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Case Study

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BIDIRECTIONAL RELATIONSHIP BETWEEN DIABETES MELLITUS AND TUBERCULOSIS

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ABSTRACT

India has a high prevalence of Tuberculosis (TB) as well as Diabetes Mellitus (DM). The risk of TB amongst DM patients is three times higher than those without. The aim of the study is to determine the prevalence of DM with TB and symptomatology, time to clinical improvement and prognosis in TB patients with DM. It is prospective observational study carried out for a period of 6 months in TB wards SVRR Govt General Hospital in Tirupati, Andhra Pradesh. A total of 31 patients with confirmed diagnosis of TB and DM were recruited. 26 (84%) were males and 5 (16%) were females. 30 (97%) was pulmonary TB and 1(3%) was extra pulmonary TB. The predominant age group of patients was 51-60 years. The mean BMI was <18.5. 23 (74%) of study population were smokers and 22 (71%) were alcoholics. 29 (94%) were positive for sputum test. 19 (55%) were daily wage workers. Cough, SOB, weight gain, loss of appetite was main symptoms. There were 6 (19%) deaths. One – way Annova was performed for FBS and PPBS levels. For FBS levels, p – value was 0.05, considered not statistically significant. For PPBS levels, P – value of 0.03 considered statistically significant. We concluded that there is bidirectional relationship between TB and DM and both impact the presentation of one another. Early screening for DM in TB patients and for TB in diabetics will prevent morbidity and mortality. Judicious control of blood sugar levels will improve the symptomatology and prognosis in TB patients.

KEYWORDS: Tuberculosis, Diabetes Mellitus, prevalence, bidirectional relationshiop, screening.

INTRODUCTION

Diabetes Mellitus is a major public health problem in India.[15] It is a very common health problem across the globe. It has a huge impact on Quality of life and on individual's subjective perception of physical, emotional and social well-being, including both a cognitive component and an emotional component.[15] It is fast gaining the status of potential epidemic in India with more than 62 million diabetic individuals currently diagnosed with the disease and represents 49 percent of the world's diabetes burden, with an estimated 72 million cases in 2017, a figure expected to almost double to 134 million by 2025.[1]

The International Diabetes Federation (IDF) estimates a current worldwide diabetes disease burden of about 415 million, which is projected to hit 642 million by 2040 (over 60% increase).[6] According to Wild et al., the prevalence of diabetes is predicted to double globally from 171 million in 2000 to 366 million in 2030 with a maximum increase in India.[1] It is predicted that by 2030 diabetes mellitus may afflict up to 79.4 million and over 85% world's diabetic individuals in India, while China (42.3 million) and the United States (30.3 million) will also see significant increase in those affected by the disease.[1&12]

Preliminary results from a large community study conducted by the Indian Council of Medical research (ICMR) revealed that a lower proportion of the population is affected in states of Northern India (Chandigarh 0.12 million, Jharkhand 0.96 million) as compared to Maharashtra (9.2 million) and Tamil Nadu (4.8 million).[1]

Rough estimates showed that the prevalence of diabetes in rural populations is one-quarter that of urban population for India and other Indian sub-continent countries such as Bangladesh, Nepal, Bhutan, and Sri Lanka.[1] Similar results showed by National Urban Survey conducted across the metropolitan cities of India reported similar trend: 11.7 per cent in Kolkata (Eastern India), 6.1 per cent in Kashmir Valley (Northern India), 11.6 per cent in New Delhi (Northern India), and 9.3 per cent in West India (Mumbai) compared with (13.5 per cent in Chennai (South India), 16.6 per cent in

Hyderabad (south India), and 12.4 per cent Bangalore (South India).[1]

A suggested explanation for this difference is that the North Indians are migrant Asian populations and south Indians are the host populations.[1] However this possible cause-and-effect has not been corroborated through further research. Similar ethnographic disparities have been observed in indigenous and non-indigenous populations in countries colonised by Great Britain: indigenous people from New Zealand and Australia have been shown to suffer from diabetes and cardio-metabolic disorders more than the non-indigenous people.[1]

