

## Original Research Article

# Incidence of tuberculosis in nondialysis-requiring CKD patients

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### ABSTRACT

**Background:** Tuberculosis is a common infection of chronic kidney disease patients in developing countries.

**Methods:** A retrospective study of 2960 non-dialysis requiring chronic kidney disease patients was made to determine the incidence and understand the demographic features of patients that lead to the development of tuberculosis on the basis of cell count, routine, ADA estimation, ZN stain, culture and PCR.

**Results:** Between Jan 2000 and March 2017, the incidence of tuberculosis in no dialysis-requiring chronic kidney disease group was 10.3% in which pulmonary tuberculosis was 3.9% while extrapulmonary tuberculosis was 6.4%. Among extrapulmonary tuberculosis, 52% positivity was seen in pleural effusion, 16.40% in ascetic fluid, 10.10% in lymphnodes, 7.4% in urinary tract, and 3.7% in CSF, 2.6% in pericardial fluid, 1.6% in adrenal tissue and 1.1% in spine. ZN stain was positive in 48.6%, culture isolated mycobacterium 98.3%, PCR 93.4%, the mean ADA levels was  $22.90 \pm 11.24$  IU/ml and  $60.49 \pm 07.24$  IU/ml in CSF and body fluids respectively. Outcome analysis revealed 15.4% mortality rate in diagnosed tuberculosis cases while maximum loss of life was seen in diabetic patients.

**Conclusions:** In the present study we observed 10.3% incidence of tuberculosis among nondialysis-requiring chronic kidney disease patients. Extrapulmonary form of tuberculosis predominates over pulmonary form. Unusual presentation and localization of symptoms should not be overlooked. Prompt and early diagnosis of tuberculosis is especially required in endemic areas.

**Keywords:** Chronic kidney disease, Extrapulmonary, Nondialysis-requiring, Pulmonary, Tuberculosis

### INTRODUCTION

There is an increased incidence of tuberculosis (TB) in patients with end-stage renal disease (ESRD) as compared with the general population. In absolute numbers, this observation is especially important in areas where the disease is endemic. It is estimated that in 1997 almost 8 million new cases of TB occurred worldwide, with more than half occurring in Southeast Asia.<sup>1</sup> The pathophysiology of chronic kidney disease (CKD)-related immunodeficiency would suggest that early stage CKD could also be a risk factor for TB.<sup>2</sup> Immunodeficiency associated with CKD appears to be multifactorial in etiology.<sup>3</sup> Advanced CKD is associated with oxidative

stress and inflammation, 25-hydroxyvitamin D deficiency, and malnutrition, with evidence of functional abnormalities in a variety of immune cells including B and T cells, neutrophils, monocytes, and natural killer cells. Changes in immunity begin as early as stage 3 CKD (defined as a glomerular filtration rate  $<60$  ml/min per  $1.73$  m<sup>2</sup>) and worsen in later stages as kidney function deteriorates and waste products accumulate.<sup>4</sup> Active TB is an infectious complication that may develop and result from progression of *Mycobacterium tuberculosis* infection after recent exposure or reactivation of latent tuberculosis infection (LTBI) from a distant exposure, often years before the disease develops. The presentation of TB in uremic patients is often quite unusual and insidious, and diagnosis and management provide the

treating physician with many special challenges.<sup>5</sup> Therefore the focus of this study is to analyze the incidence and demographic features of nondialysis-requiring CKD patients who developed TB.

