release of certain cytokines in these cells. Deflazacort administration has shown depletion of CD4+ lymphocytes along with increase in the CD8+ subset.1 Studies have shown that the average deflazacort to prednisolone potency ratio ranges from 0.69 to 0.89 and also reported that therapeutic dosage ratio ranges from 1:1.2 to 1:1.5. [2]

Anti-inflammatory and Immunosuppressive Properties:

Based on various comparative studies and with data from British National Formulary, it has been shown that deflazacort has potent anti-inflammatory activity, which is quite similar to prednisolone. The relative potency

comparison between deflazacort and prednisolone is 1 mg of prednisolone equals 1.2 mg of deflazacort. The above comparison is obtained from many in vitro study models. In more simplified terms it can be said that 5 mg of prednisolone is equivalent to 6 mg of deflazacort. Deflazacort has potent immunosuppressive action. Studies done in ex vivo on thymus explants have shown that deflazacort possesses superior immunosuppressive action than triamcinolone, prednisolone and hydrocortisone. One study also showed that deflazacort is 10-folds more effective than prednisolone in controlling experimental delayed-type hypersensitivity. Some of the other studies have shown that deflazacort's ability to produce immunosuppression is not just higher but is also sustained for a long time when compared to prednisolone. This strong immunosuppression is useful in certain diseases but it may also pose risk of opportunistic infection in some patients.[2,3,4]

Pharmacokinetics:

Deflazacort administered orally is well-absorbed and converted by plasma esterase to pharmacologically active metabolite (D21 OH), which achieves peak plasma concentration in 1.5-2 hours. Its elimination plasma half-life is 1.1-1.9 hours. It is 40% protein bound and has no affinity for corticosteroid binding globulin (transcortin). Elimination takes place primarily through the kidneys (70%). The remaining 30% is eliminated in the faeces. High elimination rate through kidney means a need for caution in patients with kidney diseases.[1]

Deflazacort (Xalcort): A Safer Corticosteroid

The common safety issues with long-term steroid therapy are: Weight gain, hyperglycaemia and osteoporosis.

Weight Gain:

Ferraris et al conducted a study on patients undergoing kidney transplant. A comparison was made between deflazacort and methylprednisolone. These patients were followed-up for 2.1 years. The study showed that number of overweight patients were significantly higher in prednisolone group.5 Another study conducted by Broyer et al in patients with idiopathic nephritic syndrome also compared deflazacort with prednisolone and patients were followed-up for 5.5 years. At the end of the study, the individual body weight change was higher in prednisolone group as compared to deflazacort.[6]

Hyperglycaemia:

Gulliford et al. found 2% of newly diagnosed cases of diabetes mellitus (DM) due to orally administered Glucocorticoid 7. Glucocorticoids may transiently or permanently induce hyperglycaemia.[8-10]

Bruno et al conducted a study in which subjects administered deflazacort/betamethasone for two months underwent glucose tolerance test. The study showed that there was significant increase in blood glucose and insulin after betamethasone as compared with deflazacort. The study also concluded that degree of glucose intolerance and insulin resistance depends on the steroid used and dose given.11 In another study conducted by Bruno et al, insulin-treated diabetic patient were randomly assigned to deflazacort or prednisolone treatment for four weeks. At the end of the study, mean plasma glucose level was 139 ± 28 versus 169 ± 32 mg/dl in deflazacort and prednisolone groups, respectively. Also, insulin requirement was significantly lower in deflazacort group.12In both short-term and long-term use, conventional oral steroids like prednisolone have various adverse effects. Deflazacort may be a step as an alternative oral steroid with fewer side-effects.

