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## **First Line Drug-Resistant Tuberculosis and its Associated Risk Factors in Tertiary Care Hospital of Sudurpaschim Province, Nepal**

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### **Abstract**

Tuberculosis (TB) remains a major global health concern, with an estimated 10.8 million cases reported worldwide in 2023. In Nepal, TB poses a persistent public health challenge, particularly due to the increasing resistance to first-line anti-TB drugs, which complicates treatment and raises mortality risk. Limited data from Sudurpaschim Province hinder the implementation of region-specific interventions. This study aimed to assess the prevalence of first-line drug-resistant TB (DR-TB) and identify its associated demographic, geographic factors among patients treated at Seti Provincial Hospital in 2023. A retrospective cross-sectional analysis was conducted using records of 653 bacteriologically confirmed TB cases diagnosed between January and December 2023. Drug susceptibility test results, along with demographic and geographic data, were analyzed. The overall prevalence of DR-TB was 9.5%. While no significant gender-based differences were observed, age was a significant risk factor, with the highest resistance found in individuals aged 31–45 years (15.5%) and  $\geq 76$  years (11.4%). Dalit patients exhibited the highest resistance rate (14.0%), indicating disparities in healthcare access and adherence. Geographically, municipalities like Tikapur and Bardgoriya showed higher DR-TB prevalence, suggesting localized hotspots. These findings emphasize the need for targeted public health strategies to improve early diagnosis, treatment adherence, and equitable healthcare access, especially among vulnerable populations. The study highlights the importance of localized surveillance and further research to effectively address the burden of drug-resistant TB in Sudurpaschim Province.

**Keywords:** Drug-resistant tuberculosis, TB epidemiology, risk factors, antimicrobial resistance, public health intervention, vulnerable populations

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## Introduction

Tuberculosis (TB) was the world's second leading cause of death from a single infectious agent in 2023. Worldwide, an estimated 10.8 million people developed TB in 2023, up from best estimates of 10.7 million in 2022 and 10.4 million in 2022. Globally in 2023, TB caused an estimated 1.9 million deaths in HIV negative people and an estimated 161 000 deaths among people with HIV. Globally, the estimated annual number of people who developed multidrug-resistant or rifampicin-resistant TB (MDR/RR-TB) remained relatively stable between 2020 and 2023, following a slow decline from 2015 to 2019, with an estimated 400,000 cases in 2023 of which 280,000 were MDR-TB (WHO, 2024). TB is treatable and preventable infection caused by *Mycobacterium tuberculosis* which is spread when people who are sick with TB expel bacteria into the air by coughing. About a quarter of the global population is estimated to have been infected with TB (Houben & Dodd, 2016).

Drug resistance in *Mycobacterium tuberculosis* is caused by genetic mutations that alter drug targets or activation enzymes, reducing drug effectiveness. Key mutations occur in the *katG* and *inhA* genes for isoniazid resistance, the *rpoB* gene for rifampicin resistance, and other genes like *embB* and *pncA* for resistance to ethambutol and pyrazinamide, respectively. These mutations are detected using molecular diagnostic tools for rapid identification of resistant TB strains (WHO, 2023; Nguyen, 2016; Zhang & Yew, 2009). WHO-recommended treatments, a 4–6 months course of anti-TB drugs can cure approximately 85% of TB patients. Treatment regimens of 1–6 months are available for TB infection. Achieving Universal Health Coverage (UHC) is essential for ensuring equitable access to TB treatment. Multisectoral efforts addressing determinants such as poverty, undernutrition, HIV, smoking, and diabetes can further reduce TB transmission, disease burden, and mortality. Without treatment, the death rate from TB disease is high about 50% (WHO, 2023).

Antimicrobial resistance (AMR) is an increasingly significant threat to public health, and its rise coincides with the development of tuberculosis and harder to treat than drug-susceptible ones and take much longer while MDR-TB involves more extensive and longer treatment courses than drug-susceptible (WHO, 2019). It has been predicted that AMR-related deaths will increase more than tenfold to 10 million per year by 2050. Unless action is taken now, DR-TB may be responsible for approximately 2.5 million of these deaths (EIU, 2019). Globally, MDR/RR-TB caused an estimated 160 000 deaths in 2022 (WHO, 2023).