**METHODS**

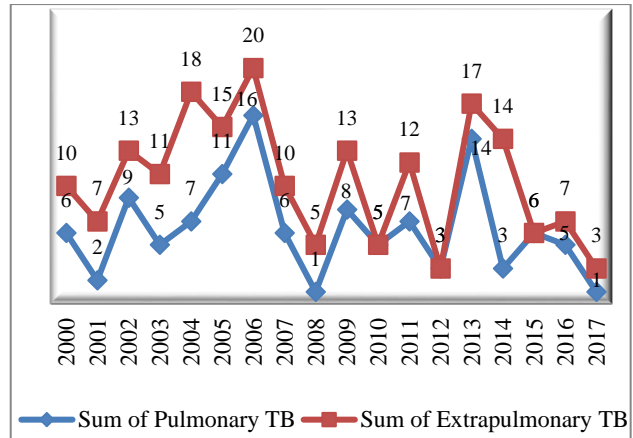
It is a retrospective study involving CKD patients registered at Allahabad over a period of 18years, from Jan 2000 to March 2017. Out of 2960 CKD patients, 376 cases were suspected for Tuberculosis clinically.

Depending on the site of involvement, specimens were collected and sent to microbiology laboratory for confirmation. Sputum, endotracheal aspirates and pus were subjected to ZN Stain, mycobacterium culture and PCR while 2-5 ml fluids and aspirates were analysed for cell count, routine, ADA estimation, ZN Stain, culture and PCR.

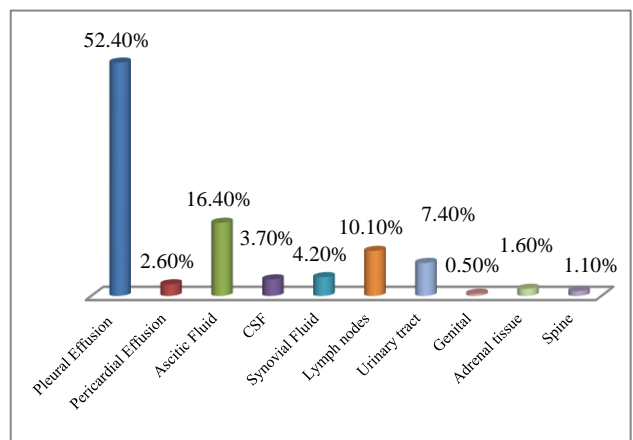
Fluids were divided into 4 parts in which 200µl was taken for routine and cell count 10µl for estimation of ADA, 500µl for PCR and 1000µl was left for ZN stain, and culture. Out of 1000µl, 900µl was inoculated in MP bottle for isolation of mycobacterium. This inoculated MP bottle was further incubated in BactAlert 3D system following standard protocols. PCR was done by Hense (Line Probe Method recommended by WHO) in the lab. ADA activity was estimated by Turbidometry and was expressed as U/l. Cut off reference range of 10U/l and 40U/l was taken as positive in CSF and fluid respectively. Sputum, endotracheal aspirates and pus were decontaminated first and then processed for Z.N. Stain, culture and Hense.<sup>6</sup> Data are expressed as mean +SD and done by IBM SPSS 24 version.

**RESULTS**

As stated above during the period from Jan 2000 to March 2017, 2960 CKD patients were registered in Nephrology OPD, Allahabad. Out of 2960 CKD patients, 376 were clinically suspected for TB in which 304 were detected positive for the same. In these 304 TB positive cases 3.9% were of pulmonary TB and 6.4% were of extrapulmonary TB. Their incidence and different sites of extrapulmonary TB are shown (Figure 1 and Figure 2). The base line and demographic data of positive TB cases are described as follows. CSF and body fluids of routine, microscopy and ADA levels of CKD patients who developed TB (Table 1).



