

<https://doi.org/10.48047/AFJBS.6.14.2024.6725-6734>



African Journal of Biological Sciences

Journal homepage: <http://www.afjbs.com>



Research Paper

Open Access

## Clinico-Radiological Profile of Drug-Resistant Tuberculosis in a Tertiary Care Center in Tirupati, Andhra Pradesh.

Bharath Kathi<sup>1</sup>, A. Udaya kiran<sup>2</sup>, Vubbara Anupama<sup>3</sup>, \*M Neethi Chandra<sup>4</sup>, Subbarao Singapati<sup>5</sup>, P.Ajoy kumar<sup>6</sup>, Katikam Sai Vikas Reddy<sup>7</sup>, Syed Mizbah Muzzain<sup>8</sup>, Devika S Nair<sup>9</sup>

<sup>1,2,3</sup>Assistant Professor, <sup>4,6</sup>Associate Professor, <sup>5</sup>Professor and Head, <sup>7</sup>Senior Resident, <sup>8,9</sup>PG Resident

Department of Pulmonary Medicine, SV Medical College Tirupati, Andhra Pradesh

\*Corresponding Author: M Neethi Chandra

Volume 6, Issue 14, Aug 2024

Received: 15 June 2024

Accepted: 25 July 2024

Published: 15 Aug 2024

[doi: 10.48047/AFJBS.6.14.2024.6725-6734](https://doi.org/10.48047/AFJBS.6.14.2024.6725-6734)

### Abstract:

**Background:** Drug-resistant tuberculosis (TB) poses a significant risk to public health and impedes global efforts to manage and eliminate tuberculosis. The objective was to assess the clinical and radiological profile of Drug drug-resistant tuberculosis in Government Tertiary care centre.

**Methods:** A Prospective observational study was done between November 2022 to August 2023 among patients attending to drug-resistant tuberculosis center. 60 Drug Resistant TB cases were enrolled and history, demographic and clinic-radiological profiles were analyzed.

**Results:** A total of 60 patients were analyzed with male predominance (80%). The drug resistance pattern observed in the study group reveals that the majority of patients (56.66%) were resistant to rifampicin and isoniazid. Among Isoniazid resistance KAT G (53.33%) is most common resistance pattern seen. The commonest presenting symptom was cough (93.33%) followed by shortness of breathe (83.3%) , fever (50%) and with diabetes(30%), PLHIV (10%), CLD (3.33%), CKD (3.33%). Most of the patients were underweight (65%). The chest X-ray revealed that the majority of individuals had a moderately extensive lesion (57%), while mild and extensive lesions were observed in 30.2% and 12.6% of cases, respectively. The bilateral lesion was greater than the unilateral lesion.

**Conclusion:** The relapse of tuberculosis in people who were previously cured is a significant factor in the development of drug-resistant tuberculosis (DR-TB). The resistance pattern indicated a low level of resistance to second-line medicines, while a significant prevalence of resistance to both Rifampicin and Isoniazid was seen.

**Keywords:** Tuberculosis, Drug Resistance, Radiological profile, Tertiary care centre, NTEP

**Introduction:**

Drug-resistant tuberculosis (TB) is a significant public health risk that impedes global efforts to provide effective care and control for tuberculosis. Tuberculosis (TB) is a disease that can typically be prevented and cured. In 2022, tuberculosis (TB) ranked as the second most common cause of death worldwide caused by a single infectious agent, following coronavirus disease (COVID-19). TB caused nearly twice as many fatalities as HIV/AIDS. Annually, almost 10 million individuals still contract tuberculosis. In 2022, approximately 410,000 individuals (95% UI: 370,000-450,000) worldwide contracted multidrug-resistant or rifampicin-resistant tuberculosis (MDR/RR-TB). The quantity of individuals diagnosed and initiated on treatment was significantly lower.<sup>1</sup>

