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RESEARCH ARTICLE

CLINICAL AND RADIOLOGICAL STUDY OF PULMONARY TUBERCULOSIS IN DIABETES MELLITUS

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ABSTRACT

Back ground: Diabetes mellitus has been reported to modify the presenting features of pulmonary tuberculosis, but there are varying data, particularly regarding the association with lower lung field involvement.
Objectives: Clinical and radiological study of pulmonary tuberculosis in diabetic patients.
Methods: 70 cases of diabetes mellitus with pulmonary tuberculosis were studied. Their clinical profile, relevant tests and chest radiograph results were analysed.
Results: The predominant clinical symptoms noted were anorexia (77.14%), cough (74.29%), and fever (64.29%). 81.63% of male patients were smokers. Clubbing was noted in 14.29% of our patients. Average duration of diabetes was 6.59 years. 74.29% of patients were anaemic and 60% of patients had an erythrocyte sedimentation rate above 50mm hr-1. The average FBS value was 227 mg/dl. 72.73% of patients were sputum positive for acid fast bacilli under the age of ≤50 years. Cavitary lesions were noted in about 52.88% of patients. 27.14% of patients had infiltration. Fibrosis was noted in 30% of patients. Lower lung field involvement was noted in 25.71% of patients and was more common in patients greater than 50 years.
Conclusion: Multiple cavities and multiple lobe involvement are more common in tuberculous diabetics and lower lung field is involved more commonly in older age group patients. Severe hyperglycaemia appears to be a contributory factor to the development of pulmonary tuberculosis in diabetics. Diabetes appears to have no effect on the presenting features of pulmonary tuberculosis to a large extent.

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INTRODUCTION

The incidence of tuberculosis (TB) is greatest among patients with impaired immunity. India is experiencing a double epidemic of HIV and Diabetes Mellitus (DM), both of which are strongly associated with immune suppression. Though more importance is been given to HIV-TB co-infection, we cannot overlook DM, which is showing higher prevalence in pulmonary TB patients compared to HIV. The rising prevalence of DM in high TB burden countries may adversely affect TB control (Gupta *et al*., 2011) Globally the numbers of persons with DM is predicted to double by 2025 (a prevalence rate of about 5.4%), with the greatest number of cases being expected in China and India (Rani Balasubramanian *et al*., 2007).

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India leads the world with largest number of diabetic subjects, earning the dubious distinction of being termed the "Diabetes Capital of the world". DM was associated with increased risk of TB regardless of study design and population. There is now good evidence that people with DM have 2–3 times the risk of developing active TB compared with those who do not have DM (Stevenson *et al*., 2007; Jeon, 2008). Not only may this lead to an increase in the TB burden, but patients with dual disease appear to have an increased frequency of adverse TB treatment outcomes, with delayed sputum culture conversion, an increased risk of death during anti-tuberculosis treatment and an increased risk of recurrent disease after successful completion of treatment (Baker *et al*., 2011). The large dual burden of disease may make management of both conditions more difficult. High quality implementation research is needed to assess the value and ways of screening for TB in patients with DM and vice versa, and to setup standardised system of monitoring and evaluation based on the DOTS model used for TB control (Rom William *et al*., 1981).

The Tuberculosis-Diabetes mellitus (TB-DM) co-morbidity is one of the rising public health problem and the studies in this part of country on TB-DM co-morbidities are lesser. We need more evidence base for the management of the dual burden of TB and DM. The merging epidemics of communicable and non-communicable diseases should be handled properly. Hence the study was taken up to assess the outcome and to suggest the measures. This study would throw light in the direction of creating an evidence base for the treatment of TB in persons with DM.

AIM

To study the clinical profile and radiographic pattern of (PT) Pulmonary Tuberculosis in diabetic patients.

METHODOLOGY

Source of data

The study was undertaken on 70 patients with DM and PT of both gender admitted to Ashram Medical College & Hospital, Eluru after approval from institutional ethical committee and informed consent from patients.

