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Original Article

Rifampicin resistance among the TB Patients in Pakistan: a retrospective cross-sectional study

Sobia Faisal[1], Syed Azizur Rab[1], Khalid F Muhammad[1], Ghulam Haider[1], Munir Alam[1], Furqan B Irfan[2,3]

[1] *Greenstar Social Marketing, Pakistan*
[2] *Manhattan Strategy Group, Bethesda, Maryland, United States*
[3] *Michigan State University, Institute of Global Health, College of Osteopathic Medicine, Department of Neurology and Ophthalmology, East Lansing, Michigan, United States*

Abstract
Introduction: Rifampicin resistant (RR) tuberculosis (TB) is a key challenge in terms of high morbidity, mortality and socio-economic burden. Pakistan has the sixth highest RR TB prevalence globally. In the absence of a national TB survey during the past decade, this study was conducted to determine prevalence estimates.
Methodology: This was a retrospective cross-sectional study (with an analytical component) of the bacteriologically confirmed TB patients whose sputum or other clinical samples were tested for RR (by Xpert® assay) in public-private mix (PPM) settings of 28 districts of Pakistan, from January 2022 to June 2024. Univariate and multivariable logistic regression analyses were performed for analysis.
Results: Among the 42,423 patients with bacteriological confirmation by the Xpert, 231 (0.5%) had indeterminate result for RR. The RR TB prevalence was 2.31% among the valid results. Univariate analysis showed that RR TB was significantly associated with province, residence, age, sputum smear microscopy results, and history of TB treatment. Multivariate analysis of significant factors showed that RR TB was significantly associated with the province; Sindh (OR = 1.65) and Khyber-Pakhtunkhwa (OR = 0.51). Risk of RR TB was significantly lower among people above 60 years of age (OR = 0.59) and higher among people previously treated for TB disease (OR = 3.73).
Conclusions: Findings support the need for evidence-based strategies aimed at timely diagnosis and management of TB, with greater focus on people at risk of developing RR TB including patients living in RR TB prevalent provinces and among those previously treated for TB.

Key words: tuberculosis; rifampicin resistance; Pakistan.

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Introduction

Pakistan is among the top ten countries contributing to 75% of the global gap between estimated incidence of multi-drug resistance / rifampicin resistance tuberculosis (MDR/RR TB) and treatment enrollment [1]. In 2023, an estimated 15,000 TB patients developed MDR/RR TB, of whom only 4,601 (30%) were diagnosed and 3,590 (24%) started MDR/RR TB treatment [2]. Both the drug sensitive (DS) TB and drug resistant (DR) TB pose great threats to individuals, communities and the economies. The major concerns related to DR TB include its substantial economic impact [3], high mortality rates [4], and unsuccessful treatment outcomes [5]. Pakistan ranks fifth in terms of DS TB and sixth in DR TB, among the high TB burden countries of the world [1]. It also carries the highest DR TB burden within the World Health Organization (WHO)'s Eastern Mediterranean region [6].

A national drug resistance survey was conducted in Pakistan during 2013 [1]. In the absence of real updated and comprehensive data, WHO estimates the prevalence of drug resistance among the TB patients using routine laboratory surveillance data. These estimates categorize MDR/RR TB prevalence primarily on the basis of previous history of TB treatment [7]. Prior history of TB treatment is a major risk factor for RR TB, largely due to exposure of anti-TB drugs, taken irregularly, resulting in propagation of resistant *Mycobacterium tuberculosis* strains. Additional factors such as inadequate treatment supervision, poor adherence to treatment, and limited access to care [8] also lead to unsuccessful TB treatment outcomes. This has created a critical gap in understanding the evolving patterns of TB drug resistance, especially among some of the RR TB prevalent groups.

Resistance to rifampicin is known to be associated with both socio-demographic [9] and clinical factors [10]. Some localized studies in Pakistan have also found a disproportionate distribution of MDR/RR TB among the different demographic and clinical sub-groups. For example, in a hospital-based study from Sialkot district of Punjab province, age, marital status,

and treatment history were identified as significant risk factors for MDR/RR TB [11]. RR TB was found to be associated with gender, history of TB treatment and ethnicity in Karachi district [12]. A study from Khyber Pakhtunkhwa province reported a significant association between RR TB and history of TB treatment [13], while research from Faisalabad district found age and gender to be significantly associated with RR TB [14]. Despite these localized findings, the national level data on the prevalence and distribution of MDR/RR TB across different socio-demographic and clinical subgroups remains limited.

Given the burden of MDR/RR TB in Pakistan, ensuring equitable access to standardized services especially for high RR TB prevalent sub-groups, is of utmost importance [15]. This study aimed to evaluate the resistance patterns among the diagnosed TB patients in the public private mix (PPM) model of Pakistan. A detailed analysis of MDR/RR TB across provinces, residence, age, gender, screening approach, history of TB treatment, and site of disease offered valuable insight for TB epidemiology and control initiatives in Pakistan. The study utilized programmatic data from all four provinces, allowing for an assessment of national population level trends and dynamics.

