ORIGINAL RESEARCH PAPER
Volume - 11 | Issue - 08 | August - 2022 | PRINT ISSN No. 2277 - 8179 | DOI : 10.36106/ijsr
INTERNATIONAL JOURNAL OF SCIENTIFIC RESEARCH

OMINOUS PROGRESSION OF MDR TUBERCULOSIS TO PRE-XDR AND XDR TUBERCULOSIS.

Microbiology

Suneel Bhooshan* Senior Demonstrator, Department of Microbiology, Dr. S N Medical College, Jodhpur Rajasthan. *Corresponding Author

Dr P K Khatri Sr. Professor, Department of Microbiology, Dr. S N Medical College, Jodhpur Rajasthan.

ABSTRACT

Tuberculosis is a serious public health problem. In recently years increase in drug resistance has made the situation worsened by a giving origin to multidrug-resistant Mycobacterium tuberculosis. We conducted a cross sectional study to identify the drug resistance prevalence in Western Rajasthan population. Prevalence rate of MDR TB was found to be 6% in presumptive tuberculosis suspected cases. Majority of these cases belonged to young working class of population (66.67% of MDR cases were from in young age group 21-30 years). Additional resistance to fluoroquinolones has become a new challenge by converting MDR isolates to pre-XDR cases. 23 (76.67%) MDR isolates were found to have fluoroquinolones and 2 (6.6%) also had resistance to injectable along with fluoroquinolones (XDR-TB). The high proportion of drug resistance TB patients is alarming in the region. Performing DST at the baseline in the initial stage of the disease is recommended to prevent further transmission of these resistant strains.

KEYWORDS

Tuberculosis, Multi Drug Resistant tuberculosis, Pre-XDR and XDR tuberculosis.

INTRODUCTION:

Tuberculosis (TB) is air-born, a communicable disease caused by Mycobacterium tuberculosis. It is on the top of the list of the leading causes of death by single infectious agents. It is worldwide prevalent with the capability of infecting any part of the body. (1) Approximately 10 million people are infected every year globally and 1.5 million people die from TB each year. (2) TB is curable and preventable however, lack of awareness and adherence to treatment is causing higher treatment failure rates and the spread of drug resistance in Mycobacterium tuberculosis. Drug resistance in tuberculosis is a serious clinical condition that might lead to poor outcomes. Multi-drug-resistant tuberculosis (MDR-TB) is defined as tuberculosis resistant to at least two first-line drugs isoniazid (INH) and rifampicin (RIF). (3) MDR-TB remains a clear threat and an obstacle to eradicating tuberculosis. Additional resistance in the life-saving second-line drugs has been reported worldwide in MDR strains and leading to pre-XDR tuberculosis or XDR strains. The global incidence of Fluoroquinolones resistance among Rifampicin/MDR-TB cases was 21% according to WHO 2019 TB report. It is crucial to recognize the drug resistance at the earliest stage before its resistance progresses to the next category and leaves no choice for treatment but unfortunately, to date limited data are available on the prevalence of Pre-XDR-TB worldwide, including in India. The aim of the present study was to determine the prevalence and resistance pattern of Pre-XDR- and XDR-TB among MDR-TB patients in Western Rajasthan.

Material and Methods:

Study design and participants-

A cross-sectional study was carried out in TB C & DST laboratory of Kamala Nehru Chest Hospital, Jodhpur which included nine districts of Western Rajasthan. Pulmonary and extra-pulmonary cases of presumptive tuberculosis were included in the study. 500 presumptive tuberculosis patients were enrolled in the study. For diagnosis of tuberculosis microscopy, CBNAAT and liquid culture (MGIT 960) were performed and for drug resistance detection Line probe assay (first-line and second-line drugs) was performed. Data were analyzed using SPSS 24 software.

Exclusion Criteria: Repeat specimen, close contact of tuberculosis-positive patient, patient with a history of previous tuberculosis treatment, Non-tuberculous Mycobacteria (NTM), or incomplete demographic data were excluded from this study.