Osteoporosis:

Olgaard et al conducted a study to assess the osteoporotic effects of glucocorticoids in patients with nephrotic syndrome, who were followed-up for 12 months. At the end of the study, bone decay rate was 2% per year in deflazacort as compared to 5.3% per year in prednisolone group ($p < 0.001$). The bone decay in lumbar spine was (6.8% per year) in deflazacort group as compared to (12.5% per year) in prednisolone group.[13] The study showed that detrimental effects of long-term steroid treatment on bone can be significantly reduced with deflazacort therapy. In another study by Gennari et al, the bone loss over 12-month therapy with deflazacort and prednisolone was compared. The study showed that bone lost with deflazacort was 9.7% in 12 months as compared to 21.4% in 12 months in prednisolone group.[14]

Withdrawal benefits:

Abrupt withdrawal of deflazacort of doses upto 48 mg daily or equivalent for three weeks is unlikely to lead to clinically relevant HPAaxis suppression in the majority of patients. However, gradual withdrawal is recommended in the following situations: [1]

- Repeated courses of systemic corticosteroids
- Patients receiving dose >48 mg/day
- Patients repeatedly taking doses in the evening.

Indications and Clinical Uses:

Duchenne muscular dystrophy (DMD):

Biggar et al have reported that deflazacort can improve gross motor and pulmonary function in boys (7 and 15 years) with DMD with limited side-effects.[15] A study by Houde et al over period of 8 years has shown that treatment with deflazacort improves cardiac function, prolongs walking and seems to eliminate the need for spinal surgery in patients with DMD, although vertebral fractures and stunted growth may occur. The overall impact on quality-of-life appears positive.[16] Deflazacort improves strength and functional outcomes compared to placebo. Deflazacort causes less weight gain than prednisolone as reported in a systematic review of trials by Campbell et al.[17]

Polymyalgia rheumatica:

Studies have reported deflazacort to be effective and safe in long-term usage in treating patients suffering from

polymyalgia rheumatic a compared to other corticosteroids.[18]

Drug-resistant epilepsy of childhood:

Grosso et al have reported that deflazacort is as effective as hydrocortisone, with a less worrying adverse-effect profile, for long-term therapy in drug-resistant childhood epilepsies.[19]

Idopathic sephrotic syndrom(INS):

Studies have suggested that deflazacort is more effective than prednisolone in preventing steroid-dependent INS.[06]

Renal transplant:

Study done on pediatric and adolescent patients have shown that deflazacort was well-tolerated and safe after renal transplantation.[20]

Asthma:

A comparative study of deflazacort and prednisolone by Gartner et al in children with acute moderate asthma has shown similar efficacy in improving pulmonary function.[21]

Deflazacort is also indicated in rheumatic carditis, ulcerative colitis, Crohn's disease, uveitis, optic neuritis, autoimmune haemolytic anaemia and idiopathic thrombocytopenic purpura.

Adverse Effects:

Deflazacort is associated with adverse effects like skin lesions such as acne, bruises or stretch marks, recurrent infections, stomach upset, muscle or bone weakness, Cushing's syndrome, menstrual cycle irregularities or hirsutism.[18]

Dosage

Adults:
120 mg/day; maintenance dose: 3- 18 mg/day
Rheumatoid arthritis: 3-18 mg/
Bronchial asthma: 48-72 mg/day

Children:
0.25-1.5 mg/kg/day.
Juvenile chronic arthritis: 0.25-1.0 mg/kg/day.
Nephrotic syndrome: 1.5 mg/kg/day
Bronchial asthma: 0.25-1.0 mg/kg/day

Conclusion:

Deflazacort (Xalcort) seems to be a promising corticosteroid with strong immunosuppressive and potent anti-inflammatory action. It also has safe pharmacokinetic profile. Many long-term studies show, lesser weight gain and hyperglycaemia with deflazacort compared to other corticosteroids. The percentage of bone loss with long-term deflazacort therapy was also lesser as compared to prednisolone. Further studies with large sample size and proper study design may be needed to establish efficacy and safety of deflazacort in wide range of indications. With currently available studies, it can be concluded that deflazacort is a safe and effective corticosteroid.

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Case Report

Intraosseous Osteolytic Meningioma of the Skull: A Rare Case Report

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ABSTRACT

Primary intraosseous meningiomas of skull are uncommon lesion often confused preoperatively with a primary bone tumour of skull. The osteolytic variants of these tumours are even rarer. When one review a bony skull lesion diagnosis is very wide and includes both malignant and benign diseases. The most common primary sources of metastatic tumour found in the skull region are the lung, kidney and prostate gland in men and the breast, genital organ and kidneys of women. The exact location of the primary tumour however, is difficult, sometimes impossible, to identify. Here we will present the case of a 52 year old woman with metastatic adenocarcinoma involving the left fronto-parietal region of skull.

