A RETROSPECTIVE STUDY RISK FACTOR ANALYSIS IN MDR TB CASES AMONG RURAL POPULATION OF THANJAVUR MEDICAL COLLEGE AND HOSPITAL, THANJAVUR, TAMILNADU

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ABSTRACT

BACKGROUND

Drug resistance in tuberculosis is one of the major problems worldwide. There is an estimated 99,000 annual incident cases of MDR-TB in India. MDR-TB poses therapeutic and treatment challenges with significantly higher rates of morbidity and mortality. It is easy to prevent multidrug resistant tuberculosis if the risk factors are known.

The aim of the study is to evaluate the risk factors in MDR TB cases among rural population of Thanjavur district, Tamilnadu, India.

MATERIALS AND METHODS

The medical record of patients with multidrug resistant tuberculosis diagnosed as per RNTCP DOTS PLUS guidelines admitted for pretreatment evaluation in DOTS PLUS centre, Thanjavur Medical College, were examined. These cases were diagnosed or registered during Jan-2015 to Dec-2015. All selected patients were categorized into four groups: Below 30 years, 31-40 years, 41-50 years, 51-60 years and above 60 years. The variables analysed include age, gender, site of the disease, personal history regarding alcoholism & smoking were recorded. Previous treatment history and default status were analysed. Each potential risk was evaluated using Univariate Conditional Logistic Regression Model / Chi-Square test.

RESULTS

Of the 96 cases studied, default majority were males (85.4%), predominant age groups 41-60 (51.1%). alcoholism (57.3%) were found to be the risk factors for drug resistance in tuberculosis. There is significant association between previous treatment and age group. Drug intolerance, default & relapse were more common in 41-60 age groups. Alcoholism plays a role in treatment failure and default.

CONCLUSION

Male gender, adult age groups (41-60), alcoholism, were the significant risk factors for MDR TB in our study and it showed statistical significance of $p<0.05$. On analysis of the risk factors, alcohol abuse was found to be the major behavioural risk factor for treatment default. Hence alcohol deaddiction could be included as an essential programme in DOTS plus strategy. Since people between age groups 41-60 were also found to be major defaulters, they should be educated about regular intake of ATT, drug toxicity, diet schedule and emergence of multidrug resistance and regular follow up. Drug intolerance symptoms like vomiting and giddiness need to be managed appropriately with due care.

KEYWORDS

Retrospective Observational Study.

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BACKGROUND

Globally in 2015 there was an estimated 480,000 new cases of MDR-TB and an additional 100,000 people have been found to be rifampicin resistant TB (RR-TB)[1], thus bringing total of 580,000 cases of MDR TB. Of this MDR TB globally XDR TB constitutes 9.7 %.

The emergence and spread of MDR-TB is threatening to destabilize global TB control.[2] WHO estimates 60% cases are in India, china, Brazil and Russia.

Based on the estimates reported in global TB report 2016, the burden of both TB and MDR TB is highest in India. India has the second highest burden of MDR-TB in the world next to China. Of the MDR TB cases in India 79,000 emerge from pulmonary[3] TB patients as per the current year status. The absence of surveillance[4] network and lack of reliable prevalence studies make it difficult to evaluate the true extent of MDR-TB in India.

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To detect drug resistance, Drug susceptibility testing (DST) is done. DST is done in all retreatment cases at diagnosis, any sputum smear positive person during follow up, cases at diagnosis, contacts of confirmed MDR-TB cases, and HIV associated TB. WHO recommends sputum examination by LED microscopy[5] over conventional microscopy.

RNTCP is implementing DOTS PLUS facility in our country to control MDR-TB burden since October 2007. Previous treatment[6] for TB is the strongest risk factor for the development of MDR-TB. One should analyse each and every risk factor for MDR TB to reduce the overall burden. Previous treatment history and default status were analysed. Treatment naïve patients are also at risk due to either spontaneous mutations or transmission of resistant strains.

Aims and Objectives

To evaluate the risk factors in MDR TB cases among rural population of Thanjavur district, Tamilnadu, India.

Tuberculosis (TB) and diabetes mellitus were individually one of the top ten cases of mortality all over the world.[7] Drug resistance tuberculosis (DR TB) has challenged all the aspects of tuberculosis management, from diagnosis till prognosis.

MDR-TB (multi drug resistant tuberculosis) is defined as isolates of mycobacterium tuberculosis resistant to isoniazid and rifampicin with or without resistance to other antituberculosis drugs.[8]

Risk factors

Primary Resistance- An inherent resistance of acid fast bacilli (AFB) to an agent may exist, which is called primary resistance.

