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ORIGINAL ARTICLE

A Comparative Study on Treatment Outcome Among Tuberculosis Patients with and without Co-morbidities in DOTS Centres Covered under Urban Health Centres (UHCs)

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Abstract

Background: Tuberculosis remains a major public health challenge in India, accounting for two-fifths of incident global cases. Despite being preventable, comorbidities can negatively impact treatment outcomes. This study assesses the impact of co-morbidities on treatment outcomes among tuberculosis patients in a tertiary care setting. **Methods:** A community-based longitudinal study was conducted among 272 drug-sensitive tuberculosis patients registered at directly observed treatment short-course centres under urban health centres of the Kurnool tuberculosis unit between January 2021 and October 2022. Data on socio-demographic factors, personal habits, co-morbidities, and treatment outcomes were collected and analysed using chi-square tests and logistic regression. **Results:** Among the 272 patients, 28.7% had comorbidities—most commonly diabetes (56.4%), hypertension (30.8%), and human immunodeficiency virus (12.8%). The overall favourable treatment outcome was 85.3%. Significant associations were found between unfavourable outcomes and male sex, smoking, alcohol use, and absence of family screening. Comorbidities, especially diabetes, chronic respiratory disease, and cardiovascular disease, were associated with significantly lower cure rates. **Conclusion:** Co-morbidities and behavioural risk factors significantly affect treatment outcomes in tuberculosis patients. Strengthening integrated care for tuberculosis and non-communicable diseases, along with family contact screening and behavioural counselling, is crucial for improving outcomes and achieving national tuberculosis elimination goals.

Keywords: Co-morbidities, Risk factors, Tuberculosis, Treatment outcomes

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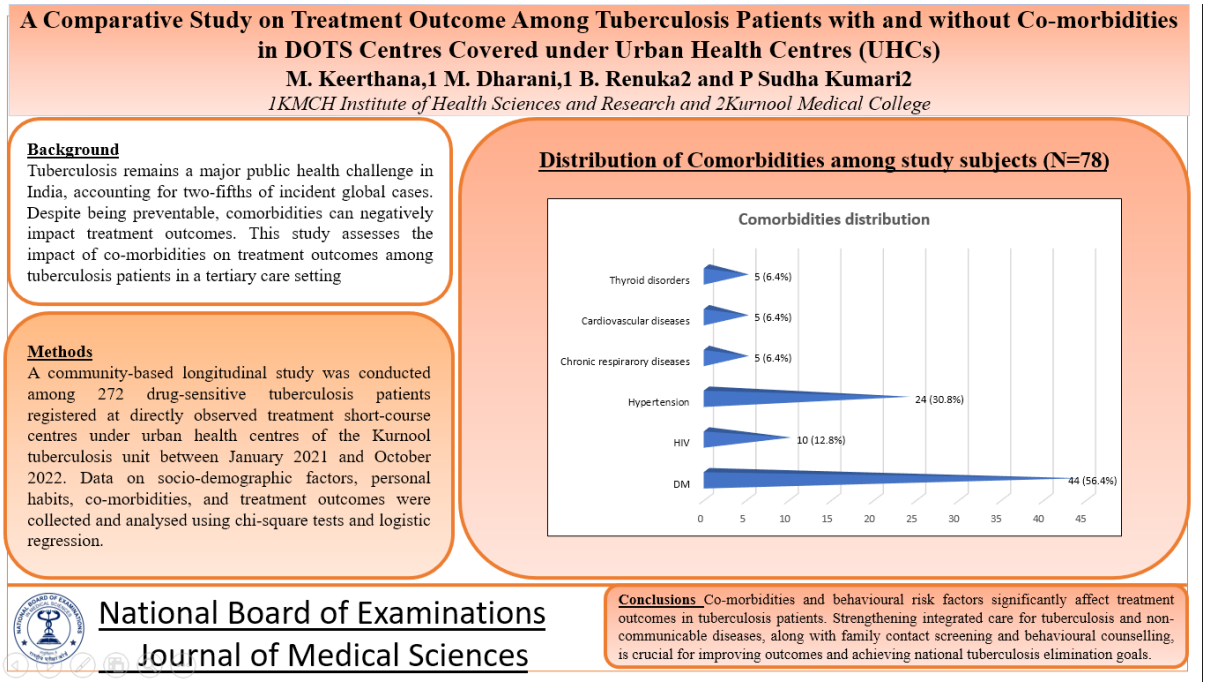
Graphical Abstract



