Journal of Population Therapeutics & Clinical Pharmacology

RESEARCH ARTICLE
DOI: 10.53555/hsezrs89

TO STUDY PATTERN OF DRUG RESISTANCE OF ANTITUBERCULAR THERAPY IN ALCOHOLIC LIVER DISEASE AND NON-ALCOHOLICS

Dr Gopika Sharma[1*], Dr.O.P. Jatav[2], Dr.K P Ranjan[3]

[1*]Junior Resident, Dept. of Medicine, GRMC Gwalior, India
[2]Professor, Dept. of Medicine, GRMC Gwalior, India
[2]Professor, Dept. of Microbiology, GRMC Gwalior, India

***Corresponding author -** Dr Gopika Sharma
*Junior Resident, Dept. of Medicine, GRMC Gwalior, India Email: gopika1995sharma@gmail.com

ABSTRACT

Introduction: Tuberculosis remains a global health threat, with drug resistance complicating its control. Alcohol use and alcoholic liver disease impair drug metabolism, immune defense, and treatment adherence, creating a higher risk of resistant TB. These factors highlight the need for integrated management addressing both addiction and comorbid liver dysfunction.

Aim and Objective: This study aimed to assess the prevalence and pattern of antitubercular therapy (ATT) resistance in patients with and without ALD, and to evaluate the relationship between alcohol consumption, liver disease severity, and treatment outcomes.

Materials and Methods: A prospective case–control observational study was conducted over 1.5 years at J.A. Group of Hospitals, Gwalior. Sixty adults (aged 30–60 years) with drug-resistant pulmonary TB, confirmed by CBNAAT, Line Probe Assay, and radiological findings, were included. Patients were stratified into two cohorts: 26 with ALD and 34 non-alcoholics. Clinical, microbiological, and radiological profiles were recorded, and drug resistance patterns were analyzed.

Results: The cohort was predominantly male (73.3%) with a mean age of 42.7 years. All alcoholics were male. Course completion of ATT was lower in alcoholics (8.3%) compared to non-alcoholics (20%). CBNAAT revealed rifampicin resistance in 53.8% of alcoholics versus 23.5% in non-alcoholics, while MDR and XDR cases were more common among alcoholics. Longer duration and severity of alcohol use correlated with higher resistance, particularly RR-TB and XDR-TB.

Conclusion: Alcohol misuse and ALD are strongly associated with poor treatment adherence and higher rates of drug-resistant TB. Integrating addiction management, liver care, and routine alcohol screening into TB programs is essential to improve adherence, reduce resistance, and achieve better outcomes.

Keywords: tuberculosis; alcoholic liver disease; drug resistance; adherence; multidrug-resistant TB

INTRODUCTION

Tuberculosis (TB), caused by *Mycobacterium tuberculosis*, continues to be one of the world's leading infectious diseases despite decades of control programs and public health interventions. The disease spreads mainly through inhalation of airborne droplets expelled during coughing or sneezing by infected individuals, making it highly transmissible. Although TB primarily targets the lungs, it can involve the lymph nodes, abdomen, skeletal system, and central nervous system, leading to severe

morbidity. Its burden is particularly heavy in low- and middle-income countries where limited healthcare resources, socioeconomic challenges, and high exposure to risk factors create a fertile ground for sustained transmission [1]. Globally, TB accounts for nearly 1.3 million deaths annually, underscoring the persistence of this preventable and treatable disease and the complexity of factors that perpetuate its spread, including delays in diagnosis, drug resistance, and coexisting comorbidities [2].

A major obstacle to TB elimination is the emergence of drug-resistant forms. Multidrug-resistant TB (MDRTB), resistant to both rifampicin and isoniazid—the cornerstone drugs of first-line therapy—poses grave challenges. Even more concerning is extensively drug-resistant TB (XDRTB), characterized by resistance to rifampicin, isoniazid, fluoroquinolones, and at least one second-line injectable. Such resistance leads to protracted, toxic, and expensive treatments with poorer success rates [3]. According to the 2019 Global TB Report, about 500,000 new rifampicin-resistant cases were identified, and the majority of these were MDRTB. The spread of resistance not only complicates treatment but also heightens costs, increases relapse rates, and sustains community transmission. Drug resistance thus represents both a clinical and public health emergency [4].