**Figure 1: Incidence of pulmonary and extrapulmonary tuberculosis in nondialysis-requiring CKD patients.**



**Figure 2: Various sites of extrapulmonary tuberculosis in nondialysis-requiring CKD patients.**

**Table 1: Incidence and different sites of extrapulmonary TB.**

Parameter	Percentage
Age	54.40±6.04
Gender	68% male and 32% female
Diabetes	135 (44.3%)
Hypertension	59 (19.4%)
Glomerulonephritis	98 (32.3%)
Others	12 (4.0%)
Zn stain	148 (48.6% positive)
PCR	284 (93.4% positive)
Bactalert	299 (98.3% positive) till 11 <sup>th</sup> day
Loss of life	47 (15.4%)

**Table 2: Details of CSF and body fluids of routine, microscopy and ADA levels of CKD patients who developed TB.**

Specimen	Cell count (cells/cumm)	Lymphocyte count	Protein level (CSF- mg/dl, body fluids -gm/dl)	Sugar (mg/dl)	ADA (u/l)
CSF	36.85 ± 16.56	87.70 ± 07.33	78.20 ± 17.63	41.15 ± 05.64	22.90 ± 11.24
Body fluids	265.85 ± 60.56	80.45 ± 05.12	05.69 ± 02.11	60.10 ± 08.14	60.49 ± 07.24

Out of 304 positive cases, the mean age of patients with TB was 54.40 + 06.04 years with males being about 68% and female about 32%. The notable symptoms and signs were weight loss 86.8%, anorexia 80%, fever 55%, vomiting 13.8% and headache 7.2%. Patients with extrapulmonary tuberculosis showed clinical presentations associated with features depending upon the site of organ involvement for example pleural infusion 52.40%, palpable nontender lymph nodes 10.10%, knee pain 4.2%, abdominal distension due to exudative ascitis 16.40%, pericardial infusion with thickened pericardium 2.60%, pyuria 7.4%, and seizure was present in a single patient 05%. None of the patients who were diagnosed with extra-pulmonary tuberculosis showed any X-ray chest findings suggestive of pulmonary tuberculosis

## DISCUSSION

The host response against intracellular pathogens, including Mycobacterium tuberculosis, is determined by the type 1 helper T-cell response with the involvement of interleukin (IL)-12, resulting in increased production of interferon (IFN)- $\gamma$ .<sup>7</sup> In uremia there is a decreased T-cell response, as indicated by the high rate of anergy to intracutaneously administered antigens, reported to be as high as 32% and 40%.<sup>8,9</sup> A reason for the decreased cellular immunity might be a defect in the costimulatory function of the antigen-presenting cells and a persistent inflammatory state of the monocytes which in turn is caused by the uremia per se, as well as by the dialysis treatment.<sup>10</sup> Other factors which might contribute to decreased immunity are malnutrition, vitamin D deficiency and hyperparathyroidism.<sup>11,12</sup>

Although TB was found in most organs of the body, it was most frequently reported in the peritoneum, bone, and lymph node. Some relatively uncommon cases were also reported, including intestinal TB, renal TB, breast TB, and tuberculous orchitis.<sup>13-16</sup> In the present study, the incidence of TB in nondialysis-requiring CKD group was 10.3% in which pulmonary TB was 3.9% while extrapulmonary TB was 6.4%. Among extrapulmonary TB, 52% positivity was seen in pleural effusion, 16.40% in ascetic fluid, 10.10% in lymphnodes, 7.4% in urinary tract, 3.7% in CSF, 2.6% in pericardial fluid, 1.6% in adrenal tissue and 1.1% in spine.

In the present case series ZN stain was positive in 48.6%, culture isolated mycobacterium 98.3%, PCR 93.4%, the mean ADA levels was 22.90 + 11.24 U/l and 60.49 + 07.24 U/l in CSF and body fluids respectively. Outcome analysis revealed 15.4% mortality rate in diagnosed TB cases while maximum loss of life was seen in diabetic patients.

The link between CKD and TB has been known for more than 40 years, but the interaction between these 2 diseases has not been understood well. This link was first reported in a 1974 case series involving dialysis patients and multiple studies have been done in different parts of

the world on ESRD patients who developed TB. As far as our knowledge goes, no study has recorded incidence of demography and TB risk in populations with nondialysis-requiring CKD patients and as such it would not be improper to say that the present case series is the largest and first study of its own type reporting from India focusing on incidence and demographic features of nondialysis-requiring CKD patients who developed TB. Therefore, the comparison of this study with other such studies could not be done as a review of literature on nondialysis-requiring CKD patients is scarce.

