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ORIGINAL RESEARCH

Occurrence of Diabetes Mellitus with Rifampicin Resistance in patients of Pulmonary Tuberculosis

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ABSTRACT

Introduction: The drug-resistant tuberculosis strains that are on track to become the world's deadliest infections are responsible for one-fourth of the deaths caused by antimicrobial resistance.[2] the prevalence of MDR-TB is between 3% & 50% among re-treatment cases. There is a rise in the number of instances of multidrug-resistant tuberculosis in the present day. Understanding the connection between diabetes & MDR-TB is becoming increasingly important as the prevalence of MDR-TB rises worldwide. Diabetes & tuberculosis (TB) have been studied together for a long time. Patients incur greater financial costs due to TB-diabetes mellitus comorbidities & delayed diagnosis & treatment. The sooner these diseases are diagnosed, the more likely they are to be treated successfully. **Material and Methods:** This study was a hospital based cross sectional research conducted in the Department of respiratory medicine, TMMC & RC, MORADABAD among 160 patients who were sputum smear positive & those who meet our inclusion & exclusion criteria was taken in study group. The aim of the research was to analyse the occurrence of DM with Rifampicin Resistance in patient of Pulmonary Tuberculosis. **Result:** It was a hospital a cross-sectional research conducted in the Department of pulmonary medicine, TMMC & RC, MORADABAD among 160 patients. Maximum participants were between the ages of 51 & 60 (26.25%), then 41 & 50 (22.50%), & the youngest were between the ages of 16 & 20 (6.88%) & 31 & 40 (10%). Male participants accounted for 69.4% of the total H/O ATT intake was reported among 10% of the study subjects in this study. Out of 160 subjects, 68.1% live in rural area while 31.9% reside in urban location. diabetes mellitus was revealed in 27.50% of the subjects. Most common clinical symptom was cough (96.9%) followed by fever (78.7%) & sputum (72.5%). Mean HbA1c among the study subjects was 6.54±2.34. Out of 43 diabetic subjects with positive AFB outcome; 27, 9 & 7 subjects had diabetes since <1 year, 1-5 year & >5 year respectively. Samples were found to be resistance in 9.09%, 2.59% & 90.91%, 97.41% of the subjects with & without diabetes mellitus respectively. Mean HbA1c level in CBNAAT resistant & sensitive outcome was 7.77±2.53 & 6.48±2.27 respectively with statistically significant difference. **Conclusion**: Our findings suggest a link between diabetes and rifampin resistance, so we recommend integrating diabetes surveillance into TB programs, especially in changing epidemiological contexts. Quantifying the disparities in TB diagnostic findings is also needed to provide a global research setting where study results may be appropriately compared.

Introduction

Since 1991, the World Health Organization has declared tuberculosis a global public health emergency because it is the greatest infectious disease killer of adults around the world.[1] The drug-

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resistant tuberculosis strains that are on track to become the world's deadliest infections are responsible for one-fourth of the deaths caused by antimicrobial resistance.[2] TB affects people of all ages & geographic locations. However, TB can be treated & prevented. However, TB in children & adolescents is commonly missed by clinicians & can be challenging to cure. Eighty-seven percent of the world's new TB infections occurred in just 30 high TB burden countries in 2021. The expected annual decline in global tuberculosis incidence is 1%, which is far below the 4-5% decline needed to meet WHO's End TB Strategy targets.[3] On the other hand, mortality rates are falling at a faster rate of 4.1 percent annually. Recent studies show that the prevalence of MDR-TB is between 3% & 50% among re-treatment cases.[4] The reported frequency of drug resistance in retreatment cases has increased over the past decade, particularly among those treated sporadically, with the incidence of MDRTB ranging from 12% to 17%.[5] Overcrowding, malnutrition, silicosis, & HIV infection are all well-known risk factors & co-morbidities for tuberculosis, but it is also necessary to treat chronic illnesses like diabetes, which weaken the immune system & increase the likelihood of infection. The treatment success & prognosis of tuberculosis (TB) are significantly affected by chronic hyperglycemia.[6] An estimated 15% of TB patients in high-burden countries have diabetes in 2019. Diabetes is a known risk factor for the development of active TB.[7] Due to the increasing prevalence of both diseases worldwide & the projected increase in diabetes incidence & fatalities over the future decades, research into the correlation between diabetes & TB is gaining momentum.[8,9] It is generally believed that people with diabetes are more susceptible to MTB infection because their cell-mediated immunity is less effective. Reactivation, recurrence, & relapse of tuberculosis (TB) are more common in patients with diabetes.[10] Patients with TB & diabetes have a higher risk of treatment failure due to delayed sputum conversion.[11,12] Understanding the connection between diabetes & MDR-TB is becoming increasingly important as the prevalence of MDR-TB rises worldwide. Diabetes & tuberculosis (TB) have been studied together for a long time. According to the International Diabetes Federation (IDF), there are approximately 175 million unrecognized instances of diabetes in the world.[13]

This figure is 62% in Africa & 54% in south-east Asia, where the prevalence of tuberculosis is also highest. Because of this, DM poses a serious threat to TB control & may have the greatest impact in resource-poor regions where TB is prevalent. Using Gene Xpert, researchers have identified a mutation in the rpo gene that causes rifampicin resistance by altering the beta component of bacterial RNA polymerase (RNAP). It's well-known that people with diabetes are at a higher risk of contracting tuberculosis. There is a rise in the number of instances of multidrug-resistant tuberculosis in the present day. However, studies connecting diabetes & rifampicin resistance are scarce. Patients incur greater financial costs due to TB-diabetes mellitus comorbidities & delayed diagnosis & treatment. The sooner these diseases are diagnosed, the more likely they are to be treated successfully.