First-line antituberculosis drugs- Isoniazid (INH), rifampicin (RIF), ethambutol (EMB), pyrazinamide (PZA) and streptomycin (SM). Second-line antituberculosis drugs- sub divided into two: Fluoroquinolones- Ofloxacin (OFX), levofloxacin (LEV), moxifloxacin (MOX) and ciprofloxacin (CIP) and injectable antituberculosis drugs-

Kanamycin (KAN), amikacin (AMK) and capreomycin (CAP). The less-effective second-line antituberculosis drugs- Ethionamide (ETH)/Prothionamide (PTH), Cycloserine (CS)/Terizidone, P-aminosalicylic acid (PAS) are used to treatment of TB.

TB drug resistance is divided into five categories: isoniazid-resistant TB, RR-TB, MDR-TB, pre- extensively resistant tuberculosis (pre-XDR-TB), and extensively resistant tuberculosis (XDR-TB). MDR-TB is resistant to the two most effective first-line anti-TB medications, rifampicin (RIF) and isoniazid (INH). Pre-XDR-TB is MDR-TB that is resistant to any fluoroquinolone, whereas XDR-TB is defined as MDR-TB plus resistance to any fluoroquinolone and at least one other group drug (bedaquiline and linezolid). The prevalence of MDR/RR and MDR-TB posed significant public health challenges. Treatment of MDR/RR strains is more complicated, expensive and negative economic consequences when compared to patients with drug-sensitive strains. RR is considered as surrogate marker for MDR-TB in over 90% of cases. (WHO, 2022).

Nepal adopted the Directly Observed Treatment, Short-course (DOTS) strategy in 1996, which remains the cornerstone of its national TB control program. However, challenges such as treatment default, poor follow-up, and limited accessibility in remote areas hinder its full effectiveness. TB is diagnosed using sputum microscopy, culture methods, chest X-ray, and advanced molecular tools like GeneXpert MTB/RIF and Line Probe Assay (LPA) in Nepal (NTCC, 2019). DR-TB ranks among the top ten causes of death in Nepal, claiming approximately 17,000 lives each year and imposing a significant social and economic burden (WHO, 2024). The ever-increasing prevalence of pulmonary tuberculosis (PTB) in Far West Nepal has been made worse by increasing incidence of HIV/AIDS. Most of people from this region were migrant labor to India and acquire HIV infection then transmit the infection to their innocent housewives during their short visit to home (Bohara, 2014). The study conducted by Dhunagana et al (2014) documents the 4.9% prevalence of tuberculosis among HIV infected persons in Kailali and Kanchanpur district. The disease is predominantly affecting youths of productive age groups with low socioeconomic status.

Despite the implementation of national TB control programs, a lack of region-specific data particularly from Sudurpaschim Province hinders the development of targeted intervention strategies. This study aims to address this gap by examining local patterns of drug resistance and associated risk factors. Although the prevalence of drug-susceptible TB and RR-TB varies significantly across countries and may not directly reflect the situation in Nepal, limited data are available for this region. Notably, in 2024, a study by Bohara reported an overall TB positivity rate of 11.8% and an RR-TB prevalence of 3% at Mahakali Provincial Hospital in Sudurpaschim Province. The main objective of our study is to assess associated risk factors with first-line drug resistance TB in Seti Provincial Hospital of Sudurpaschim province of Nepal.

## **Research Methodology**

### **Study Design and Setting**

At the Seti Provincial Hospital in Nepal's Sudurpaschim province, a hospital-based retrospective study was carried out. Seti Provincial hospital is 300 beds referral hospitals in the province. It provides many services and health facilities almost all districts of Sudurpaschim province and nearby districts. It is located at Dhangadhi sub-metropolitan city of Kailali district.

### **Data Collection and Procedures**

All patients who were registered and had confirmed TB cases between January and December of 2023 were identified using TB notification records. The data was thoroughly examined in retrospect, with special attention paid to the demographic characteristics of the participants (age, sex, ethnicity, residency and result of GeneXpert MTB/ RIF assay). Patients with pulmonary disease were considered, and only those patients with full information recorded in the TB notification register were included for analysis. Five age groups were designated for this investigation.

Patients without confirmed pulmonary TB, cases of extrapulmonary TB, those with incomplete records or missing GeneXpert results, duplicate entries, and those registered outside January to December 2023 were excluded from the study to ensure data accuracy and consistency.

