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Determinants, risk factors and spatial analysis of multi-drug resistant pulmonary tuberculosis in Jodhpur, India

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Abstract

This study was planned to estimate the proportion of confirmed multi-drug resistance pulmonary tuberculosis (TB) cases out of the presumptive cases referred to the District Tuberculosis Center (DTC) Jodhpur for diagnosis; to identify clinical and socio-demographic risk factors associated with the multidrug-resistant pulmonary TB and to assess the spatial distribution to find out clustering and pattern in the distribution of drug-resistant pulmonary TB with the help of Geographic Information System (GIS). In the Jodhpur district, 150 confirmed pulmonary multi-drug resistant tuberculosis (MDR-TB) cases, diagnosed by probe-based molecular drug susceptibility testing method and categorized as MDR in DTC's register, were taken. Simultaneously, 300 control of confirmed non-MDR or drug-sensitive pulmonary TB patients were taken. Statistical analysis was done with logistic regression. In addition, for spatial analysis, secondary data from 2013-17 was analyzed using Global Moran's I and Getis and Ordi (Gi*) statistics. In 2012-18, a total of 12563 CBNAAT (Cartridge-based nucleic acid amplification test) were performed. 2898 (23%) showed M. TB positive but rifampicin sensitive, and 590 (4.7%) showed rifampicin resistant. Independent risk factors for MDR TB were ≤60 years age (AOR 3.0, CI 1.3-7.1); male gender (AOR 3.4, CI 1.8-6.7); overcrowding (AOR 1.6, CI 1.0-2.7); using chulha (smoke appliance) for cooking (AOR 2.5, CI 1.2-4.9), past TB treatment (AOR 5.7, CI 2.9-11.3) and past contact with MDR patient (AOR 10.7, CI 3.7-31.2). All four urban tuberculosis units (TUs) had the highest proportion of drug-resistant pulmonary TB. There was no statistically significant clustering, and the pattern of cases was primarily random. Most of the hotspots generated were present near the administrative boundaries of TUs, and the new ones mostly appeared in the area near the previous hotspots. A random pattern seen in cluster analysis supports the universal drug testing policy of India. Hotspot analysis helps cross administrative border initiatives with targeted active case finding and proper follow-up.

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Key words: MDR; TB; antimicrobial resistance; GIS; spatial; clustering.

Acknowledgments: The authors would like to thank the District Tuberculosis Officer and his team of Senior Treatment Supervisor at Jodhpur, Rajasthan, India; Mr. Rajeev and Mr. Praveen, State Remote Sensing Application Centre, Jodhpur, Rajasthan, India; Prof. PK Khatri, Department of Microbiology, Dr. Sampurnanand Medical College, Jodhpur, Rajasthan, India; and Prof. Pankaja Raghav, Department of Community Medicine and Family Medicine, All India Institute of Medical Sciences, Jodhpur, Rajasthan, India.

Contributions: All the authors made a substantive intellectual contribution, read and approved the final version of the manuscript and agreed to be accountable for all aspects of the work.

Conflict of interest: The authors declare that they have no competing interests, and all authors confirm accuracy.

Ethics approval and consent to participate: Approval from the Institutional Ethical Committee was taken before starting the study. Written informed consent was taken from every participant.

Received for publication: 22 July 2021.
Accepted for publication: 20 December 2021.

Licensee PAGEPress, Italy
Monaldi Archives for Chest Disease 2022; 92:2026
doi: 10.4081/monaldi.2022.2026

Introduction

Globally, tuberculosis (TB) is among the top 10 causes of death and the leading cause from a single infectious agent. Drug-resistant TB is growing as a public health crisis. Globally, about half a million people developed TB in 2018 that was resistant to rifampicin (RR-TB), and among them, 78% had multidrug-resistant TB (MDR-TB). Around one-fourth (27%) of these cases were from India alone, followed by China (14%). Around 3.4% of new TB cases and 18% of previously treated patients had MDR/RR-TB [1].

