

Original Research Article


Association between chronic kidney disease and tuberculosis - A prospective study form a tertiary care teaching hospital

G. Elango¹, C. Ramesh², D.D. Venkataraman^{3*}

¹Professor of General Medicine, ²Professor of Chest and TB Medicine, ³Professor and HOD of General Medicine

Dhanalakshmi Srinivasan Medical College and Hospital, Siruvachur, Perambalur, India

*Corresponding author email: dd.venkataramana@gmail.com

	International Archives of Integrated Medicine, Vol. 4, Issue 9, September, 2017. Copy right © 2017, IAIM, All Rights Reserved. Available online at http://iaimjournal.com/ ISSN: 2394-0026 (P) ISSN: 2394-0034 (O)
	Received on: 04-09-2017 Accepted on: 13-09-2017 Source of support: Nil Conflict of interest: None declared.
How to cite this article: G. Elango, C. Ramesh, D.D. Venkataraman. Association between chronic kidney disease and tuberculosis - A prospective study form a tertiary care teaching hospital. IAIM, 2017; 4(9): 164-170.	

Abstract

Background: Chronic kidney disease (CKD) is emerging as a major public health problem in India. The links between CKD and Tuberculosis have long been established but the exact nature of interaction is poorly understood. Bulk of the association was studied on subjects undergoing dialysis or renal transplantation, with limited studies on CKD subjects without dialysis. The amount of data is further scarce on Indian population. Hence the present study was conducted to assess the prevalence and profile of pulmonary tuberculosis in CKD patients presenting to a tertiary care teaching hospital in south India

Materials and methods: The present study was a prospective study of all the CKD patients presenting to a tertiary care teaching hospital in south India diagnosed with chronic renal failure, as per the hospital protocol. The data was collected from the prospective case records of all the CKD patients diagnosed between April 2015 to 2017.

Results: There were a total of 2927 patients with CKD, who satisfied the inclusion criteria and were included in the study. The average prevalence of tuberculosis among the study population was 1.16%. The age distribution of the tuberculosis cases have shown that highest proportion of subjects (47.05%) was aged above 60 years. There was a high male preponderance in study population, as 88.23% affected by tuberculosis were males and 11.77% were females. The most common x-ray finding was infiltration seen in 12 (35.29%) of the patients with TB. Cavities were present in 14 (41.17%) subjects- fibrosis was seen in 4 (11.76%) subjects. There was no statistically significant difference in blood urea nitrogen (BUN) or serum creatinine values between the two groups (P value > 0.05)

Conclusion: Chronic Kidney disease patients are at high risk of tuberculosis, as the prevalence in CKD patients is higher than that of general population. Considering the alterations in the immune system, the immunological response of the host to tuberculosis infection is altered in CKD patients- this makes routine investigations like sputum examination and mantoux test less reliable in CKD patients. Chest-X-ray may be more useful in these patients.

Key words

CKD, Uraemia, Tuberculosis, Immunity.

Introduction

Chronic kidney disease (CKD) is an important, chronic, non-communicable disease epidemic that affects the world, including India. There is dearth of reliable data on exact burden of chronic kidney diseases in the community in India, as there is no population based renal registry existing till recently. Some of the community based studies have reported a prevalence of chronic renal failure ranging from 0.16% and 1.39% [1-3].

But there were differences in the operational definition and methodology adopted etc. making these estimates less reliable for extrapolation to the national level. Recently published findings from first report of national renal registry has reported Diabetic nephropathy, followed by glomerulonephritis were the commonest causes, but significant chunk of CKD was of undetermined etiology [4]. A recently published large scale SEEK-India cohort study by Singh AK et al. have reported, overall prevalence of CKD as 17.2% among patients attending hospitals [5]. There are numerous media reports and grey literature regarding high incidence of chronic kidney disease in few pockets of the country linking it to the drinking water, exposure to industrial effluents etc. [6, 7].

Tuberculosis is another important major public health problem in India and in spite of decades of organized efforts the high burden of tuberculosis still continues in India [8]. Another major problem encountered in tuberculosis prevention in recent years is its synergy with other chronic disease like HIV infection, diabetes mellitus and chronic kidney diseases [9, 10]. Even though the

link between Tuberculosis and chronic kidney disease (CKD) is known for decades, the exact nature of interaction and cause and effect relationship between the two is poorly understood. TB screening and diagnostic test performance is also reported to be suboptimal in the CKD population, due to altered immune response [11].

