Profile of pleural effusion in chronic kidney disease patients undergoing hemodialysis

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Abstract:

Background: A number of complications related to the respiratory system occur in patients with chronic kidney disease (CKD). Pleural effusion in such patients is a common diagnostic dilemma as it may arise from CKD itself or due to concomitant infections. In the present study, we retrospectively studied the occurrence, causes, clinical features and management issues of pleural effusion in patients with CKD on hemodialysis.

Material and Methods: Study is conducted on 50 CKD patients on hemodialysis admitted in the various medical wards of the Mc Gann Hospital attached to the Shimoga Institute of Medical Sciences, Shimoga from January 1st 2017 to September 30th 2017. A detailed history was taken in all the patients and a through physical examination was done. Blood was collected for analysis of Hb, blood urea, serum electrolyte, serum calcium, phosphorus, serum albumin, serum cholesterol, serum creatinine, electocardiography, HIV serology, hepatitis B surface antigen (HBsAg), anti-hepatitis C antibody (Anti HCV), sputum for Ziehl-Neelsen (Z-N) stain, urine for routine and microscopic examination recorded in the case records were studied. Echocardiography was done. Chest radiograph (postero-anterior views) was reviewed. Pleural fluid analysis for cell type, cell count, protein, sugar, gram stain and AFB were recorded.

Results: There were 35 males and 15 females. Average age is 46±11.6 years. The majority of these patients belong to the age group of 41-50 years (38%). Anemia (90%) and hypertension (88%) were commonest associations. IHD was seen in 42%. Commonest symptom was fatigue (90%) followed by dyspnea (84%) followed by cough (80%) and pedal edema (72%). Moderate pleural effusion (70%) was seen in majority of cases. Right sided (60%) unilateral (70%) effusion was common. Transudative effusion was common (64%). Out of 18 exudative pleural effusions 12 were para-pneumonic effusions. Out of 32 transudative pleural effusions 4 were due to volume overload. The Mean±SD of total leucocyte count of exudative pleural effusion was (335±145), tubercular pleural was 75±25 and cardiac failure pleural effusion was 15±9. Lymphocytes were predominant in tubercular pleural effusion (76±22) followed by uremia (75±19). Neutrophils were predominant in para-pneumonic effusions (66±23).

Conclusions: This study concludes that substantial number of patients with CKD suffers from respiratory diseases, most common of which is pleural effusion. Etiologies of these are multifactorial. Early thoracentesis should be done as management in such cases.

Keywords: CCF; CKD; Hemodialysis; Pleural effusion; Thoracocentesis.

Introduction:

Chronic kidney disease (CKD) is associated with multiple pathophysiologic in relation with Aan abnormal renal function, and a progressive decrease in glomerular filtration rate (GFR). In 1836, Bright reported that only 29% of patients with aluminous urine had healthy pleura at autopsy [1]. A number of complications related to the respiratory system occur in patients with CKD [2]. Some of these are related to alterations in volume status, plasma oncotic pressure, bone and mineral metabolism, concomitant heart failure, and an altered immune function in such patients, although in other instances the precise mechanisms were not well understood [3]. Pleural effusion in these patients could well be due to multiple factors, as it may arise from CKD itself (fluid overload, nephrotic syndrome, uraemic pleurisy) or due to associated infections (pneumonia, tuberculosis), pulmonary embolisms or autoimmune diseases like systemic lupus erythematosus [4]. Inadequate haemodialysis also leads to pleural effusion. Uremic pleurisy is a diagnosis of exclusion that persists or recurs despite aggressive hemodialysis [5]. In the present study, we retrospectively studied the occurrence, causes, clinical features and management issues of pleural effusion in patients with CKD on haemodialysis.

Material and Methods:

It is a retrospective Study, conducted on 50 consecutive patients admitted in various medical wards of the Mc Gann Hospital attached to Shimoga Institute of Medical Sciences, Shimoga from January 1st 2017 to September 30th 2017. All patients with CKD between 15-70 years on haemodialysis showing features of pleural effusion were taken for the study. An ethical committee approval was taken.

Inclusion criteria:

All CKD patients aged between 15 to 70 years on maintenance haemodialysis with pleural effusion.

