Original Article

Pleural fluid analysis in pleural effusion patient of chronic kidney disease and non chronic kidney disease: A comparative observational study

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Abstract

Introduction: Pleural effusions can occur as a complication of various diseases. The distribution of etiology of pleural effusion is also changing. Etiological distribution of bacterial pleural effusion depends on geographic region, patient age and advances in the diagnosis and treatment of the underlying causes TB, CKD, Malignancy, infection etc **Aim and Objective:** To analyse pleural fluid in Pleural effusion patient of chronic kidney disease and non chronic kidney disease, **Methodology:** This study comprises 150 cases of pleural effusion. Out of 150 cases of pleural effusion, 11 (7.3%) cases were CKD with pleural effusion and 139 (92.7%) cases were non-CKD pleural effusion. Various lab investigations done on pleural fluid like including complete blood count, BSL, 24 hour urine protein analysis (in CKD patients), Sputum Z-N stain, Gram's stain, culture and sensitivity and Thoracocentesis (USG guided) **Result and Discussion:** Pleural fluid microscopy shows WBC count, lymphocyte count, and polymorphs were more significantly associated with non-tubercular effusion than CKD effusion. ($p < 0.05$) No difference were found in appearance of pleural fluid, pleural fluid protein, sugar and ADA in pleural effusion in CKD and non CKD. ($p>0.05$) No difference were found in type (transudative or exudative) of pleural fluid in pleural effusion in CKD and non CKD. ($p>0.05$) There were no significant difference found in Gram staining of pleural fluid and Z-N staining (sputum + pleural fluid) in CKD and non CKD. ($p>0.05$).

Key Words: Pleural fluid, pleural effusion.

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INTRODUCTION

Pleural effusion is an abnormal accumulation of fluid in the pleural space. Pleural effusion indicates a pathologic process that may be of primary pulmonary origin or of an origin related to another organ system or occasionally the first evidence of some other systemic disease.(1) Chronic kidney disease (CKD) encompasses a spectrum of different pathophysiologic processes associated with abnormal renal function and a progressive decline in glomerular filtration rate (GFR). Pleural effusion in CKD patients is a common diagnostic dilemma as it may arise from CKD itself (fluid overload, nephrotic syndrome, uremic pleurisy), concomitant infections [especially, tuberculosis (TB) in our country], pulmonary embolisms or diseases causing pleuro-renal syndromes, like systemic lupus erythematosus.[2] Pleural disease is common problem in patient with chronic renal insufficiency. There are several reasons why pleural disease may be common in patient with chronic kidney disease. Uremic pleurisy results from an unknown putative agents and therefore uremic pleuritis is a diagnosis of exclusion that persist or recurs despite aggressive hemodialysis.[3] Chronic presence of pleural effusion induces atelectasis and entrapment of the lungs, as well as intermittent infections.[4,5] Most of the studies looking into the incidence of pleural effusion in patients with CKD are retrospective studies of hospitalized patients. Systemic approach to the investigations is needed because of the extensive

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differential diagnosis. So in the present study, we studied the occurrence, causes, clinical features of pleural effusion in patients with CKD and that in non-CKD.

AIM AND OBJECTIVE

To analyse pleural fluid in Pleural effusion patient of chronic kidney disease and non chronic kidney disease,

Methodology

This hospital based prospective observational study was conducted between 1st December 2014 to 31st October2016, among patients with chronic kidney disease and pleural effusion in tertiary care hospital. This study included 150 cases which were previously diagnosed as a case of pleural effusion or were diagnosed during hospital stay. Out of 150 cases of pleural effusion, 11 (7.3%) cases were CKD with pleural effusion and 139 (92.7%) cases were non-CKD pleural effusion.

Inclusion Criteria

1. Patients of pleural effusion with chronic kidney disease.
2. Patient of pleural effusion due to non-chronic kidney disease.
3. Age ≥14 yrs.

Exclusion Criteria

1. Age <14 yrs.
2. Patient of chronic kidney disease without pleural effusion.
3. Patients with HIV.
4. Patients with bleeding disorders, pregnant females.
5. Patients not willing for thoracocentesis or not giving consent.