Aim and Objectives

Aim: To study the Occurrence of Diabetes Mellitus with Rifampicin Resistance in patient of Pulmonary Tuberculosis in tertiary care hospital in western Uttar Pradesh.

Objectives

1. To confirm the diagnosis of Pulmonary TB in presumptive TB patients with sputum AFB.
2. To screen Diabetes Mellitus in Pulmonary TB patients.
3. To study the occurrence of Diabetes Mellitus in pulmonary TB patients.
4. To study the association of Rifampicin resistance in Pulmonary TB Patients with or without Diabetes.
5. To study the association of diabetic control on rifampicin resistance in Pulmonary TB patients with Diabetes.

Material and Methods

Inclusion Criteria

1. All sputum smear positive pulmonary TB patients.
2. All patients who had given informed consent for their inclusion in the study.

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Exclusion Criteria

1. All patients who are on steroid therapy.
2. All patients with extra pulmonary TB.
3. Immunosuppressive conditions.

Result

Table 1: Age distribution among the study subjects

Age Group (in years)	N	%
16-20	11	6.88
21-30	24	15.00
31-40	16	10.00
41-50	36	22.50
51-60	42	26.25
>60	31	19.38
Total	160	100

It was a hospital a cross sectional research conducted in the Department of respiratory medicine, TMMC & RC, MORADABAD among 160 patients who were sputum smear positive & those who meet our inclusion & exclusion criteria was taken in study group. The aim of the research was to analyse the occurrence of DM with Rifampicin Resistance in patient of Pulmonary Tuberculosis. Maximum subjects belonged to age group of 51-60 years (26.25%) followed by 41-50 years (22.50%) while minimum subjects were in the age group of 16-20 years (6.88%) followed by 31-40 years (10%) as shown in [Table 1].

Table 2: Clinical symptoms among the study subjects

Clinical Symptoms	N	%
Chest pain	25	16.6
Cough	155	96.9
Sputum	116	72.5
Fever	126	78.7
Hemoptysis	5	3.1
SOB	82	51.2

[Table 2] shows the clinical symptoms among the study subjects. Most predominant clinical symptom was cough (96.9%) followed by fever (78.7%), sputum (72.5%) & SOB (51.2%). Least common clinical symptom was hemoptysis (3.1%) followed by chest pain (16.6%).

Table 3: Distribution of HbA1C among the study subjects

HbA1C	N	%
<6.5	116	72.50
6.5-8.4	21	13.12
>8.4	23	14.37
Total	160	100

In present study out of 160 subjects, 116 (72.50%) subjects had HbA1c < 6.5, 23 (14.37%) subjects had HbA1c > 8.4 & 21 (13.12%) subjects had HbA1c between 6.5-8.4. [Table 3]

Table 4: Sputum AFB outcome among the study subjects

Outcome	Sample A		Sample B	
	N	%	N	%
1+	74	46.3	56	35.0
2+	58	36.3	60	37.5
3+	23	14.4	44	27.5
Negative	5	3.1	0	0

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Sputum AFB outcome among sample A outcome 1+,2+,3+ & negative were 46.3%,36.3%,14.4% & 3.1% respectively. Sputum AFB outcomes among sample B were 1+(35%), 2+(37.5%) & 3+ (27.5%). [Table 4]

Table 5: CBNAAT outcome among the study subjects

Outcome	N	%
Resistance	7	4.4
Sensitive	153	95.6

According to CBNAAT outcome; resistance & sensitivity was reported among 4.4% & 95.6% of the subjects respectively [Table 5].

Table 6: AFB status in relation to HbA1c level with history of diabetes.

HbA1C	AFB Outcome		
	+1	+2	+3
6.5-8.4	3	11	5
>8.4	7	8	10
Total	10	19	15
Chi square	1.63		
p value	0.80		

In current study AFB status in relation to HbA1c level with diabetes mellitus shows-
-AFB outcomes 1+ were seen maximum (n=7) with HbA1c >8.4 group, followed by 3 subject in 6.5-8.4 group.
-AFB outcomes 2+ were seen maximum (n=11) in 6.5-8.4 group, followed by 8 subjects in >8.4 HbA1c.
-AFB outcomes 3+ were seen maximum (n=10) with >8.4 HbA1c group, followed by 5 subjects in 6.5-8.4 HbA1c group.

