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Editor's choice

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Editorial of this issue is 'Breast cancer-a rising issue of Bangladesh. At present breast cancer is one of the most common cancer among women in Bangladesh. In this section, the incidence rate of breast cancer, risk factor, screening for early detection, treatment protocol and preventive measures are nicely discussed. Apart from that this issue also contains seven original articles, two review articles and two case reports.

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Editorial

Breast Cancer-A Rising Issue of Bangladesh

Breast cancer remains one of the most common cancer among women in Bangladesh. It has become a hidden burden which accounts for 69% of cancer death in women[1]. In Bangladesh, the incidence rate of breast cancer was about 22.5 per 100000 in females[2]. Breast cancer has been reported as the highest prevalence rate (19.3 per 100,000) among Bangladeshi women between 15 and 44 years of age when compared to other types of cancer. An increase in incidence rate has been reported due to lack of disease awareness, lack of confidence about medical treatment, improper screening tests and maltreatment of early metastasis[3]. Furthermore, patients are kept away from cancer treatment due to poor socio-economic infrastructure, social stigma of the disease and fear of the cancer treatment. The results of the maternal mortality survey conducted by the National Institute of Cancer Research and Hospital in Bangladesh (2010) showed that 21% of total number of deaths among women between 15 and 49 years of age was due to breast cancer.[3]

Some reproductive factors such as age at menarche, menopause and first pregnancy, breastfeeding, parity and non-reproductive factors such as menopausal hormone therapy, family history of cancer, body mass index, alcohol intake, and others have been linked with breast cancer risk[4]. Use of menopausal hormone therapy[5,6], greater alcohol consumption[7], older age at menopause [8].and a positive family history[9] are known to increase the risk of breast cancer.

Breast cancer can be detected at earlier stages by simple self-examination of the breasts[10] but most of the patients (more than 90%) seek medical attention at advanced stages: i.e., stages III and IV[11]. A study showed that majority of breast cancer patients presenting with a large tumor were associated with regional adenopathy, chest wall changes (often fixed to tumor or lymph nodes) and distant metastases[12].

None of the breast cancer cases is detected by organized screening in Bangladesh. Almost all breast cancer cases are detected clinically. The diagnosis of breast cancer these days, very often, is done in its subclinical form, through routine mammography or population screening programs. Mammography is the standard method for screening and diagnosis of breast cancer. Even in cases where the clinical picture is suggestive, a mammogram should be indicated in order to assess the extent of the tumor and to detect subclinical ipsilateral multicentric foci, as well as in the contralateral breast. Recently, digital mammography is introduced for diagnosis. Although ultrasound is a non-ionizing and more comfortable method, it presents a lower predictive value compared to mammogram for diagnosis of breast cancer. Magnetic resonance imaging is a new diagnostic method with increasingly important role in recent years. It is the imaging study with greater sensitivity for the detection of breast cancer, but must be requested with caution because its false positive rate is still not ideal, leading to unnecessary procedures. In addition, its cost is still high and its real impact in reducing mortality from breast cancer is unknown. It is indicated when the extent of the suspected lesion cannot be determined by conventional methods.[13-15]

In Bangladesh, approximately 95% of all breast cancers are invasive ductal carcinomas and over 63% of the patients had grade III tumors[16]. As there are no nationally applicable standard protocols or guidelines for managing breast cancer in Bangladesh, the quality of treatment varies widely. Only a few patients have the opportunity to get treatment at well-equipped private hospitals that use international standard protocols. In addition, affluent people often prefer to travel to neighboring countries including Singapore, Thailand and India – to seek high-quality treatment. Compromises are made at every step-in breast cancer care, including the appropriate diagnosis, surgical treatment and multi-modal therapy, considering various factors such as financial ability, tolerance and nutritional status of the patients.

Surgical treatment of breast cancer in its initial stage (tumor size $\leq$ 3 cm) consists in quadrantectomy and mammary segmental resection. For larger tumors, radical mastectomy sparing the pectoral muscles is usually recommended. Mastectomy is also indicated to treat the in situ multicentric form or invasive disease. Occasionally, when the breast is large and the relationship between tumor volume and breast volume is favorable, conservative surgery may be indicated for tumors between 3 and 5 cm, associated with oncoplastic techniques. In case of radical mastectomy, breast reconstruction may be performed, reducing the impact of breast amputation. Axillary lymphadenectomy is performed when the axilla is medically compromised or when the tumor is large (greater than 5.0 cm). Otherwise, the surgeon will remove the sentinel lymph node, which is the first lymph node to receive lymphatic drainage from the mammary gland. In quadrantectomy, or segmental excision of the breast, radiation therapy is formally indicated to prevent local recurrence in the rest of the gland. Chemotherapy is indicated in metastatic (palliative chemotherapy) and locally advanced (neoadjuvant or primary chemotherapy) disease. Neoadjuvant chemotherapy is also recommended to reduce the tumor volume and allow conservative surgery in cases that initially would be eligible for mastectomy.[17-19]

In low-income countries, the general population as well as healthcare staff are mostly unaware of the importance of screening for early detection of breast cancer and its improved treatment outcomes. Access to anticancer drugs is also inadequate and expensive as well. From this perspective, most people consider cancer as a death sentence. Massive awareness campaigns and access programs are

essential to educate communities that cancer is not inevitably a death sentence and that the risk of dying from breast cancer can be minimized significantly through screening and healthy lifestyles.[20]

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Original Article

Surgical Outcome of Extradural Spinal Tumour:

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ABSTRACT

Introduction: *Surgical outcome of extradural spinal tumours varies depending on a number of factors such as: site of tumour, the histological characteristics of tumours, the neurological progression, patient's age, co-morbidity, tumour extension, involvement of neighbor structures and organs etc.*

Objective: *The aim of this study was to analyze the data to made conclusion for more effective surgical strategy as per site, size, type, resectibility and histological variety to establish an effective treatment protocol and prevention of per-operative and post-operative complications.*

Materials & Methods: *The 28 patients with extradural spinal tumour underwent surgery from January, 2011 to December, 2018 in Dhaka Medical College & Hospital were reviewed retrospectively. Analysis of the surgical outcome of extradural spinal tumour patients of the study was done on different variables like age, sex, presenting symptoms, neuroimaging, co-morbidities etc. The aim of surgery was decompression of the spinal cord, total removal of the tumour when possible and spinal stabilization when needed. Out of 28 patients 7 needed bony stabilization, 16 patient needed chemotherapy and radiotherapy.*

Result: *In this study 21.43% patients immediate post-operative improvement were observed. 35.71% patients were discharged at 7th post-operative day with significant improvement. 17.88% patients were improved at first month after operation. 17.8% patients were deteroit and 7.14% patients were death due to metastasis.*

Conclusion: *To bring good surgical outcome, to reduce postoperative mortality and perioperative morbidity in case of spinal tumors, each neurosurgeon has to perform meticulous anatomical dissection under microscope. Besides this, thorough perioperative planning, meticulous microsurgical techniques and early mobilization & rehabilitation are essential for good clinical outcomes.*

Key Words: *Spinal tumours, spinal cord compression, surgical outcome, extradural.*

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INTRODUCTION

Surgical outcome of extradural spinal tumours varies depending on a number of factors such as: site of tumour, the histological characteristics of tumours, the neurological progression, patient's age, co-morbidity, tumour extension, involvement of neighbor structures and organs etc. Treatment of spine and spinal cord tumors is complex and a multidisciplinary approach is required[1]. Treatment options are surgery, radiation therapy and chemotherapy[2].This study was conducted to analyze factors affecting on the functional outcome in a series of 28 surgically treated patients with extradural spinal tumours and to point out the characteristics of the different histological entities and planning of subsequent modalities of treatment for more survival.

The signs and symptoms of extradural tumors varies depending on site of tumor, histologic type, bony or neural involvement, primary or secondary tumour. Because of the slow growth of benign extradural tumors, symptoms may be subtle and progress slowly over time before diagnosis[3]. The benign nature of ordinary spinal neurofibroma is well documented[4-7]. Total surgical removal can usually be achieved and short-term outcome is favorable in those who are not too severely crippled before operation[5,7]. But those tumor from metastasis having needed complete removal with fixation and chemo-radiotherapy, even though outcome is unsatisfactory.

Fortunately, good numbers of extradural primary tumor are benign but thus surgical excision represents the possibility of a curative result [8]. Surgical outcomes have generally been quite positive, with multiple studies quoting gross total resection rates approaching 100% with minimal morbidity and mortality regardless of histologic subtype [9,10]. Surgical excisions in majority cases are incomplete due to metastasize to the surrounding structure. Post-operative radio-chemotherapy needed even through recurrence is very high.

Fig-A

Fig-B

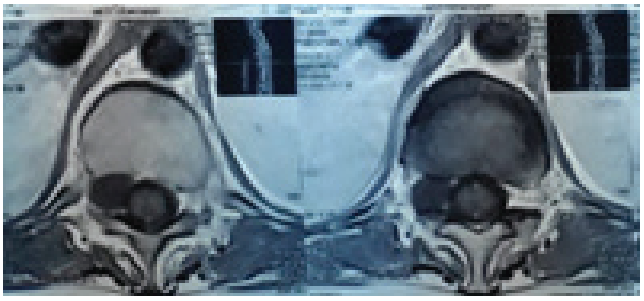

Fig-C

Figure: MRI of dorsal spine showing extradural spinal tumor: A. Sagittal section (T1WI), B: Sagittal section (T2WI), C: Axial section (T1WI)

MATERIALS & METHODS

The 28 patients with extradural spinal tumours underwent surgery in between January, 2011 to December, 2018 were reviewed retrospectively.

Characteristics of patients

Variable	Number (%)
Age	
<20	4 (14.29%)
21-40	5 (17.86%)
41-60	17 (60.71%)
61-80	2 (7.14%)
Sex	
Male	17 (60.71%)
Female	11 (39.29%)
Presenting Symptom	
Pain	28 (100%)
Numbness	20 (71.43%)
Paraparesis	14 (50%)
Paraplegia	9 (32.14%)
Quadriparesis	3 (10.71%)
Cauda equina syndrome	2 (7.14%)
Neuro-imaging	
Plain X-ray	28 (100%)
CT scan	5 (17.86%)
MRI	28 (100%)
Co-morbidity	
Hypertension	19 (67.86%)
Diabetes	10 (35.71%)
COPD	5 (17.86%)
Heart failure	1 (3.57%)
Lung Carcinoma	1 (3.57%)
Breast carcinoma	1 (3.57%)

The aim of surgery was decompression of the spinal cord, total removal of the tumor when possible. All cases were operated by laminectomy and 7 patients needed stabilization.

RESULTS

Many factors have influenced the outcome of surgical treatment. The most important are the histological characteristics of tumor, spinal segment affected and the degree of decompression.

Trait	Number (%)
Spinal level	
Cervical	7 (25%)
Cervico-dorsal junction	14 (50%)
Dorsal spine	5 (17.86%)
Conus level	2 (7.14%)
Nature	
Metastasis	16 (57.14%)
Neurofibroma	6 (21.43%)
Tuberculosis	2 (7.14%)
Sarcoma	2 (7.14%)
Multiple Myeloma	1 (3.57%)
Aneurysmal bone cyst	1 (3.57%)

Extent of tumor resection

Trait	Number (%)
Gross total	16 (57.14%)
Near total	8 (28.57%)
Subtotal	3 (10.71%)
Biopsy only	1 (3.57%)

Patient onset of improvement

Trait	Number (%)
Immediate improvement	6 (21.43 %)
Improvement at discharge (7 days)	10 (35.71%)
Improvement at first month follow-up	5 (17.88%)
Deterioration	5 (17.88%)
Death	2 (7.14%)

The most frequent difficulties encountered during surgery were the per-operative bleeding, anesthetic hazard, instrumentation failure due to tumor infiltration.

Postoperative complications include

Complication	Number (%)
Wound infection	3 (10.71%)
Stabilization failure	2 (7.14%)
Deformity	1 (3.57%)
Pneumonia	1 (3.57%)

DISCUSSION

In this study, the most of the patients were male 17 (60.71%) and belong to the age group of 41-60 years 17 (60.71%).

The patients presented with multiple symptoms among which pain contributes as 100% and numbness as 71.43%. In this study 14 cases were at Cervico-dorsal junction which was highest in location (50%). Regarding nature of tumor the most frequent cases were metastasis 16 (57.14%) followed by neurofibroma 6 (21.43%), tuberculosis 2 (7.14%) , multiple myeloma 1 (3.57%) and aneurismal bone cyst 1 (3.57%).

The extent of tumor resection and decompression correlates directly with a good outcome. The extent of excision either complete or incomplete was found to positively correlate with postoperative improvement. In our study 16 cases(57.14%) were underwent operation with gross total removal of tumor, 8 cases (28.57%) were underwent operation with near-total removal of tumor, 3 cases (10.71%) were underwent operation with sub-total resection of tumor and rest 1 case (3.57%) only biopsy were taken.

In this study, 10 patients (35.71%) were discharged at 7th post-operative day with significant improvement. In 6 patients (21.43%), immediate post-operative improvement were observed. There was improvement in 5 cases (17.88%) at first month after operation; there was deterioration in 5 cases (17.8%) and death in 2 (7.14%) cases due spinal tumor with metastasis.

Postoperative complications vary 10-52%[11-26]. In our study there were different type of post-operative complication wound infection in 3 cases (10.71%), stabilization failure in 2 cases(7.14%), deformity in 1case (3.57%) and pneumonia in 1case (3.57%).

CONCLUSION

To bring good surgical outcome, to reduce postoperative mortality and perioperative morbidity in case of spinal tumors, each neurosurgeon has to perform meticulous anatomical dissection under microscope.

Besides this, thorough perioperative planning, meticulous microsurgical techniques and early mobilization & rehabilitation are essential for good clinical outcomes. Metastatic lesion is the commonest extradural spinal tumor. Even after complete removal of tumor along with chemotherapy and radiotherapy reveals high rate of recurrence and high morbidity and mortality.

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Original Article

Frequency & Pattern of Complications in COPD Patients

Kabir MA[1], Zaman N[2], Yasmin D[3]

ABSTRACT

Background: *Chronic Obstructive Palmonary Diseases (COPD) is a generally progressive inflammatory disease of the lungs that is characterized by airflow limitation that is not fully reversible and is often complicated by significant systemic manifestations and co-morbidities. The two main types of COPD are chronic bronchitis and emphysema. COPD exacerbations and complication like cor-pulmonale, pneumonia, respiratory failure etc. In long-standing and severe condition COPD associated complication like cor-pulmonale, pneumonia, respiratory failure etc. Pulmonary artery hypertension and subsequent right heart failure are observed in COPD patients as a consequence of pulmonary artery remodeling. Early detection, preventive measures and proper treatment prevent the burden of fatal complication of COPD.*

Objectives: *Aim of this study was to find out the frequency and pattern of different complications of COPD admitted into medical wards of a tertiary care hospital.*

Materials & method: *This cross sectional study was conducted in Gazi Medical College Hospital , Khulna over a period of eight months. All study subjects had COPD (diagnosed on the basis of history, examination and previous medical records) attended in the hospital. Sample was selected from the population by convenient and purposive sampling technique. Sample size was 50. Complications of COPD were evaluated. Detail demographic data were collected from the patients and recorded in structured case report form. Clinical examination and relevant investigations were done meticulously.*

Result: *In this study more than 50% of patients were 61-75 years age group, mean age of the patient was 68.2±9.37 years. Male and female ratio was 1.12:1. In this study prevalence of complications of COPD recorded as 86%. Among these patients, 24 cases were male and 19 cases were female. This study demonstrated that, prevalence of cor-pulmonale was common among overall complications of COPD, present in 26% of patients. Cases failure was 14%, pneumonia (20%), lung cancer and pneumothorax in 20% cases respectively.*

Conclusion: *Chronic obstructive pulmonary disease is a leading cause of morbidity and mortality prevalence of cor-pulmonale is common among overall complications of COPD, present in 26% of patients. Respiratory failure was 14%, pneumonia 20%, lung cancer and pneumothorax in 20% respectively. Early detection and proper treatment can prevent fatal complication of COPD. Proper and multidisciplinary medical interventions are urgently needed for COPD management in order to decrease direct and indirect health care burden.*

Key words: *COPD, Cor-pulmonale, Respiratory failure, Pneumonia, Lung cancer, Pneumothorax.*

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Introduction

COPD is a generally progressive inflammatory disease of the lungs that is characterized by airflow limitation that is not fully reversible, and is often complicated by significant systemic manifestations and co-morbidities[1]. In Bangladesh the overall prevalence of COPD in the general population is 3%[2]. The Centers for Disease Control and Prevention (CDC) has been collaborating with icddr,b reported that Chronic Obstructive Pulmonary Disease is third leading (7%) causes of Death in Bangladesh[3]. COPD constitutes a huge

hidden burden of disease in people of 40 years of age or older in Bangladesh. Prevalence of COPD was higher among rural than urban residents and in males than females[4]. Factors associated with increase prevalence of COPD in Bangladesh may relate to smoking habit, occupational dust and chemicals, outdoor and indoor air pollution, and environmental change. Regarding signs and symptoms of COPD, dyspnea is the most suffering and devastating symptom.