This study was approved by institutional ethics committee. Patient were explained regarding the study purpose in local language and written informed consent of patient was taken. A clinically suspected case of pleural effusion patient, diagnosed by chest X-ray and ultrasound chest. Patient enrolled in study were divided into two groups, pleural effusion with chronic kidney disease and pleural effusion with non-chronic kidney disease.. All patients were subjected to blood investigations including complete blood count, erythrocyte sedimentation rate (ESR), Blood sugar (BSL), complete renal profile including blood urea, serum creatinine, serum total protein, serum Na+, K+ (in CKD cases), and Liver function tests, HIV, HBsAg, HCV antibody and urine routine examination, 24 hour urine protein analysis (in CKD patients), chest x-ray, electrocardiogram (ECG). Sputum (if present) is sent for Z-N stain, Gram's stain, culture and sensitivity. Ultrasonography (USG) abdomen done to know renal size, corticomedullary differentiation (CMD), echostructure cyst and to evaluate liver, pancreas and whole abdomen grossly for malignancy. Renal doppler for renal blood flow (in selected cases). Thoracocentesis (USG guided, in septate effusion) is studied for the gross appearance, total TLC count, differential count (lymphocyte, polymorphonuclear neutrophils, mesothelial cells), protein, glucose, ADA, cytology, Gram staining and AFB staining, pleural fluid culture and CB-NAAT (cartridge based nucleic acid amplification test) or Gene Xpert. Pleural fluid was classified as exudative effusion or transudative effusion by applying LIGHT's Criteria[68] (pleural fluid protein divided by serum protein greater than 0.5).

RESULTS

Table 1: Pleural fluid microscopy in CKD and Non CKD

Etiology	WBC (Mean/dL)	Lymphocyte (Mean/dL)	Polymorphs ((Mean/dL)	P value
Chronic kidney Disease (N=11)	462.7± 242.44	55.45 ± 20.30	46 ± 20.74	X^2 = 13.73
Non-CKD (N=139)	792.42±200.53	49.87 ± 16.58	50.29 ± 12.71	P < 0.05

Table 2: Pleural fluid microscopy in non-CKD etiologies

Etiology	WBC (Mean/dL)	Lymphocyte (Mean/dL)	Polymorphs (Mean/dL)
Pulmonary Tuberculosis(N=54)	308.39 ± 57.64	74.81 ± 15.59	26.04 ± 17.17
Parapneumonic Effusion (N=33)	1388.2 ± 158.5	16.9 ± 12.35	83.1 ± 24.78
Malignancy (N=20)	870.70 ± 404.25	74.5 ± 11.68	25.5 ±11.68
Congestive cardiac failure (N=16	134 ± 18.62	60.62 ± 7.00	39.37 ± 7.00
Liver cirrhosis	249.6 ± 74.2	60 ± 10	40 ±10
Other*(N=5)	689.4 ± 470.5	50.8±21.3	49.2±21.3
Total	**792.42 ± 200.53**	**49.87 ± 16.58**	**50.29 ± 12.71**

Other*-includes hypothyroidism (1case), undiagnosed (1 case), chronic pancreatitis (2 cases), postoperative (perforation peritonitis) pleural effusion case (1case).

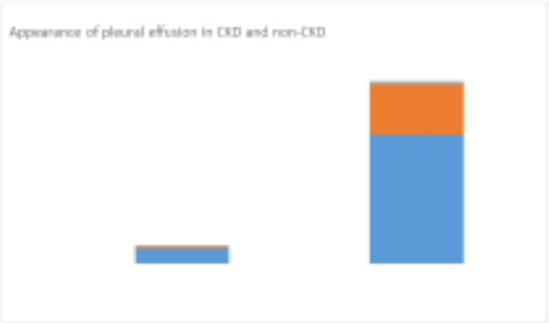

Figure 1: Appearance of pleural effusion in CKD and non-CKD

Table 3: Pleural fluid Protein, Sugar, ADA in CKD and non-CKD

Etiology	Sugar (mg/dL)	Protein (mg/dL)	ADA (IU/L)	P value
Chronic Kidney Disease	43 ± 8.49	3.1 ± 0.67	37.63 ± 23.28	X^2 = 0.022
Non- CKD	42.49 ± 8.34	3.25 ± 0.4	35.87± 9.36	P >0.05

Table 4: Pleural fluid Glucose, protein and ADA in non-CKD

Etiology	Glucose (mg/dL)	Protein (mg/dL)	ADA (IU/L)	P value
Pulmonary Tuberculosis	48.52± 8.01	3.2 ± 0.32	67.51± 17.34	X^2 = 22.48
Parapneumonic Effusion	36.52± 7.9	3.86 ± 0.2	33.55± 6.16	P < 0.05
Malignancy	41.25± 4.70	3.01±0.47	24.05± 6.16	P < 0.05
Congestive cardiac failure	52 ± 14.97	2.7 ± 0.57	17.87± 2.41	
Cirrhotic effusion (N=5)	39.8 ± 1.8	2.44 ± 0.3	34.8 ± 3.8	
Other* (N=5)	40.5 ± 6.48	2.85 ±0.61	38.7± 14.77	