Host-related factors are increasingly recognized as pivotal in TB epidemiology and resistance development. Alcohol misuse stands out as a particularly influential factor. Chronic alcohol consumption weakens immune defenses, thereby increasing susceptibility to infection and reducing resilience during treatment. Additionally, alcohol alters drug metabolism, complicates pharmacokinetics, and is closely tied to treatment non-adherence. These effects increase the likelihood of drug resistance. Research consistently demonstrates higher rates of MDRTB among individuals with alcohol misuse, marking them as a high-risk subgroup requiring targeted interventions [5].

The complications of alcohol extend further when liver health is considered. Alcoholic liver disease (ALD), a common result of prolonged misuse, severely impairs hepatic function. Since the liver is central to drug metabolism, its dysfunction disrupts the processing of anti-tubercular therapy (ATT). Patients with ALD face heightened risks of ATT-induced hepatotoxicity, which may necessitate interruptions, dose adjustments, or treatment discontinuation—all of which can promote resistance. Moreover, advanced ALD is associated with weakened immunity and poorer prognoses, further compounding treatment difficulties. Thus, alcohol misuse creates a dangerous cycle of increased TB risk, drug toxicity, and resistance [6].

TB is further complicated by the dual burden of communicable and non-communicable diseases, particularly in developing regions. Rising prevalence of diabetes, cardiovascular diseases, and chronic respiratory conditions often overlaps with TB. These comorbidities not only exacerbate disease severity but also complicate both diagnosis and management. Alcohol misuse illustrates this intersection vividly: it predisposes individuals to TB, worsens outcomes, and complicates care through comorbid conditions like ALD. The convergence of infectious and chronic diseases in such populations demands integrated care approaches that consider both sets of health challenges [7].

The public health consequences of alcohol misuse in TB go beyond individual-level effects. Alcohol-related behaviors often delay healthcare seeking, prolong periods of infectiousness, and increase the risk of treatment default. The dual stigma associated with both TB and alcohol abuse further discourages timely care, creating barriers to early diagnosis and sustained treatment. Additionally, the socioeconomic fallout of alcohol misuse—such as poverty, unemployment, and homelessness—intersects with TB risk factors, reinforcing cycles of vulnerability. This interplay of medical, behavioral, and social determinants creates a complex challenge for TB control programs [8].

Host-related factors like smoking, low BMI, HIV, diabetes, chronic kidney disease, COPD, and malignancies increase susceptibility to TB and worsen treatment outcomes, often by impairing immunity, complicating adherence, and altering drug metabolism. Diabetes predisposes to relapse, while HIV strongly links with MDRTB due to profound immunosuppression. Managing TB in patients with alcohol misuse and comorbidities requires comprehensive strategies, including timely ALD screening, alcohol cessation programs, nutritional support, and close monitoring for hepatotoxicity. Equally crucial are systemic approaches—reducing stigma, improving access, and

strengthening healthcare infrastructure. Integrated medical, behavioral, and social interventions provide the best means to curb resistance and improve outcomes [9].

This study explores anti-tubercular therapy resistance among individuals with and without alcoholic liver disease (ALD), focusing on how alcohol consumption and liver disease severity influence outcomes. By examining correlations between duration of alcohol intake, ALD severity, and resistance development, it highlights mechanisms by which alcohol abuse worsens TB. Insights gained could clarify MDRTB and XDRTB epidemiology in this subgroup, guiding targeted interventions. Addressing TB effectively requires attention to both medical regimens and behavioral determinants, with integrated care models tackling alcohol-related complications to improve adherence, reduce resistance, and strengthen public health responses in vulnerable populations through holistic, stigma-free approaches [10].

This study investigates the prevalence and patterns of antitubercular therapy (ATT) resistance in alcoholic and non-alcoholic individuals, while examining the correlation between alcohol consumption duration and resistance. It also explores how the severity of alcoholic liver disease influences resistance development. By addressing these associations, the research aims to clarify the impact of alcohol misuse and liver dysfunction on treatment outcomes, offering insights to guide tailored interventions for reducing TB drug resistance.