India has a long way to reach the level of TB control achieved by developed countries in the last century. Under the World Health Organization's End Tuberculosis strategy, the 2035 targets reduce

the TB incidence rate by 90% to ≤10 cases per 100,000 populations per year and reduce the absolute number of TB deaths by 95% of the baseline 2015. These correspond to the overall goal of ending the global TB epidemic by 2035 [2]. An intensified case detection of TB and drug-resistant TB (DR-TB) can help achieve this goal by helping in an early start of proper treatment and preventing the mortality and transmission of DR-TB. However, it is also essential to identify those who are at high risk of DR-TB. For this, major risk factors and determinants of the DR-TB should be known at the regional or local level and in specific settings. Another vital factor proven in many infectious and vector-borne diseases is the geographic distribution of cases. It helps in the early identification of clusters, which can help in targeted testing or other preventive measures. Combined with other regional risk factors, this information will further support the optimal planning and implementation of the TB control program [3]. Drug treatment without achieving control will only result in the development of drug resistance. Therefore, the determinants and risk factors must be known and focused on to control growing MDR-TB.

Different studies [4-7] have been done to show the clinical risk factors of MDR-TB. Very few [8,9] are done, focused on biosocial risk factors, but none is from India's northwestern region.

This study was done in a period (i.e., 2018) when the National Program known as Revised National TB Control Program (RNTCP) was undergoing transaction. With elimination as the target, India was changing many national program strategies. Universal drug resistance testing, i.e., every TB patient, will be offered a test to identify the drug-resistant, was one of them. Other than this, active surveillance was also underway [10]. This study was planned to generate evidence to help with the changing strategy of the national program and provide a rationale for expanding the program in a resource-poor setting like India. A case-control study will help identify the multiple risk factors and determinants of MDR-TB further strengthened by spatial analysis to better understand the geographical spread of disease.

Add to the existing pool of knowledge and help tailor the program on a regional level, this study aims to identify clinical and socio-demographic risk factors associated with multi-drug-resistant pulmonary TB. This study also estimates the proportion of confirmed multi-drug resistance pulmonary TB cases out of the presumptive cases (based on either history of previous treatment or contact with confirmed drug-resistant cases or based on clinical judgment) referred to District Tuberculosis Center (DTC) and also assess the spatial distribution to find out clustering and pattern in the distribution of pulmonary TB with the help of Geographic Information System (GIS). Evidence generated at the district level helps in state-level planning, which allows forming national strategy.

Materials and Methods

Study design and area

This case-control study was done in the Jodhpur district of Rajasthan, situated in India's northwestern part. Rajasthan State is the largest state in India, with a population of 786.6 lakh. It reports the fourth-highest no. of TB cases in India, *i.e.*, 7.62% of the total. Jodhpur is one of the largest districts of Rajasthan state and is centrally situated in the state's Western region, having a geographical area of 22850 sq. Km. It has a population of 36.85 lacs as *per* the 2011 census. The district stretches between 2600' and 27037' at North Latitude and between 72 55' and 73 52' at East Longitude.

Test negative case-control design was used. Both cases and controls were selected from a similar pool of TB patients whose sample was sent for drug-resistant testing. A patient of either gender, of any age, diagnosed as confirmed pulmonary MDR-TB by probe-based molecular drug susceptibility testing (DST) method (CB NAAT/Gene-XPert or LPA) showing *M. tuberculosis* strain resistant to rifampicin and categorized as MDR in DTC's register were taken as cases and confirmed non-MDR pulmonary TB by the same test were chosen as control. This approach helped to control biases related to health-seeking behavior, access to testing, and case ascertainment. Two controls were taken for each case. The study duration was 18 months, and only those patients from whole district were taken who were currently on treatment during the study.

Sample size

The sample size was calculated taking the help of Epi Info™ (Division of Health Informatics and Surveillance, Center for Surveillance; https://www.cdc.gov/ddphss/) by taking 'inadequate anti TB drug therapy' risk factor's proportion in DR-TB as 24% and in DS-TB as 13% from a previous study [11] and keeping two-sided confidence interval at 95%, power as 80%, odds ratio as 2.1. A total of 150 cases and 300 control were recruited in the present study. The sample size was also following the sample size mentioned in Section- Treatment of Drug- Susceptible and MDR-TB: Optimal access, delivery and community participation in the document "Priorities in Operational Research to improve Tuberculosis Care & Control," published by WHO 2011 [3]. For spatial analysis, previous 5-year data of the Jodhpur district's MDR-TB cases were used.