Introduction

Tuberculosis (TB) is a contagious disease caused by *Mycobacterium tuberculosis* (MTB), a bacillus first identified by Robert Koch in 1882. While TB primarily affects the lungs, it can also involve lymph nodes, intestines, meninges, bones and joints, skin, and other tissues [1]. Around 10 million new cases occur each year, with India contributing nearly two-fifths of the global TB incidence in 2021 [2]. Treatment success is a key indicator of the effectiveness of the National TB Elimination Program (NTEP). The treatment success rate for drug-susceptible TB (DS-TB) patients in India was reported at 87.6% [3]. One of the health targets under the Sustainable Development Goals (SDGs) is to end the TB epidemic by 2030. India has set an even earlier goal—to eliminate TB by 2025 [4].

TB often becomes active when the immune system is compromised. Managing TB along with other health conditions is very important, as co-morbidities can make TB harder to diagnose and treat, increase the risk of complications, delay recovery, cause drug interactions, and lead to poor outcomes or even death. A shred of growing evidence highlights the association between TB and various co-morbidities such as diabetes, HIV, malnutrition, chronic respiratory diseases, cancer, smoking, alcoholism, and cardiovascular conditions. These co-morbidities can negatively influence TB treatment outcomes, especially in developing countries like India, where a "double burden of disease" persists [5]. Previous studies have shown that TB is associated with several factors, including prior TB treatment, poor adherence to therapy, lung cavities, contact with active TB cases, HIV, diabetes or impaired glucose tolerance, alcohol use, malnutrition, and smoking. In addition, social and demographic factors such as income, place of residence, and family size influence the occurrence of TB [6,7].

The WHO's End TB strategy has closely studied the factors affecting TB cases and deaths, especially focusing on managing other chronic illnesses alongside TB [8]. Although diabetes and HIV affect TB treatment outcomes, there remains limited evidence regarding the impact of other co-morbid conditions. Understanding the effects of these comorbidities on TB treatment outcomes is essential for improving patient care. Hence, this study aimed to assess the prevalence of co-morbidities among registered TB cases and their impact on treatment outcomes in a tertiary care setting.

Methodology

A community-based longitudinal study was conducted at DOTS (Directly observed treatment short-course) centres under Urban Health Centres (UHCs) of the Kurnool TB Unit from January 2021 to October 2022. Ethical clearance was obtained from the Institutional Ethical Committee. The study included all drug-sensitive (DS-TB) patients—both newly diagnosed and previously treated—of any age or sex, who were registered in the first and second quarters of 2021, and all received the same TB treatment regimen. Drug-resistant TB (DR-TB) cases were excluded. Considering the prevalence of successful treatment outcomes as 80.5% from a study by Ramya MS et al[9] and a 5% margin of error, the required sample size was 241, which was adjusted to 265 after accounting for a 10% non-response rate.

The study purpose was explained to all the participants in their language, and written consent was obtained. Data were collected using a pre-tested semi-structured questionnaire covering socio-demographic details, personal habits, co-morbidities, adverse events, clinical progress, and treatment outcomes. Follow-ups included assessment of sputum status and adverse events. At the end of treatment, patients are classified into one of six outcomes [10]: cured, treatment completed, died, treatment failed, lost to follow-up, or transferred out with unknown outcome. Cases marked as cured or treatment completed are grouped as favourable outcomes, while all others are considered unfavourable.

Data were analysed using SPSS 26, with results expressed as means and percentages. The link between comorbidities and treatment outcomes was assessed using chi-square tests, cure rates, risk ratios (RR), attributable risk (AR), and attributable fraction (AF). Variables that showed statistical significance in the chi-square test were included in the Multivariate logistic regression to identify adjusted odds ratios (aOR) of unfavourable treatment outcomes, while adjusting for confounders.

Results

Almost half of the participants (43.8%) were between 19 and 39 years old. There were equal numbers of men and women. Most of them were Hindus (70.6%) and married (66.2%). Many lived in nuclear families (74.6%). About one-fourth (23.9%) had no formal education. More than half (53.7%) were not working, and most (52.9%) belonged to the lower middle-income group. Most patients were newly diagnosed TB cases (89%), while the rest (11%) were retreatment cases (Table 1).

