Tuberculosis in Chronic Kidney Disease

Mahesh Kumar Lal¹*, Satpal Singh²

Abstract

Introduction: Given the increasing prevalence of chronic kidney disease (CKD) in tuberculosis (TB) endemic areas, a merging of CKD and TB epidemics could have significant public health implications, especially in low to middle income countries like India, which is experiencing rapid increase in CKD prevalence. The aim of this study is to analyze the prevalence of TB in patients with CKD.

Methods: A prospective study was done on 160 patients with CKD at Safdarjung Hospital, New Delhi, both with and without dialysis. The patients were investigated to detect any form of TB.

Results: 22 patients showed evidence of tubercular infection (13.7%). Of these 22 subjects, 17 had extra-pulmonary and only 5 had pulmonary TB. TB infection was more prevalent among the patients on dialysis (18) than those who were not on dialysis (4).

Conclusion: Therefore, we infer that TB is more common in patients of CKD and patients of CKD need to be screened for TB more so due to their over lapping signs and symptoms.

Further, TB screening and diagnostic test performance is suboptimal in the Indian CKD population. Most of the previous studies have been done on a single group of patients, either on dialysis or without. We report incidence of TB in CKD comparing both the groups. A clear relationship between these two conditions needs to be established, necessitating the study.

Materials and Methods

This was a prospective study on patients attending the Medicine OPD and admitted in the Medical Wards of Safdarjung Hospital, New Delhi.

Inclusion Criteria

After obtaining an informed consent and clearance from the hospital ethical committee, adult patients with CKD were enrolled. They were further sub-grouped into patients on or without dialysis.

Exclusion Criteria

The following patients were excluded from the study:
1. Patients taking steroids
2. HIV positive
3. Renal transplant patients

4. Concomitant hepatic disease
5. Patient taking immuno-suppressive medications

A detailed history was taken with special mention of symptoms of tuberculosis and past tubercular infection. The patients were inquired about the duration of CKD and dialysis. The patients were subjected to a detailed clinical general and systemic examination.

All the subjects underwent the following investigations:
i. Routine investigations: including haemogram, random blood sugars, LFT, KFT, Urine R/M
ii. Mantoux test using 5 units of Purified Protein Derivative (PPD)
iii. Sputum examination: 3 early morning sputum samples were taken for AFB staining and culture
iv. Chest X-ray (PA View)

Special investigations (as and when required):
1. Pleural/ ascitic fluid/CSF cytology/ biochemistry
2. AFB staining of pleural and ascitic fluid
3. Histopathological examination of tissue samples
4. ADA levels
5. AFB culture of tissue and fluid specimens

Results

A total of 160 patients were enrolled, out of which 97 (61%) were males and 63 (39%) were females. The age span of the subjects ranged from 30 to 60 years. 40.6% of the subjects represented the age group of 30 - 40 years, 33.7% belonged to the 41 - 50 years group and...
about 25.6% were in the 51 - 60 years age group (Figure 1).

Subjects were arranged according to the stages of CKD, based on the GFR values. It revealed that there were 81 cases in stage IV and 76 cases in stage V. Only 3 cases were found to be in stage III and no case qualified to be in stages I and II. (Table 1). The study population had equal representation of patients on dialysis and without dialysis.

The notable symptoms were weight loss, anorexia, fever and cough. Out of the total 160 subjects, only 3 had positive Mantoux Test. Further, the positive results were seen only in patients with extra-pulmonary TB infection, who were on dialysis.

Of the 160 subjects, 22 showed evidence of tubercular infection (13.7%). Of these, 17 had evidence of extra-pulmonary tubercular TB while only 5 had pulmonary TB. TB infection was more prevalent among the patients on dialysis (18) than those who were on not on dialysis (4). Further, extra-pulmonary TB (17) was more prevalent as compared to pulmonary TB (5) (Table 2). The most common extra-pulmonary presentations were lymphadenopathy followed by pleural effusion.

Discussion

Tuberculosis is a serious health problem in India. The incidence of TB in children and adults in India has been reported to be high. Tuberculosis in CKD is an important problem in developing countries like India because of its endemic and environmental causes.

The incidence of tuberculosis in the general population is about 6.6%. Patients with CKD run a high risk of developing tuberculosis and an incidence, 6 to 16 times that of general population, has been reported from many countries. Our study revealed that 22 CKD patients had evidence of some form of TB infection, an incidence of about 13.7%.

Majority of the our patients were in the third to fourth decade of life (74.3%). Study by Malhotra, in the North Indian population, also revealed a young population with the average age being 46.4 years,’ emphasizing that more and more younger population is being affected by CKD, imposing a huge financial burden. It may be attributed to the better availability of investigative and diagnostic facilities, thereby detecting CKD earlier.