The risk factors peculiar for developing diabetes among Indians include high familial aggregation, central obesity, insulin resistance and life style changes due to urbanization. Screening for gestational diabetes and impaired glucose tolerance among pregnant women provides a scope for primary prevention of the disease in mothers as well as in their children.[12]

Prevalence of Tuberculosis

Tuberculosis [TB] is an air born infection caused by Mycobacterium Tuberculosis. It is a major global health problem. India is facing the dual problem of being the highest TB-burden country having a large number of people with diabetes posing a serious challenge for the health system that is high TB burden along with DM prevalence.[4&2]

In 2016, as a result of new information being available, the GoI together with the World Health Organisation revised upwards the estimates for the burden of TB in India and estimated 28 lakh cases occurred and 4.5 lakh people died due to TB. India also has more than a million "missing" cases every year that are not notified and most remain either undiagnosed or unaccountably and inadequately diagno sed and treated in the private sector.

In 2015, across world-wide there were 10.4 million new cases noticed and World Health Organization (WHO) estimated that 1.4 million died from the disease in 2015 despite several preventive strategies to reduce the burden and impact.[2&6]

In India, the average prevalence of all forms of tuberculosis estimated to be 5.05 per thousand, prevalence of smear-positive cases 2.27 per thousand and average annual incidence of smear-positive cases at 84 per 1,00,000 annually.[3]

Some epidemiologists forecast a rise of 20 percent in incidence in the next 20 years, with a cumulative rise of 46 million cases of tuberculosis during that period, largely as a consequence of HIV epidemic.[3]

Prevalence of both Diabetes and Tuberculosis

Diabetes and Tuberculosis often present together and complicate each other at many levels.[4] India has a high prevalence of tuberculosis (TB) as well as diabetes mellitus (DM).[11] DM is a chronic disease caused by deficiency of insulin production by the pancreas. The risk of TB amongst DM patients is three times higher than those without. The estimated national prevalence of DM is 7.3%.[11] The prevalence of diabetes in tuberculosis patients was found to be 29% (known diabetics - 20.7%, new Diabetes cases - 8.3%).[4]

Screening TB patients for fasting blood sugar estimation will help in early detection of diabetes. About 95% of patients with tuberculosis (TB) and 70% of patients with diabetes mellitus (DM) live in the low and middle income countries.[4]

The epidemic growth of DM has occurred in developing countries where TB is highly endemic. As a result, DM and TB are increasingly present together.[4] The involvement between DM and TB is supported by the fact that patients with DM have impaired cell-mediated immunity, renal failure, micronutrient deficiency and pulmonary microangiopathy, all of which augment their vulnerability to develop TB.[14]

Interactions between Diabetes and TB

- TB occurs 10 times more frequently in DM.[5]
- In most cases TB develops after onset of DM.[5]
- The PTB occurrence increases with duration of DM.[6]
- Host defence and immune cell functions become defective with the increased incidence of pulmonary TB in diabetics.[6]
- Immune disorganization involves the cell mediated arm of immune system.[6]
- There is a distinct influence of hyperglycemia on the microbial function of macrophages with even brief exposures to blood sugar level of 200 mg% significantly increasing the respiratory burst of these cells.[6]
- DM causes delayed clearance of infection and spread of infection in host.[6]

Cause Of Glucose Intolerance In Tuberculosis

- Epinephrine, glucagon, cortisol and growth hormones are stimulated by fever. Inactivity and malnutrition raise blood sugar level in excess amounts.[6]
- Plasma level of tumor necrosis factor alpha (TNF ALPHA) and interleukin (IL-1) are also raised in severe illness which can stimulate the anti insulin hormones.[7]
- Serum levels of adrenocorticotropins hormone, cortisol, and T3 have been found to be decreased in patients with TB.[7]
- In severe TB, endocrine function of pancreas also has been found to be adversely affected.[8]
- Disorganization of lipid metabolism has been described in patients with TB.[8]

Effects of Anti- TB Drugs on Blood Sugar Level

- Rifampicin- powerful inducer of hepatic microsomal enzyme which lower serum levels of anti-diabetes drugs sulphonyl ureas and biguanides.[9]
- Pyrazinamide- Causes hyperglycemia.[9]

Diabetics have three to four times higher risk of developing TB than those without diabetes.[5] TB induces glucose intolerance and worsens the glycemic control in people with DM.[5]

