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Editorial

Healthy Diet Trends in Recent Years

A healthy lifestyle is about making little changes that make a big difference. It's not about being perfect or having zero fun. Eating healthy can be doable with the diets if one has the right mindset. A healthy diet helps to protect against malnutrition in all its forms, as well as non-communicable diseases (NCDs), including diabetes, heart disease, stroke and cancer.

Energy intake (calories) should be in balance with energy expenditure. To avoid unhealthy weight gain, total fat should not exceed 30% of total energy intake.[1, 2, 3] Intake of saturated fats should be less than 10% of total energy intake and intake of trans-fats less than 1% of total energy intake, with a shift in fat consumption away from saturated fats and trans-fats to unsaturated fats[3] and towards the goal of eliminating industrially-produced trans-fat.[4, 5, 6]

Limiting intake of free sugars to less than 10% of total energy intake is part of a healthy diet. A further reduction to less than 5% of total energy intake is suggested for additional health benefits.[7]

Keeping salt intake to less than 5 g per day (equivalent to sodium intake of less than 2 g per day) helps to prevent hypertension, and reduces the risk of heart disease and stroke in the adult population.[8]

WHO Member States have agreed to reduce the global population's intake of salt by 30% by 2025; they have also agreed to halt the rise in diabetes and obesity in adults and adolescents as well as in childhood overweight by 2025.[9,10]

The National Institute of Health claims a 22-year study showed that people who ate a healthy diet lived an average of seven years longer than those who didn't. So, let's see the list of healthy diet trends for 2024.[11] Often including weight loss resolutions it seems to be hard to keep up with different diet trends, but following are all covered. Now the trend is not only to ensure weight off but also to add years in our life.

1. The Keto Diet

It is a high-fat, low-carb diet that was originally developed as a treatment for epilepsy in the 1920s and is now used for weight loss and various health benefits.

The main idea behind the keto diet is to reduce carbohydrate intake to a very low level and replace it with fat. This process forces our body into a state called ketosis, which is when our body starts burning fat instead of carbohydrates for energy.

The benefits of a ketogenic diet are vast and include weight loss, improved energy levels, better mental clarity, and decreased risk of certain chronic diseases. But it can be very restrictive in terms of food choices. Additionally, it is important to follow the diet correctly and to ensure getting all the necessary vitamins and minerals from other sources such as supplements.[12]

The ketogenic diet which is still popular is being tweaked. Health experts are now recommending a moderate amount of carbohydrates, as well as protein. This may prevent short-term side effects of KD referred to as "keto flu," which encompasses symptoms including fatigue, headache, dizziness, nausea, vomiting, constipation, and low exercise tolerance. Long-term side effects include hepatic steatosis, kidney stones, hypoproteinemia, and vitamin deficiency.[13]

2. The Paleo Diet

The Paleo diet (Paleolithic Era2.5Milion -10000yrs ago) is based on the idea of eating like our ancestors did. It focuses on a diet of whole foods, including vegetables, fruits, nuts, seeds, and lean proteins such as fish and poultry. The basis of the diet is that our bodies are best suited to eat what we have been evolved to eat over thousands of years.

It has been linked to reducing inflammation, promoting weight loss, increasing energy levels, improving mental clarity, and reducing the risk of chronic diseases.

Some of the foods allowed on the Paleo diet include: grass-fed meats, wild-caught seafood, eggs, nuts and seeds, non-starchy vegetables, low-sugar fruits, and healthy fats such as olive oil, coconut oil, and avocado

oil. Foods to avoid on this diet include processed grains and refined sugars, dairy products, legumes, and most processed foods.

3. The Mediterranean Diet
The Mediterranean Diet is based on the traditional eating habits of countries around the Mediterranean Sea, such as Spain, Italy, Greece, and Morocco. It focuses on consuming whole foods, such as fruits, vegetables, nuts, seeds, legumes, olive oil, and whole grains. The diet also incorporates moderate amounts of fish, eggs, poultry, and dairy products.

One of the main benefits of the Mediterranean Diet is its emphasis on healthy fats like monounsaturated and polyunsaturated fatty acids found in olive oil, nuts, and avocados. These are known to reduce inflammation and help lower your risk of heart disease. Additionally, the diet emphasizes plant-based foods that are high in fiber, vitamins, minerals, and antioxidants, all of which can improve overall health.

Overall, the Mediterranean Diet is a great option for those looking to improve their health and wellness while still enjoying their food. It provides a wide range of nutritional benefits while still allowing for flexibility.

4. The Vegan Diet
The vegan diet is based on the principle of avoiding animal-derived products such as meat, dairy, eggs, and other animal-derived ingredients, instead opting for plant-based foods like fruits, vegetables, nuts, seeds, and grains.

It is high in fiber, antioxidants, vitamins, minerals, and phytochemicals, which can help reduce the risk of chronic diseases such as heart disease and certain types of cancer. Additionally, research suggests that a vegan diet may help reduce inflammation in the body and improve mental health.

In addition to the health benefits of a vegan diet, it is also much more sustainable than diets based on animal products. According to the United Nations, livestock production accounts for 14.5 percent of global greenhouse gas emissions. Eating a vegan diet eliminates this contribution to climate change and can help protect our planet. [12]

5. The DASH diet- This is a Dietary Approach to Stop Hypertension and also to lose weight. It includes lots of fruits, vegetables, grains and low-fat dairy products with limited amounts of lean meat, poultry and fish. Being high in potassium and magnesium, the DASH diet is low in sodium.

5. MIND - It stands for the Mediterranean-DASH intervention for neurodegenerative delay. It is a hybrid of the Mediterranean diet and DASH diet. Research suggests it may reduce the risk of developing dementia or slow the decline in brain health. [14]

6. The Intermittent Fasting Diet
This involves periods of fasting and eating within a specified time frame. There are several different methods of Intermittent Fasting, including the 5:2 diet, which involves eating normally for five days and restricting calories to 500-600 calories for two non-consecutive days. Another popular method is the 16/8 diet, which involves fasting for 16 hours a day and eating all meals within an 8-hour window.

Intermittent Fasting cite numerous potential health benefits, such as weight loss, improved mental clarity, increased energy, better digestion, and improved insulin sensitivity. Additionally, Intermittent Fasting may help to improve cardiovascular health and reduce inflammation in the body.

When it comes to the actual process of Intermittent Fasting, it is important to ensure that one's calorie intake is still healthy and nutritious. It is also important to take breaks if needed.[12]

7. Flexitarian Diet- A flexitarian or semi-vegetarian diet (SVD) is one that is primarily vegetarian with the occasional inclusion of meat or fish. So, flexitarian is a portmanteau of "flexible" and "vegetarian." The FD seems to recognize the fact that meat is an important source of protein, fat, and micronutrients, yet also considers the ethical sides, such as the need to avoid intensification and improve animal welfare. It also considers evidence that long-term consumption of increasing amounts of red meat and particularly processed meat may increase the risk of mortality, cardiovascular disease, type 2 diabetes and certain forms of cancer such as colon cancer. Recently, the International Agency for Research on Cancer classified red meat and processed meat as probable carcinogenic to humans [15]

This diet can be started by adding plants to every meal to start – at least 2 cups per meal, equivalent to half of the plate. Selection of one meal a day that can easily be replace animal products with plants. For example, switch out of eggs and sausages with hearty

oatmeal topped with chia seeds and berries for breakfast. For lunch, opt for a salad with beans instead of chicken.[16]

Ultimately, it is important to consult with a doctor or registered dietitian before trying out any new diet. It is important to understand the potential benefits and risks associated with any type of diet before trying it out.

Previous years the rise of diets like "veganism" and "paleo" both were viewed as a healthy life style but considered disliked due to their limited food options. So, in coming years top diet trends will not only be easy to follow diet plans but they focus on our overall health and extension of healthy life rather just the number on the scale.

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Original Article

Evaluation of Neutrophil-Lymphocyte Ratio as Inflammatory Marker in Chronic Kidney Disease Stage 3 and 4

Sumon AMI[1], Islam MN[2], Chowdhury MFH[3], Nath PKD[4], Rana MSA[5], Saha JV[6], Jannat G[7], Hossen SI[8], Naher MN[9]

ABSTRACT

Chronic kidney disease (CKD) is a worldwide health problem because of the significant morbidity and mortality which is mostly due to chronic inflammation and proteinuria. Early detection of inflammation and its proper management can prevent further CKD progression and complications. This study aims to observe the association of neutrophil-lymphocyte ratio (NLR) with inflammatory markers in chronic kidney disease stage 3 and 4. In this study, a total of 100 adult patients of CKD stage-3 and 4 were included as study subjects and patient with acute illness, known case of malignancy, cardiovascular and cerebrovascular disease were excluded from the study. From each patient all the relevant history, clinical and laboratory findings were recorded in the data collection sheet. Study subjects were divided into two groups according to NLR value; those who have NLR 0- 3 were in group normal NLR and subjects with NLR >3 in group high NLR. Then markers of inflammation ESR, CRP and serum albumin were compared between these groups. Statistical analysis was done by Statistical Package for Social Science (SPSS) version 22.0. The mean ESR of male and female patients was higher in high NLR subjects than normal NLR subjects. The mean CRP was higher in high NLR subjects than normal NLR subjects. The mean serum albumin was lower in high NLR subjects than normal NLR subjects. The difference of mean ESR, CRP was statistically significant between high NLR and normal NLR subjects but difference of mean serum albumin was not statistically significant. The study findings suggest that high NLR is significantly associated with of inflammatory markers-ESR, CRP. Hence, it can be concluded that NLR could be used as an indicator of inflammation in CKD.

Keywords: *Chronic Kidney disease, Inflammatory marker, Neutrophil-lymphocyte ratio.*

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INTRODUCTION

Chronic kidney disease (CKD) is a worldwide health problem because of the significant morbidity and mortality. CKD is associated with age-related decline of renal function accelerated in hypertension, diabetes, obesity and primary renal disorders.[1] Proteinuria shows strong association to risk of progression to chronic renal failure.[2] The presence of proteinuria generally reflects impaired glomerular filtration barrier or impaired tubular function, in which advanced immunoinflammatory activity has been found to play an important role.[3] Proteinuria is the basic finding of renal damage and is an important indicator of development of fibrogenesis and glomerulosclerosis linked to the progression of several kidney diseases.[4] It may cause an increase in

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morbidity and mortality in the general population. The effect of proteinuria is essentially due to an increase in inflammation that is already present. Evidence for this includes the amount of increased protein in the urine and is associated with increased amount of tubulointerstitial inflammatory cells, especially, T lymphocytes.[4]

Neutrophil lymphocyte ratio (NLR) is an indicator of inflammation in chronic kidney disease (CKD); it may not be an independent predictor of CKD progression except that the CKD is in a more advanced stage and reflects the associated inflammation. Classical risk factors such as DM and lower GFR are more powerful predictors of progression.[5] Neutrophil lymphocyte ratio (NLR) is a strong indicator in determining inflammation in cardiac and noncardiac diseases.[4]

There is a graded inverse relationship between CVD risk and glomerular filtration rate (GFR) that is independent of age, sex and other risk factors.[6,7] Decreased renal function is a predictor of hospitalization,[1] cognitive dysfunction and poor quality of life.[8,9] The healthcare burden is highest in early stages due to increased prevalence, affecting around 35% of those over 70 years.[10]

Atherosclerosis, which develops as a result of inflammation, is the most important cause of morbidity and mortality in CKD.[11] Neutrophil counts are increased, whereas lymphocyte counts are decreased during inflammation and recent studies have emphasized that NLR could be used as an indicator for inflammation.[12] Other studies showed that NLR is increased in inflammation in cardiovascular disorders and can be used as an indicator of prognosis.[13,14] Studies in patients with malignancies as well as cardiovascular disorders revealed that NLR and lifespan are correlated.[15] Mahmoud et al[12] found that NLR is significantly higher in patients with CKD compared to healthy individuals and NLR is increased as the stage of kidney disease progressed.

Cardiovascular mortality risk due to atherosclerosis is 10–20-fold higher in CKD patients as compared to general population.[16] In addition to conventional risk factors, CKD has nonconventional risk factors that accelerate atherosclerosis.[17] Nonconventional risk factors include inflammation and thrombogenic factors. In addition to known conventional indicators of inflammation such as C-reactive protein (CRP), fibrinogen, erythrocyte sedimentation rate, several interleukins and tumor necrosis factor alpha, several recent studies have shown that mean platelet volume (MPV) and neutrophil/lymphocyte ratio (NLR) are also increased during inflammation and may be associated with poor prognosis in CKD.[18] In addition to increased morbidity and mortality, Neutrophil-Lymphocyte ratio (NLR) is a marker of inflammation. Some recent data suggest that NLR may predict the progression of CKD.[5] Use of NLR as indicators of inflammation is very valuable as it can be evaluated by a simple blood count.

Therefore, aim of the study is to evaluate the NLR as inflammatory markers in patients with CKD stage 3 and 4.

METHODS

This cross-sectional study was conducted in the Department of Nephrology and Medicine out patient department, Dhaka Medical College Hospital, Dhaka for 12 months. After getting approval from the Research Review Committee of the Department of Nephrology and Ethical review committee of Dhaka Medical College, a questionnaire was prepared considering key variables like demographic data, clinical presentation and clinical findings. Then, informed written consent was taken from each patient. Total 100 adult patients of CKD stage-3 and 4 defined by MDRD formula were included as study subjects and patient with acute illness, known case of malignancy, cardiovascular and cerebrovascular disease were excluded from the study. After selection of the patient; aims, objectives and procedures of the study was explained with understandable language to the patient. Risks and benefits also were made clear to the patient. The patients were encouraged for voluntary participation and they were allow being free to withdraw themselves from the study. Then, relevant history, physical examination and laboratory findings were recorded in the data collection sheet. For convenience, study subjects were divided into two groups according to NLR value; subjects with NLR 0- 3 were in group normal NLR and subjects with NLR >3 in group high NLR. Then markers of inflammation ESR, CRP, serum albumin and also 24 hours urinary total protein were compared between these groups. Estimation of complete blood count, ESR, Serum Creatinine, serum albumin and CRP was done as laboratory parameters. Calculation of Neutrophil-Lymphocyte Ratio (NLR) was done dividing absolute neutrophils counts by absolute lymphocytes counts. eGFR was estimated by using MDRD formula. Statistical analysis was

done using Package SPSS version 22.0. For comparison of data, Kolmogorov–Smirnov test was used. Student's *t*-test, Mann–Whitney U-test, Chi-square test used where applicable.

RESULTS

The mean serum albumin was lower in high NLR subjects than normal NLR subjects. The difference of mean ESR, CRP was statistically significant between high NLR and normal NLR subjects but difference of mean serum albumin was not statistically significant.

Table I: *Distribution of the study population by Socio demographic parameters (n=100)*

Socio demographic parameters	Number (%)
Age (in year)	
<40	10 (10.0)
41-50	28 (28.0)
51-60	40 (40.0)
61-70	15 (15.0)
>70	7 (7.0)
Mean ± SD	54.46±11.16
Range(min-max)	(35-87)
Sex	
Male	67 (67.0)
Female	33 (33.0)

Table II: *Association of NLR with ESR (mm/1st hour) (n=100)*

	High NLR (N= 59)	Normal NLR (N= 41)	*P* value
ESR (mm/1st hour)	Number (%)	Number (%)	
Male			
High (>10)	35 (59.4)	24 (58.6)	
Normal (0-10)	1 (1.7)	7 (17.1)	
Mean±SD	30.03±13.81	23.16±8.63	0.005
Range(min-max)	10-82	10-37	
Female			
High (>20)	23 (38.9)	6 (14.7)	
Normal (0-20)	0 (0.0)	4 (9.8)	
Mean±SD	33.74±20.36	24.5±18.42	0.022
Range(min-max)	20-120	10-70	

P value reached from unpaired t-test
high NLR (NLR>3)
normal NLR (NLR 0-3)

Table III: *Association of NLR with CRP (n=100)*

	High NLR (N= 59)	Normal NLR (N= 41)	*P* value
CRP	Number (%)	Number (%)	
<6.0	1 (1.7)	0 (0.0)	
≤6.0	58 (98.3)	41 (100.0)	
Mean±SD	16.54±11.09	10.54±6.81	0.002
Range(min-max)	1-66	6-36	

P value reached from unpaired t-test

Table IV: *Association of NLR with serum albumin (n=100)*

	High NLR (N= 59)	Normal NLR (N= 41)	*P* value
Serum Albumin (gm/dl)	Number (%)	Number (%)	
Low (<3.5)	39 (66.1)	20 (48.8)	
Normal (3.5-5.5)	20 (33.9)	21 (51.2)	
Mean±SD	3.4±0.54	3.53±0.48	0.218
Range(min-max)	2.5-4.8	2.8-5	

P value reached from unpaired t-test

DISCUSSION

In present study, it was observed that more than one third 40 (40.0%) patients belonged to age 51-60 years. The mean age was 54.46±11.16 years with ranged from 35 year to 87 years. More than two third 67 (67.0%) patients were male and 33(33.0%) were female.

In this study, it was observed that 35 (59.4%) male patients had high ESR in high NLR subject and 24 (58.6%) patients in normal NLR subjects. The mean ESR of male patients was 30.03±13.81 mm/1st hour in high NLR and 23.16±8.63 mm/1st hour in normal NLR subject. 23 (38.9) female patients had high ESR in high NLR subject and 6 (14.7) patients in normal NLR subject. The mean ESR of female subject was 33.74±20.36 mm/1st hour in high NLR subjects and 24.5±18.42 mm/1st hour in normal NLR subject. The difference of mean ESR was statistically significant between high NLR and normal NLR subject in both male and female. Kocyigit et al[18], Ju et al. (2015)[16] stated that neutrophil/lymphocyte ratio (NLR) were

increased during inflammation and associated with poor prognosis in CKD. Yoshitomi et al[19] reported that a high NLR was associated with poor renal outcomes, suggesting that NLR may be a useful marker for prognostic prediction in patients with CKD.

