Original Article

Clinico-etiological profile of pleural effusion in chronic kidney disease

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Abstract

Introduction: Pleural effusion is a common complication of chronic kidney disease, arising from multiple causes. In a resource constrainted, tuberculosis endemic region like Nepal, accurate diagnosis is challenging. This study was done to assess the clinical profile and etiology of pleural effusion in CKD patients in a tertiary care center in Nepal.

Methods: This hospital based cross sectional study was conducted in the nephrology wards in Tribhuvan University Teaching Hospital over a period of 13 months. It included all patients aged ≥ 18 years with CKD stage 3 to 5D with radiologically confirmed pleural effusion who underwent diagnostic thoracentesis admitted during the study period. Pleural fluid was analyzed using Light's criteria. Final diagnosis was recorded after comprehensive evaluation as required.

Results: A total of 103 patients were included in the study. The mean age was 52.69±15.15 years with slight female predominance. Most patients (56.3%) were in maintenance hemodialysis. Diabetes Mellitus was the leading cause of CKD (41.7%). Shortness of breath was the most common symptom (86.4%). 59.2% were transudative effusion. Heart failure was the most common etiology (58.3%), followed by parapneumonic effusion (24.3%) and tubercular effusion (13.6%). Pleural fluid ADA was diagnostic in only 8 of 14 cases, remaining case required additional investigation or empirical treatment.

Conclusions: Pleural effusion in CKD has diverse causes with heart failure being the predominant cause. However, infectious etiology including tuberculosis constitute a substantial burden, necessitating a systematic evaluation especially in a TB endemic region like Nepal.

Introduction

Chronic kidney disease is a global health problem that affects >10% of the general population worldwide, amounting to >800 million individuals.[1] In Nepal, it affects more than 3 million people, although exact data is not available. It is now recognized as a major public health problem in Nepal.[2] Pleural effusion is a common presentation in patients with CKD.[3] There are numerous causes of pleural effusion ranging from cardiac failure, fluid overload, uremia, infections, malignancy and others.

The diagnostic workup for pleural effusion in CKD patients typically involves a combination of clinical assessment, laboratory studies, imaging studies and diagnostic procedures such as thoracocentesis, bronchoscopy and pleural biopsy. Congestive heart failure and infections are the most common causes of pleural effusion.[4] The management of pleural effusion in CKD patients is dependent on the underlying cause of the effusion. In cases of congestive heart failure, diuretics, heart failure medications and optimization of dry weight may be used to treat the underlying condition and reduce fluid overload. In cases of infection, antibiotics may be necessary to treat the underlying infection. If the cause of pleural effusion

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is uremia, intensifying the dialysis may be helpful. Since CKD is a disease with multi system involvement with multiple comorbidities, sometimes there are multiple causes of pleural effusion and many times the etiology is obscure. Furthermore, in many cases the usual investigation tools such as pleural fluid Adenosine Deaminase level may be falsely low even in cases of Tuberculosis and patients might have to started on Antitubercular treatment on clinical basis.

Therefore, it is important to conduct a thorough evaluation taking in account clinical features, associated symptoms and relevant investigations including bronchoscopy, pleural biopsy to determine the cause of pleural effusion as much as possible in order to treat them better. The data regarding the clinical presentation and etiology of pleural effusion in CKD patients in Nepal is scarce. Therefore, this study was conducted to evaluate the clinical features and etiology of pleural effusion in patients with CKD stage 3 to 5D admitted in tertiary care center in Nepal.

Methods

This study was a hospital based cross-sectional study. The study population included all patients aged ±18 years with chronic kidney disease (CKD) stage 3 to 5D who were admitted with radiologically confirmed pleural effusion and underwent diagnostic thoracentesis. It was conducted in the nephrology wards in Tribhuvan University Teaching Hospital, Kathmandu, Nepal over a period of 13 months from January 15th, 2025 to February 15th, 2026. Ethical approval was obtained from Institutional review committee of Institute of Medicine with reference number 519, 081/082 (dated January 10th, 2025). Written informed consent was taken from all the participants prior to enrollment. All the patients aged <18 years, those who did not undergo thoracentesis and those who did not provide consent were excluded from the study.

A consecutive sampling method was used to collect the data, where all eligible patients during the study period were included in the study. Proforma was used to collect demographic data, clinical history including presenting symptoms, cause of CKD, comorbidities and laboratory parameters. After thoracentesis, pleural fluid analysis included total count/differential count, protein, lactate dehydrogenase (LDH) and adenosine deaminase (ADA). Corresponding serum protein and serum lactate dehydrogenase were also collected. Light's criteria was used to differentiate between transudative and exudative pleural effusion.[5]

Pleural effusion was classified as exudative if it met at least one or more of the following conditions:[6]

1. Pleural fluid protein / Serum protein >0.5
2. Pleural fluid LDH / Serum LDH >0.6
3. Pleural fluid LDH > 2/3 of serum LDH upper limit of normal

Any other diagnostic tests such as sputum culture and sensitivity, acid-fast bacilli (AFB) stain, GeneXpert MTB/RIF test, echocardiography, Computed tomography (CT) of the chest, bronchoscopy, bronchoalveolar lavage and pleural biopsy were recorded if performed. The final diagnosis of the pleural effusion of all cases before discharge was recorded.

