

# Clinical spectrum of tuberculosis in chronic renal failure patients on hemodialysis – A single centre experience

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**Abstract-** This study includes one hundred fifty patients of End Stage Renal Disease (ESRD), mean age  $52.5 \pm 14.56$  years, during a period of two year from August 2009 to July 2011 were studied. Detailed clinical history, physical examination and laboratory investigations were recorded. Chi-square and Fischer-exact tests were used for statistical analysis. Thirty cases of tuberculosis were detected in 150 ESRD patients on hemodialysis. Twenty seven of them were pulmonary and three extrapulmonary cases. Increased association of tuberculosis were seen in diabetics as underlying cause for ESRD (82%), lower socioeconomic status (65%), male patients (67.3%), and patients > 30 years of age (83.3%). Anorexia was most common symptom (73.3%), followed by fever (60%) and cough (53.3%). Keeping in view of high incidence and prevalence of tuberculosis in developing countries like India patients of ESRD should always be screened for tuberculosis. If patients presenting with above symptoms requiring a high index's of suspicion.

**Index Terms-** End stage renal disease, Hemodialysis, Tuberculosis

## I. INTRODUCTION

India has almost 30% of the global burden of tuberculosis and one person dies due to disease every minute.<sup>1</sup> Currently in India there are about 14 million suspected and about 3.5 million bacteriologically proved cases of pulmonary tuberculosis and prevalence of 4.84/ 1000 cases.<sup>2</sup> More recently, average prevalence of all forms of tuberculosis (TB) in India estimated to be about 5.05 per 1000.<sup>3</sup> Due to certain risk factors like disturbance of skin and mucous membrane barrier, inadequate nutrition and acidosis, profound alteration in immune responses associated with uremia and exacerbated by dialysis, so there is increase in risk for developing active tuberculosis after primary infection.<sup>4</sup> Frequent hospital contacts, older age and use of immunosuppressive drugs are additional factors explaining the higher prevalence of tuberculosis in these patients.

Tuberculosis in end stage renal disease patients on regular hemodialysis presents a number of diagnostic challenges. In these patients the symptomatology of TB is often insidious and nonspecific, where as the localization is often extrapulmonary. This makes the disease difficult to diagnose, delaying the initiation of curative treatment, which is a major determinant of the outcome. That is why annual skin testing with tuberculin skin test (TST) and chemoprophylaxis for all hemodialysis patients is

recommended if tuberculin skin test >10mm. However, even today with increased quality of dialysis there is a high rate of anergy reported among hemodialysis patients and anergic hemodialysis patients are at increased risk of developing tuberculosis.

## II. MATERIAL AND METHOD

This was a hospital based study involved the detection of tuberculosis, both pulmonary as well as extrapulmonary in end stage renal disease on hemodialysis from outdoor and indoor patient in the Department of Medicine, CSM Medical University, Lucknow during a period of two year from May 2009 to June 2011. End stage renal disease (ESRD) from any cause in subjects of either sex and age were selected for the study.

Details of clinical history, physical examination and laboratory investigations were recorded in a special proforma. Specific symptoms which were looked in each case were persistent cough of about 3 or 4 weeks duration, continuous fever, chest pain, anorexia, weight loss and abdominal pain/distension, hemoptysis, swelling in the neck/axilla.

All patient investigated for automated blood count including general blood picture, ESR, renal function tests, creatinine clearance by Cockcroft-Gault formula, X-ray chest (PA/ lateral view), tuberculin skin test (PPD), sputum smears, ELISA for mycobacterium tuberculosis, cytology and biochemistry of fluid drawn from serous cavities, FNAC, biopsy of suspected tissues such as lymph nodes, peritoneum, pleura (when indicated), bone radiology, PCR for mycobacterium tuberculosis (if required) were done. Statistical analysis was done using Chi-Square and Fischer-exact tests.

## III. RESULT

Thirty cases of tuberculosis were seen in 150 ESRD patient on hemodialysis in this study. Twenty seven of them were pulmonary, only three was extrapulmonary. Five of the cases had history of previously treated tuberculosis, thereby 25 new cases were detected. The incidence/prevalence seen in the present study is strictly not comparable to the general population.