In present study, it was observed that 58 (98.3%) patients had high level of CRP in high NLR subject and 41 (100.0%) patients in normal NLR subject. The mean CRP was 16.54±11.09 in high NLR subjects and 10.54±6.81 in normal NLR subject. The difference of mean CRP was statistically significant between these two groups. Kocyigit et al[18]; Ju et al.[16] stated that neutrophil/lymphocyte ratio (NLR) were increased during inflammation and associated with poorer prognosis in CKD. Yoshitomi et al[19] reported that the high NLR group had significantly higher CRP level compared with the low NLR group.

It was observed that almost 39 (66.1%) patients had low serum albumin in high NLR subjects and 20 (48.8%) patients in normal NLR subjects. The mean serum albumin was 3.4±0.54 gm/dl in high NLR subjects and 3.53±0.48 gm/dl in normal NLR subjects. The difference of mean serum albumin was not statistically significant between these two groups. Hypoalbuminemia is a frequently found feature of chronic kidney disease (CKD).[20] Binnetoglu et al[4] reported that there was a moderate positive correlation between proteinuria and NLR.

CONCLUSION

The study findings suggest that high NLR is significantly associated with inflammatory markers-ESR, CRP. So, it can be concluded that NLR could be used as an indicator of inflammation in CKD.

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Original Article

Comparison of Treatment Outcome of Ganciclovir Ophthalmic Gel and Moxifloxacin Eye Drop in Acute Adenoviral Keratoconjunctivitis

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ABSTRACT

Adenoviral ophthalmic infection is a self-limiting, highly contagious, very frequent infectious process. It can present in three acute clinical forms: nonspecific acute follicular conjunctivitis, pharyngo-conjunctival fever and epidemic keratoconjunctivitis. This study aims to assess and compare the efficacy of 0.15% ganciclovir gel with Moxifloxacin eye drop in the treatment of acute adenoviral keratoconjunctivitis.This longitudinal prospective study was conducted among 40 patients of acute adenoviral keratoconjuctivitis attending in the cornea clinic of National Institute of Ophthalmology & Hospital (NIOH), Dhaka, Bangladesh. They were randomly divided into two groups: group-I (study group) with 20 patients who used 0.15% ganciclovir gel and group-ii (control group) with 20 patients who used artificial tear and 0.5% moxifloxacin eye drop. Diagnosis was confirmed by expert cornea specialist by methodical ophthalmic examination. They were followed-up on 1,2,4 and 6 weekly. Mean score of symptoms and signs were calculated in every follow-up and compared between two groups. Unpaired t test and chi square test were done in applicable cases with statistical significance p<0.05. This study showed that in study group mean age of the respondents were 36.4±9.59 years and in control group 37±11.02 years. Most of them were male (82.5%). In study group, mean score of symptoms at the beginning of the study was 1.4. It was 1.14, 0.64, 0.20 and 0.04 after1,2,4,6 weeks respectively after starting treatment and in control group mean score of symptoms at the beginning of the study was 1.48. It was 1.46, 1.125,0.59 and 0.23 after1,2,4,6weeks respectively after starting treatment. A trend towards better response was observed in the treatment group and the difference was statically significant. The mean score of signs after starting treatment in group-iwas 1.8.It was 1.35, 0.775, 0.30 and 0.175 after ,2,4,6weeks respectively and in group-ii, mean score of signs at the beginning of the study was 1.675. It was 1.725,1.35,0.725 and 0.300 after 1,2,4,6 weeks respectively after starting treatment. A trend towards improved sings were observed in the study group and the difference was statistically significant at 1 week (p=0.0283), 2 week (p= 0.0003), 4 week (p=0.0016) except 6 week (p=0.1524). At 6th week of treatment improvement of signs occur but not statistically significant because of persistence of some corneal lesion. The significant symptomatic relief and clinical improvement was found in the study group treated with Ganciclovir ophthalmic gel suggesting an effective method for treatment of acute adenoviral keratoconjunctivitis.

Keywords: *Ganciclovir, Adenoviral Keratoconjunctivitis, Moxifloxacin.*

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INTRODUCTION

Adenoviral eye infection is a highly contagious, self-limiting and very frequently occurring infectious disease that can lead to an epidemic outbreak[1,2]. The patient has complaints of burning, pain, photophobia, pruritus, irritation and tearing.[1,2] In the acute phase of the disease, follicles in the tarsal conjunctiva, serous or mucous secretion, eyelid edema, chemosis, punctate keratitis, preauricular lymph adenopathy and in the later phase, subepithelial infiltrates in the cornea are observed[1].Onset is acute, with symptoms 6 to 9 days after exposure. The ocular picture is usually bilateral, occurring simultaneously or with a difference of three days between the two eyes.[3,4]

The diagnosis of adenoviral conjunctivitis is generally clinical, based on signs and symptoms, and epidemiology.[1] Laboratory diagnosis of adenoviral infections is rarely indicated and currently is based on cell-culture in combination with immuno-fluorescence staining (CC-IFA), serologic methods, antigen detection, or PCR.[5] Cell culture in combination with immunofluorescence staining (CC-IFA) is the historical gold standard but is not widely used. Since its introduction as a laboratory test for eye disease in 1990, PCR has been used widely in clinical ophthalmology.[6,7] It has demonstrated better sensitivity compared with cell culture.[8,9,10]

Several drugs have been tested for the treatment of viral conjunctivitis, such as cyclosporine, trifluridine, povidone iodine, cidofovir, but none of them proved to be effective.[11] Topical ganciclovir is already available in the market of several countries in Europe, Asia, Africa and South America for treatment of ocular herpes.

Ganciclovir is a more selective and less toxic antiviral compared to other older antivirals[12]. Ganciclovir and aciclovir have similar pharmacological mechanisms. Topical application of gancilovir has been shown to penetrate the corneal stroma and reach the aqueous humor at therapeutic levels.[13,14,15] Ganciclovir has been shown to be a safe and effective topical antiviral, with less toxicity and more convenient in dosage schedule[15] .There are few clinical trials regarding the use of ganciclovir in adenoviral keratoconjunctivitis. Those studies suggested that ganciclovir can help achieving faster resolution of sign and symptoms reducing the contagiousness of the disease and preventing subepithelial opacities.[18,19] Due to the need for effective treatment for this common and highly contagious condition, the present study was conducted.So this study was conducted to campare the efficacy of Ganciclovir ophthalmic gel with Moxifloxacin eye drop in the treatment of acute Adenoviral keratoconjunctivitis.

METHODS

This prospective longitudinal study was conducted in the Department of Cornea, NIOH, Dhaka since June 2020 to July 2021, comprising of 40 cases of adenoviral keratoconjunctivitis who attended the cornea clinic, selecting them by non-random purposive sampling technique.

Inclusion Criteria: Patient with acute viral keratoconjunctivitis with onset of symptoms 5 days or less, over 18 years old were included in the study

Exclusion Criteria: Patients with central or para central corneal opacities, Pregnant or nursing mother immunodeficiency, corneal dystrophy, degeneration and corneal ectatic condition , previous ocular surgery (previous keratoplasty), kerato-uveitis, patient with corticosteroid or antibiotic use by any route within 30 days prior to the study and one eyed patients were excluded.

This 40 patients of viral keratoconjunctivitis with symptoms onset 5 days or less non randomly divided into two groups:group-i (Study group) with 20 patients who used 0.15%ganciclovir and group-ii (control group) with 20 patients who used artificial tear and 0.5% moxifloxacineye drop for 6 weeks. Data was collected from both groups. All patients with viral keratoconjunctivitis had gone ophthalmic examination. A data sheet was filled by interviewer by face to face interview.

They were followed-up on 1, 2, 4, 6 weekly. Mean score of symptoms and signs were calculated in every follow-up and compared between two groups. Statistical analyses were done to assess the level of significance. All the relevant data was recorded in a pre-designed data collection sheet.

The Statistical analysis was performed using the SPSS program, version 13.0. Unpaired t test and Chi square test were done in applicable cases. At 95% CI, p-value <0.05 will be considered as significant.

RESULTS

Mean age of the respondents were 36.4±9.59 years and in control group37±11.02 years. Most of them were male (82.5%). In study group, mean score of symptoms at the beginning of the study was 1.4. It

was1.14, 0.64, 0.20 and 0.04 after1,2,4,6 weeks respectively after starting treatment and in control group mean score of symptoms at the beginning of the study was 1.48. It was 1.46, 1.125,0.59 and 0.23 after1,2,4,6weeks respectively after starting treatment. A trend towards better response was observed in the treatment group and the difference was statically significant. The mean score of signs after starting treatment in group-iwas 1.8.It was 1.35 ,0.775 ,0.30 and 0.175 after ,2,4,6weeks respectively and in group-ii, mean score of signs at the beginning of the study was 1.675. It was 1.725,1.35,0.725 and 0.300 after 1,2,4,6 weeks respectively after starting treatment. A trend towards improved sings were observed in the study group and the difference was statistically significant at 1 week (p=0.0283), 2 week (p= 0.0003), 4 week (p=0.0016) except 6 week (p=0.1524). At 6th week of treatment improvement of signs occur but not statistically significant because of persistence of some corneal lesion.

Table I : *Distribution of frequency of symptoms*

Symptoms	Group-i (n=20)	Group-ii (n=20)
Foreign body sensation	19	17
Watering	18	20
Photophobia	18	18
Discharge	10	9
Eye ache	12	18
Reduced vision	6	4

Table II: *Distribution of frequency of signs*

Symptoms	Group-i (n=20)	Group-ii (n=20)
Intact corneal sensation	20	20
Punctate epithelial keratitis	20	20
Reduced visual acuity	18	20
Conjunctival congestion	18	16

Table III: *Distribution of mean score of symptoms*

Assessment periods	Group-I	Group-II	p value
Baseline	1.4±0.45 (SD)	1.48±0.26(SD)	0.6^{ns}
1 week after treatment	1.14±0.49(SD)	1.46±0.28(SD)	0.02^{s}
2 weeks after treatment	0.64±0.29(SD)	1.13±0.25(SD)	0.0001^{s}
4 weeks after treatment	0.20±0.25(SD)	0.59±0.18(SD)	0.0001^{s}
6 weeks after treatment	0.04±0.14(SD)	0.23±0.21(SD)	0.0016^{s}

ns= non-significant, s= significant, p value obtained by unpaired t test

Table IV: *Distribution of mean score of signs*

Assessment periods	Group-I	Group-II	p value
Baseline	1.8±0.41 (SD)	1.68±0.47(SD)	0.37^{ns}
1 week after treatment	1.35±0.56(SD)	1.73±0.47(SD)	0.0283^{s}
2 weeks after treatment	0.78±0.50(SD)	1.35±0.40(SD)	0.0003^{s}
4 weeks after treatment	0.30±0.47(SD)	0.73±0.30(SD)	0.0016^{s}
6 weeks after treatment	0.18±0.24(SD)	0.30±0.30(SD)	0.1524^{ns}

ns= non-significant, s= significant, p value obtained by unpaired t test

Table V: Distribution of complications of the study

Complications	Group-i(n=20)	Group-ii(n=20)	p value
Pseudo-membrane	5	6	1.12^{ns}
Sub-epithelial infiltrate	4	5	

ns= non-significant, p value obtained by a”^{2} test

Table V: Distribution of days of improvement and recovery after treatment

	Group-I	Group-II	p value
Improved	8.40±2.6 (SD)	18.70±3.6 (SD)	<0.001[s]
Recovered	34.20±8.3 (SD)	42.85±6.14 (SD)	<0.001[s]

s= significant, p value obtained by a"[2] test

DISCUSSION

Adenoviral eye infection is a serious public health problem.It is extremely contagious and can easily lead to epidemics. The cost of this disease to the citizens is high. It is needed to explore effective drugs for treatment of adenoviral keratoconjunctivitis which will provide faster recovery and should prevent any squelae and complications. Keeping all these aspects in consideration this study was conducted to evaluate the efficacy of 0.15% ganciclovir in treatment of adenoviral keratoconjunctivitis patients and showed that the drug is effective in controlling signs and symptoms of diseases.

In this study, patients were within 18-60 years of age. This age range represents the people working outside in crowd with the chance of more adenoviral infection.

Maximum number of participants were male 33 (82.5%),female were 7(17.5%).Most of the patients (70%) were service holder and middle class, most of them were engaged in outdoor activities.

Most of the patients (95%) of both groups presented with watering at the beginning of the study, which was followed by reduced vision (50%), discharge (47.5%), eye ache (75%), FB sensation (90%) and photophobia (90%). Study done by Tabbara K et al showed that patients with adenoviral kerato-conjunctivitis presented with tearing, photophobia, FB sensation and discharge was consistent with this study findings.[18] In this study corneal lesion was found in all the patients (100%) on examination at the beginning of the study. This was followed by congestion (85%) and reduced visual acuity (95%) in our study. Study done by Yabiku ST et al showed that the patients of severe adenoviral keratitis had congestion, hyperemia, corneal lesion and sub epithelial infiltration. They did not find reduced corneal sensation in adenoviral keratoconjunctivitis patients which also correlates with this study.[19]

By comparing proportion of symptomatic relief of both groups it appears that topical gancyclovir 0.15% eye gel is more effective in relieving symptoms compared to topical artificial tear and moxifloxacin after 6 weeks of treatment.

By comparing proportion of substitution of signs of both groups it appears that topical gancyclovir0.15% eye gel is more effective in relieving signs as compared to artificial tear and moxifloxacin after 6 weeks of treatment. Study done by Yabiku ST et al showed that topical gancyclovir 0.15% eye gel is more effective in relieving symptoms and signs of tearing, congestion, corneal lesion, sub epithelial opacitiesas compared to artificial tear and moxifloxacin 0.5% eye drop after 2 weeks of treatment.[19]

Study done by Yabiku ST et al showed that there is faster improvement of symptoms in study group compared to control group which supports this study findings.[19] There is statistically significant ($p<0.05$) difference in efficacy of topical gancyclovir eye gel in relieving symptoms of patients with adenoviral keratoconjunctivitis.

Study done by Jeng BH et al showed that mean score of signs after 2 weeks and 3 weeks of starting treatment with topical gancyclovir eye gel were 1.7 and 0.2 respectively which support this study findings[20]. There is statistically significant ($p<0.05$) difference in efficacy of topical gancyclovir eye gel and artificial tear and moxifloxacineye drop in relieving signs of patients with adenoviral keratoconjunctivitis.

At the end of the study, in group-i, 5 patients had pseudomembrane and 4 patients had sub-epithelial infiltrate. In group-ii, 6 patients had pseudomembrane and 5 patients had sub-epithelial infiltrate. In our study, there was corneal sub epithelial infiltrates, conjuctival pseudo membranes were higher in group-ii compared to group-i. So, study showed fewer complications in the ganciclovir group.

Tabbara K, et al found that ganciclovir significantly reduced both the duration of disease and the incidence of subepithelial infiltrates. They found mean time of adenovirus recovery was significantly shorter for ganciclovir-treated patients at 7.7 days in contrast to 18.5 days for those who received artificial tears ($P < 0.05$). In addition subepithelial opacities less developed in patients treated with ganciclovir 2

(22%) compared to 7 (77%) patients in treated with artificial tear and moxifloxacin.[18] Shiota H et al showed ganciclovir ophthalmic gel treatment shortens the recovery time and prevent complications in the keratoconjunctivitis which correlate with this study.[15]

CONCLUSION

The present study showed a tendency of faster improvement of signs and symptoms treated with 0.15% ganciclovir gel compared to the group treated with artificial tear and moxifloxacin eye drop. Which demonstrates this therapeutic modality to be an effective method of treatment for acute adenoviral keratoconjuctivitis.

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Original Article

A Comparison of Functional Endothelial Changes between Phacoemulsification with PCIOL and Manual Small Incision Cataract Surgery with PCIOL

Hasan MM[1], Kajmina N[2], Begum H[3]

ABSTRACT

Intraocular surgery e.g., cataract surgery with PCIOL implantation is one of the leading causes of corneal endothelial injury and change in the functionality of the cornea. This observational study was conducted in the Department of Ophthalmology of Combined Military Hospital (CMH), Dhaka Cantonment, Dhaka, Bangladesh, between January and July of 2016, to assess and compare functional changes in cornea (i.e., endothelial thickness) after phacoemulsification with posterior chamber intraocular lens (PCIOL) implantation and manual small incision cataract surgery (MSICS) with PCIOL implantation. A total of 80 patients of age-related cataract were randomly selected based on inclusion and exclusion criteria. All patients underwent complete ophthalmic evaluation pre- and post-operatively (at day 1, after 1 week and 3 months) specifically for observation of the endothelial changes in cornea. Specular microscopy was done to assess corneal endothelial change. The mean central corneal thickness was increased at day 1 (564.71±22.45µ vs. 555.10±40.57µ), after 1 week (539.43±22.16µ vs. 535.08±38.87µ) and 3 months (523.49±21.29µ vs. 520.05±33.68µ) after phacoemulsification and MSICS from their preoperative value (508.72±23.96µ vs. 503.62±32.06µ) respectively. However, the differences were not statistically significant between two groups (P>0.05). The mean percentage of central corneal thickness change at day1, after 1 week and after 3 months following cataract surgery were found 11.01±6.30% and 10.22±26.54% at day 1, 6.04±7.52% and 6.25±21.24% after 1 week, 2.90±11.14% and 3.26±5.05% after 3 months in phacoemulsification and MSICS cases respectively. However, no statistically significant difference was observed in percentage of central corneal thickness change of both groups (P>0.05). To summarize, an increased central corneal thickness was observed after phacoemulsification and SICS from their preoperative values.