Sample procedure-

Two sputum specimens (spot and morning) were collected in 50 mL wide-mouthed sterile falcon tubes from all participants. Each sample was examined microscopically for the presence of Mycobacterium tuberculosis using Ziehl-Neelsen (ZN) staining. All smear-positive specimens were directly processed for LPA directly from the processed specimen. In the case of smear-negative specimen, a subsequent liquid culture was performed by the N-acetyl-L cysteinesodium hydroxide method. Culture-positive specimens were subjected to immune-chromatographic assay for detection of the mpt64 antigen. MPT64 positive specimens were considered to be Mycobacterium tuberculosis complex and were further subjected to LPA (First line and second line).

Drug resistance detection-

GeneXpert procedure: Drug resistance for rifampicin was detected by CBNAAT Briefly, the reagent was added at a 2:1 ratio to clinical specimens. The closed specimen container was manually agitated twice during the incubation period for 15 min at room temperature. The reagent sample mixture was transferred to the Xpert test cartridge. The cartridge was inserted into the GeneXpert device and the results generated automatically were read after 90 min.

LPA: All smear-positive and smear negative culture-positive isolates were further tested for drug resistance detection by LPA (Genotype MTBDR plus V 2.0 assay and Genotype MTBDRsl Ver 2.0 assay) as per the manufacturer's instructions. (4)

Ethical approval:

The study protocol was approved by Ethics Committee of Dr. S N Medical College, Jodhpur.

RESULT

Out of 500 TB-positive cases, 354 patients were males and 146 females with a mean age of 38.66 (median 37.50, SD 15.97, IQR 25). 405 (81%) specimens were sensitive to both rifampicin and isoniazid in the first-line- Line probe assay. 30 (6%) specimens were found to be MDR cases (Rifampicin resistant or Rifampicin and Isoniazid resistant). These strains were further tested for any additional resistance to second-line drugs (FQ & SLID) by LPA. Out of 30 MDR strains, 5 were sensitive to second-line drugs, 23 were confirmed as pre-XDR cases and 2 (0.4%) were XDR cases.

Table 1: Frequency of isolates according to age group.

Age Group of patients	Frequency (%)
1-10 years	1
11-20 years	8
21-30 years	12
31-40 years	4
41-50 years	4
51-60 years	0
61-70	1

Males were more commonly infected in all three drug resistant categories. None of the patient had history of HIV reactivity. Predominant comorbidity observed was tobacco followed by alcohol consumption, corona and diabetes. Out of 30, both male patients had extrapulmonary site involved in disease with history of alcohol consumption. In our study percentage of Pre XDR-cases among TB positive cases was 04.6% and XDR cases were 0.4%.

Table 2. Demographic and clinical characteristics of Drug

resistant tuberculosis patients.

Patient's characteristics		MDR-TB n=30		Pre-XDR-TB n=19 XDR-TB n=2		XDR-TB n=2		P value
		n	%	n	%	n	%	
Categorical variables								
Gender	Female	10	33.3	7	36.8	0	0	0.432
	Male	20	66.6	12	63.2	2	100	
HIV status	Negative	30	100	17	89.5	2	100	0.724
	Positive	0	0	0	0	0	0	
	UK			2	10.5			
Alcohol abuse	No	16	53.3	8	42.1	0	0	0.380
	Yes	14	46.6	11	57.9	2	100	
Diabetes	No	29	96.6	18	94.7	2	100	0.808
	Yes	0	0	0	0	0	0	
	UK	1	3.3	1	5.3	0	0	
Corona	No	13	43.3	7	36.9	1	50	0.432
	Yes	0	0	0	0	1	50	
	UK	17	56.6	12	63.2	0	0	
Tobacco	No	10	33.3	6	31.6	2	100	0.432
	Yes	20	66.6	13	68.4	0	0	
Pregnancy	No	10	33.3	19	100	0	0	NA
	Yes	0	0	0	0	0	0	
Site of disease	PTB	28	93.3	18	94.7	2	100	0.808
	EPTB	2	6.6	1	5.3	0	0	