Age and smoking are common risk factors for COPD and other illnesses, often leading COPD patients to demonstrate multiple coexisting comorbidities. COPD exacerbations and comorbidities contribute to the overall severity in individual patients[5]. Several environmental exposures such as air pollution increase the risk of death in COPD patients. The aetiology of COPD is overwhelmingly dominated by smoking although many other factors could play a role. Particular genetic variants are likely to increase the susceptibility to environmental factors although little is known about which are the relevant genes. There is clear evidence about the role of the α1-antitrypsin but the fraction of COPD attributable to the relevant variants is only 1%[6]. The inhaled toxic substances, particularly tobacco smoke and the products from the burning of biomass fuels that cause inflammation of the lungs. The inflammation can lead to tissue damage if the normal protective and/or repair mechanisms are overwhelmed or defective. The results of the lung tissue damage are mucus hypersecretion, airway narrowing, fibrosis, destruction of the parenchyma and vascular changes. These pathological changes lead to airflow limitation, loss of elastic recoil and other physiological abnormalities[7].

Chronic obstructive pulmonary disease (COPD) is an umbrella term for conditions, including chronic bronchitis and emphysema that impede the flow of air in the bronchi and trachea. International organizations have more specifically defined COPD as "a disease state characterized by airflow limitation that is not fully reversible. The airflow limitation is usually both progressive and associated with an abnormal inflammatory response of the lungs to noxious particles or gases[8]. COPD can cause or contribute to the development of several other serious health problems. Complications of COPD include: heart disease, pneumonia, lung cancer, depression etc[9].

Cor pulmonale classically defined as "hypertrophy of the right ventricle resulting from diseases affecting the function and/or structure of the lungs except when these pulmonary alterations are the result of diseases that primarily affect the left side of the heart". Since this definition does not indicate the presence of right heart failure, and since the presence of edema does not always imply underlying right heart failure in stable COPD patients, the terms cor pulmonale and right heart failure are not synonymous. Pulmonary hypertension (PH) however is always the underlying pathologic mechanism for right venrticular hypertrophy in cor pulmonale.

Cor pulmonale is defined as an alteration in the structure and function of the right ventricle (RV) of the heart caused by a primary disorder of the respiratory system. Pulmonary hypertension is often the common link between lung dysfunction and the heart in cor pulmonale. Right-sided ventricular disease caused by a primary abnormality of the left side of the heart or congenital heart disease is not considered cor pulmonale, but cor pulmonale can develop secondary to a wide variety of cardiopulmonary disease processes. Although cor pulmonale commonly has a chronic and slowly progressive course, acute onset or worsening cor pulmonale with life-threatening complications can occur[10]. The pathophysiology of cor pulmonale is a result of increased right-sided filling pressures from pulmonary hypertension that is associated with diseases of the lung. Hypoxia and endothelial dysfunction play a central role in the development of pulmonary hypertension. Cor pulmonale is a maladaptive response to pulmonary hypertension. The presence of peripheral edema in cor-pulmonale is almost invariably associated with hypercapnia. Correction of abnormalities of gas exchange and ventilation can ameliorate pulmonary hypertension and improve survival[11]. The increased afterload leads to structural alterations in the right ventricle (RV) including RV hypertrophy (RVH) which can be seen in chronic cor-pulmonale.

Another important complication of COPD is lung infection or pneumonia. Community-acquired pneumonia (CAP) is one of the most frequent medical causes of hospital admission and still carries a high morbidity and mortality. COPD and chronic bronchitis are the most frequent comorbidities in hospitalised patients with CAP, ranging 25–50%[12]. Study reported that pneumonia is considered an independent entity in chronic obstructive pulmonary disease (COPD), to be distinguished from an infectious exacerbation of COPD[13].

The occurrence of a spontaneous pneumothorax represents a troubling milestone in the course of patients with moderate-to-severe COPD. A pneumothorax causes rapidly progressive and alarming degrees of dyspnea usually associated with pleuritic chest pain. Hospitalization is necessary and often prolonged, and most patients require an intercostal chest tube and consideration of a surgical procedure to induce pleurodesis. But beyond these distressing experiences, a spontaneous pneumothorax represents a significant marker of mortality for patients with COPD[14].

Patients with chronic obstructive pulmonary disease (COPD) are at increased risk for both the development of primary lung cancer, as well as poor outcome after lung cancer diagnosis and treatment. Because of existing impairments in lung function, patients with COPD often do not meet traditional criteria for tolerance of definitive surgical lung cancer therapy. Emerging information regarding the physiology of lung resection in COPD indicates that postoperative decrements in lung function may be less than anticipated by traditional prediction tools. In patients with COPD, more inclusive consideration for surgical resection with curative intent

may be appropriate as limited surgical resections or nonsurgical therapeutic options provide inferior survival[15]. The prevalence of COPD among patients with lung cancer varies from40% to70%[16, 17]. A shared genetic susceptibility to development of COPD and lung cancer may be present. Shared genetic loci have been reported on chromosome 6q for both lung cancer risk and reductions in lung function, as well as on chromosome 12 for lung cancer, COPD, and reduced lung function[18].

In the last few years, some improvements in the management of COPD have been made, owing to new drugs and management strategies, along with non-pharmacologic treatment of COPD with pulmonary rehabilitation and surgical interventions. Smoking cessation is still the best strategy to prevent COPD and prevent further progression of disease[19]. Results highlight COPD as a major public health problem in Bangladesh and call for more research and action to be directed toward preventive measures and intensive efforts to target smoking cessation and reduction of indoor air pollution due to biomass fuel burning. Illiteracy, smoking and biomass fuel burning are modifiable determinants of COPD[20].

Method

This cross-sectional study was conducted from diagnosed case of COPD admitted in medicine department. Study period was eight months from 12.1.17 to 11.9.17. Sample was selected by purposive sampling technique. Inclusion criteria were patients who clinically present with features of COPD, aged >45 years, and who gave informed written consent for this study. Critically ill patients need ICU, HDU support excluded. After fulfilling the inclusion and exclusion criteria, patients were enrolled with unique ID. Subjects were briefed about the objectives of the study, risk and benefit, freedom for participating in the study and confidentiality. Informed written consent was obtained accordingly. Present and past history of each case record evaluated in detail regarding their general & clinical informations. The case definitions of operational variable were described. Relevant investigations e.g. CBC, ECG, Echo, CXR were done in each patient. Patient data such as age, sex, clinical presentation, etc were noted. A questionnaire was used for collection of information by interviewing patients. All the collected data questionnaire were checked very carefully to identify errors in collecting data. Data processing work consisted of registration of schedules, editing, coding and computerization, preparation of dummy tables, analysis and matching data. The technical matters of editing, encoding and computerization looked by the researcher

Result

In this series, the more than 50% of patients 27(54.0%) were in the 61-75 years age group, mean age of the patient was 68.2±9.37 years. Male and female ratio was 1.12:1. (Table-I)

Table-I: Age and gender distribution of the patient (n=50)

Age (years)	Frequency		Total	Mean ± SD
	Male (n= 27)	*Female(n= 23)*		
45-60	22.2%	21.7%	11	68.2±9.37
61-75	44.4%	65.2%	27	
>75	33.3%	13.0%	12	

Large numbers of respondents came from rural area (66.0%), followed by urban area (34.0%). (Table-II).

Table-II: Distribution of patients according to residence (n=50)

Residence	Frequency		p-value
	M (n=27)	*F (n=23)*	
Urban	8(29.6)	9(39.1)	0.565544
Rural	19(70.4)	14(60.9)	

Clinical manifestation revealed that, cough with sputum, breathlessness, fever and chest pain was the commonest presentation (100%, 96%, 54% and 92% respectively) of the COPD patients. (Table-III)

Table-III: Clinical manifestation of the COPD

Clinical features	Number of patients	Percentage (%)
Cough, sputum	50	100.0%
Breathlessness	48	96.0%
Chest pain	46	92.0%
Rhonchi	36	72.0%
Fever, chill-rigor	27	54.0%
Raised JVP	25	50.0%
Leg oedema	18	36.0%
Cyanosis	15	30.0%
Hemoptysis	14	28.0%
Disorientation	13	26.0%
Weight loss	4	8.0%

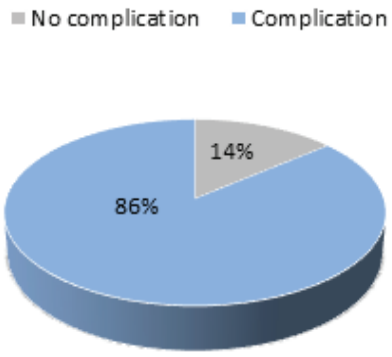
In this study, cor-pulmonale was the commonest (29.6% vs 21.7% in male and female respectively) complication of COPD. Pneumonia (14.8% vs 26.0% in male and female), respiratory failure (11.1% vs 17.3% in male and female) were the next common complications of COPD. It was observed that bronchial carcinoma was predominantly in male subject. In case of female, pneumonia and respiratory failure were common complications. Only 14% cases of hospital admission COPD patients were not detected any complication of COPD. These patients hospitalized for only acute exacerbation of disease. (Table-IV)

Table- IV: Pattern & Frequency of complications of COPD in study patient (n=50)

Complications	Number of patients		Total
	M (n=27)	*F (n=23)*	
Cor-pulmonale	8(29.6)	5(21.7)	13
Pneumonia	4(14.8)	6(26.0)	10
Respiratory failure	3(11.1)	4(17.3)	7
Pneumothorax	4(14.8)	2(8.6)	6
Bronchial carcinoma	4(14.8)	0	4
Polycythemia	1(3.7)	2(8.6)	3
No complication	3(11.1)	4(17.3)	7

Regarding the operational definition of different COPD complication, amongst the 50 case of COPD, 43(86%) of patients hospitalized for any sort of complication. Among the patients of COPD complication, 24 cases were male and 19 cases were female subject. (Figure-1)

Figure- 1: Prevalence of COPD complications amongst the hospital admission patient (n=50)



Discussion

In this study, the more than 50% of patients 27(54.0%) were 61-75 years age group, mean age of the patient was 68.2±9.37 years. Out of 50 cases 54% were male and 46% were male. Male and female ratio was 1.12:1. Highest incidence of male and female patients were in age group between 61-75 years, (44.4%) and (65.2%) respectively. Female patients were comparatively older than male.

Our findings are consistent with other studies that reported COPD being more prevalent in men, rural communities, and in older age groups[21-23]. Such gender and community variability in prevalence may result from differences in tobacco smoking and other risk factors such as higher exposure to indoor air pollution in rural settings due to extensive use of biomass fuel in the traditional cook stove, for both cooking and heating. Age is a well-established risk factor for COPD and we observed nearly three to five times higher prevalence of COPD among ages 60 years or older compared to ages 40 to 49 years. A similar steep increase in COPD prevalence by age has also been reported by others[24].

Bangladesh is undergoing a rapid demographic and epidemiological transition in which mortality and morbidity due to non-communicable diseases are increasing[25]. These shifts have great implications for COPD as it occurs more often in older than younger people. Older males in Bangladesh appear to be especially more susceptible to COPD. More than 50% of adult males over 25 years in Bangladesh (20 million men) smoke compared to less than 2% of females[26]. In a recent study it was shown that 25% of all deaths in Bangladeshi men aged 25 to 69 are attributed to smoking. In 2010, this amounted to 42,000 excess adult male deaths due to smoking[27].

In this study more than 50% of respondents came from rural area (66.0%). All result correlates with the results of similar studies at home and abroad, e.g. In a cross-sectional study in Bangladesh shows prevalence was three times higher in males compared to females (22% VS 6.4% by GOLD criteria and 16.2% VS 5.3% by LLN criteria) and about 60% higher in rural than urban populations (17% VS 9.9% by GOLD criteria and 12.5% VS 8% by LLN criteria). The prevalence of stage I (mild), stage II (moderate), stage III (severe), and stage IV (very severe) COPD was 2.7, 8, 2.3, and 0.6%, and by the GOLD severity criteria[4].

Phenotypic traits that are considered to play a role in the development of COPD include sex, with females being at a higher risk, bronchial responsiveness and atopy. There is strong causal evidence regarding the relationship between smoking and COPD. Passive smoking has been found to be associated with a small though statistically significant decline in FEV1. Other risk factors that are likely to be

relevant in the development of COPD are occupation, low socioeconomic status, diet and possibly some environmental exposures in early life[6].

Regarding the operational definition of different COPD complication, amongst the 50 case of COPD, 43(86%) of patients hospitalized for any sort of complication. Among the patients of COPD complication, 24 cases were male and 19 cases were female subject. In this study, cor-pulmonale was the commonest 29.6% vs 21.7% in male and female respectively) complication of COPD. Pneumonia 14.8% vs 26.0% in male and female), respiratory failure 11.1% vs 17.3% in male and female) were the next common complication of COPD. It was observed that bronchial carcinoma was predominantly in male subject. This study demonstrated that, prevalence of cor-pulmonale is common among overall complications of COPD, present in 26% of patients. Respiratory failure was 14%, pneumonia 20%, lung cancer and pneumothorax in 20% respectively.

Findings of other study revealed that most commonly COPD is associated with cor-pulmonale, lung cancer and other cancers, asthma, obstructive sleep apnea syndrome, hypertension, cardiovascular disease, diabetes, metabolic syndrome, dysfunctional skeletal myopathies, osteoporosis, and mental disorders[5]. Divo et al in a recent report concluded that lung, pancreatic, esophageal, and breast cancers (the last only for female patients), pulmonary fibrosis, atrial fibrillation/flutter, congestive heart failure, coronary artery disease, gastric/duodenal ulcers, liver cirrhosis, diabetes with neuropathy, and anxiety are the most significant and frequent comorbidities[5].

The pathological changes in COPD, which include chronic inflammation and structural changes resulting from repeated injury and repair due to inhaled cigarette smoke and other noxious particles, are found in the proximal airways, peripheral airways, lung parenchyma, and pulmonary vasculature. The chronic inflammation in COPD is characterised by an increase in the numbers of neutrophils (in the airway lumen), macrophages (in the airway lumen, airway wall, and parenchyma), and CD8+ lymphocytes (in the airway wall and parenchyma). The cells and mediators involved in the inflammatory processes in COPD and in asthma are different which explains the differences in physiological changes, symptoms and response to treatment in these two diseases. These pathological changes lead to mucus hypersecretion, expiratory airflow limitation with dynamic small airway collapse causing air trapping and lung hyperinflation, gas exchange abnormalities, and progressive pulmonary hypertension, rupture of bullae, pneumothorax and secondary lung infection and pneumonia.

Conclusions

The effects of COPD contribute to the deterioration of health status, functional abilities, and quality of life. Identification, reduction, control and elimination of risk factors are important steps toward effective prevention and management of any disease and its sequel. For COPD, these risk factors include tobacco smoke, occupational exposures, indoor and outdoor air pollution and irritants. Prevalence of cor-pulmonale is common among overall complications of COPD. Respiratory failure, pneumonia, lung cancer and pneumothorax also common. It is obvious that proper and multidisciplinary medical interventions are urgently needed for COPD management in order to decrease direct and indirect health case.