MATERIALS AND METHODS

This prospective case-control observational study was conducted over 1.5 years (May 2023 onwards) in the Department of Medicine, J.A. Group of Hospitals, Gwalior, after obtaining institutional ethical clearance and written informed consent. A total of 60 adults aged 30–60 years with drug-resistant pulmonary tuberculosis confirmed by CBNAAT, LPA, and radiological findings were included. Patients were stratified into two cohorts: 26 with alcoholic liver disease (based on alcohol history and ultrasonography) and 34 non-alcoholics with normal liver imaging. Exclusion criteria included extrapulmonary TB, advanced liver disease, HIV, malignancy, critical illness, or refusal to consent. Confidentiality and counseling were ensured.

RESULTS

The study population was predominantly male (73.3%) compared to females (26.7%), reflecting the higher prevalence of alcoholism among men in clinical settings. This imbalance highlights an important demographic determinant that may influence drug resistance patterns in tuberculosis. Male predominance could be linked to greater alcohol consumption, hepatic dysfunction, and poor treatment adherence, thereby impacting therapeutic outcomes. Hence, gender distribution forms an essential baseline characteristic when interpreting antitubercular drug resistance trends between alcoholics and non-alcoholics.

Table 2: Age distribution between the genders

		Frequency	Mean	Std. Deviation	Variance	Minimum	Maximum	Mean ± Std.
AGE	M	44	43.16	9.16	83.86	30	60	43.16 ± 9.16
	F	16	41.75	7.51	56.33	31	55	41.75 ± 7.51

The age distribution table shows that males (mean 43.16 ± 9.16 years) and females (mean 41.75 ± 7.51 years) were closely matched in age, with ranges of 30–60 years and 31–55 years respectively. This indicates a middle-aged study cohort where chronic alcohol use and tuberculosis both peak in prevalence. The comparable age profile minimizes age as a confounding factor when assessing drug resistance. Hence, observed differences in resistance patterns are more likely attributable to alcohol-related hepatic dysfunction rather than age disparity.

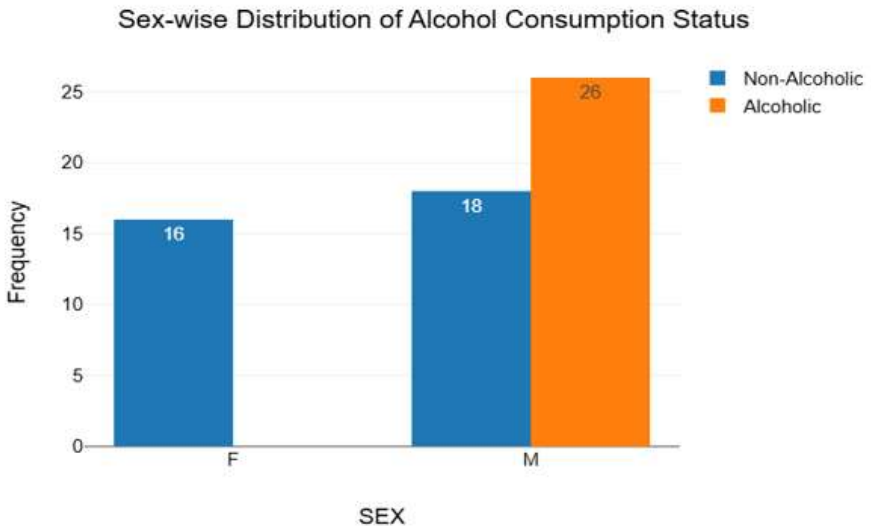

Figure 3: Bar graph showing the distribution of alcohol consumption status by sex

All females were non-alcoholic, while alcoholism was seen only in males (n=26), making men the primary high-risk group. This male predominance reflects socio-behavioral influences and increases vulnerability to hepatic dysfunction and poor TB drug response. Hence, drug resistance patterns in alcoholics are largely driven by male patients.

Table 4: Sputum AFB grade distribution between alcoholic and non-alcoholic patients

Alcohol Consumption Status	Sputum AFB grade				
	1+	**2+**	**3+**	**Scanty**	**Total**
Alcoholic	13	9	4	0	26
Non-Alcoholic	22	8	3	1	34
Total	35	17	7	1	60
	Fisher's Exact Test, p-value = 0.2977.				