Table 5: Type of Pleural fluid in CKD and non-CKD pleural effusion

Etiology	Cases (N)	Transudative	Exudative	P value
Chronic Disease Kidney	11	03 (27.27%)	08 (72.72%)	X^2 = 0.45
Non- CKD	139	52 (37.4%)	87 (62.6%)	P > 0.05
Total	**150**	**55(36.7%)**	**95 (63.3%)**	

Table 6: Type of pleural fluid in non-CKD pleural effusion

Etiology	Cases (N)	Transudative	Exudative	P value
Pulmonary Tuberculosis	54	14 (25.92%)	40 (74.07%)	X^2 = 41.15
Parapneumonic Effusion	39	05 (12.82%)	34 (87.17%)	p < 0.05
Malignancy	20	13 (65%)	07 (35%)	
Congestive Failure cardiac	16	13 (81.25%)	03 (18.75%)	
Liver cirrhosis	05	05 (100%)	00 (0%)	
Pancreatitis	02	00 (0%)	02 (100%)	
Hypothyroidism	01	01 (100%)	00 (0%)	
Undiagnosed	01	01 (100%)	00 (0%)	
Postoperative	01	00 (0%)	01 (100%)	
Total	**139**	**52 (37.4%)**	**87 (62.6%)**	

Table 7: Pleural fluid culture

Etiology	Organism grown	No of Culture positive	No of culture negative	p-value
Chronic Kidney Disease (N-11)	S. pnemonae-01	01(9.09%)	10 (90.9%)	X^2=0.19
Non- CKD (N-139)	S. pnemonae-07	10 (7.19%)	129 (92.8%)	P >0.05
	S. aurius -02			
	E. coli -1			
Total (N-150)	**S. pnemonae-08**	**11 (7.33%)**	**138 (92%)**	
	S. aurius -02			
	E. coli -1			

In microscopic study of the pleural fluid in non-CKD etiologies lymphocytes are predominant in tubercular pleural effusion (74.81±15.59), malignancy (74.5 ± 11.68), cardiac failure (60.62 ± 7.00) and neutrophils are predominant in parapneumonic effusion (83.1 ± 24.78). The Mean ± SD of Total leucocyte count of tubercular pleural was 308.39±57.64 and Cardiac failure pleural effusion was 134±18.62. Figure 1. shows pleural fluid appearance in CKD and non-CKD. 81.81% cases of CKD pleural effusion were straw colored fluid and 79/139 (56.83%) non-CKD effusion cases were straw colored fluid. 1/11 cases of CKD pleural effusion were turbid fluid and 31/139 non-CKD effusion cases were turbid fluid. 1/11 (9.09%) cases of CKD pleural effusion were hemorrhagic fluid and 28/139 (20.14%) non-CKD effusion cases were hemorrhagic fluid. 79 (52.7%) cases of non-CKD pleural effusion were straw colored, 31 (22.3%) pleural fluid sample were turbid, and 29 (20.9%) sample were hemorrhagic. Among 139 non-CKD effusion, in tubercular effusion 44/54 (81.5%) pleural fluid sample were straw colored and 10/54 (18.5%) sample were hemorrhagic. In parapneumonic effusion, 08/39 (20.5%) pleural fluid sample were straw colored, 31/39 (79.5%) samples were turbid. In malignant effusion, 1/20 (5%) pleural fluid sample was straw colored and 19/20 (95%) samples were hemorrhagic effusion. In cardiac effusion all 16/16 (100%) sample were straw colored. Table 3 shows pleural fluid sugar,