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Orginal Article

Study on Role of Socio Demographic Characteristics of Patients of Somatoform Disorders

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ABSTRACT

Background: *The somatoform disorders are a group of psychiatric disorders that cause unexplained physical symptoms. They include somatization disorder (involving multisystem physical symptoms), undifferentiated somatoform disorder (fewer symptoms than somatization disorder), conversion disorder (voluntary motor or sensory function symptoms), pain disorder (pain with strong psychological involvement), hypochondriasis (fear of having a life-threatening illness or condition), body dysmorphic disorder (preoccupation with a real or imagined physical defect), and somatoform disorder not otherwise specified (used when criteria are not clearly met for one of the other somatoform disorders).*

Objective: *To determine role of socio-demographic characteristics of patients of somatoform disorders.*

Materials and methods: *This cross sectional study carried out in tertiary level hospital of Pabna Medical college Hospital, at out-patients department of medicine in the period of January 2014 to December 2015. Total 100 samples were taken. Patients attending out-patient Department of Medicine in Pabna Medical College Hospital, firstly assessed by general physicians and subsequently they referred to the suspected cases of somatoform disorders to the investigator and finally the investigator diagnosed the cases by using diagnostic and statistical Manual of 4th edition of oext revision (DSM-4TR). Only diagnosed cases of somatoform disorders were included in this study. Cases of somatoform disorders were diagnosed clinically by using Diagnostic and Statistical manual for mental disorders of 4th edition, text revision (DSM-4TR). Subsequently, data were collected by using predesigned data collection sheet which included socio-demographic and other variables. Data were edited and cleaned by re-checking inconsistency and irrelevant information. Data were analyzed using statistical package for social science (SPSS) for windows version 20.*

Results: *This study found maximum patients were age group between 21-40 years. Regarding distribution of sexes, majority of patients were female (78%). Majority of patients were Muslim (97%), 87% were married and 13% were unmarried. Regarding educational status 23% were illiterate, 39% were primary, 26% were secondary, 8% were graduate and 4% were masters. Maximum (44%) had monthly income 5000-10000 taka. Study found 21% had marital conflict, 9% were failure in examination. This study showed common somatoform disorder were undifferentiated somatoform disorder (36%), the somatization disorder (24%), persistent somatofrom pain disorder (15%), somatoform autonomic dysfunction (13%), other somatoform disorder (7%) and hypochnondriacal disorder (5%).*

Conclusion: *Somatoform disorders are more common in young adults, females, housewife, students and belonging to lower socioeconomic status. Common somatoform disorders were undifferentiated somatoform disorder, then somatization disorders, persistent somatofrom pain disorder, somatoform autonomic dysfunction.*

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INTRODUCTION

Somatic symptom disorders are a group of disorders, all of which fit the definition of physical symptoms similar to those observed in physical disease or injury for which there is no identifiable physical cause. As such, this disorder are diagnosed of exclusion method. Somatic symptoms may be generalized in four major medical categories: neurological, cardiac, pain, and gastrointestinal somatic symptoms.[1,2] These somatic physical complaints challenge medical service providers who must distinguish between a physical and psychiatric source for the patient's complaints. Often, the medical symptoms patients experience may be from both medical and a psychiatric illnesses. Anxiety disorders and mood disorders commonly produce physical symptoms. These physical symptoms can dramatically improve with

successful treatment of the anxiety or mood disorder.[2]

The Diagnostic and Statistical Manual for Mental Disorders, Fourth Edition, Text Revision (DSM-IV-TR) includes a specific category for somatic symptoms related to psychiatric origins called the somatoform disorders. Specific somatoform disorders include (1) somatization disorder, (2) conversion disorder, (3) pain disorder, (4) hypochondriasis, and (5) body dysmorphic disorder. Somatization disorder is a relatively rare disorder that is associated with high medical resource utilization. More common somatization syndromes may not reach the diagnostic threshold for somatization disorder but may be clinically and functionally significant.[3,4]

The etiology of these disorders involves a combination of social, psychological, cultural and biological variables. There is association between period of increased stressful life events and the exacerbation of somatic symptoms. These disorders are common in women, among rural population with little education, low 10 and among low socioeconomic class.[5]

The overarching category of somatoform disorders includes conditions that share the common feature of physical symptoms that induce undue discomfort, distress, or dysfunction. In the case of hypochondriasis and body dysmorphic disorder, the disorders carry the additional component of intrusive unpleasant thoughts about disease or bodily appearance, compulsions to check for reassurance, and an accompanying negative appraisal of bodily symptoms that results in fear or avoidance. In these disorders, the meaning and implications of the symptoms are more distressing than the symptoms themselves. In the case of somatization disorder and pain disorder, the symptoms themselves are the primary focus of discomfort and distress. Because the terms hypochondriasis and somatization disorder are often used interchangeably by primary care clinicians, it is worth emphasizing that in hypochondriasis the fear of a serious illness preoccupies the patient and the compulsive checking serves to temporarily reduce the anxiety, creating a mental state and behavioral response that is quite similar to obsessive–compulsive disorder.[6]

In Bangladesh, most of the people are in economically disadvantage position, have low literacy level and lives in rural areas. Most families live as extended family with strong bondage among family members. As it is a male-dominant society, women become frequently the victims of physical, sexual and emotional abuse. Psychosocial adversity is commoner in working class subjects. Therefore, the proposed study has been designed to find out the sociodemographic variables of somatoform disorder.

METHODOLOGY

This was a cross sectional study carried out in Tertiary level Hospital of Pabna Medical college Hospital, at out-patients Department of Medicine unit in the period of January 2014 to December 2015. Total 100 samples were taken. Patients attending Out-patient Department of Medicine in Pabna Medical College Hospital, firstly assessed by General Physicians and subsequently they referred to the suspected cases of somatoform disorders to the investigator and finally the investigator diagnosed the cases by using Diagnostic and Statistical Manual for Mental Disorders of 4th edition, Text Revision (DSM-4TR). Only diagnosed cases of somatoform disorders were included in this study. Cases of somatoform disorders were diagnosed clinically by using Diagnostic and Statistical Manual Of 4th edition, Text Revision (DSM-4TR). Subsequently, data were collected by using predesigned data collection sheet which included socio-demographic and other variables. Data were edited and cleaned by re-checking inconsistency and irrelevant information. Data were analyzed using statistical package for social science (SPSS) for windows version 20.

RESULTS

Table I : Sociodemographic characteristics of the study subjects.

Characteristics	Frequency	Percentage
Age in years		
≤20	12	12
21-40	81	81
>40	7	7
Sex		
Male	22	22
Female	78	78
Religion		
Muslim	97	98
Hindu	3	3
Marital status		
Married	87	87
Unmarried	13	13
Educational status		
Illiterate	23	23
Primary	43	43
Secondary	22	22
Graduate	8	8
Masters	4	4
Occupational status		
Unemployed	4	4
Student	19	19
Service	4	4
Business	2	2
Farmer	4	4
House wife	76	77
Economic status		
5000-10000	44	44
1100-15000	33	33
16000-20000	16	16
>20000	7	7

Table 2 : Others characteristics of the study subjects

Characteristics	Frequency	Percentage
Marital conflict	21	21
Financial loss or problem	14	14
Sexual problem	17	17
Large loan	11	11
Family conflict	19	19
Failure of exam	9	9

Table-3: Frequency of different types of somatoform disorders

Characteristics	Frequency	Percentage
Somatization disorder	24	24
Undifferentiated somatoform disorder	36	36
Hypochondriacal disorder	5	5
Somatoform autonomic dysfunction	13	13
Persistent somatoform pain disorder	15	15
Other somatoform disorders	7	7

DISCUSSION

Somatoform disorders were considered as a significant proportion of case load in psychiatry clinics in a developing country. The prevalence of this disorders in developing countries are differed from than those of developed countries, hence, research findings from developed countries may not be easily generalized to the developing countries.[7]

This study found maximum patients were age group 21-40 years. Regarding distribution of sexes, majority patients were female (78%). 97% of somatoform disorder patients were in Muslim by religion. Therefore, the findings of the study are in well agreement with the findings of the other research works.[5,9]

This study found 87 were married and 13% were unmarried. Regarding educational status 23% were illiterate, 39% were educational background in primary level, 26% were secondary level, 8% were graduate and 4% were masters. Maximum patient were house wife (67%). This corresponds with the findings by Vyas et al.[8] Bagadia et al.[9] and Choudhury et al.[10] Moreover, these findings obviously support already established findings of prevalence of conversion disorder. Majority of our subjects were literate (80%). Although they were literates, they had not reached a very high educational level; and most of them had completed only 10 or less than 10 years of formal education. The predominant study populations were students (50%). This is in contrast, with the findings of Jain and Verma et al.11and Choudhury et al.[10] who found housewives and married to be the predominant group. As many as 42.5% of the subjects belonged to the rural community and 30% to the tea garden community. Therefore, it can be presumed that a majority of the subjects had a rural background as the tea gardens are usually located in the rural areas. As many as 82.5% of the study population were from nuclear families, which could be possibly due to life-style pattern changing to a modernized one. This result is not consistent with the findings by Vyas et al.8 might be due to socio-cultural variation.

Regarding economic status, 44% had monthly income 5000-10000 taka, 33% had monthly income 11000-15000 taka, 16% had monthly income 16000-20000 and 7 were monthly income >20000 taka in somatoform disorder. Therefore, the findings of the study are in well agreement with the findings of the other research works.[7,9]

This study found 21% had marital conflict, 9% were failure in examination in somatoform disorder. Sharma et al.12 studied showed that neurotic patients experienced a variety of life events in different walks of life more often than somatoform disorder. Life events, namely suspension from job, broken engagement or love affair, failure in examination etc. are more in somatoform disorder.

This study found 1% had illness of family members. Sing et al.13 reported that some events are commonly experienced by general population, e.g. death of a close family member, getting engaged or married, pregnancy of wife, illness of family member, etc. This finding of this study is similar to the finding of Sing et al.[13] Somatoform disorder patients experienced the events that are commonly experienced by general population but it does not show any significant difference between them.

This study found 17% had sexual problem, 11% were taken large loan, 19% had family conflict. In a study by Sharma et al,[12] items related to education and failure in examination and appearing for interview were found to be significant in patients.

This study shows most common somatoform disorder were undifferentiated somatoform disorder (36%), the somatization disorder (24%), persistent somatofrom pain disorder (15%), somatoform autonomic dysfunction (13%), other somatoform disorder (7%) and hypochnondriacal disorder (5%). In relation to the similar findings of this study, a study in Bangladesh showed that medically unexplained somatic symptoms were very common and these were more in women.[14]

CONCLUSION

Somatoform disorder is more common in young adults, females, housewife, students and belonging to the lower socioeconomic status. A majority of the patients had an obvious precipitating factors of which marital conflict, family conflict, sexual problem and financial loss or problem are important. Common somatoform disorders were undifferentiated somatoform disorder, then somatization disorder, persistent somatofrom pain disorder, somatoform autonomic dysfunction.

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Original Article

Clinicopathological Profile of Breast Cancer Patients Attending in Tertiary Medical College Hospital, Chattogram, Bangladesh

Chowdhury MAA[1], Alam F[2], Ahmed N[3], Tasmia SU[4], Banik A[5], Nisa J[6], Mahmud NU[7], Yusuff SM[8], Mitra T[9], Awal MA[10]

ABSTRACT

Background: *Breast cancer is the most frequent cancer of women worldwide, with considerable geographic and racial/ethnic variation. It is the most prevalent cancer in woman of Bangladesh. Prevalence is 19.3 per 100000 among Bangladeshi women between 15 and 44 years of age when compared to other types of cancer.*

Objective: *The present study aimed to describe the profile of breast cancer patients attending a tertiary hospital at chattogram in Bangladesh.*

Material and Method: *In this observational and longitudinal study, we reviewed records of pathologically diagnosed patients of breast cancer managed at our center from January, 2017 to December, 2017. Data with respect to demographic status, disease related information, pathological data and treatment related information.*

Results: *Total 192 patients were ranging in the age from 23 to 70 years (Mean age is 45 year) included in this study. Majority of the patients were in the age group of 41 to 50 years. Breast lump was the only complaints of all patients. Most patient having left sided breast cancer 57%. FNAC was done of 90% cases which is the most common modality of diagnosis before preceding to surgery at our center. Maximum number of patients belong to infiltrating ductal carcinoma (90%). 30% of them belong to stage IIB & 28% to stage IIIA. Mastectomy was the only surgical procedure.*

Conclusion: *This study shows that locally advanced breast cancer patients presented at a younger age. Lack of education and awareness of general population associated with advanced stage of breast cancer. Early detection of breast cancer as a major approach for better treatment outcome.*

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Introduction

Women of all races and ethnicity are affected by breast cancer. The incidence, clinical presentation and survival rates vary in different geographic areas and among different races &ethnicity within same geographic region. It is also most common cancer among women in Bangladesh. Incidence of breast cancer is 22.5 per 100000 in female and prevalence is 19.3 per 100000 among Bangladeshi women between 15 and 44 years of age when compared to other types of cancer [1]. Death rate from breast cancer is 11.85 per 100000 population of Bangladesh. WHO also ranked Bangladesh 2nd in terms of mortality rate of women in the country from breast cancer. This can be attributed to poor access to adequate treatment and absence of specialized center for cancer directed treatment. Not much information on breast cancer is available in Bangladesh. We want to conduct a retrospective study of clinicopathological profile of breast cancer patients and type of diagnostic modality used with treatment given to patients. Today whole literature focus on screen detected breast cancers and breast conservative surgeries[2]. Mortality increases with more advanced stage of presentation which may be due to low awareness, lack of education, financial issues, incomplete treatment regimens, limited access to effective treatment at regional cancer centers among rural populations [3-8] Despite of all the advanced management of breast cancer is still controversial topic [9]. It continues to be the focus for clinical research. Breast conservative surgery is demand of time for surgeons whether it is applicable to our centre is questionable because of poor follow up as most of the patients come to our center are from rural areas. Based on this background we proposed to study clinical and pathological profile of Breast cancer patients attending at our tertiary care hospital.

Material and Methods

This is a observational and longitudinal study of breast cancer patients who attended at Radiotherapy Department, CMCH between January, 2017 to December, 2017. 192 medical records of patients were reviewed over 1 year. Demographic details, clinical presentation, laterality, diagnostic modality, histopathological findings, molecular typing, treatment given to all patients were entered into our study proforma.

Staging of the breast cancer was done according to Tumour, Node and Metastasis cancer staging system.

After extracting necessary records data was compiled in the Microsoft Excel.

Results

Majority of the patients were in the age group 41 years to 50 years and mean age was 45 years and none of the patients were reportedly below the age of 23 years. And the oldest patient was 70 years old.

Age	Number of patients (n=192)	Percentage (%)
21-30	20	10.42%
31-40	49	25.52%
41-50	72	37.5%
51-60	38	19.79%
61-70	12	6.25%
Total	192	100%

Table-1: Age of the study population.

Approximately 50% patients were poor, 30% from lower middle class and 20% from middle class. (fig-1)

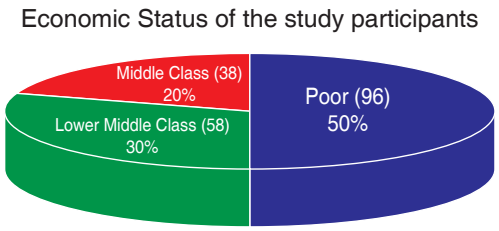

Fig-1: Economic status of the study population.

All patients came with the complaint of breast lump. A predominance of left sided cancers was noted (57%).

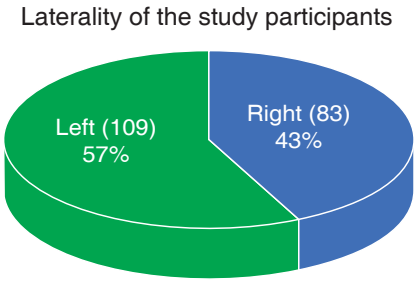

Fig-2: Laterality of the study population.