Key words: Primary intraosseous meningioma, ectopic meningioma, osteolytic lesion, resection, skull, Metastatic adenocarcinoma.

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Introduction:

Meningiomas without any dural connections are uncommon and often referred to as ectopic. Ectopic meningiomas have been reported to occurs in the subcutaneous tissue of the skin, paranasal sinuses, orbit, neck, salivary gland and calvaria[3,6,7,11] .The lesion appears as a hard osteoblastic tumours which appear as hyperdense areas of the calvarial bones in X-ray/CT studies[2].Of ,a rarer prevalence are lytic skull meningioma that are not readily suspected because of their radiological appearance; rather they are investigated first for a primary source of malignancy elsewhere in the body or are thought to be other lytic lesions of the skull[2,5,13]. Primary intraosseous meningiomas are seldom correctly diagnosed pre-operatively and are usually mistaken for primary bone tumour or metastatic cancer[1, 3,7,11].

Case Report:

A-52 year old female was admitted with persistent left sided headaches and one episode of unconsciousness. The Headache was described as dull aching, centered over the left parietal region, mild to moderate in intensity and present on daily basis for approximately 7 months.

On examination :

She showed no physical and neurological abnormality except there is a subcutaneous hard mass (8×5×2cm) in her left fronto-parietal region with ill-defined margin and irregular surface and was continuous with the calvarium.The overlying skin showed no abnormalities. Results of Laboratory examinations were all within normal limit.

Radiological examination:

- X-ray of skull and computed tomogram (CT) of head showed lytic lesion of the skull in the left fronto-parietal region.
- Magnetic resonance imaging (MRI) of head showed an area of iso to hypointense in T1W image and mildly hyperintense in T2 & FLAIR images with contrast enhancement inT1W image with contrast and reactive hyperplasia of left fronto-parietal region. The lesion was extradural, intradiploic and without any intracranial extension.
- CT angiogram demonstrated that the small branches of the superficial temporal artery were the feeders of the mass.

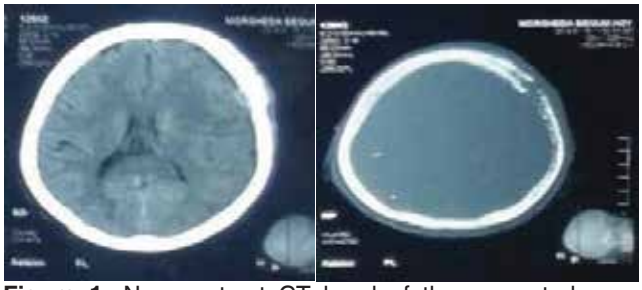

Figure 1: Non contrast CT head of the presented case showing a destructive, osteolytic mass lesion involving left fronto-parietal region.

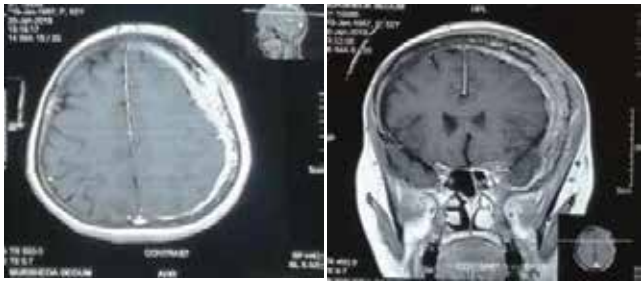

Figure 2: Contrast MRI of head, axial and coronal view showing a extradural, intradiploic enhancing mass lesion without intracranial extension occupying left fronto-parietal region.

Operation:

The patient underwent surgery in order to resection of the mass lesion. The skin was reflected easily and the mass was not adhered to it. The outer table of the skull was thinned and elevated and the tumour partly infiltrated the overlying pericranium. The tumour was resected totally including the surrounding normal bone. The inner table of the removed bone was smooth and intact. The dura was easily separated from the bone and it's outer surface showed no tumour infiltration.

