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Research Article

INCIDENCE OF PULMONARY TUBERCULOSIS IN IMMUNOCOMPROMISED PATIENTS

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ABSTRACT

Objective:-

1. To study the individual incidence of Pulmonary Tuberculosis among different immunocompromised patients.
2. To assess the diagnostic sensitivity of various modalities in Pulmonary Tuberculosis among different immunocompromised patients.
3. To study the clinical spectrum of pulmonary TB in different immunocompromised conditions.
4. To study the laboratory and radiological changes in different immunocompromised conditions in reference to Pulmonary Tuberculosis.

Materials and Methods:-

The present study was conducted in tertiary care centre in India. The study was carried out on 100 patients admitted during the period from June 2020 to October 2022 in the hospital.It was a prospective observational study. A detailed history was taken followed by a thorough clinical examination to assess clinical severity and complications.

Result:-

HIV infection (30%) was the most common immunocompromised condition associated with Pulmonary Tuberculosis followed by Diabetes Mellitus (20%) and Malnutrition (20%).Incidence of Pulmonary Tuberculosis in Chronic Liver Kidney Disease/Chronic Liver Disease was lower in our study (10%). However, in Chronic Kidney Disease; females were found to have higher incidence (50%) as compared to other immunocompromised conditions.

Conclusion:-

Immunocompromised diseases particularly HIV and Diabetes Mellitus definitely affect the incidence of Pulmonary Tuberculosis as evident by radiological presentation of disease (more atypical changes and frequent cavity occurrence in patients with poor glycemic control and Malnutrition and may also show more sputum positivee rates among patients with low CD4 count, poor glycemic control and Malnutrition. The implementations of Tuberculosis interventions and network collaborations; particularly in HIV infected patients; needs to be highlighted to help and generate common feasibilities to improve life expectancy among these patients and to curb the future incidence of Pulmonary Tuberculosis.Our study shows the there is higher occurrence of Pulmonary Tuberculosis in Immunocompromised Patients and they should be screened routinely for detection of pulmonary tuberculosis.

INTRODUCTION

After human immunodeficiency virus (HIV) infection, tuberculosis is the second most frequent cause of death among infectious diseases in the world. Annually, 8–10 million people are infected, and around 2 million people die.[1] One person with active tuberculosis infects 10–15 individuals per year. It is believed that one third of the entire human population is infected with Mycobacterium tuberculosis (M. tuberculosis).[2] The epidemiological situation of tuberculosis has changed during recent years, primarily due to an increasing number of patients with immunocompromising diseases (the patients with transplanted organs, patients undergoing immunosuppressive therapy, people infected with HIV, people suffering from malignant diseases, diabetes mellitus, liver cirrhosis, renal insufficiency, alcoholism) that change the course of tuberculosis infection.[3] An increase in the number of these patients can be expected in the future.[4]Aquired cell mediated immunodeficiency is the most common kind of immunodeficiency and it is very important in pathogenesis of

