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Original Research Article**A study of respiratory manifestations in chronic kidney disease****Venkatesh Moger¹, Arun B S^{*2}, Suresh H³, and Sagar Reddy S. L.⁴**¹Associate Professor, Department of Nephrology, Karnataka Institute of Medical Sciences, Hubli, Karnataka State, India 580022²Assistant Professor, Department of Internal Medicine, MVJ MC & RH, Bangalore, Karnataka State, India- 562114³Associate Professor, Department of Cardiology, Karnataka Institute of Medical Sciences, Hubli, Karnataka State, India 580022⁴Junior Resident, Department of Internal Medicine, Karnataka Institute of Medical Sciences, Hubli, Karnataka State, India 580022

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***Correspondence Info:**Dr. Arun B.S.,
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MVJ MC & RH, Bangalore, Karnataka State, India- 562114***Article History:****Received:** 18/01/2017**Accepted:** 11/02/2017**DOI:** <https://dx.doi.org/10.7439/ijbr.v8i2.3876>**Abstract****Introduction:** Diseases of the kidneys can intimately affect lungs by multiple pathological mechanisms, and adversely affect outcome in these patients.**Objectives:** To study the prevalence of various respiratory diseases in the patients with CKD.**Methods:** One hundred patients with CKD who were being treated at KIMS, Hubli, from 1st October 2015 to 30th June 2016 were considered for the study. Clinical evaluation and relevant investigations including chest radiography, USG chest, CT chest, sputum analysis, pleural fluid analysis and pulmonary function test were done. Echocardiography was done to assess left ventricular function. Polysomnography was done in selected patients.**Results:** Mean age of study population was 45.50± 13.25 yrs. Sex ratio was 55:45 (M:F). Respiratory diseases were prevalent in 70% of them, commonest being Pulmonary edema (67%), followed by pleural effusion (54%). Pleural effusion was predominantly right sided and transudative. Pulmonary tuberculosis was present in 6% and tuberculous pleural effusion in 2%. Pneumonia occurred in 5% of them. Pleural thickening was present in 11%. Pulmonary calcification was noted by chest X-ray and CT chest in 13%. Sleep apnea was present in 12 out of 20 patients studied. (60%). 2 patients with pneumonia and tuberculosis did not have classical symptoms.**Conclusion:** The prevalence of respiratory diseases is substantially high in patients with CKD and carries adverse outcome in relation to patient management.**Keywords:** CKD, Pulmonary edema, Pulmonary tuberculosis, pleural calcification sleep apnea.**1. Introduction**

The relationship between the lungs and the kidneys are clinically important in both health and disease. A number of complications related to the respiratory system occur in patients with chronic kidney disease (CKD).[1] Some of these are related to alterations in volume status, plasma oncotic pressure, bone and mineral metabolism, concomitant heart failure, and altered immune function in such patients, although in other instances the precise mechanisms are not well understood.[2]

There are limited studies reported on respiratory manifestations of CKD, which have protean presentations. Hence, this study was conducted in our institute, Karnataka Institute of Medical Sciences, a Government run Tertiary care hospital and Medical college at Hubli, Karnataka.

1.1 Objectives

To know the prevalence of various respiratory diseases and their presentation in the patients with CKD.

2. Designs and Settings

It was a cross-sectional observational study conducted at Karnataka Institute of Medical Sciences, from 1st October 2015 to 30th June 2016. One hundred patients with CKD were considered for the study after explaining the objectives of the study. Informed written consent was taken from all of them. The study was conducted after obtaining the approval by the Institute Ethics Committee.

2.1 Inclusion criteria

1. CKD diagnosed based on 'KDIGO 2012 Clinical Practice Guidelines for the Evaluation and Management of CKD'.

2. Those aged 18 years or more.

2.2 Exclusion criteria

1. Those who were not willing to participate in the study.

2. Those with respiratory disease onset before the diagnosis of CKD.

3. Age less than 18 years.

4. Valvular heart diseases.

5. Congenital heart diseases.

6. Connective tissue diseases.

7. Hypothyroidism and Hyperthyroidism.

2.3 Methods

2.3.1 Protocol

The history was obtained from the patients with special reference to the symptoms of CKD and respiratory disease, co-morbid conditions, duration of diagnosis of CKD and duration of hemodialysis. Clinical examination was done with emphasis on signs of CKD and respiratory diseases.