Pathology:

Histological study of the lesion revealed metastatic adenocarcinoma. The absence of the tumour tissue at the margin of the resected bone indicates that the tumour had been removed completely. Regarding calvarial defect after resection of the tumour cranioplasty was planned on a later session. The patient was advised for chemotherapy postoperatively.

Discussion:

Extradural meningioma constitutes 1-2% of all Meningioma[14]. The term "primary extradural meningioma" differentiates tumour that arise separately from the dura from those that originate from dura but have an extra cranial extension[2,5]. Lang et. al. have proposed a classification system for these tumours 2,10: tumours that are purely extracalvarial are type I, purely calvarial tumours are type II and calvarial tumours with extra cranial extension are type III. Extradural meningioma, including intraosseous meningioma, are reported to occur with the same frequency in each sex or with a slight female predominance, unlike intradural meningioma, which occur twice as frequently in women as in men[5,16]. Like intradural meningioma, extradural meningioma predominantly occurs later in life, with a median patient age at diagnosis in the fifth decade [4,5,16]. Ectopic meningioma is a well recognized entity and it has been reported to occur in various sites such as subcutaneous regions 1,7, paranasal sinuses 1,4 and orbits 1,8. The histogenetic origin of these tumors is speculated to be ectopic embryonal arachnoids cell rests 1,12, especially those located in the midline or cells normally distributed around cranial nerves and sensory organs (orbital, aural, nasal, buccal) [12]. There is no answer as yet to the question on why intraosseous calvarial meningiomas preferentially occur at the cranial sutures. The assumption provided by Azar-Kia et al. 6 is interesting, that is a part of the dura containing arachnoid cells may have been trapped in the suture lines during molding of the skull at birth and later develops into meningioma. Alternatively, Turner et al. [15] reported that trauma may play a role in the development of some primary intraosseous meningiomas. As there is no history of head injury in our case, the former may well explain our case. Primary intraosseous meningiomas are usually of osteoblastic subtype. More rarely, these lesions may present as an osteolytic skull lesion 2,5. The differential diagnosis of an osteolytic lesion of the skull includes chondroma, epidermoid cyst, osteogenic sarcoma, myeloma, metastatic cancer, or fibrous dysplasia [13]. Due to benignity of meningiomas, and hence their different natural history, the intraosseous meningiomas should be considered in evaluation of a lytic skull lesion since definite treatment (i. e., complete surgical resection) is available. If there is doubt about complete resection, the lesion should be followed with appropriate imaging studies [17].

Conclusion:

Intraosseous meningiomas are rare lesions that originate in the skull and represent the most common type of extradural meningioma. The lesions are often asymptomatic, but can cause proptosis and neurological symptoms depending on their size and location. Radiographic and clinical presentations generate diagnostic suspicion that may assist with preoperative planning. The majority of these tumors cause hyperostosis that may mimic fibrous dysplasia. Although most are benign, intraosseous meningiomas are more likely to be malignant than their intradural counterparts. The osteolytic subtype of intraosseous meningiomas are more likely to be malignant than the osteoblastic subtype. Intraosseous meningioma should be considered in the differential diagnosis for patients presenting with osteoblastic or osteolytic skull lesions.

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Case Report

A Case Of Oral Contraceptive Pill (OCP) – Induced Carpal Tunnel Syndrome

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Introduction:

Carpal Tunnel Syndrome (CTS) is the most common compressive neuropathy affecting the hand. The symptoms are caused by pressure applied to the median nerve in the carpal tunnel, presumably by the transverse carpal ligament, but the precise etiology for the development of the pressure is unknown in most cases. It is estimated to affect 8 percent of women and 0.6 percent of men. The cause of most CTS is not known, but a number of diseases that affect local architecture of the wrist are associated with it, included rheumatoid arthritis and Colles fracture. Individuals with occupation that involve repetitive or forceful hand movements are also at risk of developing the condition. Those with certain hormonal and metabolic problems, notably thyroid disease and diabetes mellitus, have a higher prevalence of CTS. An influence of specific risk factors for females on CTS is suggested by the higher incidence in women compared with men and the observation that incidence in women peaks around menopause. Furthermore, uses of combined oral contraceptives, bilateral oophorectomy and pregnancy have all been reported to be associated with CTS. If CTS is not treated, the patient may develop pain, numbness, loss of strength. CTS can be treated with surgical decompression in the later period. For this reason, we found it appropriate to present a case with carpal tunnel syndrome.