Keywords: *Central corneal thickness, phacoemulsification, small incision cataract surgery*

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INTRODUCTION

The cornea is the transparent, avascular front part of the eye, refracts light and accounting for approximately two-thirds of the eye's total optical power.[1] It has five layers – outer epithelium, Bowman's layer, stroma, Descemet's membrane and innermost endothelial layer.[2] Corneal Endothelium is a simple squamous or low cuboidal monolayer, approximately 5ìm thick and consists of 5,00,000 of mitochondria-rich cells.[2] These cells are responsible for regulating fluid and solute transport between the aqueous and corneal stromal compartments and maintenance of corneal optical transparency via active Na/K ATPase pump.[2,3] The cells of the endothelium do not regenerate. Instead, they stretch to compensate for dead cells which reduces the overall cell density of the endothelium; however, it affects fluid regulation. If the endothelium can no longer maintain a proper fluid balance, stromal swelling ensues from excess fluids and subsequent loss of transparency occurs in cornea.[3]

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Intraocular surgeries are one of the leading causes of endothelial injury and cataract surgeries

comprise of 80% eye surgeries.[4] Phacoemulsification is considered the gold-standard procedure for cataract.[5] However, manual small incision cataract surgery (MSICS) has appeared as a popular procedure of choice in the surgical treatment of cataracts as it is less expensive and is as effective as phacoemulsification.[5] Both techniques are advantageous for being suture less procedure and required small incision.[6] However, in both surgeries, the invasive trauma leads to endothelial cell injury. Endothelial injury may occur during surgery due to several factors, such as corneal distortion, ricocheting of nuclear fragments, intraocular lens (IOL) contact and release of free radicals.[7,8] The traumatized endothelium continues to loosen cells and endothelial dysfunction may develop gradually years after the surgery. After surgical trauma, the endothelium shows practically no proliferative activity, and the damaged area is covered by means of cell migration.[8,9] Moderate damage to corneal endothelium during the surgery can cause a transient increase in corneal thickness.[9] Evidence showed that the central corneal thickness (CCT), as an indicator of the physiological (functional) condition of the corneal endothelium, is generally used in diagnoses like keratoconus, Fuchs' dystrophy, and glaucoma.[10]

Several studies done in different countries reported no significant difference in percentage of endothelial cell loss and increased corneal thickness among the manual small incision cataract surgery (MSICS) and phacoemulsification surgery.[4-6,9,11] However, in our country, no such reports are available. Therefore, the present study aims to assess and compare functional changes (central endothelial thickness) in cornea after phacoemulsification with posterior chamber intraocular lens (PCIOL) implantation and manual small incision cataract surgery (MSICS) with PCIOL implantation.

METHODS

This observational study was conducted in Department of Ophthalmology of Combined Military Hospital (CMH), Dhaka Cantonment, Dhaka, Bangladesh, between January and July of 2016. After taking written informed consent, a total of 80 cataract patients with age ranging from 40 to 70 years were selected. They were randomly allocated into two groups. One group consists of 40 cataract patients who underwent phacoemulsification with PCIOL implantation, while the other group consists of 40 cataract patients who underwent manual small incision cataract surgery (MSICS) with PCIOL implantation. Patients with pre-operative astigmatism more than ±1.00 D and post-operative more than ±1.5 D with K1-K2 in keratometric reading, intra-operative use of sutures, corneal diseases like any pre-existing scar, any interstitial keratitis, peripheral corneal degeneration, dry eye, limited visual potential after cataract surgery like amblyopia, maculopathy, glaucoma, diabetic retinopathy, previous retinal detachment surgery, optic atrophy were excluded from the study. Detailed history and physical examination of each patient was performed and recorded. The anterior segment was examined by torch and slit lamp biomicroscope to evaluate lids, conjunctiva, cornea, anterior chamber, pupil, iris, lens and anterior vitreous (where possible). Visual acuity and extra- ocular muscle balance were tested. The posterior segment was examined by direct and indirect ophthalmoscope. Retinal and macular functions were tested by projection of rays in different quadrants, two-points discrimination, Maddox rod and colour perceptions test. Intra-ocular pressure was measured by applanation tonometer and sac patency test was done to exclude the possible source of infection. All patients were examined preoperatively and post operatively at day 1, after 1 week and after 3 months for evaluation of corneal endothelial change. Keratometric cylinder was measured by using an Autorefractometer (Nidek AR-1, Tokyo, Japan) and Autokeratometer (Grand Seiko; GR-3100K, Shigiya Machinery Works Ltd, Japan) to find out the K1 and K2 reading for flat and steep meridian. Astigmatism was calculated from keratometric data using vector analysis. A specular microscopy was done to analyze corneal endothelial cell count, central corneal thickness and hexagonal cells. Uncorrected and Best corrected visual acuity for all patients were measured in all examination visits. Subjective refraction was done for all patients with Snellen chart, trial frame and trial lens. Most of the operation was done under local anesthesia and few with topical anesthesia. Standard operative procedure was followed in the phacoemulsification and posterior chamber IOL implantation and manual small incision cataract surgery and posterior chamber IOL implantation.

All the data were compiled, sorted properly, and analyzed statistically using Statistical Package for

Social Science (SPSS) version 20.0. Chi-square test, unpaired and paired Student's 't' tests were performed to compare between the groups. P value <0.05 was considered as significant. Ethical clearance was obtained from the Institutional Review Board (IRB) of Combined Military Hospital, Dhaka Cantonment, Dhaka, Bangladesh.

RESULTS

Most of the patients belonged to the age group of e"50 years. The mean age was 52±9.1 years in phacoemulsification group and 55±8.9 years in manual small incision cataract surgery (SICS) group. Men (62.50%; 70%) had a higher incidence rate than women (37.5%; 30%) in both groups. Male female ratio was 1:1.7 in Phacoemulsification group and 1:2.3 in SICS group. Statistically no significant (P>0.05) difference was observed in age and sex between the groups (Table-I). Table-II showed that mean central corneal thickness was increased at day 1 (564.71±22.45μ vs. 555.10±40.57μ), after 1 week (539.43±22.16μ vs. 535.08±38.87μ) and 3 months (523.49±21.29μ vs. 520.05±33.68μ) after phacoemulsification and MSICS from their preoperative value (508.72±23.96μ vs. 503.62±32.06μ) respectively. However, the differences were not statistically significant (P>0.05) between the groups. Table-III showed that mean central corneal thickness changes at day 1, and 1 week and 3 months after surgery respectively. In this study, central corneal thickness was significantly (P<0.001) increased at day 1 and after 1 week than that of preoperative value in both phacoemulsification and MSICS. Table-IV showed that the mean percentage of central corneal thickness changed at day1, after 1 week and after 3 months following cataract surgery. Mean central corneal thickness was found 11.01±6.30% and 10.22±26.54% at day 1, 6.04±7.52% and 6.25±21.24% after 1 week, 2.90±11.14% and 3.26±5.05% after 3 months in phacoemulsification and MSICS cases respectively. However, no statistically significant difference was observed in percentage of central corneal thickness change of both groups (P>0.05).

Table-I: Distribution of study subjects according to age and gender (N=80)

	Phacoemulsification (n=40)	MSICS (n=40)	P value
Age (Years)			
<50	17 (42.5%)	13 (32.5%)	0.356^{NS}
e"50	23 (57.5%)	27 (67.5%)	
Mean±SD	52± 9.1	55± 8.9	
Sex			
Male	25 (62.50%)	28 (70%)	0.478^{NS}
Female	15 (37.50%)	12 (30 %)	
Ratio	1:1.7	1:2.3	

Data were expressed as frequency, percentage and Mean±SD. Chi-Square test was performed to compare between the groups. NS=not significant.

Table-II: Mean central corneal thickness of the study subjects at different follow-up (N=80)

Follow-up	Phacoemulsification (n=40)	MSICS (n=40)	P value
Pre-operative (in μ)	508.72±23.96	503.62±32.06	0.995^{NS}
Post-operative (in μ)			
At day 1	564.71±22.45	555.10±40.57	0.848^{NS}
After 1 week	539.43±22.16	535.08±38.87	0.998^{NS}
After 3 months	523.49±21.29	520.05±33.68	1.000^{NS}

Data were expressed as Mean±SD. Unpaired student's t test was performed to compare between the groups. NS= not significant.

Table-III: Mean central corneal thickness change after surgery at different follow-up (N=80)

Follow-up	Phacoemulsification (n=40)		MSICS (n=40)	
	Corneal thickness (in μ)	P value	Corneal thickness (in μ)	P value
At day 1	55.99±1.51	<0.001^{S}	51.48±8.51	<0.001^{S}
After 1 week	30.71±1.80	<0.001^{S}	31.46±6.81	<0.001^{S}
After 3 months	14.77±2.67	0.367^{NS}	16.43±1.62	0.233^{NS}

Data were expressed as Mean±SD. Paired student's t test was performed to compare pre and postoperative values of each group. NS= not significant, S= significant.

Table-IV: Mean percentage of central corneal thickness change at different follow-up (N=80)

Follow-up	Phacoemulsification (n=40) (%)	MSICS (n=40) (%)	P value
At day 1	11.01±6.30	10.22±26.54	1.000^{NS}
After 1 week	6.04±7.52	6.25±21.24	0.825^{NS}
After 3 months	2.90±11.14	3.26±5.05	1.000^{NS}

Data were expressed as Mean±SD. Unpaired student's t test was performed to compare between the groups. NS= not significant.

DISCUSSION

In the present study, the majority of the study subjects belongs to age group of e"50 years. Mean±SD age was 52± 9.1 years in Phacoemulsification group and 55± 8.9 years in manual small incision cataract surgery (SICS) group. Men (62.50%; 70%) had a higher incidence rate than women (37.5%; 30%) and male female ratio was 1:1.7 in Phacoemulsification group and 1:2.3 in SICS group. Participants were matched by age and gender. Almost similar findings were observed by various researchers of different countries.[11,12]

Our study showed that the mean central corneal thickness was found to increase at day 1, after 1 week and 3 months in both phacoemulsification and MSICS patients from their preoperative values respectively. However, statistically no significant (P>0.05) difference was observed in mean central corneal thickness of both groups. In this study, central corneal thickness was significantly (P<0.001) increased more at day1 and after 1 week than preoperative value in both phacoemulsification and MSICS. Mean central corneal thickness was increased 11.01±6.30% at day-1, 6.04±7.52% at 1st week, and 2.90±11.14% at 3 months after Phacoemulsification and increased 10.22±26.54% at day-1, 6.25±21.24% at 1st week, 3.26±5.05% at 3 months after SICS. There is no significant difference in percentage of change in central corneal thickness between the groups with respect to increase in central corneal thickness postoperatively. Present study demonstrated that the central corneal thickness shows a decreasing trend over 1 week and 3 months; however, it remains higher than that of its preoperative value. Several other studies found similar results with significant increase in central corneal thickness over 1 week and 1 month after surgery.[12-16] A study by Goldenberg et al. also showed similar results with significant increase in CCT post manual small incision cataract surgery when compared to preoperative values on first post-operative week and first month post-operatively. However, the study also showed a return to normal values by the end of third month.[14] Two other studies showed a return of the CCT to normal thickness one month postoperatively after phacoemulsification.[15,16] Mathew et al. showed an increasing trend in CCT after SICS for the first two weeks followed by a decrease in the thickness.[17] Similar study was done in the same hospital setting to compare the morphological changes between those two procedures which revealed that a decreased endothelial cell count was observed after cataract surgery in both

phacoemulsification and MSICS procedures from their preoperative values respectively. However, the difference was not significant between those two procedures.[18]

CONCLUSION

To summarize, a significant change was observed in the functionality of the corneal endothelium i.e., central corneal thickness after both phacoemulsification with PCIOL and MSICS with PCIOL. It is evident by a decreased endothelial cell count and increased central corneal thickness after Phacoemulsification and SICS from preoperative value. Though corneal thickness increased initially after surgery, but it almost decreased to its pre-operative value after surgery. However, a large-scale study can be conducted to make the findings of the study generalizable to the reference population.

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Original Article

Anthropometric Study of Correlation between the Selected Craniofacial Measurements with the Stature in Adult Bangladeshi Manipuri Males

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ABSTRACT:

Cephalofacial anthropometry can be useful for racial identification, forensic scientist, physical anthropologist, genetic counsellors as well as reconstructive surgery for the purposes of identification of an individuals and understanding human physical variation, gender and ethnicity especially with facial recognition as a tool in recent advances in biometrics. Stature is one of the important criteria for personal identification which has a proportional biological relationship with every parts of the human body like head, face, trunk, extremities and vertebral column. In this study, our main goal is find out the correlation between the selected craniofacial measurements with the stature in Adult Bangladeshi Manipuri males. This cross-sectional study was carried out in 100 healthy adult males from March 2017 to February 2018 in the Department of Anatomy, Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka, Bangladesh. Descriptive statistics and testing of hypotheses were used for the analysis using SPSS software (version 22.0). Here non- significant positive correlations of the stature with the mandible height and significant positive correlations of the stature with mandible breadth was found. The Mean (±SD) of Mandible height (sto-gn) was 4.44 (±0.69), Mandible breadth (go-go) was 11.45 (±0.57). This study will be anticipated to provide baseline quantitative data on the linear craniofacial measurements and the stature of adult Bangladeshi Manipuri males. And using larger samples with non-contact measurement technique will help in defining craniofacial anthropometric profiling of the adult Bangladeshi Manipuri males.

Keywords: *Anthropometry, Craniofacial measurement, Stature, Manipuri male.*

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INTRODUCTION

One of the primordial concerns is defining the physical size and shape of the human body. Measurements are the important tools for comparisons and the branch of physical anthropology that deals with measurements of different body parts is called Anthropometry.[1] Anthropometry is a Greek word, 'Anthrops' meaning human and 'metry' meaning measurement. So, anthropometry is being used to take the measurements of human body.[2] Cephalometry is one of the important divisions of anthropometry, which is a

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Measurement of the head and face. Facial anthropometry provides a suggestion of the variation in facial shape in a population. Facial features and facial dimensions vary in different races and ethnic groups. Studying of human face and the assessment of facial dimensions draw the attention of the artist, poets and scientists, genetic counsellors and takes a prime importance in medical and dental fields in both diagnosis and treatment planning such as rhinoplastic surgery, orthognathic and orthodontic surgery for any congenital or post traumatic facial disfigurements in members of local population and different ethnic groups, otherwise lose their ethnic. Moreover, cephalofacial parameters are useful in forensic scientist, physical anthropologist for the purposes of identification of an individual and understanding human physical variation, gender, and ethnicity especially with facial recognition as a tool in recent advances in biometrics. Craniofacial anthropometry is also used for design of clothing, equipment, military, and industrial helmets. Craniofacial anthropometric measurements are a major consideration in the aircraft cockpit design and layout requires the knowledge of human anthropometric dimensions to facilitate aircrew-aircraft compatibility for the local population of the country. Stature is one of the important criteria for personal identification which have a proportional biological relationship with every part of the human body like head, face, trunk, extremities, and vertebral column. This relationship helps in calculating stature from decomposed, mutilated, and amputated body fragments in recent times due to natural disasters like earthquakes, tsunamis, floods and man-made disasters like bomb blasts, car accidents, wars, plane crashes etc. It is important both for legal and humanitarian reasons.

The human populations have been divided into divergent races based on morphological and anthropometric characters. As in Bangladesh, varieties of ethnic population groups, ecological and nutritional conditions are present; so different formulae are required for measurements of bones or body parts to identify different populations as well as various ethnic communities and sexes. Therefore, for successful treatment of any congenital or post-traumatic facial disfigurements of people of different ethnic groups, surgeons require accessing the normative craniofacial measurements of the ethnic group.[3] The Manipuri community is one of the oldest tribes in Bangladesh. The present study will be useful in comparing of Manipuri males features with the features of Manipuri females and different other ethnic communities of Bangladesh. Therefore, the contribution of the present study will be expected to help in setting a standard of normative value of stature, craniofacial anthropometric values of adult Bangladeshi Manipuri males. Therefore, in this study, our main goal is find out the correlation between the selected craniofacial measurements with the stature in Adult Bangladeshi Manipuri males.

METHODS

Study design and participants: The study was cross-sectional with some analytical components. The study was carried out on a hundred healthy adult Bangladeshi Manipuri males.

Place and period of the study: The study was carried out on the healthy adult Bangladeshi Manipuri males of Madhavpur village at Kamalganj upazila of Moulvibazar district of Sylhet, Bangladesh. The period of the study was March 2017 to February 2018.

Inclusion criteria : Each participant was selected who met the following criteria:

a) Aged between 25 to 45 years
b) Bangladeshi by nationality
c) Manipuri by ethnicity
d) Male by sex

Exclusion criteria: The following exclusion criteria were used to screen out the ineligible participants through history taking and physical examinations:

a) Mixed ethnic origin- if there was any history of marriage of last three generation of participant with Bengali people or with any other ethnic minority.
b) History or evidence of congenital craniofacial anomalies, major craniofacial trauma, orthodontic treatment, or craniofacial reconstructive surgery that might affect craniofacial measurements.
c) History of recent respiratory distress or common cold (as they might hamper the measurement process).
d) Malocclusion of teeth that might affect cranio-facial measurements.
e) Common genetic, endocrine, or neurological disorders that might affect craniofacial measurements and stature (Down's syndrome, acromegaly, myxedema, facial palsy).
f) Baldness or presence of beard or mustache.