Exclusion criteria:

1. Those not on regular haemodialysis

2. Immunosuppressive medication
3. Valvular heart disease

Methods:

A total 50 consecutive patients with CKD on haemodialysis fulfilling the inclusion and exclusion criteria were taken into study. In all these patients, detailed clinical history and detailed clinical examination as recorded in the case sheet was studied. The presence of hypertension, diabetes mellitus, ischaemic heart disease, HIV, tuberculosis and carcinoma was entered. Blood for complete blood count, blood sugar, blood urea, serum creatinine, liver function tests, serum electrolyte, serum calcium, phosphorus, serum albumin, cholesterol and CRP. ECG, hepatitis B surface antigen (HBsAg), anti-hepatitis C antibody (Anti HCV), sputum for Ziehl-Neelsen (Z-N) stain, urine routine examination as recorded in the case records were studied. Echocardiography was done to look for decreased ejection fraction (<50%) indicative of CCF. Chest radiograph (PA view) was reviewed.

Pleural fluid was studied for cell type, cell count, protein, sugar, Gram stain and AFB and thus divided as transudative or exudative as per Light's criteria [6].

Exudative pleural effusion was studied for Z-N stain, Gram stain and culture was also done wherever necessary. AFB negative Sputum sent for *M. tuberculosis* CBNAAT (cartridge based nucleic acid amplification assay) was studied.

Results:

Demographic data: 50 consecutive patients with CKD on hemodialysis were studied.

Table 1: Showing Sex distribution

Sex	No. of patients	Percentage
Male	35	70
Female	15	30

The male to female ratio was 1.3:1.

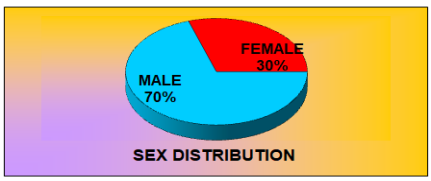

Chart 1: Showing sex distribution

Table 2: Showing age distribution

Age group	No. of patients	Percentage
15-20	2	4
21-30	3	6
31-40	11	22
41-50	19	38
51-60	8	16
61-70	7	14

The age distribution ranged from 15 years to 70 years with maximum number of patients in the age group 41 to 50 years (38%). Average age is 46±11.6 years.

The mean age among men was 44.22±9.72 years and in women was 46.45± 8.61 years. Majority of the patients were in the age group of 40-50 years (table 2).

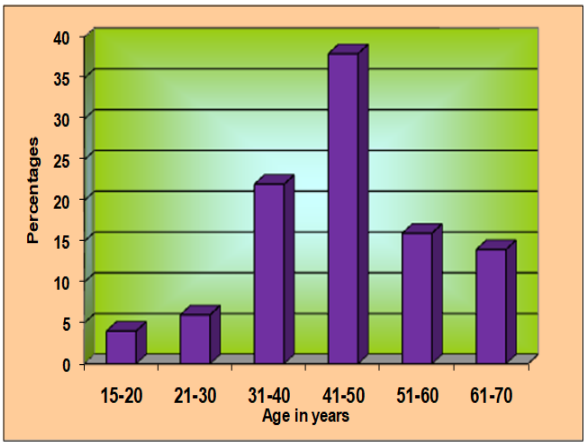

Chart 2: Showing age distribution

Table 3: Patient profile

Ranges	Number	Percentage
Hypertension	44	88
Diabetes mellitus	25	50
Anemia	45	90
IHD	21	42
Duration of Haemodialysis	2.8 years ± 1.2 years	

Anemia (90%) and hypertension (88%) are commonest associations. IHD is seen in 42%.

Table 4: Symptomatology

Symptoms	No of Patients (n=50)	Percentage
Dyspnea	40	84
Paroxysmal nocturnal dyspnea	14	28
Orthopnea	8	16
Fatigue	45	90
Cough	42	80
Pedal edema	36	72
Abdominal distension	14	28
Chest pain	11	22
Cyanosis	5	10
Fever	9	18
Hemoptysis	7	14
Sputum	6	12

Commonest symptom is fatigue (90%) followed by dyspnea (84%) followed by cough (80%) and pedal edema (72%).