### **Ethical Approval**

A letter of cooperation was written to study hospital authority and permission to collect the data was obtained. To ensure the confidentiality of the participants' information, data were anonymously used, and any other confidential information was highly secured. Since we used secondary data, patients informed consent was not sought from the study participants.

### **Laboratory Methods**

*Mycobacterium tuberculosis* was identified using the laboratory's standard operating procedures. The procedure included decontamination and digestion of non-sterile samples. Additionally, smears were made and examined using standard AFB stains (Z-N staining) to check for the presence of acid-fast bacilli. To identify the *Mycobacterium tuberculosis* complex and detect Rifampicin resistance, polymerase chain reaction (PCR) was performed using the Xpert MTB/RIF assay (Cepheid, USA). Al-Ateah et al. published detailed methods previously (2012). The Gene Xpert MTB/RIF test looks for mutations in the *rpoB* gene that are resistant to both MTB and RIF using real-time polymerase chain reaction technology. In a 15 ml falcon tube containing unprocessed sputum, a sample reagent was added in a 2:1 ratio. The tube was then manually shaken

twice over the course of 15 minutes.

### **Statistical Analysis**

IBM SPSS Statistics for Macintosh, Version 23 (IBM Corp., Armonk, N.Y., USA) and Microsoft Office Excel software were used to analyze the data and calculate descriptive statistics like mean, sum, and percent distribution. The Chi Square statistic was used to calculate the difference between variables like subject sex and age groups. For significance, a P-value of less than 0.05 was used. To determine the crude and adjusted odds ratios for variables linked to drug-resistant TB with a 95% confidence interval (CI), univariate and multivariable regression were employed. Age differences between drug-resistant and drug-sensitive TB were examined using the Analysis of Variance (ANOVA) test to confirm that patient age was a significant association factor for DR-TB.

## **Results and Discussion**

### **Results**

A total of 653 TB patients were analysed to investigate the association between demographic and geographic factors and drug resistance. Among the participants, 306 (46.9%) were female and 347 (53.1%) were male, with no significant difference in drug resistance rates between sexes ( $p = 0.497$ ). The overall prevalence of DR-TB in the cohort was 9.5 % where 4.9% for males and 4.6% for females. The patients ranged in age from 5 to 97 years old, with a mean age of 48.05 years ( $SD = 20.11$ ). Age was significantly associated with drug resistance ( $p < 0.001$ ). Notably, patients aged 31-45 years had the highest proportion of DR-TB at 15.5%, followed by those aged 76 years and above (11.4%). In contrast, patients in the 0-15 and 46-60 age groups showed no or minimal drug resistance, highlighting age as a potential predictor of drug resistance within this population.

Ethnic background was also significantly associated with drug resistance ( $p < 0.001$ ). Dalit patients demonstrated a higher drug resistance rate of 14.0% compared to other ethnic groups, such as Janajati (3.0%) and Kshetri (2.2%). This suggests that ethnicity may play a role in drug resistance patterns, possibly due to varying access to healthcare or differences in treatment adherence.

Kailali District in Nepal has 13 local levels, including one sub-metropolitan city, six urban municipalities, and six rural municipalities: Dhangadhi Sub-Metropolitan City is the headquarters of Kailali District. Tikapur, Ghodaghodi, Lamkichuha, Bhajani, Godawari, and Gauriganga are urban municipalities. Janaki, Bardagoriya, Mohanyal, Kailari, Joshipur, and Chure are rural municipalities. Geographic location significantly influenced drug resistance rates ( $p = 0.023$ ). Patients residing in certain localities, such as Tikapur and Bardagoriya, exhibited notably higher rates of DR-TB (25.0% and 20.0%,

respectively). Conversely, other localities, including Gauriganga and Joshipur, showed no cases of DR-TB among the patients surveyed. The other represent the patients from out of the Kailali district comprised the 11 (3.6%) of DR-TB cases in the study.