Figure 1. Public private mix model.

RR: rifampicin resistance; MTB: Mycobacterium tuberculosis; SSM: sputum smear microscopy; TB: tuberculosis; DRTB: drug resistant TB.

Methodology

This was a retrospective cross-sectional study, with an analytical component, based on routine program data of bacteriologically confirmed TB patients diagnosed between January 2022 to June 2024, in 28 districts of Pakistan across all four provinces; Punjab, Sindh, Khyber-Pakhtunkhwa, and Balochistan.

Setting

The data were sourced from the PPM intervention (Figure 1) implemented by Greenstar Social Marketing (GSM) at 6000 healthcare facilities. The PPM program was launched in 2005 in five districts and gradually expanded to 28 districts by the end of 2021. Site selection followed a pre-defined mapping and selection criterion. After selection, the healthcare providers of these sites received training on national TB guidelines, followed by signing of memorandum of understanding (MOU). These facilities included general physicians (GPs) and private hospitals. Once a TB presumptive patient was identified at any of these sites, a sputum sample (for pulmonary TB) or other clinical sample (for extra-pulmonary TB) of the patient was either tested directly on Xpert® assay (Cepheid, Sunnyvale, CA, USA) alone, or both sputum smear microscopy (SSM) and Xpert®, depending on the availability and access (Figure 1). This study analyzed the data of TB patients who presented at PPM sites through consecutive sampling.

Participants

All bacteriologically confirmed TB patients who were tested using the WHO recommended rapid diagnostic test, Xpert® assay, through GSM's PPM network facilities during the study period and within the study settings were included in the analysis. Patients whose samples were not processed by the Xpert® assay, or for whom the test result was unavailable or invalid, were excluded from the study. TB diagnostic approaches varied depending on the available resources and the logistic arrangements. Some patients were tested directly using Xpert®, while others underwent both Xpert® and SSM, particularly in cases where delays in receiving Xpert® results were anticipated due to distance. In the case of patients who were tested with both methods, SSM results were included in the analysis to find its potential association with RR TB. However, the study used only Xpert® result for defining RR TB.

Variables

The study analyzed variables including

demographic characteristics (residence, age and gender), screening approach (active and enhanced case finding, A/ECF), and clinical profile (disease site, history of TB treatment, and date of diagnosis). The primary outcome of interest was the prevalence of RR among TB patients. Secondary outcomes included the association of covariate variables with DS TB and RR TB.

Under the PPM model, patients accessed TB care either by presenting at a TB facility for care (passive case finding) or through strategies designed to enhance access to services (A/ECF). A/ECF in the study context included patients who did not reach TB care facility by themselves; rather the service providers reached the patient in community or other formal or informal healthcare settings. A/ECF aimed for early detection in the course of the disease through community camps, mobile diagnostic camps, screening initiatives, referrals from pharmacies and informal sector providers, and contact screening of bacteriologically confirmed TB patients.

In this study, pulmonary TB referred to involvement of lung parenchyma and/or tracheobronchial tree, regardless of whether other anatomical sites were also affected. Extra-pulmonary TB was defined as TB involving any site other than lungs or tracheobronchial tree. A patient was classified as a new TB patient if the patient had never taken anti TB (ATT) drugs or if the duration was less than a month. Patients who had received ATT for more than a month were categorized as retreatment cases. Retreatment cases were further classified on the basis of outcome of prior TB treatment, including relapse; patients with unknown previous history; other history and treatment after failure; and loss to follow-up.

Data sources/measurement

The program data were initially recorded at the facility level using national recording and reporting (R&R) tools. The field team of GSM subsequently entered the data on the Management Information System (MIS), which served as the source of data used in the study. The R&R tools contained standardized variables to capture information on demographic aspects, morbidity patterns, diagnostic details, and treatment approaches. Since the PPM model adheres to national guidelines for data collection and reporting, all data classifications in this study followed national protocols and definitions. Residential address of the patients was mentioned as city or tehsil in a separate field, however rural residence was determined based on the keywords indicating rural residence in local language.

Ethical approval

The study was conducted in accordance with the standard ethical guidelines. The patients' biographic data were coded to ensure confidentiality, and no personal identifiable information of the patient was used at any stage of the study. Ethical approval had been taken from the Institutional Review Board (IRB) of National Iqra University (INU/ERC/24-1).