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tuberculous infection. The patients who have impared cell mediated immunity are predominantly susceptible to infections caused by intracellular microorganisms including M. tuberculosis inside alveolar macrophages.[3]Individuals suffering from immunocompromising diseases with latent tuberculosis infection (LTBI) have an increased risk of developing active tuberculosis. The HIV infected patients have dominantly impared cell immunity with lower number of CD4+ lymphocites. If these patients suffer from latent tuberculosis infection, they have 20–30 times higher risk to develop active tuberculosis then the immunocompetent persons. The HIV positive patients exhibit more frequent occurrences of disseminated and extrapulmonary forms of tuberculosis, more frequent occurrence of sputum smear negative pulmonary disease, and an atypical radiological presentation of changes in the patients with CD4+ lymphocyte number lower than 200 cells/uL. The adverse effects of drugs are also more frequent. Hepatotoxicity is connected to the overlapping of adverse effects of antituberculotics, antiretroviral therapy, antibiotics and antimycotics that are used simultaneously.[5]The patients with liver cirrhosis have increased risk to develop tuberculous infection due to the multifactorial process, dominantly reticuloendothelial system dysfunction. These patients more frequently exhibit extrapulmonary forms of tuberculosis with predominant peritoneal localization of the disease. The tuberculosis treatment regimen must be modified in accordance with the level of damage to the liver functions. Considering that the basal function of the liver is often disturbed, the most common adverse effect during the treatment is hepatotoxicity. Three out of four of the first-line antituberculotics are potentially hepatotoxic. Pyrazinamide is considered to be the most frequent cause of hepatotoxicity, followed by isoniazid, and thirdly by rifampicin. According to the recommendation of the World Health Organization (WHO), the larger extent of damage to the liver function, the smaller number of the hepatotoxic drugs can be used.[6] The patients with chronic renal failure have 10–15 times higher incidence of tuberculosis mostly due to impaired cellular immunity.[7] In those patients, tuberculosis is usually diagnosed later on, because of unspecific clinical signs and due to 50% more frequent occurrence of extrapulmonary form of the disease, especially with peritoneal localization.Mortality rate in the patients on hemodialysis who develop tuberculosis is two times higher compared to the patients without tuberculosis. The tuberculosis treatment regimes usually last six or nine months. Duration of treatment is individual reflecting the different clinical circumstances, immunosuppression level, or the spread of disease. Usually, the standard doses of antituberculotics are used and they are administered daily or in an intermittent therapy regimen, depending on the drug metabolism and creatinine clearance. Hemodialysis eliminates most of the antituberculotics, therefore they are administered after hemodialysis. The adverse drug effects are observed in a majority of cases, the most common being neurotoxicity, hepatotoxicity, and optic neuropathy.[8]Systemic diseases are connected with the increased risk of tuberculosis infection. It remains unknown whether that risk is linked only to the use of immunosuppressive therapy or to the immunologic disease itself as well. The cases of active tuberculosis were reported in the patients who used corticosteroid therapy in doses of 15–20 mg of prednisone or equivalent for a month or longer.[9]The cases of active tuberculosis following the usage of methotrexate and cyclophosphamide were also reported.[10] Recently, a biological therapy has been successfully applied in rheumatoid arthritis which entails the use of tumor necrosis alpha (TNF-alpha) inhibitors. TNF-alpha is an important proinflammatory cytokine which plays an important role in the tuberculosis granuloma formation. There is an increasing amount of data that suggests that the use of these drugs is linked to the risk of developing active tuberculosis.[11]In the patients with malignancies, the increased risk of developing tuberculosis occurs due to the drop in immunity conditioned by the local or systemic effect of the tumor mass itself, or as a consequence of chemo- and radiotherapy.[12] The patients with transplanted organs require the application of immunosuppressive therapy with the aim of preventing the rejection of organs which significantly increases the risk of active tuberculosis. Alcohol is the most commonly abused substance throughout numerous countries.[13] The chronic alchocolics have impaired the neutrophils function and the impaired alveolar macrophage phagocytosis and superoxide production. T cells of the alchoholics show the impiared delayed type hypersensitivity responses. It has been proven that individuals who use more than 40 g of alcohol per day are three times more likely to develop active tuberculosis.[14]Diabetes mellitus is predisposing factor for developing tuberculous infection. The frequency of tuberculosis is four times higher in diabetics then in nondiabetics.[15] The diabetic patients show the neutrophil and macrophage dysfunctions which includes: impaired chemotaxis, adherence, phagocytosis and ability to kill the phagocyted microorganisms. These patients show alternations in the T lymphocyte subsets. Tuberculosis incidence among the diabetics increases proportionally with the duration of the diabetes and the increase of insulin doses required for glucoregulation.[16] If diabetes is well-regulated, the course of tuberculosis and the response to the antituberculotics therapy shows no significant difference compared to the individuals without diabetes, whereas poorly-regulated diabetes has a negative impact on the course of pulmonary tuberculosis.[17] The aim of the present study is to evaluate the incidence of pulmonary tuberculosis in the immunocompromised patients in the local population.

MATERIALS AND METHODS

100 cases of immune-compromised patients fitting the inclusion criteria admitted over the period of 2 years from June 2020 to October 2022.Subjects were selected from Medicine ward, Pulmonology ward and Tuberculosis ward under RNTCP. The diagnosis of Pulmonary tuberculosis was made with Sputum analysis, GENE XPERT, Microbiological Culture, Pleural Fluid Analysis and Clinical examination supported by radiological studies and histopathological examination.

Inclusion Criteria

- Patient above the age of 12 years were taken for study
- Patient having underlying immune-compromised status
- Patient diagnosed with pulmonary tuberculosis as per the case definition of RNTCP (2017-2018).

Exclusion Criteria

- Patients below the age of 12 years
- Patients having extra pulmonary tuberculosis.
- All critical ill patients
- Pregnant patients