All patients presenting to our center with breast carcinoma are female(100%). FNAC was the most common modality of diagnosis before proceeding to surgery at our center. About 173 patients had done FNAC initially from them 100 patients had done Biopsy following FNAC. 19 patients had done Biopsy initially.

Diagnostic Modality	Number of patients (Total, n=192)	Percentage(%)
FNAC	173	90%
Biopsy	119	62%

Table-2: Diagnostic modality of the study population.

Histopathology	Number of patients (Total, n=192)	Percentage(%)
Infiltrating Duct Cell Carcinoma	190	99%
Infiltrating Lobular Cell Carcinoma	2	1%

Table-3: Histopathology of the study population.

Maximum patients belong to stage IIB. Overall patients present at operable advanced stages at our institute. Infiltrating ductal carcinoma was the major histological types.

Staging	Number of patients (Total, n=192)	Percentage (%)
IA	10	5%
IIA	27	14%
IIB	58	30%
IIIA	53	28%
IIIB	10	5%
IIIC	6	3%
IV	28	15%

Table-4: Staging of the study population.

Only 89 patients had done molecular typing. Commonest molecular typing was HR +ve, HER-2/neu-ve(30.34%) and TNBC was 28.08%.

Molecular Type	Number of patients (Total, n=192)	Percentage (%)
HR +ve, HER-2/neu + ve	21	11%
HR +ve, HER-2/neu - ve	27	14%
HR -ve, HER-2/neu + ve	16	8%
TNBC	25	13%
Not Done	103	54%

Table-5: Molecular type of the study population.

78 patients had done CA 15-3, among them CA 15-3 raised only in 10 cases. Only 1 patient had done CT scan of chest and whole abdomen. 10 patient had done mammogram where only in 4 cases it revealed malignant growth.

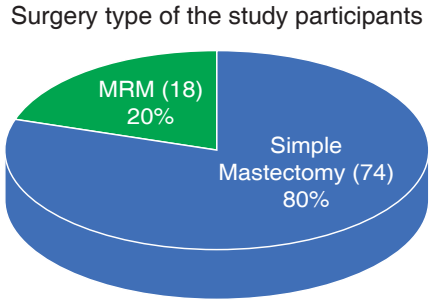

Fig-4: Surgery type of the study population.

NACT was given to 48 (25%) patients, ACT was given to 99 (51.56%) patients, palliative CT was given to 28(14.58%) patients. 92 (47.92%) patients had undergone to surgery. Among them simple mastectomy with axillary clearance was done in 74 (80.43%) patients and modified radical mastectomy was done in 18 (19.57%) patients. Radiotherapy was given to 24 (12.5%) patients. 22(11.46%) patients were taking hormone therapy.

Discussion

In the present descriptive retrospective study we analyzed institutional data from January, 2017 to December, 2017 in breast cancer patients with regards to baseline demographic, clinical and pathological profile. Data from clinical practice concerning profile of breast cancer is limited from our region. Hence we intended to study the status of breast cancer patients including clinical and pathological profile.

In our study mean age was 45. Where a study at NICRH during 2005 to 2010 the mean age of breast cancer patient was 41.8 year [10] and at UK/US was 62.8 year[11]. Our majority of the patients (37.5%) were in the age group 41 to 50 years. The younger age at presentation is a feature of breast cancer patients in most of the developing countries like India [12, 13], Sri Lanka [14] and Cameroon [15]. The younger age range of patients in developing countries may be explained by the younger age structure and the lower life expectancy of their women. In western countries breast cancer is most prevalent in women in fifth and sixth decade of life [16]. Most of the patients of our study were from rural area (66.67%) where it is most common in urban female of India[17]. All our patient presented with lump in the breast. Most of the patients had left sided breast cancer (57%) which is similar to national figures. FNAC was the most common modality before proceeding to surgery at our center (90.10%) which is similar to a study in Haryana, India [16, 17].

In our study histopathology of 98.96% patients were infiltrating duct cell carcinoma where another study in Bangladesh showed 95% of all breast cancer are IDCC [18, 19].Stagewise analysis (TNM) of our patients showed most of the patients were in the stage of IIB (30%) and IIIA (28%). One of the

study from Maharashtra, India found 71.35% women presenting in late stage at the time of diagnosis of breast cancer [19, 20]. Similar observations were noted by studies from north and south Indian populations also [21, 22, 23, 24]. Molecular typing results were available only in 89 case records with Hormone receptor +ve, HER-2/neu overexpression in 23.6% cases, HR +ve but HER-2/neu -ve in 30.34% cases, HR-ve but HER-2/neu + ve in 17.98% cases and triple negative type is observed in 28.08% cases. Another study in Bangladesh demonstrated that 69% and 73% of the cases were ER and PR- positive respectively. About 28% showed HER-2/neu overexpression. Only 9% patients had TNBC [19]. A study in Chennai, India showed among 162 cases 47% was with hormone receptor positive sub type, 30% was with HER-2/neu overexpression and 22% was with TNBC subtype [25].

Conclusion

Breast cancer is one of the most common cancer in women in Bangladesh. It is a big threat to women's health, inspite of advanced diagonostic and therapeutic options. Lack of education and awareness of general population associated with advanced stage of breast cancer. Early detection of breast cancer as a major approach for better treatment outcome. Massive awareness campaigns and access programs are essential to minimize the death rate from breast cancer and ensure healthy life.

Limitations of the study

Limitations of the study is hospital based observational study, so may not represent underlying general populations.

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Original Article

Comparative Study of Oral Tranexamic Acid with Topical Tripple Therapy Versus Topical Triple Therapy Alone in The Treatment of Melasma

Akter A[1], Afroz R[2] , Mannan MA[3]

ABSTRACT

Background: *Melasma is a common, acquired, circumscribed hypermelanosis of sun exposed skin. It presents as symmetric, hyper pigmented macules having irregular, serrated, and geographic borders. Tranexamic acid has shown promising results by enhancing the efficacy of conventional melasma treatment like LASER and hydroquinone. Considering the atrophogenic and other side effects of individual components of triple combination regimen, concomitant use of oral tranexamic acid would help in decreasing the duration of topical steroid based treatment.*

Objectives: *The primary objective was to assess the degree of improvement in pigmentation objectively using Melasma area severity index (MASI) at baseline, 4 weeks and 8 weeks of treatment.*

Material and Method: *It was an open labeled randomized comparative trial conducted on 40 patients of melasma of either sex attending to dermatology OPD. Participants were randomly divided into two groups with 20 patients in each group. Group A patients were asked to apply the cream only and Group B patients received oral tranexamic acid 250 mg twice daily and applied a triple combination cream containing fluocinolone acetonide 0.01%, tretinoin 0.05%, and hydroquinone 2% once daily for 8 weeks. Response was evaluated using melasma area severity index (MASI) at baseline, 4 weeks, and 8 weeks.*

Results: *There were 40 patients included in the study among them 32 were female and 8 were male. It had showed promising result. Objective response to treatment as studied by fall in MASI scoring after 8 weeks was 54.65% reduction (from 15.425 to 6.995) in group A and 88% reduction (from 18.243 to 2.19) in group B.*

Conclusion: *Combining these two treatment modalities in our study resulted in greater and statistically significant improvement in MASI scores with fewer side effects.*

Keywords: *Tranexamic acid, Tripple therapy, Melasma.*

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Introduction

Melasma is a common, acquired, circumscribed hypermelanosis of sun exposed skin. It presents as symmetric, hyper pigmented macules having irregular, serrated, and geographic borders. Tranexamic acid has shown promising results by enhancing the efficacy of conventional melasma treatment like LASER and hydroquinone. Considering the atrophogenic and other side effects of individual components of triple combination regimen, concomitant use of oral tranexamic acid would help in decreasing the duration of topical steroid based treatment.

Method

It was an open labeled randomized comparative trial conducted on 40 patients of melasma of either sex attending to dermatology OPD. Participants were randomly divided into two groups with 20 patients in each group. Group A patients were asked to apply the cream only and Group B patients received oral tranexamic acid 250 mg twice daily and applied a triple combination cream containing fluocinolone acetonide 0.01%, tretinoin 0.05%, and hydroquinone 2% once daily for 8 weeks. Response was evaluated using melasma area severity index (MASI) at baseline, 4 weeks, and 8 weeks

Inclusion criteria

Patients with facial melasma belonging to both sexes, any age group and willing to undergo treatment and to come for follow up were included in the study.

Exclusion criteria

1. Pregnant and lactating females,

2. Patients with history of thrombosis or a tendency of blood coagulation approved by laboratory tests,

3. Those who had taken other melasma therapies within last 6 months.

4. Those who refused to allow photographs were excluded from study.

All the patients were explained about the study. Written informed consent was

Results

There were 40 patients included in the study and with 32 females and only 8 males of age between 24 and 55 years with a mean age 35.85 + 7.614 years [Table 1]. In Group A, 15 patients were female and 5 were male and in Group B 17 patients were female and 3 were male.

	Gr A (n=20)	Gr B (n=20)	Total
Mean age (in years)	36+8.932	35.7+6.258	35.85+7.614
	No of patients (%)		
Age group (in years)			
<25	1 (5)	0 (0)	1 (2.5)
25–34	7 (35)	8 (40)	15 (37.5)
35–44	9 (45)	10 (50)	19 (47.5)
≥45	3 (15)	2 (10)	5 (12.5)
Total	20 (100)	20 (100)	40 (100)

Table 1: Age Distribution among melasma patients

The MASI scores at baseline, 4 weeks and 8 weeks in group A were 15.425 + 1.09, 11.075 + 9. 167 and 6.995 + 6.056 respectively and in group B 18.243 + 1.05, 6.135 + 4.94 and 2.19 + 3.38 [Figure 1]

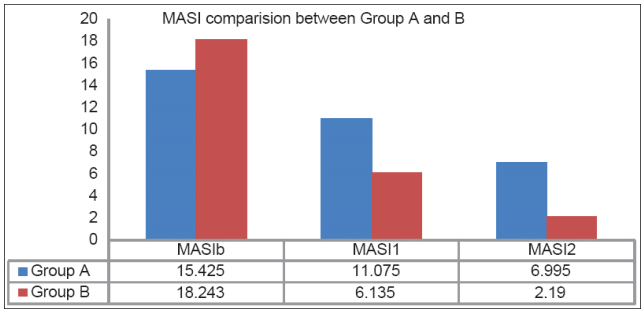

Figure 2: Objective assessment of melasma area severity Index (MASI), MASIb score at baseline, MASI 1 score at 4 weeks, MASI 2 score at 8weeks

Objective response to treatment as studied by fall in MASI scoring after 8 weeks was 54.65% reduction (from 15.425 to 6.995) in group A and 88% reduction (from 18.243 to 2.19) in group B. Of 20 cases of melasma which were treated with oral tranexamic acid there was greater decrease in MASI scores at 4 weeks and 8 weeks [Figure 3] and [Figure 4]. Also the results were statistically significant at both 4 and 8 weeks with $P < 0.05$ [Table 2].

Figure 3: Pre-and post-treatment photographs in Group A at 0 and 8 weeks

Figure 4: Pre-and post-treatment photographs in Group B at 0 and 8 weeks

	Mean MASI 0	P value	Mean MASI 4	P value	Effect size	Mean MASI 8	P value	Effect Size
Group A	15.425+1.09	0.883	11.075+9.167	0.014	0.7	6.995+6.056	0.000	1.0
Group B	18.243+10.5		6.135+4.94			2.19+2.378		

MASI: Melasma area severity index

Table 2: Melasma area severity index-comparison between Group A and Group B at baseline, 4 weeks and 8 weeks

When the MASI scores were compared within the groups at 0, 4 and 8 weeks, the result was also statistically significant among those taking oral tranexamic acid at the end of 4 and 8 weeks with P < 0.05 [Table 3].

	Mean			P value (ANOVA)
	MASI 0	MASI 4	MASI 8	
Group A	15.425+1.09	11.075+9.167	6.995+6.056	0.016
Group B	18.243+1.05	6.135+4.94	2.19+2.378	0.000

ANOVA: Analysis of variance, MASI: Melasma area severity indes

Table 3: Melasma area severity index-comparison within the Group at baseline, 4 weeks and 8 weeks

Effect sizes: The evaluation of the intervention magnitude was considered large with effect size being 1.0 at the end of 8 weeks when MASI scores were compared between group A and B.

When adverse effects were compared between the groups, the results were almost identical. Systemic side effects including ophthalmological adverse effects, a major concern in patients taking tranexamic acid, were not seen in any of the patients receiving the drug [Table 4].

Adverse effects	Present in no of patients	
	Group A	Group B
Erythema	3	2
Burning	2	2
Hypopigmentation/ Depigmentation	0	2
Oligomenorrhoea	0	1
Other systemic side effects	0	0

Table 4: Comparison of adverse effects among both groups

The patients were followed up for 6 months and there was no recurrence.

Discussion

Finding a cure for melasma has always been a challenge for the treating dermatologist. Various treatment modalities, all of them aiming at reducing melanin synthesis, exist but come with their own side effect profile. Moreover, none of them are very effective in inducing a long term remission.

Tranexamic acid (trans-4-aminomethyl cyclohexanecarb oxylic acid) is a synthetic derivative of the amino acid lysine.[3] Primarily it is used as an agent to reduce blood loss in menorrhagia or after major surgical procedures by virtue of its plasmin inhibiting action. It exerts its antifibrinolytic action by blocking the lysine binding sites on plasminogen molecule. [3] It is well known that increased level of plasmin in keratinocytes induces synthesis of arachidonic acid and also increases level of α- melanocyte - stimulating hormone (α - MSH) both of which in turn stimulate melanogenesis. [7] UV radiation increases plasmin level and being a plasmin inhibitor, tranexamic acid is believed to block UV-induced melanogenesis. [8,9] Moreover, because of structural similarity with tyrosine, tranexamic acid is also believed to be competitively inhibiting tyrosinase action. [9] Use of tranexamic acid in patients of melasma has shown reduction of melanin in the epidermis and decrease in vascularity and mast cell numbers in the dermis. [10] The safety profile of long-term use of oral tranexamic acid has been well established and use up to 4.5 gm/day has not been associated with any serious side effects in menorrhagia and post-surgical blood loss.[11] Whereas the conventional dose of tranexamic acid as a hemostatic is 1500 mg per day, most of the studies evaluating the depigmenting effect of the drug have used either 500 mg or a maximum of 750 mg per day.

In the study conducted by Karn D et al., from Nepal, clinical effect of oral tranexamic acid combined was compared with that of topical hydroquinone alone.[6] Patients were advised to take tranexamic acid orally 500 mg per day for 12 weeks. Statistical analysis was done between within the groups only, i.e. intra-group and not inter-group and the fall in MASI was statistically significant in both the groups at eighth week but not significant in those receiving topical hydroquinone at 12 th week. This study MASI was calculated at baseline, 4 and 8 weeks time and fall in MASI was significant at 8 weeks in patients receiving oral tranexamic acid compared with those receiving topical treatment .

The effect of oral tranexamic acid was studied by Wu et al., in which patients received the treatment for 6 months.[4] They did not compare it with any other modality and their criteria of evaluation were reduction in melasma size (expressed as percentage) at the end of 6 months. They graded outcome as follows: excellent: 90% reduction in size, good: 60%, fair: 30%, and poor: <30% reduction in size. After 6 months of treatment, the results were as follows: excellent (10.8%, 8/74), good (54%, 40/74), fair (31.1%, 23/74, and poor (4.1%, 3/74). Thus, the total improvement rate for melasma was 95.9% of the subjects.

Kato and his colleagues had used oral tranexamic acid at a dose of 750 mg for 4 weeks in patients who underwent treatment with Q-switched Ruby laser for lentigenes and they found no significant change in post inflammatory hyper pigmentation.[12] They concluded that tranexamic acid might be having depigmenting effect but it may not be effective in preventing post inflammatory hyper pigmentation following laser therapy.

Like most other studies, we found a better response rate with combination of TA and triple therapy.

Conclusion

Addition of oral Tranexamic acid to a conventional fluocinolone based triple regimen may enhance the clinical efficacy of topical treatment. Combining these two treatment modalities in our study resulted in greater and statistically significant improvement in MASI scores with fewer side effects. Therefore, it may be helpful in treatment of all cases of melasma, especially the refractory ones.

