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Original Article

Etiology of Exudative Pleural Effusion in Type 2 Diabetic Patients Admitted in a Tertiary Care Hospital in Dhaka

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Abstract:

Background: *There is limited data on the etiological pattern of pleural effusion in diabetic patients. Therefore, it is imperative to understand the cause of pleural effusion in diabetic patients so that it may help in adoption of regionally optimized diagnostic & therapeutic approach.*

Methodology: *This was a hospital based cross-sectional study carried out in the Department of Internal Medicine and Respiratory Medicine of BIRDEM General Hospital, Dhaka, Bangladesh over a duration of 6 months. All hospitalized adult (≥18 years) type 2 diabetic patients of either sex with exudative pleural effusion were included in the study. Pregnant women, non diabetic patients, patients with other forms of diabetes, bleeding disorders, chest trauma and non-aspirable pleural effusion were excluded. Investigations were done to find out the etiology of pleural effusion.*

Results: *The mean age was found 57.9±16.7 years, ranging from 19 to 91 years. Almost three-fourth (72.0%) patients were male. Male to female ratio was 2.7:1. Forty four patients had tubercular pleural effusion, among them 27 (61.4%) were right sided and 17 (38.6%) were left sided pleural effusion. Thirty patients had pneumonia, among them 19 (63.3%) were right sided and 11 (36.7%) were left sided pleural effusion. Twenty six patients had malignancy, among them 15 (57.7%) were right sided and 11 (42.3%) were left sided pleural effusion. Causes of malignant pleural effusion were adenocarcinoma (42.3%), squamous cell carcinoma (26.7%), small cell carcinoma (19.2%), lymphoma (7.7%) and mesothelioma (3.8%).*

Conclusion: *The most common cause of exudative pleural effusion in type 2 diabetic patients was tubercular pleural effusion.*

Keywords: *Diabetic, Dhaka, Etiology, Exudative pleural effusion.*

Introduction

Pleural effusion may be classified as exudative and transudative based on the Light's criteria, which is being used since 1972.[1] Exudative pleural effusion is a result of inflammatory fluid leakage due to local capillary injury[2] and the causes are parapneumonic effusion, emphysema, tuberculosis and malignancies.[3] The accumulation of pleural fluid due to increased pressure without capillary injury is termed as transudative pleural effusion, which is a consequence of congestive cardiac failure, renal failure, superior vena cava obstruction, constrictive pericarditis, liver cirrhosis, fluid overload and hypoalbuminaemia.[2]

The geographical location and local prevalence of common diseases vastly influences the etiologic spectrum of pleural effusion.[4] While cardiac failure malignancy and pneumonia are common causes of pleural effusion in developed countries, tubercular and parapneumonic effusion are more predominant in developing countries.[5, 6] Even though with the recent advances of medicine, up to 20-25% cases the pleural effusion etiology still remain undiagnosed.[3, 7]

In a prospective observational study carried out in Khulna, Bangladesh, on 54 patients with pleural effusion, about 79.63% patients had exudative and 21.57% patients had transudative pleural effusion. The most common cause of pleural effusion was tuberculosis (46.29%) followed by pneumonia (18.52%), malignancy (12.96%), nephrotic syndrome (5.55%), cirrhosis of liver disease (3.71%), congestive cardiac failure (3.71%), systemic lupus erythematosus (1.85%) and 7.41% patients remained undiagnosed.[2] In a study by Maikap et al. done on 250 patients of pleural effusion in a tertiary level hospital in India, demonstrated the causes of pleural effusion were tuberculosis

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(68.8%), malignancy (14%), empyema (6%), and transudative effusion (2.8%). Pleural effusion was commonly right sided and more in male (66%). Younger patients of 21-30 years had more tubercular pleural effusion and older patients above 60 years of age suffered more from malignant pleural effusion.[8] In a retrospective analysis of 101 patients in Riyadh medical complex, Saudi Arabia, found 71% patients with exudative pleural effusion. The causes of pleural effusion were pneumonia (30.8%), congestive cardiac failure (22.4%), malignancy (13.1%) and tuberculosis (11.2%). Younger patients presented with tuberculosis when compared to those with congestive cardiac failure and malignancy. Most common presenting features were cough and breathlessness.[7] In a prospective study of 1000 patients with pleural effusion conducted by Villena et al. in a tertiary care hospital in Madrid, Spain, showed neoplasm (n = 364 patients) was the most common cause of pleural effusion. The second most common cause was tuberculosis (n = 155). About 118 patients had transudative pleural effusion, mainly secondary to heart failure. Tuberculosis was the most common cause of pleural effusion in human immune deficiency virus positive patients and in patients under 40 years of age.[9]

