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RESEARCH ARTICLE
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TREATMENT OUTCOMES IN DRUG-SENSITIVE TUBERCULOSIS PATIENTS WITH AND WITHOUT NON-COMMUNICABLE CO-MORBIDITIES AT A TERTIARY HEALTH CARE FACILITY IN NORTHERN INDIA: A PROSPECTIVE COHORT STUDY

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Abstract

Background: Tuberculosis is a leading global health issue, with a high burden in developing countries. Non-communicable co-morbidities (NCCs) such as diabetes, hypertension, and chronic respiratory diseases are increasingly recognized as factors that complicate TB treatment. This study investigates the impact of NCCs on treatment outcomes in drug-sensitive TB patients**.**

Methods: This prospective cohort study was conducted at UPUMS Saifai Etawah between January 2023 and July 2024. A total of 144 drug-sensitive TB patients were divided into two groups: group 1 (TB patients with co-morbidities) and group 2 (TB patients without co-morbidities). The primary outcomes assessed were cure rate, treatment completion, treatment failure, mortality, and loss to follow-up. Statistical analyses, including Chi-square tests and relative risk (RR) calculations, were performed to evaluate the impact of co-morbidities.

Results: Group 1 had a significantly worse treatment outcome compared to group 2. The cure rate was lower in group 1 (23.61% vs. 38.89%), while mortality was higher (22.22% vs. 8.33%). Treatment failure occurred in 5.56% of group 1 but was absent in group 2. Smoking/tobacco use (73.61%) and malnutrition (44.44%) were the most common co-morbidities in group 1, both contributing to poorer treatment outcomes. Group 1 also had a higher mean age, a predominance of males, and lower literacy rates, all of which contributed to the disparity in outcomes.

Conclusions: The presence of NCCs significantly worsens treatment outcomes in TB patients, leading to lower cure rates and higher mortality. Diabetes and hypertension were the most impactful co-morbidities. Integrated care approaches that address both TB and NCCs are essential to improve treatment success and reduce mortality in TB patients with co-morbidities.

Key words: Co-morbidity impact, Drug-sensitive TB, non-communicable co-morbidities (NCCs), Tuberculosis (TB), Treatment outcomes.

Introduction

Tuberculosis (TB) is a chronic infectious multi-systemic disease caused by mycobacterium tuberculosis and is one of the leading causes of mortality worldwide[1]. The World Health Organization (WHO) has estimated that 2 billion people, almost a third of the world's population have latent tuberculosis [2]. Every year about eight million people develop this disease, and some three million dies of it, over 95% of these from developing countries. In 2005 the highest rates per capita were from Africa (28% of all TB cases), and half of all new cases were from five Asian countries, namely India, Bangladesh, China, Indonesia and Pakistan[3,4]. India accounts for one-fourth of the global TB burden of Tuberculosis in the world, with an estimated 2.8 million cases in 2015.[5] About 40% of the Indian population is infected with TB, the majority having latent infection, which can potentially flare up into active disease. While extra-pulmonary tuberculosis accounts for a quarter of the annual incidence of TB globally[5]. Current reports show increasing evidence of links between Tuberculosis and non- communicable disease such as tobacco use, physical inactivity, unhealthy diet, harmful use of alcohol, and cardio-metabolic risk factor such as high blood pressure, overweight, and dyslipidemia[6,7,8]. Models of TB/HIV co-management such as 'two disease one patient' have improved early TB diagnosis and treatment amongst people with HIV infection and improved clinical outcomes for both disease[9]. This concept could also be applied to non-communicable comorbidities and tuberculosis. Clinicians receiving suspected patients of pulmonary tuberculosis / extrapulmonary tuberculosis will need to acknowledge that they may encounter more than one disease of which some might be beyond their core expertise area, in a single patient. Integrated screening and management can improve early diagnosis and health outcomes for both conditions[10]. Some studies have reported NCD screening in tuberculosis patients[11], however they focused mainly on diabetes. The burden of other common non-communicable diseases (NCDs) and risk factors in tuberculosis patients has not been thoroughly explored. The absence of investigation of NCD co-morbidity and multi-morbidity among the patient may negatively impact on the success of TB control programmes[12,13]. The primary objective of this study is to determine the prevalence of NCD (diabetes mellitus, hypertension, under-nutrition alcohol use, smoking) in drug sensitive tuberculosis patients. The secondary objective of the study to assess the impact of comorbidity on treatment outcome at tertiary care centre UPUMS, Saifai, Etawah (Uttar Pradesh).