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Original Article

Functional Outcome of Treatment of Supracondylar Humeral Fracture in Children

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ABSTRACT

Purpose: *To assess the functional outcome of treatment of supracondylar humeral fracture in children.*

Method: *This is a prospective study and conducted in 250 bedded district hospital attached Colonel Malek medical college,Manikganj from June 2016 to June 2017. 14 patients were supracondylar humeral fracture of age 4-10 yrs in this study. Severity of fracture was classified according to the Gartland system: Type-I and type-II fractures were treated with closed reduction and immobilization with long arm posterior cast in flexion, type-III fractures, closed reduction was first attempted followed by percutaneous kirschner wire fixation under general anaesthesia. If closed reduction failed, open reduction and internal fixation with smooth cross kirschner wire fixation was performed.*

Result: *Patients were followed up for one year. Treatment results were excellent in 7 patients, good in 4 patients, fair in 3 patients, and poor in none of the patient. All Patients were pain-free and none suffered in any activity restriction.*

Conclusion: *Closed reduction is a good treatment option for type I, II and type-III supracondylar humeral fractures.*

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INTRODUCTION

Supracondylar humeral fractures are the most common fractures around the elbow in children[1]. The injury results from a fall directly onto the elbow[2]. The distal fragment may be displaced posteriorly and anteriorly and may migrate proximally in a completely displaced fracture. The ulnar nerve and also brachial vassel may be vulnerable and may be entrapped in the fracture or in the healing callus[7]

Various treatment options have been described : manipulation and casting in flexion[8] manipulation and casting in extension,[5,9] traction,[10] closed reduction and percutaneous pinning by Kirschner wires,[2] and open reduction and internal fixation.[7]

This fracture is inherent instability, difficult in achieving reduction and specially holding reduction, and potential for loss of range of movement of elbow by keeping the elbow with posterior cast in flexion for a long time and also in case of inadequate reduction.

METHODS

The mean age of the patients of 10 boys and 4 girls were 6.4 years .

Nine patients were injured in the left side and 5 patients were in the right side. No patient had any other associated fracture.

Only one had an ulnar nerve palsy at presentation from which the patient had recovered within 12 days of reduction.

Fracture severity was classified according to the Gartland system : type I- minimally displaced, type II- displaced with some integrity of the anterior or posterior cortex, type- III displaced with no cortical contact, type-IIIA posteromedial displacement, type-IIIB posteroterolateral displacement. In this study 3 Patients were type I, 5 patients were type II, 2 patients type IIIA, and 4 patients type IIIB.

Patients with type-1 and type-II fractures were treated with immobilisation in long arm posterior cast for 3 weeks and removed the posterior cast followed by gradual extend the elbow from flexion upto pain permit and then allowed gradual early active movement. Patients having type-II were treated with closed reduction under general anaesthesia long arm posterior cast in flexion and type-III fractures were treated with closed reduction and percutaneous pinning under general anaesthesia and long arm posterior cast in flexion .

Close reduction was done under general anaesthesia by the

following step wise manoeuvre- traction for 2-3 minutes in the long axis of length of the forearm with counter traction at the arm above the elbow,correction of any sideways tilt or shift and compare with the normal elbow and gradual flexion of the elbow to 120º, gentle traction was applied with the elbow in flexion and pronation of the forearm while maintaining traction and exerting posterior pressure infront of the proximal part of fracture and milking the posterior aspect of the lower arm and elbow to check posterior tilt and sideways pressure on the both humeral condylar area by the palm of the hand to correct medial or lateral shift , check the capillary filling was change by feeling the radial pulse. If the distal circulation sluggish gradually extending the elbow at where position pulse reappear and at this position long arm posreior cast applied after checking the reduction by image intensifier and confirm satisfactory reduction by x-rays of elbow anteroposterior and lateral views .

In case of type-III fractures rotation and adequate reduction was checked following above manoeuvre with image intensifier and two percutaneous crossed pinning was undertaken under general anaesthesia, also guided by image intensifier with the elbow in 45º flexion position, pin introduce at the direction to opposite cortex from the medial or lateral epicondyle in 40º inclination from midline and 10º in posterior angulation continue to opposite cortical area and adequate fixation was checked and elbow was immobilised in a long arm posterior cast in 90º or more in flexion for 4 weeks; kirschner wires removed after 3weeks and plaster was removed after 4 weeks and then gradual early range of movement exercises were initiated.

In this study 3 patients were failed closed reduction (1 patient type IIIA, 2 patients type IIIB), open reduction and internal fixation was performed through an anterior approach. A transverse incision was made across the antecubital space to develop a plane between biceps and brachialis to release the bicipital aponeurosis and protect brachial artery, the biceps and brachialis were retracted medially and brachioradialis laterally to protect radial nerve and posterior interosseous artery. To expose the fracture site and note its alignment with the proximal fragment ,use small curette to remove haematma at the fracture site and matching if any comminuted fragments and reduction was done of the fracture and crossed percutaneous smooth pinning was performed under visualisation at 45º flexion in 40º inclination from midline and 10º posterior angulation. Image intensifier was used to help adequate position of the pin and also direct visualisation of the fracture site and after adequate fixation cutting the pins outside of the skin and bending outside portion and again stability was checked and the wound closed with interrupted prolene sutures and an above-elbow posterior long cast applied in 90º flexion; the wires were removed at 3 weeks and cast removed at 4 weeks respectively and early range of movement exercises initiated.

All Patients were followed up weekly for the first 3 weeks and then monthly for one year.

RESULTS

Treatment results were assessed according to Flynn criteria (Table 1); outcome was deemed excellent in 7 patients, good in 4, fair in 3, and poor were none .Among 14 patients 3 patients were type-I and 5 patients were type-II, 2 patients were typeIIIA, 4 patients typeIIIB were performed closed reduction, 1 patient type-IIIA and 2 patients type-IIIB were performed open reduction and percutaneous pinning.All patients of type-I and type-II closed reduction done without percutaneous pinning and 1patient of type-IIIA and 2 patient of type-IIIB closed reduction with percutaneous pinnig done, 1 patient of type-IIIA and 2 patients of type-IIIB open reduction and percutaneous pinning were done

(Table 2).

Grading	type-I,n=3		type-II,n=5		type-IIIA,n=2		type-IIIB,n=4	
	CR	ORIF*	CR	ORIF	CR	ORIF	CR	ORIF
Excellent	3	0	3	0	0	0	1	0
Good	0	0	2	0	0	0	1	1
Fair	0	0	0	0	1	1	0	1
Poor	0	0	0	0	0	0	0	0

CR-Close reduction, ORIF-open reduction internal fixation

Three patients had superficial pin tract infections that resolved after wire removal. All the patients were pain-free and satisfied and no one in any permanent activity restriction.

DISCUSSION

supracondylar humeral fractures are common fracture in children. In flexion-type injuries are usually rare 2% -3% of all supracondylar fractures and it is unstable fracture, where as in extension type fracture is comperatively stable and occurs usually 97%-98% in all supracondylar fractures .Flexion type supracondylar fracture are not includded in this study. Common complications are cubitus varus deformity and reduction of carring angle and extension lack . In this study 7 patients were excellent, extension lack were 0%-5% and reduction of carrying angle were 0%-5% ,4 patients were good results 6%-10% reduction of carrying angle and extension lack, 3 patients were fair results 11%-15% reduction of carrying angle and extension lack and none of the patiets were poor results with more than 15% varus and carrying angle deformity.

Table 1 Flynn's criteria[12]

Grading	Loss of functional movement(extension)	Change in carrying angle (varus angle reduction)
Excellent	0º–5º	0º–5º
Good	6º–10º	6º–10º
Fair	11º–15º	11º–15º
Poor	>15º	>15º

The overall excellent results were 50% of patients,good results were 28.6% patients, fair results were 21.4% patients. In our study demonstrates the superiority of closed reduction and percutaneous pinning of supracondylar fractures. Only three patient need open reduction in

CONCLUSION

Closed reduction is a good treatment option for supracondylar fracture.

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Original Article

Thyroid Associated Orbitopathy: A Concern of Thyroid Dysfunction Diseases

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ABSTRACT

Background: *The purpose of this study is to find out the relation between hormonal status and radiological imaging status in thyroid associated orbitopathy, at a tertiary care hospital, Bangladesh.*

Methods and Materials: *A retrospective observational study of 48 patients was conducted at a tertiary care hospital of Bangladesh from 2009 to 2017 time period. Patients of Thyroid associated orbitopathy were selected by comprehensive ophthalmological examination as well as from CT scan of orbit and thyroid function tests. Serum FT4 and FT3, TSH, TGAb titre and TPOAb titre were taken in account to see the thyroid function status of the cases.*

Results: *A total 48 patients were evaluated, of them Male: Female ratio was 0.92:1 with mean age 35.08±13.05 years. Among all cases, 20(41.7%) were hyperthyroid and 15(31.3%) were euthyroid and rest 13(27%) were hypothyroid. CT scan findings revealed that 12(92.3%) hypothyroid and 16(80%) hyperthyroid patients got extraocular muscle enlargement. Extraocular muscle enlargement was not statiscally significantly associated with different types of thyroid dysfunction (p-0.431).*

Conclusion: *Though Thyroid associated orbitopathy is well established with hyperthyroidism state, but in the current study hypothyroidism was also noted as remarkable percentage. So, all thyroid dysfunction patients, both hypothyroidism and hyperthyroidism, should be evaluated by ophthalmologists to see the orbital status.*

Keywords: *Thyroid associated orbitopathy, Extraocular muscle enlargement, Thyroid function.*

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Introduction

Thyroid Associated Orbitopathy (TAO) refers to the inflammatory response and its sequel in and around the orbit, which is associated with autoimmune thyroid disease. Thyroid Associated Orbitopathy (TAO) varies in its pattern and presentation. Affected patients suffer distressing and disfiguring eye disease with a small risk of sight loss in severe cases. It results from infiltration of the orbit by auto-reactive T-lymphocytes, proliferation of orbital fibroblasts and increased orbital fat[1,2]. This leads to periorbital edema, lid retraction, proptosis, diplopia and in severe cases, dimness or loss of vision. It is an orbital autoimmune disease. The thyroid stimulating hormone receptor (TSH-R) is an antigen found in orbital fat and connective tissue and is a target for autoimmune assault. However, some patients with this present, with neither anti microsomal nor anti-thyroglobulin nor anti TSH receptor antibodies, the antibodies identified in TAO or in Graves' disease. On histological examination, there is an infiltration of the orbital connective tissue by lymphocytes, plasmocytes and mastocytes. The inflammation results in a deposition of collagen and glycosaminoglycans in the muscles, which leads to subsequent enlargement and fibrosis. There is also an induction of lipogenesis by fibroblasts and preadipocytes, which causes orbital volume enlargement due to fat deposition. Thyroid eye diseases affect between 25-50% of

patients with TAO. It is identified in approximately 20% of those seen with Graves' disease on initial examination. About 10% of cases do not have Graves' disease, but do have auto antibodies. Systemic lymphomatous involvement may be associated in 20% of cases and through clinical examination of opposite orbit, oral cavity and oropharynx is mandatory along with systemic examination. In the majority of patients, TAO is associated with thyrotoxicosis [3,4]; often the diagnosis is made simultaneously, although the temporal relation is not consistent. A small fraction have Hashimoto's thyroiditis or, more rarely, primary hypothyroidism. Approximately 55 have no evidence of thyroid dysfunction at the time of presentation of TAO[5], although this may develop later and antibodies to thyroid tissue may be detected. The pathology mostly affects persons of 30 to 50 years of age. Females are four times more likely to develop TAO than males. When males are affected, they tend to have a later onset and a poor prognosis. The temporal relationship between the thyroid and orbital diseases is variable. Whereas in 80% of patients the onset of the glandular and orbital diseases occurs within 18 months of each other, the clinical appearance of the two can be separated by as much as 20 years in some cases [6-8]. Most cases of TAO are initially seen with symmetric- appearing orbital involvement. However, a few patients exhibit marked asymmetry of the orbital disease [9-11,7]. Still fewer have unilateral disease that resolves before acute disease affects the second orbit, sometimes more than 1 year later. The most common presenting symptoms are soft tissue symptoms (periorbital puffiness, redness, grittiness, watering, or itching), or altered appearance of the eyes due to either lid retraction or proptosis. Other presenting symptoms relate to impaired ocular motility or to reduced visual acuity. The most common presenting symptom was slowly growing orbital mass. The presentation of TAO also varies in different ethnic groups. Upper eyelid retraction and soft tissue involvement are reported as the commonest manifestations in Caucasians, in contrast to increased risk of exophthalmos and lower eyelid retraction in Asians. TAO is diagnosed clinically by the presenting ocular signs and symptoms, but positive tests for antibodies (anti- thyroglobulin, anti-microsomal and anti-thyrotropin receptors) and abnormalities in thyroid hormones level (FT3, FT4, and TSH) help in supporting the diagnosis.

Orbital imaging is an interesting tool for the diagnosis of TAO and is useful in monitoring patients for progression of the disease. It is, however, not warranted when the diagnosis can be established clinically. Ultrasonography may detect early TAO in patients without clinical findings. It is less reliable than the CT scan and magnetic resonance imaging (MRI), however, to assess the extraocular muscle involvement at the orbital apex, which may lead to blindness. The CT scan will reveal a mass lesion of homogenous characteristics and rule out any bony involvement. An intriguing feature of TAO is the age-related variation in disease expression. Patients younger than 40 years are more likely to exhibit orbital fat expansion and proptosis in the absence of infiltration of the extraocular muscles and eyelid retractors. Thus, CT scan or MRI is necessary when optic nerve involvement is suspected. On neuroimaging, the most characteristic findings are thick extraocular muscles with tendon sparing, usually bilateral, and proptosis.

CT or MRI imaging of the orbit is essential in excluding other causes of orbital disease including meningiomas, lymphomas, cavernous carotid fistula, orbital cellulitis, cushing's disease, sarcoidosis, pseudotumor cerebri, and primary and metastatic tumors [12]. Imaging will also confirm the features of TAO such as extraocular muscle enlargement, adipose tissue expansion, or the sight threatening complication of dysthyroid optic neuropathy (DON), which may require urgent intervention to prevent sight loss. CT or MRI will also detect bilateral disease may present with unilateral symptoms and signs.

Methods and Materials

It was a retrospective observational study comprising of 48 cases of thyroid associated orbitopathy at oculoplastics department of a tertiary care hospital in Dhaka, Bangladesh. The study cases were selected from 2010 to 2017. All patients were diagnosed with clinical examination as well as CT scan of brain and orbit findings for the diagnosis of thyroid associated orbitopathy. Their thyroid function tests were included S. FT3, S.FT4, S.TSH, S. Anti TG antibody and S. Anti TPO. Normal reference range were taken as, normal: TSH: 0.4 -4.5U/L, S.FT4: 11.0-24.0 pmol/L and S.FT3: 2.67-7.03 pmol/L of thyroid disease. TRAb measurement was performed using a commercial third generation ELISA kit that detects both thyroid stimulating (TSAbs) and blocking antibodies (TBAbs) with manufacturer

Thyroid Status of patients	n(%)	Thyroid function findings Mean±SD				
		S.FT3	S.FT4	S.TSH	S.Anti TGAb	S. Anti TPO
Euthyroid	15(31.2)	4.15±1.92	11.53±7.01	1.43±0.94	162.56±251.57	269.70±474.21
Hyperthyroid	20(41.7)	27.39±64.73	22.68±27.62	0.57±1.73	514.19±1201.85	513.62±1082.78
Hypothyroid	13(27.1)	29.25±44.82	10.67±5.51	22.62±31.57	319.68±362.54	1688.89±3680.46

specificity and sensitivity of 100 and 95%, respectively, and positive cut –off > 0.4 U/L 13. And reports and photographs of CT Scan of brain and orbit of each patient were collected.

Their information was collected from register book of hospital. Prior to the study, permission from Ethical Review Committee of National Institute of Ophthalmology and Hospital.