Data source and variables in the study

After getting approval from Institutional Ethics Committee, a list of MDR pulmonary TB patients registered under the Revised National Tuberculosis Control Program (RNTCP) was procured from DTC. With contact details (phone numbers, residential addresses), the cases and controls were contacted. Accordingly, the visit was made either at their residences or the directly observed treatment short-course (DOTS) center from where they were procuring medicines. After a detailed explanation of the purpose of the visit and confidentiality, informed written consent was taken. Data was collected with the help of a structured questionnaire (having both closed-ended and open-ended questions). Details of clinical, demographic, socio-economic variables were also taken in both cases and controls.

Statistical analysis

After a descriptive analysis of variables, crude and adjusted odds ratios were calculated for individual risk factors with their 95% confidence intervals with logistic regression adjustment using SPSS v. 21. All the factors (regardless of statistical significance) were taken into account to calculate the adjusted odds using logistic regression.

Geographic Information System analysis

For this objective, a secondary source of data was used. The previous 5-year data of the Jodhpur district's MDR TB cases were procured from registers maintained under RNTCP in DTC. ArcGIS

10.6.3 was used. Global Moran's I and Getis and Ordi (Gi*) statistics were used to analyze the disease's spatial distribution and clusters across settings.

The spatial autocorrelation (Global Moran's I) measures spatial autocorrelation based on feature locations and feature values simultaneously. It evaluates whether the pattern expressed is clustered, dispersed, or random with a set of features and an associated attribute. The tool calculates the Moran's I index value and both a z-score and p-value to evaluate that index's significance. These p-values are numerical approximations of the area under the curve for a known distribution, limited by the test statistic. Following the best practice guideline rather than analyzing the number of cases at the TU level, a geographic resolution was decreased to the village level because there were only 14 TU in the Jodhpur district, and results are unreliable with less than 30 features. A fixed distance band was used in the conceptualization of spatial relationships. It makes sure that all features will have at least one neighbor. Row standardization was done, following best practice guidelines as villages are polygon features [12].

The Hot Spot Analysis tool gives the Getis-Ord Gi* statistic (pronounced G-i-star) for each feature in a dataset. The resultant z-scores and p-values tell where features of either high or low values are clustered spatially. This tool looks at each feature within the context of neighboring features. A feature with a high value is exciting, but this hot spot may not be statistically significant. For this, a feature should have both a high value and be surrounded by features with high values, too.

The sum local for a feature and its neighbors is compared to the sum of all features proportionally; when the sum local is very different from the expected local sum, and when that difference is too large to result from random chance, a statistically significant z-score results. False discovery rate (FDR) correction was applied to adjust statistical significance to account for multiple testing and spatial dependency. The choice for the conceptualization of spatial relationships parameter should reflect inherent relationships among the features being analyzed. The more realistically we can model how features interact in space, the more accurate our results. The present study used a fixed distance band, the default for threshold distance band for this modeling. This method ensured that each feature would have at least one neighbor [13].

Results

From the year 2012 till 2018, a total of 12,563 CBNAAT tests were performed. Out of these, 2898 (23.07%) showed M.tb positive but rifampicin sensitive. The proportion of rifampicin resistant M.tb cases were 4.70% (n=590). In 2018, 3170 CBNAAT tests were performed compared to 2012, where only 1100 tests were performed. With increasing capacity, the number of CBNAAT tests is rising each year. Accordingly, no. of drug-sensitive tuberculosis is also growing, ranging from 195 to 704. Meanwhile, the no. of Drug-resistant tuberculosis cases is more or less the same each year, ranging from 2-5% of total tests (Table 1). The geographic information system (GIS) was used to prepare the map of different Tuberculosis Units (TUs) of the Jodhpur district as it was different from the administrative boundary, i.e., panchayat samitis. A choropleth thematic map was prepared from 2013 to 2017, i.e., five years (Figure 1). These maps were prepared with the incidence cases of drug-resistant pulmonary tuberculosis using DTC's secondary data. It shows that all the four urban TUs, i.e., Pratap Nagar, Paota, Chopasani Housing Board, and District Tuberculosis Center, had the highest proportion of drug-resistant pulmonary TB except in 2014, Bilara TU also had a high number.