Sputum AFB grading showed similar distribution between alcoholics and non-alcoholics, with no statistically significant difference (p=0.2977). Both groups had a predominance of 1+ and 2+ grades, indicating comparable bacterial loads at presentation. This suggests that alcohol use did not independently influence baseline smear positivity. Hence, drug resistance differences, if present, are more likely due to host-related hepatic and adherence factors rather than initial bacillary burden.

Table 6: ATT course completion among alcoholic and non-alcoholic patients

Alcohol Consumption Status	YES	%	NO	%	Total	Total %
Non-Alcoholic	12	20.00%	22	36.70%	34	56.70%
Alcoholic	5	8.30%	21	35.00%	26	43.30%
Total	17	28.30%	43	71.70%	60	100.00%
p = 0.2805						

ATT course completion was lower in alcoholics (8.3%) compared to non-alcoholics (20%), though the difference was not statistically significant (p=0.2805). This trend suggests that alcoholism adversely affects adherence, likely due to poor compliance, hepatic side effects, and social factors. Incomplete treatment among alcoholics increases the risk of resistance emergence and treatment failure. Thus, alcohol use remains a clinically relevant barrier to successful TB therapy despite the lack of statistical significance.

Table 7: Sputum CBNAAT distribution among alcoholic and non-alcoholic patients

Alcohol Consumption Status	MTB DETECTED	RIF RESISTANT	RIF+INH RESISTANT	Total
Alcoholic	9	14	3	26
Non-Alcoholic	25	8	1	34
Total	34	22	4	60

CBNAAT results revealed markedly higher rifampicin resistance among alcoholics (14/26) compared to non-alcoholics (8/34), with additional combined RIF+INH resistance also more frequent in alcoholics. This pattern indicates a stronger predisposition to multidrug resistance in patients with alcohol use, likely due to poor adherence, hepatic compromise, and altered drug metabolism. In contrast, non-alcoholics showed higher rates of MTB detection but lower resistance. These findings highlight alcoholism as a significant clinical risk factor for drug-resistant tuberculosis.

Table 8: DR-TB Status among the alcoholics and non-alcoholics

DR-TB Status	Non-Alcoholic	Alcoholic	Total
RR TB	7	10	17
MDR TB	1	2	3
Pre XDR TB	1	1	2
XDR	0	1	1
NO DR	25	12	37
Total	34	26	60
p-value 0.2432			

Alcoholics showed higher rates of RR-TB, MDR-TB, and XDR-TB than non-alcoholics, though not statistically significant (p=0.2432). The trend reflects poor adherence, altered metabolism, and immune compromise in alcoholics, making them more vulnerable to resistant TB forms.

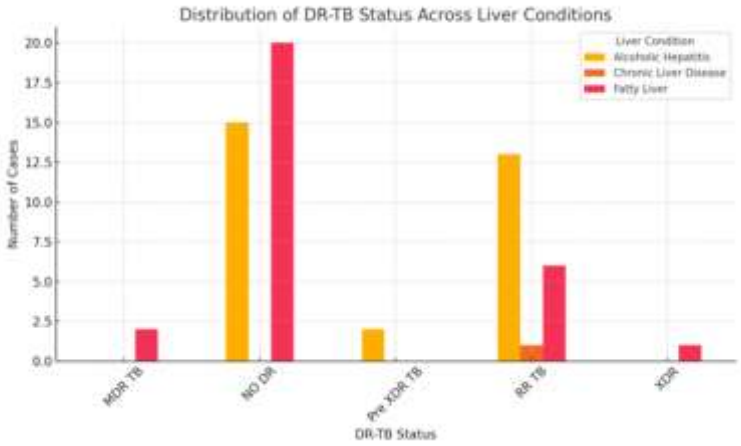

Figure 8: Grouped bar chart showing the distribution of different DR-TB statuses across liver condition categories

The chart shows that RR-TB and MDR-TB were more frequent in patients with alcoholic hepatitis and chronic liver disease, while most fatty liver cases had no drug resistance. This indicates that severe alcohol-related liver damage predisposes patients to higher resistance patterns. Poor drug metabolism and adherence in advanced liver disease likely drive this trend. Thus, liver condition severity is an important modifier of TB drug resistance risk.