Keywords:

Carpal tunnel syndrome, oral contraceptive pill.

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Case Report:

A 29 years old female presents with a complaints of “tingling” affecting the thumb, index and middle fingers of the right hand. These symptoms began spontaneously about four months previously and were not associated with any injury or change in her activities. She first noted this symptom at night when it disrupted her sleep, sporadically at the outset but in recent weeks on almost a nightly basis. She is a housewife. Her right hand is dominant. She has a long term history of taking oral contraceptive pills (OCP) around 4 years with no history of using any vibrating tools as well.

The physical examination of the right hand does not reveal abnormalities on inspection; in particular the bulk of the intrinsic musculature of the hand, including the thenar eminence, is normal. There is no tenderness to palpation in the hand. The neurological examination shows that the strength of the abductor pollicis brevis muscle is normal and is rated as grade V. Two point discrimination in the distribution of the median nerve is normal. The Phalen test is positive. The Tinel sign is positive – light tapping over the median nerve at the level of the carpal tunnel causes paraesthesiae radiating into the index and middle fingers.

Investigations Findings:

TSH: 2.56 mIU/L (0.4 – 4.0 mIU/L)
RA Factor: Negative
Anti CCP Antibody: Negative
X ray cervical spine: doesn’t reveal any abnormality
The Electrophysiological Study of Right Hand is suggestive of Right Sided Carpal Tunnel Syndrome (severe)

On the basis of history, physical examination and investigation a diagnosis of CTS is made. She was advised surgery and to avoid OCP. The patient was reluctant for undergoing surgery and took the medicines for 7 days, but had no relief. After 7 days she came to the Outpatient department (OPD). The patient was advised to undergo a steroid injection into the carpal canal and in addition, to begin splinting of the hand in the wrist brace preventing wrist flexion during sleep. Within 2 weeks the symptoms of tingling have been fully addressed. The patient has continued with her usual work activities and gradually reduces her splint use over the next 6 weeks. She avoided to use OCP and planned for intra uterine contraceptive devices.

She returns for further follow up about 1 year later. In the interim she states that the sensory symptoms gradually returned about 6 months after splinting was fully discontinued. She resumed nighttime splinting but the symptoms have persisted despite this treatment. She intermittently experiences the symptoms during the day as well but she finds that daytime splinting is not practical because it disrupts her household works to an unacceptable degree. The physical examination has not changed since the initial assessment. Because the surgical release of carpal tunnel is now a treatment option she is advised to undergo

electro diagnostic tests of median nerve function. These are performed within several weeks and confirm median nerve dysfunction at the level of carpal tunnel. She was advised to undergo a carpal tunnel release.

As a result of surgical release of the transverse carpal ligament the patient experiences an immediate resolution of the sensory symptoms. Although she is troubled by mild wound tenderness for the next 6 weeks but she is able to return to all of her work activities within 3 weeks of the surgical procedure and without any formal program of post-operative rehabilitation. The wound tenderness has resolved by the time she is seen for a final follow-up 3 months after the surgical procedure. The sensory symptoms remain fully resolved at that time. She was advised to discontinue OCP fully and adopt other intrauterine contraceptive devices.

Discussion:

Diabetes, rheumatoid arthritis, hypothyroidism, OCP and pregnancy can cause CTS. Gender, age, body mass index and thyroid function affect CTS development.[1] Female gender has been reported as a risk factor for CTS.[2] They reported recurrent CTS by reason of connective tissue diseases such as gout.[3] CTS can be caused by a variety of causes, including inflammatory or non-inflammatory arthropathy, wrist trauma or fractures, diabetes mellitus, obesity, hypothyroidism, pregnancy, OCP and genetic factors. The risk of CTS increases by progressive age at premenopausal women.[1] The use of vibration tools in the workplace, installation work, food processing and packaging can cause CTS.[4] CTS has been reported to be associated with repetitive movements in the upper extremity, strong manual forcing, wrist flexion and elbow vibration.[5] To establish a job-related carpal tunnel syndrome diagnosis; the job story should be related to CTS and the CTS should be recognized by the clinician. Repeated, long-term, hand-wrist movements, hand wrist strength in the workplace are risk factors for CTS.[1] It is found that current use of OCP increase the risk of CTS. It was found that the longer a woman used OCP , the greater her chances were developing CTS severe enough for hospital referral. The hypothesis is that OCP exerts their effects through fluid retention, causing pressure on the median nerve. It is difficult to reconcile such a mechanism with observation that former users of OCP are those with the elevated risk of CTS and that the risk declines with duration of use. One possible explanation is that women who develop pain or neurologic symptoms in the upper limb while using OCP may advised by their family doctor to stop using them and that the actual CTS diagnosis was made at later date, by which time the woman was a “former” user. If this happened soon after a woman started the OCP, it would lead to an apparent link of CTS with short duration former use, while continuing users would be “healthy survivors”.[6] For the diagnosis of CTS disease, EMG evaluates the median nerve and assists for the diagnosis.[7] Carpal tunnel syndrome should be operated. The general approach is to remove the median nerve pressure in the trap area by the surgical procedure. CTS can be improved by treatment of underlying disease such as pregnancy, cessation of OCP use and myxedema. Patients may not have surgery if the symptoms are mild for CTS. Medical treatment is given for CTS if there is median paralysis in the future. [8, 9] Complication rarely develops after CTS operation. However, a case with postoperative epidermal inclusion cyst was reported.[10] In another case, they reported a neuroma following the median nerve injury after operation.[11]

Conclusion:

Hormonal factors, both endogenous and exogenous, may account for some of the differences in the frequency of CTS between men and women, including past use of the pill in older women and obesity. Further research is required to see the link between CTS and other musculoskeletal syndrome.

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Case Report

Gaucher's Disease and Pregnancy: A Case Study in Bangladesh.

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ABSTRACT

Background: *Gaucher disease is a lysosomal storage disorder due to deficiency of glucocerebrosidase enzyme. In this study, a case of newly diagnosed patient with gaucher's disease during her pregnancy was reported.*

Case Presentation: *A 35-year old woman with type I Gaucher disease was managed for pregnancy until delivery. A conservative approach with close monitoring of both mother and baby was planned.*

Results: *In the 39th week of pregnancy, a healthy male baby of 3180 g was delivered via cesarean section.*

Conclusion: *Apart from mild hematological complications, the pregnancy, the delivery and the puerperium were uneventful. In this case report, the issue of therapy and risk assessment in pregnancy in patients with type I Gaucher disease was discussed.*

Keywords: Gaucher's Disease, Pregnancy

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Introduction:

Gaucher disease is a lysosomal storage disorder due to deficiency of glucocerebrosidase. The association with pregnancy exposes the worsening of the disease and complications of pregnancy and puerperium [1]. This disease is one of the group of lipidoses, which are hereditary metabolic storage disorders. In Gaucher's disease the lipid cerebroside, kerasin, infiltrates the histiocytic cells of the lymph nodes, liver, spleen and bone marrow; these are the Gaucher cells, derived from reticuloendothelium [2]. According to Thannhauser, this disorder is caused by a disturbance of intracellular metabolism. The large spleen in this disorder is reddish purple and homogeneous. On section it has a uniform, granular, reddish-pink colour. Microscopically, there is replacement of the normal pattern by accumulation of Gaucher cells, which are large, pale and polyhedral [3]. Data presented at the WORLDSymposium meeting in San Diego last month and published in the clinical journal Molecular Genetics and Metabolism concludes that pregnant women receiving enzyme replacement therapy (ERT) for Gaucher disease can continue taking it and can continue labour [2].

The disease has a familial tendency and may appear in infancy or childhood. Females are more often affected than males and it has a greater predilection for the Jewish race. It may be suspected in an otherwise healthy individual who has a large liver and spleen, usually without ascites. Yellowish, spotty thickenings of the conjunctiva, known as pingueculae [5]. Data presented at the WORLDSymposium meeting in San Diego last month and published in the clinical journal Molecular Genetics and Metabolism concludes that pregnant women receiving enzyme replacement therapy (ERT) for Gaucher disease can continue taking it and can continue labour [2].