RESULT

Patients were informed about the deatils of the tests performed and all investigations were collected with consent. Among 100 patients, 64(64%) were males and 36(36%) were females (table 1). 30% patients had HIV infection , 20% patients had diabetes mellitus, 20% patients had chronic kidney diseases/chronic liver disease / chronic obstructive pulmonary disease, 10% patients had malignancy and 10% patients had connective tissue disorder. Malignancy (10%) constituted the least population in our study. HIV (30%) was the leading immuno compromised condition among immuno compromised patients followed by diabetes mellitus (20%), malignancy (20%) and chronic kidney disease (15%) (table 2,3). In our study, male-female ratio was predominant. Highest male-female ratio was observed in HIV infection (2.75:1) followed by chronic kidney disease (2.33:1). Connective tissue disorder population had the lowest male-female ratio(0.67:1) due to more occurence of autoimmunity in them (table 4). Most significant age group affected was 20-40 years (60%) followed by 41-60 years (25%) .Among 20-40 years age group, HIV (66.67%) followed by Diabetes Mellitus (55.5%) were the most common underlying immuno compromised condition (table 5). Among the socio economic factors, labourers (45%), were commonly affected among pulmonary tuberculosis in immunocompromised patients (table 6). In the present study, fever (66.67%) and cough (72.2%) were the major clinical presentation among immuno compromised patients. Fever was the most common clinical presentation in HIV (77.7%) followed by Malignancy (66.67%). Pleural effusion was least observed clinical presentation and was observed only in HIV patients(11.11%). However, night sweats as a symptom was more prevalent in hiv patients (72.22%) compared to any other immunocompromised patients (table 7). Hb values (>10) were maximally (45%) observed in all immunocompromised patients in our study. Expect in Chronic Kidney Disesase (33.33%) were Hb value (>7) was observed. Hb values (>10) was mostly observed in Diabetes mellitus patients (50%) (table 8). Total leukocyte count (4-11) were most commonly observed among immunocompromised patients (70%). Total leukocyte count (<4) was only observed among HIV (5%) patients. Total leukocyte count (>11) was maximally observed in malignancy (50%) followed by chronic kidney disease (33.3%) (table 9). Atypical findings (33.3%) were the most common radiological findings in chest x-ray among immunocompromised patients. Atypical findings were predominant among HIV patients (55.5%).Upper zone consolidation was most observed in malignancy (50%), Connective Tissue Disorders followed by chronic kidney disease (33.33%).Cavitation was most common among diabetes mellitus patients (50%) followed by malignancy (50%) (table 10). In present study, Consolidation (40%) was the most common finding in HRCT thorax followed by Atypical Findings (30%). Atypical finding (55.55%) were predominantly observed in HIV patients. Cavitation were frequent among Malignancy (50%) and diabetes mellitus (50%). Consolidation was common in Malignancy (50%) followed by Chronic Kidney Disease patients(33.33%). Military opacities were found only among HIV patients (22.22%) (table 11). Comparing the diagnostic sensitivity of sputum analysis, sputum culture (66.67%) had the highest sensitivity followed by sputum CBNAAT (60%) . Sputum AFB (15%) was the least sensitive method found in our study (table 12). Comparing different modalities, the most sensitive modality was combination of sputum analysis and chest x-ray (85%) followed by sputum analysis (65%) and HRCT thorax (60%). Chest x-ray(55.5%) was the least sensitive method found in our study (table 13). In our present study, there is higher occurrence of sputum CBNAAT positivity (54.5%) with CD4 count <500, while sputum CBNAAT positivity decreases to 10.5% with CD4 count >500.So, sputum positivity was commonly observed with CD4 count <500 as compared to CD4 count >500 (table14).In our present study, glycosylated Hb values (>8) was frequently associated with sputum positivity and cavitation as compared to glycosylated Hb values (<8).So, in our study, there was higher occurrence of sputum positivity and cavitation with higher glycosylated Hb values (>8) (table 15).

Table 1 Distribution of patients according to gender

Gender	Number	Percent
Male	64	64%
Female	36	36%
Total	100	100%

Table 2 Distribution of patients according to underlying immunocompromised condition

Immunocompromised condition	No. of Patients	Percent
HIV	30	30%
Diabetes Mellitus	20	20%
Chronic Kidney Disease/ Chronic liver disease/ Chronic obstructive pulmonary disease	20	20%
Malignancy	10	10%
Connective tissue disorders/ Immunosuppressive drugs	20	20%
Total	100	100%

Table 3 Incidence of pulmonary TB in immunocompromised patients

Immunocompromised condition	Total no. Immunocompromised patients [n = 100]	Total no. of pulmonary Tuberculosis in immunocompromised patients [n=20]	Incidence of pulmonary Tuberculosis in immunocompromised patients
HIV	30	9	30%
Diabetes Mellitus	20	4	20%
Chronic Kidney Disease/ Chronic liver disease/ Chronic obstructive pulmonary disease	20	3	15%
Malignancy	10	2	20
Connective tissue disorders/ Immunosuppressive drugs	20	2	10
Total	100	20	

Table 4 Distribution of immnucompromised patients according to male female ratio

Gender	HIV (n=30)	Diabetes Mellitus (n=20)	Chronic Kidney Disease/ Chronic liver disease/ Chronic obstructive pulmonary disease (n=20)	Malignancy (n=10)	Connective tissue disorders/ Immunosuppressive drugs (n=20)
Male	22 (73.33%)	12 (60%)	14 (70%)	6 (60%)	8(40%)
Female	8 (26.67%)	8 (40%)	6 (30%)	4 (40%)	12 (60%)
Male:Female ratio	2.75:1	1.5:1	2.33:1	1.5:1	0.67:1