While there are many studies on pleural effusion in the general population, there is limited data on the etiological pattern of pleural effusion in diabetic patients. Diabetes mellitus (DM) is a metabolic disease that also has a high prevalence worldwide. Epidemiological data reveals that in 2011 there were 366 million people with diabetes globally and it is expected that by the year 2030 about 552 million people would be affected by the disease.[10] Type 2 diabetes mellitus (T2DM) affects about 7% of the population.[11] International diabetic federation (IDF) estimates show that the prevalence of diabetes in Bangladesh was 9.6% in 2011 and it would rise to 13.3% by 2030. Bangladesh is ranked eight with 8.4 million people affected with diabetes between 20-79 years of age.[10]

Pulmonary infections are common in diabetes mellitus.[12, 13] The susceptibility to infections may be due to severity of microvascular and neurologic complications associated with chronic hyperglycaemia, and decreased pulmonary cell immunity.[14, 15] Chemotaxis to the site of infection, adherence to bacterial surface and phagocytosis by the neutrophils and macrophages are inhibited by diabetes mellitus.[16] Hyperglycaemia causes decreased production of free radicals, impairing the respiratory burst; hence the intracellular killing of the phagocytosed microorganisms are also reduced.[17] Reduction of serum complement levels and T4 lymphocytes, alteration of capillary endothelium function, rigidity of red blood cells, changes in the oxygen dissociation curve and pulmonary microangiopathy as a result of chronic hyperglycemia can lead to the impairment of the host's ability to fend off infection.[12, 13, 17]

Therefore it is imperative to understand the cause of pleural effusion in diabetic patients so that it may help in adoption of regionally optimized diagnostic & therapeutic approach. Thus this study aims to identify the etiology of exudative pleural effusion in type 2 diabetic patients admitted in a tertiary care hospital in Dhaka.

Materials and Methods

This was a cross-sectional observational study conducted in Internal Medicine and Respiratory Medicine department of Bangladesh Institute of Research and Rehabilitation in Diabetic, Endocrine and Metabolic disorder (BIRDEM) General Hospital from June 2019 to November 2019. All hospitalized adult (≥18 years) type 2 diabetic patients of either sex with radiological evidence of pleural effusion were considered. Pregnant women, non diabetic patients, patients with other types of diabetes, bleeding disorders, chest trauma and non-aspirable pleural effusion were excluded from the study. With all aseptic precaution, pleural fluid aspiration was done and sent for biochemistry (protein and LDH). Blood was also drawn for routine investigations including serum total protein and LDH. According to Light's criteria, if the effusion was exudative, only then the patient was included in this study and later searched for etiology. By consecutive sampling of all eligible patients in above mentioned period, 100 patients were incorporated in the study.

Tuberculosis was diagnosed on the basis of pleural fluid cytology, adenosine deaminase (ADA), Ziehl-Nelson stain, Gene X-pert, pleural biopsy and FNAC from lymph node. Sputum, if present, was analyzed for cytology, Ziehl-Nelson stain and Gene X-pert for mycobacterium tuberculosis. Pneumonia was diagnosed on the basis of cytology, Gram's stain, culture and sensitivity (C/S) of pleural fluid and sputum. Malignancy was diagnosed on the basis of presence of malignant cell in pleural fluid, pleural biopsy, bronchoscopy guided biopsy or CT guided FNAC with histopathology from suspected lesion/ lymph node if found in imaging. Samples of blood, sputum & pleural fluid were collected in presence of an expert doctor who was able to manage any emergency.

Data regarding age, gender, co-morbidities, presenting complaints, clinical findings, cause of pleural effusion, complete blood count, serum for total protein and LDH, pleural fluid for protein, LDH, ADA, cytology, C/S, Gram's stain, AFB stain, Gene X-pert and malignant cell were collected in a case record form and the data was analyzed using Statistical Package for Social Sciences (SPSS) software (version 23). Collected data were checked every day carefully to identify any error in collected data. Qualitative data were presented as numbers and percentages while quantitative data were expressed as mean ± standard deviation (SD). Pleural fluid etiology was shown in a table and pie chart was used to represent the etiological distribution of malignant pleural effusion.

Basic principles of research ethics according to 52 World Medical Association declarations of Helsinki-2000 and Council for International Organizations of Medical Sciences (CIOMS) guidelines were maintained during the research processes. Permission was taken from the Institutional Review Board (IRB) of BIRDEM General Hospital. Patients were informed about the nature of the study and about the collection of data. Informed written consent was taken from every patient in the study. The participants were assured of confidentiality and anonymity, emphasizing that all the information acquired was used for academic purpose and data analysis only.