Materials and Methods

This hospital-based prospective cohort study was conducted at UPUMS, Saifai, Etawah, from January 2023 to July 2024. A total of 144 drug-sensitive TB patients were enrolled from the outpatient department (OPD) and indoor patient department (IPD) of Respiratory Medicine and other clinical departments of UP UMS, Saifai, Etawah and divided into two groups: Group 1 (patients with co-morbidities such as DM, hypertension, chronic respiratory diseases) and Group 2 (patients without co-morbidities) who were fulfilling the inclusion and exclusion criteria. The sample size has been calculated by using the following formula

$n = [Z (1-\alpha/2\ 2P(1-P)\} + Z1-\beta\ P1(1-P1) + P2(1-P2)\}]/(P1-P2)$

where, n= sample size Z1-α/2 will be 1.96 at 95% confidence level Z1-β will be 0.84 at 80% power of study P=average value of P1 and P2, P1=proportion of success of treatment in case cohort (with co-morbidities) P2=proportion of success of treatment in control cohort (without co-morbidities) On applying formula - n =72 Hence sample size will be 72 for case cohort and 72 for control cohort.

INCLUSION CRITERIA:
1. Drug sensitive Pulmonary and Extrapulmonary TB Patients between 14 years and 80 years of age and having any non-communicable comorbidity.
2. Patients who will be haemodynamically stable and co-operative.
3. Patients who will provide consent to participate in the study.

EXCLUSION CRITERIA:
1. Drug-resistant pulmonary and extrapulmonary TB patients
2. Patients diagnosed to be infected with non-tubercular mycobacteria
3. Patients with associated communicable diseases like HIV, Hepatitis-B, Hepatitis-C and sexually transmitted diseases, etc.
4. Critically ill and hemodynamically unstable patients
5. Patients with Mental retardation / Significant head injury / Epilepsy / Dementia &Dementia like syndrome and Any significant Neurodevelopmental disorders.

The diagnosis of Drug-sensitive pulmonary and extrapulmonary tuberculosis will be made according to NTEP guideline. A detailed history regarding clinical features, personal habits like smoking, alcohol, or any substance use or known coexisting illness will be recorded and general examination and systemic examination will be done. The diagnostic criteria for various co-morbidities include several key health indicators. Diabetes Mellitus is diagnosed when fasting blood sugar levels are ≥ 126 mg/dL, postprandial blood sugar levels are ≥ 200 mg/dL, or HbA1c is ≥ 6.5% [14]. Smoking is identified in individuals who are current smokers or have a history of smoking within the past 12 months [15]. Undernutrition is defined by a Body Mass Index (BMI) of less than 18.5 kg/m^2 [16]. Regular alcohol consumption is assessed using the CAGE questionnaire to identify alcohol use disorder [17]. Hypertension is characterized by a systolic blood pressure of ≥ 140 mmHg and/or a diastolic blood pressure of ≥ 90 mmHg, or by the use of antihypertensive medication [18]. Chronic Obstructive Pulmonary Disease (COPD) is diagnosed based on spirometry results showing a FEV1/FVC ratio of less than 0.7 [19]. Treatment outcome of TB patients is defined by as per NTEP guideline [20]. These criteria are essential for identifying and managing the co-morbidities that may complicate TB treatment. The primary outcomes assessed included cure rate, treatment completion, mortality, loss to follow-up, and treatment failure. Ethical clearance was obtained from our institutional ethical committee before the study enrolment and written informed consent was obtained from each subject in response to a fully written and verbal explanation of the nature of the study. Statistical analysis was performed using SPSS statistical software version 25 (IBM). Continuous variables were expressed as mean ± standard deviation while proportions were expressed as percentage. Comparison of categorical variables between the groups was done by Chi-square tests. Relative risk (RR), and attributable risk (AR) calculated for various co-morbidities. A 'p' value of less than 0.05 was considered to be significant.