Numerous studies have reported higher prevalence of TB in patients undergoing dialysis and renal transplant [12]. But the studies documenting the association between CKD patients not on dialysis or renal transplantation are very limited across the globe [13]. Further, the association between the tuberculosis and CKD is the least explored aspect in Indian population.

Objectives

To study the prevalence of pulmonary tuberculosis in CKD patients presenting to a tertiary care teaching hospital in south India.

Materials and methods

The present study was a prospective study of all the CKD patients presenting to a tertiary care teaching hospital in south India with symptoms suggestive of CKD and diagnosed with CKD as per the hospital protocol. The data was collected from the retrospective case records of all the CKD patients diagnosed between April 2015 to 2017.

The case records of the study subjects were meticulously reviewed for any associated symptoms suggesting of pulmonary tuberculosis like cough, difficulty in breathing, fever etc. The

data regarding the relevant investigation findings like, chest X-ray, Complete blood picture including ESR, Sputum examination results were reviewed and documented onto a structured proforma.

Any patients who were diagnosed either with sputum positive or negative pulmonary tuberculosis a positive for tuberculosis. The study was approved by institutional human ethics committee. Informed written consent obtained from all the participants.

The quantitative data was summarized as mean and standard deviation and categorical data was summarized as frequency and proportions. The association between the tuberculosis and renal function parameters (Blood urea nitrogen and serum creatinine) was assessed comparing the mean and standard deviation, using independent sample t-test. IBM SPSS statistical software version 21 was used for data analysis.

Results

There were a total of 2927 patients with CKD, who satisfied the inclusion criteria and were included in the study. The average prevalence of tuberculosis among the study population was 1.16%. Year wise analysis has shown that, the prevalence was 1.15% (0.63% to 2.11%) in year 2015, 1.16% (0.73% to 1.83%) in year 2016 and

1.18% (0.54% to 2.55%) in year 2017 (**Table - 1**).

The age distribution of the tuberculosis cases have shown that highest proportion of subjects (47.05%) were aged above 60 years. The proportion of subjects Blow 20 years was only 5.88%, 20.58% were aged between 21 to 40 years and the remaining 26.47% were aged between 41 to 60 years. There was a high male preponderance in study population, as 88.23% affected by tuberculosis were males and 11.77% were females (**Table - 2**).

The most common x-ray finding was infiltration seen in 12 (35.29%) of the patients with TB. Cavities were present in 14 (41.17%) subjects, fibrosis was seen in 4 (11.76%) subjects. The other findings seen on chest X-ray were cavity plus effusion and infiltration plus fibrosis seen in 2 (5.88%) subjects each (**Table - 3**).

The mean blood urea nitrogen in patients with TB was 65.38 ± 18.91 gm/dl and in non TB CKD cases it was 64.02 ± 17.21 . The difference in mean blood urea nitrogen values between the two groups were statistically not significant (P value 0.76). The mean serum creatinine in patients with TB was 2.71 ± 1.04 and in patients without TB was 2.39 ± 1.02 gm/dl, and the difference between the two groups was statistically not significant (P value 0.20) (**Table - 4**).

Table - 1: Year wise proportion of TB cases diagnosed among CKD patients in the study setting.

Year	No of CKD patients	No of TB patients	Proportion (95% CI)
2015	867	10	1.15% (0.63% to 2.11%)
2016	1550	18	1.16% (0.73% to 1.83%)
2017 (Till April)	510	6	1.18% (0.54% to 2.55%)
Total	2927	34	1.16% (0.83% to 1.62%)

Discussion

The current study was conducted to explore the possible association of tuberculosis and Chronic Kidney Disease in a tertiary hospital located in south India, with high incidence of CKD in the community. The average prevalence of tuberculosis among the study population was

1.16% (0.83% to 1.62%) in the study population and there was no increasing or decreasing trend in the prevalence during the three year study period. The reported prevalence in the study was lesser than the prevalence reported by few other Indian studies. Venkata RK, et al. [14] have reported a prevalence of 4% in their study of

over 900 chronic renal failure patients. Ostermann M, et al. [15] have reported a Cumulative incidence of TB of 1267/100,000 in hemodialysis patients. Lee SS, et al. [16] have reported Compared to the healthy controls, a high prevalence of Latent TB infection (62.5%) among ESRD patients undergoing haemodialysis patients. But the key reasons for this huge difference in the prevalence was due to the nature of the study population included, the diagnostic approach used and the spectrum of the

tuberculosis included in the study. Whereas the current study was only limited to pulmonary tuberculosis and primary modes of evaluation was only done by chest radiography, sputum examination and Mantoux. But the other studies have included patients on dialysis, and used immunological methods for the diagnosis of tuberculosis, which are much more sensitive than the methods used in current study. Including entire spectrum of tuberculosis was also another important reason.