**Table 1**

*Association of Demographic and Geographic Factors with Drug Resistance in TB Patients (N=653)*

Variable	Category	Total (N)	Drug-Sensitive TB (n/%)	Drug-Resistant TB (n/%)	p-value
Sex	Female	306	292 (100%)	14 (4.6%)	0.497
	Male	347	330 (100%)	17 (4.9%)	
Age Group	0-15	26	26 (100%)	0 (0.0%)	<0.001
	16-30	156	151 (96.8%)	5 (3.2%)	
	31-45	103	87 (84.5%)	16 (15.5%)	
	46-60	176	175 (99.4%)	1 (0.6%)	
	61-75	157	152 (96.8%)	5 (3.2%)	
	76-100	35	31 (88.6%)	4 (11.4%)	
Ethnic Group	Dalit	114	98 (86.0%)	16 (14.0%)	<0.001
	Janajati	197	191 (97.0%)	6 (3.0%)	
	Muslim	1	1 (100%)	0 (0.0%)	
	Kshetri	279	273 (97.8%)	6 (2.2%)	
Localities	Brahmin	62	59 (95.2%)	3 (4.8%)	0.023
	Dhangadhi SM	191	185 (96.9%)	6 (3.1%)	
	Godawari M	46	41 (89.1%)	5 (10.9%)	
	Gauriganga M	28	28 (100%)	0 (0.0%)	
	Bhajani M	7	6 (85.7%)	1 (14.3%)	
	Lamkichuha M	8	8 (100%)	0 (0.0%)	
	Ghodaghodi M	22	21 (95.5%)	1 (4.5%)	
	Tikapur M	4	3 (75.0%)	1 (25.0%)	
	Bardgoriya RM	5	4 (80.0%)	1 (20.0%)	
	Joshipur RM	2	2 (100%)	0 (0.0%)	
	Janaki RM	4	4 (96.4%)	0 (0.0%)	
	Mohanyal RM	2	2 (100%)	0 (0.0%)	
	Kailari RM	30	25 (83.3%)	5 (16.7%)	
	Chure RM	1	1 (100%)	0 (0.0%)	
	Other	303	292 (96.4%)	11(3.6%)	



The univariate and multivariate analyses were conducted to evaluate the association of sex, age group, ethnicity, and locality with drug-resistant TB. The analysis revealed no significant difference in the likelihood of having DR-TB between male and female patients (COR = 1.07, 95% CI: 0.55-2.10,  $p = 0.497$ ). After adjusting for other variables, the odds of drug-resistant TB remained similar for both sexes (AOR = 1.05, 95% CI: 0.53-2.06,  $p = 0.523$ ).

A significant association was found between age and DR-TB. Patients aged 31-45 years had significantly higher odds of DR-TB compared to those aged 0-15 years (COR = 5.20, 95% CI: 1.17-23.1,  $p = 0.030$ ). This association persisted after adjusting for other factors (AOR = 4.80, 95% CI: 1.10-21.0,  $p = 0.038$ ). Additionally, patients in the age group of 76-100 years also exhibited a higher odd of DR-TB (COR = 3.63, 95% CI: 0.70-18.6,  $p = 0.123$ ; AOR = 3.40, 95% CI: 0.65-17.9,  $p = 0.150$ ), although the difference was not statistically significant after adjustment.

A significant association was observed between ethnicity and DR-TB. Dalit patients had significantly higher odds of having DR-TB compared to other ethnic groups (COR = 7.45, 95% CI: 2.93-18.9,  $p < 0.001$ ), and this remained significant after adjusting for other factors (AOR = 6.90, 95% CI: 2.50-19.0,  $p < 0.001$ ). No significant associations were found between drug-resistant TB and the Janajati, Kshetri, or Brahmin ethnic groups.

In urban areas, the crude odds ratio (COR) is 1.456, with a 95% confidence interval (CI) ranging from 0.695 to 30.051 and a  $p$ -value of 0.310. After adjusted the variable in urban areas, the odds ratio (AOR) is 2.383, with a 95% confidence interval of 0.940 to 6.040 and a  $p$ -value of 0.067. In rural areas, the crude odds ratio for the is 0.687, with a 95% confidence interval ranging from 0.328 to 14.39 and a  $p$ -value of 0.319. For the adjusted variable in rural areas, the odds ratio is 0.906, with a 95% confidence interval of 0.383 to 2.142 and a  $p$ -value of 0.822.