Signs and Symptoms of Tuberculosis

- Tiredness or weakness,[8]
- Weight loss,[8]
- Fever,[8]
- Night sweats.[8]

If the infection in the lung worsens, then further symptoms can include:[8]

- Coughing,[8]
- Chest pain,[8]
- Coughing up of sputum (material from the lungs) and/or blood,[8]
- Shortness of breath.[8]

Risk Factors

1. Poverty.[10]
2. Malnutrition.[10]
3. Overcrowding.[10]
4. Immunosuppression including HIV/AIDS.[10]
5. Diabetes.[6]
6. People with silicosis.[6]
7. Chronic renal failure and persons on hemodialysis.[6]
8. Peptic ulcer patients.[10]

Diagnosis

1. Sputum for AFB, CBNAAT.[6]
2. Chest X-ray.[6]
3. CT Chest.[6]
4. Tuberculin test.[6]
5. Blood test- ESR.[6]
6. TB culture of body fluids.[6]

METHODOLOGY

Aim

The aim of the study is to determine the prevalence of diabetes mellitus with Tuberculosis, and symptomatology, time to clinical improvement and prognosis in TB patients with Diabetes attending SVRR Govt General Hospital in Tirupati, Andhra Pradesh.

Objectives

The objectives of the study are to estimate the prevalence of DM amongst adult hospitalized TB patients at SVRR Govt. General Hospital, Tirupati and determine factors associated with the likelihood of DM-TB co-prevalence.

Methodology

- **Study design:** A Prospective observational study.
- **Study site:** TB wards SVRR Govt General Hospital, Tirupati.
- **Study duration:** 6 months (July to December 2018).
- **Sample size:** 31 Patients.
- **Inclusion criteria:** Patients of either sex who are diagosned with diabetes and TB.
- **Exclusion criteria**

- Patients not willing for study.
- Patients lost to follow up

Study Materials

- Patient demographic data collection forms.
- Patient informed consent forms.

Method of Study

- A total of 31 patients with confirmed diagnosis of TB with diabetes and were recruited. The symptomatology, sputum status, blood sugar levels both fasting and post prandial were studied at the time of admission, after 15 days and 1 month.

Ethical Justification

Written and oral informed consent was taken from the patients after explaining the nature of the study. No additional charge was incurred on the patients for the various investigations- all were free of cost, and those who wanted to leave the study were allowed to leave.

Statistical Analysis

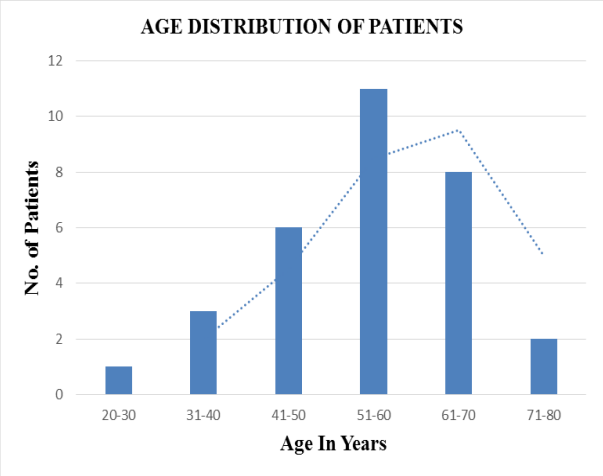
Percentages were calculated for all categorical variables considering the literature prevalence. Data was entered into MS – excel spread sheets. Mean and standard deviation was calculated for all continuous variables. After obtaining the data from the patients diagnosed with both TB and diabetes mellitus, one – way Annova was performed for FBS and PPBS levels. For FBS levels, p – value was 0.2 considered not statistically significant. For PPBS levels, P – value was 0.03 considered statistically significant.

RESULTS

In our study a total of 31 patients were enrolled with both Pulmonary and extra pulmonary tuberculosis and diabetes mellitus.