Secondary Drug Resistance

If ATT mono therapy or the regimen is inappropriate, it leads to secondary drug resistance. This patient can spread resistant disease to contacts, that can develop primary drug resistant disease in them.

Immunology of MDR TB

There is a possibility of genetic predisposition of the bacteria to being resistant to the anti TB drugs by-

1. Point mutation in IFN-g receptor gene located on chromosome 6q.
2. Absence of IFN-g receptor 1 on cell surfaces

MATERIALS AND METHODS

The medical records of 96 patients with MDR TB were diagnosed and registered during Jan 2015 to Dec 2015 who came to Thanjavur Medical College Hospital, Thanjavur. These patients had drug resistant to first line anti tuberculosis drugs (isoniazid and rifampicin). Ages were categorized in to groups- Below 30 years, 31-40 years, 41-50 years, 51-60 years and above 60 years. The following signs are evaluated as treatment failure in MDR-TB. They include persistent positive smears or culture, after two months of treatment, progressive extensive and bilateral lung disease on chest X-ray with no options for surgery, overall deteriorating clinical conditions that usually include weight loss, and respiratory insufficiency. Mode of TB diagnosis, Treatment history in detail; initiation of ATT at private DOTS centre, default statistics during the course of treatment were assessed. Reasons for default was noted including analysis by sex, age group and behavioural pattern including smoking and alcoholism.

Results of bio clinical analysis of blood for surgery, sputum AFB smear, AFB culture and sensitivity pattern were noted. Reports of chest X-ray, CT chest were analysed. Any associated immunological investigations were noted. MDR Tb was confirmed by CBNAAT and Line probe assay as per RNTCP guidelines issued by Govt. of India & Central TB control Division.

MDR TB was evaluated by univariate conditional logistic regression model.

RESULTS

Of the 96 cases studied, among the defaulters, these are the following observations, males (85.4%), predominant age groups 41-60 (51.1%). alcoholism (57.3%), were found to be the major risk factors for drug resistance in tuberculosis. Drug intolerance, default & relapse were more common in 41-60 age groups. Alcoholism plays a role in treatment failure and default. Of the 96 cases defaulters constitutes 28, treatment failure - 54 and relapse – 14. Each potential risk had been evaluated by Univariate conditional logistic regression model / Chi-Square test.

	q14a-PREVIOUS TREATMENT (Reason for default)														Statistical Inference
	NA		Alcoholic		Drug Adverse Effects		Native Treatment		Occupation		private Treatment		Total		
	(n=22)	(100%)	(n=36)	(100%)	(n=20)	(100%)	(n=3)	(100%)	(n=11)	(100%)	(n=4)	(100%)	(n=96)	(100%)	
Male	18	81.8%	36	100.0%	16	80.0%	3	100.0%	7	63.6%	2	50.0%	82	85.4%	X^2=15.575 Df=5.008<0.05 Significant
Female	4	18.2%	0	.0%	4	20.0%	0	.0%	4	36.4%	2	50.0%	14	14.6%	

Table 1. Sex

In our study, Out of 96 cases, 82 were male, constituting 85.4% with significant P = value < 0.05.

	q14a-Previous Treatment (Reason for Default)														Statistical Inference
	NA		Alcoholic		Drug Adverse Effects		Native Treatment		Occupation		Private Treatment		Total		
	(n=22)	(100%)	(n=36)	(100%)	(n=20)	(100%)	(n=3)	(100%)	(n=11)	(100%)	(n=4)	(100%)	(n=96)	(100%)	
Below 30 yrs.	7	31.8%	5	13.9%	1	5.0%	0	.0%	2	18.2%	0	.0%	15	15.6%	X^2=42.257 Df=20 .003<0.05 Significant
31 to 40 yrs.	5	22.7%	8	22.2%	1	5.0%	0	.0%	6	54.5%	1	25.0%	21	21.9%	
41 to 50 yrs.	1	4.5%	12	33.3%	12	60.0%	3	100.0%	3	27.3%	0	.0%	31	32.3%	
51 to 60 yrs.	4	18.2%	9	25.0%	3	15.0%	0	.0%	0	.0%	2	50.0%	18	18.8%	
Above 61 yrs.	5	22.7%	2	5.6%	3	15.0%	0	.0%	0	.0%	1	25.0%	11	11.5%	

Table 2. Age Wise

In our study MDR TB was predominant in the age group 41-60 years (51.1%) P= value < 0.05 deemed significant.