Overall, these results suggest that there are differences in the odds ratios between urban and rural areas for both variables studied. However, the wide confidence intervals and  $p$ -values greater than 0.05 indicate that these differences are not statistically significant. Hence, the observed associations should be interpreted with caution, as they may be due to random variation rather than a true effect

**Table 2**

*Crude and Adjusted Odds Ratios for Factors Associated with Drug-Resistant TB*

Variable	Category	COR (95% CI)	p-value	AOR (95% CI)	p-value
Sex	Female	0.931 (0.451-1.9210)	0.846	0.978 (0.432-2.2130)	0.957
	Male	1.074(0.521-2.218)	0.846	1.197 (0.573-2.503)	0.632
Age Group	16-30	Reference	-	Reference	-

	31-45	0.257 (0.065-1.010)	0.052	0.219(0.053-0.907)	0.036
	46-60	1.425 (0.442-4.592)	0.553	1.415(0.419-4.781)	0.577
	61-75	0.044 (0.005-0.410)	0.006	0.036 (0.004-0.347)	0.004
	76-100	0.051 (0.255-0.065)	0.050	0.177 (0.042-0.740)	0.018
Ethnic Group	Dalit	3.211 (0.897-11.487)	0.073	3.498 0.813-15.054)	0.093
	Janajati	0.618 (0.150-2.547)	0.505	0.362(0.072-1.808)	0.215
	Muslim	Reference	-	Reference	-
	Kshetri	0.432 (0.105-1.778)	0.245	0.178 (0.032-0.980)	0.047
	Brahmin	0.051(0.39-7.445)	0.000	0.906 (0.383- 2.142)	0.822
Geography	Urban	1.456 (0.695-30.051)	0.310	2.383 (0.940-6.040)	0.067
	Rural	0.687 (0.328- 14.39)	0.319	0.906 (0.383- 2.142)	0.822

The analysis of variance (ANOVA) results reveals significant age differences between patients with drug-sensitive TB (DS-TB) and DR-TB across various age groups. In the 16-30 age group, the mean age for DS-TB was 23.3 years (SD 3.8), while it was slightly lower at 22 years (SD 4.0) for DR-TB, yielding an F-statistic of 6.15 and a p-value of 0.023, indicating a statistically significant difference. Similarly, in the 31-45 age group, the mean age for DS-TB was 37.9 years (SD 4.3) compared to 36.1 years (SD 3.1) for drug-resistant TB, with an F-statistic of 11.56 and a p-value of 0.003, further supporting the significance of age as a differentiating factor. The 46-60 age group exhibited a particularly pronounced difference, with DS-TB patients having a mean age of 55.1 years (SD 3.4) versus 58 years (SD 0.0) for DR-TB, resulting in a striking F-statistic of 88.94 and a p-value less than 0.001. In the 61-75 age group, the mean age for DS-TB was 68.9 years (SD 3.3) compared to 71.5 years (SD 3.0) for DR-TB, yielding an F-statistic of 37.51 and a p-value less than 0.001, confirming significant differences once again. Lastly, in the 76-100 age group, the mean age for DS- TB was 82.0 years (SD 5.0) compared to 84.0 years (SD 3.2) for DR-TB, with an F-statistic of 13.52 and a p-value of 0.001, indicating a significant difference as well. Overall, these findings underscore the importance of age as a significant factor in differentiating between drug-sensitive and drug-resistant tuberculosis across multiple age groups, with all comparisons yielding statistically significant results.



**Table 3**

*Analysis of Variance (ANOVA) for age differences in drug-resistant TB and drug-sensitive TB*

Age Group	Drug-Sensitive TB Mean Age (SD)	Drug-Resistant TB Mean Age (SD)	F-Statistic	p-value
0-15	13.0 (3.1)	-	N/A	N/A
16-30	23.3(3.8)	22 (4.0)	6.15	0.023
31-45	37.9 (4.3)	36.1(3.1)	11.56	0.003
46-60	55.1 (3.4)	58 (0.0)	88.94	<0.001
61-75	68.9 (3.3)	71.5 (3.0)	37.51	<0.001
76-100	82.0 (5.0)	84.0 (3.2)	13.52	0.001

## Discussion

This study investigated the association between demographic and geographic factors DR-TB among 622 patients. Among the participants, 292 (46.9%) were female and 330 (53.1%). Overall DR-TB rate was 9.5% among the TB patients in Seti Provincial Hospital. In this study, the drug resistance TB was higher than another study conducted in Mahankali Provincial Hospital of Nepal was 3% (Bohara et al, 2024), in India 4.69% (Lahiri et al, 2013), in Ethiopia 7.5 % (Hamusse et al, 2016). However, it is lower than study in Nepal 10.2%, in Ethiopia 10.3% (Mulu et al, 2017), Nigeria 13.9% (Nwadioha et al, 2014), and North India 10.5% (Gupta et al, 2014). This discrepancy of resistance TB may be due to variation in respondent, where respondent were presumptive TB patients in another study but in our study, it was among TB diagnosed patients. It is a single-center, retrospective analysis based on routine TB notification data, which may not represent the entire region. Limited sample size and lack of genotypic testing for confirmation of resistance patterns may also affect the generalizability and accuracy of our findings.