Age Distribution of Patients

Tuberculosis and diabetes mellitus was observed in our study in 11 patients (35%) in the age group of 51-60 years, followed by 8 (26%) in the age group of 61 – 70 years, 6 (19%) in the age group of 41 -50, 3 (10%) in the age group of 31-40, 2 (6%) in the age group of 71-80 and 1 (3%) in the age group of 20-30 was shown in figure 1. The mean± SD age of patients was 55.9 ±11.94.



MEAN ± SD = 55.9± 11.94

Fig.1: **Age Distribution of Patients.**

Gender Distribution of Patients

In our study of 31 patients with both tuberculosis and diabetes mellitus, 26 (84%) were males and 5 (16%) were females was shown in table 1.

Table 1: Gender Distribution of Patients.

Sr.No	Gender	Frequency	Percent
1.	Females	5	16
2.	Males	26	84

Body Mass Index (BMI)

In our study, out of 31 patients 10 (32%) patients were found with BMI > 18.5 and 21 (68%) patients with BMI < 18.5 was shown in figure 2.

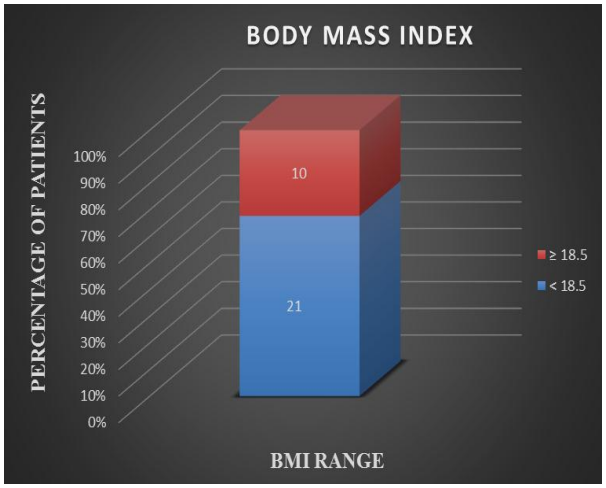


Fig. 2: Body Mass Index.

Sputum Test

In our study, the patients with positive result for sputum are 29 (94%) and negative for sputum are 3 (10%).

Category I And II

In our study, patients on CAT I Anti- TB drug are 13 (42%) and patients on CAT II Anti- TB drug are 18 (58%).

Type of TB

In our study, out of 31 patients, 30 (97%) were of pulmonary TB and 1 (3%) is extrapulmonary TB was shown in Table 2.

Table 2: Type of TB.

S.No	Type of TB	No. of patients
1.	Pulmonary	30
2.	Extra Pulmonary	1
	Total	31

Smoking History

In our study among 31 patients diagnosed with both tuberculosis and diabetes mellitus, 23 (74%) were smokers and 8 (26%) were non smokers was shown in figure 3.

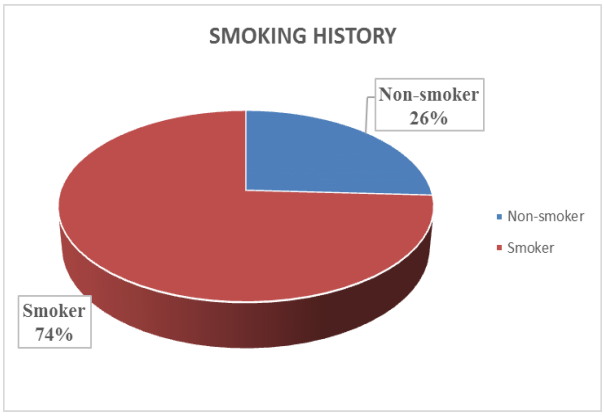


Fig. 3: Smoking History.

Alcohol History

In our study among 31 patients diagnosed with both tuberculosis and diabetes mellitus, 71% (22) were alcoholics and 29% (9) were non-alcoholics was shown in figure 4.