Table 5 Distribution of pulmonary Tuberculosis in immuno-compromised patients according to age group

Age group	HIV (n=9)	Diabetes Mellitus (n=4)	Chronic Kidney Disease/ Chronic liver disease/ Chronic obstructive pulmonary disease (n=3)	Malignancy (n=2)	Connective tissue disorder(n=2)	Total (n=20)
<20 years	-	-	-	-	-	-
20-40 years	6 (66.67%)	2 (50%)	1 (33.33%)	1 (50%)	2	12 (60%)
41-60 years	2 (22.22%)	2 (50%)	1 (33%)	-		5 (25%)
>60 years	1 (11.11)	-	1(33%)	1(20%)		3(15%)

Table 6 Distribution of pulmonary Tuberculosis in immuno-compromised patients according to Socioeconomic factors

Socioeconomic factor	HIV (n=9)	Diabetes Mellitus (n=4)	Chronic Kidney Disease/ Chronic liver disease/ Chronic obstructive pulmonary disease (n=3)	Malingnancy (n=2)	Connective Tissue Disorder(n=2)	Total (n=20)
Labourer	4 (20%)	1 (5%)	-	2 (10%)	2(10%)	9(45%)
Farmer	2 (10%)	2 (10%)	1 (5%)	-	-	5(25%)
Unemployed	1 (5%)	-	1 (5%)	-		2(10%)
Workers	2 (10%)	1 (5%)	1 (5%)	-		4(20%)

Table 7 Distribution of pulmonary Tuberculosis in immuno-compromised patients according to Clinical presentation

Clinical presentation	HIV (n=9)	Diabetes Mellitus (n=4)	Chronic Kidney Disease/ Chronic liver disease/ Chronic obstructive pulmonary disease (n=2)	Malignancy (n=3)	Connective tissue disorder (n=10)	Total (n=18)
Fever	7 (77.77%)	2 (50%)	1 (50%)	2 (66.67%)	5(50%)	12(66.67%)
Cough	7 (77.77%)	3 (75%)	1 (50%)	2 (66.67%)	6(60%)	13(72.2%)
Hemoptysis	1 (11.11%)	1 (25%)	-	1 (33.33%)	1(10%)	2(11.11%)
Dyspnea	2 (22.22%)	1 (25%)	1 (50%)	-	1(10%)	4(22.2%)
Weight loss	7 (77.77%)	-	1 (50%)	1 (33.33%)	-	9(50%)
Others	2 (22.22%)	1 (25%)	-	1 (33.33%)	1(10%)	4(22.2%)
Pleural effusion	1 (11.11%)	-	-	-	1(10%)	1(5.5%)

Table 8 Distribution of pulmonary Tuberculosis in immunocompromised patients according to Hemoglobin

Hemoglobin	HIV (n=9)	Diabetes Mellitus (n=4)	Chronic Kidney Disease/ Chronic liver disease/ Chronic obstructive pulmonary disease (n=2)	Malignancy (n=2)	Connective Tissue Disorder(n=2)	Total (n=20)
>10	4 (44.44%)	2 (50%)	1(33.33%)	1 (50%)	1(50%)	9(45%)
8-10	3 (33.33%)	1 (25%)	1 (33.33%)	1 (50%)	1(50%)	7(35%)
<8	2 (22.22%)	1 (25%)	1 (33.33%)	-	-	4(20%)

Table 9 Distribution of pulmonaryTuberculosis in immunocompromised patients according to Total leukocyte count

Total leukocyte count	HIV (n=9)	Diabetes Mellitus (n=4)	Chronic Kidney Disease/ Chronic liver disease/ Chronic obstructive pulmonary disease (n=3)	Malignancy (n=2)	Connective tissue disorder(n=2)	Total (n=20)
>11	1 (11.11%)	1 (25%)	1 (33.33%)	1 (50%)	1 (50%)	5(25%)
4-11	7 (77.77%)	3 (75%)	2 (66.67%)	1 (50%)	1 (50%)	14(70%)
<4	1 (11.11%)	-	-	-		1(5%)

Table 10 Distribution of pulmonary Tuberculosis in immunocompromised patients according to Radiological features of Chest Xray

Immunocompromised status	Lower zone consolidation	Upper zone consolidation	Cavitation	Pleural effusion	Atypical findings
HIV (n=9)	2 (22.22%)	1 (11.11%)	1 (11.11%)	-	5 (55.55%)
Diabetes Mellitus (n=4)	-	1 (25%)	2 (50%)	-	1 (25%)
Chronic Kidney Disease/ Chronic liver disease/ Chronic obstructive pulmonary disease (n=3)	1(33.33%)	1 (33.33%)	-	1 (33.33%)	-
Malignancy (n=2)	-	1 (50%)	1 (50%)	-	-
Connective Tissue Disorders (n=2)	1(50%)	1(50%)	-	-	-
Total (n=20)	4(20%)	5(25%)	4(20%)	1(5%)	6(30%)