The present study being a hospital-based study, prevalence tends to be higher since the sample is not truly representative owing to selection bias. Mean age of patients was  $52.5 \pm 14.56$  years. Majority of patients were male (57.3%). Majority of ESRD patients were in age group 51-60 years (Table I). Major

baseline parameters were deranged. Patients were moderately anemic (mean Hb 7.8 gm%). Creatinine clearance was <10 (mean 7.1835). PPD (Mx) was positive in a three patient (10%). Mean ESR in persons suffering from tuberculosis was 82.92 mm/1st hour.

The main underlying etiology for ESRD was diabetes mellitus (54.6%), chronic glomerulonephritis (25.3%), and hypertension (13.3%) (Table II). Anorexia (73.3%), fever (60%) and cough (53.3%) were the most common symptoms (Table III).

Most of the patients suffering from tuberculosis were older than 35 years (88%). Males (67.3%) were more affected by tuberculosis than females. 13.3 per cent of diabetics as underlying cause for ESRD had tuberculosis. More of tuberculosis was seen in patients with lower socio-economic status. Twenty out of 30 tuberculosis patients belonged to lower socio-economic status.

#### IV. DISCUSSION

Worldwide TB infection in dialyzed patients range from 5-25% and a 6.9-52.5 fold risk of TB is reported as compared to the general population.<sup>5,6</sup> India has almost 30 per cent of the global burden of tuberculosis<sup>1</sup>. Advance age, diabetes mellitus and low BMI, are known factors of immunological imbalance, associated with TB development in the general population. In hemodialysis patients they have been also associated with depressed cell-mediated immune responses and anergy.<sup>7-11</sup> In our study, they were proved to be factors predisposing to active TB in the dialysis setting. Along with lymphocyte dysfunction and decrease in absolute lymphocyte counts, furthermore interferon production is depressed in uremia. In chronic renal failure the functions of polymorphonuclear leucocytes known as first line of non-specific defense against microbial infection, involving chemotaxis, bactericidal activity have been reported as diminished.<sup>12</sup>

As per etiology of the patients with end stage renal disease, diabetes mellitus (54.6%), chronic glomerulonephritis accounted for (25.3%) followed closely by then hypertension (13.3%), obstructive uropathy (3.33%) and others (3.33%). As for age is concerned, majority of patients were in age group 51 to 60 years, comprising of 28 males (27.7%) and 17 females (34.69%). Mean age was 52.5 years with standard deviation of 14.56. Majority of the patients were male (67.3%).

In the present study, we found 30 cases of tuberculosis out of 150 ESRD patients. 27 out of these were pulmonary and 3 was extrapulmonary. Amongst pulmonary, 24 cases were infiltrative, 4 cases of pleural effusion and 2 cases of consolidation. Extrapulmonary case included abdominal tuberculosis in form of intra-abdominal lymphadenopathy in which ultrasound guided FNAC revealed granulomatous lesion. IgM for mycobacterium tuberculosis was positive in it. Among pulmonary, 12 of the cases had sputum for AFB positive. In the rest, clinical suspicion, supportive investigations and response to the treatment were the criteria. Pulmonary form of tuberculosis as main form of tuberculosis was also observed in the studies done by Cengiz *et al.*<sup>13</sup>, Shohaib *et al.*<sup>14</sup>, Taskapan *et al.*<sup>15</sup>, Mohammed Al *et al.*<sup>16</sup>, Erkok *et al.*<sup>17</sup>. While extrapulmonary as

main form of tuberculosis was observed in several other studies.<sup>4,11,18</sup>

As far as clinical symptoms amongst tuberculosis patients were concerned, anorexia was the most common symptoms seen in 73.3 per cent patients, next was fever seen in 60 per cent, cough in 53.3 per cent, weight loss in 60 per cent, chest pain in 33.3 per cent, hemoptysis in 40 per cent, pain abdomen in 3.33 per cent patients.

Thus, anorexia, fever and cough were the most common symptoms. Fever, weight loss, malaise were common symptoms noticed by Venkata *et al.*<sup>18</sup>, undiagnosed pyrexia, lethargy, weight loss by Kwan *et al.*<sup>19</sup>. Anorexia, loss of weight, low grade fever by Mitwalli *et al.*<sup>20</sup>; anorexia, weight loss, fever by Cengiz *et al.*<sup>13</sup>; similar symptoms found by Shohaib *et al.*<sup>14</sup>, Mohammed Al *et al.*<sup>16</sup>.