UK – Unknown, PTB – Pulmonary TB, EPTB- Extra-pulmonary

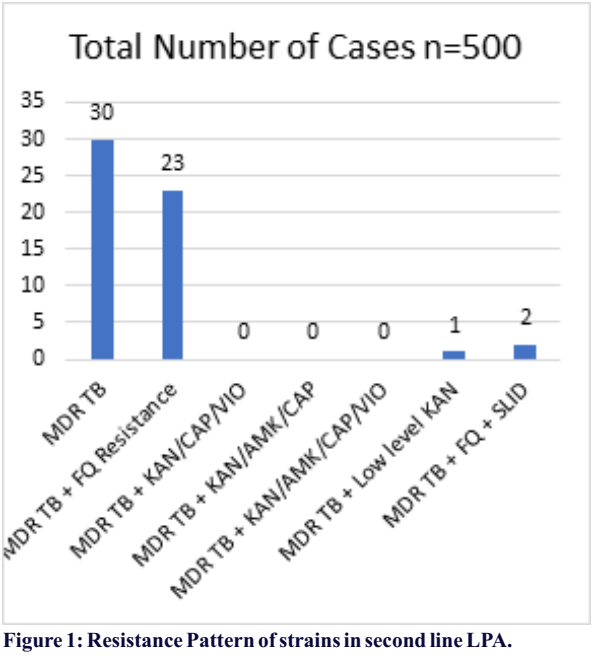

Figure 1: Resistance Pattern of strains in second line LPA.

DISCUSSION

In our study mean age of participants was 38.66 ± 15.97. In the case of multi-drug resistant patients mean age was 27.73 years. The mean age of male was higher (28.5) as compared to females (26.2), this difference was found to be statistically insignificant (P value = 0.432). Similar findings were observed by Venkatesh U. (5) Majority of the TB burden is among the working-age group. Men alone accounted for 66.67% of cases in our study which is in parallel to data published by TBC India in the 2021 TB annual report. 93.3% of TB cases come from the age group of 11-50 years. Age sex distribution shows a preponderance of TB (40%) among the age group 21-30 years for both males and females similar to published data by the Government of India. (6) Our findings were constant with a study from Mumbai, India, in which 69% of patients belonged to the younger (15–35 years) age group with a median age of 26 years (interquartile range: 20–37 years). (7) A study from Ahmedabad, India, in which 83.7% of patients were in the reproductive age group of 16–45 years with the mean age of 33.64 ± 11.03. 68.5% were males. (8) Prevalence of MDR cases (6%) in presumptive tuberculosis cases was high in our population compared to found in a meta-analysis study by A Lohiya. (9) Our findings were in correlated to a study conducted by Ahmed Hersi MD et al in 1999 where they reported a 6.6% prevalence of MDR patients. (10) However, this percentage was higher a (19.1%) in study conducted by Prabha Desikan from Central India. (11) Our study population showed that 66.67% of MDR cases were from in young age group 21-30 years. Both patients of XDR TB in our study were below 43 years of age. Udwadia also reported a prevalence of younger age group among MDR-TB patients with the mean age of their study groups being 29.7 years and 33.25 years, respectively. (12) Involvement of the younger population in drug resistant cases may be due to high mobile to outdoor activities. A total of 56 (11.20%) patients with drug-resistance to any first-line or second-line drugs were seen during our study period. Overall 30 (6%) patients had MDR tuberculosis out of which, 23 (76.67%) were found to have pre-XDR-TB and 2 (6.6%) had XDR-TB (both males). The prevalence of XDR-TB observed in our study between December 2020 and January 2021 was similar to that estimated globally by the WHO. (1) Among MDR patients, 28 cases of the pulmonary site were involved and 2 cases of extra-pulmonary site. None of the cases had a history of HIV reactivity. Alcohol consumption was the most common factor in all three-drug-resistant categories. Reason behind this might be the decline in immunity due to high consumption of alcohol. However, it was not statically significant (P-value-0.38). High alcohol consumption (34.1%) association, was also reported by Olena Oliveira et al 2021. (13) During the enrolment process none of the patients had a history of diabetes and a corona. One XDR TB patient developed corona infection during the treatment phase. The countrywide prevalence of pre-XDR TB over the 20-year period was 7.9%. Global resistance to second-line drugs is still underestimated (14) because many countries do not have the capacity to perform second-line DST. Due to limited data from previous studies for pre-XDR and XDR-TB, a comparative analysis based on regions and decades could be performed.