Selected variables studied through direct physical measurement

Stature

Stature is natural heights of subject in an upright position. It is measured as vertical distance from the vertex (height point on the head) to the floor, when the head is held in Frankfurt horizontal plane, barefooted with heels and knees kept together.[4]

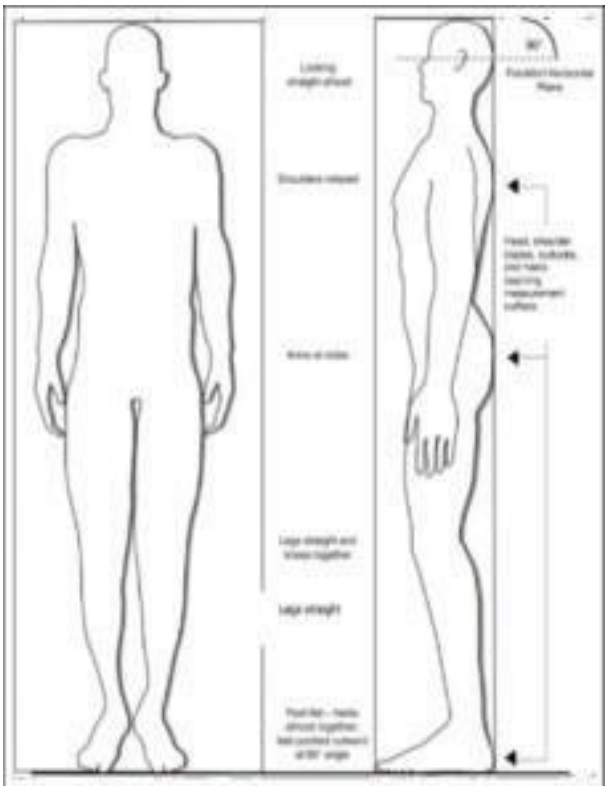

Fig. 1. *Diagrammatic representation of frontal and lateral views of the stature.*[5]

Craniofacial measurements

Mandible height (sto-gn): It is the linear distance between the 'stomion' and 'gnathion' (Figure-2).[6]

Mandible breadth (go-go): It is the linear distance between the left and right soft tissue 'gonions' points (Figure 2).[7]

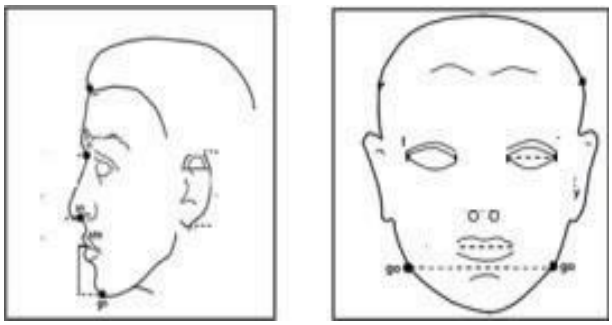

Fig. 2. *Diagrammatic representation of mandible height and mandible breadth measurements.*[8]

Procedure for measuring stature

The stature was taken by using steel plate and steel tape (shown in Figure 2.24B and Figure 2.24C). Then the subject stood in a position that the weight distributed equally on both feet, heel together and toes apart. Each participant's head was positioned in the Frankfort horizontal plane and arm hung freely from the sides. After asking the participant to take a deep breath and holding it, a steel plate was placed against the head and the wall to determine maximum height on the wall, and this was marked.[2] The height was then measured in centimetres from the floor to the mark on the wall with steel tape.[9] Figure 3 shows the procedure for measuring the stature.

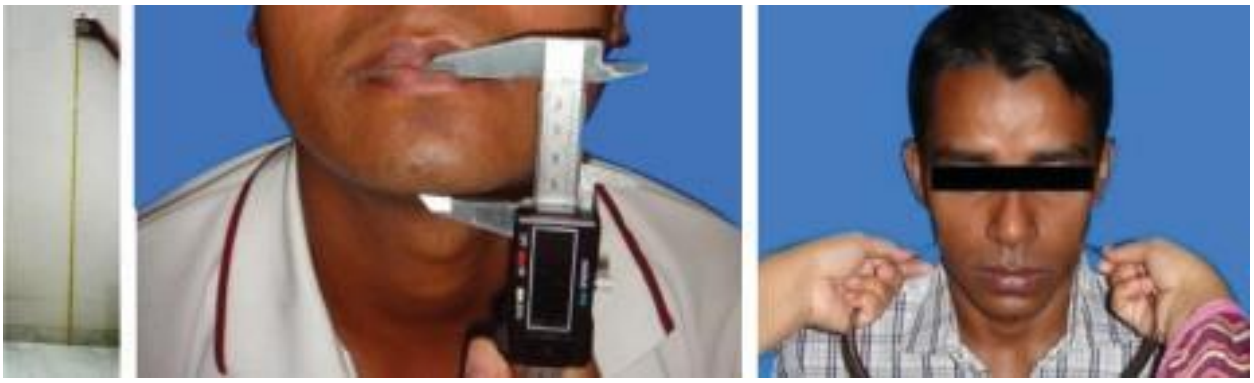

Fig. 3. *Procedure of measuring (A) Stature from the marked point on the wall to the floor by using steel tape (B) mandible height (from stomion to gnathion) using a digital sliding caliper and (C) Mandible breadth (from gonion to gonion) using a spreading caliper.*

Procedure for measuring mandible height

To measure the height of the mandible, the sliding caliper was vertically placed with the inner edge of the fixed arm placed to the stomion, holding it in place with the thumb and index fingers. The movable arm was slided up to the gnathion[6] cautiously not pressing down on the lower lip (Figure 3).

Procedure for measuring mandible breadth

The Mandibular breadth was measured by using spreading caliper. To measure the Mandibular breadth, left and right gonion points were felt with the index and middle fingers. The tips of the spreading caliper were placed on the lateral aspect of the angles of the mandible,[10] and gentle pressure was applied until the bone could be felt (Figure 3).

Data analysis

Data analysis was carried out in the Department of Anatomy, Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka. The statistical analyses of the results were obtained by using window-based computer software devised with Statistical Packages for Social Sciences (SPSS version 22.0) and Microsoft Excel.

RESULTS

The range, mean values and standard deviations of different variables related to the stature and selected linear craniofacial measurements of 100 adult Bangladeshi Manipuri males were obtained through direct physical procedure. The Mean (±SD) of Mandible height (sto-gn) was 4.44 (±0.69), Mandible breadth (go-go) was 11.45 (±0.57) are presented in Table I.

Table I: *Values of stature, mandible height and mandible breath measurements in adult Bangladeshi Manipuri males (n= 100)*

Measured Stature and linear craniofacial measurement	Value (cm) Range Minimum – Maximum	Mean (±SD)*
Stature	150.10 – 177.10	163.47 (±7.06)
Craniofacial measurements		
Mandible height (sto-gn)	3.13 – 6.01	4.44 (±0.69)
Mandible breadth (go-go)	10.00 – 12.70	11.45 (±0.57)

***SD:** Standard deviation

The non-significant positive correlation between the stature and mandible height, the significant positive correlation between the stature and mandible breath are shown in Table II.

Table II: *Correlation coefficients of mandible height and mandible breath with the stature in adult Bangladeshi Manipuri males (n= 100)*

Linear craniofacial measurement	Correlation coefficient (r)	Coefficient of determination (r^2)	Significance (p)* of correlation with the stature
Mandible height (sto-gn)	+0.022	0.000	0.828
Mandible breadth (go-go)	+0.227	0.052	0.023

*p: Probability

If p value ≤ 0.05 was considered as significant (S)

The mandible height showed non-significant positive correlation (r= +0.022, r^2= 0.000, p= 0.828) with the stature of the adult Manipuri males (Table 3.2 and Figure 3.5).

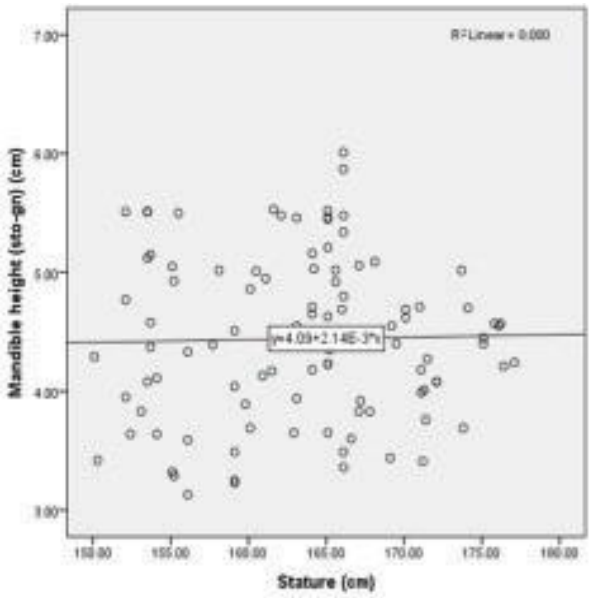

Fig. 4. *Regression analysis shows non-significant positive correlation between the mandible height and the stature.*

The mandible breadth showed significant positive correlation (r= +0.227, r^2= 0.052, p= 0.023) with the stature of the adult Manipuri males (Table 3.2 and Figure 3.6).

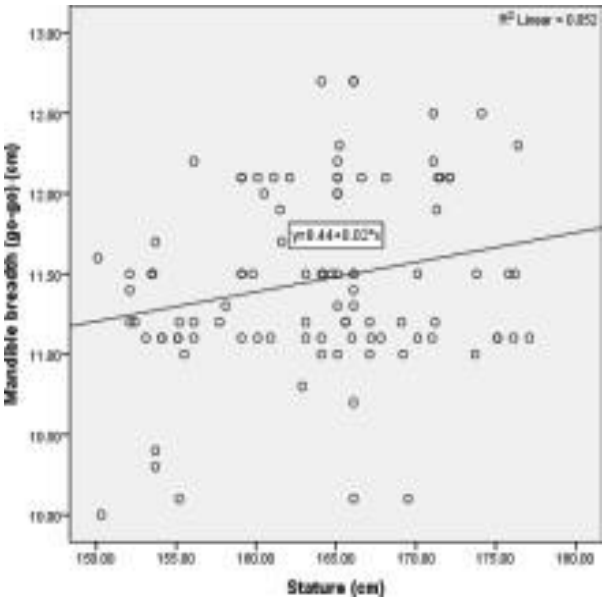

Fig. 5. *Regression analysis shows significant positive correlation between the mandible breadth and the stature.*

DISCUSSION

The present anthropometric study was carried out in 100 adult Bangladeshi Manipuri males which provide new data pertaining to the selected craniofacial measurements and stature by means of physical procedures. Manipuri belongs to the Kuki-Chin group of the Tibeto-Burman family of the Mongolian race.[2] The Mongolians are mostly Inhabitants of China Mongolia, Tibet, North America, Siberia, Greenland, Burma, Thailand, Malay Peninsula, Philippines, Japan and North-East India.[11] The age range of the Manipuri study participants was kept between 25 to 45 years. This age limit was based on the concept that anthropometric measurements in adults should be standardized normative values at such an age when the development of the respective body parts is complete.[9] The relationship between the stature and other craniofacial measurements are likely to differ according to age, sex, race, and ethnic background.[3] Physical changes occur in the human body at every stage of life. Most of the physical body dimensions reach their peak forms within 20 to 35 years of age.[12] This is because bone length and stature are related to ossification and epiphyseal fusion with diaphysis and both these events are age dependent. Body height increases with age from childhood to adulthood. Ossifications of the long bones are completed by the age of 20 to 25 years.[13] On the other hand, the normal growth and development of human head and face is one of the most attractive fields of anatomical and anthropological implication to determine the time, duration, and prognosis of malocculation. Facial skeletons is made from the fusion of fronto-nasal and two pair of maxillary, mandibular prominence from 4th to 10th weeks of development.[14] Paranasal sinuses also reach their maximum size during puberty and fully developed at 17 years of age and contribute to the definitive shape of the face.[15] According to Datta the growth of base of the skull continues until synostosis of the cartilaginous joint between the occipital and sphenoid bone occurs. This joint is replaced by bone usually after 25 years.[16] Moreover, A loss of height begins about 45 years of age that continues steadily throughout the rest of the life of an individual.[8] The loss of body height occurred due to diminution of bone mineral density, compression of cartilage, loss of elasticity and shrinkage of intervertebral disc, osteoporotic vertebral collapse, and anatomical distortion of the skeleton. Thus, it can be a misleading index of stature.[17]

The above-mentioned observations and descriptions keeping in mind; the age of the participants of the present study was limited between 25 and 45 years. In order to keep the effects of the age-related changes on the stature and craniofacial features could be kept to the minimum. It is apparent from Table2 that the values of the two craniofacial measurements found to be positively correlated with stature. Devi and Singh found a positive correlation between stature and cranial measurements with each other in males.[18] Ilayperuma recommended that the stature and cranial measurements were found to be statistically significant and positively correlated with each other in both males and females.[19] Agnihotri et al showed that positive correlation between the stature and cranial measurements in both males and females.[20] Mansur et al noted that head circumference showed highly significant positive correlation with height.[13] Shah et al. suggested that the stature and craniofacial measurements showed week and statistically insignificant relation with each other in both males and females.[21] Datta and Sawant found that statistically significant week positive correlation in between stature and facial measurements in males.[22]

CONCLUSION

The results of the present anthropometric study of the adult Bangladeshi Manipuri population can provide the basic framework for formulating standards of linear craniofacial measurements and the stature for Bangladeshi Manipuri male population. However, using larger samples with non-contact measurement technique will help in defining craniofacial anthropometric profiling of the adult Bangladeshi Manipuri males.

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Anti-inflammatory Effect of Methanolic Extract of *Mangifera Indica* Leaves on Inflammed Rats in Comparison to Indomethacin

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ABSTRACT

In the context of inflammation and immunity, there are fragmented and observational studies relating the pharmacological effects of Mangifera indica leaves and its main active component-mangiferin. Hence, this study aims to evaluate the anti-inflammatory effects of this leaf extract (MIE) in comparison to Indomethacin on inflammed rats. The methanolic extract of Mangifera indica leaves in different doses, Indomethacin and normal saline were orally administrated in experimental and control groups of rats. Then acute inflammation was induced by administration of 0.1 ml of 1% Carrageenan in sterile saline solution into the sub-plantar surface of the right hind paw of each rat. Anteroposterior diameter of rat paw oedema was measured at 0 hour and at the end of 3 hours of Carrageenan injection. In the group treated with higher dose of methanolic extract of Mangifera indica leaves, acute inflammation in rats was improved significantly. But in the group treated with lower dose acute inflammation was not improved significantly in comparison to Indomethacin administered group. The methanolic extract of Mangifera indica (MEMI) leaves has potential health benefits as it showed dose dependent anti-inflammatory activity. The mangiferin in the MEMI leaves inhibits COX 2 enzyme and exerts the anti-inflammatory effects.

Keywords: *Mangifera indica leaves, indomethacin, anti-inflammatory drug.*

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INTRODUCTION

Inflammation is the immune response of body to injury or infection. At the site of injury cells release molecular signals that cause a number of changes in the affected area. These are vasodilation, increased blood flow, increased vascular permeability, exudation of fluids containing protein like antibodies and invasion by several different types of leukocytes including granulocytes, monocytes and lymphocyte. Neutrophils are the first leukocytes to appear at the injured site[1].

The occurrence of inflammatory disorder is seen worldwide with no racial predilection. However, the poor and developing countries are lacking proper management of inflammatory diseases. As a result, the prevalence of inflammatory conditions is considerably high in developing countries like Bangladesh. The anti-inflammatory drugs that are now available includes non-steroidal anti-inflammatory drugs, like indomethacin, corticosteroids, gold, disease modifying anti-rheumatic drugs (DMARD) such as methotrexate, cyclosporine etc. Indomethacin is mostly used worldwide as an anti- inflammatory drug[2].

Carrageenan-induced inflammation has long been used as an in vivo model of local inflammation.

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Carrageenan can stimulate through TLR4 signaling pathways. It initiates an inflammatory response in these cells that differs from a typical endotoxin effect such as LPS stimulation in terms of the pathways and gene products altered, suggesting that activation of TLR2/6 and TLR4/6, the predominant pathways through which carrageenan induces inflammatory responses[3].

Numerous communities employ herbal medicines derived from medicinal plants to treat and avoid a wide range of illnesses[4]. Plant barks, leaves, flowers, and other parts have been utilized in medicine. The similar chemicals found in plants have just lately been used to generate synthetic pharmaceuticals[5]. Medicinal plants are a significant source of biologically active natural chemicals and are used as an alternate and/or supplementary treatment method due to their extensive pharmacological, therapeutic, and other biological properties[6].

Given the recent increase in microbial infections in humans, scientists have turned their attention to medicinal plants as low-cost and efficient forms of treatment[7]. Due to the development of microbial resistance to numerous antibiotics, the utilization of extracts and bioactive chemicals produced from medicinal plants has expanded[8]. Plant-based medicines are garnering popularity because of their minimal toxic effects and negligible health consequences[9].

Several Mangifera species have been discovered to offer therapeutic benefits as antidiabetic, antiviral, antibacterial, anti-Alzheimer, antioxidant, and anticancer agent[10]. Furthermore, this has a wide range of bioactive compounds, including vitamins A and C, protein, carotenoids, benzoic acid, gallic acid, carbohydrates, fiber, minerals, and phenolic compounds (such as iriflophenones, quercetin, catechin, and gallotannins). Several pharmacological actions are hypothesized to originate from these bioactive molecules[11].

Mangiferin (C19H18O11), a natural glucoxanthone, is one of the major bioactive compounds present in different parts of M.indica, including the leaves, barks, and peels, as well as many other plants[12]. Mangiferin has been shown in numerous studies to have a wide spectrum of biological actions, making it a viable agent for the food and pharmaceutical sectors. It offers several health-promoting properties, such as anti-inflammatory, antiviral, immunoregulatory, and anticancer capabilities[13].

The side effects of the currently available anti-inflammatory drugs pose a major problem during their clinical uses. Therefore, the development of newer and more potent anti-inflammatory drugs with lesser side effects is necessary[14].

METHODS

This experimental study was carried out at the Department of Pharmacology, Dhaka Medical College, Dhaka during the period from July 2015 to June 2016. Sample size was 28 Long Evan Norwegian rats. Rats were divided into 4 groups, 7 rats each for each group of treatments. The experimental rats were of either sex, weighing between 150 to 200gm. They were allowed to feed on standard laboratory diet and to drink water ad libitum. The animals were maintained at room temperature under condition of natural light and dark schedule. The leaves of Mangifera indica were cut into pieces, shade-dried and grounded to coarse powder. The leaves of Mangifera indica was soaked in methanol (900ml) with continuous shaking at 25.C for 3 days and filtered. The organic extract was evaporated under vacuum to obtain a semisolid residue (10g). The methanolic extract of Mangifera indica leaves was given orally by nasogastric tube at doses of 200 mg/kg body weight and at a dose of 500 mg/kg body weight. Indomethacin was given orally at a dose of 10 mg/kg body weight as standard anti-inflammatory drugs. The group of rats given only saline solution was served as control group. After one hour of drug administration, 0.1 ml of 1% Carrageenan in sterile saline solution was injected into the sub-plantar surface of the right hind paw for the production of acute inflammation. Antero-posterior diameters of paw was measured by slide calipers at zero hour and at the end of three hours of carrageenan injection. Progress of the inflammatory exudative lesion - oedema was assessed by measuring the maximum linear cross section of the joint at zero hour and at the end of three hours.