The poster presentation, "Reported outcomes of 453 pregnancies in patients with Gaucher disease: an analysis from the Gaucher Outcome Survey," reports that this patient population can continue the treatment regimen with small risk of a miscarriage or issues in delivery of the baby [2].

Pregnancy can worsen Gaucher disease symptoms and increase patients' risk of having disease-related complications [3]. GD affects most female events during the

reproductive age, particularly, fertility, pregnancy, delivery and puerperium. While pregnancy in GD may exacerbate disease manifestations, the disease may have deleterious effect on female reproductive health milestones [4].

Case Presentation:

The patient was 35 years old Bangladeshi woman and was full term pregnant (37+ weeks). She had some skeletal and visceral abnormalities, such as spleenomegaly which was non tender and diagnosed by USG. Also complained for pain in hip and ankle joint. Because of repeated episodes of bone pain, we suspected and did her beta glucosidase leukocyte (BGL) assay and found low enzyme activity. Invasive bone marrow testing to rule out leukemia and blood cancer.

She was characterized as suffering from GD Type 1, as she had skeletal and visceral abnormalities, with no involvement of the central nervous system. The avoidance of bone crises, normal size of liver, a normal platelet count and normal haemoglobin.

From the gynaecological point of view, the woman had regular menstrual cycles (every 32-35 days) and normal periods lasting for 4-5 days. She was on combined oral contraceptive pill (OCP) and before attempting any pregnancies, her husband was tested and found not to be carrier for GD. Her father and mother, in their sixties, were living and well.

Her platelet count was almost normal throughout pregnancy, ranging between 100 and 125 and she was not anaemic. The anomaly ultrasound scan revealed no anatomical abnormalities of fetus. The course of the pregnancy, in general, was uneventful and the fetus showed a normal growth pattern. When pregnancy complicates the condition, a decision must be made concerning the advisability of terminating the pregnancy. There is anxiety about possible rupture of the spleen during the stress of labour and mechanical interference with the natural uterine enlargement.

Because of the favorable reports, her general good health, and her strong desire to continue the pregnancy, it was decided to perform caesarean section. As it turned out, she had a very satisfactory delivery, free of complications, and was fit to be discharged on the eighth postpartum day, with a completely healthy baby.

On follow-up checkup day at 20 postoperative day, the mother and baby was satisfactorily healthy. The mother was advised for enzyme replacement therapy [ERT], to improve hematological abnormalities, reverse the visceromegaly, ameliorate bone symptoms.

Discussion:

Gaucher's disease is not often seen in practice, general or specialized in Bangladesh. However, it should be remembered that it occurs. An otherwise healthy young patient who presents with a large spleen for which no etiological factor is discernible should have a bone marrow aspiration. In this way, by the demonstration of the cells that are a specific feature of this disease, the correct diagnosis can be made. Other evidence in the form of skin pigmentation, bone changes and blood abnormalities due to hypersplenism may also be present [4].

The signs and symptoms of Gaucher disease may have an impact on pregnancy and birth, particularly hepatosplenomegaly may be massive and may alter the normal growth in pregnancy; anemia and thrombocytopenia may be exacerbated by pregnancy and the bleeding tendency may be mild in a nonpregnant patient but may become critical during birth. On the other hand, pregnancy may affect the course of Gaucher disease, with regard to signs and symptoms that existed previously as well as the possibility of triggering new features, i.e. bone pains [5]. The ability of enzyme therapy to rapidly stabilize the disease, especially hematological parameters, has been reported previously [6].