Age of the patients suffering from tuberculosis varied from 22 to 70 years (mean 52.5 years). Most of the patients of tuberculosis in ESRD were more than 35 years old comprising 27 of 30 patients (90%) matching Taskapan *et al.*<sup>15</sup>, where age of the patients suffering from tuberculosis varied from 19 to 70 years with mean age  $43.05 \pm 3.72$  years. Mean age in Shohaib *et al.*<sup>14</sup> was 48 years in males and 47 years in female.

In present study, out of 20 patients, 14 patients (70%) were male and 6 (30%) patients were female. Similarly, Venkata *et al.*<sup>18</sup> and Murthy and Pereira<sup>21</sup> reported more males affected by tuberculosis.

Mean ESR was 33.12 in 150 patients whereas mean ESR was 82.92 in case of patients with tuberculosis with standard deviation of 20.64. ESR was found to be varied in tuberculosis patients of ESRD. Mean PPD (Mx) in 150 patients was 5.87. A recent conversion of positive has more value than an isolated positive PPD test in these situation. In contrast, a positive PPD test can be taken as an diagnostic aid to detect tuberculosis infection, in countries with low prevalence of tuberculosis. However, among dialysis patients, a positive PPD test was observed only in 40 to 60 per cent of patients with tuberculosis.<sup>4</sup> The defective cell mediated immunity associated with uremia is the likely cause of low sensitivity of the PPD test in these patients.

Among 30 cases, 12 had sputum for AFB positive, 4 cases had IgM positive for mycobacterium tuberculosis. All the 4 pleural effusion cases had fluid as exudate and lymphocytic predominance. One of the pleural fluids had positive PCR for mycobacterium tuberculosis. Rests of the cases were unable to afford PCR. Once diagnosed, all the patients were put on short course chemotherapy.

All the patients were on regular follow-up except 3 patients who did not report for follow-up despite reminders. Five patients died during treatment. Cause of mortality was not directly attributed to tuberculosis in any of them. Rest of the patients improved symptomatically and radiologically. The present study conclude that keeping in view of high incidence and prevalence of tuberculosis, patients of ESRD should always be screened for tuberculosis, annually, testing with tuberculin test and chemoprophylaxis for all patients on hemodialysis if tuberculin test response is positive ( $\geq 10$  mm), is recommended. Similarly recommended by American Thoracic Society: Controlling tuberculosis in United States 2005.

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Table-1: Epidemiological data

Age group (in Years)	Number of patients		Total number of cases
	Male (%)	Female (%)	
10-20	3(2.97)	2(4.08)	5
21-30	15 (14.8)	5 (10.2)	20
31-40	18(17.8)	7(14.2)	25
41-50	22(21.7)	8(16.3)	30
51-60	28(27.7)	17(34.69)	45
61-70	11(10.8)	8(16.3)	19
>71	4(3.96)	2 ( 4.1 )	6
Total	101 (67.3)	49 (32.7)	150

**Table-2: Co-morbid conditions.**

<b>Etiology of ESRD</b>	<b>With tuberculosis (N= 30 )</b>	<b>Without tuberculosis ( N= 120 )</b>	<b>Total ( N = 150 )</b>
Chronic glomerulonephritis	8	30	38 (25.3%)
Diabetes mellitus	20	62	82 (54.6 %)
Hypertension	2	18	20 (13.3 %)
Obstructive uropathy	Nil	5	5 (3.33 %)
Others	Nil	5	5 (3.33 %)

**Table-3: Clinical presentation**

<b>Symptoms</b>	<b>Positive (N=30)</b>	<b>Frequency (%)</b>
Anorexia	22	73.3
Weight loss	18	60
Fever	18	60
Cough	16	53.3
Hemoptysis	12	40
Pain chest	10	33.3
Pain abdomen/distension	4	13.3

Male (n= 22) 73.3% and Female (n= 8) 26.7% positive for Tuberculosis.