In 2022, a total of 175,650 individuals with MDR/RR TB were registered for treatment worldwide.<sup>2</sup> India has the greatest burden of Tuberculosis and multi drug resistant TB (MDR TB) globally, which is abnormally high even when considering India's population. India holds the top position in the global standings for identifying new cases annually. India accounts for around 25% of all active tuberculosis cases identified worldwide.<sup>3</sup>

Currently, the National TB Elimination Program (NLEP) has five categories to classify drug-resistant tuberculosis. Isoniazid-resistant tuberculosis (TB), rifampicin-resistant (RR) TB, and multi-drug resistant TB (MDR-TB), pre-extensively drug-resistant TB (Pre-XDR-TB) and extensively drug-resistant TB (XDR-TB).<sup>4,5</sup>

The first national anti-tuberculosis drug resistance survey (NDRS), found that 28% of tuberculosis patients were resistant to any form of medication (22% among new patients and 36.82% among those who had been treated before), and 6.19% had multidrug-resistant tuberculosis (2.84% among new patients and 11.62% among previously treated individuals). A previous history of tuberculosis infection, together with alcohol consumption and smoking, heightens the risk of multidrug-resistant tuberculosis (MDR-TB).<sup>6</sup>

The primary objective of the National Tuberculosis Elimination Program is to promptly detect instances of tuberculosis through the use of molecular testing techniques. Nationwide implementation of comprehensive drug susceptibility testing for tuberculosis patients using the CBNAAT method, including the universal medication Rifampicin, has been in effect since January 2018. Currently, the incidence of Isoniazid monoresistance is on the rise. The identification of a case with Isoniazid and other drug resistance patterns can be achieved using a different test called Line Probe Assay, which has a turnaround time of 3 days.<sup>7,8,9</sup>

This study was undertaken by analyzing the data of tuberculosis (TB) patients from a Tuberculosis Unit in SVRR Government General Hospital - Tirupati, Andhra Pradesh. The aim was to study the clinico-radiological profile of the patients and identify the characteristics associated with drug-resistant TB (DR-TB). There is a scarcity of research in this area about cases of Drug Resistant Tuberculosis. The study results will address the academic requirements of healthcare practitioners who deliver comprehensive and continuous care to tuberculosis (TB) patients. Additionally, the findings will highlight the obstacles and factors that contribute to achieving the country's goal of eliminating TB.

**Aim:** To assess the clinical and radiological profile of Drug Resistant Tuberculosis in a Government Tertiary care centre - Tirupati.”

**Objectives:**

- To determine the drug resistance patterns among tuberculosis patients who visit the Government Tertiary care centre in Tirupati.
- To study the role of comorbidities in drug resistant tuberculosis.

**Material and Methods:**

A Prospective observational study was done at the drug-resistant tuberculosis center of Sri Venkateswara Medical College in Tirupati, Andhra Pradesh, India, from November 2022 to August 2023, spanning a duration of 10 months. During the study period, a total of 60 cases with Drug Resistant TB were included.

The Study Population comprised individuals who enrolled in the DR/MDR/XDR-TB treatment regimen. Participants who provided informed consent after receiving a thorough description of the study's objectives were included in the study. A semi-structured questionnaire was used to collect information from all the patients diagnosed with DR TB in Sri Venkateswara Medical College.

The questionnaire consists of information about the participants' sociodemographic characteristics, previous tuberculosis treatment history, resistance patterns, clinical results, radiological findings, and any other relevant laboratory investigation records that are accessible. Data were gathered through conducting face-to-face interviews, reviewing medical records, and doing clinical examinations. Essential data was obtained by a thorough examination of the PMDT treatment register, PMDT therapy card, and clinical information booklet. A comprehensive medical history was obtained, which included an assessment for substance addiction involving drugs or alcohol. Chest X-ray was performed at the beginning of the study. For patients who were suspected to have Pulmonary TB, CBNAAT was done. If in CBNAAT, MTB is detected then the samples were sent for LPA which is done in Vishakhapatnam TB centre. With the results of LPA, the resistance patterns was analyzed. Those patients who were registered in this TB unit with sputum samples resistant to any of anti TB drugs were included in the study.