Method of collection of data

PT was diagnosed by detailed history, clinical examination, sputum examination for acid fast bacilli, chest radiography. DM was diagnosed using the national diabetes data group and WHO diagnostic criteria. Adult patients who fulfilled the above criteria were included in the study, diabetic patients with extra pulmonary tuberculosis is excluded from the study.Patients were examined in detail and subjected to relevant laboratory and radiological investigations. The clinical profile which was evaluated in this study include age and sex distribution, symptom of presentation, past history of tuberculosis, duration of DM, history of smoking, incidence of clubbing, haemoglobin level, erythrocyte sedimentation rate(ESR), total leukocyte count(TLC), blood sugar levels(BSL), sputum AFB results and radiological pattern. The results of the above clinical profile, relevant tests and radiological findings were tabulated and analysed.

Statistical analysis

Statistical analysis was done by descriptive statistics as mean, SD etc. Comparison of mean values of continuous parameters under study was done by applying Student's Unpaired't' test. Mann Whitney test, Chi-square and Independent t test have been used to find the significance of study categorical data as appropriate. 'P' value of <0.05 was considered to be statistically significant. The statistical software namely SYSTAT version 12 (made by Cranes Software's, Bangalore) was applied.

RESULTS

Patients were divided into two groups

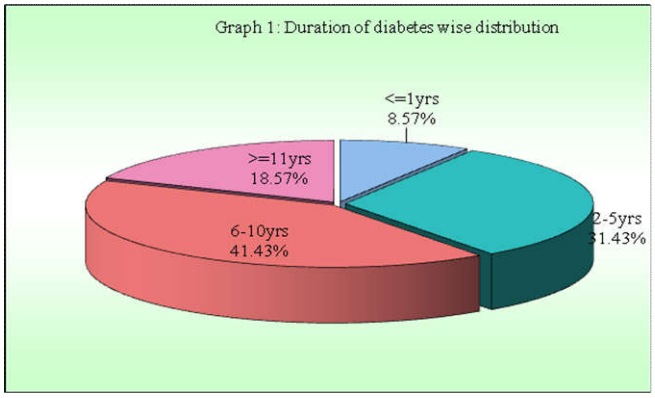
First group: Age ≤50 years - 33 patients (47.14%).

Second group: Age >50 years - 37 patients (52.85%).

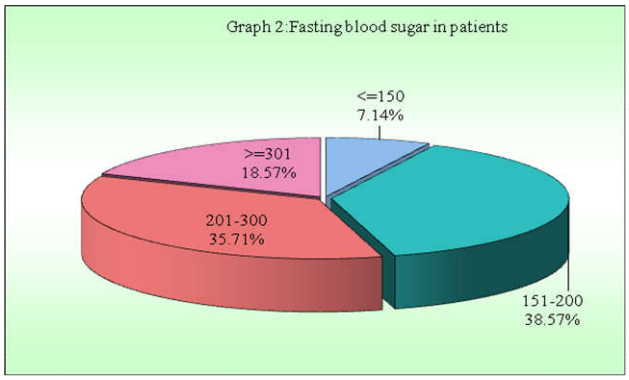
Table 1. Age and sex wise distribution of patients

Age groups	Male	%	Female	%	Total	%
≤40yrs	10	62.50	6	37.50	16	22.86
41-50yrs	12	70.59	5	29.41	17	24.29
51-60yrs	11	68.75	5	31.25	16	22.86
≥61yrs	16	76.19	5	23.81	21	30.00
Total	49	70.00	21	30.00	70	100.00
Mean age	52.53		49.24		51.54	
SD age	11.11		13.85		11.99	

Number of males in this study group were 49(70%) and females were 21 (30%). Male to Female ratio is 2.3:1. The maximum incidence of pulmonary TB was noted above the age of 40 years. The peak incidence was in the age group of 41 – 50 years and > 60 years. (Table 1).The predominant symptoms noted were cough (74.29%), fever (64.29%), and anorexia (77.14%). Other symptoms noted were haemoptysis (12.86%), loss of weight (50%), dyspnoea (21.43%), chest-pain (21.43%), and night sweats (41.43%) (Table 2). 24.29% of the patients had a past history of TB, 12.86% of the patients had associated hypertension, 8.57% of the patients had associated ischemic heart disease, 81.63% of male patients were smokers and 8.57% of the patients had family history of tuberculosis (Table 3). 41.43% of the patients had a duration of DM between 6 – 10 years, 31.43% between 2 – 5 years, 8.57% less than 1year and in 18.57% for more than 10yrs (Graph 1). Fasting blood sugar (FBS) showed a definite co-relation with pulmonary TB. 35.71% of the patients had FBS Value between 201 to 300 mg dl-1, 38.57% had value between 151 – 200 mg dl-1 and 18.57% of the patients had value above 300 mg dl-1. Mean FBS value was 227 mg dl-1 (Graph 2).