Table 11 Distribution of pulmonary Tuberculosis in immunocompromised patients according to HRCT thorax findings

HRCT thorax findings	HIV (n=9)	Diabetes Mellitus (n=4)	Chronic Kidney Disease/ Chronic liver disease/ Chronic obstructive pulmonary disease (n=3)	Malignancy (n=2)	Connective Tissue Disorders (n=2)	Total (n=20)
Atypical findings	5 (55.55%)	1 (25%)	-	-	-	6(30%)
Consolidation	3 (33.33%)	1 (25%)	1 (33.33%)	1(50%)	2(100%)	8(40%)
Cavitation	-	2 (50%)	1(33.33)	1(50%)	-	4(20%)
Miliary opacities	2 (22.22%)	-	-	-	-	5(25%)
Lymphadenopathy	-	-	-	-	-	-
Pleural effusion	-	-	1 (33.33%)	-	1(50%)	2(10%)

Table 12 Diagnostic sensitivity of sputum analysis

Method	Positive	Negative	Not required	Total	Sensitivity
Sputum AFB	3	17	-	20	15%
Sputum CBNAAT	12	8	-	20	60%
Sputum culture	7	3	10	20	70%

Table 13 Comparing diagnostic sensitivity of different modalities in pulmonary Tuberculosis in immunocompromised patients

Investigation	Total patients detected	No. of patients requiring investigation	No. of patients not requiring investigation	Sensitivity
Sputum analysis	13	20	-	65%
Chest Xray	11	20	-	55%
HRCT thorax	6	10	10	60%
Pleural fluid analysis	1	1	18	-
Sputum analysis + Chest Xray	17	20	-	85%

Table 14 CD 4 count and their relationship with Sputum CBNAAT result

CD 4 count	Sputum CBNAAT positive	Sputum CBNAAT negative	Total
<500	6 (54.5%)	5 (45.45%)	11
>500	2 (10.5%)	17 (89.5%)	19

Table 15 HbA1C (Glycosylated Hemoglobin) and their relationship with Sputum CBNAAT and Cavitation

Glycosylated hemoglobin value	Sputum positivity	Sputum negative	Cavitation	Total
>8	2(25%)	6(75%)	1(12.5%)	8
<8	1(8.3%)	0	0	12

DISCUSSION

In present study,100 Immunocompromised patients were taken followed by incidence of Pulmonary tuberculosis was found. For review and comparison, with present study, available studies of Pulmonary Tuberculosis with different immunocompromised conditions were considered and their sub-data of each were compared with present study.

Table 1A Comparing incidence of pulmonary tuberculosis in immunocompromised patients.

Immunocompromised Patients in present study (n=100)	Pulmonary Tuberculosis in Immunocompromised Patients in Present study (n=20)	GOLSHAR *et al*.(n=143)
HIV	9 (45%)	-
Diabetes Mellitus	4(20%)	23%
Chronic Kidney Disease	3(15%)	5.8%
Malignancy	2(10%)	5%
Connective Tissue Disorders	2(10%)	2.5%
Overall Incidence	20%	-

In our study, 45% of the patients who had pulmonary tuberculosis had HIV as the underlying disease. This was followed by 20% of patients having diabetes mellitus and 15% of the patients having chronic kidney disease as the underlying disease. Malignancy and connective tissue disorders formed the smallest group with contribution 10% of each as the underlying disease. This was compared to Golshar *et al* wherein diabetes mellitus was the underlying disease in 23% of the patients followed by chronic kidney disease and malignancy with the least percentage having connective tissue disease as the underlying disease. Patients with HIV were not included in this study.

The other results are comparable to our study.

Table 1B Comparing incidence of pulmonary tuberculosis in immunocompromised patients according to male: female ratio

Gender distribution	Present Study(n=20)	Soham Gupta *et al*.(n=207)
Male	14(70%)	130 (62.8%)
Female	6(30%)	77(37.20%)
M:F ratio	2.33:1	1.7:1

In the present study, the male to female ratio was 2.33:1. The male female ratio was compared with the study by Soham Gupta *et al*.Both the study show that the proportion of males with tuberculosis is greater than the proportion of females.