Statistical analysis

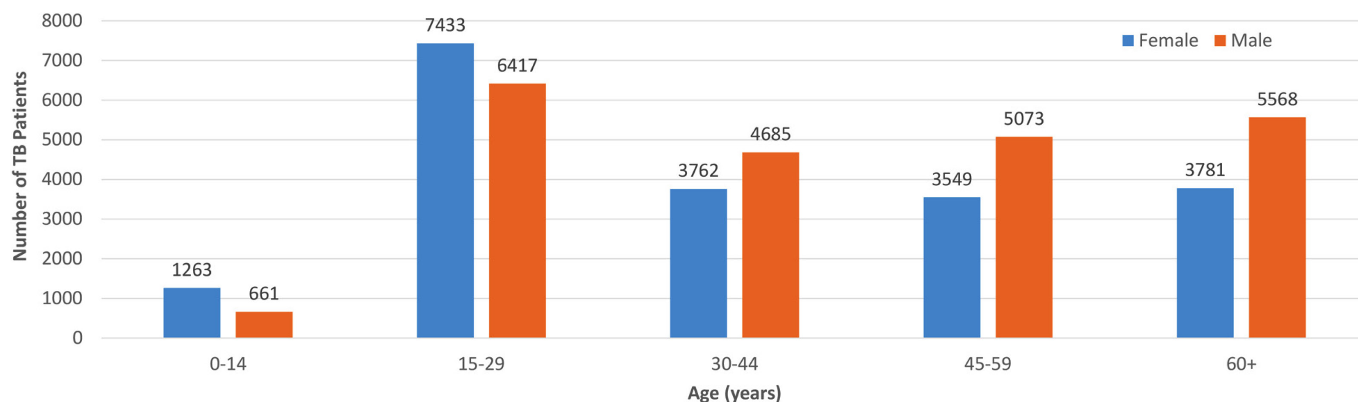
Descriptive analysis of categorical variables included frequencies and percentages; whereas normal distributions, means, and standard deviation were calculated for continuous variables. Additionally, independent t-test was performed to analyze age. Univariate analysis (Chi-square test) was conducted where variables with p value ≤ 0.05 were considered eligible for inclusion in multivariable analysis. Multivariable logistic regression was performed to determine the predictors of secondary outcome predictors. The Hosmer–Lemeshow goodness-of-fit test was utilized to assess model fit. The model demonstrated a good fit (Hosmer and Lemeshow test, 0.065; Omnibus test, $p < 0.001$). Punjab province was selected as the reference category for provincial comparisons in the multivariable logistic regression analysis. This selection was based on the fact that Punjab had the largest sample size among all provinces, providing greater statistical stability and more precise estimates. Another approach could be made by selecting the province with lowest RR TB prevalence; however, the choice of Punjab helped minimize the variability in odds ratio estimates due to its representative and high-volume data. The data was entered and analyzed using SPSS version 26 [16].

Results

During the study period, 42,423 TB patients were bacteriologically confirmed using the Xpert test, among whom 231 (0.5%) had an indeterminate result for RR TB, 974 (2.3%) were RR TB detected, and RR was not detected in 41,218 (97.2%) TB patients. Further analysis was carried out on the data of 42,192 TB patients with valid RR results (i.e., either RR detected or not detected).

The mean age ± SD of the study population was 40.27 ± 19.48 years. An independent samples t-test showed statistically significant difference in age among the patients with RR and those without ($t = 3.34$, $df = 42{,}190$, $p = 0.001$). The mean age of TB patients with

Figure 2. Age and gender distribution of TB patients.



RR TB (M = 38.20 ± 18.34 years) was significantly lower than the patients without RR TB (M = 40.32 ± 19.50 years).

There were fewer women than men (46.9% (n = 19,788): 53.1% (n = 22,404)) among the study population (n = 42,192). Further disaggregation showed that there were more women till the age of 29 years (55% (n = 8,696): 45% (n = 7,078)), while from age 30 years onwards, there were fewer women (42% (n = 11,092), 58% (n = 15,326)) (Figure 2). The women had a greater prevalence of RR TB (2.45%) as compared to the men (2.19%), however, the difference in RR TB occurrence was not statistically significant. RR TB was highest among the 15–29-years age group (n = 13,850, 2.66%), followed by those aged 45–59 years (n = 8,622, 2.42%), and 30–44 years (n = 8,447, 2.40%). The lowest prevalence was found among people aged ≥ 60 years (n = 9349, 1.70%), followed by the youngest age group of 0–14 years (n = 1,924, 1.82%) (Table 1). Univariate analysis showed that age groups were significantly associated with RR TB (Table 2). Multivariable analysis indicated that individuals ≥ 60 years had statistically significant reduction in the odds of the outcome (41% lower) as compared to the youngest age group (Table 3).

The study found statistically significant geographical variation in RR TB detection across provinces on univariate analysis ($p = 0.004$). Sindh had the highest RR TB (n = 16,915, 2.51%), followed by Punjab (n = 21,942, 2.28%), Balochistan (n = 57, 1.75%), and Khyber-Pakhtunkhwa (n = 3,278, 1.46%) (Table 1). Multivariable analysis showed that the odds

Table 1. Chi square analysis of rifampicin resistance across various socio-demographic sub-groups.