Table 5: Classification of pleural effusion according to investigation

S. No		Number	Percentage
1	Grades of pleural effusion		
	Mild	10	20
	Moderate	35	70
	Massive	5	10
2	Unilateral effusion	35	70
	Right	30	60
	Left	5	10
3	Bilateral effusion	15	30
4	Recurrent pleural effusion	17	34
5	Hemorragic effusion	4	8
6	Tansudative effusion	32	64
7	Exudative effusion	18	36

Moderate pleural effusion (70%) is seen in majority. Right sided (60%) unilateral (70%) effusion is common. Transudative effusion is common (64%).

Table 6: Pleural fluid characteristics in different causes

	Pleural fluid characteristics	Transudative (32)	Exudative (18)	Tubercular (8)	CCF (28)	Uremic (5)
1	Total cell count (cells/cubic mm)	30±19	335±145	75±25	15±9	70±24
	Neutrophil %	39±16	66±23	26±11	33±16	28±18
	Lymphocytes%	60±23	33±15	76±22	66±25	75±19
	Eosinophils%	Nil	Nil	Nil	Nil	6±3
	Glucose (mg/dl)	45±11	15±6	48±12	66±8	68±11
2	Protein (gm/dl)	2.1±0.8	4.5±1.1	3.9±0.7	1.8±0.6	3.8±0.4
	RBC's	Nil	7±5	3±1	Nil	15±7
	Gram stain	Negative	Bacteria present	Negative	Negative	Negative
3	AFB	Negative	Negative	Positive	Negative	Negative

Out of 18 exudative pleural effusions 12 were para-pneumonic effusion. Out of 32 transudative pleural effusions 4 were due to volume overload.

Discussion:

A pleural effusion in CKD arises from multiple causes. There were 35 males (70%) and 15 females (30%) in the present study. The male to female ratio was 1.3:1. This finding is consistent with that of Ray et al., with male to female ratio of 2:1 [7]. The age distribution of these patients ranged from 15 years to 70 years with maximum number of patients in the age group 41 to 50 years. There were 38% of patients in this age group. Average age is 46±11.6 years. This is in sync with the study by Moger *et al[8]* where average age is 45.50±13.25 years. In study by Ray et al., The mean age (mean±SD) was 37.2±1.8 years [7]. The average duration of haemodialysis in our patients is 2.8 years ± 1.2 years.

Table 7: Symptomatology

Symptoms	Our study (%)	Moger et al. [8] (%)	Ray et al. [7] (%)	Rashid-Farokhi et al. [9]
Dyspnea	80	89	93	84
Paroxysmal nocturnal dyspnea	28	54	-	-
Orthopnea	16	23	-	
Fatigue	90	85	-	
Cough	84	64	71	55.6
Pedal edema	72	54	90	
Abdominal distension	28	40	-	
Chest pain	22	33	42	33.3
Cyanosis	10	9	-	
Fever	18	8	45	14
Hemoptysis	14	6	-	
Sputum	12	-	-	

Most common symptom was dyspnea. Most of the symptoms presentations in our study correlate with other studies [7-9].

Table 8: Clinical profile comparison with various studies

	Clinical profile	In our study (%)	Moger et al. [8] (%)	Ray et al. [7] %)	Rashid-Farokhi et al. [9]
1	Grades of pleural effusion				
	Mild	20	18	-	
	Moderate	70	65	-	
	Massive	10	16	-	
2	Unilateral effusion	70	77	62	69.7
	Right	60	74	--	
	Left	10	3		
3	Bilateral effusion	30	23	38	30.3
4	Recurrent pleural effusion	34	22	-	
5	Hemorragic effusion	8	5	-	10
6	Tansudative effusion	64	55	68	
7	Exudative effusion	36	45	32	74.1

Pleural disease is common in CKD. It was predominantly right sided and transudative. In our study transudative effusion was more common (64%) than exudative (36%) which is in line with study done by Moger et al.,[8] (55%) and Ray et al.,[7] (68%), However in study done by Rashid-Farokhi et al.,[9] the exudative pleural effusion was seen in 74.1%. Dyspnea was the common symptom found in these patients, being present in all with massive effusion and 30 of 35 patients (86%) of moderate effusion and 7 of 10 patients (35%) of those with mild effusion. All those with mild effusion also had pulmonary edema, which could be the cause of their dyspnea.

