Original Article

Aetiology of pleural effusion among patients with chronic kidney disease

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ABSTRACT

Background: *Pleural effusion is common in patients with chronic kidney disease (CKD). Aetiology of pleural effusion is diverse like heart failure, tuberculosis (TB), pneumonia, uraemia etc. Proper diagnosis of the cause is necessary as treatment plan varies from case to case. This study was designed to evaluate the aetiology of pleural effusion in patients with CKD.*

Methods: *This cross-sectional study was conducted in the Departments of Nephrology and Dialysis, Internal Medicine and Respiratory Medicine of BIRDEM General Hospital, Dhaka, from July to December, 2022. Sixty-two patients, aged e 18 years with CKD stage 3 to 5 with pleural effusion were included in this study. Patients having bleeding disorder, recent myocardial infarction or patients unwilling for thoracocentesis were excluded. Patients were evaluated clinically and by aspiration of pleural fluid.*

Results: *Of the 62 patients, 42 (67.7%) were male and 20 (32.3%) were female. The mean age was 52 years. Commonest symptom was dyspnea (47, 75%), cough (33, 53%), weight loss (23, 37%) anorexia (22, 35%), fever (16, 25%), pleuritic chest pain (15, 24%), bilateral basal crepitations (15, 24%), abdominal swelling (9, 14%), engorged neck veins (7, 11%). Diabetes mellitus (DM) (50, 80%) was the commonest comorbidity in our patients. A previous history of TB was present in 9 (14%) patients (most of whom completed treatment) and 7 patients had history of malignancy (including 2 on treatment). In our study, 38 (61%) patients were in CKD stage 4, 6 (9%) patients were on dialysis. In most cases (51, 81%), effusions were bilateral transudative. Fluid overload (32, 62%), heart failure (29, 56%) and nephrotic syndrome (11/21%) were common transudative effusion. Etiology of exudative pleural effusion were TB, uremia, empyema and hypothyroidism.*

Conclusion: *Aetiologiy of pleural effusion in CKD are mostly fluid overload, heart failure, nephrotic syndrome, TB and empyema.*

Key words: *chronic kidney disease, pleural effusion, aetiology.*

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INTRODUCTION

Chronic kidney disease (CKD) is kidney damage as defined by structural or functional abnormalities of the kidney, with or without decreased glomerular filtration rate (GFR), that manifests by either: pathological abnormalities or markers of kidney damage, including abnormalities in the composition of blood or urine or abnormalities in imaging tests or GFR <60 ml/min/1.73 m^2 for 3 or more months, with or without kidney damage. Kidney failure or end-stage renal disease (ESRD) is defined as a GFR of less than 15 ml/min/ 1.73 m^2 or the need for treatment with dialysis or transplantation.

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Classification of CKD in to 5 stages is based on GFR as proposed by Kidney Disease Outcomes Quality Initiative (KDOQI) guidelines.

CKD including ESRD is associated with an increased susceptibility to infection due to advanced age, immune dysfunction, underlying disease and the dialysis procedure itself leading to increased morbidity and mortality.[1] Pleural effusion is one of these common problems that is often encountered in this group of patients. There are several reasons why pleural disease may be common in patients with CKD. These include congestive heart failure, fluid overload, an increased risk of infection (especially tuberculosis, TB), the presence of diseases associated with renal and pleural manifestations (e.g. systemic lupus erythematosus, SLE), uremic pericarditis, an increased risk for certain malignancies and pulmonary embolism. Uremic pleurisy results from an unknown putative agent and therefore uremic pleuritis is a diagnosis of exclusion, that persists or recurs despite aggressive haemodialysis. Management of TB in these patients raises issues of drug dosing and interactions.

Patients with CKD have immune dysfunction manifested by depressed cell-mediated immunity (CMI). This impairment of CMI makes infection with *Mycobacterium tuberculosis* more difficult to detect and more likely to progress to TB disease than in immune competent individuals.[2] Increased risk for ischemic heart disease and potential for dilated cardiomyopathy makes these patients especially prone to problems with fluid balance.

In CKD, diseases such as SLE are associated with renal and pleural manifestations. Patients with CKD are immune compromised and some studies have suggested that this group of patients may be at increased risk for certain malignancies, such as non-Hodgkin's lymphoma and renal, prostate and uterine cancer. All of these malignancies can involve the pleura. Uraemia per se has been shown to cause a pleuritis by an unknown mechanism. Co-morbid conditions associated with or contributing to CKD may indirectly cause pleural abnormalities.