Results

In this study, we analysed 144 TB patients, with 72 in group 1 (TB patients with co-morbidities) and 72 in group 2 (TB patients without co-morbidities). Table 1 summarizes the baseline characteristics, revealing that group 1 had a significantly higher mean age (50.26 years) than group 2 (39.99 years, $p < 0.001$). Gender distribution favoured males in group 1 (88.89%) compared to group 2 (55.56%, $p < 0.001$). Educationally, only 13.89% of group 1 were literate versus 40.28% in group 2 ($p = 0.001$) shows a significant difference between two groups and occupational differences were pronounced, with 55.56% of group 1 was farmers compared to 20.83% in group 2 ($p < 0.001$) which was significant. Socioeconomic status showed no significant difference ($p = 0.228$). Table 2 presents the co-morbidity distribution, highlighting smoking/tobacco use (73.61%) and malnutrition (44.44%) as the most prevalent conditions in group 1, with respective relative risks of 1.21 and 1.05. Figure 1

showing distribution of comorbidities among group 1. Treatment outcomes, detailed in Table 3, and figure 2 indicated that only 23.61% of group 1 achieved cure status compared to 38.89% in group 2 (p = 0.009), while treatment failure was reported in 5.56% of group 1, with no failures in group 2. Mortality was significantly higher in group 1 (22.22% vs. 8.33% in group 2). These results underscore the substantial challenges faced by TB patients with co-morbidities, necessitating targeted interventions for improved outcomes.

Table 1: Baseline Characteristics of Group 1 (TB patients with co-morbidities) and Group 2 (TB patients without co-morbidities)

Variable	Group 1 (n=72)	Group 2 (n=72)	Chi-Square	p-Value
Age (Mean ± SD)	50.26 ± 16.18	39.99 ± 18.07	3.59	<0.001
Gender				
Male	64 (88.89%)	40 (55.56%)	18.31	<0.001
Female	8 (11.11%)	32 (44.44%)		
Education				
Literate	10 (13.89%)	29 (40.28%)	11.39	0.001
Illiterate	62 (86.11%)	43 (59.72%)		
Occupation				
Farmer	40 (55.56%)	15 (20.83%)	39.82	<0.001
Student	1 (1.39%)	12 (16.67%)		
Labourer	16 (22.22%)	5 (6.94%)		
Housewife	9 (12.50%)	31 (43.06%)		
Others	6 (8.33%)	9 (12.5%)		
Socioeconomic Status				
APL	7 (9.72%)	13 (18.06%)	1.45	0.228
BPL	65 (90.28%)	59 (81.94%)		

*Statistically Significant at 95% CL (P <0.05)

Table 2: Distribution of Co-morbidities, Relative Risk, and Attributable Risk in Group 1

Co-morbidity	Group 1 (n=72)	Relative Risk (RR)	Attributable Risk (AR)
Diabetes Mellitus	22 (30.56%)	1.34	0.1509
Hypertension	7 (9.72%)	1.20	0.0945
Chronic Respiratory Disease	21 (29.17%)	1.62	0.2549
Malnutrition	32 (44.44%)	1.05	0.0250
Alcohol Use Disorder	29 (40.28%)	1.25	0.1098
Smoking/Tobacco use	53 (73.61%)	1.21	0.0883