Table 1C Comparing incidence of pulmonary tuberculosis in immunocompromised patients according to Age group

Age group (in years)	Present Study(n=20)	Soham Gupta *et al*.(n=207)
<20	10%	11.78%
21-40	55%	42.78%
41-60	25%	30.67%
>60	10%	14.77%

In the present study, the greatest proportion of patients belonged to the age group of 21-40 years followed by 41-60 years. Equal proportions of patients belonged to the group of less than 20 and greater than 60 years. This was compared to the study by Soham Gupta *et al* which also showed the greatest proportion of patients in the age group of 21-40 years followed by 41-60 years. This shows that majority of the patients belonged to the economically productive age group of 21-60 years.

Table 1D Comparing incidence of pulmonary tuberculosis in immunocompromised patients according to occupation

Socioeconomic Factors	Present Study(n=20)	Soham Gupta *et al*.(n=207)
Labourer	44.44%	43.96%
Farmer	27.77%	27.05%
Unemployed	11.11%	6.28%
Workers	16.67%	10.63%

In the present study, when the occupational status of the patients was compared, it was found that 44.44% of the patients belonged to the group of labourers. This was followed by farmers constituting 27.77%, workers constituting 16.67% and 11.11% being unemployed. This was compared to the study by Soham Gupta *et al* which also showed 43.9% patients being labourers, 27.05% patients being farmers, 10.63% being workers and 6.28% being unemployed. Thus, similar occupational status was found in our study as well as the compared study with labourers being most affected. This is probably due to the increased incidence of malnourishment and outdoor working conditions in labourers.

Pulmonary Tuberculosis and HIV

Table 2A Comparison of age group in pulmonary tuberculosis with HIV infection

Age group (Years)	Present Study(n=9)	Soham Gupta *et al*.(=22)	Kuppusamy *et al*.(n=67)
12-20	Nil	Nil	4%
20-40	66.66%	63.63%	76%
40-60	33.37%	36.36%	20%

The age group of patients with HIV who presented with tuberculosis was compared. In the present study, majority belonged to the age group of 20-40 years followed by 33.37% belonging to 40-60 years. This was comparable to the study by Kuppusamy *et al* wherein also the majority of the patients belonged to 20-40 years age group followed by 40-60 years. This is in line with the fact that most patients who are infected with HIV are in the sexually active age and economically productive age group.

Table 2B Comparison of pulmonary tuberculosis with HIV infection according to gender

Gender distribution	Present Study(n=9)	Soham Gupta *et al*.(=22)	Kuppusamy *et al*.(n=67)
Male	64%	86.36%	88%
Female	36%	13.74%	12%
M:F ratio	3.5:1	6.33:1	7.3:1

In the present study, 64% of males were infected with TB and 36% of females were infected with TB when HIV was the underlying comorbidity. This was compared to the study by Soham Gupta *et al* and Kuppusamy *et al* which also showed that the incidence of tuberculosis was much higher in males compared to females when HIV was the underlying comorbidity. The slightly higher male to female ratios in the compared studies may be due to larger population size.

Table 2C Comparison of pulmonary tuberculosis with HIV infection patients according to clinical symptoms

Clinical Symptoms	Present Study(n=9)	Kuppusamy *et al*.(n=67)
Fever	77.7%	80.6%
Cough	77.7%	83.6%
Weight loss	77.7%	82%
Night sweats	66.67%	22.4%
Hemoptysis	11.11%	15%

In the present study, fever, cough, weight loss were all present in 77.7% of the patients as the clinical symptoms; night sweats in 66.67% and least commonly, hemoptysis in 11.11% of the patients. In the study by Kuppusamy *et al*, fever, cough and weight loss were the most common symptoms, all present in almost 82% patients which was comparable to our study. The incidence of night sweats was slightly lower than in our study. Hemoptysis as the clinical symptom was present in 15% of the patients which was also comparable to our study.

Table 2D Comparison of pulmonary tuberculosis with HIV patients According to CD4 count

CD4 count (cells/mm^3)	Present Study(n=9)	Srujana akella *et al*. al.(=56)	Dixit kumar kapadiya *et al*. (n=360)
<200	55.68%	49.88%	43.3%
201-350	22.22%	25%	26.2%
351-500	11.11%	12.5%	17.3%
>500	11.11%	12.5%	13.1%

In the present study, almost half of the patients had CD4+ count of less than 200 cells/mm^3. This was followed by 22.22% of patients with counts between 200 and 350 cells/mm^3. An equal proportion of patients were found in the groups with CD4+ counts between 350 to 500 cells/mm^3 and those with CD4+ counts more than 500 cells/mm^3 (11.11%).This was comparable to the studies by Srujana akela *et al* and Dixit Kumar Kapadiya *et al* where almost half the patients had CD4+ count less than 200 cells/mm^3, followed by 26.2% patients with counts between 200 to 350 cells/mm^3 and the least proportions present in the groups with counts between 350 to 500 and greater than 500 cells/mm^3.This shows that lower CD4+ counts are associated with an increased prevalence of pulmonary tuberculosis.