By Global Moran's I, there was no significant clustering seen for drug-resistant pulmonary tuberculosis cases in any year except the year 2013 and year 2017. In 2013, the pattern showed statistically significant clustering with a p-value of 0.009 (Moran's I=0.021, z score=2.622). Whereas in 2017, the statistically significant clustering had a p-value of 0.048 (Moran's I=0.016, z score=1.979). Year 2014 had Moran's I=0.012, z score=1.557, p=0.119; year 2015, Moran's I=0.010, z score=1.304, p =0.192 and year 2016 had Moran's I=0.008, z score=0.993, p =0.321.

Getis and Ordi (Gi*) statistics or hot spot analysis of village-wise drug-resistant pulmonary tuberculosis using fixed distance model also showed no meaningful clustering or identifiable pattern (Figure 2). Most of the hot spots were random, but many were located on the Jodhpur district's southeast side every year except in 2017.

Most participants were male (68.2%) in the current study and belonged to the 21-60 years of age group (79.8%). Most were from the lower class (35.6%) or lower-middle-class (31.1%). Cases were more or less similar to the controls except regarding gender and socio-economic status, where a statistically significant difference was present. The majority of participants were living in a condition of overcrowding (62.4%), and more than half (52.9%) were using smoke appliances (chulha) with traditional fuel for cooking. This use of chulha was significantly different in cases and controls. Only one-fifth (21.1%) of participants had an average or higher body mass index (BMI) (>18.5 kg/m^2) at the time of diagnosis. Approximately three fourth (73.8%) of participants had a previous history of TB treatment. Other than this factor, past contact with someone with MDR TB, History of living in congregated settings, past uses of tobacco in the form of smoking or chewing were other

Table 1. Distribution of cases referred to DTC according to their status of CBNAAT report.

Year	Test performed n	M.tb positive and rifampicin sensitive n (%)	M.tb positive and rifampicin resistant n (%)
2018	3170	704 (22.2)	83 (2.6)
2017	2191	515 (23.5)	93 (4.2)
2016	1320	357 (27.0)	58 (4.4)
2015	1084	204 (18.8)	59 (5.4)
2014	1478	495 (33.5)	180 (12.2)
2013	2220	428 (19.3)	62 (2.8)
2012	1100	195 (17.7)	55 (5.0)

Source: Data provided by District Tuberculosis Center, Jodhpur.

factors that showed a statistically significant difference between cases and control (Table 2).

After logistic regression, age, sex, overcrowding, and cooking fuel were the independent socio-demographic risk factors. Other than this, history of TB treatment, contact with MDR TB patient, came out to be other independent risk factors after adjusting for other factors (Table 3).

Discussion

India is a high MDR-TB burden country, and this study has provided baseline information about factors associated with MDR-TB, which will support the implementation of targeted interventions to achieve the goal of elimination.

Among socio-demographic factors, the younger age group (≤60 years) is at higher risk of MDR TB, having three times higher odds than more than 60 years of age group. Similar as shown in the study done by Nair *et al.* [8]. Further, age distribution shows that this disease primarily affects economically productive age groups and can affect the family's economic status. Thus, social assistance must be provided to such patients and their families to prevent them from going into the poverty trap. In line with this Government of India started the Direct Benefit Transfer (DBT) schemes for TB patients' adequate nutrition during treatment. Under this, 500 INR per month is deposited in installments to the patient's bank account.

Males had 3.5 times higher odds of having MDR TB in comparison to females. It may be explained as males socially come into contact with a larger population, which may increase TB and MDR TB risk. Another reason can be gender bias in reporting to and securing health care facilities. A similar result has been shown in other studies [14-17], but few studies show the same risk [8] or more risk in females [4,9]. Although the culture is changing now, males are still the primary earner in a family at most places, and