Table 1. Socio-demographic profile of TB patients in relation to their treatment outcomes

Variables	Sub-types	Favourable outcome n (%)	Unfavourable outcome n (%)	Total N=272	P-value
Age (in years)	<19	35 (92.1)	3 (7.9)	38	
	19-39	101 (84.9)	18 (15.1)	119	
	40-59	69 (85.2)	12 (14.8)	81	0.501
	>60	27(79.4)	7 (20.6)	34	
Sex	Female	121 (90.3)	13 (9.7)	134	**0.022***
	Male	111 (80.4)	27 (19.6)	138	
Religion	Christians	10 (100)	0	10	
	Muslims	60 (85.7)	10 (14.3)	70	0.511
	Hindus	162 (84.4)	30 (15.6)	192	
Socio-economic status	upper middle (ii)	31 (96.9)	1 (3.1)	32	
	Lower middle (iii)	123 (85.4)	21 (14.6)	144	0.081
	Upper lower (iv)	71 (82.6)	15 (17.4)	86	
	Lower (v)	7 (70.0)	3 (30.0)	10	
Marital status	Death of spouse	12 (70.6)	5 (29.4)	17	
	Married	155 (86.1)	25 (13.9)	180	0.208
	Unmarried	65 (86.7)	10 (13.3)	75	
Type of family	Three generation	21 (27)	6 (22.2)	27	
	Joint	29 (87.9)	4 (12.1)	33	0.486
	Living alone	7 (77.8)	2 (22.2)	9	
	Nuclear	175 (86.2)	28 (13.8)	203	
Overcrowding	Present	61 (89.7)	7 (10.3)	68	
	Absent	171 (83.8)	33 (16.2)	204	0.236
Smoking	Yes	40 (70.2)	17 (29.8)	57	**0.001***
	No	192 (89.3)	23 (10.7)	215	
Type of smoking (n=57)	Smoke	33 (67.3)	16 (32.7)	49	
	Smokeless	7 (87.5)	1 (12.5)	8	0.413
Smoking tobacco (n=49)	Current	14 (53.8)	12 (46.2)	26	
	Former	19 (82.6)	4 (17.4)	23	**0.032***
Alcohol consumption	Yes	18 (62.1)	11 (37.9)	29	**0.001***
	No	214 (88.1)	29 (11.9)	243	

*P<0.05 Statistically significant

Relative risk was calculated for significant variables

Sex: RR: 2.3, 95% CI: 1.1–4.6

Smoking: RR: 3.5, 95% CI: 1.7–7.2

Alcohol consumption: RR: 4.5, 95% CI: 1.9–10.5

Co-morbidities

In this study, 28.7% of the participants had co-morbidities (Figure 1). Among them, diabetes mellitus (56.4%) was the most common.