protein and ADA level in CKD effusion and non-CKD effusion. In pleural effusion with CKD, pleural fluid sugar was 43 ± 8.49 mg/dL, protein 3.1 ± 0.67 mg/dL and ADA 37.63 ± 23.28 IU/L. In pleural effusion with non-CKD, pleural fluid sugar was 42.49 ± 8.34 mg/dL, protein 3.25 ± 0.4 mg/dL and ADA 35.87± 9.36IU/L. In non-CKD pleural effusion, tubercular pleural fluid glucose was 48.52 ± 8.01 mg/dL, protein 3.2 ± 0.32 mg/dL and ADA 67.51 ± 17.34 IU/L, parapneumonic pleural fluid glucose was 36.52 ± 7.9 mg/dL, protein 3.86 ± 0.2 mg/dL and ADA 33.55 ± 6.16IU/L, malignant pleural fluid glucose was 41.25 ± 4.70 mg/dL, protein 33.01±0.47 mg/dL and ADA 24.05 ± 9.32IU/L, cardiac failure pleural fluid glucose was 52 ± 14.97mg/dL, protein 2.7 ± 0.57 mg/dL and ADA 17.87 ± 2.41IU/L. Out of 150 pleural effusion samples, 55/150 (36.7%) pleural fluid samples were transudative and 95 (63.3%) were exudative. In CKD with pleural effusion, 03/11 (27.27%) pleural fluid samples were transudative and 08/11 (72.72%) were exudative. In non-CKD with pleural effusion, 52/139 (37.4%) pleural fluid sample were transudative and 87/139 (62.6%) samples were exudative. Table 6. shows type of pleural fluid in non-CKD etiologies. Out of 139 non-CKD pleural effusion samples, 52/139 (37.4%) pleural fluid sample were transudative and 87/139 (62.6%) samples were exudative. In tubercular effusion, 14/54 (25.92%) pleural fluid sample were transudative and 40/54 (74.07%) samples were exudative. In parapneumonic effusion, 05/39 (12.82%) pleural fluid sample were transudative and 34/39 (87.17%) samples were exudative. In malignant effusion, 13/20 (65%) pleural fluid sample were transudative and 07/20 (35%) samples were exudative. In cardiac failure effusion, 13/16 (81.25%) pleural fluid sample were transudative and 03/16 (18.75%) samples were exudative. In cirrhotic effusion, 05/05 (100%) pleural fluid sample were transudative. In pancreatic effusion, 2/2 (100%) samples were exudative. Hypothyroidism 01/01 (100%), undiagnosed 01/01 (100%) pleural fluid samples were transudative. Gram stain was positive in 7/150 (4.6%) pleural fluid sample. CKD pleural fluid does not stained any organism. In non CKD pleural effusion, 05/139 (3.26%) pleural fluid samples demonstrate Gram positive organisms and 2/139 (1.33%) samples demonstrate Gram negative organism. Total 40/150 (26.7%) (Sputum + pleural fluid) demonstrate Acid fast bacilli (AFB) in Z-N staining. 3/11 (27.27%) patient with CKD with pleural effusion were sputum positive for Acid Fast bacilli (AFB). 37/139 (26.6%) pleural effusion patient with non CKD were sputum positive for AFB. All pleural fluid Z-N staining found negative for AFB. Table 7 - shows the result of culture of pleural fluid in CKD and non-CKD. A total of 11 (7.33%) were culture positive. Also 1/11 (9.09%) pleural fluid sample shows growth of organisms in CKD patient while 10/139 (7.19%) in non-CKD effusion. Total 8 pleural fluid samples found culture positive for S. pneumoniae, 02 were S. aurius and 01 were E. coli. Out of all 11 (20.37%) NCKD cases found CB-NAAT positivity.

DISCUSSION

Pleural fluid microscopy was showed in table 1 and 2. Arup I. [7] found mean of TLC of tubercular pleural was 327.50±114.75, parapneumonic pleural effusion was 1712.00±1167.80 and mean of DLC (PMN and lymphocyte) of tubercular pleural effusion was and 19±1, parapneumonic effusion was 81±1 and 21±1, respectively. Mridul B.[8] found mean pleural fluid cell count in tubercular, malignant, transudative and synpneumonic are 1061±410, 574±190, 139±31 and 1332±571 respectably. Predominance of polymorph cells indicates acute process (pneumonia) affecting the pleura and lymphocyte indicates chronic disease like tuberculosis, malignancy.[9] In tubercular pleural effusion lymphocytes are predominant (>74%). But lymphocytic pleural effusion also common in cancer, rheumatoid pleurisy, lymphoma etc.[10] From Spain Castro *et al*.[11] also reported that lymphocytic exudate which was seen with tubercular pleuritis, also occur with other diseases such as malignancy and collagen vascular diseases. Figure 1 shows pleural fluid appearance in CKD and non-CKD. 9/11 (81.81%) cases of CKD pleural effusion fluid were straw colored and 79/139 (56.83%) non-CKD effusion cases were straw colored fluid. In Premkumar A[12.] pleural fluid appearance 15 (48.9%) were straw colored, 9 (25.7%) were hemorrhagic and 4 (11.4%) were turbid. No difference is found in appearance of pleural fluid in pleural effusion in CKD and non CKD. ($p>0.05$). In comparison with the study Victoria villena *et al*.[13] majority of effusions were straw colored of which tuberculosis (74%) and transudates (67%) were predominant and 34% of malignant effusions were hemorrhagic. A. Islam [7] found parapneumonic pleural effusion 07 (70.0%) In tubercular pleural effusion pleural fluid Adenosine deaminase level (ADA) has got a good diagnostic index after excluding other causes of raised ADA levels. An ADA level less than 40IU/L very much unlikely of pleural tuberculosis. But different authors have used different cut off levels for pleural fluid ADA ranging between 33 IU/L to 50 IU/L. In comparison to other studies: Asmita Mehta *et al*.[14] >40U/l, S.K.Verma *et al*.[15] pleural fluid ADA 36U/l and Kalpana Dave *et al*.[16] pleural fluid ADA >60U/l was taken as diagnostic cut off for tuberculous effusion. Table no 5,6 shows type of pleural fluid in CKD and non-CKD. In CKD with pleural effusion, 03/11 (27.27%) pleural fluid samples