	MTB detected RR detected (n)	MTB detected RR not detected (n)	MTB detected with valid RR result (n)	RR (%)	*p* value
		n = 42192			
Province					**0.004**
Punjab	501	21441	21942	2.28%	
Sindh	424	16491	16915	2.51%	
Khyber-Pakhtunkhwa	48	3230	3278	1.46%	
Baluchistan	1	56	57	1.75%	
Residence					**0.000**
City	668	30516	31184	2.14%	
Sub-district / Tahsil	113	4701	4814	2.35%	
Village	193	6001	6194	3.12%	
Age (years)					**0.000**
0–14	35	1889	1924	1.82%	
15–29	368	13482	13850	2.66%	
30–44	203	8244	8447	2.40%	
45–59	209	8413	8622	2.42%	
60+	159	9190	9349	1.70%	
Gender					**0.077**
Female	484	19305	19789	2.45%	
Male	490	21913	22403	2.19%	
Year of RR TB Detection					**0.058**
2022	320	12241	12561	2.55%	
2023	425	18224	18649	2.28%	
2024	229	10753	10982	2.09%	

RR: rifampicin resistance; MTB: *Mycobacterium tuberculosis.*

of RR TB were significantly higher in Sindh (OR = 1.65, 95% CI 1.37–2.00, p = 0.000) and lower in Khyber Pakhtunkhwa (OR = 0.512, 95% CI 0.33–0.8, p = 0.003), in comparison to Punjab (Table 3).

Univariate analysis indicated that RR TB detection was highest among patients residing in rural areas (n = 6194, 3.12%), followed by tehsils (sub-district) (n = 4,814, 2.35%), and cities (n = 31,184, 2.14%) (p = 0.000) (Table 1). However, multivariable logistic regression indicated that there was no statistically significant association between residence and RR TB detection, indicating no meaningful difference after adjusting for covariates.

Screening/testing

A lower prevalence of RR TB was observed among patients diagnosed through ACEF (n = 3,769, 1.91%), as compared to the patient's seeking healthcare from a facility by themselves (n = 38,423, 2.35%); however, the association was not significant (p = 0.088) (Table 2).

TB patients with positive SSM results had a higher prevalence of RR TB (n = 13602, 2.71%) compared to those with negative SSM results (n = 5977, 2.23) (p = 0.050) (Table 2).

Clinical factors

More TB patients with pulmonary TB had RR TB (n = 41,112, 2.32%) than those with extra-pulmonary TB (n = 1,080, 1.94%). The association between the site of disease and RR TB was not statistically significant (p = 0. 420) (Table 2).

Among the extra-pulmonary TB patients, the highest RR TB rate was observed in patients having meningeal involvement (n = 47, 4.26%) followed by patients having abscess (n = 74, 4.05%) and abdominal TB (n = 90, 3.33%). The lowest rate was observed in patients with pleural involvement (n = 368, 0.54%). These differences were not statistically significant (p = 0. 094) (Table 2).

A statistically significant association was found between the history of previous TB treatment and RR TB (p < 0.000). The prevalence of RR TB was 1.95% among new TB patients and 5.48% among retreatment patients (Table 2). Multivariable analysis revealed that the retreatment patients had 3.7 times higher odds of RR TB as compared to new patients (OR = 3.73, 95% CI 3.04–4.57, p < 0.000) (Table 3).

Among the retreatment TB patients, the highest RR TB was seen among patients who were enrolled again after previous history of TB treatment failure (n = 88, 13.64%), followed by unknown previous TB treatment

Table 2. Chi square analysis of rifampicin resistance across programmatic and clinical sub-groups.

	MTB detected RR detected (n)	MTB detected RR not detected (n)	MTB detected with valid RR result (n)	RR (%)	*p* value
			n=42192		
Referral					**0.088**
ACF	72	3697	3769	1.91%	
PCF	902	37521	38423	2.35%	
Site of disease					**0.420**
Pulmonary TB	953	40159	41112	2.32%	
Extra-pulmonary TB	21	1059	1080	1.94%	
Site of extrapulmonary TB					**0.094**
Pleural	2	366	368	0.54%	
Lymph nodes	8	271	279	2.87%	
Abdomen	3	87	90	3.33%	
Abscess	3	71	74	4.05%	
Meningitis	2	45	47	4.26%	
Other	3	219	222	1.35%	
Sputum smear microscopy					**0.050**
Positive	368	13234	13602	2.71%	
Negative	133	5844	5977	2.23%	
History of treatment					**0.000**
New	742	37219	37961	1.95%	
Retreatment	232	3999	4231	5.48%	
History of TB treatment					**0.001**
Relapse	171	3127	3298	5.18%	
Treatment after LTFU	20	381	401	4.99%	
Other previously treated	15	300	315	4.76%	
Unknown previously treated	14	115	129	10.85%	
Treatment after Failure	12	76	88	13.64%	
History of LTBI treatment					**0.387**
Yes	0	33	33	0.00%	
No	779	34300	35079	2.22%	

RR: rifampicin resistance; MTB: *Mycobacterium tuberculosis*; ACF: active case finding; PCF: passive case finding; LTBI: latent TB infection; LTFU: loss to follow-up.