	q14a-PREVIOUS TREATMENT (Reason for default)														Statistical Inference
	NA		Alcoholic		Drug Adverse Effects		Native Treatment		Occupation		Private Treatment		Total		
	(n=22)	(100%)	(n=36)	(100%)	(n=20)	(100%)	(n=3)	(100%)	(n=11)	(100%)	(n=4)	(100%)	(n=96)	(100%)	
No	20	90.9%	0	.0%	9	45.0%	1	33.3%	8	72.7%	3	75.0%	41	42.7%	X2=53.632 Df=5 .000<0.05 Significant
YES	2	9.1%	36	100.0%	11	55.0%	2	66.7%	3	27.3%	1	25.0%	55	57.3%	

Table 3. Behavioural Pattern – (a)- Alcoholism

Among the behavioural patterns, alcoholism contributed (57.3 %) as the major risk factor for MDR TB P= value was < 0.05 showed significant.

	q14a-PREVIOUS TREATMENT (Reason for default)														Statistical Inference
	NA		Alcoholic		Drug Adverse effects		Native Treatment		Occupation		Private Treatment		Total		
	(n=22)	(100%)	(n=36)	(100%)	(n=20)	(100%)	(n=3)	(100%)	(n=11)	(100%)	(n=4)	(100%)	(n=96)	(100%)	
No	17	77.3%	13	36.1%	11	55.0%	1	33.3%	6	54.5%	2	50.0%	50	52.1%	X2=9.798 Df=5 .081>0.05 Not Significant
YES	5	22.7%	23	63.9%	9	45.0%	2	66.7%	5	45.5%	2	50.0%	46	47.9%	

(b)- Smoking

In our study smoking was not found to be a risk factor for MDR TB.

DISCUSSION

Sex

In our study, Out of 96 cases, 82 were male, constituting 85.4% with significant P = value less than 0.05. In Addis Ababa,[9] a case control study. Male had higher incidence of MDR TB because of nonadherence to therapy. In a population based study conducted in republic of Georgia[10] previous TB treatment and female gender are important risk factors. An Ethiopia based study conducted in Amhara[11] National regional state, also showed female preponderance. An Ahmedbad[12] MDR TB, RNTCP study showed 2/3 rd of the study population were males.

Age

In our study MDR TB was predominant in the age group 41-60 years (51.1%) P= value < 0.05 deemed significant. In a Mumbai[13] based RNTCP study, risk of MDR seems to be higher among elderly>45 yrs. In a case control Bangladesh[14] based MDR TB study, majority were aged between 18-45 years. An epidemiological study of MDR-TB under RNTCP of Ahmedabad city.[12] showed MDR TB was common among 16-45 years aged males.

Alcohol Abuse

Among the behavioural patterns, alcoholism contributed (57.3 %) as the major risk factor for MDR TB P= value was <0.05 showed significant. An Egypian[15] study, showed cigarette smoking as the most frequent risk factor. Harrison's principles of Internal medicine stresses about, alcoholism as a risk factors & hence educating the alcoholic patients about drug induced hepatitis and to do monthly monitoring of amino transferases[16] level. Based on RNTCP guidelines one should do base line LFT before starting ATT, provided there are no risk factor. If the patient has abnormal base line elevation of transaminases level and those with risk factors for DILI[17] (Drug induce liver injury) should be monitored by repeat LFTs.

CONCLUSION

Of the 96 cases studied, reasons for default being majority were males.

Predominant age groups fall in 41-60 years. Alcoholism plays a role in treatment failure and default. All three showed statistical significance that is P value < 0.05.

MDR-TB poses therapeutic and treatment challenges with significantly higher rates of morbidity and mortality early detection and effective treatment of source of infection[18] is crucial in reducing DR-TB transmission.

Unavailability of proper laboratory setup[19] at the gross root level was the most probable reason for MDRTB.

The major advantage of genexpert[20] is that it allows for the rapid initiation of second line drugs while awaiting DST culture.

Having more than one PTB episode and non-adherence to first line ATT had a significant association with MDR-TB. Patients with ≥2 previous[21] episodes of PTB had a risk for development of MDR-TB.

The commonest side effects of prescribed drugs are GI disorders[15] (vomiting, nausea, gastritis).

Adverse[22] effects of anti-TB medication were associated with MDR-TB among previously treated TB patients.

It is easy to prevent MDR TB if the risk factors are known. By doing this study we would be able to identify risk factors for MDR-TB, cause for failure, default, and relapse and identify people at risk population there by able to find methods to prevent transmission and control of MDR-TB.

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