



ISSN: 0976-3031

Available Online at <http://www.recentscientific.com>

International Journal of Recent Scientific Research
Vol. 6, Issue, 8, pp.5976-5979, August, 2015

**International Journal
of Recent Scientific
Research**

RESEARCH ARTICLE

IDENTIFICATION AND EVALUATION OF SUSPECTIBLE RISK FACTORS FOR MULTI DRUG RESISTANT TUBERCULOSIS

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ARTICLE INFO

Article History:

Received 14th, July, 2015
Received in revised form 23th,
July, 2015
Accepted 13th, August, 2015
Published online 28th,
August, 2015

ABSTRACT

There are susceptible risk factors/criteria which our study aimed to identify and evaluate for multi-drug resistant tuberculosis (MDR TB) in order to overcome the barriers in effective Tuberculosis control and treatment. The study population was divided TB center wise, Gender wise and Age wise. In our study, according to the seven criteria for MDR TB, which are Failure, Re-treatment case Sputum positive (S+) at 4th month, Contact of known MDR TB, S+ at diagnosis, re-treatment, Any follow up S+, Sputum negative (S-) at diagnosis, re-treatment and HIV TB cases, the ratio of MDR TB cases to Non- MDR TB cases were found to be 1:3, 1:1, 1:1, 1:3, 1:3, 1:6 and 1:6 respectively. Based on this criteria; Re-treatment case S+ at 4th month and Contact of known MDR TB showed higher risk for MDR-TB. The risk was found to be equally strong in all age groups and both genders.

Key words:

Multi-drug Resistant
Tuberculosis, Susceptible
Criteria, HIV TB, and Ratio.

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INTRODUCTION

Tuberculosis (TB), also called as Koch's disease; is an infectious disease caused by infectious strains of Mycobacterium (M), the most common being *M. Tuberculosis* and other infectious strains like *M. avium* and *M. bovis*. Lungs are the most commonly affected part of the body, nevertheless it affects almost all parts (Leon shargel et al, 2009). The transmission of the infection is via the droplets from the throat and lungs of people with the active TB infection that are present in the air. Some of the symptoms of active TB include chronic cough with sputum with or without blood, weakness, weight loss, fever, chest pain and night sweats. The complications of TB include long-term lung damage, organ damage when infection spreads beyond the lungs, joint damage, eye problems, heart disorders, liver or kidney problems, meningitis and spinal pain (Leon shargel et al, 2009). The first line drugs used to treat TB are Isoniazid, Rifampicin, Ethambutol, Pyrazinamide and Streptomycin. Multiple drugs are used to avoid resistance and duration of treatment is long in order to avoid relapse (Leon shargel et al, 2009). Drug-Resistance in Mycobacterium is defined as a decrease in sensitivity to a sufficient degree to be reasonably certain that the strain concerned is different from a sample of wild strains

of human type that have never come in contact with the drugs (C.N. Paramasivan et al, Oct 2004). Multi-drug resistant tuberculosis is defined as disease due to *M. tuberculosis* that is resistant to Isoniazid (H) and/or Rifampicin (R) with or without resistance to other drugs (Grover GS et al, Oct 2005). Drug resistance is of two types. A) Primary Resistance is seen in a patient who has not received any anti-tubercular treatment in the past now called 'Drug resistance among new cases'. B) Acquired Resistance is seen in a patient who has received prior TB treatment now called 'Drug resistance among previously treated cases' (Rajendra Prasad, 2005). Resistance for Rifampicin alone or in combination with Isoniazid is detected by using the Line Probe Assay (LiPA) (Surajeet Kumar Patra et al, 2012). Risk factors such as cases previously treated with inappropriate, incomplete or erratic anti-tubercular drugs, Community acquired drug resistant tuberculosis, Contact with a patient known to have drug resistant tuberculosis, Co-morbidities such as HIV, Socioeconomic factors such as financially deprived groups, unhygienic surroundings, enclosed areas such as prisons, in intravenous drug abusers and other immune compromised states as in transplant recipients, anti cancer therapy patients, and patients with diabetes mellitus have been identified in the causation of drug resistant tuberculosis (Rajendra Prasad, 2005).

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The seven criteria for a TB case to be a suspected MDR TB case are Failure, Re-treatment case Sputum positive (S+) at 4th month, Contact of known MDR TB case, S+ at diagnosis, re-treatment case, Any follow up S+, Sputum negative (S-) at diagnosis, re-treatment case and HIV TB Case. A TB case, having met one or more of these criteria will be considered as a potential case for performing the line probe assay to further rule out multi-drug resistance. The emergence and spread of multi-drug resistant tuberculosis (MDR-TB) is threatening to destabilize tuberculosis control in India and globally, at large. The prevalence of MDR-TB is increasing both among new tuberculosis cases as well as among previously-treated ones. In the present scenario, there is high likelihood that what initially seems to be drug-sensitive TB in a treatment-naive patient might in fact be MDR-TB from the outset. Therefore, the study sought to determine the prevalence of MDR-TB among the TB cases enrolled at various TB centers in the Telangana state of India. The study identifies and evaluates the susceptible risk factors for MDR - TB in order to overcome the barriers in effective TB control and treatment.

