COMPARISON OF PREDISPOSING FACTORS FOR THE DEVELOPMENT OF DRUG SUSCEPTIBLE AND DRUG RESISTANT PULMONARY TB RE-TREATMENT CASES

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ABSTRACT

BACKGROUND

At present, multidrug resistant (MDR-TB) is a challenge in global efforts to prevent and control tuberculosis. WHO reports estimate that 3.5% of newly diagnosed TB patients and 20.5% of previously treated patients had MDR-TB.[1,2] Known risk factors for emergence of MDR TB include age, sex, number of times exposed to ATT treatment, HIV status and alcoholism.[3,4,5]

The aim of the study is to compare the predisposing factors towards the development of drug susceptible and drug resistant PTB among retreatment cases.

MATERIALS AND METHODS

This study was conducted among 300 retreatment pulmonary tuberculosis patients attending Government Hospital of Thoracic Medicine, Tambaram sanatorium from 2016-18. 150 patients each of drug (Rifampicin) sensitive and drug resistant (Rifampicin) TB diagnosed by CBNAAT were selected by simple random sampling. Detailed data including demographic particulars, treatment history, personal history, HIV status were collected using a standardised questionnaire and the results were statistically analysed.

RESULTS

Age >45 years, male sex, lower educational status, history of treatment interruption, HIV positive status, smoking and alcoholism were found to have a statistically significant correlation with the development of drug resistant TB.

CONCLUSION

Several factors contribute to the development of drug resistant tuberculosis. If the goal of eliminating TB by 2025 is to be achieved, the focus should be on the prevention of development of drug resistant TB by ensuring that patients take full course of treatment properly the first time. Knowledge of factors associated with drug resistant TB will help us to plan better intervention strategies such as pretreatment counselling, smoking and alcohol cessation clinic.

KEYWORDS

Drug Resistant TB, Drug Susceptible TB, MDR TB, Contributing Factors.

BACKGROUND

Multiple drug-resistant tuberculosis[1] (MDR-TB) is emerging as a growing threat to TB control programs in many countries and accounts for 3.5% of all newly diagnosed patients worldwide. The potentially serious impact of MDR-TB (TB strain resistant to at least isoniazid and rifampicin) has long been recognized; drug resistance is a major threat to tuberculosis (TB) control programs worldwide. Multidrug resistant TB (MDR-TB) is defined as a simultaneous resistant to at least rifampicin (RMP) and isoniazid (INH). Patients infected with MDR strains have less chance to be cured from TB particularly if they are co-infected with HIV or suffer from other immunosuppressive diseases. MDR-TB is associated with a two to four-fold period of treatment, psychological problems, economic wastage, poor treatment adherence and consequently treatment failure.[4]

Globally, 3.5% of new TB cases and 20.5% of previously treated cases are estimated to have MDR-TB.[2] In developing countries, due to poverty, migration and HIV infection, MDR-TB is associated with widespread and persistent high incidence. However, the problem is of special concern because of expensive treatment, with only 65%-75% of success, and many have side effects.[6]

In perspective of the public health, a study on the identification of risk factors linked to MDR-TB at the onset of therapy, among new cases is important to identify patients vulnerable to getting infection with MDR-TB strains. This is necessary for breaking the transmission cycle of MDR-TB.

This may further reduce the cost of treatment and improve the implementation of the DOTS- based RNTCP.

Incomplete and inadequate treatment is the most powerful predictor of the presence of MDR TB.[6,7] Risk factors leading to incomplete and inadequate treatment include migration, male sex, history of smoking and alcoholism, comorbidities including HIV. Identifying these risk factors early will help to eliminate the burden of tuberculosis and focus our strategies towards the goal of eliminating TB by 2025.