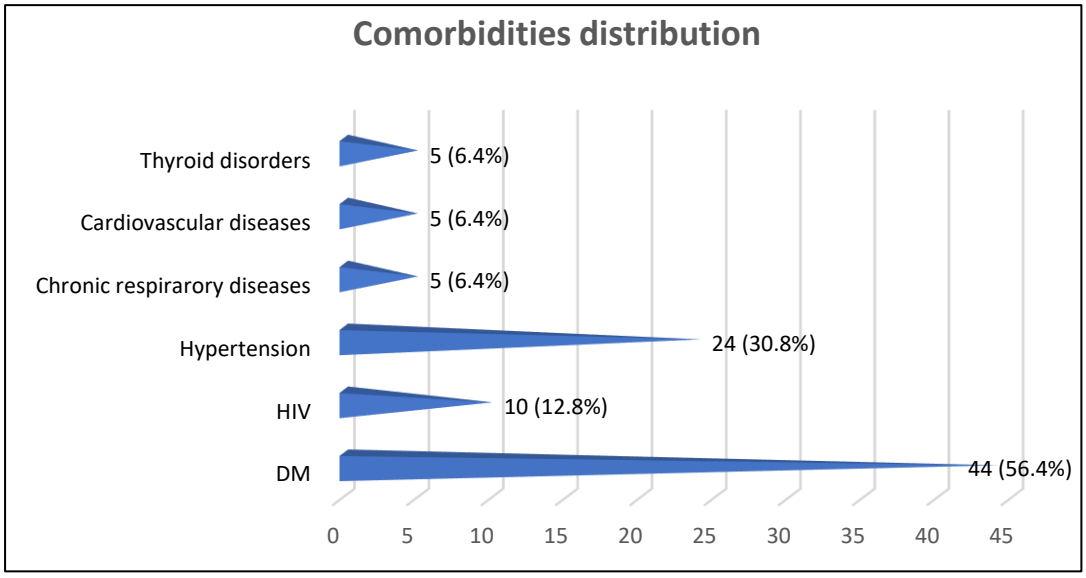


Figure 1. Distribution of Comorbidities among study subjects (N=78).

Treatment outcome

The favourable treatment outcome (85.3%) includes treatment completed and cured. The unfavourable outcome (14.7%) includes death, loss to follow-up, and treatment failure (Figure 2).

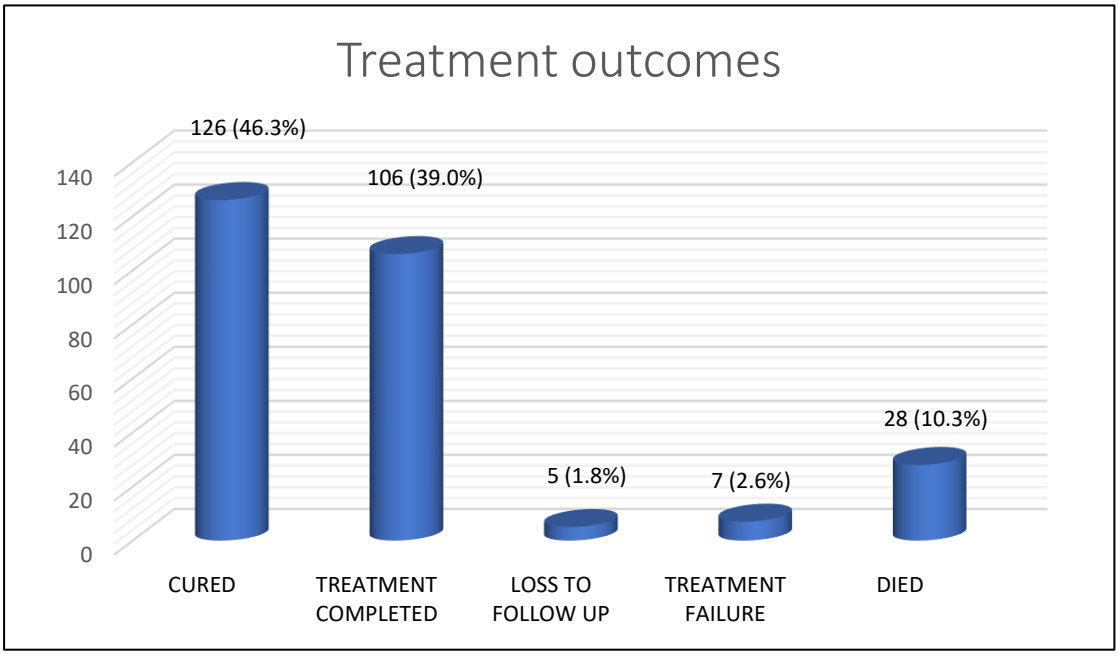


Figure 2. Distribution of the study subjects based on TB treatment outcomes

Factors influencing treatment outcome

A significant association was found between sex and treatment outcomes, with females having better outcomes than males (RR: 2.3, 95% CI: 1.1–4.6). Lifestyle factors such as smoking and alcohol use

significantly affected outcomes. Non-smokers had better treatment outcomes compared to smokers (RR: 3.5, 95% CI: 1.7–7.2), although current smokers were not at increased risk (RR: 0.2, 95% CI: 0.1–0.9). Alcohol users (RR: 4.5, 95% CI: 1.9–10.5) had significantly worse outcomes than non-users (Table 1).

Screening family members for TB was also linked to better outcomes, with families who underwent screening showing a lower risk of poor outcomes (RR: 0.2, 95% CI: 0.1–0.6). In addition, newly treated TB cases (RR: 2.9, 95% CI: 1.2–6.9) had better outcomes than previously treated patients (Table 2).