Graph 1.Duration of diabetes wise distribution



Graph 2. Fasting blood sugar in patients

45.71% of the patients had post prandial blood sugar (PPBS) value above 350 mg dl-1, 27.14% had values between 251 – 350 mg dl-1 and 27.14% of the patients had value less than 250 mg dl-1.

Table 2. Clinical symptoms

Symptoms	Male	%	Female	%	Total	%	Chi-square	P-value
Cough	37	75.51	15	71.43	52	74.29	0.1280	0.7200
Fever	30	61.22	15	71.43	45	64.29	0.6670	0.4140
Hemoptysis	6	12.24	3	14.29	9	12.86	0.0550	0.8150
Dyspnea	12	24.49	3	14.29	15	21.43	0.9090	0.3400
Anorexia	40	81.63	14	66.67	54	77.14	1.8670	0.1720
Loss of weight	25	51.02	10	47.62	35	50.00	0.0680	0.7940
Chest pain	9	18.37	6	28.57	15	21.43	0.9090	0.3400
Night sweats	18	36.73	11	52.38	29	41.43	1.4830	0.2230

Table 3. Past history

Past history	Male	%	Fem -ale	%	Total	%	Chi-square	p-value
Tuberculosis	15	30.61	2	9.52	17	24.29	3.5550	0.0590
Hypertension	6	12.24	3	14.29	9	12.86	0.0550	0.8150
Ischemic heart disease	5	10.20	1	4.76	6	8.57	0.5560	0.4560
Smoking	40	81.63	0	0	40	57.14	40	0.0001*
Family history of Tuberculosis	3	6.12	3	14.29	6	8.57	1.2500	0.2640

*P<0.05

Table 4. Sputum AFB

Age groups	Sex	Yes	%	No	%	Total
≤50yrs	Male	15	68.18	7	31.82	22
	Female	9	81.82	2	18.18	11
	Total	24	72.73	9	27.27	33
>50yrs	Male	12	44.44	15	55.56	27
	Female	8	80.00	2	20.00	10
	Total	20	54.05	17	45.95	37

Table 5. Side of lesion (right/left/bilateral)

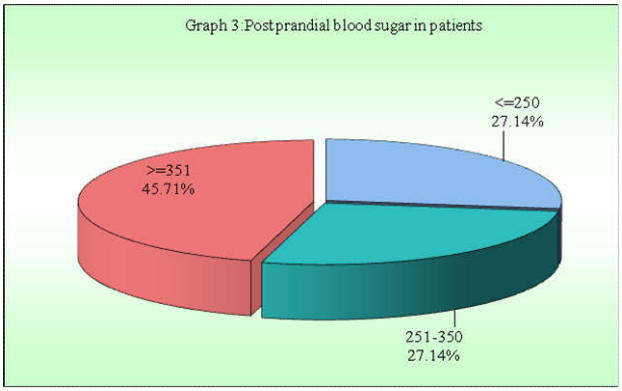
Age groups	Sex	Left	%	Right	%	Bilateral	%	Total
≤50yrs	Male	6	27.27	10	45.45	6	27.27	22
	Female	3	27.27	5	45.45	3	27.27	11
	Total	9	27.27	15	45.45	9	27.27	33
>50yrs	Male	7	25.93	10	37.04	10	37.04	27
	Female	3	30.00	2	20.00	5	50.00	10
	Total	10	27.03	12	32.43	15	40.54	37

Table 6. Lower lung field tuberculosis

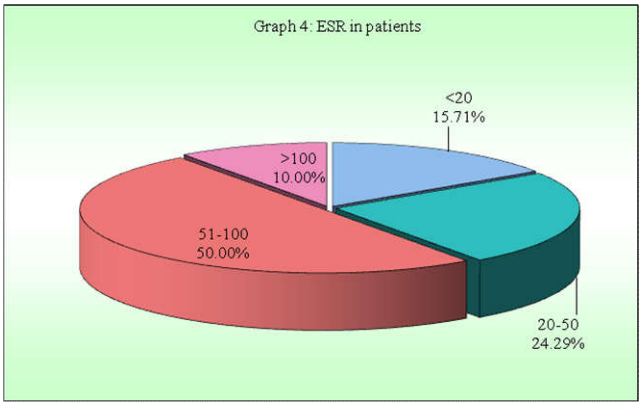
Age groups	Sex	Yes	%	No	%	Total
≤50yrs	Male	6	27.27	16	72.73	22
	Female	4	36.36	7	63.64	11
	Total	10	30.30	23	69.70	33
>50yrs	Male	3	11.11	24	88.89	27
	Female	5	50.00	5	50.00	10
	Total	8	21.62	29	78.38	37