Statistical Analysis were performed using the SPSS software package (version 17.0; SPSS Inc, IL, USA). Continuous variables are reported as mean±standard deviation (SD). The chi-squared test was used to compare categorical variable.

Results

A total 48 patients of TAO were enrolled in this study. Among them Male: Female ratio was 0.92:1. Mean age of them were 35.08±13.05 years. According to thyroid function status 15(31.2%) were euthyroid patients and 20(41.7%) were hyperthyroid and 13(27.1%) were hypothyroid.

Table 1: Gender distribution of all respondents

Gender	Number	Percentage	Ratio
Male	23	47.9	0.92: 1
Female	25	52.1	

Mean±SD S.TSH of Euthyroid, hyperthyroid and hypothyroid were 1.43±0.94, 0.57±1.73 and 22.62±31.57 accordingly. Details distribution of all thyroid function tests were described in table 2.

Table 2: Thyroid function status of all respondents

On chi squared analysis it was noted that there was no significant relationship between thyroid status of the patients and the extraocular muscle enlargement, (p=0.431). Hyperthyroid patients as well as hypothyroid patients were also vulnerable to develop Thyroid associated orbitopathy (TAO). Table 3 showed the association between them.

Table 3: Association of Thyroid function status and extraocular muscle enlargement in TAO patients

Thyroid Status of Patients(n)	Extraocular Muscle Findings on CT Scan		x^2 value	P value
	Enlarged	Normal		
Euthyroid (15)	11(73.3)	4(26.7)	1.681	0.431
Hyperthyroid (20)	16(80.0)	4(20.0)		
Hypothyroid (13)	12(92.3)	01(7.7)		
Total (48)	39(81.3)	9(18.8)		

Results were expressed as number(percentage) and comparison done by chi-squared test, significant at p-value<0.05

Discussion

From 2010 to 2017, total 48 cases were enrolled in the current study. Mean±SD age of them were 35.08±13.05 years. Bartley GB, et al.3 found in their study that the mean age of onset of TAO is about 45 years, with bimodal peaks in the age groups 40 to 49 and 60 to 69.

In the present study it was noted that male and female patients were almost same, 23 and 25 in number. Though Jacobson DH, et al.[14-16] found in their study female preponderance with a F:M ratio 2-5: 1, which is not pronounced as for TAO, where the F:M ratio is 5-10: 1[14-17]. They found a positive relation between gender and TAO and men tend to be more severely affected than women 17-19. Women are considerably more likely to develop TAO and upto 8 times more likely to exhibit severe orbital involvement. Yet, among patients with TAO, men are more likely to develop optic neuropathy[9,11,19-22].

The initial symptoms and signs of onset of the disease lasted 10.5 months (range 1-54 months) because of the slow development of a palpable mass. Out of 48 cases, 17(35.4%) were presented with proptosis and 1 (2.1%) case with exophoria.

It is widely accepted that TAO is an autoimmune disease and is not believed to result directly from the metabolic perturbations caused by thyroid hormone over production [9-11,19]. However, evidence supported that TAO is largely circumstantial and includes the frequent coincidence of other auto immune processes such as systemic lupus erythematosus, rheumatoid arthritis and vitiligo in patients with TAO[11,28]. But in the current study we couldn't explore the other auto immune diseases history.

In this study it was noted that mean S. Anti TPO were 269.70±474.21 in euthyroid and 513.62±1082.78 in Hyperthyroid That means from euthyroid to hyperthyroid state it had a increasing pattern. Similar findings were noted by Khoo DH, et, al. in their study. They have observed a progressively increasing prevalence of TAO with increasing TRAb titres and TRAb titres were independent risk factors for TAO.

In our study, 23 cases among 39 were not hyperthyroid state. Among 23 who had enlarged extraocular muscles 11 were euthyroid and 12 were hypothyroid patients. The advent of sensitive second and third generation TRAb has simplified the clinical recognition of TAO, especially in patients with atypical presentation such as euthyroid grave's ophthalmopathy (EGO) 30. This condition occurs in approximately 5% of the cases of Grave's ophthalmopathy and refres to the occurance of ophthalmopathy in the absence of current or past history of hyperthyroidism 30.

TAO classically occurs in patients with Graves' hyperthyroidism, but 5-10% of patients have hypothyroidism or normal thyroid function 30.Individuals with TAO or Graves' orbitopathy and normal thyroid tissue are said to have euthyroid Graves' opthalmopathy (EGO), the diagnosis of which is supported by the presence of one or more thyroid specific antibodies, namely antibodies to thyroid

peroxidase(TPOAb) and the THS receptors(TRAbs). In the present study 41.7% TAO patients presented with hyperthyroid status, on the other hand, 27.1% had hypothyroid state and 31.2% were in euthyroid state. Among the hyperthyroid patients 80% were found with enlarged extraocular muscles on CT scan findings and among hypothyroid paercentage was 92.3%. A study demonstrated that at the time of diagnosis, 90% of the patients with clinical orbitopathy were hyperthyroid according to thyroid function tests, 3% Hashimoto's thyroiditis, 1% were hyperthyroid and 6% did not have any thyroid function tests abnormality 31. Of patients with Graves' hyperthyroidism, 20 to 25 percent have clinically obvious Graves' ophthalmopathy, while only 3-5% will develop severe ophthalmopathy. So, any form of thyroid dysfunction may presented with thyroid associated orbitopathy. Meticulous examination as well as antibody titres tests are very important to diagnosis their status.

Conclusion

Though Thyroid Associated Orbitopathy (TAO) is well established with hyperthyroidism state, but in the current study hypothyroidism was also noted as remarkable percentage. So, all thyroid dysfunction patients, both hypothyroidism and hyperthyroidism, should be evaluated by ophthalmologists to see the orbital status. Patients with orbital symptoms in the absence of thyroid disease or auto antibodies presents a diagnostic dilemma, and the clinician may be tempted to attribute such cases to non-thyroid cases. So, every individual requires thorough clinical and radiological evaluation and close monitoring of long-term thyroid status in such individuals.

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Review Article

Management of Nutrition Status in Liver Cirrhosis Patients

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ABSTRACT

Malnutrition is a common event in chronic liver disease. The aetiology of this condition is more complex than simple protein and calorie malnutrition. Over nutrition and obesity can also be observed mainly in patients with Non-alcoholic fatty liver disease (NAFLD) cirrhosis. Sarcopenia (loss of muscle mass) is the main finding in these patients. Reduced calories intake, metabolic alterations and modifications in the disposal of energy sources are among the causes of malnutrition. Recent studies have increased our knowledge of the molecular mechanism involved in muscle wasting in liver cirrhosis. Nutritional problems are frequently disregarded in liver diseases and an ideal tool for their diagnosis is missing. Composite scores try to overcome this difficulty. The presence of sarcopenia is evaluated by measuring the muscle area on CT scan at the level of the third lumbar vertebra. Malnutrition and sarcopenia are indicators of a worse outcome and a lower survival in cirrhosis. Treatment of malnutrition starts from its recognition patient education, use of late evening snacks, intake of in multiple meals to shorten periods of starvation, branched chain amino acid supplementation and high protein/high calorie diet like 35–40kcal/kg/daily and 1.2–1.5g/protein/daily. Improved understanding of the multiple mechanisms involved should allow the development of more effective therapies, which target the specific underlying metabolic derangements.

Keywords: *Nutrition Status, Liver Cirrhosis.*

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INTRODUCTION

The liver plays a central role in energy disposal and is involved in protein, carbohydrate, and fat metabolism, therefore nutritional status can be profoundly affected in patients with chronic liver disease.[1] The term malnutrition covers two main groups of conditions: under nutrition and over nutrition. In the present study utilize the term malnutrition for under nutrition, while for over nutrition the terms overweight or obesity was used.

The prevalence of malnutrition in cirrhosis ranges between 60% and 90% [2, 3]. An Italian study showed that malnutrition was more frequent (50%) in Child class C patients and less frequent (20%) in those belonging to Child class A [3]. Muscle loss is more severe in males, while females more frequently experience a decrease in fat deposits. Active alcoholism causes malnutrition per se and patients continuing alcohol abuse are at higher risk for nutritional failure. Malnutrition may affect different body compartments (fat mass or body cell mass) and may cause micronutrient depletion, osteopenia, and osteoporosis. The main focus has recently concentrated on the depletion of skeletal muscle mass (i.e. sarcopenia) [4]. Its pathogenesis is multifactorial and the causes are not limited to a reduced nutrient intake, but also to alterations in nutrient absorption and in nutrient handling through the different metabolic pathways.

In the last decades overweight and obesity have also been reported in patients with cirrhosis, particularly given the rise in cirrhosis due to non-alcoholic fatty liver disease (NAFLD). In spite of the excess of body fat, even these patients may experience muscle loss with negative effects.

Malnutrition is not only a consequence of progressive liver insufficiency, but it is also a condition that may itself affect the natural history and complications of cirrhosis (encephalopathy, ascites, sepsis), thus influencing patient outcome and survival. New treatment approaches will derive from an improved knowledge of the pathogenesis of this syndrome.

CAUSES OF MALNUTRITION

Multiple factors contribute to malnutrition in cirrhosis (Table

1). The diet of a majority of patients with cirrhosis is inadequate/unbalanced and is sometimes influenced by unnecessary self-restrictions or by a superficial approach to the problem by their physician. In advanced liver disease appetite is decreased either due to dysgeusia (altered taste sensation), early satiety, or dyspepsia. Hospital admission is frequently a further cause of starvation due to changes in eating habits or the need for fasting prior to diagnostic and/or therapeutic procedures. In this setting, attention to dietary intake is generally disregarded. In the presence of ascites, indication of a salt-restricted diet makes food unpalatable and tense ascites causes a reduction in stomach compliance contributing to rapid satiety.

TABLE 1. FACTORS AFFECTING NUTRITION STATUS IN PATIENTS WITH CIRRHOSIS

1. QUANTITY AND QUALITY OF ORAL INTAKE

a. Socioeconomic limitations to food

b. Dietary excesses (e.g., alcohol intake or salt)

c. Dietary restrictions

d. Poor dentition

e. Dysgeusia

f. Nausea (and vomiting)

g. Early satiation (ascites related in some cases)

h. Altered mentation (e.g., recurrent HE episodes or intoxicants)

2. MALDIGESTION/ABSORPTION, LOSSES

a. Altered gut motility

b. Bowel resection (e.g., patients with inflammatory bowel disease)

c. Bowel edema (portal hypertension related)

d. Protein-losing enteropathies

e. Bile acid insufficiency/cholestatic disease (e.g., primary biliary cholangitis)

f. Pancreatic insufficiency (e.g., chronic pancreatitis)

g. Altered gut microbiota

h. Increased bowel movements (iatrogenic or otherwise)

i. Proteinuria/nephrotic syndrome

3. METABOLIC ABNORMALITIES

a. Glucose intolerance

b. Decreased glycogenic storage

c. Increased gluconeogenesis, lipolysis

d. Sarcopenia

e. Ascites per se as a hypercatabolic state (and with paracenteses losses of vitamins, minerals, and proteins)

f. Electrolyte abnormalities related to altered dietary intake, iatrogenic medications (e.g., diuretics), and degrees of kidney injury

AETIOLOGY OF SARCOPENIA IN CIRRHOSIS

Sarcopenia results from an imbalance between muscle formation and muscle breakdown.

1 Malnutrition – reduced substrate for muscle production.

There are many potential causes of reduced dietary intake in cirrhotics including nausea and anorexia induced by elevated inflammatory mediators such as TNF-alpha; increased intra-abdominal pressure from ascites; abdominal pain and altered gut motility[6]. Dysgeusia is common in cirrhosis,and salt restriction may also affect enjoyment of food, both of which also may affect caloric intake[7]. Patients may also have inadequate dietary protein intake due to inappropriate and outdated advice that protein restriction is required to prevent encephalopathy. Even with adequate caloric intake, malabsorption may contribute to net negative energy balance in cirrhosis. It is well recognised that reduced bile flow can cause malabsorption of fats and fat-soluble vitamins including vitamin D[8]. There is also increasing evidence that altered gut motility, small bowel bacterial overgrowth and changes to the gut microbiota in cirrhosis can each affect both absorption and utilisation of nutrients. Alcohol abuse may result in concomitant pancreatic insufficiency, which can also impair nutrient absorption.

2 Elevated myostatin and inhibition of muscle growth

Myostatin is the predominant negative regulator of satellite cell differentiation and proliferation. Elevated myostatin levels are thought to be one of the major driving forces underlying the sarcopenia of ageing, however, the reasons for this elevation are not fully understood. Patients with cirrhosis have been shown to have significantly higher serum levels of myostatin than controls (0.53 µg/mL vs. 0.13 µg/mL in cirrhotics and controls respectively, P = 0.002)[9]. Muscle biopsies in cirrhotics have also demonstrated significantly increased myostatin expression compared to controls[10]. One possible mechanism is that ammonia levels are frequently elevated in cirrhosis, and that this increases myostatin expression. The reduction in serum testosterone levels and IGF-1 levels in cirrhosis are likely also contribute to elevated myostatin levels since these mediators normally act to suppress myostatin expression.

3 Altered metabolism – abnormal use of protein as an energy source

Cirrhosis mimics the state of starvation, with inappropriate use of body fat and protein stores for gluconeogenesis. This proteolysis and lipolysis can occur even during short periods of fasting such as overnight, which should not happen under normal physiological conditions. This switch to the use of fat and protein as an energy source is thought to due to a reduction in hepatic glycogen stores which results in a need to generate glucose from alternate sources. This study

demonstrated that energy use derived from carbohydrate during a 12 h overnight fast was only 13% in cirrhotics compared to 39% in normal subjects. In controls at least 36 h of fasting was required for the proportion of calorie production from fat and protein to approach that in overnight fasted cirrhotic. Several other studies have documented increased ketogenesis and amino acid consumption in cirrhosis[11&12] and respiratory quotient (carbon dioxide production as compared to oxygen consumption) has been shown to be reduced in cirrhosis (0.63 ±0.05 vs. 0.84 ± 0.06 in controls (< 0.001), which again reflects a lower proportion of energy derived from carbohydrate[13]. In keeping with these findings, whole body protein turnover was found to be increased from 1.8 ± 0.3 g of lean body mass per 9 h to 3.14 ± 1.2 g of lean body mass per 9 h in cirrhotics[11]. The consumption of body fat and protein stores in cirrhotic is likely further exacerbated by an overall increase in resting energy expenditure, in part driven by the chronic up regulation of inflammatory mediators. This metabolic switch to the use of amino acids to create glucose results in reduced levels of circulating branched chain amino acids (BCAAs) in patients with cirrhosis. This may further compounds muscle breakdown since BCAAs are the preferential energy source of skeletal muscle and muscle tissue[14].

4 Relationship between hepatic encephalopathy and muscle mass

The prevalence of sarcopenia was found to be 30% in patients without encephalopathy, 49% with minimal change encephalopathy and 56% with overt encephalopathy[15]. This may reflect a causative relationship between these two common sequelae of cirrhosis. Although BCAAs are utilized for energy production in cirrhosis, the main cause for reduced BCCA levels is their uptake by muscle to assist in ammonia detoxification via glutamine synthase. Muscle uptake of BCAAs is significantly higher in cirrhotics than controls (32 vs. 12 mol/L blood) and leads to a reduced BCAA/aromatic amino acid ratio (1.65 vs. 2.73, P < 0.05)[14]. Thus in sarcopenic cirrhotic patients, both reduced circulating BCAA levels and reduced muscle mass may contribute to impaired ammonia clearance. A Cochrane review has concluded the BCAA therapy has a beneficial effect on hepatic encephalopathy (RR 0.76, 95% CI 0.63–0.92) which reflects the important role BCAAs play in ammonia clearance but few studies investigate the impact of BCAAs on muscle mass.

5 Activation of the ubiquitin–proteasome pathway (UPP) and autophagy – increased muscle breakdown

Cirrhosis is a pro-inflammatory state, in which levels of TNF-alpha and other inflammatory mediators such as interleukin-1 and interleukin- 6 are elevated. In experimental cirrhosis a strong correlation was demonstrated between muscle TNF-alpha and muscle ubiquitin levels (r = 0.86, P < 0.001), which reflects the activation of the UPP, suggesting that in cirrhosis, inflammation may also contribute to sarcopenia activity or the UPP,[7] indicating that alcohol induced autophagy may directly contribute to sarcopenia in patients with alcoholic liver disease.