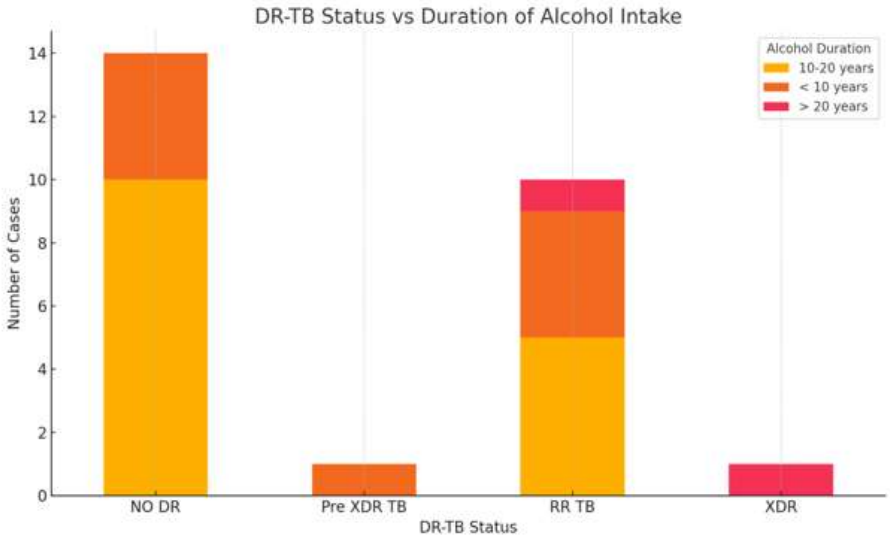

Figure 9: stacked bar chart visualizing the relationship between DR-TB status and duration of alcohol intake

The chart demonstrates that longer duration of alcohol intake is associated with higher drug resistance, particularly RR-TB and XDR-TB, while shorter duration (<10 years) is mostly linked with no resistance. Patients with more than 20 years of alcohol use showed the greatest burden of resistant TB. This highlights a clear dose–duration effect of alcohol on resistance risk. Thus, chronicity of alcohol exposure is a strong determinant of TB drug resistance patterns.

DISCUSSION

Tuberculosis (TB), caused by *Mycobacterium tuberculosis*, primarily affects the lungs but may involve other organs including the bones, glands, abdomen, and nervous system [11]. Despite being both preventable and treatable, TB continues to pose a global health challenge due to the emergence of multidrug-resistant (MDR) and extensively drug-resistant (XDR) strains. MDR-TB, defined by resistance to rifampicin and isoniazid, complicates therapy, while XDR-TB extends resistance to fluoroquinolones and second-line injectables, making management far more challenging [12]. Treatment for MDR/XDR-TB is prolonged, costly, and associated with high failure, relapse, and mortality rates.

Comorbidities significantly influence TB outcomes. Large cohort studies show that 10–20% of MDR/XDR-TB patients have coexisting conditions such as HIV, diabetes mellitus (DM), or alcohol misuse [13]. These factors impair immunity, compromise adherence, and contribute to treatment failure. With the rising burden of non-communicable diseases (NCDs) like diabetes, CKD, and COPD in developing countries, TB patients often experience a "double burden," increasing susceptibility to drug-resistant TB (DR-TB) and complicating public health control efforts [14]. According to the Global TB Report 2019, nearly 500,000 new rifampicin-resistant cases were reported, 78% of which were MDR-TB [15]. Prior anti-tuberculosis therapy (ATT), especially if incomplete or inappropriate, further predisposes to drug resistance.

Host-related risk factors such as smoking, alcohol abuse, low BMI, HIV, DM, CKD, malignancies, and COPD have repeatedly been linked to poor TB outcomes [16]. Alcohol abuse, in particular, has a strong association with MDR-TB and poor adherence. Our study demonstrated male predominance (73.3%), aligning with findings by Duraisamy K et al. (2014), who reported similar proportions [117]. The mean age of participants (43.16 years for males; 41.75 years for females) reflected a middle-aged cohort, comparable to Duraisamy's distribution in the 25–44 and >44-year age groups.

Alcohol use emerged as a significant gender-associated factor, with 43.3% of males consuming alcohol, while none of the females did. Sinha P et al. (2017) also identified alcohol consumption as a strong risk factor for both TB prevalence and MDR-TB [18]. Although our sputum AFB grading did

not show significant association, Baskaran N et al. (2021) reported higher positivity rates among alcoholics, suggesting sample-related variations [19].