Table 2. Clinical characteristics of TB patients in relation to their treatment outcomes

Variables	Sub-types	Favourable outcome n (%)	Unfavourable outcome n (%)	Total N=272	P-value
Screening status among the family	Yes	84 (95.5)	4 (4.5)	88	**0.001***
	No	148 (80.4)	36 (19.6)	184	
Family history of TB	Yes	22 (84.6)	4 (15.4)	26	1.000
	No	210 (85.4)	36 (14.6)	246	
Contact history of TB	Yes	29 (87.9)	4 (12.1)	33	0.445
	No	203 (84.9)	36 (15.1)	239	
Category of TB patients	New	211 (87.2)	31 (12.8)	242	**0.012***
	Retreatment	21 (70.0)	9 (30.0)	30	
Site of involvement	Pulmonary	162 (84.4)	30 (15.6)	192	0.474
	Extrapulmonary	70 (87.5)	10 (12.5)	80	
Treating Facility	Public	187 (83.5)	37 (16.5)	224	0.047
	Private	45 (93.8)	3 (6.2)	48	
Duration of complaints	<3 weeks	215 (85.3%)	37 (14.7%)	252	1.000
	>3 weeks	17 (85.0%)	3 (15.0%)	20	
Delay in the initiation of treatment	<1 week	137 (85.1)	24 (14.9)	161	0.918
	>1 week	10 (90.9)	1 (9.1)	11	
	No delay	85 (85.0)	15 (15.0)	100	
Adverse effects on treatment	Yes	57 (87.7)	8 (12.3)	65	0.531
	No	175 (84.5)	32 (15.5)	207	

*P<0.05 Statistically significant
Relative risk was calculated for significant variables
Screening status among the family: RR: 0.2, 95% CI: 0.1–0.6
Category of TB patients: RR: 2.9, 95% CI: 1.2–6.9

Patients with co-morbid conditions had a lower cure rate (74.4%, *P* 0.001) with an attributable fraction of 17.09%. Diabetics had a lower cure rate (75%, *P* 0.035), with an attributable fraction of 14.07%. Patients with chronic respiratory diseases had a lower cure rate (40%, *P* 0.024) with an attributable fraction of 53.57%. Patients with cardiovascular disease (CVD) had a lower cure rate (40%, *P* 0.024) with an attributable fraction of 53.57%. Hypertension, HIV, and thyroid disorders do not influence the observed cure rates (Table 3).

Table 3. Impact of comorbidities on treatment outcomes in TB patients

Study variables	Favorable outcomes	Unfavorable outcomes	Cure Rate (%)	Risk Ratio Ie/Io	Attributable Risk Ie-Io	Attributable fraction in exposed Ie-Io/ Io *100 (%)
Chronic illness						
Yes	58	20	74.4	0.83	15.33	17.09
No	174	20	89.7			
Diabetes mellitus						
Yes	33	11	75.0	0.86	12.28	14.07
No	199	29	87.3			
Hypertension						
Yes	21	3	87.5	1.03	2.42	2.84
No	211	37	85.1			
HIV						
Reactive	7	3	70.0	0.82	15.88	18.49
Non-reactive	225	37	85.9			
Chronic respiratory illness (COPD, Asthma)						
Yes	2	3	40.0	0.46	46.14	53.57
No	230	37	86.1			
Cardiovascular diseases (coronary artery disease)						
Yes	2	3	40.0	0.46	46.14	53.57
No	230	37	86.1			
Thyroid disorders (Hypothyroidism)						
Yes	5	0	100	1.18	14.98	17.62
No	227	40	85.0			

Logistic regression

Multivariate logistic regression was conducted to identify the predictors of unfavourable TB treatment outcomes (Table 4). The full model containing all predictors was statistically significant, $\chi^2(9) = 37.794$, $P < 0.001$ (Omnibus Test), indicating that the model was able to distinguish between patients with favorable and unfavourable outcomes. The model explained 22.9% of the variance in TB treatment outcomes (Nagelkerke $R^2 = 0.229$) with a *P*-value <0.05.