Table 7. Chest X-ray Diagnosis

Chest X-ray Diagnosis	≤50yrs	%	>50yrs	%	Total	%
Parenchymal opacity	1	100.00	0	0.00	1	1.43
Parenchymal opacity, Infiltration	1	100.00	0	0.00	1	1.43
Bronchiectasis	2	66.67	1	33.33	3	4.29
Cavity	9	45.00	11	55.00	20	28.57
Cavity, Infiltration	1	33.33	2	66.67	3	4.29
Consolidation	2	40.00	3	60.00	5	7.14
Fibrous cavity, Infiltration	2	40.00	3	60.00	5	7.14
Fibrous cavity	3	33.33	6	66.67	9	12.86
Fibrosis	2	33.33	4	66.67	6	8.57
Fibrosis,Infiltration	1	100.00	0	0.00	1	1.43
Hydro pneumothorax	1	50.00	1	50.00	2	2.86
Infiltration,Hydro pneumothorax	1	100.0	0	0.00	1	1.43
Infiltration	4	57.14	3	42.86	7	10.00
Pleural effusion	2	40.00	3	60.00	5	7.14
Pleural effusion, Infiltration	1	100.00	0	0.00	1	1.43
Total	33	47.14	37	52.86	70	100.00



Graph 3. Post prandial blood sugar in patients



Graph 4. Erythrocyte sedimentation rate in patients

Mean PPBS value in the study group was 327.57 mg dl-1 (Graph 3). 10% of the patients had anerythrocyte sedimentation rate (ESR) of more than 100 mm hr-1. 50% of the patients had values between 51 – 100 mm hr-1. Only 15.71% of the patients had value below 20 mm hr-1. 84.29% of the study group had an elevated ESR (Graph 4). Sputum AFB was demonstrated in 72.73% of cases ≤ 50 years and in 54.05% of cases >50 years (Table 4). Right sided lung lesions were noted in 45.45% of the cases of age ≤50 years and 32.43% of cases with age > 50 years, left sided lesions were noted in 27.27% of the cases of age ≤ 50 years and 27.03% of cases with age >50 years. Bilateral lesion were noted in 27.27% of the cases of age ≤50 years and 40.54% of cases with age >50 years (Table 5). Lower lung field lesions were noted in 25.71% of the cases. Of these 10 cases were observed in age group ≤ 50 years and 8 cases of age > 50 years (Table 6). Chest x-ray showed cavitary lesions in 52.85 %, fibrosis in 30% of the patients and infiltrative lesion in 27.14% of the patients. Other lesions noted are consolidation (7.14%), pleural effusion (8.57%), hydro pneumothorax (4.28%), parenchymal opacity (2.85%) and bronchiectasis (4.28%) (Table 7).

DISCUSSION

A clinical and radiological evaluation of 70 cases of pulmonary tuberculosis with diabetes mellitus was done. The high incidence of tuberculosis in diabetic patients, reported by western and Indian workers suggest a significant association between these two diseases (Vishwanath, 1981; Davies *et al*., 1996). In our study the total number of males were 70% and females were 30%. The male to female ratio was 2.3:1.In a study done by Desmukh and others among the 138 cases of diabetes with pulmonary tuberculosis, 72.4% were males and 27.53% were females (Deshmukh, 1984).