The type of resistance pattern was classified as 1. Isoniazid monoresistance with Gene's either inhA or katG, 2.Rifampicin along with inhA or KatG and 3. Rifampicin resistance with inhA and katG. Postero-anterior chest x ray features were classified as unilateral or bilateral. Lesions in the x ray were further divided into cavity, nonhomogeneous opacity, fibrosis or combination of above.

Ethical clearance was from Institutional Ethics Committee of SVMC, Tirupati obtained before starting the study (IEC Ref.Lr.No.64/2023 dated 27.03.2023). Data obtained and analysed using the Microsoft Excel and Epiinfo software 7.4 version of CDC, Atlanta, USA. All categorical variables like age, gender, comorbidities, and pattern of resistance will be expressed in the form of frequency and proportion while the continuous variables like Age, BMI will be expressed in form of Mean & Standard Deviation.

**Results**

Among the 60 patients included in this study, the largest proportion of instances of drug-resistant tuberculosis (DR-TB) (32%) were found in the middle age group (41-50 years). The median age of the patients was 45 years. The current study observed a predominance of males, accounting for 80% of the participants. Majority of them were daily wage laborers. Out of all the patients, 65% were undernourished with a Body Mass Index (BMI) below 18.5 kg/m<sup>2</sup>. (Table 1)

**Table 1: Socio-demographic details and BMI**

Socio-demographic factors and BMI		Frequency	Percentage
Gender	Male	48	80
	Female	12	20
Age	≤20 years	3	5
	21-30 years	10	17
	31-40 years	8	13
	41-50 years	19	32
	51-60 years	10	17
	61-70 years	7	12
	71-80 years	3	5
BMI	Underweight	39	65
	Overweight	1	1.7
	Healthy	20	33.3

**Table 2: History, habits, type of regimen and comorbidities wise distribution**

History, habits, type of regimen and comorbidities		Frequency	Percentage
Type of Disease	Pulmonary	57	95
	Extra Pulmonary	3	5
Presenting complaints	Cough	56	93.3
	SOB	50	83.3
	Fever	30	50
	Streaky Hemoptysis	5	8.3
Substance abuse	Alcoholics	30	50
	Smokers	35	58.3
Previous history of ATT	Newly diagnosed MDR	6	10
	Previous h/o DSTB	49	81.6
	Past h/o MDR lost to follow up	5	8.3
Associated comorbidities	Diabetes Mellitus	18	30
	PLHIV	6	10
	Chronic Lung disease	2	3.3
	Chronic Kidney disease	2	3.3
	Coronary arterial Disease	2	3.3

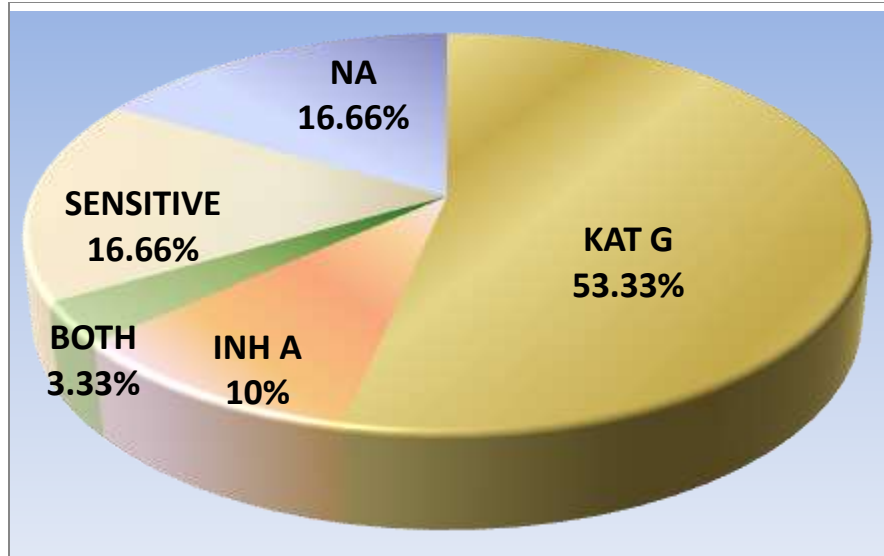
	COPD	2	3.3
	Hypertension	1	1.6
	Hypothyroidism	1	1.6
Type of regimen initiated	H mono	4	6.6
	Shorter oral BDQ	40	66.6
	AOL	14	25
	Not initiated (Expired)	2	3.3