All the data were entered in Microsoft Excel sheet and then analyzed using SPSS version 26. Continuous variables were expressed as mean with standard deviation and categorical variables as frequency and percentage.

Results

A total of 103 patients with CKD and pleural effusion were included in the study. The mean age of the patients was 52.69±15.15 years with a range of 23 to 76. Among them, 55 (53.39%) patients were female and 48 (46.6%) were male. Most patients (56.3%) were CKD stage 5D (on maintenance hemodialysis) followed by CKD stage 5 (33%) and rest were in CKD stage 4 (10.7%). There were no patients admitted with CKD stage 3 with pleural effusion. Diabetes mellitus was the most common cause of CKD accounting for 41.7% of cases, followed by chronic glomerulonephritis (15.53%) and hypertension (13.59%). In a substantial number of cases (25.24%), the cause of CKD was undetermined. The demographic and clinical parameters of the study participants are summarized in Table 1.

Table 1: Demographic and Clinical Characteristics of Study Participants (N=103)

Parameters	Mean±SD/ Frequency(%)
Age	52.69±15.15
Minimum age	23
Maximum age	76
Sex	
Male	48(46.60%)
Female	55(53.39%)
Stage of CKD	
Stage 4	11(10.7%)
Stage 5	34(33%)
Stage 5D	58(56.3%)
Cause of CKD	
Diabetes Mellitus	43(41.7%)
Chronic Glomerulonephritis	16(15.53%)
Hypertension	14(13.59%)
Chronic pyelonephritis	2(1.94%)
Lupus Nephritis	1(0.97%)
Anti GBM disease	1(0.97%)
Undetermined	26(25.24%)

The most common presenting symptom in patients with pleural effusion was shortness of breath (86.4%) followed by cough and swelling of legs. Other presenting complaints were anorexia (24.3%), fever (21.3%) and chest pain (7.7%). The presenting symptoms of patients with pleural effusion are shown in Table 2.

Table 2: Presenting symptoms of patients with pleural effusion (N=103)

Presenting Symptoms	Frequency(%)
Shortness of breath	89 (86.40%)
Cough	51 (32.03%)
Swelling of legs	30 (23.30%)
Anorexia	24 (23.3%)
Fever	22 (21.35%)
Chest pain	8 (7.7%)

Based on Light's criteria, 59.2% of effusions were classified as transudative and 40.8% as exudative. Heart failure was the most common cause of pleural effusion, accounting for 58.3% of the cases followed by parapneumonic effusion (24.3%). Tubercular pleural effusion was diagnosed in 13.6% of cases. Uremic pleural effusion, diagnosed after exclusion of other causes, was diagnosed in 3.9% of patients. (Table 3) Among the 60 patients with heart failure, 22 patients (36.66%) had systolic dysfunction and the rest had diastolic dysfunction in echocardiography. 4 out of 25 patients (16%) with parapneumonic effusion and 7 out of 14 patients (50%) with tubercular effusion had systolic dysfunction in echocardiography.

Table 3: Causes of Pleural Effusion (N=103)

Cause of pleural effusion	Frequency (%)
Heart failure	60 (58.3%)
Parapneumonic pleural effusion	25 (24.3%)
Tubercular pleural effusion	14 (13.6%)
Uremic Pleural effusion	4 (3.9%)

Out of the 14 cases of Tubercular pleural effusion, only 8 were diagnosed with the help of the pleural fluid ADA in exudative pleural effusion taking a cutoff value of 40 IU/L. In the remaining cases, 1 case was diagnosed by Sputum GeneXpert MTB/RIF, 2 cases by Bronchoalveolar lavage with GeneXpert testing. Thoracoscopy with pleural biopsy established the diagnosis in 1 case and in 2 remaining cases Anti-Tubercular drugs were started empirically based on strong clinical suspicion. Both patients showed clinical improvement before discharge.

Discussion

This study evaluated the clinical presentation and etiology of pleural effusion in patients with chronic kidney disease stage 3 to 5D admitted to a tertiary care center in Nepal. The results highlight the diverse causes of pleural effusion in this population and the challenges in establishing an accurate diagnosis.

The demographic analysis showed a mean age of 52.69±15.15 years with a slight female predominance. Diabetes mellitus was the most common cause of CKD with 41.7%. This is consistent with the global scenario with diabetic kidney disease as the leading cause of CKD.[7] In our study, more than half of the patients were on maintenance hemodialysis. This indicates that clinically significant pleural effusion requiring admission is more common in advanced stage of CKD.