Table 3. Analysis of rifampicin resistance across various significant socio-demographic and clinical sub-groups through logistic regression.

	Variable	OR (Exp(B))	95% CI for OR	*p value*
Province	Punjab (Ref)			0.000
	Sindh	1.652	(1.37, 2.00)	0.000
	Khyber-Pakhtunkhwa	0.512	(0.33, 0.80)	0.003
	Balochistan	0.000	(0.00, 0.00)	0.999
Residence	District level (Ref)		(0.00, 0.00)	0.457
	Sub-district level	1.045	(0.80, 1.37)	0.748
	Village	1.157	(0.92, 1.45)	0.211
Age	0–14 (Ref)		(0.00, 0.00)	0.002
	15–29	1.007	(0.62, 1.63)	0.978
	30–44	0.796	(0.48, 1.32)	0.373
	45–59	0.933	(0.57, 1.53)	0.782
	60+	0.588	(0.35, 0.98)	0.043
History of TB Treatment	New (Ref)			
	Retreatment	3.730	(3.04, 4.57)	0.000
SSM	Positive (Ref)			
	Negative	0.821	(0.67, 1.01)	0.059

SSM: sputum smear microscopy; TB: tuberculosis.

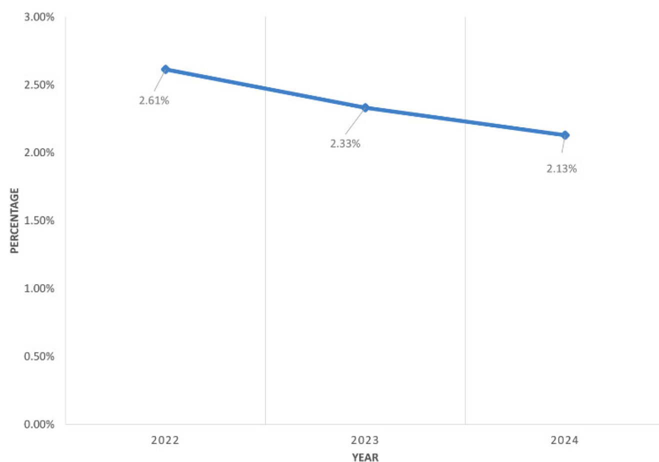
history (n = 129, 10.85%), treatment after previous relapse (n = 3,298, 5.18%), treatment after loss to follow up (n = 401, 4.99%), and other previously treated (n = 315, 4.76%). The Chi square test indicated that the association was statistically significant (p = 0.001) (Table 2).

RR TB showed a decreasing trend over time. The highest RR TB prevalence was observed in 2022 (2.55%) followed by 2023 (2.28%) and 2024 (2.09%). The relation was not statistically significant on univariate analysis (p = 0.058) (Figure 3).

Discussion

In this study, the prevalence of RR TB was 2.31% among all forms of TB patients. The findings revealed that RR TB prevalence was not uniform across all subgroups. Higher RR TB prevalence was observed among patients who were SSM positive, those who were previously treated for TB, and residents of Sindh province; while the lowest prevalence was observed among individuals aged over 60 years.

Figure 3. Rifampicin resistance among newly diagnosed bacteriologically confirmed TB patients.



RR: rifampicin resistance; MTB: Mycobacterium tuberculosis.

The highest prevalence of RR TB was observed in Sindh province. Our findings are comparable with the National TB Control Program data, which also reported variation in RR TB positivity across provinces. According to the Annual Report TB 2019 (the most recent available report), RR TB positivity was highest in Punjab (4.8%), followed by 4.7%, 4.5%, and 3.9 in Sindh, Khyber-Pakhtunkhwa and Balochistan respectively [17].

Although univariate analysis showed a higher RR TB detection among patients residing in rural areas, this association did not remain statistically significant in multivariable analysis. Therefore, while limited access to standardized TB care in rural and remote settings has been a possible contributor to drug resistance [18], the findings of this study do not provide conclusive evidence of an independent association between the residence of patient and RR TB.

This study found that RR TB was higher among the younger age groups as compared to children (0–14 years) and those above 60 years of age. This was similar to findings in China where MDR TB detection was 14.1% among the patients under 51 years of age, as compared to 9.3% among the over 51 years' age group [19]. A meta-analysis also found that the risk of RR TB was lower among the elderly (65+ years) and pediatric TB patients [20].