**Table 3: Type and pattern of drug resistance**

Type of resistance		Frequency	Percentage
Type of resistance	RIF R with LAPA details not available	10	16.6
	RIF+INH+FQ resistance	2	3.3
	RIF+INH Resistance	34	56.6
	RIF mono resistance	10	16
	H Mono resistance	4	6.6
Pattern of Isoniazid resistance	KAT G	32	53.3
	INH A	6	10
	Both KAT G and INH A	2	3.3
	H sensitive	10	16.6
	Pattern of resistance not known	10	16.6

**Table 4: Radiological Profile**

Radiological profile	Frequency	Percentage
Non homogeneous opacities	23	38
Reticulo nodular opacities	9	15
Fibrosis	8	13
Bronchiectasis	6	10
Fibro cavity	5	8.3
Pleural effusion	2	3.3
Right loculated pneumonia	1	1.3
Lung abscess with fibrosis	1	1.3
Hilar adenopathy	1	1.3
Normal	3	5



**Figure 1: Pattern of Isoniazid Resistance**

Among 60 patients' pulmonary disease (95%) was found to be predominant followed by extrapulmonary TB (TB Lymphadenopathy 5%). Majority of them presented with complaints of cough (93.33%), followed by SOB (83.33%), FEVER (50%) and few presented with streaky hemoptysis (8.3%). Smoking was the most prevalent form of substance abuse, accounting for 58.3% of cases, followed by alcohol at 50%. The current study found that individuals with longer duration of substance use had a greater chance of moderately extensive and extensive Koch's lesion. The majority of participants in our study had previously had anti-tubercular treatment, and the majority of them achieved a state of cure. (Table 2)

In this study, 10.1% had not received Anti-Tuberculosis Treatment (ATT) before, while 81.66% had a history of receiving ATT for Drug-Susceptible Tuberculosis (DSTB) and 8.33% had taken ATT for Drug-Resistant Tuberculosis (DRTB). The majority (89.9%) of cases had previously undergone treatment under the Revised National Tuberculosis Control Program (RNTCP) and received Anti-Tuberculosis Treatment (ATT) for a duration of 6 months or longer. Additionally, the majority of these cases had been successfully cured in the past. The most prevalent comorbidity in this study was diabetes mellitus, affecting 30% of the participants. This was followed by PLHIV (10%), CLD (3.33%), CKD (3.33%), CAD (3.33%), COPD (3.33%), HTN (1.66%), and Hypothyroidism (1.66%). (Table 2)

The drug resistance pattern observed in this study group showed that the majority of the cases were both Rifampicin and Isoniazid resistant (56.66%) followed by Rifampicin mono resistance (16.66%), H mono resistance (6.66%), Rifampicin +Isoniazid +FQ Resistance (3.33%). In approximately 16.66% of cases with Rifampicin Resistance, Isoniazid resistance pattern was not known as LPA reports are not available in the medical records. As per the LPA Reports available, among H resistant 53.33% are KAT G RESISTANT followed by 10 % INH A resistant and both KAT G and INH A resistant were 3.33%. (Table 3 and Figure 1)

The chest X-ray showed that the majority of individuals had a moderately extensive lesion (62.3%), while mild and extensive lesions were observed in 30.2% and 12.6% of cases, respectively. The bilateral lesion was greater in size than the unilateral lesion. (Table 4)