The presence of unilateral effusion suggests a diagnosis other than heart failure, like TB or parapneumonic or atelectasis. The reduced humoral and cellular immunity, in addition to delay in diagnosis because of an attenuated clinical response, may explain the high rate of empyema. Most of the studies looking into the incidence of pleural effusion in patients with CKD are retrospective studies of hospitalized patients. We planned to do the present study prospectively to know the causes, clinical features and management issues of pleural effusion in patients with CKD.

METHODS

It was a cross-sectional study, conducted in the Department of Nephrology and Dialysis, Internal Medicine and Respiratory Medicine of BIRDEM General Hospital, Dhaka, over a period of six months (July to December, 2022). Sixty-two patients, admitted during the study period who were aged 18 years or above with an eGFR <60 ml/min/1.73 m^2 for 3 or more months (CKD stage 3 to 5) with pleural effusion were included purposively excluding patients with known bleeding disorder, severe comorbidities like recent myocardial infarction or patients unwilling for thoracocentesis.

A clinically suspected case of pleural effusion in a CKD patient was diagnosed by chest X-ray and ultrasound of chest. Detailed demographic parameters including age, sex, history of smoking or alcoholism and systemic examination for the co-morbid illness were evaluated in all patients. Co-morbid illnesses were defined as the presence of coexisting cardiac failure, ischemic heart disease, chronic lung disease (COPD), chronic liver disease, malignancies, neurological diseases and diabetes mellitus. All patients were subjected to pleural fluid aspiration and analysis, blood investigations including complete blood count, erythrocyte sedimentation rate (ESR), blood sugar, renal function tests and liver function tests and urine routine examination. Sputum if present was sent for ZN stain, Gram's stain, culture and sensitivity. Statistical analysis was done by SPSS version 22.

RESULTS

Of the 62 patients, 42 (67%) were male and 20 (33%) were female. Mean age was 52 ±8 years. Smoking history was evident in 35 males but no history of alcohol intake was found. Dyspnea (47, 75%) was the commonest clinical feature followed by cough (33, 53%), weight loss (23, 37%), anorexia (22, 35%), fever (16, 25%), pleuritic chest pain (15, 24%), bilateral basal crepitations

(15, 24%), abdominal swelling ((9,14%), engorged neck veins (7, 11%). The most frequent comorbidity (Table I) was diabetes mellitus (DM) followed by hypertension (HTN) and ischaemic heart disease (IHD). Multiple co-morbidities were present in 52% patients. Chronic liver disease was found in 11 patients, of them HBV (4) and nonalcoholic fatty liver disease (NASH) (4) predominated. COPD (5) and hypothyroidism (4) were also found. A previous history of TB was present in 9 (14%) patients, most of whom completed treatment and 7 (11%) patients had history of malignancy (2 of them were under treatment). Most of the effusions were bilateral transudative (51, 83%) (Table II). Pleural fluid characteristics in different causes (Table III) were variable. Etiology of exudative pleural effusion was variable consisting of TB, uremia, empyema and hypothyroidism (Table IV). Among the causes of transudative pleural effusion, 52% patients were suffering from fluid overload due to unrestricted oral or intravenous fluids, whereas heart failure (29, 48%) was the second most common cause followed by nephrotic syndrome (11, 17%) (Table V). In our study, the majority of patients (38 patients were in CKD stage 4), (6, 9%) were on dialysis (Table VI). Most patients were discharged within 2 weeks without any complications however 5 of them needed chest tube drainage because of rapid reappearance and massive amount of pleural fluid (Table VII).

Table I. Co-morbidity of study patients with chronic kidney disease and pleural effusion (N = 62)

Variables	n (%)
Diabetes mellitus	50 (80)
Hypertension	40 (64)
Ischaemic heart disease	30 (48)
Malignancy	7 (11)
Treatment completed	5 (9)
Ongoing treatment	2 (3)
History of tuberculosis	9 (14)
Treatment completed	7 (11)
Ongoing treatment	2(3)
Chronic liver disease	11 (17)
Hepatitis B virus associated	5 (9)
Hepatitis C virus associated	1 (1.6)
Non-B non-C	1 (1.6)
Non-alcoholic fatty liver disease (NASH)	4 (7)
Hypothyroidism	4 (7)
Chronic obstructive pulmonary disease (COPD)	5 (9)

Table II. Pattern of pleural effusion (N = 62)

Pleural effusion	Number (%)
Unilateral	20 (32)
Bilateral	42 (68)
Exudative	11 (18%)
Transudative	51 (82%)

Table III. Pleural fluid characteristics in different causes (N = 62)