Table - 2: Age and gender distribution of the Tuberculosis cases among CKD patients (N=34).

Parameter	Number	Proportion
Age group		
Below 20	2	5.88%
21 to 40	7	20.58%
41 to 60	9	26.47%
Above 60	16	47.05%
Gender		
Male	30	88.23%
Female	4	11.77%

Table - 3: Radiological findings in Study population (N=34).

Parameter	Number	Proportion
Chest X-ray findings		
Infiltration	12	35.29%
Cavity	14	41.17%
Fibrosis	4	11.76%
Cavity plus effusion	2	5.88%
Infiltration plus fibrosis	2	5.88%
Sputum for AFB		
Positive	8	23.52%
Negative	26	76.47%
Monteux		
Less than 5 mm	6	17.64%
5 to 10 mm	19	55.88%
More than 10 mm	9	26.47%

Table - 4: Comparison of mean Blood urea and serum creatinine levels between Tuberculosis and non-tuberculosis CKD patients.

Parameter	TB cases among CKD (Mean ±SD)	Non TB CKD cases (Mean ±SD)	P value
Blood Urea	65.38 ± 18.91	64.02 ± 17.21	0.76
Serum Creatinine	2.71 ± 1.04	2.39 ± 1.02	0.20

But the prevalence of TB reported in the CKD patients is considerably higher than the general population in India which is reported to be about 0.5% in general population, less than half of the reported prevalence in current study [17]. Patients with advanced kidney disease are susceptible to tuberculosis infection and disease. Immunity is impaired in CKD patients through reduced function of T and B cells and neutrophils. But the key issues which have to highlight are insignificant mantoux, and equivocal blood counts and high reliance on chest x-ray in the current study for tuberculosis diagnosis. This would have resulted in significant underestimate of true burden.

The age distribution of the tuberculosis cases have shown that no age group is immune to tuberculosis among CKD patients and the highest proportion of subjects (47.05%) were aged above 60 years. There was a high male preponderance in study population, as 88.23% affected by tuberculosis were males and 11.77% were females This was in line with findings from study by Venkata RK, et al. [14], which has reported age range of 25 - 77 years and high male preponderance of 33 : 3 ratio. Other studies done on CKD patients have also revealed similar findings [13, 18, 19].

Our patient's population of CKD positive chest x-ray findings confirmed tuberculosis while history and TST were non-specific. The most common x-ray finding was infiltration seen in 12 (35.29%) of the patients with TB. Cavities were present in 14 (41.17%) subjects, fibrosis was seen in 4 (11.76%) subjects. In the current study no differences were found between TB and Non TB subjects, with respect to renal function parameters. These findings are in contrast to studies by Ostermann M, et al. [15] and Shu CC, et al. [12] which have documented high proportion of TB subjects to have higher grade of CKD with poorer renal function compared to non TB subjects.

But there are many debatable aspects of the association between the two diseases. As many

studies have debated the cause and effect relationship and the role of other co-morbidities like diabetes, HIV or vitamin D deficiency while assessing the association between CKD and tuberculosis. A recent meta-analysis Rogerson TE, et al. [20] and Al-Efraij K, et al. [13] have clearly highlighted this issue. Hence TB in patients with CKD continue to be challenging and screening for both active and latent TB is essential and also it is essential to evaluate the relative contribution by various Co morbidities.

Conclusion

Chronic Kidney disease patients are at high risk of tuberculosis, as the prevalence in CKD patients is higher than that of general population. Considering the alterations in the immune system, the immunological response of the host to tuberculosis infection is altered in CKD patients, which makes routine investigations like sputum examination and mantoux test less reliable in CKD patients. Chest-X-ray may be more useful in these patients.

Limitations

- Considering the limited resource availability, extensive battery of investigations required could not be done in study population, hence the reported prevalence may be an underestimate of actual burden of tuberculosis in CKD patients.

Recommendations

Clinicians should have high index of suspicion for tuberculosis in CKD patients and also should be aware of the atypical presentation. Timely screening of CKD patients for tuberculosis and initiation of treatment may have tremendous positive impact on the morbidity and mortality.