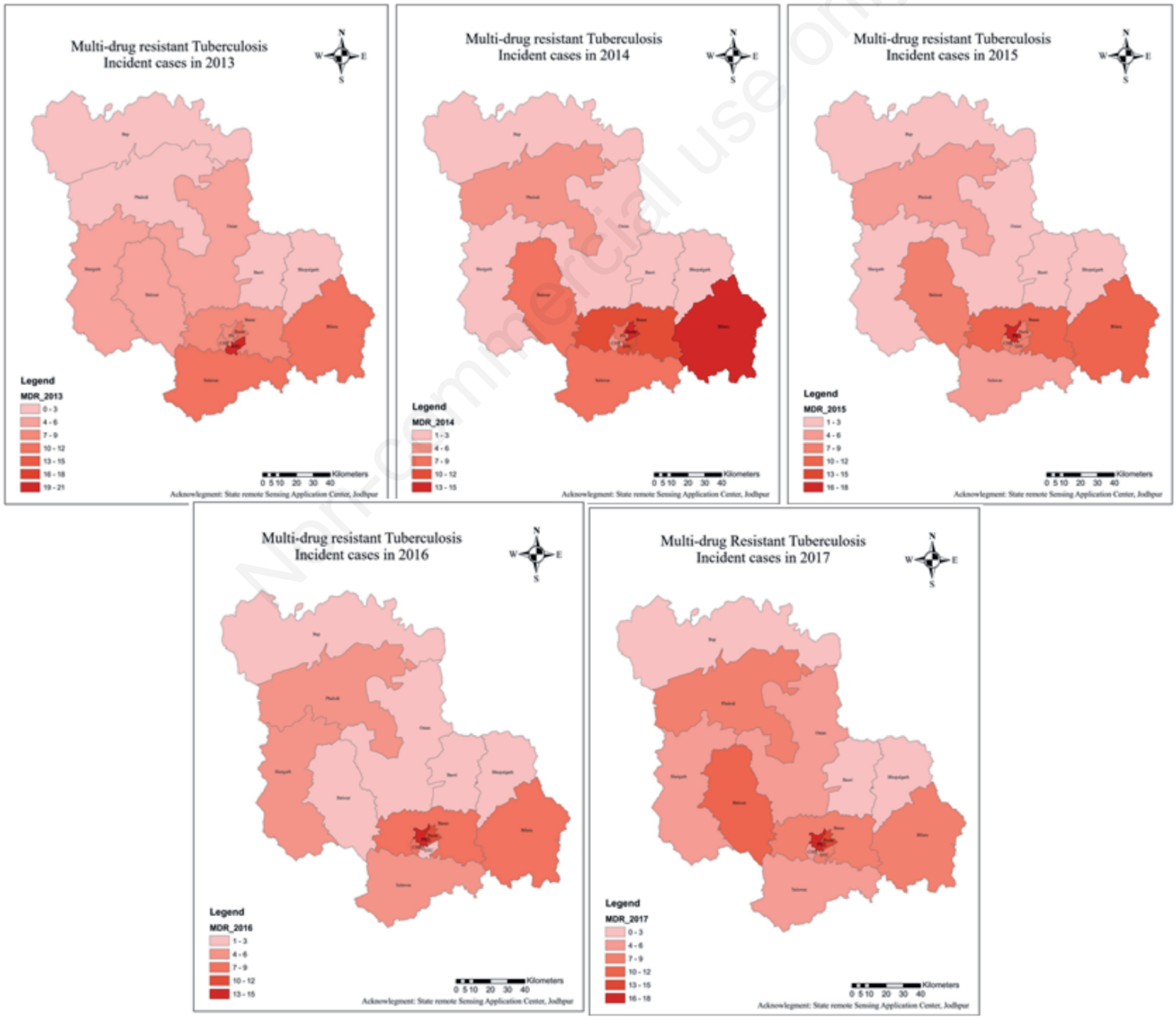

Figure 1. Choropleth thematic maps of Incident cases of multi-drug resistant tuberculosis according to tuberculosis unit for 2013-2017.

Table 2. Distribution of study participants according to their socio-demographic profile and risk factors for having multi-drug resistant tuberculosis.