Experimental design: Carrageenan induced rat paw edema in control group (Group I) and experimental group (Group II, III, IV) (Fig.-1)

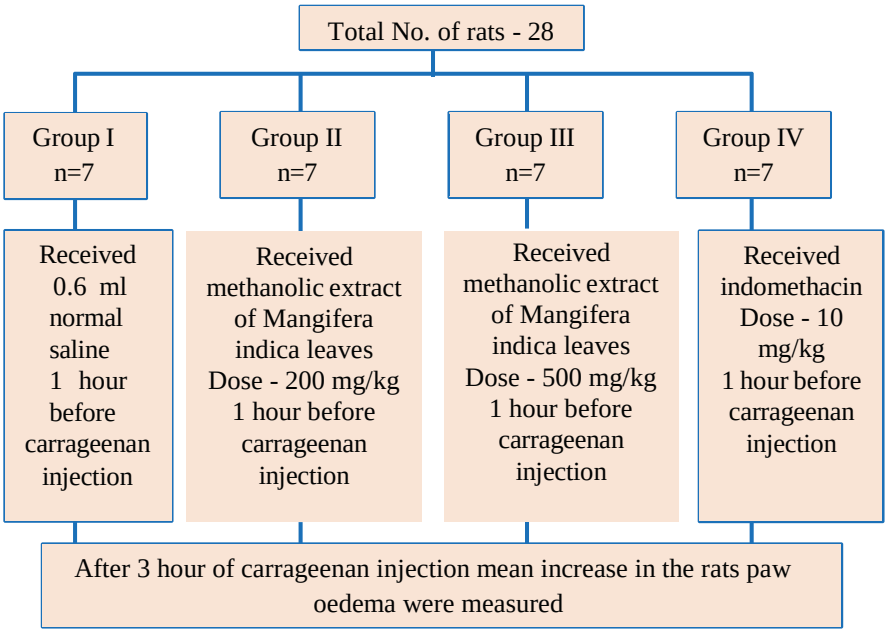

Fig.-1: *Design of experiment for acute inflammation*

RESULTS

The mean initial antero-posterior diameter of rat paw of control group (group I) and experimental group (group II, III, IV) were 3.86+0.03 mm, 3.82±0.04 mm, 3.81±0.02 mm and 3.84±0.02 mm respectively. The mean antero-posterior diameter of rat paw of control group (group I) and experimental group (group II, III, IV) after 3 hours of carrageenan injection were 7.49±0.03 mm, 5.86±0.03 mm, 5.49±0.04 mm and 5.39±0.03 mm respectively. The percentage of inhibition of edema was in case of Indomethacin 57.3%, in case of test extract (200 mg/kg) 43.8%, in case of test extract (500 mg/kg) 53.7%. The extract showed dose dependent anti-inflammatory activity, which was found to be statistically significant at higher concentration.

Table I: *Comparison between Control group and Experimental group (500 mg/kg body wt. of methanolic extract of Mangifera indica leaves) (n=7)*

Group	Group I Control group	Group III Experimental group	P value
Initial antero-posterior diameter (mm)(mean + SEM)	3.86±0.03	3.81±0 .02	0.12
Antero-posterior diameter after 3 hrs of carrageenan (mm) (mean±SEM)	7.49±0.03	5.49±0 .04	0.04

Table II: *Comparison between Control group and Experimental group (Indomethacin 10mg/per kg body weight) (n=7)*

Group	Group I Control group	Group IV Experimental group	P value
Initial antero-posterior diameter (mm)(mean + SEM)	3.86 + 0.03	3.84 + 0.02	0.09
Antero-posterior diameter after 3 hrs of carrageenan (mm)(mean ±SEM)	7.49 + 0.03	5.39 + 0.03	0.02

Table III: *Comparison between 2 Experimental groups (200 mg/kg body wt and 500 mg/kg body wt methanolic extract of Mangifera indica leaves) (n=7)*

Group	Group II Experimental group	Group III Experimental group	P value
Initial antero-posterior diameter (mm)(mean±SEM)	3.82±0.04	3.81±0.02	0.08
Antero-posterior diameter after 3 hrs of carrageenan (mm) (mean±SEM)	5.86±0.03	5.49±0.04	0.05
P value	0.04	0.05	

Table IV: *Comparison between 2 Experimental groups (500mg/kg body wt. of methanolic extract of Mangifera indica leaves and Indomethacin 10mg/per kg body weight) (n=7)*

Group	Group III Experimental group	Group IV Experimental group	P value
Initial antero-posterior diameter (mm)(mean ± SEM)	3.81±0.02	3.84±0.02	0.06
Antero-posterior diameter after 3 hrs of carrageenan (mm) (mean±SEM)	5.49±0.04	5.39±0.03	0.04
P value	0.05	0.04	

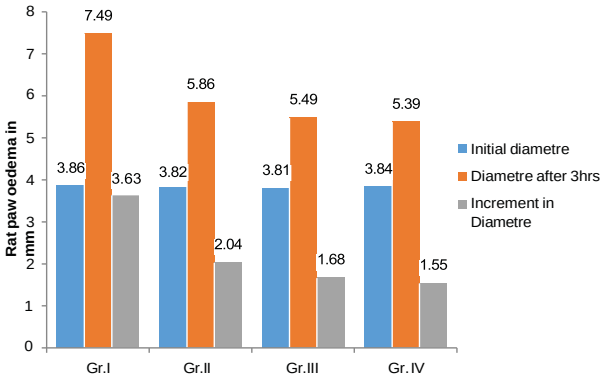

Fig.-1: *Bar diagram showing initial, after 3 hour of carrageenan injection & increment of antero-posterior diameter of rat paw*

DISCUSSION

The present study was carried out to evaluate the anti-inflammatory effect of methanolic extract of Mangifera indica leaves. Its anti-inflammatory effects were tested on Long Evan Norwegian rats. The crude methanolic extract showed presence of chemical constituent with presence of mangiferin. The methanolic extract of mangifera indica leaves is devoid of toxicity up to 5 g/kg in Long Evan Norwegian rats. Carrageenan induced rat paw edema was taken as a prototype of exudative phase of acute inflammation. Inflammatory stimuli like microbes, chemicals and necrosed cells activate the different mediator systems through a common trigger mechanism. The development of carrageenan induced edema is believed to be biphasic. The early phase is attributed to the release of histamine and serotonin and the delayed phase is sustained by the leukotrienes and prostaglandins [15]. In case of carrageenan induced acute rat paw edema technique: the percentage inhibition of edema- in case of standard (Indomethacin; 10 mg/kg) is 57.3%, in case of test extract (200 mg/kg) is 43.8%, in case of test extract (500 mg/kg) is 53.7%. The extract showed dose dependent anti-inflammatory activity, which was found to be statistically significant at higher concentration, 500 mg/kg, in acute carrageenan induced rat paw oedema model. The extract as well as indomethacin showed anti-inflammatory activity. The present study shows that the activity profile of extract at 500 mg/kg closely resembled to that of Indomethacin (standard drug). However, this activity was less potent as compared to indomethacin in low dose extract. This activity appears not to be significant in early phases of acute inflammation. Thus, extract shows anti- inflammatory activity at various acute phases of inflammation[16].

CONCLUSION

Mangifera indica is a unique source of various types of compounds having diverse function. This study has revealed the anti-inflammatory effect of methanolic extract of Mangifera indica leaves. Anti-inflammatory drugs have many adverse effects but methanolic extract of Mangifera indica leaves have less significant side effects. Therefore, it can be used as alternative medicine for its easy availability, cost effectiveness and minimum side effects. However, extensive basic and clinical studies are required in order to identify the exact active ingredient responsible and to determine the precise mechanism of action.

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Original Article

Modified D2 Gastrectomy operation in Gastric Cancer Patients and Outcome

Hossain MM[1], Rahman J[2], Khandaker T[3]

ABSTRACT

Gastric cancer remains the fifth most commonly diagnosed cancer and the third leading cause of cancer-related deaths worldwide. In 2018, there were an estimated 1,033,701 newly diagnosed cases and 782,685 related deaths. The aim of this study was to evaluate outcome of modified D2 gastrectomy operation in gastric cancer patients with or without comorbidities. This prospective observational study was conducted at the Department of Surgical Oncology, National Institute of Cancer Research and Hospital, Mohakhali, Dhaka, from July 2019 to March 2021. A total of 53 patients were included in the study. The outcome of the surgery was assessed by monitoring postoperative complications for a period of 30 days. Statistical analysis was performed using SPSS (Statistical Package for the Social Sciences) version 28. Prior to the commencement of the study, the research protocol was approved by the Research Review Committee of the Department of Surgical Oncology and the Ethical Committee of the National Institute of Cancer Research and Hospital, Dhaka. There was no significant association observed between postoperative complications of modified D2 gastrectomy and patients' age, gender, or smoking status. Among the 53 patients, the highest proportion (92.45%) experienced anorexia, followed by vomiting (81.13%), and approximately 71.69% had dyspepsia. Among the patients, 52.83% had diabetes mellitus (DM) and 45.28% had hypertension (HTN). Patients with gastric cancer and DM were found to be more susceptible to developing wound infections. Based on the analysis of the study results, it can be concluded that modified D2 gastrectomy is a safe procedure that yields acceptable postoperative outcomes for the treatment of gastric cancer in a tertiary care center.

Keywords: *Gastric cancer, gastrectomy, infection, diabetes mellitus.*

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INTRODUCTION

Gastric cancer remains the fifth most common cancer and the third leading cause of cancer-related deaths worldwide. In 2018, an estimated 1,033,701 new cases and 782,685 related deaths were reported globally.[1] The highest incidence rates are found in Eastern Asia, particularly in Mongolia, the Republic of Korea, and Japan.[2] The first successful gastrectomy was performed by Bill Roth in 1881[3]. Since then, radical gastrectomy, which involves the removal of the primary lesion with a satisfactory resection margin (R0), along with radical dissection of regional lymph nodes, has been the primary treatment for resectable gastric cancer.[3] Surgeons have also explored more extensive surgeries, such as super-extended (D3) lymphadenectomy or standardized extended (D2) lymphadenectomy plus para-aortic nodal dissection (PAND), combined with prophylactic splenectomy or bursectomy.[4] In Japan, radical gastrectomy with D2 dissection has been the standard procedure for locally advanced gastric cancer (LAGC) since 1961.[5] This approach has also gained acceptance in Western

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countries, given the latest 15-year follow-up results of the Dutch D1D2 trial, which showed significant survival benefits of D2 over standardized limited (D1) lymphadenectomy.[5] However, the United Kingdom Medical Research Council Gastric Cancer Surgical Trial (MRC, ST01) found no survival advantages of D2 over D1 dissection.[6] Similarly, the Dutch D1D2 trial in the Netherlands showed that D2 dissection was associated with a higher risk of postoperative morbidity and mortality compared with D1 dissection, with no differences in overall survival rate after an 11-year follow-up period.[7] Pancreatic resection often leads to complications such as pancreatic juice leakage, subphrenic abscess, and postoperative diabetes. To mitigate these risks, Maruyama et al. developed pancreas-preserving surgery in 1979.[8] They found that gastric cancer tumors only invaded the pancreas directly, rather than metastasizing to the pancreas. Pancreas-preserving surgery proved superior to pancreas resection in terms of operative mortality, hospital mortality, surgical morbidity, and 5-year survival rate.[9] Furukawa et al.'s randomized controlled trial (RCT) also supported the superiority of pancreas-preserving surgery over pancreas resection in terms of surgical risk and postoperative glucose tolerance.[9]

METHODS

This prospective observational study was conducted at the Department of Surgical Oncology, National Institute of Cancer Research and Hospital, Mohakhali, Dhaka, Bangladesh, from July 2019 to March 2021. The study aimed to evaluate outcome of modified D2 gastrectomy operation in gastric cancer patients with or without comorbidities. A total of 53 patients who met the inclusion criteria were enrolled in the study. The inclusion criteria consisted of patients with biopsy-proven and operable adenocarcinoma of the stomach. Patients with stage IV diseases, previous gastric surgery, individuals unfit for surgery, and those unwilling to participate in the study were excluded. Preoperative evaluations were performed, including basic laboratory tests such as complete blood count (CBC), random blood sugar (RBS), serum creatinine, serum electrolytes, serum albumin, liver function tests, electrocardiogram (ECG), chest x-ray, ultrasound of the whole abdomen, contrast-enhanced computed tomography (CT) scan of the abdomen, and serum carcinoembryonic antigen (CEA) levels. Patients were selected for the surgical procedure based on proper staging evaluation. The surgery was performed as per standard guidelines, and modifications to the extent of lymph node dissection were implemented based on the procedure. Postoperative complications were monitored for a duration of 30 days to assess the outcome of surgery.

Statistical analysis was conducted to analyze the data using SPSS (Statistical Package for the Social Sciences) version 28. The available statistical analysis focused on determining the significance of the association between diabetes mellitus and wound infection. A single table presenting the p-value for this association was generated. No other tables, such as those displaying confidence intervals or odds ratios, were included in this study.

The study was approved by the Ethical Review Committee of National Institute of Cancer Research and Hospital, Mohakhali, Dhaka, Bangladesh,

RESULTS

Postoperative complications in this study were categorized as major complications including anastomotic leak and duodenal blow out and minor complications including wound infection, wound dehiscence, pulmonary infection, and paralytic ileus.

Table I : *Association of different demographic parameters, and postoperative complication in gastric cancer (n=53)*

Parameters	Complications			
	no	minor	major	P value
Age				
<45	9(32.1%)	3(14.3%)	1(25.0)	0.356a
≤45	19(67.9)	18(85.7)	3(75)	
Sex				
Male	21(75)	17(81)	3(75)	0.88b
Female	7(25)	4 (19)	1(25)	
Smoking				
Yes	18(64.3)	15(71.4)	3 (75)	0.827c
No	10(35.7)	6(28.6)	1(25)	

a.X^2= 2.068 df=2, b.X^2=.256 df=2 c.X^2=.380 df=2

The study analyzed the association of demographic parameters with postoperative complications in gastric cancer patients. Age was categorized into two groups: below 45 , 45 and above. In case of patients with major complications 25% patients were below 45yrs and 75% were 45 and above. Among minor complications group 14.3% patients were below 45 and 85.7% were 45 and above. Among patients with no complications, 32.1% were below 45 and 67.9% were 45 and above. However, the association between age and postoperative complications was not statistically significant (p=0.356, chi-square test, df=2). The study also examined the association between sex and postoperative complications. In case of patients with major complications 75% patients were male and 25% were female. Among minor complications group 81% patients were male and 19% were female. Among patients with no complications, 75% were male and 25% were female. The association between sex and postoperative complications was not statistically significant (p=0.88, chi-square test, df=2). Similarly, the association between smoking status and postoperative complications was investigated. In case of patients with major complications 75% patients were smoker and 25% were non-smokers. Among minor complications group 71.4% patients were smokers and 28.6% were non-smokers. Among patients with no complications, 64.3% were smokers and 35.7% were non-smokers. The association between smoking status and postoperative complications was not statistically significant (p=0.827, chi-square test, df=2). Although the associations did not reach statistical significance, it is noteworthy that chi-square values and degrees of freedom were reported for each association: age (X2=2.068, df=2), sex (X2=0.256, df=2), and smoking status (X2=0.380, df=2). These values provide insights into the strength and significance of the associations in this analysis.

Table II : *Distribution of patients according to clinical presentation (n=53)*

Clinical presentation	Frequency (%)
Anorexia	49(92.45%)
Dyspepsia	38(71.69%)
Vomiting	43(81.13%)
Epigastria pain	19(35.84%)
Abdominal lump	11(20.75%)
Hematemesis	3(5.67%)
Melena	5(9.43%)
Weight loss	12(22.64%)

Table II provides the distribution of patients according to their clinical presentation in a cohort of 53 individuals. The clinical presentations evaluated in this study include anorexia, dyspepsia, vomiting, epigastric pain, abdominal lump, hematemesis, melena, and weight loss. Among the patients, 49 (92.45%) reported experiencing anorexia, indicating a loss of appetite. Dyspepsia, characterized by recurrent or persistent discomfort or pain in the upper abdomen, was reported by 38 individuals (71.69%). Vomiting, defined as the forceful expulsion of stomach contents, was observed in 43 patients (81.13%). Epigastric pain, felt in the upper central part of the abdomen, was reported by 19 individuals (35.84%). Furthermore, 11 patients (20.75%) presented with an abdominal lump, which refers to a localized swelling or mass in the abdominal region. Hematemesis, the vomiting of blood, was reported by 3 individuals (5.67%). Additionally, 5 patients (9.43%) presented with melena, which is the passage of dark, tarry stools containing blood. Weight loss, defined as a reduction in body weight, was observed in 12 individuals (22.64%).

Table III : *Distribution of patients according to postoperative findings (n=53)*

Postoperative findings	Frequency (%)
Postoperative wound infection	
Present	16. (30.19%)
Absent	37. (69.81%)
Wound dehiscence	
Present	2 (3.77%)
Absent	51 (96.23%)
Anastomotic leakage	
Present	2 (3.77%)
Absent	51 (96.23%)
Postoperative ileus (in days)	
>4	8 (15.09%)
≤4	45 (84.91%)
Duodenal blow out	
Present	2 (3.77%)
Absent	51 (96.23%)
Pulmonary infection	
Present	8 (15.09%)
Absent	45 (84.91%)

Regarding postoperative wound infection, 16 patients (30.19%) presented with this complication, while 37 patients (69.81%) did not. Similarly, for wound dehiscence, only 2 patients (3.77%) experienced this condition, while the majority, 51 patients (96.23%), did not exhibit wound dehiscence. The occurrence of anastomotic leakage was also low, with 2 patients (3.77%) demonstrating this complication, while 51 patients (96.23%) did not experience it. Postoperative ileus, defined as a disruption of normal bowel function after surgery, was observed in 8 patients (15.09%) for more than 4 days, while 45 patients (84.91%) had a postoperative ileus duration of 4 days or less. In terms of duodenal blowout, 2 patients (3.77%) presented with this complication, while 51 patients (96.23%) did not. Lastly, pulmonary infection was observed in 8 patients (15.09%), while 45 patients (84.91%) did not experience this postoperative complication.