## CONCLUSION

The above observations lead us to the conclusion that there is an increased prevalence of TB (10.3%) amongst the patients of CKD with the extrapulmonary form of tuberculosis predominating over the pulmonary form. Renal physicians should not be unaware of the unusual presentation and localization of symptoms and should include TB in their differential diagnosis. Efforts must be made promptly for an early diagnosis. However, if it is not possible or the result is in negative and the diagnosis is strongly suspected, an empirical trial with an anti-TB medication is justified, especially in endemic areas.

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## REFERENCES

1. Dye C, Scheele S, Dolin P, Pathania V, Raviglione MC. Consensus Statement. Global Burden of Tuberculosis: Estimated Incidence, Prevalence, and Mortality by Country. WHO Global Surveillance and Monitoring Project. JAMA. 1999;282:677-86.
2. Romanowski K, Clark EG, Levin A, Cook VJ, Johnston JC. Tuberculosis and chronic kidney disease: an emerging global syndemic. Kidney Int. 2016;90:34-40.
3. Zuo L, Wang M. Current burden and probable increasing incidence of ESRD in China. Clin Nephrol. 2010;74:S20-2.
4. Carrero JJ, Stenvinkel P. Inflammation in end-stage renal disease-what have we learned in 10 years? Semin Dial. 2010;23:498-509.
5. Hussein MM, Mooij JM, Roujouleh H. Tuberculosis and Chronic Renal Disease. Semin Dial 2003;16:38-44.
6. Giusti G. Adenosine deaminase. In Bergmeyer HU, editor. Method of enzymatic analysis. Vol. II VCH Weinheim: Florida; 1974:1072
7. Chatenoud L, Descamps-Latscha B. Immunological disturbances in uremia. In: Massry SG, Glasscock RJ, editors. Textbook of Nephrology, 4th edn. Philadelphia: Lippincott Williams & Wilkins; 2001. p. 1433-8.
8. Woeltje KF, Mathew A, Rothstein M, Seiler S, Fraser VJ. Tuberculosis infection and anergy in

- hemodialysis patients. *Am J Kidney Dis.* 1998;31:848-52.
9. Smirnoff M, Patt C, Seckler B, Adler JJ. Tuberculin and anergy skin testing of patients receiving long-term hemodialysis. *Chest* 1998;113:25-7.
  10. Girndt M, Sester U, Sester M, Kaul H, Kohler H. Impaired cellular immune function in patients with end-stage renal failure. *Nephrol Dial Transplant.* 1999;14:2807-10.
  11. Chan TY. Vitamin D deficiency and susceptibility to tuberculosis. *Calcif Tissue Int.* 2000;66:476-8.
  12. Tzanno-Martins C, Futata E, Jorgetti V, Duarte AJ. Restoration of impaired T-cell proliferation after parathyroidectomy in hemodialysis patients. *Nephron.* 2000;84:224-7.
  13. Peces R, de la Torre M, Alcazar R. Visceral leishmaniasis and renal tuberculosis in a patient on maintenance haemodialysis. *Nephrol Dial Transplant.* 1996;11:707-8.
  14. Alper M, Balbay O, Akman Y, Arbak P, Cam K. Tuberculous orchitis in chronic renal failure. *Med J Malaysia.* 2004;59:118-9.
  15. Siu YP, Tong MK, Kwok YL, Leung KT, Kwan TH, Lam CS, et al. An unusual case of both upper and lower gastrointestinal bleeding in a kidney transplant recipient. *Transpl Infect Dis* 2008;10:276-9.
  16. Yazici O, Mescigil P, Kepenekci I, Celepli P, Sengul S, Azap A, et al. Tuberculosis of the breast in a patient undergoing hemodialysis. *Int Urol Nephrol* 2011;43:241-4.

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