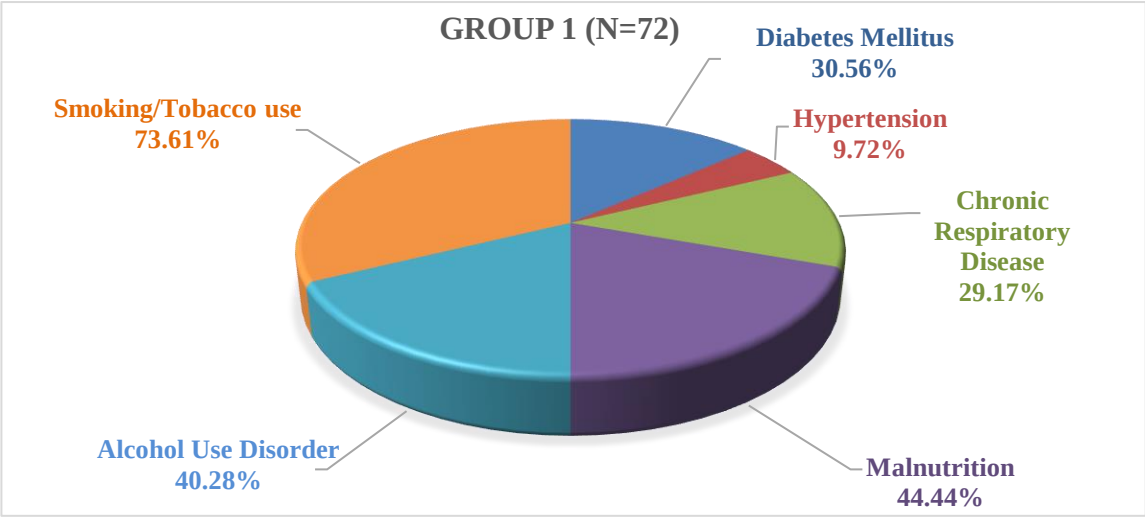

Figure 1

Table 3: Comparison of Treatment Outcomes Between Group 1 and Group 2

Treatment Outcome	Group 1 (n=72)	Group 2 (n=72)	Chi-Square	p-Value
Cure	17 (23.61%)	28 (38.89%)	15.345	0.009
Treatment Completed	20 (27.78%)	28 (38.89%)		
Treatment Failure	4 (5.56%)	0 (0.00%)		
Death	16 (22.22%)	6 (8.33%)		
Lost to Follow-up	8 (11.11%)	8 (11.11%)		
Not Evaluated	7 (9.72%)	2 (2.78%)		

*Statistically Significant at 95% CL (P <0.05)