Table IV: *Distribution of patients according to co-morbidities (n=53)*

Co-morbidities	Frequency (%)
Diabetes mellitus (DM)	17(32.07%)
Hypertension (HTN)	13(24.52%)
Both DM & HTN	11(20.75%)
No Co-Morbidities	12(22.66%)

Among the patients, 17 individuals (32.07%) had diabetes mellitus (DM). Additionally, 13 patients (24.52%) presented with hypertension (HTN). Moreover, 11 patients (20.75%) had both diabetes mellitus and hypertension (DM&HTN), indicating a co-occurrence of these two conditions. 12patients (22.66%) had no co-morbidities.

Table V : *Association of DM with Wound infection in gastric cancer(n=53)*

DM	Wound infection		P value
	No (n=37)	Yes (n=16)	<.001
Non Diabetic (25)	23	2	
Diabetic (28)	14	14	

Among the 25 patients without DM, 23 did not experience wound infection, while 2 had wound infections. In contrast, among the 28 patients with DM, 14 had wound infections, while the remaining 14 did not. The association between DM and wound infection was found to be statistically significant, with a p-value of less than 0.001.

DISCUSSION

In this study, the mean age was observed to be 48.9 ± 9.36 years, with the most common age group affected being 45-54 years (49%). These findings closely resemble those reported by Dr. Sahu et al., who observed a mean age of 49.10 ± 8.32 years.[10] However, Galata et al., reported a higher mean age of 65 years in their study, which differs from the current study.[11] The proportion of females was considerably lower than males in this study, with 41 (77.35%) male patients and 12 (22.64%) female patients. The male-to-female ratio was 3:1. Similar findings were reported by Lam et al., who found a male-to-female ratio of 2:1, closely resembling the present study.[12] Galata et al. also observed a male predominance in their study.[11] The majority of the patients in this study were smokers, accounting for 36 (67.92%) cases. This finding aligns with the study by Crumley et al., which also found an association between smoking and gastric cancer.[13] However, due to the small sample size, it was challenging to comment on the correlation between smoking and gastric cancer. No association was observed between smoking and postoperative complications in this study. The most commonly observed symptoms in the patients were anorexia (92.45%), vomiting (81.13%), dyspepsia (71.69%), epigastric pain (35.84%), weight loss (22.64%), and abdominal lump (20.75%). These clinical findings are consistent with those reported by Nafae et al., who also found anorexia, dyspepsia, abdominal pain, and weight loss as the most common symptoms.[14] Postoperative complications in this study were categorized as major complications, including anastomotic leak and duodenal blow out, and minor complications, including wound infection, wound dehiscence, pulmonary infection, and paralytic ileus. Prolonged postoperative ileus, lasting more than 4 days, is a known complication following gastric cancer surgery.[15] In this study, postoperative ileus duration was determined based on the patient's appreciation of flatus and bowel sounds returning together, as bowel activity typically resumes within 3 days following abdominal surgery. However, in the context of this study's perspective and open surgery, a cutoff of more than 4 days was arbitrarily chosen. The majority of cases had timely return of bowel activity, while 8 (15.09%) cases experienced

postoperative ileus lasting longer than 4 days. Among these cases, anastomotic leakage was a major complication observed in only 2 (3.77%) cases. Another major complication, duodenal blowout, was observed in 2 (3.77%) patients. The remaining 4 cases of postoperative ileus were considered idiopathic. Wound infection was present in 16 (30.19%) cases, which is higher compared to the 13% wound infection observed by Nafae et al., with a positive statistical significance associated with DM.[14] Postoperative pulmonary infection was observed in 8 (15.09%) patients, and no association was found between pulmonary infection and smoking based on the statistical analysis. Only 2 (3.77%) patients developed wound dehiscence in this study. The majority of patients (29, 54.71%) did not experience any postoperative complications. The mortality rate in this study was only 1.08%, which aligns with findings from previous studies by Nafae et al. and Sahu et al[10,14]. The presence of preoperative comorbidities, particularly in oncologic patients, can contribute to the occurrence of postoperative complications. In this study, the most common comorbidity observed was DM in 28 (52.83%) patients, followed by hypertension in 24 (45.28%) patients, consistent with a previous Indian study by Dr. Sahu et al.[10]. This study also found that gastric cancer patients with DM were more prone to developing wound infection, and a statistical association was observed between DM and postoperative wound infection.

CONCLUSION

Modified D2 gastrectomy is safe procedure and provide with acceptable postoperative outcomes in treatment of gastric cancer. Diabetes mellitus should be well controlled in gastric cancer patients before surgery for better postoperative outcome.

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Review Article

Ophthalmic Manifestations of Leukemia and Their Management

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ABSTRACT

Patients with leukemia often have ophthalmic manifestations. These occur either from direct infiltrations of neoplastic cells or from indirect or secondary causes. Nearly all ocular structures can be affected by leukemia. Sometimes, ophthalmic involvement can be the first sign of disease relapse. This review article aims to highlight different ocular manifestations of leukemia along with treatment. It involves studying the available material in textbooks, printed and online journals. As there is high prevalence of ocular findings in leukemia, it can be a standard practice that all leukemic patients should have screening by ocular examination. Awareness of the clinical spectrum of leukemic infiltration of ocular region is essential for rapid diagnosis, prompt initiation of treatment and better outcome. If prompt diagnosis and treatment can be done, worsening of vision may be minimized or prevented.

Keywords: *Leukemia, ophthalmic manifestations, leukemic infiltrate*

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INTRODUCTION

Leukemias are a category of malignant neoplasm originated in the hematopoietic stem cells due to proliferation of blood cells in the bone marrow.[1] Leukemia is categorized according to the mode of presentation, i.e., acute or chronic and the predominant proliferating cell type. Consequently, the diagnosis of leukemia will be either acute myelogenous leukemia (AML), acute lymphocytic leukemia (ALL), chronic myelogenous leukemia (CML), chronic lymphocytic leukemia (CLL), as well as other types of leukemia.[2] Generally maturity of the WBCs, their morphology, cyto-chemical findings, and immune phenotype are used to classify the type of leukemia.[3]

Leukemic infiltration of the orbit is considered rare. If prompt diagnosis and treatment can be done, worsening of vision may be minimized or prevented. Ocular symptoms can present after the systemic diagnosis, they can be existing signs of the disease or they can be the first expression of a relapse after remission.[4,5] Ophthalmic involvement by leukemia is divided into two major categories: "primary" or direct infiltration of neoplastic cells(leukemic infiltration and white-centered retinal hemorrhages), and "secondary" or indirect involvement from nonviable or dysplastic cells, or from chemotherapy leading to hematological alterations and immunosuppression causing opportunistic infections.[6] Direct leukemic infiltration may have the following paradigms:

I) Direct infiltration of the anterior segment, vitreous, choroid, iris, ciliary body and retina resembling uveitis, choroiditis and retinitis.

II) Infiltration of the optic nerve presenting with or without another cranial nerve involvement

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(cranial nerves III, IV or VI) clinically resembling palsies and swollen disks.

III) Infiltration of the orbit resembling orbital inflammatory diseases. Intraocular leukemic involvement most commonly presents in the posterior segment. Leukemic manifestations frequently have diminished vision, pain and reduced mobility of the eye. Hemorrhages in the retina are the most common feature of leukemia.[7] Some forms of hemorrhages occur due to leukemic cell infiltration whereas other forms of hemorrhages in leu kemic patients are secondary to the systemic conditions. Secondary hemorrhages mimicking as dots or blots, flame-shaped etc. Additionally, the hemorrhage may spread into the sub retinal or vitreous spaces. Cotton wool spots in leukemic patients may be attributed to nerve fiber layer infarcts or to localized collections of leukemic cells. Peripheral micro aneurysms and peripheral neovas-cularization are also ocular signs of chronic leukemia.[8] Leukemia with ophthalmic manifestations are rarely examined extensively and hardly ever biopsied.

The contemporary treatment of patients with ophthalmic leukemia includes systemic chemotherapy (although it may not be adequate due to insufficient penetration of systemic chemotherapy to the involved ocular structure) and biological treatments.[9,10] Irradiation is another treatment option (Although it commonly produces local complications). Hence, treatments with intravitreal injections of dexamethasone[11], anti–vascular endothelial growth factor (anti-VEGF)[12] or methotrexate (MTX)[13] have been recently considered.

This review aims to outline the ocular manifestations and outcomes of patients with ocular leukemia. Awareness of the clinical spectrum of leukemic lesion of ocular region is essential for rapidly establishing the accurate diagnosis and start immediate treatment.

OPHTHALMIC MENIFESTATIONS

Retinal involvement: Retina is the most common site of ocular manifestations. Leukemic retinopathy is noticed in both the acute and chronic leukemia, more frequently in acute form.[14] Retinal vascular irregularity is due to hyper viscosity resulting from increased number of circulating leukocytes or platelets. The hyper viscosity leads to diminishing blood flow and vascular stasis which then give rise to peripheral retinal capillary dropout, microaneurysm formation and proliferative retinopathy. The classic feature of retinopathy includes retinal venous dilatation and tortuosity.[15] The dilatation may be irregular in diameter. Retinal vascular sheathing is frequently present. In the sheathing there are perivascular infiltration by leukemic cells. Hard exudates and cotton wool spots may also be seen. The most prominent finding is retinal hemorrhage, more frequently noticed in the posterior pole. The hemorrhages are usually red or flame-shaped confined to retina. Rarely boat-shaped hemorrhage in the sub hyaloid space extends up to vitreous, leading to obvious obscuration of visualization of the posterior pole. The intraretinal hemorrhage may contain white dots in the center which represent cellular debris, capillary emboli or accumulation of leukemic cells.[16]

Retinal infiltrate: In patients with chronic myelogenous leukemia large grayish-white nodular retinal infiltrates are found which may be associated with local destruction, necrosis, and hemorrhage. Histopathological examination reveals that internal limiting membranes are well preserved without spreading into the vitreous cavity. These nodular retinal infiltrates are noticed in association with increased leucocyte counts with major proportion of blast cells.[17] When they are associated with increased leucocytes count, it is a dangerous prognostic sign.[17]

Retinal microaneurysm and neovascularization: Several studies demonstrated that retinal micro aneurisms with occasional capillary dropout are more commonly found in patients having chronic myelogenous leukemia.[18,19] They observed that prolonged leukocytosis is an obligatory factor in the development of peripheral retinal micro aneurysm. But they were unable to find any association between duration of the disease and retinal vascular abnormality. Although in some case reports no correlation was observed between micro aneurysm formation and hematocrit level, significant correlation was noticed between retinal neovascularization and increased number of circulating platelets.[20]

Orbit and eye lid involvement: Around 2-6% of the orbital tumors of childhood are considered due to leukemia.[21] A recent study has demonstrated that about 11% of children presented with unilateral proptosis having some form of acute leukemia.[22]

There is increase prevalence of orbital involvement in leukemia due to soft tissue infiltration by leukemic cells or due to hemorrhage. Infiltration of the eye lid, orbit, or lacrimal gland may also be noticed. When retrobulbar hemorrhage occurs, it may extend forward into the subconjunctival space. Hemorrhage into the lids is also not an uncommon finding. Granulocytic sarcoma involving orbit is a typical feature of myelogenous leukemia. It may occur at any time of development of myelogenous leukemia and sometimes even before the appearance of systemic involvement. Due to diffuse orbital involvement the patient may present with proptosis following discrete orbital growth.[22]

Optic nerve infiltrates: Leukemic infiltration of the optic nerve has been considered that the disease progress to the point of involvement of the central nervous system (CNS), which is more commonly observed in acute compared with chronic leukemia, children compared with elderly people and acute lymphoblastic leukemia (ALL) compared with acute myelogenous leukemia (AML).[23] The optic nerve can be bulged from increased intracranial pressure, retro laminar leukemic invasion or by direct infiltration of the optic nerve head.[24] Retinal perivascular infiltration is the differentiating point between direct optic nerve head infiltration and papilledema. Vision is more likely to be maintained in direct infiltration of the optic nerve head compared with retro laminar involvement of the optic nerve.[25]

Anterior segment involvement: The anterior segment is rarely involved by leukemic infiltration. Comma-shaped venous irregularities of the conjunctiva have been noticed, possibly due to hyper viscosity.[26] Conjunctival tumors result in subconjunctival protrusion in AML or ALL.[27] Iris involvement is characterized by color change and a gray or yellow pseudohypopyon.[28] Due to involvement of trabecular meshwork the intraocular pressure is likely to increase.[28]

Vitreous leukemic infiltration: Despite the internal limiting membrane predominantly acts as barrier to leukemic cell infiltration, cells can infiltrate the vitreous from optic disc neovascularization and vitreous hemorrhage can permit neoplastic cells to infiltrate the vitreous cavity.[29,30]

Choroid leukemic infiltration: Although the ophthalmologic changes are not predominantly found, the choroid infiltration with leukemic cells is frequently found in histopathological examination.[31] Kincaid et al. have noticed bilateral serous detachment of the retina with diffuse infiltration of the choroid by leukemic cells.[32] Furthermore, large choroid masses with chronic myelogenous leukemia and overlying serous retinal detachment have also been observed in adults.[32] Fluorescein angiographic examinations in patients with choroidal infiltration and overlying serous detachment of the retina show innumerable retinal pigment epithelial leakage points in the early phase of the angiogram. With time these leakage points become more diffuse, and dye is found to leak into the sub retinal space.[32]

Unusual ocular manifestations in leukemia: The ophthalmologist should be aware of the unusual and diverse ophthalmological disorders in which leukemia can be presented to them. At the initial stage, leukemic process can be found as redness and swelling of the lower palpebral conjunctiva (in acute lymphocytic leukemia),[33] corneal ring ulcer (in acute monocytic leukemia),[34] Sjogren's syndrome with lacrimal gland enlargement (in chronic lymphocytic leukemia),[35] anterior segment ischemia (in chronic myelogenous leukemia),[36] open-angle glaucoma considered to be due leukemic infiltration of the trabecular meshwork (in both chronic lymphocytic leukemia and chronic myelogenous leukemia),[37,38] and finally, acute leukemic infiltration of the vitreous in a patient with acute lymphocytic leukemia.[39]

SYSTEMIC EVALUATION BY THE OPHTHALMOLOGISTS

When leukemia is suspected, the principal test is complete blood count with platelet count. If it reveals markedly elevated or decreased WBC count, the ophthalmologist should consult hematologist or oncologist. In acute leukemia, at least 20% or more blast cells are seen.[41] It is a medical emergency and patients should be immediately referred. Sometimes, extraocular deviations are visible. However, if the CBC with platelet parameter reveals no blast, lymphocyte predominance with mature appearing cells and basophilia, findings indicate chronic leukemia.[41] These patients should be referred to consult with hematologist/oncologist within 1-2 weeks.

TREATMENT

We must be aware of the basis of our management in such cases, that is to treat the underlying malignancy.

In Acute lymphoblastic leukemia: The prognosis for a patient having acute lymphoblastic leukemia mainly depends on the underlying cytogenetic and molecular characteristics. In the induction phase chemotherapeutics minimize the tumor burden by clearing leukemic cells in the bone marrow. Acute lymphoblastic leukemia tends to infiltrate the CNS. Therefore, intrathecal prophylaxis is judgmental. In the consolidation phase, the target is to eliminate any leukemic cells which remain viable. In the maintenance phase, chemotherapeutics and steroids are considered in combination to prevent recurrence. In unfavorable acute lymphoblastic leukemia, allogeneic stem cell transplantation may be considered. However, immediate radiotherapy administration to the eye, combined with systemic chemotherapy, may be useful in preservation of vision and for reaching long term disease-free survival.

In Acute myeloid leukemia: The biologic aggressiveness of AML is often anticipated on the underlying chromosome abnormalities and molecular characteristics. Treatment is categorized into induction and consolidation phases. The patients who carry unfavorable cytogenetic or molecular features are likely to undergo stem cell transplantation for consolidation therapy.[40]

In Chronic Lymphocytic Leukemia: Patients having chronic lymphocytic leukemia often do not need therapy at the initial phase as the disease can be indolent course. However, therapy is often indicated for those patients who have constitutional symptoms, hepatosplenomegaly, gross lymphadenopathy, anemia and or thrombocytopenia.[41] The treatment for chronic lymphocytic leukemia has undergone regime changes in the last few years. Although chemotherapy and immunotherapy are considered as first-line treatment, some selective oral agents including ibrutinib, idelalisib and venetoclax are recommended which disrupt several signaling pathways inside the chronic lymphocytic leukemia cell.[42]

In Chronic Myeloid Leukemia: Chronic myeloid leukemia can progress from an indolent chronic phase to a more invasive accelerated or blast phase.[43] The approach with tyrosine kinase inhibitors has extremely upgraded the treatment and prognosis of patients with chronic myeloid leukemia.[44]

PROGNOSIS

Several studies suggest that ophthalmic leukemic infiltrations are more aggressive and have worse outcomes.[45,46] The prognosis also related to some other factors of bone marrow or CSF involvement and the length of initial hematological remission. Among patients with leukemic retinopathy, the mean survival rate was significantly lower who have cotton wool spots, compared with those without those spots. As there is high prevalence of ocular findings in leukemia, it should be a standard practice that all leukemic patients should have a screening through ophthalmic examination.

CONCLUSION

Ophthalmic manifestations of leukemia can result from direct infiltration of leukemic cells or indirect causes along with hematologic abnormalities. It has been observed that mostly all parts of the eye can be involved in leukemia. Sometimes, ophthalmic involvement can be the first sign of disease relapse. Awareness of the clinical spectrum of leukemic infiltration of ocular region is essential for rapid diagnosis, prompt initiation of treatment and better outcome.