The most common presentation of pleural effusion was shortness of breath followed by cough and swelling of legs. This is expected given the combined effect of pleural fluid accumulation, anemia, volume overload and cardiac failure in this population. Fever was present in one fifth of the patients. This may provide crucial clue pointing towards infectious etiologies, necessitating a thorough diagnostic workup.

Using Light's criteria, 59.2 % of effusions were transudative and 40.8% were exudative. In a study conducted by Virupakshappa et al in India, transudative effusion was also predominant in pleural effusion in CKD patients.[8] This may be attributable to heart failure and fluid overload, both of which are highly prevalent in CKD patients. However, a substantial proportion of effusion were exudative as well, underscoring the need for routine pleural fluid evaluation rather than empirical treatment alone in CKD patients with pleural effusion who require admission.

Heart failure was the most common cause of pleural effusion in our study with 58.3%. This is in accordance with a study done by Bakirci et. al. in Turkey, which showed that heart failure was the most common cause (71.1%) of pleural effusion in 52 patient on maintenance hemodialysis.[9] CKD is associated with increased prevalence of heart failure, ischemic heart disease, arrhythmias and valvular calcification.[10] Possible mechanisms for the cardiac involvement in CKD might be due to pressure overload, volume overload and CKD associated non hemodynamic factors that alter the myocardium. Long standing hypertension and vascular calcification leads to pressure overload. Salt and water retention compounded by diastolic and systolic dysfunction leads to volume overload. Inappropriate activation of renin-angiotensin system, oxidative stress and inflammation also contribute to cardiac pathology.[11] LV diastolic dysfunction is more frequent than systolic dysfunction and is associated with increased mortality in CKD patients.[11] Diastolic dysfunction was found predominantly in patients with heart failure in our study. Even in patients with exudative picture with parapneumonic effusions and tubercular effusion, echocardiography showed systolic dysfunction in many patients highlighting the fact that multiple comorbidities may be interplaying in CKD patients. The high prevalence of heart failure related pleural effusion in this study suggests the importance of routine cardiac evaluation, including echocardiography for all CKD patients admitted with pleural effusion.

Infectious causes represented a significant burden of cases, accounting for 37.9% of case with parapneumonic effusion (24.3%) and tubercular effusion (13.6%). Infection is one of the common cause of hospitalization in CKD patients.[12] Multiple comorbidities, uremia, anemia, malnutrition, immunosuppressive therapy and hypoalbuminemia are the risk factors for infection among patients with CKD.[13] Uremia has also been associated with impaired lymphocyte function making them prone to infections.[14] In previous studies, the risk of pneumonia in hospitalized CKD patients was found to be 2.17 times higher compared to patient without CKD.[15] In a study done by Virupakshappa et al in India, infectious causes accounted for 40% of cases of pleural effusion in patient with CKD under hemodialysis done in 50 patients.[8] In our study as well, exudative effusion secondary to infection constituted more than one third of cases. So, infectious causes have to be considered in all cases of pleural effusion in CKD.

Nepal being an endemic region for Tuberculosis, tubercular pleural effusion was also common, as shown in this study with 13.6% of cases. In a similar study done in India, tubercular pleural effusion accounted for 16% of pleural effusion in patients with CKD.[8] In previous studies, the rate of TB was found to be higher in CKD as compared non CKD patients with the risk of TB increasing as the stage of CKD increases.[16] In our study, pleural fluid ADA had limited utility in diagnosing tubercular pleural effusion in this population

with only 8 patients out of 14 showing high ADA. So, overreliance on ADA as a single diagnostic marker might lead to underdiagnosis in CKD patients. Additional measures such as sputum test such as GeneXpert, bronchoalveolar lavage, thoracoscopy and pleural biopsy might be needed for diagnosis especially in exudative pleural effusion. Sometimes, empirical treatment based on clinical judgement might also play a role in selected patient with strong suspicion as shown in 2 cases who improved after treatment. Uremic pleural effusion was relatively uncommon in our study. This may reflect improved dialysis adequacy in our setting. It also points out that uremic pleural effusion is a diagnosis of exclusion and should only be considered after an extensive workup for other causes.

Limitations

This study has several limitations. It was a single center study where most of the cases were from advanced stage of CKD. So, the result may not be generalized to all the CKD population at different stages. Advanced diagnostics procedures like pleural biopsy could not be done in all the patients because of financial constraints and unavailability of equipment or expertise.

Despite these limitations, this study provides detailed clinico-etiological data from TB endemic, resource limited setting where such data are scarce. These findings have direct relevance for clinical practice in Nepal.

Conclusions

Pleural effusion in CKD has diverse causes with heart failure being the predominant cause. However, infectious etiology including tuberculosis constitute a substantial burden, necessitating a systematic evaluation especially in a TB endemic region like Nepal.

Conflict of Interest: None

Acknowledgement: None

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