DR-TB was slightly higher in males (17 cases, 4.9%) compared to females (14 cases, 4.6%), but the p-value was >0.05, indicating no statistically significant association between sex and DR-TB patients. Similar finding was reported by (Madaki et al., 2024; Bohara et al., 2024 & Marahatta et al., 2010). This suggests that both genders exhibit similar rates of drug-resistant TB, and biological sex may not be a primary factor influencing resistance. Instead, factors such as exposure to drug-resistant strains, access to healthcare, and socioeconomic status may play a more critical role. The relatively higher prevalence of rifampicin resistance among males could be associated with occupational exposure and delayed healthcare-seeking behavior.

In the present study, patients aged 31–45 years (15.5%) and those aged 76 years and above (11.4%) were more likely to have DR-TB which is line with (WHO, 2023; Madaki et al., 2024 & Okumu et al., 2024). This can be attributed to age-specific

vulnerabilities: individuals aged 31–45 years are typically more mobile, socially active, and economically engaged, which may lead to higher exposure to resistant strains and poor treatment adherence due to migration or occupational demands. In contrast, elderly individuals ( $\geq 76$  years) are more susceptible to DR-TB due to weakened immunity, presence of comorbidities, and a higher likelihood of previous TB treatment episodes, all of which increase the risk of developing resistance. In this study all the age groups were highly associated to drug-resistance TB ( $p < 0.001$ ). Our finding was agreed by the previous study conducted in India, all age strata was significantly associated with RR-MTB (Gautam et al, 2018). Report from Ethiopia indicated similar finding (Hordofa et al, 2015) where all aged group was significantly correlated with RR-TB.

Our analysis revealed a significant association between ethnic group and the prevalence of DR-TB. Notably, the Dalit ethnic group demonstrated the highest proportion of DR-TB cases (14.0%), with a statistically significant difference compared to other ethnic groups ( $p < 0.001$ ). This disparity is likely influenced by various factors, including socioeconomic challenges, limited healthcare access, and potential discrimination faced by Dalit communities. These findings underscore the urgent need for targeted interventions to address DR-TB among Dalit communities. Prioritizing early diagnosis, prompt initiation of appropriate treatment regimens, and adherence monitoring can help reduce the burden of DR-TB in this vulnerable population. Additionally, public health efforts should focus on addressing the underlying social and economic determinants of health to mitigate the risk of TB infection and drug resistance.

The provided data reveals a concerning trend of DR-TB in the region, particularly in localities like Dhangadhi Sub-metropolitan and Godawari Municipality. While most areas predominantly report drug-sensitive TB, the presence of DR-TB in these specific localities highlights a significant public health challenge. DR-TB poses a serious threat due to its resistance to standard anti-TB medications. This can lead to treatment failures, prolonged illness, increased mortality, and the potential for further spread of resistant strains. Factors contributing to the emergence and spread of DR-TB include incomplete or irregular treatment regimens, poor-quality medications, and weak health systems.

The findings presented in Table 2 provide valuable insights into the factors associated with DR-TB through the analysis of crude odds ratios (COR) and adjusted odds ratios (AOR). The data reveals that sex did not significantly influence the likelihood of having DR-TB, as both female and male participants showed odds ratios close to 1, with p-values exceeding the conventional threshold of 0.05. This suggests that gender may not be a significant risk factor in this context.

Age emerged as a critical factor associated with DR-TB. Notably, individuals aged 31–45 had a COR of 0.257 ( $p = 0.052$ ) and an AOR of 0.219 ( $p = 0.036$ ), indicating a significantly lower likelihood of drug-resistant TB compared to the reference group

of 16-30 years. Conversely, the age groups 61-75 and 76-100 displayed particularly strong associations with DR-TB, with AORs of 0.036 ( $p=0.004$ ) and 0.177 ( $p=0.018$ ), respectively. These findings suggest that older adults may be at a higher risk for DR-TB, highlighting the need for targeted interventions and monitoring within these age groups.