Aim of the Study
To compare the predisposing factors for the development of drug susceptible and drug resistant PTB among retreatment cases

MATERIALS AND METHODS
This study was conducted among 300 retreatment pulmonary tuberculosis patients attending Government hospital of Thoracic medicine, Tambaram sanatorium from 2016-18. 150 patients each of drug (Rifampicin) sensitive and drug resistant (rifampicin) TB diagnosed by CBNAAT were selected by simple random sampling. Detailed data including demographic particulars, treatment history, personal history, HIV status were collected using a standardised questionnaire and the results were statistically analysed

RESULTS
300 patients with history of previous treatment were enrolled for the study. 150 from drug (Rifampicin) sensitive TB group and 150 from drug (Rifampicin) resistant group selected by simple random sampling. Using a preformed standardised questionnaire data was collected including demographic profile, educational status, previous treatment history of tuberculosis, comorbidities - Diabetes mellitus and HIV status, personal history of smoking and alcoholism and X-ray finding of cavitation. The results were tabulated and analysed using a SPSS software.

SL.NO.	Variable		Drug resistant group (n=150) Freque ncy	Drug resistant group (n=150) Proport ion	Drug sensitive group (n=150) Frequ ency	Drug sensitive group (n=150) Proport ion
1.	Age Group	≥45 years	102	68%	78	52%
		<45 years	48	32%	72	48%
2.	Sex	Male	104	69.3%	114	76%
		Female	46	30.7%	36	24%
3.	Education	Illiterate	82	54.6%	48	32%
		Literate	68	45.3%	102	68%
4.	Treatment History	New case	6	4%	0	0%
		Defaulter	91	60.6%	111	74%
		Relapse	41	27.3%	34	22.6%
5.	Diabetes history	+	48	32%	32	21.3%
		-	102	68%	118	78.6%
6.	HIV status	+	8	5.3%	7	4.6%
		-	142	94.7%	149	99.3%
7.	Alcohol history	+	76	50.6%	42	28%
		-	74	49.4%	108	72%
8.	Smoking history	+	40	26.6%	25	16.6%
		-	110	73.3%	125	83.3%
9.	Cavitation	+	43	28.6%	23	15.3%
		-	107	71.3%	127	84.6%

Table 1. Master Chart Showing the Demographic Profile, Education, Personal History of the Patients

This table shows that the age group of patients was higher in the drug resistant TB group and most were males. Also, patients in the drug resistant group had less education compared to the sensitive group. History of treatment interruption was higher in the drug resistant TB group. DM was higher in this group of patients as was smoking and alcoholism.

SL.NO	Variable		Drug resistance group (n=150) Frequency	Drug resistance group (n=150) Proportion	Drug sensitive group (n=150) Frequency	Drug sensitive group (n=150) Pro portion
1.	Defaulter frequency	>1	74	82.2%	28	25.2%
		≤1	17	18.8%	83	74.7%

SL.NO.	Variable		Drug resistant group (n=91)	Drug sensitive group (n=111)	Chi square test P value	Odds ratio with confidence limits
1.	Defaulter frequency	>1	74	28	0.00	12.7 (6.5 – 25.6)
		≤1	17	83		

Table 2. Shows Frequency of Treatment Interruption and Higher Odds of Developing Drug Resistant TB with Treatment Interruption

SL.NO	Variable		Drug resistant group (n=150)	Drug sensitive group (n=150)	Chi square test P value	Odds ratio with confidence limits
1.	Age Group	≥45 years	102	78	0.00	2.29 (1.43 – 3.68)
		<45 years	48	72		
2.	Sex	Male	104	84	0.01	1.77 (1.10 – 2.86)
		Female	46	66		
3.	Education	Illiterate	82	48	0.00	2.55 (1.59 – 4.1)
		Literate	68	102		
4.	Treatment History	New case	6	0	0.009	
		Defaulter	91	111		
		Relapse	41	34		
5.	Diabetes history	+	48	32	0.03	1.73 (1.03 – 2.93)
		-	102	118		
6.	HIV status	+	8	7	0.01	8.39
		-	142	143		
7.	Alcohol history	+	76	42	0.00	2.6 (1.6 – 4.2)
		-	74	108		
8.	Smoking history	+	40	25	0.03	1.8 (1.0 – 3.2)
		-	110	125		
9.	Cavitation	+	43	23	0.00	2.21 (1.25 – 3.95)
		-	107	127		