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Review Article

Managing Substance Use Disorders and Addiction: How to Integrate Professionalism and Ethics with the Complexity of Diagnosis and Therapy

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ABSTRACT

Physicians and other healthcare staff who work with the patients having substance use disorders (SUDs) and addiction have to deal with different and complex scenario invariably in comparison to other healthcare providers dealing with regular medical services sought by the patients. Hence, the unconventional nature of practice regarding patients of SUDs and addiction and the diverse range of backgrounds among substance use workers, e.g., psychiatrist, general physician, nurse, psychotherapist, counsellor, social worker, and public health specialist highlights the universal relevance of being more professional and more ethical in practice. They are expected to demonstrate a variety of ethical and professional competences to safeguard themselves and others involved. Clinical team engaged in such activities requires specific ethical training that can help them face specific ethical dilemmas and guide through deeper consideration of those pressing and complex issues, using specific framework, professional guidelines, or institutional management approaches. Professional societies and accrediting institutions should apply their authority to establish practice standards, competencies, regulatory procedures, and codes of ethics to help guide practice and protect public trust and confidence. For the team involved in practice, it is important to become familiar with and adhere to the principles and values that define professionalism and ethical conduct in care for patients suffering from SUDs and addiction. The review paper aims to examine the intersection of professionalism and ethics with the complexity of diagnosis and therapy in this specific area of practice. Besides, some frameworks will be highlighted which may help healthcare providers to foster ethical decision making. It is also a modest effort to show some new insights for improving the quality of care in addiction and mental health by the professional team and healthcare organization from both clinical and operational viewpoint.

Keywords: *Substance use disorders, addiction, addiction related practice, professionalism, medical ethics.*

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INTRODUCTION

Substance use disorders (SUDs) and addiction are responsible for substantial health, economic and social costs in any society.[1] Substance abuse has become a substantial public health concern across the globe, as per estimation of the World Health Organization (WHO), over 275 million people use illicit drugs; of them, 31 million have an addiction problem.[2] Providing proper treatment environment, optimal management and prevention for SUDs and addiction is a crucial part of the national mental health strategy of Bangladesh. However, evidence showed that Bangladesh, a resource-poor, developing country of South Asia, has a high burden of mental health disorders with few mental health services.[3,4] Recently, Bangladesh has enacted the Mental Health Act 2018 (MHA), which replaced a century old Lunacy

Act of 1912.[5] The MHA is now the prime legislation in Bangladesh that outlines procedures for admitting, assessing, and treating individuals with any mental health condition including SUDs and addiction.[5] Moreover, UN Sustainable Development Goal (SDG) 3 sets out a commitment by governments to strengthen the prevention and treatment of substance abuse.[6] However, there are numerous barriers have been identified to quality treatment uptake and recovery process among patients of SUDs and addiction. Evidence showed that an interplay of social and clinical factors including treatment cost, lack of availability, consultation style, social stigma, lack of professionalism and unethical beahaviour of the service providers are some of the burning issues that bar access to optimum care for patients with SUDs and addiction.[7-9] Specifically, Social stigma (i.e., how society views persons with drug abuse and addiction is fraught with emotion, misperceptions, and biases) and self-stigma all together including stereotyping, prejudice, rejection, social isolation, status loss, ignorance, low self-esteem, low self-efficacy, discrimination, and marginalization regarding SUDs and addiction are the some important reasons that compel them suffer in silence without any treatment.[7-11] Physicians and other healthcare staff who work with the patients having substance use disorders (SUDs) and addiction have to deal with different and complex scenario invariably in comparison to other healthcare providers dealing with regular medical services sought by the patients. Hence, the unconventional nature of practice regarding patients of SUDs and addiction and the diverse range of backgrounds among substance use workers, e.g., psychiatrist, general physician, nurse, psychotherapist, counsellor, social worker, and public health specialist highlights the universal relevance of being more professional and more ethical in practice. They are expected to demonstrate a variety of ethical and professional competences to safeguard themselves and others involved.[12] Moreover, the MHA has brought hope for those patients suffering from SUDs and addiction protecting their rights to health and keeping provisions for treatment and rehabilitative services.[5] Under the circumstances, this review paper aims to examine the intersection of professionalism and ethics with the complexity of diagnosis and therapy in this specific area of practice. Besides, some frameworks will be highlighted which may help healthcare providers to act with professionalism and foster ethical decision making. It is also a modest effort to show some new insights for improving the quality of care in addiction and mental health by the professional team and healthcare organization from both clinical and operational viewpoint.

PROFESSIONALISM AND ETHICS IN SUBSTANCE USE DISORDERS AND ADDICTION RELATED PRACTICES

While working with people with SUDs and addiction, at any level from the individual to the systemic, it is important to "evaluate decisions, policies and practices from the perspective of professionalism and ethics".[12] Generally speaking, professionalism (which may be defined as skillful actions and behaviours guided by the practitioners' values and knowledge) and ethics (the way of determining and doing what is good and right in specific situation) combinedly benefit service users and contribute much to ensure patient safety and support quality delivery of services and address mental health issues related to substance use disorders (SUDs) and addiction in the community as well.[13,14] In other words, ethics is an intellectual approach to moral issues that deals with "some fundamental principles that provide a framework for addressing dilemmas" in healthcare or reviewing our conventional practices as physician or other healthcare providers.[13] As per 'Principlism' described by Beauchamp and Childress,[15] the 'four principles' (autonomy, beneficence, non-maleficence, and justice) are still governing mostly our ethical considerations in clinical and hospital based practices in Bangladesh.[16-18] However, we have felt that it demands much more beyond those 'four principles' encompassing some other elements like "compassion, non-abandonment, non-oppression, confidentiality and client empowerment," while being engaged in the field of addiction and mental health.[13] In reality, healthcare workers in the substance abuse treatment field are constantly facing ethical dilemmas on an individual as well as a societal level.[13,19] We are aware that ethics provide some "foundational values to guide conduct, thinking and decision making in the complex scenarios" that often surround problematic substance use disorders or addiction – those include "fairness, privacy, respect, safety, meaningful life and hope".[13] In our country, the supreme regulatory authority in medical profession, Bangladesh Medical and Dental Council has Code of Medical Ethics.[20] However, there is no specific direction for such sensitive and sophisticated practice like dealing with

people having SUDs and addiction. Moreover, there are no guidelines from the respective professional societies to date. Even the curricula of undergraduate and postgraduate medical education of the country lack formal clinical ethics training.[21] Therefore, in most cases, when rules are not available, individuals turn to their own moral compass. Usually, professionals and care providers start by identifying a value, such as "courage and integrity" which defines a particular attitude, such as "the courage to do the right things consistently without regard to personal consequences," which then results in an ethical behavior, such as to make "unpopular decisions based on fair consideration of the facts."[22]

ETHICAL ISSUES FOR THE HEALTHCARE PROVIDERS

Ethical issues are both personal (micro) and societal (macro) in nature. There is an ongoing struggle between legislating morality for the "public good" and fighting to retain the "right to autonomy" of the patient. It is the intense emotional nature of such concerns that takes an issue from a personal level to a societal level.[22,23]

Another crucial task is balancing personal and professional standards. Substance abuse treatment professionals need to be familiar with the Code of Ethics and may have to reconcile personal beliefs with the profession's code. There also may be institutional standards/guidelines that conflict with an individual's personal beliefs. In either case, there is a constant need to weigh what may "feel right" personally with the standards and policies of the workplace environment and profession.[13,22,23]

Perhaps the most difficult dilemma occurs when there are conflicts between the clinician's values and the client's behaviours. For example, does an adult with an SUD have the ability to make his or her own decisions? Some views of addiction might say "no," while others might demand strict proof before accepting that such a person is incapable of making a decision. In other cases where professionals know that if a client threatens suicide or homicide, there is a duty to report. However, most of the daily concerns that arise are not so simple. For example, did the client understand what the release of information stated, or did he/she rush so that the provider could make the next appointment? Did the clinician listen to what the client said about his/her gender-specific demands or issues, cultural norms and religious beliefs, and how the treatment plan would not work because it was not created in a culturally or faith-based competent manner? Was information about the client shared with another helping agency, even though he/she did not give a release to that specific agency? These are the kinds of issues that arise every day, affecting client care and reflecting on one's status as a clinician, as well as on the institutional reputation.[22-27]

Another crucial ethical debate, which is mostly popular in western society, revolves around safe injection sites (for drug abusers) which is based on the counteraction in between the abstinence model and the harm reduction model. Those who oppose the safe injection sites are the proponents of the "abstinence model" of drug policymaking. The mechanism of action of this model is to decrease the number of illicit drug users in the society by "criminalizing drug use and implementing demand and supply reduction strategies".[28,29] On the contrary, those who are in favour of the operation of safe injection sites are the proponents of the harm reduction model. This model aims to decrease the possible negative outcomes in people and society related to drug use, which does not require any abstinence.[28-30] Here we suggest that involved professionals must weigh and consider these two mechanisms based on their existing legislation, respective institutional policies and practice guidelines.

In modern health care, ethics also calls on us to be open to examining routine practices and conventional beliefs. In the SUDs treatment field, for example, the view of effective treatment has evolved from a focus on people with severe SUDs who are willing to commit to abstinence goals to the need for a broadened spectrum of services that address a continuum from mild to severe substance use problems. This evolution reflects the advancement in knowledge and growth of evidence-informed approaches, as well as a shift in the moral frame that influences how professionals, policy makers and the public view people with SUDs and the prevention and management of these health conditions.[13,31,32]

SOME USEFUL RESOURCES FOR ETHICAL DECISION MAKING

Ethical decisions are informed by a full consideration of the circumstances, seeking a thorough understanding of the implications of all available mechanisms of action. Ethical reflection, discussion

and decision making are especially important in complicated situations where each of the available options makes things better in some ways, but worse in others.[13] Hence, it needs to be compatible with country's legislation, institutional policies, and professional Code of Ethics.

Making good ethical decisions requires a trained sensitivity to ethical issues and a practiced method for exploring the ethical aspects of a decision and weighing the considerations that should impact our choice of a course of action.[33] It is an essential part of healthcare to explore an ethical dilemma and decide on the best decision; to do so we could consider the following common approaches in our practice (as directed by the Markkula Center for Applied Ethics at Santa Clara University, USA):[33]

1. *Utilitarian Approach:* Which option produces the most good and the least harm?
2. *The Rights Approach:* Which option respects the rights of everyone involved?
3. *The Justice Approach:* Which options treat people equally or proportionally?
4. *The Common Good Approach:* What best serves the community as a whole?
5. *The Virtue Approach:* Which action best represents your personal values?

Generally, we, as healthcare providers, always need to value human relationships and work with individuals and families alike. At times, the entire family can be defined as the client, while in other situations, an individual member of that family is the client. This can be challenging when there are conflicting principles such as confidentiality, self-determination and informed consent.[14,22] Considering all those, the following chart could be used as a common guideline/framework for ethical decision-making for the healthcare providers (Fig. 1):

Another important option is the *CLEOS* model, which is a practical approach to working through complex ethical decisions in health care that integrates easily into practice. Health care professionals may review the situation considering each of five key perspectives of the *CLEOS* model:[13]

1. **C**linical, including client history, concerns and goals, intervention options and the expected benefits, risks and burdens, and therapeutic relationship and engagement;
2. **L**egal, such as laws, regulations, guidelines, occupational health and safety rules, and professional college standards;
3. **E**thical, informed by principles and values;
4. **O**rganizational, such as resource availability (including staffing and space), policies, funding and workplace culture;
5. **S**ystemic, including social determinants of health, stigma, social values and priorities.

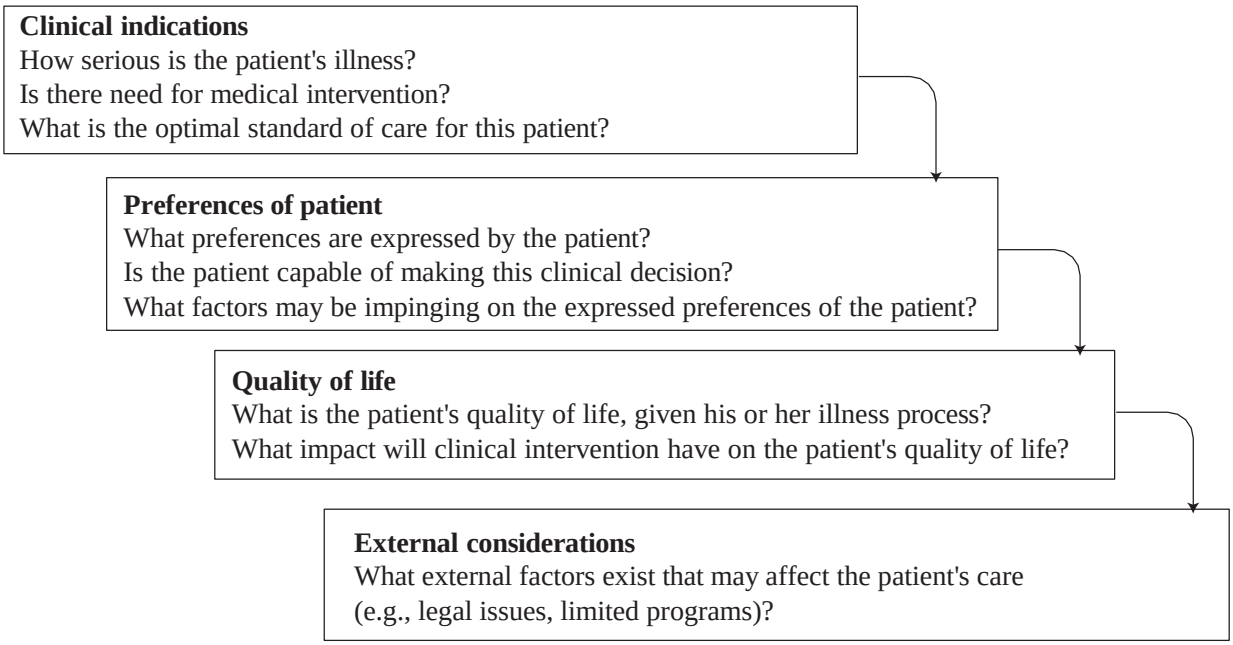

Fig. 1: *Steps for clinical ethical decision making (Adopted from Roberts & Dyer, 2004).*[22]

In recent times, clinical team engaged in such activities requires specific ethical training that can help them face specific ethical dilemmas and guide through deeper consideration of those pressing and complex issues, using specific framework, professional guideline or institutional management approaches, e.g., by following the *CLEOS* model.

Last but not the least, these are only some examples of resources to facilitate the team engaged in the treatment of SUDs and addiction. The more novel and difficult the ethical choice we face, the more we need to rely on discussion and dialogue with others about the dilemma. Only by careful exploration of the problem, aided by the insights and different perspectives of others, can we make good ethical choices in such situations.[33-35]

Additional factors such as patient preferences and quality of life considerations can be included in discussing options for care. This comprehensive model moves ethical considerations from being an add-on to becoming integral to individual, collaborative professional practice. It is important to become familiar with and adhere to the principles and values that define professionalism and ethical conduct in care for people with substance use or addiction problems.[13,34,35] By being guided by professional Codes of Ethics, professionals engaged in such practice must demonstrate that they are practicing in ways that are both professional and ethical as well as fulfilling the demands of the MHA.

CONCLUSION

Professional teams dealing with patients suffering from substance use disorder (SUD) and addiction must establish and maintain their professional and ethical standards consistent with the specialty and national standards. We have shown the necessity to formulate some directions specific to managing substance use disorders and addiction patients in the code of ethics; we believe that those are very foundational, must be followed by all physicians and other professionals and residents involved in practices related to substance use disorder (SUD) and addiction. However, it falls upon the senior faculty members and largely on the institution to teach these attributes to the healthcare providers working in this sector and trainees/residents. We have also discussed here some of the available frameworks for ethical practice in the field of addiction and mental health. Besides, online resources for ethics education and discussion on this trendy topic may be warranted. We hope that this knowledge dissemination is relevant to everyone working in substance use, addiction and mental health care, from residents, to specialized physicians to highly experienced consultants/supervisors to administrators and policy makers.

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Case Report

Ramsay Hunt Syndrome: A Rare Disease of Multiple Cranial Nerve Involvement

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ABSTRACT

Ramsay Hunt Syndrome (RHS) also known as herpes zoster oticus is a viral disease, a member of the human herpes virus family, is a late complication of varicella-zoster virus infection that results in inflammation of the geniculate ganglion of cranial nerve VII. Ramsay Hunt is a clinical diagnosis. The hallmark of the condition is multiple unilateral erythematous vesicles, which are distributed over the auricle and preceded by severe otalgia. If these symptoms are associated with facial nerve palsy, the condition is called RHS which is usually accompanied by vestibulocochlear abnormalities. Diagnosis is often missed or delayed, which can lead to an increased incidence of long-term complications. The condition is self-limiting, but treatment is targeted at decreasing the total duration of the illness as well as providing analgesia and preventing the complications that can occur. This activity reviews the role of the inter professional team in the diagnosis and treatment of RHS.