Higher RR TB was reported among patients visiting health facilities for seeking care as compared to patients reached through A/ECF strategies; however, this finding was not significant on multivariate analysis. A well-planned study is needed to evaluate the outcome of various initiatives and their reach to target population. The difference in this study may be attributed to the fact that A/ECF helped in early

diagnosis and care [21].

Female gender was an important determinant for RR TB detection in Pakistan [11], and also in other parts of the world [22]. In addition, females had slightly higher prevalence of RR in comparison to males (2.45% vs. 2.19%), however the correlation cannot be established due to statistical insignificance. This may be due to small absolute differences, potential confounders, or insufficient statistical power for detection of subtle variations. Access to healthcare services and stigma may have played a role in detection. There is a need to have an in-depth analysis on the impact of gender on RR TB detection for reaching out to RR TB prevalent communities.

Globally, prevalence of RR TB is higher among people who were previously treated for TB [21]. In China, drug resistance was 5.7% (95% CI, 4.5–7.0) among the new TB patients and 25.6% (95% CI, 21.5–29.8) among those who were previously treated [22]. In Russia, the patients who were previously treated for TB were 2.82 times (95% CI, 2.16–3.66) more likely to have drug resistant TB [23]. In Egypt, the RR TB prevalence was 3.32 among the new patients, while it was 9.46 among the retreatment cases [25]. Previous history of interrupted TB treatment is also a risk factor for RR TB [25,26]. A study in China found a lower risk of drug resistance among patients who had taken TB drugs for less than 6 months [27]. This study also found a significant association between the history of TB treatment and the RR TB detection; the retreatment patients were around 3 times more likely to have RR TB as compared to new TB patients. TB treatment history remained the strongest predictor of RR TB. Requirement to retreat TB is driven by a complex interplay of patient-level, health system, and socio-economic factors. Interruption to TB treatment is found to be associated with challenges in access to TB care services, limited support for adherence, and requirement for hospitalization [8,28]. Additionally, unsuccessful treatment (failure and loss to follow up) correlates with male gender, substance use, missed doses of treatment, adverse drug reactions, and lack of community support [29,30]. The barriers to treatment success may be minimized through the engagement of community health workers in service provision, small treatment cohorts, patient education, and implementation of directly observed treatment short-course (DOTS) throughout the course of treatment [28].

The most recent national drug prevalence survey was conducted over a decade ago, and there is need for updated survey data to reflect the current epidemiological situation.

This study shows a decreasing trend in RR over the study years, which is consistent with data from China where RR TB decreased among both the new and retreatment TB patients [31]. In contrast, a meta-analysis showed that in India, RR TB was increasing among the new TB patients, while decreasing among the retreatment patients [32].

This study could not find any significant association between the RR TB and the site of disease. This lack of significant association may be attributed to the small sample size of the extrapulmonary cases or a smaller absolute difference in RR rate, resulting in low statistical power. The bacteriological confirmation of extra-pulmonary (EP) TB is always a challenge, due to involvement of obscure or nearly inaccessible sites requiring invasive procedures for obtaining adequate samples. The non-uniform distribution of *Mycobacterium tuberculosis* at EP TB sites and the paucibacillary nature of the disease may lead to false negative results [33]. These challenges are more pronounced in resource limited settings [33], like Pakistan. There is a need to plan a study that can explore the relation between the site of TB and RR TB more robustly. Additionally, the magnitude of drug resistance burden among different sites of EP TB should also be studied to plan the need-based interventions.

Limitations

The researchers found some limitations despite the significant findings. This was a cross sectional study which lacked causal inference. The study used consecutive sampling with its inherent limitations of generalizability. There was limited sample population in Balochistan which made it difficult to generalize provincial results. Some potential confounders like socio-economic factors and comorbidity were not studied due to unavailability of data. Some the potential risk factors like diabetes, HIV, malnutrition, and history of contact with RR TB patients were not recorded during the study period since the screening services were not available for these risks in routine program implementation.

Conclusions

In Pakistan, around 25% of the estimated RR TB patients receive treatment, indicating a need to find the missed RR TB cases through innovative, targeted and evidence-based approaches for TB care. This will require mobilization of the resources and efforts in the right direction. This could be achieved through the provision of equitable diagnostic and treatment services to all those at risk of developing drug resistant TB. TB

patients who were previously treated for TB disease were at greater risk of RR TB; therefore, efforts should be directed to address the potential barriers to successful TB treatment.

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Corresponding author
Sobia Faisal, MBBS (Pak), MPH (US)
Greenstar Social Marketing, House number 13, Street 59, F 8/4 Islamabad, Pakistan.
Tel: +92323-510-1246
Email: sobiahina@gmail.com; sobiafaisal@greenstar.org.pk

Conflict of interest
No conflict of interest is declared.