6 Hormone deficiency

In men, testosterone levels correlate with muscle mass. This hormone has dual positive effects in muscle, by both inhibiting myostatin production which leads to less inhibition of satellite cell activity, and increasing IGF-1 levels, mTOR activation and muscle protein synthesis. Up to 90% of men with cirrhosis have low testosterone levels, due to defects at all levels of the hypothalamic–pituitary– testicular axis[16]. In addition, SHBG is often elevated, which strongly binds testosterone and can thereby lead to an even greater reduction in free testosterone. The possibility that low testosterone levels contribute to sarcopenia in men with cirrhosis is supported by a recent study which demonstrated a correlation between testosterone levels, sarcopenia and overall mortality (P = 0.019)[2].

CONSEQUENCES OF MALNUTRITION

Malnutrition is associated with worse outcomes and increased mortality (Table 2). [1]

TABLE 2. CONSEQUENCES OF MALNUTRITION, SARCOPENIA, AND OVER NUTRITION IN ADVANCED LIVER DISEASE

MALNUTRITION AND/OR SARCOPENIA

- Higher rate of encephalopathy (both overt and covert)
- Higher rate of bacterial infections
- Increased development of complications of cirrhosis
- Decreased survival (in outpatients and in hospitalized patients with cirrhosis)
- Decreased survival on the waiting list for liver transplantation (LT)
- Higher surgical risk
- More resources required after LT (longer stay in ICU and in the hospital)
- Lower survival after transplantation (controversial)
- Higher rate of complications during treatment of hepatocellular carcinoma
- Lower survival in patients with hepatocellular carcinoma

OVERNUTRITION

- Decreased survival at transplantation with BMI >40
- Decreased survival in sarcopenic obese patients
- Higher rate of decompensation in obese patients with cirrhosis

DIAGNOSIS AND ASSESSMENT

While malnutrition is easily recognized in cachectic patients with decompensated cirrhosis, it might be more difficult to identify in the early stages. There are, however, many reasons why attention should be drawn to nutritional status at earlier stages: (1) to make patients aware of the

TABLE 3. NUTRITIONAL ASSESSMENT IN PATIENTS WITH CIRRHOSIS

PARAMETER	*ADVANTAGES*	*DISADVANTAGES*
Body weight Body mass index (BMI)	Easy and inexpensive	Not reliable due to water retention, oedema, or ascites.
Visceral proteins (albumin, transferrin, retinol binding protein)	None	Influenced more by liver function than nutritional status
Anthropometry to evaluate muscle (AMC) and fat (TSF)	Easy, rapid, bedside evaluation. Low cost	Severe water retention may affect measurements
Dual energy X-ray Absorptiometry (DEXA)	Informs about body composition. Regional analysis possible	Measures body fat, fat-free mass, and bone mineral density. Low-dose radiation. Influenced by hydration
Bioelectrical impedence analysis (BIA)	Bedside tool moderately expensive	Unreliable in patients with ascites and oedema
CT or MRI	Frequently CT scan is already available, not influenced by muscle activity and water retention.	High costs and X-ray exposure if CT is not available
Handgrip strength	Easy, rapid, bedside evaluation. Low cost	Patient may be unable or uncooperative to perform the task
6minutes' walk test	Inexpensive functional evaluation	Patient may be unable or uncooperative to perform the task.Need for dedicated space

importance of his/her nutritional status and to discuss how to remove possible obstacles to a correct nutritional regime as a preventive intervention; (2) to make an early diagnosis, because it is much easier to intervene when nutritional impairment is mild or the patient is at 'risk of malnutrition'; (3) to monitor the course of nutritional status, independent of whether nutritional treatment is initiated or not; and (4) to obtain additional relevant information regarding prognosis and transplant candidacy. Unfortunately, there is no accepted gold standard for the assessment of nutritional status in cirrhosis, because of the many significant drawbacks encountered with the use of standard nutritional parameters (Table 3).

TABLE 4. MICRONUTRIENTS FOR POTENTIAL ASSESSMENT IN PATIENTS WITH CIRRHOSIS AND CONSIDERATIONS FOR REPLETION

MICRONUTRIENT	*POTENTIAL IMPACT IN CIRRHOSIS*	*CONSIDERATIONS FOR REPLETION*
Vitamin A	Symptoms including night blindness; potential role in disease progression in cholestatic liver disease	Fat soluble. Avoid toxicity; serum levels do not necessary correlate with tissue levels.
Vitamin D	Relationship with hepatic osteodystrophy	Fat soluble. Serum level potentially influenced by inflammation. Check 1,25-dihydroxy vitamin D with concomitant renal disease.
Vitamin E	Potential role in nonalcoholic steatohepatitis, antioxidant	Dosing guidance remains unclear.
Vitamin K	Elevated INR seen in cirrhosis; potential for improvement if Deficient.	No clear evidence of toxicity in adults.
Thiamine	Deficiency is common in cirrhosis; association with Wernicke–Korsakoff (WK) syndrome.	If increased risk for WK syndrome, give thiamine repletion prior to sugar-containing fluids.
Folate	Potential source of anemia	Toxicity rare but can cause neurological problems.
Zinc	Deficiency potentially associated with hepatic encephalopathy	Oral zinc could interfere with copper absorption. High doses can sometimes cause GI symptoms.
Vitamin B_{12}	Potential source of anemia	Replete sublingual or intramuscular.
Selenium		Toxicity rare but can cause neuropathy and mental status changes.
Copper	Deficiency seen with zinc repletion/supplementation	Biliary excretion; avoid toxicity.

MANAGEMENT

We recommend checking micronutrients at admission or shortly thereafter. (Table 4) The mechanisms for such deficiencies in cirrhosis are multifactorial in nature and outside the scope of this review. Repletion and supplementation strategies for micronutrients should take into account the relationship to liver clearance as well as potential risks associated with toxicity[5] (Table 4).

1. Stop - alcohol, smoking & tobacco. Please attend Alcohol De addiction program.

2. High energy, high protein diet- 1.2–1.5 g of protein per kg of body weight per day (total 35–40 kcal/kg total energy intake per day Improves nitrogen balance. 4.3 ± 3.2 g of nitrogen/day on a high energy, high protein diet vs. -2.2 ± 1.9 g/day on usual diet, P = 0.01[17].

3. Caloric restriction- Patients with compensated cirrhosis who are overweight or obese, moderate caloric restriction (20–25kcal/kg body weight) is recommended, as obesity is an independent risk factor for clinical decompensation in cirrhosis of all etiologies[18] and lifestyle changes (diet and exercise) leading to weight loss as low as 10% from baseline have been shown to decrease portal pressure in obese patients with compensated cirrhosis[19].

4. Salt - A moderately low sodium diet (2g or 88mmol/day) Recommended when ascites present, as excessive restriction may cause unpalatable diets.

5. Fluid - Clean water intake. Restrict Fluid intake ~ 1L/day, only if serum sodium (Na) < 125 mmol/L (Check Na, K monthly)

6. Exercise- 30 min of moderate intensity walking 3–4 times per week in combination with resistance

training such as light hand weights three times per week as tolerated

7. BCAA supplementation- Oral granules leucine/ isoleucine/valine 7.5 g/ 3.75 g/3.75 g (dissolved in carbonated beverage). Activate muscle protein synthesis via mTOR signalling pathway. BCAA reduced whole body protein Ra (representing reduced proteolysis) and increased GCN2 (muscle regulator of mTOR activity), P < 0.01[20 & 22]

8. Testosterone therapy- Intramuscular testosterone decanoate or topical testosterone gel. Activates androgen receptors in muscle which inhibits myostatin, activates muscle protein synthesis via the mTOR pathway and downregulates the UPP. Testosterone gel in 12 hypogonadal men with

cirrhosis increased hand grip strength from 34.03 ± 7.24 kg to 39.18 ± 5.99 kg, P < 0.001.[21]

9. Normalization of portal HTN- Insertion of trans-jugular intrahepatic porto-systemic shunt. May improve nutrient absorption by reducing gastropathy/ enteropathy, and may reduce systemic inflammatory driver of muscle breakdown. Psoas muscle area improved in 41 of 57 patients with a mean increase from 22.8±0.9 to 25.1± 0.9 cm2, P < 0.001 [22].

10. Rifaximin - 550 mg twice daily. Hypothetically may down regulate myostatin levels by reducing serum ammonia which may also release more BCAAs for use as muscle fuel.

CONCLUSION

Treatment of malnutrition starts from its recognition patient education, use of late evening snacks, intake of in multiple meals to shorten periods of starvation, branched chain amino acid supplementation and high protein/high calorie diet like 35–40kcal/kg/daily and 1.2–1.5g/protein/daily. Improved understanding of the multiple mechanisms involved should allow the development of more effective therapies, which target the specific underlying metabolic derangements.

Abbreviations: BMI, body mass index; HE, hepatic encephalopathy; UPP,ubiquitin–proteasome pathway; NAFLD, non-alcoholic fatty liver disease; BCAA, branched chain amino acids; mTOR ,mammalian

target of rapamycin ; LT,liver transplantation

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Review Article

Twelve Years Demographic Profile of Cancer Patients at a Selected Medical College Hospital

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ABSTRACT

Background: *Globally cancer has higher trend of morbidity and mortality. The number of new cases is apprehended to rise by about 70% over the next 2 decades. According to cancer registry report 2008-2010, NICRH lung cancer topped the list in all patients followed by breast, cervix, oesophagus, stomach, liver, Gall bladder, rectum, larynx and ovary.*

Objective: *To assess the socio-demographic profile of cancer patients admitted in a selected Medical College.*

Methods: *In Bangladesh Medical College Hospital, we have documented total number of 12,226 newly diagnosed cancer patients in 12 years from 2003 to 2014. All of the patients belonged to adult group.*

Results: *Among 12,226 patients male: female was 1.05:1; 50% of the patients belonged to lower middle to poor socioeconomic group, 10% were well to do and rest (40%) belonged to middle class group. We found 60% literate. Forty percent of the total patients were smoker. Gastrointestinal cancer were 16%, breast cancer 15%, lung cancer 10%, gynaecological cancer 10%, lymphoma 10%, Head & Neck 9 % and hepato-billiary 6%.*

Conclusion: *Epidemiology of cancer is changing and it is now prevailing as a modern or slow epidemic. Lifestyle and behavioral modification as an intervention can bring the desirable changes in the population characteristics.*

Keywords: *Cancer, Demographic profile.*

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Introduction:

Cancer is the most dreaded disease in the world. The incidence of cancer is increasing with each year and it is attributed to the changes in lifestyle and increase in life expectancy.[1,2,3] The cancer profile varies in different parts of the world and an epidemiological study helps to know the common cancers prevalent in particular segments of a population and the risk factors involved.[2,3] Cancers figure among the leading causes of morbidity and mortality worldwide,with approximately 14 million new cases and 8.2 million cancer related deaths in 2012. The number of new cases is expected to rise by about 70% over the next 2 decades.[4] Tobacco use is the most important risk factor for cancer causing around 20% of global cancer deaths and around 70% of global lung cancer deaths. Cancer causing viral infections such as HBV/HCV and HPV are responsible for up to 20% of cancer deaths in low- and middle-income countries.[5]

In 2002, 4.2 million new cancer cases—39% of new cases worldwide—were diagnosed among 3.2 billion persons (48% of the world population) living in the fifteen most highly developed countries in South, East, and Southeast Asia: Japan, Taiwan, Singapore, South Korea, Malaysia, Thailand, China, Philippines, Sri Lanka, Vietnam, Indonesia, Mongolia, India, Laos, and Cambodia. China and India, together accounting for 37% of the worldwide population, reported 3 million of these newly diagnosed cancer cases. Greater than 50% of the world's new cases of stomach cancer, and greater than 70% of newly diagnosed esophageal cancer worldwide occur in these Asian countries. In 7 of these Asian countries, lung cancer has the highest incidence rate (age-standardized) of all cancers in males, and breast cancer is the highest incident cancer for females.[6]

Globally, cancers in all forms are causing about 12% of all deaths. In developed countries cancer is the second leading cause of death accounting for 21% of mortality by other causes and in developing countries it ranks third, accounting for 9.5% of all deaths.[7]

Cancer has become one of the ten leading causes of death in India. Around, 1.5-2 million cancer cases occur at any

given point of time. Over 7 lakh new cases of cancer and 3 lakh deaths occur annually due to cancer. Nearly 15 lakh patients require facilities for diagnosis, treatment and follow up at a given time.[8]

The global community can expect an increase of incidence of about 1% each year, with larger increase in China, Russia and India. In 2030, incidence may increase to 20-26 million with around 13-17 million mortality. Cancer cases doubled globally between 1975 and 2000, will double again by 2020 and triple by 2030. The rapid increase in the global cancer burden represents a real challenge for health systems worldwide.[9]

According to Bangladesh Cancer Society the burden of new adult cancer patients is 250000/yr, and the total cancer burden is 10,00000/yr. This is an institutional based statistics, the actual picture probably far away from it due to many barriers. The majority of the patients cannot reach to final diagnosis or avail the treatment facilities.

According to cancer registry report 2008-2010, NICRH lung cancer topped the list in all patients followed by breast, cervix, oesophagus, stomach, liver, Gall bladder, rectum, larynx, ovary.[10]

Material and Methods

This cross sectional retrospective descriptive study was conducted in 2015 at the Department of Oncology, Bangladesh Medical College to find out the demographic distribution of the cancer patients from 2003 to 2014. Data was collected from hospital records (Register of Department of oncology)

Result

In Bangladesh Medical College Hospital, we have documented total number of 12,226 newly diagnosed cancer patients from 2003 to 2014.

Fig 1: Distribution of the study population by gender and year from 2003-2014

Table 1: Socio demographic characteristic of the patients (n=12226)

Variables	Frequency	%
Age group		
Below 20 years	1222	10
20 -39 years	2446	20
40 – 59 years	7335	60
60 yrs and above	1223	10
Sex		
Male	6272	51.3
Female	5954	48.7
Educational status		
Illiterate	5098	41.7
Literate	7128	59.3
Socio economic status		
Lower Middle	6113	50
Middle	4889	40
Well to do	1221	10
Tobacco consumption		
Ever use	4890	40
Never use	7336	60
Tobacco consumption by gender (Both smoke and smokeless) n=4890		
Male	3925	80.3
Female	965	19.7

Table 1 shows that among the total 12,226 cancer patients 6,272 (51.3%) were male and rest 5,954 (49.7%) were female. Male: Female ratio is 1.05:1. Majority 7335(60%) of the patients belongs to 40-59 years of age, followed by 2446(20%) between 20-39 years of age and 10% were <20 years and >60 years of age.

More than half (59.3%) of the patients were literate and rest 41.7% were illiterate. Fifty percent of the patients belonged

to lower middle class, 4889(40%) middle class and only 1221(10%) belonged to well to do class. According to tobacco consumption history (both smoke and smokeless form), 4890(40%) ever consume tobacco where 60% never consume. Among the 4890 tobacco consumer majority (80.3%) were male and 19.7% were female.

Fig 2: Distribution of Cancer patients from 2003-2014

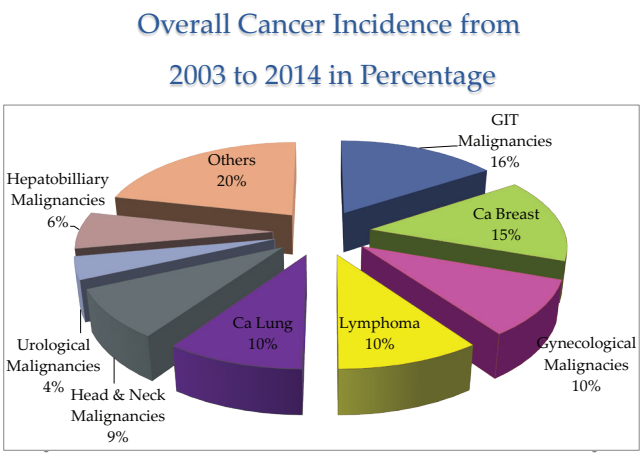

Fig-1 shows majority of the patients were of GIT(16%) followed by breast (15%), lung (10%), gynaecological (10%)malignancies and lymphoma (10%).