Each subject underwent the following investigations: Renal function tests, chest X-ray, ultrasonography of thorax and CT chest as indicated. Sputum examination, pleural fluid analysis, pulmonary function test were done. Echocardiography was done to look for left ventricular function. Sleep study was conducted in selected patients.

2.3.2 Statistical analysis

The continuous variables were expressed in terms of mean \pm S.D. The categorical measurements were expressed in number (percentage).

3. Results

3.1 General characteristics

Mean age of the study population was 45.50 \pm 13.25 years (mean \pm SD). Majority were of the age 41 years to 50 years (60%). Majority of the patients were in stage 5 CKD. [Table 1]

Table 1: General characteristics of the patients studied

	Variables	Data
1.	Age (years)	
	Mean \pm SD	45.50 \pm 13.25
	Range	18-65
2.	Sex ratio(M:F)	55:45
3.	Hypertension	74%
4.	Diabetes mellitus	43%
5.	Anemia	96%
6.	CKD stages [No. (%)]	
	Stage 3	4%
	Stage 4	7%
	Stage 5	89%
7.	Mean duration of CKD (weeks)	48.65 \pm 24.32
8.	Mean duration of hemodialysis (Weeks)	38.95 \pm 28.73

3.2 Clinical findings

Dyspnea was the most common respiratory symptom (89%), followed by cough (64%). Prevalence of other symptoms is depicted in Table 2.

Table 2: Prevalence of various symptoms and signs in the patients studied.

	Symptoms	No of Patients (n=100)
1.	Dyspnea	89
2.	Paroxysmal nocturnal dyspnea	54
3.	Orthopnea	23
4.	Fatigue	85
5.	Cough	64
6.	Pedal edema	54
7.	Abdominal distension	40
8.	Chest pain	33
9.	Cyanosis	9
10.	Fever	8
11.	Hemoptysis	6
12.	Hiccough	5
14.	Pleuritic pain	4
15.	Pleural rub	3

3.3 Respiratory diseases in the patients studied.

Most common respiratory manifestation was pulmonary edema, prevalent in 67%, followed by pleural effusion (54%). Rests of the manifestations are as depicted in Table 3.

Table 3: Prevalence of various respiratory manifestations in the patients studied.

	Respiratory diseases	No .of patients (n=100)
1.	Pulmonary edema	67
2.	Pleural effusion	54
3.	Pleuritis	12
4.	Pulmonary Tuberculosis	6
5.	Pleural tuberculosis	2
6.	Pneumonia	5

Tuberculosis was present on 8 of them. 3 of them had pulmonary cavity and where positive for Acid Fast Bacilli in sputum. 2 patients had diffuse pulmonary infiltrates and 1 had military mottling. 1 of these patients with pulmonary tuberculosis had disseminated tuberculosis in form of tuberculous meningitis. All of them had cough as a predominant complaint. Fever was present in 3 out of 8 patients (37.5%). 1 patient had minimal cough as the only presenting cough.

1 patient had exclusively extrapulmonary tuberculosis in the form of cervical tuberculous lymphadenitis. He presented with neck swelling with no fever.

In our study pneumonia was present in 5%, 3 patients had lobar pneumonia and 2 had bronchopneumonia. 3 of them had cough and low grade fever. 2 were asymptomatic. Sputum culture showed Streptococcus pneumoniae in 3 of them.

Chest X-ray revealed pulmonary calcification in 13 of them, majority of whom were asymptomatic. (10 out of 13) It was predominantly in the form of nodular opacification.