Out of 60 patients, majority were started on shorter oral BDQ Regimen (66.66%) followed by AOL regimen (25%), H MONO (6.66%), and 3.33% expired before treatment initiation due to respiratory failure. The medical records were examined and the laboratory investigation reports that were accessible were gathered. The average hemoglobin (Hb) level was  $11.5 \pm 1.78$  gm/dl, and the average fasting blood sugar (FBS) level was  $96 \pm 37$  mg/dl. A total of 18 patients, accounting for 30% of the sample, were found to have a fasting blood sugar level greater than 110mg/dl. The average creatinine level was  $0.84 \pm 0.28$  mg/dl, while the average urea level was  $23.8 \pm 9.37$  mg/dl. The average TSH level was  $2.3 \pm 2.23$  mIU/L. The complete abdominal reports of all patients were found to be normal according to the USG. During the assessment of the respiratory system, the admission of air into the lungs was found to be reduced in the left lung in 12.8% of patients and in the right lung in 8.6% of patients. 75.5% of the patients had bilateral equal air entry. An adventitious sound was detectable in 4.4% of the patients. The prevalence of bilateral lesions was 62.3%, whereas unilateral lesions accounted for 37.7%. There were 5 cases, which accounted for 8.33% of the total, that had cavitory lesions.

## Discussion:

Despite the widespread availability of comprehensive treatment, the control of Tuberculosis continues to pose a problem for public health personnel. In order to reduce the negative health effects and death rates associated with tuberculosis (TB), it is crucial that individuals who develop TB disease have timely access to both diagnosis and treatment. Multidrug-resistant tuberculosis (MDR-TB) continues to be a significant public health emergency and poses a threat to health security.<sup>10</sup> Approximately 40% of individuals with drug-resistant tuberculosis received medical therapy in 2022.<sup>10,11</sup>

Universal Drug Susceptibility Testing (U-DST) should be conducted for all individuals who have been diagnosed with pulmonary tuberculosis, as well as those who are suspected to have tuberculosis or drug-resistant tuberculosis. This testing should be done using the GeneXpert method. LPA is employed to identify genetic changes that make *M. tuberculosis* strains resistant to H, R (first-line LPA, FL-LPA), SLIs, and FQs (second-line LPA, SL-LPA).<sup>12,13,14</sup>

In this study, 10.1% had not received Anti-Tuberculosis Treatment (ATT) before, while 81.66% had a history of receiving ATT for Drug-Susceptible Tuberculosis (DSTB) and 8.33% had taken ATT for Drug-Resistant Tuberculosis (DRTB). The majority (89.9%) of cases had previously received treatment under the NTEP and had undergone Anti-Tuberculosis Treatment (ATT) for a duration of 6 months or more. Additionally, the majority of these cases had been successfully cured in the past. A study done by More SW et al<sup>15</sup> observed that 68.75% had developed medication resistance, and 73.95% of the cases were diagnosed as MDR-TB. Out of the total number of patients (70), 72.91% had previously received treatment for tuberculosis. Additionally, the majority of these patients had sought treatment from government agencies. Deoskar et al.<sup>16</sup> conducted a study and discovered that 65% of the cases had multi-drug resistant tuberculosis (MDR-TB), whereas 33.3% of the cases had acquired drug resistance. Several studies have clearly established the correlation between a patient's history of receiving anti-TB treatment and the development of drug resistance. This suggests that the development of drug resistance may be a consequence of prior failure to adhere to treatment. Another possible explanation could be the spread of TB strains from persons who are infected with MDR-TB.<sup>15,17,18</sup>

In this study, most of the cases were both Rifampicin and Isoniazid resistant (56.66%) followed by Rifampicin mono resistance (16.66%), H mono resistance (6.66%), Rifampicin +Isoniazid +FQ Resistance (3.33%). Study done by More SW et al<sup>15</sup> shown that resistance to just RIF was observed in 26% of the patients. Other researchers have also seen the development of RIF resistance following the implementation of short-term treatment.