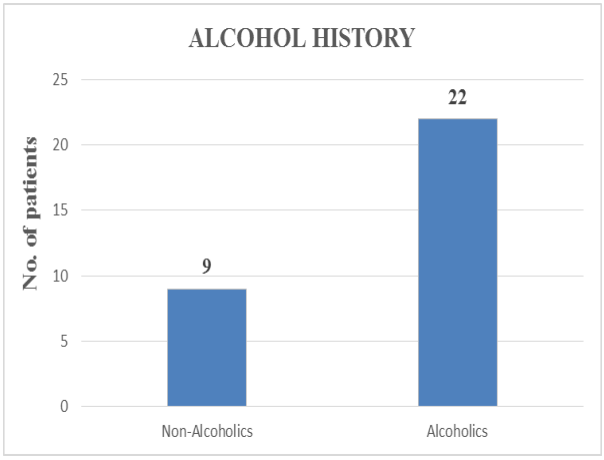


Fig. 4: Alcohol History.

Occupation

The occupation of both tuberculosis and diabetes mellitus patients observed were, 19 (55%) coolies, 9 (20%) farmers, 2 (6%) chefs, 2 (6%) drivers and 1 (3%) contractor was shown in Figure 5.

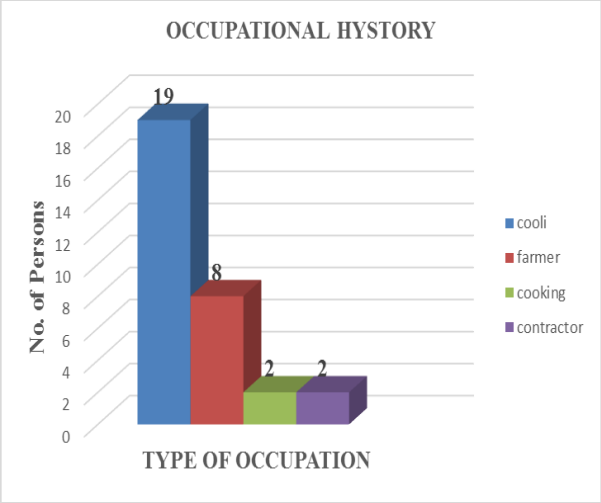


Fig. 5: Occupational History.

Sputum Test

In our study of 31 patients with both tuberculosis and diabetes mellitus, 28 (90%) were found to be positive for sputum test, where as 3 (10%) were found to be negative for sputum test.

Symptoms

In our study,common symptoms observed were- cough, breathlessness, fever, weight loss, loss of appetite. After 15 days of follow up symptoms improved as follows: Improvement of cough among 20 (65%), SOB 20 (65%), weight gain 24 (77%) and Appetite 28 (90%) was shown in Figure 6.

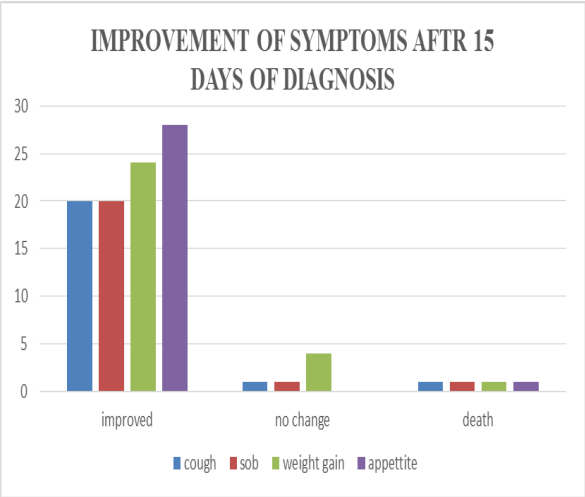


Fig. 6: Symptoms after 15 Days of Follow Up.

After 30 days of follow up symptoms improved are as follows: Improvement of cough among 23 (74%), SOB 23 (74%), weight gain 25 (81%) and 27 (87%) was shown in Figure 7.

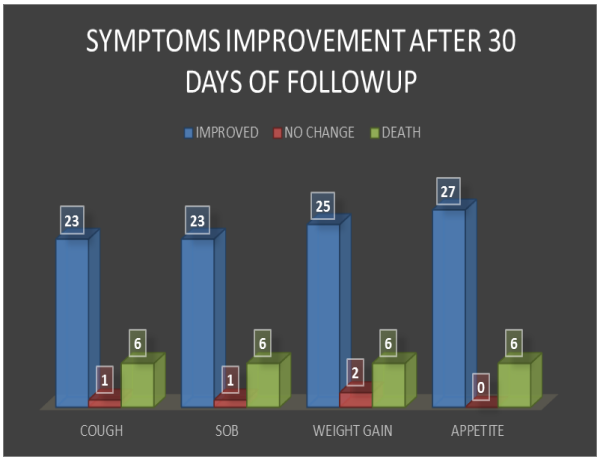


Fig. 7: Symptoms after 30 Days of Follow Up.