There is accumulating evidence that replacement therapy with imiglucerase during pregnancy might stabilize the patient's condition for physiological changes of pregnancy, and reduce the incidence of complications during delivery and the postpartum period [7, 8, 9]. The treatment has been related to a reduced risk of spontaneous abortion in women treated with alglucerase and/or imiglucerase, reduced risk of Gaucher-related complications during delivery, and a reduced risk of Gaucher-related complications during the postpartum period [8]. The first antenatal appointment should include a comprehensive assessment of patient, drafting a birth plan, and a multidisciplinary approach to management of pregnancy in such a way that assessment should ideally be performed in a center with experienced experts in pregnancy management. Genetic counseling is recommended and indications for prenatal diagnosis should be explained to the patient. For example, the facts about whether Gaucher disease mutations in one of parents are associated with a risk of neuro-nopathic Gaucher disease and the other parent is a carrier of unknown genotype should be explained thoroughly [10]. Monitoring in pregnancy should be adapted to the needs of the individual patient based on the disease status. Clinicians are advised to concentrate on direct parameters of Gaucher disease status, such as platelet count and platelet function that could affect patients during pregnancy and delivery. Ferritin concentrations are often elevated in the serum of Gaucher patients as part of the sustained acute inflammatory response [10]. This usually does not indicate iron overload but may mask the presence of iron deficiency especially in pregnancy. Iron supplementation is advisable in pregnant Gaucher patients with hypochromic microcytic anaemia who do not have evidence of a haemoglobinopathy (e.g. β thalassaemia trait), reduced concentrations of serum iron and decreased serum transferrin saturation.

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Even when most of the patients with Gaucher disease underwent splenectomy before the reproductive period, a reversible massive progressive splenic enlargement during pregnancy occurred [11]. Accumulated data presented here provide no evidence of any teratogenic effects even when given in the first trimester of pregnancy. Imiglucerase and alglucerase are generally well tolerated in Gaucher patients and have an excellent safety record [12]. Pharmacovigilance data shows that imiglucerase is also well tolerated in pregnant women and there is no evidence of any adverse events specifically related to pregnancy [11].

Even if vaginal delivery is preferred and there is no specific indication for caesarean section, often a surgical delivery is preferred for the risk of splenic rupture during labor. Caesarean sections in Gaucher patients are more likely to occur because of disease profile of patients, such as orthopaedic considerations, rather than acute complications during delivery. Caesarean sections cannot alone be perceived as an indication of risk of complications, as these are increasingly carried out without medical indication at maternal request or because of caution on the obstetrician's part, despite associated risks [11].

Although hemorrhagic tendency may be observed in such patients [8], the state could be successfully managed conservatively, for example, by a low transversal Yoel-Cohen incision or a Pfannenstiel curved incision. Surgeons should avoid exploration of the peritoneal cavity unless there is a surgical indication, as palpation of enlarged organs in Gaucher disease may precipitate bleeding.

Because Gaucher disease is a disease with multi-organic involvement, preoperative assessment should be carried out in order to determine the extent to which the different organs are affected. General anesthesia should be avoided because of maternal aspiration syndrome and the risk of neurological and respiratory depression in the new-born. The use of regional anesthesia for patients with Gaucher disease undergoing surgery remains controversial; however, some authors point out that local anesthetics, as for cesarean section, may be safe provided that no other formal contraindications for their use is present, such as clotting parameter alterations, severe spinal deformities or spinal cord abnormalities, that would put the patient at risk of neurological sequelae [13, 14].

Perinatal demise of the newborn affected by Gaucher disease is very rare and is considered a variant of type 2 Gaucher disease that occurs in the neonatal period. The most frequent features are non-immune hydrops fetalis, in utero-fetal demise, and neonatal distress. In some cases without hydrops, neurological signs occur in the first week of life and lead to death within 3 months and some common signs of the disease are hepatosplenomegaly, ichthyosis, arthrogryposis and facial dysmorphy [15].

Few data to date are available on patients with Gaucher disease treated with imiglucerase during the lactation period, on its excretion into human breast milk and its effects on the newborn [16, 17].

Even when during breastfeeding, the enzyme was likely to be digested in the child's gastrointestinal tract suggesting minimal risk to infants [18], a continued healthy development of children breast-fed by alglucerase or imiglucerase treated mothers has been reported [19]. The European Medicines Agency and the US Food and Drug Administration indicate that caution should be exercised when imiglucerase is administered in nursing women. Postpartum, bone mineral density assessment using DEXA should be considered in cases of prolonged breastfeeding and checked at appropriate intervals after breastfeeding is completed.

Conclusion:

This case study confirms that the relatively benign nature of disease in the adult female, and the case with which a normal pregnancy can be carried to term, in the presence of splenomegaly.

Competing Interests:

The authors declare that they have no competing interests.

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