In the present study, diabetes mellitus (30%) was commonest comorbidity followed by PLHIV(10%), CLD(3.33%), CKD(3.33%), CAD(3.33%), COPD(3.33%), HTN(1.66%) and Hypothyroidism(1.66%). Study done by More SW et al<sup>15</sup> found that 28.13% reported having a comorbidity. The most commonly observed comorbidity was diabetes mellitus, reported by 29.62% of the patients. Substance abuse was reported by 33.33%, while HIV infection was reported by 14.81%. A study conducted by Elmi et al.<sup>17</sup> revealed that diabetes mellitus was present in 26.7% of MDR-TB cases, while HIV infection was observed in 5.7% of cases.

The study found that the majority of individuals in the chest X-ray had a moderately extensive lesion (62.3%), while mild and extensive lesions were observed in 30.2% and 12.6% of cases, respectively. The bilateral lesion was larger than the unilateral lesion. SW et al<sup>15</sup> reported that Fibro cavitary lesions were the most commonly seen abnormalities on X-ray, present in 38.54% of cases. A study<sup>18</sup> discovered that 89.5% of the cases exhibited cavitary lesions on X-ray, while another study<sup>19</sup> indicated that cavitary lesions were present in 63.4% of cases.

Patients suffering from drug-resistant tuberculosis (TB) get care and assistance from a comprehensive network of DR-TB centers, NTEP staff, general health system staff, community volunteers, and private health facilities throughout the country. Prior to therapy, a thorough screening is conducted to identify any relevant risk factors. The selection of the regimen is guided by considering the DST results, previous treatment history, and any adverse reactions to medicines. The initiation of treatment can occur either in the ward or on an outpatient basis, depending on the patient's clinical condition, availability of resources, and patient preferences.<sup>20,21</sup>

**Conclusions:** The study concluded that middle-aged males were more susceptible to DR-TB. A significant proportion of patients had a history of smoking. A significant number of DR-TB patients exhibited a high prevalence of undernutrition and pallor. The recurrence of tuberculosis in patients who were previously cured has been identified as the primary cause of drug-resistant tuberculosis infections. Detecting drug resistance in all cases of tuberculosis at an early stage can be beneficial for promptly identifying cases of drug-resistant tuberculosis.

The prevention of drug-resistant tuberculosis (DRTB) should prioritize the young and middle age groups, as there is a growing prevalence of resistance among these populations. It is important to highlight the rigorous adherence to Directly Observed Treatment, Short-course (DSTB) for the treatment of Drug-Resistant Tuberculosis (DRTB) cases, as it has been identified as a significant factor contributing to the prevalence of such cases. Emphasis should be placed on promptly identifying drug resistance in all tuberculosis patients by initial nucleic acid amplification testing (NAAT). Conducting IEC campaigns and providing re-orientation to recently diagnosed tuberculosis (TB) patients, specifically focusing on the importance of following treatment protocols and the risks of drug resistance, could be beneficial in preventing cases of drug-resistant TB (DR-TB).