	Case (n=150) n (%)	Control (n=300) n (%)	Total (n=450) n (%)	*p-value (χ2, df)
Age (years)				
≤ 60	140 (93.3)	259 (86.3)	399 (88.7)	0.027 (4.876, 1)
> 60	10 (6.7)	41 (13.7)	51 (11.3)	
Sex				
Male	117 (78.0)	190 (63.3)	307 (68.2)	0.002 (9.922, 1)
Female	33 (22.0)	110 (36.7)	143 (31.8)	
Place of residence				
Rural	96 (64.0)	173 (57.7)	269 (59.8)	0.196 (1.668, 1)
Urban	54 (36.0)	127 (42.3)	181 (40.2)	
Socio-economic status				
Upper middle class	16 (10.7)	41 (13.7)	57 (12.7)	0.016 (10.366, 3)
Middle class	30 (20.0)	63 (21.0)	93 (20.7)	
Lower middle class	61 (40.7)	79 (26.3)	140 (31.1)	
Lower class	43 (28.8)	117 (39.0)	160 (35.6)	
Exposure to silica as occupational hazard				
No Exposure	76 (50.7)	170 (56.7)	246 (54.7)	0.347 (2.118, 2)
0-10 years	28 (18.7)	42 (14.0)	70 (15.6)	
>10 years	46 (30.7)	88 (29.3)	134 (29.8)	
Type of house				
Kuchha or mixed	73 (48.7)	142 (47.3)	215 (47.8)	0.790 (0.071, 1)
Pucca	77 (51.3)	158 (52.7)	235 (52.2)	
Overcrowding #				
Present	101 (67.3)	180 (60.0)	281 (62.4)	0.130 (2.293, 1)
Absent	49 (32.7)	120 (40.0)	169 (37.6)	
Cooking fuel				
Chulha	94 (62.7)	144 (48.0)	238 (52.9)	0.003 (8.633, 1)
LPG	56 (37.3)	156 (52.0)	212 (47.1)	
Pervious exposure to TB treatment	136 (90.7)	196 (65.3)	332 (73.8)	<0.001 (33.173, 1)
Past hospitalization due to causes other than TB	18 (12.0)	50 (16.7)	68 (15.1)	0.193 (1.698, 1)
Past contact with someone having MDR-TB	24 (16.0)	6 (2.0)	30 (6.7)	<0.001 (31.500, 1)
Lived in congregate setting	16 (10.7)	6 (2.0)	22 (4.9)	<0.001 (16.153, 1)
Diabetes	5 (3.3)	16 (5.3)	21 (4.7%)	0.343 (0.899, 1)
Use of tobacco	83 (55.3)	182 (60.7)	265 (58.9)	0.278 (1.175, 1)

*p<0.05 taken as significant; #to define overcrowding, criteria of persons per room was used.