Results

One hundred patients were included in the study to see the etiology of exudative pleural effusion in type 2 diabetic patients admitted in a tertiary care hospital in Dhaka.

Table I shows socio-demographic parameters of the study population. Majority of the patients (38%) belonged to 61-80 years age group. The mean age was found 57.9 ± 16.7 years with range from 19 to 91 years. Almost three-fourth of the patients were male (72.0%) and 28% patients were female. Male to female ratio was 2.7:1. Multiple co-morbidities were present in some patients. All the patients were diabetic as the study was done on type 2 diabetic population. However, the second most common comorbidity was hypertension (61%). Majority of the patients presented with cough (57%) followed by fever 56% and difficulty in breathing (53%). Most of the patients had right sided effusion (61%). Tracheal shifting was seen in approximately half of the patients (55%). Around 88% patients had dull percussion note and reduced breath sound was noted in 86% of patients. Only 33% patients had bronchial breath sound.

Biochemical characteristics are seen in table II. In blood, mean white blood cell count was 10859.30 ± 3990.18/cmm, LDH was 453.25 ± 114.42 U/L and total protein was 67.12 ± 5.70 gm/L. In pleural fluid analysis, mean white blood cell count was 638.25 ± 442.01/cmm, protein was 41.1 ± 16.3 gm/L, LDH was 737.16 ± 515.44 U/L and ADA was 40.1 ± 46.5 U/L.

The etiology of pleural effusion in the current study was tuberculosis (44%), pneumonia (30%) and malignancy (26%) (Table 3). Among those with malignant pleural effusion, 11 (42.3%) patients had adenocarcinoma, 7 (26.7%) had squamous cell carcinoma, 5 (19.2%) had small cell carcinoma, 2 (7.7%) had lymphoma and 1 (3.8%) had mesothelioma (Figure 1).

Table I: Socio-demographic characteristics of the study population (N=100)

Socio-demographic characteristics	Number of patients (n)	Percentage (%)
Age (in years)		
≤20	1	1
21-40	16	16
41-60	36	36
61-80	38	38
>80	8	8
Mean±SD	57.9±16.7	
Sex		
Male	72	72
Female	28	28
Comorbidities		
Diabetes Mellitus	100	100
Hypertension	61	61
Chronic pbstructive pulmonary disease	16	16
Ischemic heart disease	14	14
Renal disease	12	12
Presenting complaints		
Cough	57	57
Fever	56	56
Difficulty in breathing	53	53
Chest pain	18	18
Weight loss	7	7
Sputum	5	5
Hemoptysis	2	2
Clinical findings		
Tracheal shift	55	55
Dull percussion note	88	88
Bronchial breath sound	33	33
Reduced breath sound	86	86
Location of effusion		
Right	61	61
Left	39	39

Table II: Biochemical characteristics of the study population (N=100)

Biochemical characteristics		Mean±SD
Blood		
Haemoglobin (gm/dl)		11.0±2.0
ESR (mm/hr)		62.5±22.2
White blood cell (/cmm)		10859.30±3990.18
Platelet (/mm^3)		370043.95±149625.89
S. LDH (U/L)		453.25±114.42
S. Total protein (gm/L)		67.12±5.70
FBS (mmol/l)	8.6	±4.2
		40.1±46.5
ADA (U/L)		
Two hours ABF (mmol/L)	9.8 ±2.5	
HbA1c(%)	8.5	±2.3
Pleural fluid		
White blood cell (/cmm)		638.25±442.01
Red blood cell (mcL)		13672.7±30494.6
Protein (gm/L)		41.1±16.3
LDH (U/L)		737.16±515.44

Table III: Etiology and site of pleural effusion (N=100)

Etiology	Total (N=100)	Site of pleural effusion (n=100)	
		Right (n=61)	Left (n=39)
Tubercular	44	27 (61.4%)	17 (38.6%)
Parapneumonic	30	19 (63.3%)	11 (36.7%)
Malignant	26	15 (57.7%)	11 (42.3%)

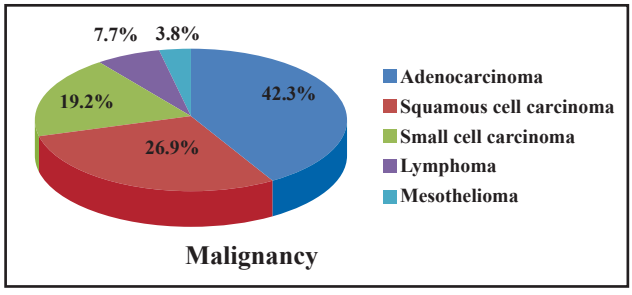

Figure 1: Etiological distribution of malignant pleural effusion (n=26)