Pulmonary tuberculosis and DM

Table 3A Comparison of age group in patients of pulmonary tuberculosis with diabetes mellitus

Age group(Years)	Present study(n=4)	Soham Gupta(n=64)
12-20	0%	1.56%
21-40	25%	10.9%
41-60	50%	68.75%
>60	25%	18.75%

In the present study, half of the patients who had tuberculosis with diabetes mellitus as the underlying cause were found to be in the age group of 41 to 60 years, followed by an equal incidence in the age groups of greater than 60 years and 21 to 40 years. This was compared to the study by Soham Gupta *et al* which also showed that in patients having tuberculosis with diabetes as the underlying cause, 68.75% belonged to age group of 41 to 60 years followed by 18.75% in greater than 60 years and 10.9% in the age group of 21 to 40 years. This is probably due to the greater prevalence of diabetes mellitus in the age group of 40 and above.

Table 3B Comparison of clinical feature in pulmonary tuberculosis infection with DM infection

Clinical symptoms	Present study(n=4)	Kuppusamy *et al*.(n=69)	Bachti *et al*.(n=94)
Fever	75%	50.7%	80.9%
Cough	75%	82.6%	98.9%
Night sweats	75%	72%	79.9%
Weight loss	75%	69.6%	96.8%
Hemoptysis	25%	26.1%	42.6%
Dyspnea	25%	17.%	69.1%

The clinical features of patients who had pulmonary tuberculosis with diabetes mellitus as the underlying cause were studies. In the present study, 75% of the patients had fever, cough, night sweats and weight loss as the clinical features. 25% had hemoptysis and dyspnea as the clinical features. This was compared to studies by Kuppusamy *et al* and Bachti *et al*, which also showed that fever, cough, night sweats and weight loss were found more commonly than hemoptysis and dyspnea as presenting clinical features. The discrepencies may be present due to the higher number of study subjects in the comparable studies.

Table 3C Comparison between glycemic control and pulmonary tuberculosis

Hb1AC (%)	Present study(n=4)	Li-kuo huang *et al* (n=214)
<8	25%	47%
>8	75%	53%

The glycemic control of patients with tuberculosis and underlying diabetes was studies.It was found in the present study, that 75% of patients had poor glycemia control with HbA1C levels of greater than 8%.This was compared to the study by Li-kuo huang *et al* where almost similar proportion of

patients were found having HbA1C less than 8% and greater than 8%.This may be due to differences in the study subjects in the present study and the compared study.

Table 3D Comparison of radiological finding in patients of pulmonary tuberculosis with DM

Radiological feature in CXR	Present study(n=4)	QAZI M.A. *et al*(n=150)	Anand *et al*(n=50)
Type of of lesion			
1) Non-homogenous opacities	50%	50%	60%
2) Cavity	25%	20%	30%
3) Homogenous opacities	NIL	15%	36%
4) Multiple opacities	25%	15%	22%
Lung Zone Affected			
Upper zone	25%	50%	16%
Middle zone	50%	13%	-
Lower zone	75%	87%	84%

In the present study, non-homogenous opacities were the most common types of lesions present in half of the patients followed by equal proportion of patients having cavities and multiple opacities. The lower zone was the most common zone affected in 75% of the patients followed by middle zone in 50% of the patients. The upper zone was least commonly affected in 25% of the patients. This was compared to the studies by Qazi MA *et al* and Anand *et al* which also showed that non-homogenous opacities were the most common type of lesions. The most common lung zone affected in these studies was also lower zone. This shows that lower zone is most commonly affected in diabetic patients (in contrast to the typical findings that affect the upper zone) because of high perfusion in the lower zones and increased blood glucose levels, favouring the growth of mycobacteria in the lower zones.

Pulmonary tuberculosis and CKD

Table 4A Comparison of age group in pulmonary tuberculosis with CKD

Age group(Years)	Present study(n=3)	Sohan Gupta *et al*(n=46)
12-20	NIL	NIL
21-40	33.33%	23.94%
41-60	66.67%	56.5%
>60	NIL	19.56%

The age group of the pulmonary tuberculosis with patients having CKD as the underlying comorbidity was compared. In the present study, age group of 41 to 60 years was the most commonly involved which was comparable to the study by Sohan Gupta *et al* which also showed the maximum patients in the same age group.