Keywords: *Ramsay Hunt syndrome, herpes zoster oticus, varicella-zoster virus, erythematous vesicles.*

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INTRODUCTION

Ramsay Hunt Syndrome (RHS) also known as herpes zoster oticus or geniculate ganglion herpes zoster, is a late complication of varicella-zoster virus (VZV) infection, resulting in inflammation of the geniculate ganglion of cranial nerve VII.[1] The syndrome is named after James Ramsay Hunt (1872-1937), an American neurologist and Army officer in first world war who described three different syndromes, the most famous of which is the second, which is discussed herein as "Ramsay Hunt syndrome."[2] Early stages of VZV infection cause fever and diffuse vesicular rash, a condition that is commonly referred to as chickenpox. After the initial infection, the virus will often remain dormant in the body. Subsequent reactivation of the virus causes a "zoster" or "herpes zoster" phenomenon. This syndrome consists of pain and a vesicular rash along the involved nerves distribution, typically corresponding to a single dermatome. The distribution and associated symptoms depend on the nerve involved. Less than 1% of zoster cases involve the facial nerve and result in Ramsay Hunt syndrome.[3]

Although the classic triad of RHS is ipsilateral facial paralysis, otalgia and a vesicular rash, there is significant variability in clinical presentation, with some patients demonstrating facial paralysis before the rash or sometimes, no rash at all.[4,5] In the latter,

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the patient's chief complaints are severe ear pain and facial weakness; this variant is known as zoster sine herpete and can be very difficult to clinically distinguish from Bell's palsy. Zoster sine herpete has been reported to comprise up to 30% of Ramsay Hunt cases.[6] If a rash is present, it may be frankly vesicular or maculopapular and can involve the affected side of the face, scalp, palate, and tongue. Additional symptoms that may be reported include a change in taste sensation, dry eye, tearing, hyperacusis, nasal obstruction, and dysarthria. Hearing loss, tinnitus, and vertigo can be seen with involvement of the vestibulocochlear nerve, and hoarseness or aspiration may indicate involvement of the vagus nerve.

CASE SUMMARY

A 42-year-old diabetic normo tensive woman 9 days back presented at the Otolaryngology clinic with a sudden onset of dysphagia, odynophagia and hoarseness of voice,after 4-5days of these symptoms she complained of left-sided mild deafness, tinnitus, severe otalgia and erythematous vesicular eruptions over the left pinna and face. After that 2 day she developed complete left lower motor neuron facial nerve palsy, House Brackmann grade III, with dry eye.(Fig-1)

Fig-1: *VII N palsy at p resentation & days later*

Fig-2: *Vesicle over face & pinna, at presentation-a & 15 day later-b*

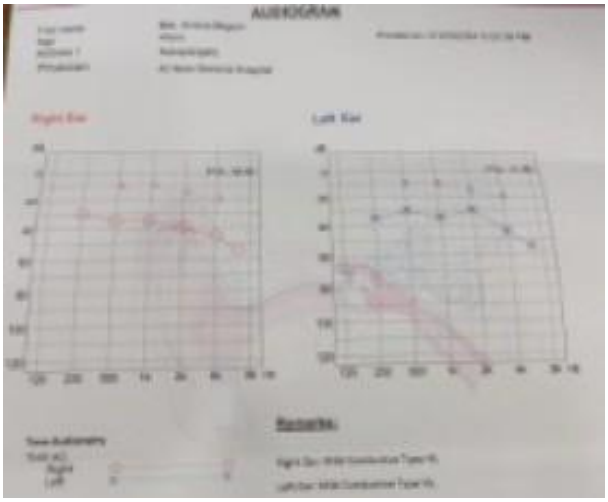

Fig-3:*Pure tone audiogram, mild sensory hearing loss, left ear*

Fig-4 :*Palatal palsy(IX, X Nerve palsy), at presentation & 15 day later*

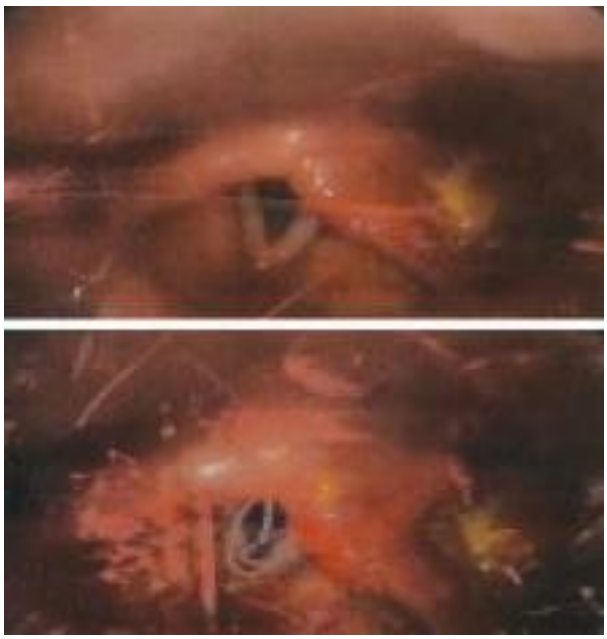

Fig-5:Videolaryngoscopy showed left vocal cord palsy & aytenoid oedema(X Nerve palsy)

Fig-6:*Showing weakness-a and sterngth-b of sternoclaidomastoid muscle(CN XI)*

She was apparently healthy before presentation of these symptoms. The patient's past medical history was unremarkable. Neither the patient nor her family had similar problem. Physical examination revealed(after 9 days of presentation) erythematous vesicular eruptions over the left auricle, angle of mouth, temple (Figure-2).Tuning fork tests showed that the Rinne test was positive on both sides, the Weber test lateralized to the right ear and the absolute bone conduction test reduced on the left side. In pure tone audiometry there was also mild sensoryneural hearing loss in the left ear(Fig-3). Oropharyngeal examination revealed that the uvula –soft palate deviated to the right side on phonation and reduced gag reflex on the left side(Fig-4).Telelaryngoscopic examination revealed erythema and white exudate covering the mucosa over the left arytenoid, accompanied by vocal cord palsy(Figure-5).Blood tests revealed that the erythrocyte sedimentation rate (ESR) was 25 mm in 1st hour (reference range 0-15 mm/hour) and C-reactive protein was 12 mg/ dL(Normal range). On serological test, the IgM and IgG antibody against VZV was not done due to unavailability.MRI with gadolinium enhancement of the brain revealed no abnormal lesions.No definite abnormal findings were found on neck and chest CT scan. The patient was diagnosed with RHS with polyneuropathy. She was hospitalized and a loading dose of 1 mg/kg/day of prednisolone orally were started. Subsequently, gradual tapering was done over three weeks. In addition, oral acyclovir was given at a dose of 25 mg/kg/day for 14 days and acyclovir cream over the skin lesion also applied. Dressing of the ear on a daily basis was performed and a pain killer was given with pregabalin 50mg bid 7days, carboxymethylcellulose sodium eye drop applied in left eye. Physiotherapy of the patient was initiated in the physiotherapy & rehabilitation unit. No side effects were detected during or following the completion of the treatment regimen. After two weeks of follow-up, the vesicles dried up changed to scabs and dropped off. Her hearing impairment partially recovered with partial improvement of facial movement but palatal palsy and vocal cord palsy persisted.She is now under observation, continuing treatment and follow up.

DISCUSSION

RHS affects both immunocompetent and immunocompromised patients and has an incidence of about 5 per 100,000 people per year; in contrast, the incidence of Bell palsy is much higher, at about 15-30 per 100,000 people per year.[7,8] RHS accounts for roughly 7% of acute facial paralysis cases, with zoster sine herpete comprising up to 30% of those. RHS mostly presents in individuals aged 60-80 years, any age from 19 to 89 years can be involved [2].However, the more severe disease form and less favorable outcomes occur in patients with hypo immunity. There are many predisposing factors that can increase the incidence of RHS, such as stress, infection, malnutrition, cytotoxic drugs, diabetes mellitus and malignant tumors. The classical presentation of RHS is a triad of unilateral severe otalgia which is preceded by the appearance of erythematous vesicular lesions over the auricle, external ear canal ,eardrum and lower motor neuron facial nerve paralysis. The vestibulocochlear nerve is the most common cranial nerve associated with the syndrome [2]. The oculomotor, trigeminal, abducent, glossopharyngeal, and vagus nerves are also associated with RHS also reported in the literature as RHS with polyneuropathy [4,6,7]. Moreover, non-classical presentations such as RHS without the involvement of the facial nerve have also been reported [8]. There are five possible mechanisms of simultaneous cranial polyneuropathy, namely, VZV induces occlusive vasculitis which results in ischemic neuropathy, the spread of the infection through the synapse, a neuroinvasive feature of the virus, inflammation of contiguous ganglia, and anastomoses between the affected nerves and other cranial nerves [9,10]. The reason for the slowly developed facial paralysis was probably the result of reactivation of the VZV that remained dormant in the nerve root ganglion. Trigeminal and vestibulocochlear

nerves and spinal ganglia C2-C4 are known to be the commonly affected nerves. Severe inflammation in one ganglion can spread to another ad jacent ganglion. It can also cause infarction by invading microvascular structures that have a common distribution in other brain nerves. VZV can directly invade the brainstem parenchyma by way of nerve axons or via synapses. Recently, a hypothesis that, VZV causes synaptic conduction along the reflex pathways of the brainstem, causing multiple neuropathies, has also been raised[11]

On serologic test, the positive rate of serum VZV IgM in patients with RHS was reported to be significantly higher (30.8%) than that in patients with Bell's palsy (9.8%).[12] Serologic screening for IgG against VZV will aid in identifying non immune individuals. The presence of IgM against VZV is suggestive of an acute or recent infection. However, results should be correlated with the clinical presentation because the patient's symptoms are the most important criteria in RHS diagnosis. RHS with multiple CN palsy has rarely been reported 11 patients with 10 years of RHS with polyneuritis, and the frequency of CN involvement was VII, VIII, IX, X, and V in that order reported, 11 cases for 15 years, and the following CN VII, VIII nerves, the frequency of other CN was CN X, IX, and V in that order[13,14] In a paper analyzing RHS with polyneuritis combined with vocal cord palsy (CNX) reported in the literature for 50 years; of the 14 patients, the incidence was CN VII,VIII,IX,V and XII.[15]There are few prospective controlled studies for RHS with multiple CN involvement in the medical literature.

The diagnosis of RHS is usually based on the classical presentation of the syndrome. Confirmation of the diagnosis is carried out with serological tests of IgG and IgM antibodies against VZV. Brain MRI is mandatory for the exclusion of tumors or demyelinated lesions or when there is a suspicion of infective brain tissue complications of the VZV. Although RHS is considered to resolve without treatment, early initiation of treatment is advised to reduce long-term complications such as postherpetic neuralgia and spastic facial nerve palsy. Several investigations have reported a significant reduction in late complications with the combination of steroid and antiviral therapy[12,14]. Our patient showed partial improvement of all presentation with these two treatment modalities till date. The prognosis of RHS is less favorable than Bell's palsy [14]. The full recovery rate was reported to be 63.63% in patients with an RHS with cranial polyneuropathy [7]. Furthermore, the prognostic factor that seems as reported in the literature is the severity of the presenting features [13]. Even though there was slow recovery of the involved cranial nerves in the presenting case, complete recovery was achieved at the four-month follow-up.

CONCLUSION

RHS affects patients in a myriad of ways and behavioral health concerns all occurring commonly in the acute period. While most patients do recover the majority of their pre morbid function when managed appropriately, long-term pain, facial dysfunction, scarring, and behavioral health concerns may all persist. For this reason, optimal patient outcomes occur when healthcare teams include members with expertise across a broad range of specialties. In the short term, primary care, otolaryngology, neurology, ophthalmology, and psychology/psychiatry are often required. In the long-term, facial plastic surgery or otolaryngology, pain management, ophthalmology, speech or physical therapy, and psychology/psychiatry may be needed. It is critical to surround these patients with an experienced inter professional team early on in the treatment process in order to provide the care and support they need to maximize their quality of life outcomes.

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Case Report

Endometrioid Carcinoma Four Years After Hysterectomy: A Rare Case Report

Rahim R[2], Hira NA[2], Banerjee R[3]

ABSTRACT

It is quite a fascinating case as we have recently experienced in Mugda Medical College Hospital, a tertiary level teaching hospital in Dhaka, Bangladesh, that a woman was diagnosed and treated for endometrioid adenocarcinoma four years after her vaginal hysterectomy had been done. Our patient was presented with abdominal pain for nearly 2 weeks along with nausea, vomiting and generalized weakness. Ultrasound evaluation revealed a complex pelvic mass (8.6cm × 4.9cm). Chest x-ray revealed a left sided pleural effusion, while CT scan of the abdomen revealed heterogeneously enhancing complex pelvic mass and mild ascites. After a clinical correlation with all the pathological investigations, the patient was advised for a core biopsy. Ultrasonogram guided core biopsy was done. Histopathological examination showed a malignant ovarian epithelial tumor. Then she underwent an interventional or surgical procedure, which included an exploratory laparotomy, bilateral salpingo-oophorectomy with bilateral pelvic lymph node dissection and infracolic omentectomy done under general anesthesia. The final histopathological examination of the removed mass showed an endometrioid adenocarcinoma (Grade 2). Meanwhile, she was referred for radiation therapy (both vaginal brachytherapy and external pelvic radiation) after the patient had recovered from surgery. We will discuss this case as a part of our clinical interest and continuing education for our clinicians and residents.

Keywords: *Endometrioid carcinoma, gynaecological malignancy, diagnostic laparotomy, hysterectomy, salpingo-oophorectomy*

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INTRODUCTION

Endometrial cancer (also referred to as 'corpus uterine cancer' or 'corpus cancer') is the leading cause of gynecologic cancer mortality in high-income countries and also increasing in incidence in low- and middle-income countries, with adenocarcinoma of the endometrium the most common type.[1,2] The incidence of endometrial cancer is raising among elderly women in Bangladesh, as per hysterectomy statistics in government hospitals across the country; however, there is no such data regarding incidence of endometrial cancer registered in the country.[3]

It is quite a fascinating case as we have recently experienced in Mugda Medical College Hospital, a tertiary level teaching hospital in Dhaka, Bangladesh, that a woman was diagnosed and treated for endometrioid adenocarcinoma (FIGO grade 2) four years after her vaginal hysterectomy had been done. Our patient was presented with abdominal pain for nearly 2 weeks along with nausea, vomiting and generalized weakness. We will discuss this case as a clinical interest and continuing education for our clinicians and residents.

CASE SUMMARY

A 48-year-old lady hailing from Dholpur area of Dhaka City Corporation (South) was admitted into Mugda Medical College Hospital, Dhaka, in December 2023, with complaints of abdominal pain for nearly two weeks along with nausea, vomiting and generalized weakness. She belonged to a low-

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socio-economic group. She had a vaginal hysterectomy 4 years back. She had no co-morbidities like diabetes, hypertension, or asthma. She had two grown up children with normal vaginal deliveries. She experienced menopause 6 years back. On general examination, the patient was found normotensive with bradycardia and mildly anemic. Par abdominal examination revealed a distension with irregular mass (about 6cm × 5cm) located at hypogastrium, which was mildly tender, and mobile. Overlying skin of the mass was free; however, it was fixed with the underlying structures. Par vaginal examination revealed a puckered vault (a portion) of the uterus along with a tender mass felt through vault. Ultrasound evaluation revealed a complex pelvic mass (8.6cm × 4.9cm). Her blood glucose levels were within normal limit. CA-125 was >1200 u/ml, while CA 19-9 was 20.49 u/ml. LDH was found 299 u/ml, and CEA was 2.63 ng/ml. CRP was >200. Chest x-ray revealed a left sided pleural effusion, while CT scan of the whole of the abdomen revealed heterogeneously enhancing complex pelvic mass and mild ascites. After a clinical correlation with all the pathological investigations, the patient was advised for a core biopsy. Ultrasonogram guided core biopsy was done. Histopathological examination showed a malignant ovarian epithelial tumor. Then she underwent an interventional or surgical procedure, which included an exploratory laparotomy, bilateral salpingo-oophorectomy with bilateral pelvic lymph node dissection and infracolic omentectomy done under general anesthesia. The final histopathological examination of the removed mass showed an endometrioid adenocarcinoma (FIGO grade 2). Meanwhile, she was referred for radiation therapy (both vaginal brachytherapy and external pelvic radiation) after the patient had recovered from surgery. Monthly follow-up after surgery was done for 3 months. Her last biochemical report showed – SGPT level 23 u/L and CA-125 32 u/ml, while follow-up ultrasonogram revealed normal findings.

DISCUSSION

Our patient had a history of vaginal hysterectomy due to fibroids 4 years back. However, she could not tell anything about other morbidities like endometriosis. She was admitted into the hospital with complaints of abdominal pain for nearly two weeks along with nausea, vomiting and generalized weakness. Further investigations revealed endometrioid carcinoma. In the presented case a secondary implantation of endometrial tissue during the earlier laparotomy is a possibility. The former histology report was not available though.

After the reproductive period ends, endometriosis is thought to resolve or remain in a state of inactivity. Although the hypoestrogenic state related to menopause may suggest it, postmenopausal endometriosis can affect up to 4% of women.[4] Although endometriosis is widely deemed as a benign disease, affected patients inherently have an increased risk of developing malignancy.[5,6] Therefore, recurrences or malignant transformations are rare but possible events.

Similar incidence was described by Abu et al. as a 38-year-old woman was diagnosed with endometrial adenocarcinoma arising from pelvic endometriosis thirteen years after hysterectomy with bilateral salpingo-oophorectomy, followed with hormone replacement therapy[7], while Debus & Schuhmacher reported a case of a 50-year-old woman with endometroid adenocarcinoma arising from endometriosis seventeen years after total abdominal hysterectomy and bilateral salpingo-oophorectomy followed with estrogenic hormone replacement therapy.[8] Another case was described by Al-Talib et al. as a 68-year-old woman who underwent total abdominal hysterectomy and bilateral salpingo-oophorectomy subsequently presented with left-sided pelvic mass which was later reveled as endometrioid carcinoma after 13 years of her hysterectomy.[9]

In our case, the woman underwent vaginal hysterectomy due to fibroids, as per her own description. Women often want a procedure that retains the cervix as because they want to retain as much of their reproductive system as possible and some of them believe it will preserve the sexual function.[10] However, evidence showed that total hysterectomy does not affect sexual satisfaction and libido.[10,11] Moreover, there might be chances of technical difficulties involved in removing the uterus and adnexa via the vagina and a potential high risk of cancer either developing in the cervical stump or disseminated from inadvertently morcellated uterine fragments. Hence, supracervical hysterectomy does not have clear benefits over total hysterectomy and should not be recommended as a superior technique.[12]

CONCLUSION

To summarize, although the risk of histological diagnosis of endometrial carcinoma is very low in

patients having their uterus removed previously, practitioners should always bear in mind that it may indeed occur.

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