Table 9: Comparison of types of pleural effusion with other studies.

Symptoms	Our study Percentage	Moger et al. [8] (%)	Ray et al. [7] (%)	Rashid-Farokhi et al. [9]	Jarett et al. [10] (%)
Transudative	64	58	46	26	
Exudative	36	42	6	74	
Tubercular	16	4	26	6.6	
CCF	56	74	42	19.7	46
Uremic	10	6	26	23.7	16
Nephrotic			6		
Parapneumonic effusion	24			23.7	15
Volume overload	8			6.6	

The tuberculous etiology was found in 16% of patients. Cardiac evaluation revealed CCF in 56% of patients. In a study conducted by Moger *et al.,[8]* CCF is found in 74% and in Jarett et al.,[10] it is 46. CCF was the commonest cause (56%) followed by para-pneumonic effusion and tubercular effusion (16%). Tubercular pleural effusion is high in study done by Ray et al.,[7] (26%). Patients on dialysis are at higher risk of developing pulmonary tuberculosis all over the globe due to immune-compromised state of CKD, uremia, malnutrition and also, due to presence of diabetes mellitus and prolonged use of corticosteroids. Immunosuppressive medications also predispose patients to tuberculosis. A higher incidence of pulmonary tuberculosis had been reported in patients with CKD on hemodialysis in India, 8.7% in patients on maintenance hemodialysis and 12.3% in renal transplant patients [11].

AFB negative and extrapulmonary tuberculosis are more common than in normal people. Pleural effusion was the commonest mode of presentation. This may be the reason for increase in the incidence of TB in our patients. Due to reduced immunity status, synpneumonic effusion and pyothorax are common in dialysis patients; once again this may be the reason for increased incidence of para-pneumonic effusion in our study (24%). Mortality in pneumonia is 10 times higher than general population in the setting of CKD [12].

In microscopic examination of the pleural fluid in CKD patients with pleural effusion lymphocytes were predominantly seen in TB pleural effusion (76±22) followed by uremia (75±19). Neutrophils were predominant in para-pneumonic effusion (66±23). The Mean±SD of total leucocyte count of exudative pleural effusion was (335±145), tubercular pleural was 75±25 and cardiac failure pleural effusion was 15±9.

Bhushan M [13] found mean± SD of pleural fluid cell count in TB, carcinoma, transudative and para-pneumonic effusion are 1061±410, 574±190, 139±31 and 1332±571 respectively. Predominance of polymorphs points toward acute process like bacterial pneumonia affecting the pleural space and predominance of lymphocyte indicates chronic disease processes like TB, neoplasms [14]. In TB pleural effusion lymphocytes are seen more in number (>74%). But lymphocytic pleural effusion was also seen in malignancy, uremia etc. [15].

Management of TB in CKD patients is more complicated than usual TB patient management since most of the drugs except rifampicin requires dose

modification and RNTCP regimen is very difficult to administer. Higher incidence of vomiting and gastritis further complicates the compliance for the drugs. Adverse drug effects are more frequent and require a very close follow-up and care. Uremic pleural effusion was first identified in 1955 by Hopps and Wissler by showing fibrinous pleuritis in 20% of uremic patients during autopsy [16]. In our study 10% had uremic pleural effusion. Jarratt et al.,[10] reported an incidence of uremic pleural effusion of 16% while many other studies have shown a three percent incidence, which is lesser compared to our or Jarrat et al., study [10]. The exact pathogenesis of uremic pleural effusion is still not clear, but many uremic toxins like phosphates, uremic acid and retained immune complexes have been thought to be involved in the pathogenesis [17].

Uremic effusion is not related to the severity of uremia [18] and may develop during any stage of the uremia. Uremic effusions cannot always be cured by hemodialysis, but it can recur in spite of hemodialysis [17].

In four of our cases refractory pleural effusion necessitated intercostal tube insertion. Aerobic Gram-negative organisms [19] or catheter associated aerobic Gram-positive organisms [20] are the predominant pathogens. In our study, *Staphylococcus aureus* and *Klebsiella pneumoniae* were recovered in pleural fluid culture.