CONCLUSION

The high proportion of at least one second-line drug resistance among MDR-TB patients is alarming in the region. Performing DST at the baseline in the initial stage of the disease is recommended for RR/MDR-TB patients to monitor and evaluate the pre-XDR and XDR-TB patient status. This will ensure clinical improvement and adjust the treatment regimen to prevent treatment failure and also reduce its transmission to the community in the study area and the country at large. Further study is warranted to explore the role of various factors (Demographic or ecological) on the observed high distribution of DR-TB, and treatment outcomes and identify transmission networks in the community to locate hotspots for targeted interventions.

REFERENCES:

1. Global tuberculosis report 2021 [Internet]. [cited 2022 Apr 14]. Available from: https://www.who.int/publications-detail-redirect/9789240037021
2. Tuberculosis [Internet]. [cited 2022 Apr 14]. Available from: https:// www. who.int /health-topics/tuberculosis
3. WHO announces updated definitions of extensively drug-resistant tuberculosis [Internet]. [cited 2021 Jul 19]. Available from: https://www.who.int/news/item/27-01-2021-who-announces-updated-definitions-of-extensively-drug-resistant-tuberculosis
4. IFU | Instructions for use from Hain Lifescience [Internet]. [cited 2022 Apr 15]. Available from: https://www.hain-lifescience.de/en/instructions-for-use.html
5. Venkatesh U, Srivastava DK, Srivastava AK, Tiwari HC. Epidemiological profile of multidrug-resistant tuberculosis patients in Gorakhpur Division, Uttar Pradesh, India. J Family Med Prim Care. 2018;7(3):589–95.
6. Annual Reports :: Central TB Division [Internet]. [cited 2022 Jun 7]. Available from: https://tbcindia.gov.in/index1.php?lang=1&level=1&sublinkid=4160&lid=2807
7. Johansson E, Diwan VK, Huong ND, Ahlberg BM. Staff and patient attitudes to tuberculosis and compliance with treatment: an exploratory study in a district in Vietnam. Tuber Lung Dis. 1996 Apr;77(2):178–83.
8. Hudelson P. Gender differentials in tuberculosis: the role of socio-economic and cultural factors. Tuber Lung Dis. 1996 Oct;77(5):391–400.
9. Lohiya A, Suliankatchi Abdulkader R, Rath RS, Jacob O, Chinnakali P, Goel AD, et al. Prevalence and patterns of drug resistant pulmonary tuberculosis in India—A systematic review and meta-analysis. Journal of Global Antimicrobial Resistance. 2020 Sep 1;22:308–16.
10. Lee JH, Chang JH. Drug-resistant tuberculosis in a tertiary referral teaching hospital of Korea. Korean J Intern Med. 2001 Sep;16(3):173–9.
11. Desikan P, Panwalkar N, Mirza S, Chaturvedi A, Ansari K, Varathe R, et al. Line probe assay for detection of Mycobacterium tuberculosis complex: An experience from Central India. Indian J Med Res. 2017;145(1):70.
12. Udwadia ZF. Totally drug resistant-tuberculosis in India: The bad just got worse. - J Assoc Chest Physicians [Internet]. [cited 2022 Jul 2]. Available from: https://www.jacpjournal.org/article.asp?issn=23208775;year=2016;volume=4;issue=2;spage=41;epage=42;aulast=Udwadia
13. Oliveira O, Gaio R, Correia-Neves M, Rito T, Duarte R. Evaluation of drug-resistant tuberculosis treatment outcome in Portugal, 2000–2016. PLOS ONE. 2021 Apr 20;16(4):e0250028.
14. Abubakar I, Zignol M, Falzon D, Raviglione M, Ditiu L, Masham S, et al. Drug-resistant tuberculosis: time for visionary political leadership. The Lancet Infectious Diseases. 2013 Jun 1;13(6):529–39.