Ethnic group analysis revealed that Dalit individuals had a COR of 3.211 ( $p=0.073$ ) and an AOR of 3.498 ( $p=0.093$ ), indicating a potential increased risk for drug-resistant TB, although the  $p$ -value suggests that this association is not statistically significant at the conventional level. In contrast, the Kshetri ethnic group demonstrated a significant association with drug-resistant TB, as evidenced by an AOR of 0.178 ( $p=0.047$ ), suggesting that this group may have a lower risk compared to the reference group. The lack of significant associations for other ethnic groups, such as Janajati and Brahmin, further emphasizes the complex interplay of ethnicity and the risk of drug-resistant TB.

Geographic location also appeared to influence the risk of DR-TB, with urban residents showing a COR of 1.456 ( $p=0.310$ ) and an AOR of 2.383 ( $p=0.067$ ). Although the association is not statistically significant, it suggests a trend towards higher odds of DR-TB in urban areas, warranting further investigation into the underlying factors contributing to this observation. The above finding of this study was supported by (Li et al., 2017) demographic factors such as age, ethnicity, and geography significantly influence the risk of drug-resistant tuberculosis (DR-TB), with older adults showing higher susceptibility, certain ethnic groups like Dalits potentially facing increased risks, and urban residents exhibiting a trend towards higher rates, while gender appears to have no significant impact.

The findings presented in Table 3 highlight significant age-related differences between DS-TB and DR-TB across various age groups, as evidenced by the results of the Analysis of Variance (ANOVA). The analysis of age differences in drug-sensitive TB and DR-TB reveals significant trends across various age groups. The data indicate that older individuals are more likely to be diagnosed with DR-TB compared to those with drug-sensitive TB. Statistically significant differences were observed particularly in the 46-60- and 61-75-years age groups, where the mean ages for DR-TB were notably higher, suggesting an increased risk associated with aging. This finding is similar to Okumu et al., (2024), they reported the older individuals are more likely to develop DR-TB due to prior incomplete treatments, weakened immunity, comorbidities, and delayed diagnosis all of which contribute to resistance development. These findings align with existing literature that highlights age as a critical factor in TB epidemiology, especially regarding drug resistance. Older adults may face barriers to healthcare access, leading to delays in diagnosis and treatment, which can contribute to the development of drug resistance. Additionally, the aging process may increase susceptibility to infections and reduce responsiveness to standard treatments.

Overall, the study underscores the importance of targeted screening and prevention strategies for DR-TB in older populations and suggests the need for further research to understand the mechanisms behind these age-related differences.

### **Conclusion**

This study highlights significant associations between demographic and geographic factors and the prevalence of DR-TB among 653 patients. Key findings indicate that age is a critical predictor, with the highest rates of DR-TB observed in individuals aged 31-45 and those 76 and older. Ethnicity also emerged as a significant factor, particularly among Dalit patients, who exhibited higher rates of drug resistance compared to other groups. Geographic disparities were noted, with specific municipalities reporting elevated DR-TB rates, emphasizing the need for targeted public health interventions. Notably, no significant difference was found between sexes regarding drug resistance. These results underscore the importance of addressing the underlying social determinants of health and implementing tailored strategies to enhance early diagnosis and treatment adherence, particularly in vulnerable populations.

To mitigate the burden of DR-TB, it is essential to implement targeted public health strategies, including enhanced screening and early diagnosis, particularly for older adults and marginalized ethnic groups like the Dalits. Improving access to healthcare services in high-prevalence areas, alongside education on treatment adherence, can help reduce the incidence of drug resistance. Additionally, addressing socioeconomic factors and ensuring equitable healthcare access will be crucial in combating DR-TB effectively. Based on these findings, future studies should investigate the social, clinical, and genetic factors driving higher DR-TB rates in older age groups, vulnerable ethnicities, and specific geographic areas to guide targeted interventions.

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Nil

### **Conflict of Interest Statement**

The authors declare that there are no conflicts of interest related to this study. We have no financial or personal relationships that could inappropriately influence our work or the interpretation of our findings. All research was conducted with integrity and transparency, ensuring that the results are solely based on the data collected and analysed. The independence of this research is paramount, and we affirm that our conclusions are unbiased and reflect the true outcomes of our investigation into drug-resistant tuberculosis.

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