MATERIALS AND METHODS

The study was a Retro-Prospective Observational study and was carried out for a period of 9 months at the Government TB hospitals in Telangana state. During the study period, the data was collected as and when TB cases were reported at the hospital and on follow-up visits as well. The study criteria was set; the inclusion criteria include both the genders and diagnosis by line probe assay where as the exclusion criteria include more than two co-morbidities, newly diagnosed TB cases and diagnosis by liquid culture test. The data was collected through the data collection forms designed for the recording of only those parameters essential to establish the objectives of the study. The results were then obtained after filtering for the required data, and after applying the statistics (prevalence, percentage and ratio).

RESULTS

It is a retrospective and prospective observational study in which we were able to identify and evaluate the criteria for MDR-TB in the TB population of Telangana state. Total number of TB cases (N=2033) enrolled in the study during the study period were again categorized according to age-groups, gender, TB center, drug resistance and MDR-TB suspect criteria. The percentages & ratios were calculated and the most susceptible MDR-TB criteria were established.

Table 1 Gender Wise Prevalence

SEX (n)	MDR TB	NON-MDR TB
Male (1641)	355 (21.63%)	1286 (78.37%)
Female (392)	98 (25.00%)	294 (75.00%)
Total	453	1580

The population having been divided into two groups; males and females, the gender-wise prevalence was found to be as follows: Out of the total 1641 males, 355 (21.63%) were MDR TB cases and 1286 (78.37%) were Non-MDR TB cases. Out of the total 392 females, 98 (25.00%) were MDR TB cases and 294 (75.00%) were Non- MDR TB cases. On the whole, there were 453 MDR TB cases and 1576 Non-MDR TB cases.

Considering the above results, both males and females are at equal risk to develop MDR TB.

Table 2 Age Wise Prevalence

AGE (n)	MDR TB	NON-MDR TB
<40 years (1046)	236 (22.56%)	810(77.44%)
41- 60 years (822)	183 (22.26%)	639 (77.74%)
>61 years (165)	34 (20.61%)	131 (79.39%)
Total	453	1580

The population having been divided into three age groups;< 40 years, 41 to 60 years, and > 61 years, the age-wise prevalence is as follows in the above mentioned age groups. In the < 40 years age group, the total number of MDR TB cases are 236 (22.56%) and the total number of Non - MDR TB cases are 810 (77.44%). In the 41 to 60 years age group, the total number of MDR TB cases are 183 (22.26%)and the total number of Non - MDR TB cases are 639 (77.74%). In the > 61 years age group, the total number of MDR TB cases are 34 (20.61%) and the total number of Non - MDR TB cases are 131 (79.39%). Considering the above results, all age groups are at equal risk to develop MDR TB.

Table 3 Area Wise Prevalence

AREA (n)	MDR TB	NON-MDR TB
Warangal (610)	136 (22.30%)	474 (77.70%)
Karimnagar (565)	144 (25.49%)	421 (74.51%)
Khammam (444)	98 (22.07%)	346 (77.93%)
Badrachalam (244)	47 (19.26%)	197 (80.74%)
Nizamabad (170)	28 (16.47%)	142 (83.53%)
Total	453	1580

The population having been divided into two groups; MDR TB and Non-MDR TB. The district-wise prevalence is as follows: In Warangal, out of the suspected 610, the number of MDR TB patients are 136 (22.30%) and the number of Non - MDR TB patients are 474 (77.70%). In Karimnagar, out of the suspected 565, the number of MDR TB patients are 144 (25.49%) and the number of Non - MDR TB patients are 421 (74.51%). In Khammam, out of the suspected 444, the number of MDR TB patients are 98 (22.07%) and the number of Non - MDR TB patients are 346 (77.93%). In Badrachalam, out of the suspected 244, the number of MDR TB patients are 47 (19.26%) and the number of Non - MDR TB patients are 197 (80.74%). In Nizamabad out of the suspected 170, the number of MDR TB patients are 28 (16.47%) and the number of Non-MDR TB patients are 142 (83.53%). The total number of MDR TB cases are 453 and Non - MDR TB cases are 1576.

Table 4 Criteria Wise Prevalence

CRITERIA (n)	MDR TB	NON-MDR TB	Ratio
Failure (60)	17 (28.33%)	43 (71.67%)	1:2.5
Re-treatment case S+ at 4th month (19)	11 (57.89%)	8 (42.11%)	1:0.7
Contact of known MDR TB case (18)	8 (44.44%)	10 (55.56%)	1:1.2
S+ at diagnosis, re-treatment case (1307)	291 (22.26%)	1016 (77.74%)	1:3.4
Any follow up S+ (334)	84 (25.15%)	250 (74.85%)	1:2.9
S- at diagnosis, re-treatment case (69)	10 (14.49%)	59 (85.51%)	1:5.9
HIV TB Case (226)	32 (14.16%)	194 (85.84%)	1:6.0
Total	453	1580	1:3.4