Table 4. Independent factors influencing TB treatment outcomes

Independent Variables	**Standard Error**	**Significance**	**Exp(B)**	**95% C.I. for EXP(B)**	
				Upper	**Lower**
Sex	0.430	0.489	1.347	0.580	3.130
Screening status of family members	0.594	**0.003**	6.001	1.875	19.207
Smoking status	0.575	0.465	1.522	0.493	4.697
Alcohol Intake	0.642	0.328	1.872	0.532	6.585
Category of TB patients	0.516	0.050	2.748	0.999	7.556
Chronic illness	0.642	0.720	1.258	0.358	4.425
DM	0.684	0.784	1.207	0.316	4.615
Respiratory disease	1.237	0.148	5.992	0.531	67.626
Cardiovascular disease	1.116	0.165	4.707	0.528	41.965
Constant	0.642	0.000	.020	-	-

<0.05 Statistically significant
Degrees of freedom (dof):1
Exp(B): Exponential of the regression coefficient (B)
CI: Confidence Interval

Patients whose family members were not screened for TB had significantly higher odds of experiencing unfavourable outcomes (adjusted OR = 6.001; 95% CI: 1.875–19.207; $P = 0.003$). Retreatment cases also showed higher odds of unfavourable outcomes compared to new TB cases (adjusted OR = 2.748; 95% CI: 0.999–7.556; $P = 0.050$), but there is no statistical significance. Other variables, including smoking (aOR = 1.522; $P = 0.465$), alcohol use (aOR = 1.872; $P = 0.328$), chronic illness (OR = 1.258; $P = 0.720$) and sex (aOR = 1.347; $P = 0.489$), were not statistically significant. Comorbidities such as diabetes mellitus (aOR = 1.207; p = 0.784), respiratory illness (aOR = 5.992; $P = 0.148$), and CVD (aOR = 4.707; $P = 0.165$) had higher odds ratios, but no statistical significance.

Discussion

In this study, overcrowding was observed in 25% of participants, which is lower (11.7%) than that of Tagaram et al[11] but much higher (79.8%) in Pooja S

et al[12]. Most of the participants (87.9%) had no prior TB contact, which is comparable to the 89.1% reported by Mathavaswami V et al[13]. Tobacco use was noted in 21% of subjects, aligning with the findings of previous studies[13,14]. Alcohol consumption was reported by 10.7%, which is lower than in studies by Ramya et al. [9] (36.9%) and Rupali et al. [14] (30.3%). Clinically, 55.9% of participants had positive sputum smear results. Pulmonary TB was more common (70.6%) than extrapulmonary TB (29.4%), with lymph nodes being the most frequently affected extrapulmonary site. These findings are in line with reports by Avinash et al. [15] and Mohandas et al. [16]. Adverse drug effects were reported in 23.9% of participants, which is lower than the 36.7% reported by Rupali et al. [14].

Comorbidities were observed in 28.7% of TB patients, with diabetes mellitus being the most common (56.4%), followed by hypertension (30.8%), HIV (12.8%), chronic respiratory diseases (6.4%), CVD (6.4%), and thyroid disorders (6.4%). The high prevalence of diabetes among TB patients in this study is notably higher compared to previous studies. For instance, Viswanathan et al. [17] reported diabetes in 23% of TB cases, Balakrishnan et al. [12] in 44%, and Murali et al. [18] in 31.4% of TB cases. Similarly, Kunoor et al. [19] reported diabetes in 28% of TB patients, which was the most common comorbidity in their study. In contrast, Anwith HS et al[20] found that with Chronic obstructive pulmonary disease (COPD) being the most prevalent (22.5%), followed by diabetes (16.3%), HIV (7.5%), and hypertension (5.0%). Likewise, Ramya MS et al[9] reported COPD in 25% of TB patients, followed by diabetes (16.1%), hypertension (12.1%), and HIV (10.7%).

Treatment success (cured or treatment completed) was observed in 85.3% of cases. Similarly, the treatment success rate among notified drug-sensitive TB (DS-TB) cases was 87% in India (2023) [3]. The success rate is consistent with studies like Ramya et al[9] (80.5%), Kumar et al. [21] (84.4%), and Mohandas B et al[16] (89%), suggesting similar program performance across various regions. Slightly higher rates in studies like Sengul et al. [22] (92.6%) and Srinivas et al. [23] (91.2%) may reflect variations in healthcare services or patient compliance.