Pleural fluid characteristics (mean)	Transudative (51, 81%)	Exudative (11, 17%)	Tubercular (6, 11%)	CCF (29, 46%)	Uremic (2, 3%)	Empyema (2, 3%)
Total cell count (cells/cubic mm)	40	33588	16	75	656	
Neutrophil %	32	7633	23	31	99	
Lymphocytes%	66	2457	77	69	01	
Glucose (mg/dl)	44	1646	66	67	12	
Protein (gm/dl)	2.3	5.65.1	2.1	3.2	5.8	
RBC	Nil	11 8	nil	5	9	
Gram stain	Negative	Bacteria present	Negative	Negative	Negative	Negative
AFB	Negative	Negative	Positive	Negative	Negative	Negative

Table IV. Etiology of Exudative pleural effusion (n = 11)

Tuberculosis (TB)	6 (52%)
Uremic pleurisy	**2** (18%)
Empyema	**2** (18%)
Hypothyroidism	1 (16 %)

Table V. Etiology of transudative (51) pleural effusion (n =51)

Fluid overload due to chronic kidney disease	32 (62%)
Fluid overload due to heart failure	29 (56%)
Fluid overload due to nephrotic syndrome	11 (21%)

Table VI. CKD stage of patients with pleural effusion

Stage 3	9 (14%)
Stage 4	38 (61%)
Stage 5	7 (11%)
On hemodialysis (stage 5D)	6 (9%)

Table VII. Treatment and outcome of patients with CKD and pleural effusion

Total stay in hospital in days		Days
Medically treated	32	14
Intervention required	5	22
Improved	41	14
Resistant effusion	4	17
Recovered	60	14
Referred	2	20

DISCUSSION

In our study transudative effusion was more common than exudative which is in line with study done by Venkatesh et al. and Ray et al.[3,4] However in study done by Rashid-Farokhi et al. the exudative pleural effusion was seen in 74.1% cases.[5] The reason could be chronic HD patients are predisposed to several complications associated with pleural effusion and in addition, uremia can directly cause pleuritis.

Dyspnea was the commonest symptom found in these patients. Some of those with mild effusion, who also had pulmonary edema, could be the cause of their dyspnea. Several studies have been done that have evaluated the frequency of pleural effusion in the CKD population. One study showed the incidence of pleural effusion of 6.7% in various stages of CKD who were not on HD[6] while few studies have reported a higher incidence in patients on maintenance dialysis.[7]

The mean age of our study subject was 52 years with male predominance, which was similar to study done by Ray et al in 2013.[4] In CKD, there are several reasons for pleural effusion as these patients are immuno-compromised. They have decreased cellular and humoral immunity and reduced macrophage and phagocytic activity. Mostly the patients had a history of IHD, which further precipitates the symptoms and these patients mostly have excessive fluids in their bodies. The comorbid conditions associated with or attributed to CKD may indirectly cause pleural abnormalities too.[8]

With regard to comorbidities, most patients were diabetic and many had a history of IHD. In a study done among the CKD population having PE, eight out of 31 patients had DM and most of them had a transudative PE, 70% were hypertensive.[9] Similar findings were observed by Fonarow GC et al in which out of 35 patients, 62.8% had DM followed by hypertension (42.48%).[8]

After fluid overload (32/62%), heart failure (29/56%) was the second commonest cause found in our analysis, which is also similar to the Jarrat and Sahn study.[10] Concomitantly, a study done by Bakirci et al found the incidence of heart failure to be 9.6% in their patients.[6]

A previous history of TB was found in 14% of patients, which is different from a study done in 2016 on 35 CKD patients and concluded that out of them, 11 (31.42%) had a past history of TB.[11] In our study we found three major causes for exudative effusion: TB was the most frequent cause (52 %). Many studies support the increased rate of TB in CKD patients, which causes exudative PE. While opposite to our study, Bakirci et al[6] showed only 1.9% of TB. Another study by Kumar et al showed 28.5% of cases of PE due to TB.[12] The association of TB with immunocompromised states like

ESRD patients is well known for many years.[13] A worldwide summary article demonstrated a 6.9 to 52.5-fold increased risk of TB in CKD patients. The characteristic feature of exudative effusion is serosanguinous fluid with increased lymphocytes and its frequency has been reported in 1 to 58% of the patients with ESRD.[14] It is difficult to confirm TB in these patients because defective cell-mediated immunity caused difficulty in detecting mycobacterium TB and in many patients empirically antituberculous therapy started to cure the symptoms. We also found that maximum number of patients with pleural effusion belonged to stages 4 CKD (61%).

Conclusion

Transudative effusions are more common than exudative one in CKD. Shortness of breath was the most common clinical presentation; fluid overload and heart failure were the commonest causes of bilateral transudative pleural effusion and TB was the common cause of exudative effusion. In haemodialysis patients, pleural effusions most commonly occur due to underdialysis state, which needs proper thrice weekly dialysis for longer duration.

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