Table 2: Distribution of the patients by types of cancer and gender

Types of Malignancies	Male	Female	Total
	Frequency (%) (%)	Frequency (%) (%)	Frequency (%) (%)
GIT	1209(60.72) (19.32)	782(39.28) (13.11)	1991(100) (16.28)
Breast	2(0.11) (0.03)	1893(99.89) (31.72)	1895(100) (15.50)
Lymphoma	894(71.18) (14.28)	362(28.82) (6.07)	1256(100) (10.27)
Gynaecological	0(0.00) (0.00)	1235(100.00) (20.70)	1235(100) (10.10)
Lung	1197(99.67) (19.12)	4(0.33) (0.07)	1201(100) (9.82)
Head & Neck	655(59.98) (10.46)	437(40.02) (7.32%	1092(100) (8.93)
Hepato-Biliary	542(65.46) (8.66)	286(34.54) (4.79)	828(100) (6.77)
Urological	407(81.24) (6.50)	94(18.76) (1.58)	501(100) (4.10)
Others	1353(60.75) (21.62)	874(39.25) (14.65)	2227(100) (18.22)
Total	6259(100) (100)	5967(100) (100)	12226(100) (100)

Gastrointestinal cancers were the most frequent malignancy (16%) found in our study. Male: Female is 3:2.

Breast Cancer is second common cancer (15%) found in this study and. It constitutes 1895 cases; 1893 cases were female (99.89%) and 2 (0.11%) were male. Gynecological cancer comprises 10% in this study. This group includes cervical cancer and ovarian cancer mostly.

Among Lung cancers majority 1197 (99.67%) were male and only 4 were female.

Among the total male cancer patients (6,259) majority were GIT malignancies (19.32%) followed by Lung cancer (19%).

Among total female cancer patients (5967) majority were diagnosed as breast cancer (31.72%) followed by gynecological malignancies (20.7%)

Table 3: Distribution of patients by top ten malignancies in adult

Cancer sites	Number	percentage
GIT Malignancies	1991	16.2
• Colorectal • Stomach, Oesophagus	1493 498	12.2% 4%
Breast	1895	15%
Lymphoma	1256	10%
Cervix, Ovary	1235	10%
Lung	1201	10%
Head & Neck	1092	9%
Hepatobilliary	828	6%
Urological	501	4%
Total	12226	100

This above table shows that top most cancer among the cancer patients 16% are GIT malignancies, followed by breast, cervix, lung, lymphoma (each 10%). GIT malignancies include colorectal, stomach and oesophageal cancer.

Discussion

The incidence and cancer profile varies in developed and developing countries. Incidence is high in developed countries because of the affluent society, diet and lifestyle.2,11 Globally life expectancy at birth has increased from 45 years in 1950 to 66 in 2000 and is expected to reach about 77 years in 2050.2

This cross sectional retrospective descriptive study was conducted in 2015 at the Department of Oncology Bangladesh Medical College to find out the demographic distribution of the cancer patients from 2003 to 2014.

This current study revealed that among the total 12,226 cancer patients 6,272 (51.3%) were male and rest 5,954 (49.7%) were female. Male: Female = 1.05:1. According to age of the patients majority 7335(60%) of the patients belonged to 40-59 years of age, followed by 2446(20%) between 20-39 years of age and 10% were below 20 years and more than 60 years of age. More than half (59.3%) of the

patients were literate and rest 41.7% were illiterate By economical distribution 50% of the patients belongs to middle to poor class, 4889(40%) middle class and only 121(10%) belonged to well to do. According to tobacco consumption history (both smoke and smokeless form), 4890(40%) ever consume tobacco where 60% never consume. Among the 4890 tobacco consumer, majorities (80.3%) were male and 19.7% were female.

A Hospital based study on socio-demographic characteristics of cancer patients was conducted in India by Puri, Ashat and others and they found that 52.5% were female and most of the (32.3%) patients were in the age group 60- 69 years. Only 0.8% patients were aged <10 years, and 2.6% were of age 80 years or older. Majority (42.7%) of the patients were illiterate and only 4.5% were postgraduate. Out of 684 cancer patients, 33.4% belonged to the low socioeconomic status, while 6.6% belonged to the high socioeconomic status.[12]

Smoking in males was more as compared to that in females. Similar findings were evident in research done by Murthy.[13] Another study of Trivandrum too had emphasized that smoking increased the risk of oral cancer in men by as much as 90%.[14]

A similar study conducted by Kalyani, Bindra Singh and others in Kolar, India and they observed among 19,615 cases of histopathology and FNAC reported a total of 2744 (13.98%) were malignant, of which 1200 were males and 1544 females with male: female ratio of 0.7 : 1, indicating female preponderance. Among all the cancers, cancer of the oral cavity was the leading cancer in both sexes (total n = 814 cases). In lymph node malignancies (n = 369 cases), metastatic cancers outnumbered (n = 292 cases), Hodgkin's disease and NHL (total n = 77) in both sexes. The top ten sites most frequently involved by cancer in males were oral cavity, stomach, esophagus, bone, NHL, prostate, liver, larynx, penis, and Hodgkin's disease / bladder cancer, whereas, the sites in females were oral cavity, cervix, breast, stomach, esophagus, thyroid, ovary, bone, rectum, and melanoma skin.[15]

Gastrointestinal cancers were the most frequent malignancy (16%) found in this study with M: F=3:2. Breast Cancer is second frequent cancer (15%) found in our study and it was highest (1893; 31.72%) among female. Gynecological cancer comprises 1235 (10%) in our study and 1256 (10%) patients with lymphoma. Types of lymphoma could not be properly documented due inadequate information.

Among the lung cancer cases male patients were 1197(99.67%) and female patients were only 4 (0.33%) documented.

Head and Neck cancer comprises almost 9% of all cancer. Female are approx 40% sufferer. Hepatobilliary cancer (6%) and 4% Urological cancer in this study. Mostly 81.24% male patients were found.

In this study miscellaneous group comprises 20%. This large number is due to inadequate documentation, some are due to diagnostic dilemma. This group includes Carcinoma of unknown origin, sarcomas, leukemia, brain tumor, skin cancers.

Conclusion

Magnitude of cancer is increasing day by day as modern or slow epidemic. Distribution in terms of population characteristics is variable due to the change of life style & behavior, dietary habit, eco-system etc. Mass awareness regarding primordial and primary prevention of cancer through lifestyle modification and behavioral change would play a very significant role. In addition legislative measures are to be made more strengthened to order to have an effective control over the risk factors of cancers.

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Case Report

Neuroleptic Malignant Syndrome Associated with Haloperidol-A Case Report

Bhuiyan F K[1] , Sarker M R[2]

ABSTRACT

Introduction: *An adult schizophrenic patient developed neuroleptic malignant syndrome after the treatment with parenteral haloperidol. Early recognition of the syndrome, immediate discontinuation of the haloperidol and prompt treatment with bromocriptine and lorazepam produced a good recovery.*

Case presentation: *A 42 year-old man was admitted for the first episode of suspiciousness, irrelevant speech and aggressive behaviour for three month. There was no history of any organic illness in the patient. He was diagnosed as a case of NMS and started orally on bromocriptine and lorazeparn . along with nutritional support and serial monitoring of serum CPK and urine .* The patient made a remarkable recovery from NMS and was discharged.

Conclusion: *Bromocriptine, dantrolene sodium and bezodiazepines are shown to be effective in the treatment of NMS. A need for awareness of the syndrome in view of the widespread use of neuroleptics and its potential lethality which can be averted by early detection and specific treatment have prompted the present report.*

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Introduction

A 42 year-old man was admitted for the first episode of suspiciousness, irrelevant speech and aggressive behaviour for three month. There was no history of any organic illness in the patient. His physical examination was normal and his psychiatric examination revealed a fearful mood, thought disturbances and auditory hallucinations. He was diagnosed as acute schizophrenic episode and put on injection haloperidol 5 mg i.m. every 8 hours. The dose was increased after two days. Three days later the patient became confused and febrile. Haloperidol was discontinued and the patient was closely monitored. after the next two days he was noted to have alteration of consciousness, marked rigidity and disphoresis.

His vital signs showed significant fluctuations - temperature:103-105 F, pulse rate: 100-110 beats/minute, blood pressure: 120-150/90-110 mm of Hg and respiratory rate:18-22/minute. His investigations revealed WBC count of 24,100/cmm and serum CPK levels of 2000 IU/L. His X-ray skull and chest, ECG, liver and renal function tests, serum electrolytes were within normal limits.

he was diagnosed as a case of NMS and started orally on bromocriptine and lorazeparn . along with nutritional support and serial monitoring of serum CPK and urine . Over the next five days the patient became alert and afebrile and his vital signs stabilised. The serum CPK levels and WBC count decreased with clinical recovery.

Discussion

All neuroleptics have been implicated in the genesis of NMS, although, high-potency agents like haloperidol is reported most often with NMS.[1,2] NMS is an idiosyncratic reaction independent of the dose and may occur at any time during treatment. Predisposing risk factors include dehydration, agitation, substance abuse, parenteral administration, high doses or rapid upward titration of neuroleptics.[1,2,3] NMS is characterised by the development of hyperthermia, muscle rigidity, change in mental status and autonomic dysfunction. Approximately 16% of cases of NMS develop within 24 h after initiation of antipsychotic therapy, 66% within the first week and nearly all cases within 30 days. NMS usually lasts for 7–10 days; however, duration may be longer when depot injections of the drug is implicated.[3]

The predisposing factors that probably led to the development of NMS in our patient included high dose, rapid titration of initial haloperidol dose. This patient exhibited classic symptoms of NMS with development of hyperthermia and muscular rigidity. This patient's creatine kinase (CPK) level was elevated . The dramatic response to dantrolene with improvement in temperature was consistent with the diagnosis of NMS. The patient made a remarkable recovery from NMS and was discharged .As demonstrated by this case, high dose and quick up-titration of the haloperidol dose can

lead to the development of NMS. Bromocriptine, dantrolene sodium and bezodiazepines are shown to be effective in the treatment of NMS[4,5,6] .A need for awareness of the syndrome in view of the widespread use of neuroleptics and its potential lethality which can be averted by early detection and specific treatment have prompted the present report.

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Case Report

Metastatic Mucosal Melanoma–A Rare Case Report in Bangladesh

ALAM MM[1], HASAN MN[2], ALAM MJ, AFROZ R[4]

ABSTRACT

Mucosal melanoma is a rare cancer that is distinct from its cutaneous counter part in biology,clinical course & prognosis. Activating mutations in the C-KIT gene are detected in a significant number of patients with mucosal melanoma. We describe our clinical experience with a case of mucosal melanoma. Early diagnosis and prompt treatment can significantly reduce the mortality & morbidity.

Primary mucosal melanoma arises from melanocytes located in mucosal membranes lining respiratory, gastrointestinal & urogenital tract.They can also arise in almost any part of mucosal membranes.Most of mucosal melanoma occurs in occult sites,which together with the lack of early and specific signs contribute to late diagnosis and poor prognosis. Primary mucosal melanomas are aggressive tumors.

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Introduction

Mucosal melanoma is a rare form of melanoma, making up only about 1% of melanoma cases. As with other areas of the skin, melanocytes, the pigment producing cells of the body, are also present in the mucosal surfaces of the body, lining the sinuses, nasal passages, oral cavity, vagina, anus and other areas. Just like melanocytes in other parts of the body, these can transform into cancerous cells, resulting in mucosal melanoma.

Approximately 50% of mucosal melanomas begin in the head and neck region, 25% begin in the ano-rectal region and 20% begin in the female genital tract. The remaining 5% include the esophagus, gallbladder, bowel, conjunctiva and urethra.

Unlike most cases of melanoma of the skin, mucosal melanoma is not considered to be related to or affected by UV exposure. Additionally, there are no obvious identified risk factors, not even family history. Lacking an identifiable culprit and given its rare occurrence, most cases of mucosal melanoma are quite advanced once identified.[4]

Case Report

A 28 years young men non diabetic, normotensive presented with weight loss, abdominal pain for one month, hemoptysis and blood vomiting for 10 days. On examination hyperpigmented patches on oral mucosa and black maculae on sclera on left eye. Anemia was moderate. On investigation, Hb 9.4 gm/dl, ESR 90 mm in first hour. Chest X-Ray shows multiple dense almost rounded opacities of different sizes seen in both lung field and diffusely involved suggestive of secondary's in the lungs. Finding of ultra-sonogram of whole abdomen showed bilateral adrenal mass, biliary sludge within the gall bladder. Morning cortisol level was 16.18 mcgm/dl. ALT 21U/l and amylase 92 U/L. Upper GI endoscopy revealed ulcerative blackish lesions in the stomach and duodenum. Tissue biopsy from stomach ulcers showed malignant melanoma. CT scan of abdomen showed cholelithiasis with biliary sludge within the gall bladder, bilateral adrenal mass and pancreatic solid mass.

Based on the clinical examination, radiologic and histopathology features the patient was suspected as a case of primary mucosal melanoma in adrenal gland then metastasis to surrounding structures including stomach and duodenal mucosa. Medical information was provided to the patient and his family regarding the diagnosis, staging, therapeutic options and prognosis. The patient was consulted with oncologist for chemotherapy and further management.

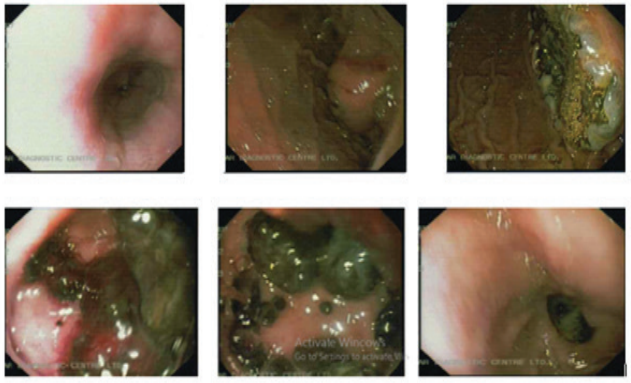

Figure : UPPER G.I. TRACT ENDOSCOPY– Ulcerative lesions in the stomach and duodenum with blackish lesions.

Discussion

Malignant melanomas are malignant tumors arising from pigment cells melanocytes. Melanocytes are derived from neural crest and migrate to several sites including skin and mucous membrane. Mucosal melanomas are rare, but they are known to behave more aggressive and have less favourable prognosis compared to other melanoma subtypes. Incidence of mucosal melanomas is increasing with age. Rates of mucosal melanomas are approximately twice higher among whites than among blacks. Based on the clinical examination, radiologic, histopathologic feature the patient has suspected as a case of primary mucosal melanoma in adrenal gland that metastasize to surrounding structures. He was advised for palliative chemotherapy. Rates of mucosal melanomas are approximately twice higher among whites than among blacks.[1]

Risk factors for development of mucosal melanomas have not been identified. Sun radiation, major risk factor for cutaneous melanoma, cannot be associated with mucosal melanomas, which arise in sun-shielded sites. Differences are also present in age, gender and racial distribution, survival rates. Discovery of different genetic mutations in different subtypes of melanomas, but also presence of different mutations within same subtype. Compared to cutaneous melanomas (80.8%), mucosal melanomas have the lowest percent (25%) of five-year survival rate3. Primary adrenal melanomas represent distant metastasis. However, because of occult site of occurrence and unspecific symptoms, diagnosis is usually delayed. Each anatomical site requires specific surgical approach, and in many cases completes removal of tumor limited by surrounding structures. Radiotherapy can provide better local control, but does not improve survival. Role of chemotherapy and immunotherapy is not clear.[2]

Recently revealed genetic changes underlying mucosal melanomas offer new hope for development of more effective systemic therapy for these aggressive tumors. Since risk factors are not well known, improvement of prevention seems not possible.

Conclusion

To conclude, we would recommend any pigment lesion in mucous membrane and mucocutaneous junction deserves attention.

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