References

1. Agarwal SK. Chronic kidney disease and its prevention in India. *Kidney international Supplement*, 2005; 98: S41-5.

2. Mani MK. Experience with a program for prevention of chronic renal failure in India. *Kidney international Supplement*, 2005; 94: S75-8.
3. Agarwal SK, Dash SC, Irshad M, Raju S, Singh R, Pandey RM. Prevalence of chronic renal failure in adults in Delhi, India. *Nephrology, dialysis, transplantation: official publication of the European Dialysis and Transplant Association - European Renal Association*, 2005; 20(8): 1638-42.
4. Rajapurkar MM, John GT, Kirpalani AL, Abraham G, Agarwal SK, Almeida AF, et al. What do we know about chronic kidney disease in India: first report of the Indian CKD registry. *BMC nephrology*, 2012; 13: 10.
5. Singh AK, Farag YM, Mittal BV, Subramanian KK, Reddy SR, Acharya VN, et al. Epidemiology and risk factors of chronic kidney disease in India - results from the SEEK (Screening and Early Evaluation of Kidney Disease) study. *BMC nephrology*, 2013; 14: 114.
6. Reddy DV, Gunasekar A. Chronic kidney disease in two coastal districts of Andhra Pradesh, India: role of drinking water. *Environmental geochemistry and health*, 2013; 35(4): 439-54.
7. Siddarth M, Datta SK, Mustafa M, Ahmed RS, Banerjee BD, Kalra OP, et al. Increased level of organochlorine pesticides in chronic kidney disease patients of unknown etiology: role of GSTM1/GSTT1 polymorphism. *Chemosphere*, 2014; 96: 174-9.
8. John TJ, Vashishtha VM, John SM. 50 years of tuberculosis control in India: progress, pitfalls and the way forward. *Indian pediatrics*, 2013; 50(1): 93-8.
9. Martinez N, Kornfeld H. Diabetes and immunity to tuberculosis. *European journal of immunology*, 2014; 44(3): 617-26.
10. Chiang CY, Bai KJ, Lin HH, Chien ST, Lee JJ, Enarson DA, et al. The influence of diabetes, glycemic control, and diabetes-related comorbidities on pulmonary tuberculosis. *PloS one*, 2015; 10(3): e0121698.
11. Romanowski K, Clark EG, Levin A, Cook VJ, Johnston JC. Tuberculosis and chronic kidney disease: an emerging global syndemic. *Kidney international*, 2016; 90(1): 34-40.
12. Shu CC, Hsu CL, Lee CY, Wang JY, Wu VC, Yang FJ, et al. Comparison of the Prevalence of Latent Tuberculosis Infection among Non-Dialysis Patients with Severe Chronic Kidney Disease, Patients Receiving Dialysis, and the Dialysis-Unit Staff: A Cross-Sectional Study. *PloS one*, 2015; 10(4): e0124104.
13. Al-Efraij K, Mota L, Lunny C, Schachter M, Cook V, Johnston J. Risk of active tuberculosis in chronic kidney disease: a systematic review and meta-analysis. *The international journal of tuberculosis and lung disease : the official journal of the International Union against Tuberculosis and Lung Disease*, 2015; 19(12): 1493-9.
14. Venkata RK, Kumar S, Krishna RP, Kumar SB, Padmanabhan S, Kumar S. Tuberculosis in chronic kidney disease. *Clinical nephrology*, 2007; 67(4): 217-20.
15. Ostermann M, Palchadhuri P, Riding A, Begum P, Milburn HJ. Incidence of tuberculosis is high in chronic kidney disease patients in South East England and drug resistance common. *Renal failure*, 2016; 38(2): 256-61.
16. Lee SS, Chou KJ, Su IJ, Chen YS, Fang HC, Huang TS, et al. High prevalence of latent tuberculosis infection in patients in end-stage renal disease on hemodialysis: Comparison of QuantiFERON-TB GOLD, ELISPOT, and tuberculin skin test. *Infection*, 2009; 37(2): 96-102.
17. Chakraborty AK. Epidemiology of tuberculosis: current status in India. *The Indian journal of medical research*, 2004; 120(4): 248-76.

18. Fang H, Lee P, Chen C, Wu M, Chou K, Chung H. Tuberculosis in patients with end-stage renal disease. The International Journal of Tuberculosis and Lung Disease, 2004; 8(1): 92-7.
19. Hussein MM, Mooij JM, Roujouleh H. Tuberculosis and chronic renal disease. Seminars in dialysis, 2003; 16(1): 38-44.
20. Rogerson TE, Chen S, Kok J, Hayen A, Craig JC, Sud K, et al. Tests for latent tuberculosis in people with ESRD: a systematic review. American journal of kidney diseases : the official journal of the National Kidney Foundation, 2013; 61(1): 33-43.