Conclusions:

This study concludes that substantial number of patients with CKD suffers from respiratory diseases, most common of which is pleural effusion. Etiologies of these are multifactorial. Transudative effusions are found to be common among the patients on long-term haemodialysis. Though CCF is the single most common cause of pleural effusion, other causes like TB, uremia, synpneumonic effusions, to be considered and investigated especially in the settings of a unilateral pleural effusion. All types of effusions should be differentiated in view of the different management strategies. Early thoracentesis should be done in the patient with a unilateral pleural effusion who is receiving hemodialysis, as other causes of pleural effusions are frequent in this population. Hence high degree of suspicion is needed when investigating cases of pleural effusion in CKD patients on hemodialysis.

Conflicts of interest: None declared
Acknowledgements: None

References:

1. Bright R. Tabular view of the morbid appearance in 100 cases connected with albuminous urine, with observation. *Guys Hosp Rep.* 1836;1:380-480.
2. Pierson DJ. Respiratory Considerations in the Patient with Renal Failure. *Respiratory care.* 2006;51:413-22.
3. Hassan IS, Ghalib MB. Lung Disease in Relation to Kidney Diseases. *Saudi J Kidney Dis Transpl.* 2005;16:282-87.
4. Mark CM, Sahn SA. Resolution of pleural effusions. *Chest.* 2001;119:1547-62.
5. Berger HW, Rammohan G, Neff MS, Buhain WJ. Uremic pleural effusion: a study in 14 patients on chronic dialysis. *Ann Intern Med.* 1975;82:2-4.
6. Light RW, Macgregor MI, Luchsinger PC, Ball WC Jr. Pleural effusions: the diagnostic separation of transudates and exudates. *Ann Intern Med.* 1972;77:507-13.
7. Ray S, Mukherjee S, Ganguly J, Abhishek K, Mitra S, Kundu S. A Cross-sectional Prospective Study of Pleural Effusion Among Cases of Chronic Kidney Disease. The Indian Journal of Chest Diseases & Allied Sciences. 2013;55:209-13.
8. Venkatesh M, Arun BS, Suresh H, Sagar Reddy SL. A study of respiratory manifestations in chronic kidney disease. *International Journal of Biomedical Research.* 2017;8(2):70-4.
9. Rashid-Farokhi F, Pourdowlat G, Nikonia MR, BehzadniA N, Kakoi S, Nasiri AA. Pleural effusion in hemodialysis patients with chronic kidney disease. *Iranian Journal of Kidney Diseases.* 2011;5(2):40-1.
10. Jarratt MJ, Sahn SA. Pleural effusions in hospitalized patients receiving long-term hemodialysis. *Chest.* 1995;108(2):470-74.
11. John GT. Infections after renal transplantation in India. *Indian J Nephrol.* 2003;13:14.
12. Sarnak MJ, Jaber BL. Pulmonary infectious mortality among patients with end-stage renal disease. *Chest.* 2001;120:1883-887.
13. Bhushan M, Kumar R, Nigam P. A clinical study of diagnostic efficacy of adenosine deaminase levels in tubercular pleural effusion. Int J Adv Med. 2016;3(1):92–6.
14. Maskell NA, Batt S, Hedley EL, Davies CWH, Gillespie SH, Davies RJO. The bacteriology of pleural infection by genetic and standard methods and its mortality significance. Am J Respir Crit Care Med. 2006;174(7):817–23.
15. Sahn S. The differential diagnosis of pleural effusions. West J Med. 1982;137(2):99–108.
16. Hopps HC, Wissler RW. Uremic pneumonitis. *Am J Pathol.* 1955;31:261-73.
17. Maher JF. Uremic pleuritis. *Am J Kidney Dis.* 1987;10:19-22.
18. Berger HW, Rammohan G, Neff MS, Buhain WJ. Uremic pleural effusion: a study in 14 patients on chronic dialysis. Ann Intern Med. 1975;82:2-4.
19. Chen CH, Hsu WA, Chen HJ, Chen W, Shih CM, Hsia TC, *et al*. Different bacteriology and prognosis of thoracic empyemas between patients with chronic end-stage renal disease. *Chest.* 2007;132:532-9.
20. Sarnak MJ, Jaber BL. Pulmonary infectious mortality among patients with end-stage renal disease. *Chest.* 2001;120:1883-7.