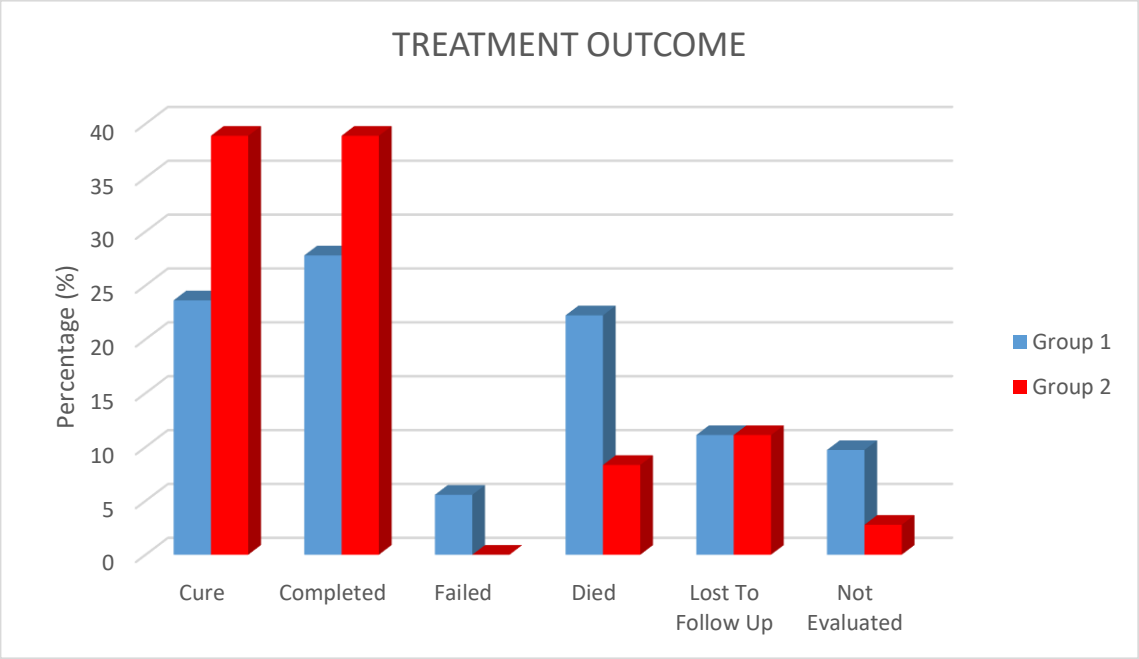

Figure 2

Discussion

The findings from this study highlight significant disparities in demographics, co-morbidities, and treatment outcomes between TB patients with co-morbidities (Group 1) and those without (Group 2). The higher mean age of patients in group 1 aligns with existing literature suggesting that older individuals are more likely to have concurrent health issues, which complicate TB management. The pronounced gender imbalance, with a higher proportion of males in group 1, may reflect social and occupational factors that predispose men to both TB and associated health conditions. These results were similar to the study conducted by Balakrishnan et al and Shivalingaiah et al. Balakrishnan et al found that male TB patients in Kerala, India, had more diabetes, suggesting that males had more comorbidities [21]. Shivalingaiah et al emphasized the need for gender-sensitive health care, especially in TB treatment, to meet the needs of both male and female patients [22]. Educational status is another critical aspect; the lower literacy rates in group 1 may hinder health-seeking behaviour and adherence to treatment protocols. Similarly, Adane et al also compared TB patients with and without diabetes by education level. This suggests that educational interventions could be vital for improving outcomes in this group [23]. Additionally, the occupational data indicating a predominance of farmers in group 1 may expose these individuals to environmental risks, further exacerbating their health challenges. Our study compares TB patients with and without comorbidities supported by the findings of Adane et al. Which provides a broader context for how occupation affects TB prevalence and treatment and emphasize the importance of occupational factors in TB treatment strategy [23]. The prevalence of co-morbidities, particularly diabetes Mellitus and hypertension, emphasizes the need for integrated care approaches. The relative risks associated with these conditions underline their significant role in TB morbidity and mortality. Co-morbid conditions not only complicate the clinical management of TB

but also contribute to poorer treatment outcomes. The findings indicate a lower cure rate and higher mortality in group 1, which is consistent with other studies that have demonstrated that co-morbidities can negatively impact TB treatment efficacy and increase the risk of adverse events. Furthermore, the notable difference in treatment failure rates between the two groups suggests that patients with co-morbidities may face additional barriers to successful treatment, including drug interactions and the complexity of managing multiple health issues simultaneously. These results advocate for a holistic approach in treating TB patients, particularly those with co-morbidities, focusing on comprehensive management strategies that address both TB and associated health conditions. Nowiński et al. emphasize the need for integrated treatment of TB and associated comorbidities to improve treatment outcomes [24].

Conclusion

This study highlights the significant impact of non-communicable co-morbidities (NCCs) on tuberculosis (TB) treatment outcomes, demonstrating that patients with co-morbidities experienced notably worse results than those without, evidenced by lower cure and treatment completion rates alongside higher rates of treatment failure and mortality. Chronic respiratory diseases and diabetes were identified as the most influential co-morbidities, with chronic respiratory diseases increasing the risk of unfavourable outcomes by 62% and diabetes contributing an additional 15% risk. Furthermore, lifestyle factors such as alcohol use and smoking exacerbated treatment outcomes, increasing risk by 10.98% and 8.83%, respectively. Other co-morbidities like hypertension, malnutrition, and also had a smaller yet significant impact. These findings underscore the critical need for integrated care approaches that address both TB and associated co-morbidities, particularly chronic respiratory diseases and diabetes, to enhance treatment success and reduce mortality, while also emphasizing the importance of addressing lifestyle factors like smoking and alcohol consumption in TB management protocols. The small sample size in this study may restrict the applicability of its findings to a wider population. Additionally, since the study was conducted at a single tertiary care center, the results cannot be generalized to the entire population. This highlights the need for further research on a larger scale.

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