According to the 7 MDR TB suspect criteria, the number of MDR TB cases and the number of Non - MDR TB cases are as follows. Out of the total number of 60 Failure cases, 17 (28.33%) were MDR TB cases and 42 (71.67%) were Non - MDR TB cases. Out of the total number of 19 Re-treatment

case S+ at 4th month cases, 11 (57.89%) were MDR TB cases and 8 (42.11%) were Non - MDR TB cases. Out of the total number of 18 Contact of known MDR TB cases, 8 (44.44%) were MDR TB cases and 10 (55.56%) were Non - MDR TB cases. Out of the total number of 1307 S+ at diagnosis, re-treatment cases, 291 (22.26%) were MDR TB cases and 1016 (77.74%) were Non - MDR TB cases. Out of the total number of 334 Any follow up S+ cases, 84 (25.15%) were MDR TB cases and 250 (74.85%) were Non- MDR TB cases. Out of the total number of 69 S- at diagnosis, re-treatment cases, 10 (14.16%) were MDR TB cases and 59 (85.51%) were Non - MDR TB cases. Out of the total number of 226 HIV TB cases, 32 (14.16%) were MDR TB cases and 194 (85.84%) were Non - MDR TB cases.

Given the number of 'Failure' cases, for every three Non-MDR TB cases there is one MDR TB case. Given the number of 'Re-treatment case S+ at 4th month cases, the ratio of MDR TB cases: Non-MDR TB cases is 1:1. Given the number of 'Contact of known MDR TB' cases, the ratio of MDR TB cases to Non-MDR TB cases is 1:1. Given the number of 'S+ at diagnosis, re-treatment' cases, for every three Non-MDR TB cases there is one MDR TB case. Given the number of 'Any follow up S+' cases, for every three Non-MDR TB cases there is one MDR TB case. Given the number of 'S- at diagnosis, re-treatment' cases, for every six Non-MDR TB cases there is one MDR TB case. Given the number of 'HIV TB' cases, for every six Non-MDR TB cases there is one MDR TB case. Given the total number of suspected cases, for every 3 Non-MDR TB cases, there is one MDR TB case.

DISCUSSION

Multi Drug Resistant (MDR) TB is a condition caused when a TB patient develops resistance to Isoniazid or Rifampicin or both.

According to a study conducted in Milan, Italy in the years 2000 to 2010, a retrospective evaluation (Alice Repossi *et al*, 2011) was done to identify risk groups for MDR TB and to limit its transmission. In our study, it was concluded both males and females are at equal risk to develop MDR TB. This finding opens important questions about equal access to health care and for targeted studies.

According to a study conducted on MDR-TB in children with evidence from global surveillance (Matteo Zignol *et al*, 2013), MDR-TB can affect persons of any age, but it remains unknown whether children are more or less likely than adults to have MDR-TB. Representative drug resistance surveillance data reported to the World Health Organization between 1994 and 2011 (Alena Skrahina *et al*, 2013) were analyzed to test the association between MDR-TB and age group (children aged >15 years versus adults), using odds ratios derived by logistic regression with robust standard errors. In our study all age groups are at equal risk to develop MDR TB.

A study was conducted in Belarus (Alena Skrahina *et al*, 2013) to identify the associated risk factors, 1420 TB patients were screened and 934 new and 410 previously treated TB cases were selected. The risk factors identified to have a strong

association with MDR-TB was found to be re-treatment cases, HIV infection, and history of imprisonment physical disability, alcohol abuse and smoking. In our study, the risk was found to be high in Re-treatment case S+ at 4th month and Contact of known MDR TB shown higher risk for MDR-TB.

According to a study conducted by the department of Microbiology, Armed Forces Institute of Pathology, Rawalpindi, Pakistan (Tahir Ghafoor *et al*, 2014) drug susceptibility testing (DST) was performed for first line agents namely INH, RIF, STR and ETH. A total of 4050 samples was tested out of which 689 (17%) were culture positive. Out of these culture-positive cases, 303(44%) were pan sensitive, 52 (7.5%) pan-resistant, 84 (12.2%) sensitive to one drug only, 171 (24.8%) resistant to one drug only and 49 (7.1%) were resistant to 2 drugs other than MDR-TB cases that were 132 (19.16%) in number. In our study, the total number of MDR TB cases were 453 (sum of cases resistant to one drug and two drugs) and Non - MDR TB cases were 1576. The highest prevalence of MDR TB cases was found in Karimnagar (144) followed by Warangal (136) and then followed by Khammam (98).

CONCLUSION

Thus the study concludes that the risk for MDR-TB was found to be equal in both genders and all age groups with criteria such as Re-treatment case S+ at 4th month and Contact of known MDR TB showing higher risk for MDR-TB. When such high-risk criteria for MDR TB and risk groups- gender, age and area-wise are identified, measures can be undertaken to eradicate the barriers of effective TB control and treatment.

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How to cite this article:

Venkateswarlu K *et al.*, Identification And Evaluation Of Susceptible Risk Factors For Multi Drug Resistant Tuberculosis. *International Journal of Recent Scientific Research* Vol. 6, Issue, 8, pp.5976-5979, August, 2015