Patel JC showed a similar ratio of male: female. In the 179 cases he studied, 76% were males and 24% were females (Patel *et al*., 1977). Above mentioned studies showed an increased incidence of the disease in males as compared to females and our study also noted the same. The high incidence of disease in males is possibly due to the fact that both tuberculosis and diabetes are more common in males. Another reason could be that the number of male patients seeking medical attention or evaluation is more than females. In the present study, maximum incidence of pulmonary TB was noted above the age of 40 years. The number of patients above 40 years were 77.14%. The peak incidence was seen in the age group of 41 – 50 years and above 60 years. Which correlates well with study done by Desmukhwhoreported that majority of cases of tuberculous diabetics belong to the age group of 45 years and above (82.6%) (Deshmukh, 1984). Reason might be general morbidity increase with age, and progressive waning off of immunity with age. The predominant symptoms noted in our study was anorexia (77.14%), cough (74.29%), fever (64.29%), Loss of weight was also more (50%). night sweats (41.43%). In a study done in Ethiopian diabetic patients with tuberculosis by Fleke Y, three most common symptoms of tuberculosis were fever (80.5%), sweating (80.4%) and cough (70.5%) (Feleke *et al*., 1999). In our study also the percentage of anorexia, cough and fever was high.Anorexia is because many patients are having less immunity or toxaemia, no proper nutritional diet, cough is common because many are smokers which can be a contributing factor during disease process and fever may be due to host immune response to bacteria and could be due to auto immune response to maintain thermoregulatory system.

24.29% of our patients had past history of TB. In India TB being an endemic disease relapse is common in association with both DM and TB. Concomitantly 12.86% of the patients were detected to have hypertension.This could be because hypertension is common in the age group of 40-50 years along with DM and TB. Incidentally 8.57% of patients in our study had family history of TB in recent past. 40 out of 49 males (81.63%) were smokers in our study. Our study is comparable to studies done by S den Boon, S W P Van lill, M W Borgdoffand others who concluded more than 82% were smokers. Pulmonary TB is less common in non-smokers and light smokers, and more common in moderate and heavy smokers compared to controls of same age suffering from other diseases (Lowe, 1956). Smoking may be a contributing factor in developing tuberculosis in these patients. Suggested mechanism could be decrease immune response, CD4 lymphophenia, defect in macrophage immune response and mechanical disruption of ciliary function in airways. Clubbing was noted in 14.29% of the patients in our study. Of these 85% had far advanced TB as evidenced by clinical and radiological examination. In study done by Gordonleitch A, incidence of 21% of clubbing was reported and was associated with more severe pulmonary damage. Gross clubbing occurs with long standing TB (Gordonleitch, 2000). Finger clubbing is of value in assessing patients with pulmonary TB because it helps to identify those with severe disease. 74.29% of the patients in our study were found to be anaemic. In a study done byPavan Malhotra, it was found that 88.76% of tuberculosis patients were anaemic. 50% of patients in this study group showed an ESR between 51 to 100 and 24.29% had values between 20 – 50 mm hr-1. Values above 100 were noted in 10% of patients. In study done by Gordonleitch A, 52% of the patients has ESR <50 mm hr-1.

The total white cell count (WBC) in our study showed an average value of 10714. Few patients who had far advanced TB showed a normal WBC, and certain others with mild to moderately advanced TB had a higher WBC. So there was no correlation noticed between the severity of TB and total WBC. Knelle has proved that leukocyte picture is of no help in diagnosis of TB and our study also shows the same. In general a normal total WBC count in the presence of extensive pulmonary shadowing on a chest radiograph favours a diagnosis of TB rather than acute pneumonia or lung abscess (Gordonleitch, 2000). The study of the duration of DM in relation to the onset of TB showed that in most of the cases, DM was diagnosed before the development of TB (Feza, 2001). Prior to the onset of TB, 41.43% patients had duration of DM between 6 – 10 years, 31.43% of the patients had duration of DM between 2 – 5 years and 8.57% of the patients less than 1year. The average duration of DM in this study was 6.59 years with standard deviation ± 3.52. The interval between detection of DM and the onset of pulmonary TB was studied by Tripathy and others. They reported that it varied from several months to 15 years, mean interval being about 6 years (Tripathy *et al*., 1984; Nihalani, 1978). In Anand AL study, DM was detected before TB in 70% of cases. 32% of patients had DM for 1 – 5 years, 32% had it for 6 – 10 years and 20% more than10 years (Anand, 1984). The duration of DM is significant because there is an increased opportunity for infections with increased duration of DM. The result of the present study is comparable to other studies. The FBS value of 200 – 300 mg% was noted in 35.71% of the patients and values above 300mg% were noted in 18.57% of the cases. Mean FBS was 227 with a standard deviation of ± 61.00.