Table 7: CBNAAT outcome among the study subjects according to HbA1c level

CBNAAT	Mean HbA1c	SD	t test	p value
Resistance	7.77	2.53	3.41	0.021*
Sensitive	6.48	2.27		

*: statistically significant

[Table 7] shows CBNAAT outcomes among 160 study subjects according to HbA1c level, mean HbA1c level in subjects with rifampicin resistance were 7.77±2.53 & in rifampicin sensitive subjects were 6.48±2.27. The CBNAAT outcomes i.r.t HbA1c level was statistically significant (p value=0.021).

Table 8: CBNAAT in relation to HbA1c level

HbA1C	CBNAAT	
	Resistance	Sensitive
<6.5	3	116
6.5-8.4	2	16
>8.4	2	21
Total	7	153
Chi square	3.96	
p value	0.13	

CBNAAT resistant & sensitive outcome was found among 3, 2, 2 & 116, 16, 21 subjects with HbA1c level of <6.5, 6.5-8.4 & >8.4 respectively. When HbA1c level was compared according to CBNAAT outcome, insignificant difference was found as p>0.05. [Table 8]

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Discussion

It was a hospital based cross-sectional research conducted in the Department of pulmonary medicine, TMMC & RC, MORADABAD among 160 patients who were sputum smear positive & those who meet our inclusion & exclusion criteria were taken in study group. The aim of the research was to analyse the occurrence of Diabetes Mellitus with Rifampicin Resistance in patient of Pulmonary Tuberculosis. In the present study, Maximum participants were between the ages of 51 & 60 (26.25%), then 41 & 50 (22.50%), & the youngest were between the ages of 16 & 20 (6.88%) & 31 & 40 (10%). Male participants accounted for 69.4% of the total, while females made up only 30.6% of the sample. Similar findings were found in a research by Panyachot et al,[14] in 2022, which found that the average age was 60 (with a range of 53-73) years. It has been noted that males, starting in their early adult years, & continuing into later life, have a greater TB rate than females. This has been noted for quite some time, & researchers believe it reflects the fact that men are more likely to be exposed to tuberculosis in the community than women.[15] H/O ATT intake was reported among 10% of the study subjects in this study. Out of 160 subjects, 68.1% live in rural area while 31.9% resided in urban location. In this study, diabetes mellitus was revealed in 27.50% of the subjects. Out of 44 subjects; duration of diabetes mellitus viz. <1 year or newly diagnosed, 1-5 year & >5 year was found among 16.88%, 6.25% & 4.38% of the subjects respectively. Most common clinical symptom was cough (96.9%) followed by fever (78.7%) & sputum (72.5%). Least common clinical symptom was hemoptysis (3.1%) followed by chest pain (16.6%). Scanty, whitish & yellowish sputum was revealed in 11.9%, 52.5% & 8.2% of the subjects respectively. Mean HbA1c among the study subjects was 6.54±2.34. HbA1C level viz. <6.5, 6.5-8.4 & >8.4 was found among 74.38%, 11.25% & 14.37% of the study subjects respectively. AFB outcome 1+, 2+ & 3+ was reported in 35%, 37.5% & 27.5% of the subjects respectively. According to CBNAAT outcome; resistance & sensitivity was reported among 4.4% & 95.6% of the subjects respectively. AFB 1+, 2+ & 3+ was reported in 10, 19 & 15 subjects suffering from diabetes mellitus. Out of 43 diabetic subjects with positive AFB outcome; 27, 9 & 7 subjects had diabetes since <1 year, 1-5 year & >5 year respectively. Hence AFB outcome was comparable according to diabetes duration as $p>0.05$.

Samples were found to be resistance & sensitive are 9.09%, 2.59% & 90.91%, 97.41% among subjects with & without diabetes mellitus respectively. Hence CBNAAT outcome was comparable among the subjects with & without diabetes mellitus. CBNAAT resistant & sensitive outcome was found among 3, 2, 2 & 116, 16, 21 subjects with HbA1c level of <6.5, 6.5-8.4 & >8.4 respectively. When HbA1c level was compared according to CBNAAT outcome, insignificant difference was found as $p>0.05$. Mean HbA1c level in CBNAAT resistant & sensitive outcome was 7.77±2.53 & 6.48±2.27 respectively with statistically significant difference.

Conclusion: Based on our findings, we recommend that all patients be screened for diabetes before beginning ATT, as both resistance & blood sugar control are crucial to reducing morbidity & helping to stop the spread of resistant tuberculosis in the general population. Patients who test positive for diabetes may then be placed on a sensitive ATT regimen to ensure a full recovery from pulmonary tuberculosis, even in resistant cases.

Our findings suggest a link between diabetes and rifampin resistance, so we recommend integrating diabetes surveillance into TB programs, especially in changing epidemiological contexts. Quantifying the disparities in TB diagnostic findings is also needed to provide a global research setting where study results may be appropriately compared.

Limitations

Most patients with rifampicin resistance were found to have poor glycemic control, but further case control research is needed to prove this as a causal component because the research was cross-sectional & the study population was small.

Furthermore, the study's framework did not allow for tracking participants' responses to therapy or their long-term outcomes with diabetes.

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