**References:**



1. WHO. Global TB Report 2023. Available from <https://www.who.int/teams/global-tuberculosis-programme/tb-reports/global-tuberculosis-report-2023>. Last accessed on 22.04.2024.
2. Basu R, Kundu S, Biswas D, Nath S, Sarkar A, Bhattacharya A. Socio-Demographic and Clinical Profile of Drug Resistant Tuberculosis Patients in a Tertiary Care Centre of Kolkata. *Indian J Comm Health*. 2021;33(4):608-614.
3. Revised National Tuberculosis Programme. National Strategic Plan for Tuberculosis: 2017 2025, Elimination by 2025. Ministry of Health and Family Welfare. March 2017. Available from: <https://www.tbcindia.gov.in/>. Last Accessed on 24.04.2024.
4. Central TB Division. India Tb Report 2023. Available from <https://tbcindia.gov.in/showfile.php?lid=3680>. Last accessed on 22.04.2024.
5. Guidelines for Progmmatic Management of Drug Resistance in India. National Tuberculosis Elimination Programme, GOI. March 2021. Available from: <https://tbcindia.gov.in/>. Last accessed on 23.04.2024.
6. Cental TB Division. Report of the First National Anti TB Drug Resistance Survey. Available from <https://tbcindia.gov.in/showfile.php?lid=3315>. Last accessed on 23.04.2024.
7. National TB Elimination Programme. Cartridge Based Nucleic Acid Amplification Test [CBNAAT]. Available from <https://ntep.in/node/397/CP-cartridge-based-nucleic-acid-amplification-test-cbnaat>. Last accessed on 23.04.2024.
8. Kranti Garg, Varinder Saini, Ruchika Dhillon, Prakhar Agarwal. Isoniazid mono-resistant tuberculosis: Time to take it seriously. *Indian Journal of Tuberculosis* 2019;66 (2):247-252.
9. WHO. National tuberculosis prevalence surveys: what diagnostic algorithms should be used in future? Geneva: World Health Organization; 2023. Available from <https://iris.who.int/handle/10665/367909>. Last accessed on 23.04.2024
10. Global HIV & AIDS statistics – fact sheet [website]. Geneva: UNAIDS; 2023 Available from <https://www.unaids.org/en/resources/fact-sheet>. Last accessed on 23.04.2024
11. Interim policy collaborative TB/HIV activities. Geneva: World Health Organization; 2004. Available from <https://iris.who.int/handle/10665/78705>. Last accessed on 23.04.2024
12. WHO consolidated guidelines on tuberculosis, Module 4: Treatment – drug-susceptible tuberculosis treatment. Geneva: World Health Organization; 2022 Available from <https://iris.who.int/handle/10665/353829>. Last accessed on 23.04.2024.
13. Global tuberculosis report 2021. Geneva: World Health Organization; 2021 Available from <https://iris.who.int/handle/10665/346387>). Last accessed on 23.04.2024
14. Global tuberculosis report 2022. Geneva: World Health Organization; 2022. Available from (<https://iris.who.int/handle/10665/363752>). Last accessed on 23.04.2024

15. More SW, Parande MA, Kamble SW, Kamble MS. Profile of drug-resistant tuberculosis in Western Maharashtra. *J Family Med Prim Care*. 2017 Jan-Mar;6(1):29-33.
16. Deoskar RB, Sengupta B, Rajan KE, Barthwal MS, Falleiro J, Sharma SK. Study of drug resistant pulmonary tuberculosis. *Med J Armed Forces India*. 2005;61:245-8.
17. Elmi OS, Hasan H, Abdullah S, Mat Jeab MZ, Bin Alwi Z, Naing NN. Multidrug-resistant tuberculosis and risk factors associated with its development: A retrospective study. *J Infect Dev Ctries*. 2015;9:1076-85.
18. Shamaei M, Marjani M, Chitsaz E, Kazempour M, Esmaeili M, Farnia P, et al. First-line anti-tuberculosis drug resistance patterns and trends at the national TB referral center in Iran – Eight years of surveillance. *Int J Infect Dis*. 2009;13:e236-40.
19. Chuchottaworn C, Thanachartwet V, Sangsayunh P, Than TZ, Sahassananda D, Surabotsophon M, et al. Risk factors for multidrug-resistant tuberculosis among patients with pulmonary tuberculosis at the Central Chest Institute of Thailand. *PLoS One*. 2015;10:e0139986.
20. WHO. Rapid communication: key changes to treatment of multidrug- and rifampicin-resistant tuberculosis (MDR/RR-TB). Geneva: World Health Organization; 2018 Available from <https://iris.who.int/handle/10665/275383>. Last accessed on 23.04.2024
21. WHO. Tackling the drug-resistant TB crisis BY WHO NOV 2023. Available from <https://www.who.int/activities/tackling-the-drug-resistant-tb-crisis>. Last accessed on 23.04.2024