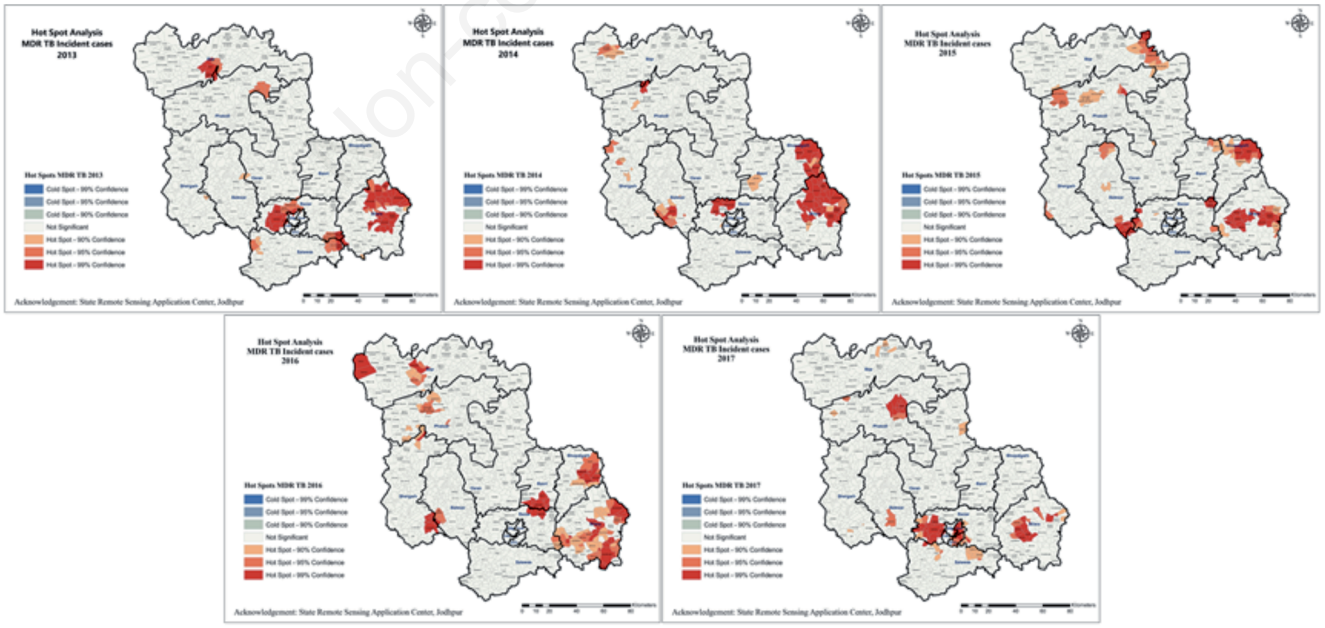

Figure 2. Result of Getis and Ordi (Gi*) statistics or hot spot analysis of village-wise multi-drug resistant tuberculosis incident cases using fixed distance model for years 2013-2017.

being affected by a debilitating disease like TB having a long course of treatment, affects the whole family dynamics. It forces the younger generation to drop out of school in search of jobs to feed the family.

The residence, socio-economic status, and type of housing didn't show any statistical significance regarding MDR-TB, indicating that TB may be considered a disease of the poor, but MDR-TB is a universal problem present in all strata of society. Exposure to silica dust also came out to be a non-significant factor.

Overcrowding, a known risk factor for tuberculosis infection, also became a significant risk factor for MDR. For defining overcrowding, criteria of persons per room were used. Living in an overcrowded house had 1.7 times higher odds of MDR-TB. Indoor air pollution (using chulha with traditional fuel like wood, coal, or dried cow dung as a proxy marker) increases the odds of getting MDR-TB by 2.5 times. It shows that indoor air pollution or biomass fuel use makes people prone to having respiratory diseases like MDR-TB, and the risk increases further if proper ventilated living spaces are not available [18,19]. It poses a challenge in a country like India, the second-largest country by population, having 16.7% of the world population but only 2.4% of the landmass. Innovative engineering techniques and architects are needed to solve this dilemma.

Past contact with MDR-TB cases increases the odds of having

Table 3. Bivariate logistic regression analysis of determinants and risk factors associated with MDR-TB.

Risk factors	Crude odds ratio (95% CI)	Adjusted odds ratio (95% CI)
Age		
≤ 60	2.22 (1.08-4.56)	3.06 (1.32-7.13)
> 60	Reference	
Sex		
Male	2.05 (1.31-3.23)	3.45 (1.76-6.75)
Female	Reference	
Place of residence		
Rural	1.30 (0.87-1.96)	0.92 (0.51-1.62)
Urban	Reference	
Socioeconomic status		
Lower class	0.94 (0.48-1.85)	0.56 (0.23-1.36)
Lower middle class	1.98 (1.02-3.86)	1.36 (0.60-3.04)
Middle class	1.22 (0.59-2.51)	1.19 (0.51-2.78)
Upper middle class	Reference	
Exposure to silica as occupational hazard		
No exposure	Reference	
0-10 years	1.49 (0.86-2.58)	0.72 (0.34-1.51)
>10 years	1.17 (0.75-1.83)	0.58 (0.31-1.09)
Type of house		
Kuchha or mixed	1.05 (0.71-1.56)	0.64 (0.35-1.20)
Pucca	Reference	
Overcrowding		
P resent	1.37 (0.91-2.07)	1.66 (1.01-2.74)
Absent	Reference	
Cooking fuel		
Chulha	1.82 (1.22-2.72)	2.47 (1.23-4.95)
LPG	Reference	
History of TB treatment in past		
Present	5.15 (2.83-9.39)	5.72 (2.90-11.28)
A bsent	Reference	
History of contact with MDR-TB patient		
Present	9.33 (3.72-23.39)	10.73 (3.69-31.23)
Absent	Reference	
Past hospitalization due to causes other than TB		
Yes	0.68 (0.38-1.22)	0.58 (0.29-1.17)
No	Reference	
History of living in congregate settings		
P resent	5.85 (2.24-15.28)	2.36 (0.77-7.17)
Absent	Reference	
Diabetes		
Yes	0.61 (0.22-1.70)	0.64 (0.19-2.15)
No	Reference	
Use of tobacco		
Yes	0.80 (0.54-1.19)	0.64 (0.37-1.08)
No	Reference	

MDR-TB by 10.7 times, making it one of the most critical risk factors. Similarly, having TB treatment in the past had 5.7 times higher odds of MDR-TB. Other studies have also shown similar results [8,16]. Therefore, it further strengthens that strategies must focus on contact tracing and uninterrupted, complete treatment for TB elimination.