References
1. World Health Organization (2024) Global tuberculosis report 2024. Geneva: WHO.
2. World Health Organization (2024) Tuberculosis profile Pakistan. Geneva: WHO.
3. Cannon LAL, Oladimeji KE, Goon DT (2021) Socio-economic drivers of drug-resistant tuberculosis in Africa: a scoping review. BMC Public Health 21.1: 488. doi: 10.1186/s12889-021-10267-0.
4. Atif M, Mukhtar S, Sarwar S, Naseem M, Malik I, Mushtaq A (2022) Drug resistance patterns, treatment outcomes and factors affecting unfavourable treatment outcomes among extensively drug resistant tuberculosis patients in Pakistan: a multicentre record review. Saudi Pharm J 30: 462–469. doi: 10.1016/j.jsps.2022.01.015.
5. Massud A, Khan AH, Syed Sulaiman SA, Ahmad N, Shafqat M, Ming LC (2023) Unsuccessful treatment outcome and associated risk factors: a prospective study of DR-TB patients from a high burden country, Pakistan. PLoS One 18: e0287966. doi: 10.1371/journal.pone.0287966.
6. Bennani K, Van den Boom M, El Medrek M, Hutin Y (2024) Progress in programmatic management of drug-resistant TB in the WHO Eastern Mediterranean Region, 2018–2023. Int J Tuberc Lung Dis Open 1: 398–403. doi: 10.5588/ijtldopen.24.0348.
7. World Health Organization (2023) Global tuberculosis report 2023. Geneva: WHO.
8. Brasil PEAAd, Braga JU (2008) Meta-analysis of factors related to health services that predict treatment default by tuberculosis patients. Cademos de Saude Publica 24: S4. doi: 10.1590/S0102-311X2008001600003.
9. Okumu A, Orwa J, Sitati R, Omondi I, Odhiambo B, Ogoro J, Oballa G, Ochieng B, Wandiga S, Ouma C (2024) Factors associated with tuberculosis drug resistance among presumptive multidrug resistance tuberculosis patients identified in a surveillance study in Western Kenya. J Clin Tuberc Other Mycobact Dis 37: 100466. doi: 10.1016/j.jctube.2024.100466.
10. Vyawahare C, Mukhida S, Khan S, Gandham NR, Kannuri S, Bhaumik S (2024) Assessment of risk factors associated with drug-resistant tuberculosis in pulmonary tuberculosis patients. Indian J Tuberc 71: S44–S51. doi: 10.1016/j.ijtb.2023.07.007.
11. Saifullah A, Mallhi TH, Khan YH, Iqbal MS, Alotaibi NH, Alzarea AI, Rasheed M (2021) Evaluation of risk factors associated with the development of MDR- and XDR-TB in a tertiary care hospital: a retrospective cohort study. PeerJ 9: e10826. doi: 10.7717/peerj.10826.
12. Ejaz M, Siddiqui AR, Rafiq Y, Malik F, Channa A, Mangi R, Habib F, Hasan R (2010) Prevalence of multidrug resistant tuberculosis in Karachi, Pakistan: identification of at-risk groups. Trans R Soc Trop Med Hyg 104: 511–517. doi: 10.1016/j.trstmh.2010.03.005.
13. Ali S, Khan MT, Khan AS, Mohammad N, Khan MM, Ahmad S, Noor S, Jabbar A, Daire C, Hassan F (2020) Prevalence of multidrug resistant *Mycobacterium tuberculosis* in Khyber Pakhtunkhwa, a high endemic area of Pakistan. Pol J Microbiol 69: 133–137. doi: 10.33073/pjm-2020-005.
14. Arif S, Mehboob Q, Arif W (2020) Prevalence and analysis of drug resistance pattern of MDR-TB in retreatment cases at Allied Hospital, Faisalabad, Pakistan. Ann Punjab Med Coll 14: 331–335. doi: 10.29054/apmc/2020.994.
15. Citro B, Soltan V, Malar J, Katlholo T, Smyth C, Sari AH, Klymenko O, Lunga M (2021) Building the evidence for a rights-based, people-centered, gender-transformative tuberculosis response: an analysis of the Stop TB Partnership community, rights and gender assessment. Health Hum Rights 23: 253–268.
16. IBM Corp (2019) IBM SPSS Statistics for Windows, Version 26.0. Armonk, NY: IBM Corp.
17. National TB Control Program Pakistan (2019) Annual report 2019. Islamabad: NTP Pakistan.
18. Admassu F, Abera E, Gizachew A, Sedoro T, Gari T (2023) Risk factors of multidrug resistant tuberculosis among patients with tuberculosis at selected MDR-TB treatment centres in Southern Ethiopia: a case-control study. BMJ Open 13: e061836. doi: 10.1136/bmjopen-2022-061836.
19. Wang Z, Hou Y, Guo T, Jiang T, Xu L, Hu H, Zhao Z, Xue Y (2023) Epidemiological characteristics and risk factors of multidrug-resistant tuberculosis in Luoyang, China. Frontiers in Public Health 11: 1117101. doi: 10.3389/fpubh.2023.1117101.
20. Nair SA, Raizada N, Sachdeva KS, Denkinger C, Schumacher S, Dewan P, Kulsange S, Boehme C, Paramsivan CN, Arinaminpathy N (2016) Factors associated with tuberculosis and rifampicin-resistant tuberculosis among symptomatic patients in India: a retrospective analysis. PLoS One 11: e0150054. doi: 10.1371/journal.pone.0150054.
21. Saunders MJ, Tovar MA, Collier D, Baldwin MR, Montoya R, Valencia TR, Gilman RH, Evans CA (2019) Active and passive case-finding in tuberculosis-affected households in Peru: a 10-