ATT adherence was significantly lower among alcoholics in our study, consistent with Kumari SR et al. and Popa A et al., who highlighted forgetfulness, side effects, and lack of motivation as major barriers [20,21]. Thamineni R et al. (2022) also observed poor completion rates due to socioeconomic and psychosocial challenges [22]. CBNAAT results in our study revealed higher rifampicin resistance and MDR-TB among alcoholics, a finding corroborated by Pandhi N et al. and Ghanta PR et al., who emphasized CBNAAT's diagnostic accuracy and its value in detecting resistance in substance users [23,24].

The prevalence of DR-TB was higher among alcoholics (14/26) compared to non-alcoholics (9/34), echoing results from Dashdavaa D et al., who reported high-risk alcohol use in 78% of MDR-TB cases in Mongolia [25]. Notably, RR-TB was strongly associated with alcoholic hepatitis in our study, aligning with Pandhi N et al., who suggested altered drug metabolism and poor adherence in alcohol-related liver disease [23]. Duration of alcohol intake also influenced resistance patterns, with prolonged use correlating with XDR-TB, a trend supported by Ghanta PR et al. [24], these findings emphasize that alcoholism not only predisposes to TB but also worsens adherence, severity, and drug resistance. A holistic approach integrating TB management with screening and treatment of comorbidities, especially alcohol dependence and liver disease, is vital to improve outcomes and curb resistance.

CONCLUSION

This study emphasizes the strong association between alcohol consumption, liver disease, and drug-resistant tuberculosis (DR-TB). Alcoholics showed higher rates of resistance, poor therapy adherence, and lower treatment completion, often complicated by hepatic dysfunction. These findings highlight the urgent need to integrate addiction management and liver care into TB programs. Routine screening for alcohol use, combined with public health measures like education and cessation support, could reduce DR-TB burden. Despite limited sample size, the significant associations observed justify larger multicentric studies. Addressing alcohol abuse as a modifiable risk factor is crucial for improving TB outcomes and resistance control.

REFERENCES:

1. Lienhardt C, Glaziou P, Uplekar M, Lönnroth K, Getahun H, Raviglione M. Global tuberculosis control: lessons learnt and future prospects. Nature Reviews Microbiology. 2012 Jun;10(6):407-16.
2. Lee H, Kim J, Choi H. Review on global burden of tuberculosis in 2022.
3. Stephanie F, Saragih M, Tambunan US. Recent progress and challenges for drug-resistant tuberculosis treatment. Pharmaceutics. 2021 Apr 21;13(5):592.
4. World Health Organization. Global tuberculosis report 2021: supplementary material. World Health Organization; 2022 Mar 31.
5. Zondo NN. Environmental Factors Associated with Tuberculosis Incidence and Mortality in Tshwane District, Gauteng Province, South Africa. University of Johannesburg (South Africa); 2022.
6. Wigger GW, Bouton TC, Jacobson KR, Auld SC, Yeligar SM, Staitieh BS. The impact of alcohol use disorder on tuberculosis: a review of the epidemiology and potential immunologic mechanisms. Frontiers in immunology. 2022 Mar 31; 13:864817.
7. Goswami N. A dual burden dilemma: Navigating the global impact of communicable and non-communicable diseases and the way forward. International Journal of Medical Research. 2024 Jul 1;12(3):65-77.
8. Morojele NK, Shenoi SV, Shuper PA, Braithwaite RS, Rehm J. Alcohol use and the risk of communicable diseases. Nutrients. 2021 Sep 23;13(10):3317.