Mortality Rate

In our study out of 31 patients, 6 (19%) members died. Out of 6 (19%), 3 (50%) had hydropneumothorax, 1(17%) had renal parenchymal disease and 1(17%) had right lung abscess and 1(17%) had meningitis.

FBS Levels after Follow Up

After 15 days of follow up, FBS levels unexpectedly increased among 13 patients. Where as, after 30 days of follow up, FBS Levels continued to be high among 8 patients was shown in Table 3. So, FBS levels increased in 8 people actually.

PPBS Levels after Follow Up

After 15 days of follow up, PPBS levels increased among 15 patients.PPBS levels continued to be high in 7 people after 30 days inspite of TB treatment was shown in Table 4.

Table 3: Sugar Levels Increased After Follow Up.

SUGAR LEVELS	15 DAYS	30 DAYS
FBS	13	8
PPBS	15	7

Table 4: Summary of Data of FBS levels

		Treatments				
	1	2	3	4	5	Total
N	25	25	25			75
∑X	4295	4189	3878			12362
Mean	171.8	167.56	155.12			164.827
$\sum X^2$	827105	771873	638798			2237776
Std.Dev.	60.9727	53.9923	39.3926			52.012

Table 5: Results of FBS levels.

Source	SS	Df	MS	
Between-treatments	3757.9467	2	1878.9733	F = 0.68872
Within-treatments	196430.8	72	2728.2056	
Total	200188.7467	74		

The f-ratio value is 0.68872. The p-value is 0.0505495. The result is not significant at p<0.05.

After obtaining the data from the patients diagnosed with both TB and diabetes mellitus, one – way Annova is performed for FBS and PPBS levels. For FBS levels, p – value of 0.05 considered not statistically significant was shown in Table 5. For PPBS levels, P – value of 0.03 considered statistically significant was shown in Table 7.

Table 6: Summary of Data of PPBS levels.

		Treatments				
	1	2	3	4	5	Total
N	25	25	25			75
∑X	4295	4189	3878			12362
Mean	171.8	167.56	155.12			164.827
$\sum X^2$	827105	771873	638798			2237776
Std.Dev.	60.9727	53.9923	39.3926			52.012

Table 7: Results Data of PPBS levels.

Source	SS	Df	MS	
Between-treatments	18404.5867	2	9202.2933	F = 3.66975
Within-treatments	180548	72	2507.6111	
Total	198952.5867	74		

The f-ratio value is 3.66975. The p-value is 0.030363. The result is significant at p<0.05.

LIMITATIONS

It is too small; a larger study is needed to study prognostic factors in patients with both TB and diabetes.

SUMMARY

1. 31 patients enrolled for the study with both TB and DM, 26 (84%) were males and 5 (16%) were females.
2. 30 (97%) was pulmonary TB and 1(3%) was extra pulmonary TB.
3. The predominant age group of patients was 51-60 years.
4. The mean BMI was <18.5.
5. 23 (74%) of study population were smokers and 22 (71%) were alcoholics.
6. Sputum positivity seen in 29 (94%) of population.
7. Most of the patients 19 (55%) were coolies.
8. Cough, SOB, weight gain, loss of appetite were main symptoms and all of them improved with in first 15 days and further improved by 30 th day..
9. Fasting and PPBS levels however did not show similar improvement inspite of adequate TB treatment and 7 patients continue to show high FBS and PPBS levels at 30 th day of starting of treatment.
10. There were 6 (19%) deaths which is considerably high but can be explained by presence of Hydropneumothorax, lung absess, meningitis in the patients.

CONCLUSION

There is bidirectional relationship between TB and DM and both impact the presentation of one another. Early screening for diabetes in TB patients and for TB in diabetics will prevent morbidity and mortality. Judicious control of blood sugar levels will improve the symptomatology and prognosis in TB patients.

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