Discussion

In the present study, the majority of patients (38.0%) were aged between 61 and 80 years. The mean age was 57.9 ± 16.7 years, ranging from 19 to 91 years. Male patients constituted 72.0% of the cohort, yielding a male-to-female ratio of 2.7:1. Comparatively, Reddy et al. reported an age range of 14–85 years, with a mean age of 48.8 ± 18.7 years; 63.4% of their subjects were between 20 and 60 years and the male-to-female ratio was 1.7:1.[18] Chowdhury et al. found that 66.66% of patients were aged 20–49 years with 41 males and 13 females.[2] Adeoye et al. documented a broader age range from 2 months to 90 years, with a median age of 38 years and a male predominance of 57.7% (male-to-female ratio 1.3:1).[19] Similarly, Abba et al. reported a mean age of 48.69 ± 18.89 years (range 13–90 years) with 68.2% males.[7]

Cough was the most frequently reported symptom in this study (57.0%), followed by fever (56.0%), dyspnea (53.0%), chest pain (18.0%), weight loss (7.0%), productive sputum (5.0%), and hemoptysis (2.0%). Adeoye et al. noted that half of the patients had effusion in the right side and presented with dyspnea, while 39.4% reported cough.[19] Reddy et al. observed dyspnea in 84% of cases, followed by cough (80%), fever (65%), and chest pain (43%), with weight loss and appetite loss in 27%.[18] Soe et al. reported breathlessness (82.4%) as the commonest symptom followed by cough (81.5%), fever (80.6%), night sweats (78.7%), appetite loss (74.1%), weight loss (72.2%), and chest pain (67.6%), with hemoptysis in 7.4% patients.[20] Abba et al. highlighted productive cough and dyspnea as predominant symptoms, while Dhital et al. found shortness of breath in 83% patients, cough in 67%, fever in 66%, chest pain in 40%, edema in 22%, hemoptysis in 16%, and weight loss in 13%.[7, 21] Among 44 patients with tubercular pleural effusion, 61.4% had right-sided and 38.6% had left-sided effusion.

Increased rates of TB in people with diabetes are caused by a compromised immune system, primarily due to high blood sugar levels, which impair both innate and adaptive immune responses, reduced cell mobility and function, altered cytokine response, decreased production of free radicals, chronic low-grade inflammation, deficiency of micronutrients such as Vitamin A and D.

Of the 30 patients with parapneumonic effusion, 63.3% were right-sided and 36.7% left-sided. Among 26 patients with malignant effusion, 57.7% were right-sided and 42.3% left-sided. Chowdhury et al. reported tuberculosis in 46.29% patients, parapneumonia in 18.52%, malignancy in 12.96%, nephrotic syndrome in 5.55%, cirrhosis in 3.71%, congestive heart failure in 3.71% and systemic lupus erythematosus in 1.85%.[2] Soe et al. found tubercular effusion predominantly right-sided (58.3%), followed by left-sided (39.8%) and bilateral (1.9%).[20] Abba et al. reported 60.6% parapneumonic effusion in right-side, 36.4% in left-side, and 3.0% present bilaterally; malignant pleural effusion was seen in right-side (57.2%), left-side (35.7%) and bilaterally (7.1%); and right sided tubercular effusion was in 41.7% patients, left-sided in 50%, and bilateral in 8.3%.[7]

Among the 26 patients diagnosed with malignant pleural effusion, adenocarcinoma was the most common histological subtype (42.3%), followed by squamous cell carcinoma (26.7%), small cell carcinoma (19.2%), lymphoma (7.7%), and mesothelioma (3.8%) in this study. Similarly, another study in Bangladesh found adenocarcinoma (57.4%) as the most frequent cause of malignant pleural effusion followed by large cell carcinoma (21.4%), small cell carcinoma (14.28%) and mesothelioma (7.14%).[22]

There were certain limitations to the study. The study was conducted in a single center so the results may not be representative of the actual picture of the country. Study duration was relatively short (6 months) and modest sample size (100). There was no non diabetic comparison group.

Conclusion

The most common causes of exudative pleural effusion in type 2 diabetic patients was tubercular pleural effusion. Diabetes not only increases susceptibility to Mycobacterium tuberculosis infection but also associated with higher complications rate. Optimal glycemic control plays a crucial role in improving treatment outcome and reducing morbidity.

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