In this study, favourable outcomes were seen in patients aged <19 years (92.1%) and among Christians (100%), but without statistical significance. Similar findings were reported by previous studies [14,24,25], while Rupali [14] found significance for younger age (p=0.027) and Ramya MS[9] for religion (*P*=0.015). Females had significantly better outcomes than males (*P*=0.022; RR: 2.3, 95% CI: 1.1–4.6), supported by Pooja and Karanjekar et al. [25,26]. Non-smokers (89.3%) and non-alcoholics (88.1%) had better outcomes, and statistically significant (p<0.05). Ramya et al. [9] reported similar results for smoking (*P*=0.008) and alcohol (p=0.001). In contrast, Srinivas and Rupali found no significant association in their studies [14,23]. Newly treated patients had better outcomes (87.2%), which was statistically significant (RR=2.9, 95% CI: 1.2–6.9, *P*=0.012). Sengul and Mohandas reported similar findings [16,22].

Patients with **co-morbid** conditions had a significantly lower cure rate (74.4%, AF: 17.09%, *P*=0.001). Similar findings were reported by Yusupova [27] (RR=0.83, *P*=0.001), Sengul A[22] (RR=1.19; 95% CI: 0.35–4.07; *P*<0.001), and Kunoor et al. [19] (p=0.000019). Lall [28] had higher

cure rates among TB patients without comorbidities (79.6%, *P*=0.024). However, a study by Anwith et al. [20] did not find a significant association between the presence of co-morbidities and treatment outcomes.

Non-diabetic TB patients had a significantly better cure rate (87.3%, AF: 14.1%, $P = 0.035$) compared to **diabetics**. Rupali et al. [14] reported comparable findings, where non-diabetics had a better outcome (84.2%, $P < 0.05$). Yusupova et al. also found significant associations with diabetes ($P < 0.01$). Although Ramya et al. and Kunoor et al. reported higher cure rates among non-diabetics (81.6% and 83.3% respectively), the association was not statistically significant. Patients with **chronic respiratory diseases** and CVD had a much lower cure rate (40%, AF: 53.6%, $P = 0.024$). Similarly, Lal et al. had lower cure rates (60%) in COPD patients. Yusupova et al. [27] also found a significant association with COPD ($P = 0.02$). However, contrasting results were observed by Kunoor et al. [19], where 83.3% of patients with chronic respiratory diseases achieved successful treatment outcomes. **HIV patients** showed a lower cure rate (70%, AF:18.49, $P = 0.169$). Lall et al. [28] reported much lower cure rates (42.9%). In contrast, previous studies found a significant association with HIV ($P < 0.001$) [9,27]. Higher cure rates are observed in **Hypertensives** (87.5, $P = 1.000$). Lall [28] reported a lower cure rate (60%). Sengul et al. [22] observed a significant association with hypertension ($P = 0.002$). **CVD** significantly reduced the TB cure rate to 40% (AF: 53.6%, $P = 0.024$). Similarly, Kim et al. [29] reported CVD in 32.5% of TB patients, where delayed treatment was significantly associated with increased all-cause mortality. Diana et al. [30] observed CVD in 8.2% of cases, with comorbidities increasing the risk of poor treatment outcomes (OR = 2.56; 95% CI: 2.22–3.03).

Lack of TB screening among family members has been shown to significantly increase the odds of unfavourable treatment outcomes. The reason may be that untreated family members can continue to spread the infection or cause reinfection, particularly in crowded households. However, Lall et al[28] found a significant association with age (OR = 1.05), diabetes (OR = 1.82), and HIV (OR = 2.23) for disease progression.

Conclusion

The overall treatment success rate was 85.3%, consistent with national data. However, poorer outcomes were linked to male gender, alcohol and tobacco use, retreatment cases, and the absence of family screening. Comorbidities, especially diabetes, chronic respiratory diseases, and CVD, were also associated with lower cure rates. These findings emphasise the importance of addressing coexisting illnesses and ensuring household contact screening.

Recommendation

Integrating TB and non-communicable disease (NCD) services at the primary care level will support coordinated screening, treatment, and counselling. Additionally, collaboration between the National TB Elimination Programme (NTEP), other national health programs, and the private sector is crucial for reducing TB transmission, improving outcomes, and lowering the financial burden on patients.

Statements and Declarations

Ethical Approval

The ethical committee approved this longitudinal study (IEC-KMC-GGH 27/01/2021).

Authors' contribution

All authors have contributed equally.

Conflicts of interest

The authors declare that they do not have conflicts of interest.

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