9. Menzel A, Samouda H, Dohet F, Loap S, Ellulu MS, Bohn T. Common and novel markers for measuring inflammation and oxidative stress ex vivo in research and clinical practice—which to use regarding disease outcomes? Antioxidants. 2021 Mar 9;10(3):414.
10. Zade A. Investigating the Efficacy and Mechanisms of Action of Tuberculosis Drugs. Systematic Reviews in Pharmacy. 2024 Jun 1;15(6).
11. Verma A, Singh V, Singh Chouhan AP, Dutt PK. TUBERCULOSIS: SYMPTOMS, DIAGNOSIS AND THE FIGHT AGAINST DRUG RESISTANCE. Biochemical & Cellular Archives. 2024 Oct 2.
12. Goldman RC, Plumley KV, Laughon BE. The evolution of extensively drug resistant tuberculosis (XDR-TB): history, status and issues for global control. Infectious Disorders-Drug Targets (Formerly Current Drug Targets-Infectious Disorders). 2007 Jun 1;7(2):73-91.
13. Wu S, Zhang Y, Sun F, Chen M, Zhou L, Wang N, Zhan S. Adverse events associated with the treatment of multidrug-resistant tuberculosis: a systematic review and meta-analysis. American journal of therapeutics. 2016 Mar 1;23(2): e521-30.
14. Liebenberg D, Gordhan BG, Kana BD. Drug resistant tuberculosis: Implications for transmission, diagnosis, and disease management. Frontiers in cellular and infection microbiology. 2022 Sep 23; 12:943545.
15. Boyd RM. Rifampicin-resistant tuberculosis in Botswana: barriers and risk factors influencing patient outcomes, case detection, and linkage to effective care and treatment.
16. Tao NN, Li YF, Song WM, Liu JY, Zhang QY, Xu TT, Li SJ, An QQ, Liu SQ, Li HC. Risk factors for drug-resistant tuberculosis, the association between comorbidity status and drug-resistant patterns: a retrospective study of previously treated pulmonary tuberculosis in Shandong, China, during 2004–2019. BMJ open. 2021 Jun 1;11(6):e044349.
17. Duraisamy K, Mrithyunjayan S, Ghosh S, Nair SA, Balakrishnan S, Subramoniapillai J, Oeltmann JE, Moonan PK, Kumar AM. Does Alcohol consumption during multidrug-resistant tuberculosis treatment affect outcome? A population-based study in Kerala, India. Annals of the American Thoracic Society. 2014 Jun;11(5):712-8.
18. Sinha P, Srivastava GN, Gupta A, Anupurba S. Association of risk factors and drug resistance pattern in tuberculosis patients in North India. Journal of global infectious diseases. 2017 Oct 1;9(4):139-45.
19. Baskaran N, Lian LS, Jamludin NA. Factors influencing delay in sputum conversion in smear-positive pulmonary tuberculosis patients in primary care in Kuala Lipis Pahang. 3. Zhang X, Han Y, Huang W, Jin M, Gao Z. The influence of the gut microbiota on the bioavailability of oral drugs. Acta Pharmaceutica Sinica B. 2021;11(7):1789-812.
20. Kumari SR, Pandit A, Reddy CS, Shyamala KK. Comparative Study for the Assessment of Compliance in Alcoholics and Non-Alcoholic Patients on Anti-tubercular Therapy–A Prospective Observational Study.
21. Popa A, Bende F, Șirli R, Popescu A, Bâldea V, Lupușoru R, Cotrău R, Fofiu R, Foncea C, Sporea I. Quantification of liver fibrosis, steatosis, and viscosity using multiparametric ultrasound in patients with non-alcoholic liver disease: A "real-life" cohort study. Diagnostics. 2021 Apr 26;11(5):783.
22. Thamineni R, Peraman R, Chenniah J, Meka G, Munagala AK, Mahalingam VT, Ganesan RM. Level of adherence to anti-tubercular treatment among drug-sensitive tuberculosis patients on a newly introduced daily dose regimen in South India: A cross-sectional study. Tropical Medicine & International Health. 2022 Nov;27(11):1013-23.
23. Pandhi N, Kajal NC, Mahajan N, Singh H. Original Research Article Diagnostic utility of cartridge based nucleic acid amplification test (CBNAAT) in detection of rifampicin resistance in multi drug resistant suspects among sputum positive cases of tuberculosis.
24. Ghanta PR, Phatak SV, Parihar PS, Dhande RP, Reddy NG, GHANTA PR, PHATAK S, PARIHAR P, DHANDE R. Radiological evaluation of a rare case of rib caries and cold abscess in a young male patient with miliary tuberculosis: a case report with review of literature. Cureus. 2023 Feb 16;15(2).

25. Dashdavaa D, Dambaa N, Oidov B, Zuunnast K. Effects of Alcohol and Tobacco Abuse on Multi-Drug-Resistant Tuberculosis Treatment Outcome, Mongolia. InProceedings of the 6th International Conference on Medical and Health Informatics 2022 May 13 (pp. 320-324).