were transudative and 08/11 (72.72%) were exudative. Sourvik Ray [17] found exudative effusions and transudative effusions occurred with similar frequency (51% versus 48%). Jarratt and Sahn [18] also found in similar frequency. In study by Premkumar A.[12] patients with transudative effusion were 31%, exudative were 69%. In non-CKD with pleural effusion, 52/139 (37.4%) pleural fluid sample were transudative and 87/139 (62.6%) samples were exudative. Study by A. Premkumar[12] in patient of NCKD (N=35) found transudative pleural effusions were 11(31.42%) and exudative pleural effusions were 24 (68.57%). No difference is found in type (transudative or exudative) of pleural fluid in pleural effusion in CKD and non CKD. ($p>0.05$). In NCKD the exudative pleural effusion were more significantly associated with tubercular effusion [40/54 (74.07%)] and The transudative with malignant effusion [13/20 (65%)]. There is significant association in difference type of pleural fluid indifferent etiologies of pleural effusion in non-CKD. ($p < 0.05$). Gram stain was positive in 7/150 (4.6%) pleural fluid sample. Arup I. [7] describes that gram stain was positive in 3% pleural fluid. 5 samples were gram stain positive which was 5% of the total cases Barnes *et al*.[19] from USA also found gram stain positive is 2.5% cases. Boersma *et al*.[20] found gram stain positive in 2 cases out of total 9 cases. Total 40/150 (26.7%) (Sputum + pleural fluid) demonstrate Acid fast bacilli (AFB) in Z-N staining. 3/11 (27.27%) patient with CKD with pleural effusion were sputum positive for Acid fast bacilli (AFB). 37/139 26.6%) pleural effusion patient with non CKD were sputum positive for AFB. All pleural fluid Z-N staining found negative for AFB. Arup I[7] and Hasaneen *et al*.[21] from Egypt also found sensitivity of AFB stain of pleural fluid was 0%. Boersma *et al*.[22] found gram stain positive in 2 cases out of total 9 case. Vorster *et al*.[23] microscopy for AFB in the pleural fluid can identify M. tuberculosis in fewer than 10% of cases. No difference is found in Z-N staining of pleural fluid and sputum in pleural effusion in CKD and non CKD. ($p>0.05$) Total 8 pleural fluid samples found culture positive for S. pneumoniae, 02 were S. aurius and 01 were E. coli. A. Islam *et al*.[24] S. pneumoniae was culture positive in 3% cases of the total 100 cases. Kawanami *et al*.[25] reported that rate of detection of bacteria on cultivation method always <20%. Boersma *et al*. found culture positive in 1 case out of total 9 parapneumonic cases [22]. Eastham *et al*.[26] found 94% pleural fluids were culture negative in ordinary bacteriological media.[26] No difference is found in culture of pleural fluid in pleural effusion in CKD and non CKD. ($p>0.05$) 11 cases found CB-NAAT positivity in non-CKD with pleural effusion. Gopi *et al*.[27] from India reported that PCR sensitivity as 20 to 90% and specificity from 78 to 100%, Ferrer[28] from Spain also found sensitivity of PCR was 20-81% and specificity 78-100%.[27,29,28]

CONCLUSION

Exudative pleural effusion were common in both CKD and non-CKD pleural effusion. Straw color pleural fluid were most common in tubercular effusion and hemorrhagic fluid found in malignancy. There were no difference found in pleural fluid protein, sugar and ADA in pleural effusion with CKD and non-CKD. Pleural fluid Z-N staining for AFB not so much useful in diagnosing tubercular effusion

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