PPBS value at 2 hours was above 350mg% in 45.71% of patients. Mean PPBS was 327.57 with a standard deviation of ± 77.54. This showed that in most of the cases blood sugar was not controlled.In a study done by Sachdeva AK and others, it wasshowed that high incidence of pulmonary TB was associated with severe hyperglycemia (Sachdeva *et al*., 1984). Deshmukh PA also had made a similar observation (Deshmukh, 1984). In a study of 180 cases of diabetics, daily dose of more than 100 units of insulin was needed in 88.7% of tuberculous diabetics in contrast to 25.2% of nontuberculous diabetics.[18]The finding in this study is consistent with the proposal that there is association between tuberculous infection and increase plasma glucose levels (Oluboyo, 1990). 72.73% of patients ≤50 years and 54.05% of the patients>50years were sputum positive for acid fast bacilli. Reason of high sputum positive in younger age group mostly may be due to their daily social and labour activities and being working class people and their immune response is leading to break down of tuberculosis. Though cavitary lesions maintain high bacterial population, less smear positivity in elderly is noted in DM. This may be related to muscle weakness due to uncontrolled hyperglycaemia and less effective expectoration (Banerjee, 2005). The examination of chest radiographs revealed that 65.71% of the patients had unilateral lesions and 34.28% of the patients had bilateral lesions. In both these group, predominant lesions were noted in the upper zones. In our study, right sided lesion was noted in 38.57% and left sided in 27.14% and rest (34.28%) of the lesions were bilateral. The increased incidence of right sided disease is probable due to more lung mass on the right side. Bilateral distribution may be due to rapid bronchial dissemination of TB in diabetics respectively. Upper zone involvement are more common in TB because alveolar concentration is more than arterial concentration in upper zones and also bacteria being aerophilic grow better in upper zones. 25.71% of patients in our study had lower lung field involvement. It was more common in age group >50 yrs and females irrespective of age (45%). In study done by Ravindran P and others, lower lung field TB patients were 13.81% (Ravindran, 1992). In study done by Bacakoglu F and others, it was reported that in tubercles diabetes lower lung field TB was significantly associated with female gender preponderance, and in patients older than 40 yrs (Bacakoglu *et al*., 2001; Perez *et al*., 2000; Ikezoe *et al*., 1992). Hence this study is comparable to the above studies with respect to incidence.Decrease immunity seen in early pregnancy and older age could be the cause for lower lung field TB in women. In patients >50 years, cavitary lesions (64.86%) were the most common type of lesions noted followed by fibrosis (35.13%), infiltration (21.33%). In patients < 50 years, also cavitations was more common (45.45%) followed by infiltration (33.33%). Fibrosis (24.24%) was very less in this group compared to patients above 50 years of age.

Overall cavitary lesions (52.88%) were the most common type of lesions noted followed by fibrosis (30%), and infiltration (27.14%) in both the age groups. In a study done by Perez Guzman and others, it was reported that more tuberculous diabetics develop multiple cavities and also cavitations are more common radiological pattern (Anand, 1984; Ikezoe *et al*., 1992). In a study done by B vidyasagar *et al* cavities were common. As reported in Benerji Sand otherstudies, TB in diabetic patients is associated with extensive caseation of lung tissue and cavitary lesions, with little pleural involvement (Banerjee, 2005). Our study results were comparable to above studies. Cavitations, infiltration, fibrosis were more common. Higher prevalence of cavities among pulmonary tuberculosis patients is probably because it causes extensive caseous necrosis. Fibrosis is probably due to active inflammation lead to alveolar injury and maladaptive repair, resulting in fibroblast proliferation and ultimately leading to fibrosis in its chronic process, more number of relapse cases and longer duration of disease.Other radiological lesions noted were bronchiectasis, hydro pneumothorax, other parenchymal opacity, and consolidation. In other studies consolidation, infiltrations were more common in lower lung field tuberculosis. Our study correlates with most of the above radiological studies in regards to the side of lesion, site of lesion, extent of lesion as well as nature of radiological pattern.

Conclusion

Multiple cavities and multiple lobe involvement are more common in tuberculous diabetics and lower lung field is involved more commonly in older age group patients. Severe hyperglycaemia appears to be a contributory factor to the development of pulmonary tuberculosis in diabetics. Diabetes appears to have no effect on the presenting features of pulmonary tuberculosis to a large extent.

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