year prospective cohort study. Lancet Infect Dis 19.5: 519–528. doi: 10.1016/S1473-3099(18)30753-9.
22. Dorji T, Tshering K, Adhikari L, Jamtsho T, Bhujel P, Lhaden P, Sherry NL, Lin C, Horan K, Wangchuk S (2024) High incidence of multidrug-resistant tuberculosis in Bhutan: a cohort study based on national surveillance data. IJID Reg 13: 100471. doi: 10.1016/j.ijregi.2024.100471.
23. Zhao YL, Xu SF, Wang LX, Chin D, Wang SF, Jiang GL, Xia H, Zhou Y, Li Q, Ou XC (2012) National survey of drug-resistant tuberculosis in China. N Engl J Med 366: 2161–2170. doi: 10.1056/NEJMoa1108789.
24. Bykov I, Dyachenko O, Ratmanov P, Liu H, Liang L, Wu Q (2022) Factors contributing to the high prevalence of multidrug-resistant/rifampicin-resistant tuberculosis in Khabarovsk Krai, Russia: an epidemiological cross-sectional and qualitative study. BMC Infect Dis 22: 612. doi: 10.1186/s12879-022-07598-7.
25. Amin W, Gadallah M, Salah A, Rady M (2024) Prevalence of rifampicin-resistant tuberculosis among presumptive tuberculosis patients in Egypt: a national health facility-based survey. BMC Infect Dis 24: 210. doi: 10.1186/s12879-023-08807-7.
26. Nofal IMM, AbdelHalim HA, Almaraghy AA, Awad AM, Farrag MA (2024) Characteristics and treatment outcomes of patients with multidrug-resistant tuberculosis at Abbassia Chest Hospital. Egypt J Bronchol 18: 97. doi: 10.1186/s43168-024-00348-0.
27. Li Z, Zhang M, Wang J, Chen S, Wang B, Li Z, A P, Wang W, Xu W (2020) Longitudinal analysis of prevalence and risk factors of rifampicin-resistant tuberculosis in Zhejiang, China. Biomed Res Int 2020: 1–10. doi: 10.1155/2020/3159482.
28. Toczek A, Cox H, Du Cros P, Cooke G, Ford N (2013) Strategies for reducing treatment default in drug-resistant tuberculosis: systematic review and meta-analysis. Int J Tuberc Lung Dis 17: 299–307. doi: 10.5588/ijtld.12.0537.
29. Damene K, Lahlou O, Ghali I, Karimi J, El Hamdani M, Chakib I, Rguig A (2011) Risk factors for tuberculosis treatment failure, default or relapse and outcomes of retreatment in Morocco. BMC Public Health 11: 140. doi: 10.1186/1471-2458-11-140.
30. Vanitha A, Praveen AJ, Kumar S, Dutta KS, Manikandan AK, Srikanth KS, Manju M, Subramanian V (2018) Tuberculosis retreatment outcomes and associated factors: a mixed-methods study from Puducherry, India. Public Health Action 8: 187–193. doi: 10.5588/pha.18.0038.
31. Ren Y, Chen B, Zhao J, Tan X, Chen X, Zhou L, Wang F, Peng Y, Jiang J (2022) Trends of rifampicin resistance in patients with pulmonary tuberculosis: a longitudinal analysis based on screening in Eastern China, 2015–2019. Infect Drug Resist 15: 6013–6024. doi: 10.2147/IDR.S394089.
32. Lohiya A, Abdulkader RS, Rath RS, Jacob O, Chinnakali P, Goel AD, Agrawal S (2020) Prevalence and patterns of drug-resistant pulmonary tuberculosis in India: a systematic review and meta-analysis. J Glob Antimicrob Resist 22. doi: 10.1016/j.jgar.2020.03.008.
33. Purohit M, Mustafa T (2015) Laboratory diagnosis of extra-pulmonary tuberculosis in resource-constrained settings: state of the art, challenges and needs. J Clin Diagn Res 9: EE01–EE06. doi: 10.7860/JCDR/2015/12422.5792.