Pleural calcification and thickening was present in 11 of them. 4 of them had history of pleuritic pain. [Table 3] Pleural effusion was predominantly right sided, moderate and transudative. Massive effusion was present in 9, all of whom had marked dyspnea. Elevated Adenosine deaminase, suggestive of tuberculous etiology was found in 4 of them. [Table 4]

Sleep apnea was evaluated by Polysomnography in 20 patients, as majority was not willing due to financial constraints and it was present in 12 of them (60%).

Echocardiography revealed left ventricular failure in 81%, predominantly diastolic dysfunction in 72% and systolic dysfunction in 23%. All patients with pulmonary edema had left ventricular diastolic dysfunction and 23 of them (34.3%) had systolic dysfunction.

Spirometric study among the patients with pulmonary edema revealed restrictive pattern in all of them, while obstructive pattern in 10 of them.

Table 4: Radiological findings in the patients studied

	Findings	No. of patients. (n=100)
1	Pulmonary hypertension	32
2	Cardiomegaly	24
3	Pleural effusion	54
4	Pulmonary edema	62
5	Cavitary lesion	2
6	Pleural thickening	11
7	Pulmonary calcification	13
8	Consolidation	3
9	Pulmonary infiltrates	2
10	Interstitial lung disease	2

Table 5: Investigation findings in pleural effusion

		No. of patients (n=54)
1	Grades of pleural effusion	
	Mild	10
	Moderate	35
	Massive	9
2	Unilateral effusion	42
	Right	40
	Left	12
3	Bilateral effusion	12
4	Recurrent pleural effusion	12
5	Hemorrhagic effusion	3
6	Transudative effusion	30
7	Exudative effusion	24
8	Elevated Adenosine deaminase	2

4. Discussion

Respiratory diseases are quite common in CKD and were detected in 70% of our patients.

4.1 Pulmonary edema

It is a common complication in CKD, especially in ESRD, contributing to high morbidity and mortality in these patients. In our study it was present in 67% of patients and was the most common respiratory manifestation. In majority it used to be recurrent and presented with dyspnea, paroxysmal nocturnal dyspnea and orthopnea.

Its etiopathogenesis is multifactorial. Hypoalbuminemia, a characteristic of CKD, decreases plasma oncotic pressure and thus cause movement of fluid out of the pulmonary capillaries into interstitium and then into alveoli. Such movement is also promoted by the increased hydrostatic pressure that occur secondary to left ventricular failure, which is common in CKD.[1]

The capillary permeability is also altered.[1,2] Such a suggestion is supported by the occurrence of pulmonary edema in patients who are clinically euvolemic.[1] In our study, pulmonary edema was present in 13 out of 40 euvolemic patients.

Left ventricular failure and other cardiac diseases are common in CKD contributing to pulmonary edema.[1,2] In our study, left ventricular failure was present in 81%. Among the patients with pulmonary edema, diastolic dysfunction was present in all of them and systolic dysfunction 34.3%. Both forms of left ventricular failure cause elevation in left ventricular filling pressure leading to elevated pulmonary capillary pressure, which causes pulmonary edema. Left ventricular failure affects 50-70% of patients with CKD and upto 90% of patients with end stage renal disease. [3,4]

Pulmonary congestion and edema in CKD patients is associated with a restrictive pattern on pulmonary function testing, and reduced airflow can also be observed on spirometry. In our study, among the patients with

pulmonary edema, restrictive pattern was present in all of them, while obstructive pattern in 10 of them. These abnormalities have been demonstrated to improve with hemodialysis.[1]

These observations would suggest that increased lung water results primarily from overall hypervolemia in the presence of low serum albumin levels and increased pulmonary capillary hydrostatic pressure and accounts for the symptoms and signs traditionally associated with "uremic lung." [1,5]

4.2 Pleural effusion

Pleural disease is common in CKD. Pleural effusion was the second most common respiratory manifestation found in our study, occurring in 54%. It was predominantly right sided and transudative. It was of tuberculous etiology was found in 2 of them. Cardiac evaluation revealed heart failure in 40 of these 54 patients (74.07%). 12 of them had associated ascites (22.2%). 45 of them had anasarca (83.3%).