The variation in average age and the incidence of tuberculosis in different countries and communities can be ascribed to difference in environmental factors, availability of diagnostic and treatment facilities, acceptability of available facilities by the population and efficiency of treatment programmes and policies.

There were more males as compared with females who were diagnosed with TB (15:7) in our study. Ludin’ and Rutsky’ found an increase ratio of males as compared to females with TB and CKD. Malhotra and RKC Venkata also reported higher incidence of TB in the Indian male CKD patients.

Therefore, the male to female ratio in our study collaborated with majority of the studies done in India and elsewhere. The higher incidence in male subjects could be attributed to increase in the number of male patients admitted in the hospital. Also, it is equally important to note that in the general population, the annual incidence of tuberculosis in males is 2.2 times higher than that in females.

The first report of increased prevalence of tuberculosis in dialysis patients was by Pradhan et al. They reported five patients of active tuberculosis among 136 patients maintained on dialysis. Malhotra showed an incidence of 13.3%. Recently, a retrospective analysis by Upma Narain has reported the incidence of TB in non dialysis-requiring CKD patients to be about 10.3%. with higher incidence of extrapulmonary TB(6.4%) as compared to pulmonary TB (3.9%), similar to the findings of Rao et al (10.5%). Thus, the results of our study match these statistics.

Tuberculosis and CKD, both are immuno-compromised states. Host resistance to infection is primarily mediated by cellular immunity which is deficient in patients with CKD. Uremic patient are at increased risk of infection due to defective neutrophilic function, antigen processing, antibody formation and cell mediated immune response.

Uremia causes persistent and major alteration in all aspects of functions of neutrophil resulting in decrease chemotaxis, increased adherence to other polymorphonuclear neutrophils (PMN’s), platelets, endothelium with decreased phagocytosis and intracellular killing. There is abnormal superoxide production and decreased secretion of important peptides. Most of the defective neutrophil functions are due to serum factors that accumulate in uremic plasma, only some of which can be corrected by dialysis. The occurrence of infection including tuberculosis is therefore high in such patients.

Changes in immunity begins as early as stage 3 CKD and worsen in later stages as kidney function deteriorates and waste products accumulate. Uremia per se causes impaired T cell and B cell function and monocyte function which results in faulty presentation of antigens for immune recognition. Both these factors together impair response to infectious agents. These alterations in functional capacity of lymphocytes manifest as increased sensitivity and altered presentation of multiple infections leading to impaired response to vaccination.

The link between CKD and TB was first reported in 1974. Both the Western and Indian studies have revealed that TB infection is more common in dialysis patients in comparison to non dialysis patients. Our study also revealed that TB infection was more prevalent among the patients on dialysis than those who were on non-dialysis treatment, extra-

Table 1: Stages of CKD

<table>
<thead>
<tr>
<th>Stage of CKD</th>
<th>GFR (ml/min)</th>
<th>n</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>&gt;90</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>II</td>
<td>60 - 89</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>III</td>
<td>30-59</td>
<td>3</td>
<td>1.9</td>
</tr>
<tr>
<td>IV</td>
<td>15-29</td>
<td>81</td>
<td>50.6</td>
</tr>
<tr>
<td>V</td>
<td>&lt;15</td>
<td>76</td>
<td>47.5</td>
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</table>

Table 2: Comparison of tuberculosis and dialysis status

<table>
<thead>
<tr>
<th>TB patients</th>
<th>Status</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pulmonary</td>
<td>On dialysis</td>
<td>Non-dialysis</td>
</tr>
<tr>
<td>Extra Pulmonary</td>
<td>14</td>
<td>3</td>
</tr>
<tr>
<td>TB</td>
<td>Total</td>
<td>18</td>
</tr>
</tbody>
</table>

Fig. 1: Age distribution of patients
pulmonary TB being more common.

However, more research is required to ascertain the reasons for the increased TB infection in CKD, particularly extra-pulmonary type in dialysed patients.

Conclusion

The study concludes that there is an increased prevalence of TB in patients of CKD with extra-pulmonary form as compared to the pulmonary type, especially in dialysis patients. In a TB endemic area like India, physicians must be aware of the overlapping signs and symptoms of TB and CKD. Thus, all patients of CKD must be screened for TB and treatment guidelines need to be developed.

References

17. Carreo JJ, Stenvinkel P. Inflammation in End-Stage Renal Disease—What have we Learned in 10 Years? Seminar Dial 2010; 23:498-509.