Table 4B Comparison of clinical features in pulmonary tuberculosis with CKD

Clinical Symptoms	Present study(n=3)	Kuppusamy *et al*.(n=69)
cough	66.67%	82.6%
Weight loss	66.67%	69.6%
Fever	33.33%	50.7%
Hemoptysis	26.1%	26.1%
Dyspnea	17.4%	17.4%

The clinical features of patients who had pulmonary tuberculosis with CKD as the underlying comorbidity was compared. In the present study, cough (66.67%) and weight loss (66.67%) were the most common symptoms followed by fever (33.33%) and hemoptysis (26.1%) with dyspnea (17.4%) being the least common symptom. This was compared to the study by Kuppusamy *et al* which also showed that cough (82.6%) and weight loss (69.6%) were the most common symtoms followed by fever (50.7%) and hemoptysis (26.1%) with dyspnea (17.4%) being the least common symptom. These findings were comparable.

Table 4 C Comparison of pulmonary tuberculosis in CKD patients with dialysis status

	Present study (n=3)	Sanjay Vikrant *et al*(n=22)	Mahesh kumar *et al* (n=5)
Dialysis	66.67%	80%	80%
Non-dialysis	33.33%	20%	20%

In the present study, when the dialysis status of the patients of CKD who had tuberculosis was compared, it was found that 66.67% of patients who had tuberculosis were on dialysis and 33.33% were not on dialysis. This was compared to the studies by Sanjay Vikrant *et al* and Mahesh Kumar *et al* where 80% of the patients who had tuberculosis were on dialysis. This shows that patients who had advanced CKD as indicated by the dialysis status were more immunocompromised and had a greater susceptibility to develop pulmonary tuberculosis.

Pulmonary tuberculosis and Connective Tissue Disease

Table 5A Comparison of age group in pulmonary tuberculosis with connective tissue disorder

Age group(Years)	Present study (n=2)	Golshoy *et al*.(n=6)
12-20	**NIL**	**NIL**
21-40	50%	16.7%
41-60	50%	50%
>60	NIL	33%

The age group of the patients who had tuberculosis with connective tissue disorder as the underlying condition was studied. In the present study, half of the patients belonged to the age group of 21 to 40 years and half of the patients belonged to the age group of 41 to 60 years. This was compared to the study by Golshoy *et al* where in the 50% of the patients belonged to the age group of 41 to 60 years and 33% to greater than 60 years. 16.7% of the patients belonged to the age group of 21-40 years. Connective tissue disorders in general are more prevalent in the reproductive age group. The discrepancies may be due to the small sample size both in the studies. Larger studies are needed to further prove the results.

Table 5B Comparison of clinical feature in pulmonary tuberculosis among connective tissue disorder

Clinical study	Present study(n=2)	Yoshihilo study(n=14)
Fever	75%	21.4%
Cough	50%	28.5%
Weigh loss	50%	45%
Dyspnea	25%	7.1%

In present study, fever (75%) was the most common manifestation in connective tissue disorder patients leading to pulmonary tuberculosis. However, yoshihilo study showed weight loss as major manifestation. Our study might have limitations due to limited number of subjects in our study.

Pulmonary Tuberculosis and Malignancy

Table 6A Comparison of age group in pulmonary tuberculosis with malignancy

Age group(Years)	Present study(n=2)	Golshal *et al* (n=5)
12-20	NIL	NIL
21-40	NIL	20%
41-60	50%	40%
>60	50%	40%

In present study, age group 41-60 years constituted leading age group leading to pulmonary tuberculosis in malignancy patients. However, because of limited number of patients in both the study, there was similar occurrence in age group 20-40 and age group 41-60 years in both the studies.

Table 6B Comparison of pulmonary tuberculosis in different malignancy

Malignancy	Present stud(n=2)	Mark Kaplan *et al* (n=20)
Carcinoma of lung	50%	21.8%
Hematological cancer	NIL	17.8%
Head and neck	NIL	20.9%
Others(prostate cancer, GI cancer, genital cancers, etc)	50%	39.5%

In present study, carcinoma of lung(50%) was the most common cancer leading to pulmonary tuberculosis followed by other group of cancers(50%). Similar results were obtained from Mark kaplan study which constituted lung cancer as a single most leading neoplastic etiology amongst all cancers.

CONCLUSION

Immunocompromised diseases particularly HIV and Diabetes Mellitus definitely affect the incidence of Pulmonary Tuberculosis as evident by radiological presentation of disease (more atypical changes and frequent cavity occurrence in patients with poor glycemic control and Malnutrition and may also show more sputum positivee rates among patients with low CD4 count, poor glycemic control and Malnutrition.The implementations of Tuberculosis interventions and network collaborations; particularly in HIV infected patients; needs to be highlighted to help and generate common feasibilities to improve life expectancy among these patients and to curb the future incidence of Pulmonary Tuberculosis.Our study shows the there is higher occurrence of Pulmonary Tuberculosis in Immunocompromised Patients and they should be screened routinely for detection of pulmonary tuberculosis.

Consent:-

Informed consent was taken as per the standard procedures in the institution.

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Conflicts of interest

There are no conflicts of interest.

Ethical clearance

Obtained from the ethical committee of the institution.

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