In a study conducted by Ray *et al*[6], it was found that pleural effusion was found in 29 out of 430 patients with CKD (6.7%). Exudates and transudates were found in equal frequencies. Heart failure was the single most common cause (41.9%).

Although effusion is typically exudative, in our study transudative effusion was more common than exudative.

Dyspnea was the common symptom found in these patients, being present in all with massive effusion and 21 of 35 patients (80%) of moderate effusion and 3 of 10 patients (30%) of those with mild effusion. All those with mild effusion also had pulmonary edema, which could be the cause of their dyspnea.

4.3 Pleuritis

Pleuritis was present in 12 of our patients. 8 of them had pleuritic pain. 4 were asymptomatic. Pleural rub was present in 3 of them. Fairshier *et al*[7] and Nidus BD *et al*⁸ have demonstrated fibrinous pleuritis to be present in 20-40% of autopsy specimens.[1]

4.4 Tuberculosis

Patients with CKD are immunocompromised. Compared to the general population, patients with CKD and those on maintenance dialysis have at least a several-fold greater risk of developing tuberculosis. In our study it was present in 8% of patients. 6 of them had pulmonary tuberculosis and 2 of them tuberculous pleural effusion. Extrapulmonary tuberculosis was present in 2 patients, one each with tuberculous meningitis and tuberculous lymphadenitis. Few had subtle presentation.

Host resistance to infection is primarily mediated by cellular immunity which is deficient in patients with CKD. Fever, malaise and cough were the predominant

symptoms among them. The occurrence of infections including tuberculosis is therefore high in such patients. The incidence of TB in patients on CKD has been reported to be 6 to 16 times that of general populations.[9] Venkata *et al* studied tuberculosis in CKD patients and found 4% incidence.[10]

4.5 Pneumonia

In our study pneumonia was present in 5%, 3 patients had lobar pneumonia and 2 had bronchopneumonia. Streptococcus pneumonia was the commonest organism. Che-Yi Chou[11] conducted a study to assess the risk of pneumonia among patients with CKD and found that incidence density rate of pneumonia was 65.6 per 1000 person-years in patients with CKD and 28.4 per 1000 person-years in individuals without CKD. Patients' comorbidities, including diabetes, asthma, chronic obstructive pulmonary disease and cardiovascular disease were independently associated with increased risk of pneumonia.

4.6 Pulmonary Calcification

Metastatic calcification occurs as a CKD, and may be found in a wide variety of visceral organs and soft tissues. When it occurs in the lungs, it is usually asymptomatic. When visible on the chest radiograph, pulmonary calcification most often produces small nodular opacities, which may occasionally coalesce into larger infiltrates.[1] In our study it was noted in 13% of patients.

4.7 Sleep Apnea

Sleep apnea is extremely common in patients with CKD. Its prevalence is said to be 10- fold higher in patients with end-stage renal disease than in general population. In our study, its prevalence was 60%.

Studies have found that at least 60% of patients on CKD have this disorder.[12,13] Other sleep disturbances, such as restless leg syndrome and periodic limb movement disorder, are also very common in this population. Several potential explanations have been proposed, but the mechanism remains unknown. There appears to be a strong link between sleep apnea and nocturnal hypoxemia and cardiovascular complications in patients with CKD. Hemodialysis during the night is found to have an ameliorating effect on sleep apnea.[13,14] Continuous positive airway pressure is effective is an effective treatment.[14,15]

5. Conclusion

This study concludes that substantial number of patients with CKD suffers from respiratory diseases, most common of which is pulmonary edema, followed by pleural effusion. Etiologies of these are multifactorial. These two manifestations can be secondary to LV failure. Dyspnea is the most common symptom. Pulmonary edema and pleural

effusion are recurrent in these patients and sometimes refractory to treatment.

Tuberculosis is several fold increased prevalence in these patients, and may cause overlapping symptoms with CKD, like dyspnea and cough and can have subtle presentation. Hence high degree of suspicion is needed.

Conflicts of interest: All authors have none to declare.

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