The history of living in congregated settings, a risk factor on univariate analysis, was non-significant as an independent factor. Diabetes and the use of tobacco were also not significant risk factors in the current study. This result may be because of the bias caused by the loss of these individuals from the study due to a poor state of health or socio-economic status, causing early death after developing resistant TB.

In spatio-temporal analysis, in almost all years, urban TUs had a comparatively higher incidence of MDR-TB. It was expected as the density of the population is high and diagnostic facilities are easily accessible. Similarly, Tiwari *et al*., in their study done in the Almora district, showed that DTC had high cases there also [20]. Cluster analyses are essential in epidemiology to detect disease cases' aggregation, test the occurrence of any statistically significant clusters, and ultimately find evidence of etiologic factors. First, it identifies whether geographically grouped disease cases can be explained by chance or are statistically significant. Second, it detects actual clusters of disease from cases grouped around population centers. Although using spatial analysis at higher geographic resolutions improves the method's performance in cluster detection [21], having only 14 TUs (less than 30 is not a good number for analysis), in the present study, village-level data was used. In addition, cases of urban TU were excluded from the analysis to prevent bias as they always had many incidence cases. These two things may help to explain the findings of the present study. In the present study, Global Moran's I showed that except in 2013 and 2017, there was no statistically significant clustering, and the pattern of cases was primarily random. Similar results have been found in few studies also where at the global level, there was no autocorrelation pattern, but at the local level, cases were clustered [22-24]. The presence of spatial clustering or spatial autocorrelation in TB distribution was considered to reflect ongoing TB transmission, while its absence was taken to indicate reactivation [25,26]. On a similar note, the present study's findings suggest that MDR-TB cases seen in Jodhpur District may not be because of transmission of drug-resistant bacteria but because of the past TB's reactivation or treatment failure infection. In India's first national drug-resistant survey, it was noted that the prevalence of MDR was 2.8% in new cases, whereas in previously treated, it was 11.6% [27].

Another exciting thing to observe was that most of the hotspots generated were present near the administrative boundaries of TUs. More research is needed to look into the reasons for this pattern. One reason that may be possible is the administrative difficulty and confusion between the TUs about the patient's follow-up, which may lead to a high no. of loss to follow-up patients and leads to MDR on subsequent illness episodes. New hotspots mostly appeared in the area near the previous hotspot, as seen in year-wise hotspot analysis. It becomes crucial when we suspect MDR-TB in patients coming from the same place. It can help in planning active surveillance also as targetting these areas will provide better yield. It further helps in policy planning also as the area where hot spots are constant may need to have a focused approach on determinants and risk factors associated with MDR-TB. This GIS analysis would have been better if the point data of TB patients were available. In that case, a better time trend analysis was possible. Nonetheless, even using village-level data had a good outcome. Using the complete address and GPS location of each patient will further help increase the sensitivity of analysis, but it may be more laborious and may need more resources.

This study was done in the Jodhpur district, and participants were from the whole district. Jodhpur district is one of the largest districts in Rajasthan state, India's largest state. The data and evidence generated will help draw and support the strategic changes needed to eliminate TB. In this study, cases and controls were carefully selected so that the proper factors affecting MDR-TB come into the picture. For these cases and controls, both were chosen from the same pool of patients suspected of having MDR-TB. The only difference was that cases came out to be drug-resistant TB, whereas controls were drug-sensitive TB. This approach helped to control biases related to health-seeking behavior, access to testing, and case ascertainment. But as this is not a community-based study, those who were not diagnosed or died before diagnosis or before being contacted by the researcher; may have been lost. In addition, recall bias is another issue that is intrinsic in a case-control study. Though there are a few limitations, this study will hopefully help further to understand the epidemiology of MDR-TB. In addition, determinants and risk factors identified will help to plan preventive strategies.

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