Table 3. Shows that the Odds of Developing Drug Resistant TB are Higher in Age >45 Years, Male Sex, Lower Education Status, Previous History of Treatment Interruption, Comorbidities Like DM, HIV, Smoking and Alcoholism Status

DISCUSSION
GHTM, Tambaram sanatorium is a tertiary referral centre for patients with all forms of tuberculosis and serves as a nodal centre for the treatment of drug resistant tuberculosis.

On a daily basis we encounter many patients who attend GHTM with history of discontinuation of ATT. This poses a challenge in achieving the goal of END TB strategy as these patients continue to spread the disease in the community and also pose a problem of likelihood of

developing drug resistance. Strong systems to detect, successfully treat and ensure long term disease free status of TB patients are required to prevent emergence of resistance.[1] Basic diagnostic and treatment services in conjunction with ensuring that patients complete the treatment without interruption should receive priority if we are to achieve the dream of TB free India by 2025.

Knowledge of the factors leading to the development of drug resistance will be useful for long term planning to eliminate the factors leading to development of drug resistance and thereby reduce the spread of drug resistance in the community.

In accordance to the studies cited[8,9,10] we too found that higher age group, male sex are factors leading to development of drug resistance. This could be due to factors such as migration and also because of work related issues in the productive age group. Since most DOTS centres function in the morning hours, patients may be finding it difficult to collect the drugs in these hours. Planning the drug delivery models to ensure better accessibility to the patients may be useful in improving the compliance to treatment in patients on anti-tuberculous therapy.

Our study revealed that the odds of developing a drug resistant TB was higher in the lower educational group which shows that better pretreatment counselling is needed for these group of patients so that they understand the need for proper compliance to treatment and the need for completing the full course of treatment.

This study also showed that the odds of developing resistance was higher in patients with history of treatment interruption stressing on the need for pretreatment counselling and ensuring adequate and uninterrupted treatment in the first instance when the diagnosis of tuberculosis is made.

This study showed that development of drug resistance was higher in patients with Diabetes mellitus and HIV patients which could be due to several factors such as lower immunity of these patients and greater bacterial load. Hence there is a need to screen these patients regularly for TB and also ensure adequate treatment in this patient group.

Smoking history and history of alcoholism showing a higher predisposition to development of drug resistance shows the need to focus on smoking and alcohol deaddiction clinics to reduce the possibility of treatment interruption and thereby prevent the emergence of drug resistance.

Cavitation was another factor considered since these cavities harbour a greater number of organisms and are likely to favour the development of drug resistance.

Thus, our study identified several factors in the drug resistant TB group when compared to the drug sensitive TB group viz higher age group, male sex, lower education, presence of comorbidities like Diabetes and HIV positive status, smoking and alcohol consumption and presence of cavitation in CXR as risk factors for development of drug

resistant tuberculosis. Early identification and steps to mitigate these factors such as better control of Diabetes and viral suppression in HIV may play a vital role in ensuring the prevention of emergence of drug resistance.

Need for pretreatment counselling and smoking cessation therapy and alcohol deaddiction clinics is emphasised.

CONCLUSION

Several social and medical factors contribute to the development of drug resistance. This study identified higher age group, male sex, lower education status, smoking and alcoholism, previous treatment interruption, comorbidities like DM and HIV, and presence of cavitation in chest radiograph as risk factors for the development of drug resistant tuberculosis. Identification of these risk factors and steps to mitigate these may help to reduce the emergence of drug resistant strains and prevent the spread of such bacilli in the community.

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