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Original Research Paper

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PSYCHIATRIC DISORDERS IN PATIENTS RECEIVING TREATMENT FOR DRUG RESISTANT TUBERCULOSIS REGISTERED UNDER DR-TB CENTRE IN A TERTIARY CARE HOSPITAL

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ABSTRACT

BACKGROUND: The emergence of drug resistant mycobacterium has become a significant public health problem creating an obstacle to effective Tuberculosis (TB) control. Psychiatric disorder can either be induced by treatment regimens or psychosocial factors. Cycloserine administration is frequently reported to be associated with psychiatric disorders. In this study, we have examined the prevalence and characteristics of psychiatric disorders among patients receiving treatment for Drug Resistant TB registered in a tertiary care hospital

Aims and Objectives- To evaluate the psychiatric disorders of patients receiving intensive phase treatment of Multi Drug Resistant Tuberculosis (MDR) and Extensively Drug Resistant Tuberculosis (XDR) as per WHO-UMC Causality Assessment Scale.

METHODS: 76 patients of MDR and XDR Tuberculosis were admitted in DR-TB (Drug Resistant TB) centre, Burdwan Medical College and Hospital and the adverse drug reaction profile particularly the psychiatric symptoms of 2nd line drugs were analysed during the intensive phase for a year after fulfilling the inclusion and exclusion criteria. Treatment was given as per guidelines by Revised National TB Control Program PMDT (Programmatic management of drug-resistant TB).

RESULTS: Psychiatric disorders were found in 8(10.5%) patients among whom suicidal attempt 3(3.9%) and depression 3(3.9%) were the most common followed by paranoia and hallucination in 1 patient each.

CONCLUSIONS: The psychiatric reactions were common in the later phase of the regimen and in patients with BMI ≤18. Hence vigilant monitoring is required for these types of patients throughout the course of treatment and sputum smear and culture conversion is very well correlated with clinical and radiological improvement.

KEYWORDS : Psychosis, DR TB, Cycloserine, Depression, Hallucination.

BACKGROUND

Mycobacterium tuberculosis (M. tuberculosis) is an ancient human pathogen, which has plagued countless human societies despite the introduction of curative and preventive therapy in the last century. In recent years, international attention has turned toward the evolving burden of drug resistance. Multi-drug resistant tuberculosis (MDR TB) has emerged in epidemic proportions in the wake of widespread HIV infection in the world's poorest populations, including sub-Saharan Africa. Extensively drug-resistant TB (XDR TB) was first reported in 2006 but has now been documented on six continents[1]. These trends are critically important for global health, since drug-resistant TB mortality rates are high and second and third-line agents for the treatment of drug-resistant TB are less potent and less tolerable than first-line therapies.

Drug resistant tuberculosis (DR-TB) poses a great threat to the eradication of TB. Therefore, preventing the disease is the key to saving lives and resources. Social and behavioural variables play a big part in this prevention. It is important to determine the social factors that may lead to DR-TB in order to set up prevention programs and more efficient treatment regimens Drug resistance in tuberculosis is a global problem and India is no exception to this. However, this rise is mainly among the previously treated cases as previous anti-tuberculosis therapy is the single most important risk factor for the development of drug resistance. The worldwide prevalence of drug resistant tuberculosis is on the rise and multiple studies give varying data regarding the adverse drug reaction of multi drug resistant tuberculosis. This study was taken up to determine the adverse drug reactions profile of a patient, previous history of anti tubercular drug intake and pattern of drug resistant. Globally, 5% of TB cases were estimated to have had MDR-TB in 2013 (3.5% of new and 20.5% of previously treated TB cases). Drug resistance surveillance data show that an estimated 480,000 people developed MDR-TB in 2013 and 210,000 people died. Extensively drug-resistant TB (XDR-TB) has been reported by 100 countries in 2013. On average, an estimated 9% of people with MDR-TB have XDR-TB[2].

WHO 2014 Global report on tuberculosis- 97,000 patients were started on MDR-TB treatment in 2013. 2nd line drugs have a lot of side effects.

In India, the prevalence of multi-drug resistant TB (MDR-TB), defined as resistance to Isoniazid and Rifampicin with or without resistance to other drugs, is found to be at a low level in most of the regions. Data from several studies conducted by TRC and NTI, have found MDR-TB levels of less than 1% to 3% in new cases and around 12% in re-treatment cases[3,4]

The disease is not only medical problem or a public health problem but is also a critical social problem of great magnitude. Base line and adequate information on adverse drug reactions profile of 2nd line drug in MDR and XDR TB, is required for its control and effective treatment. Psychiatric disorder can either be induced by treatment regiments or psychosocial factors. Cycloserine administration is frequently reported to be associated with psychiatric disorders.[9]

India may be considered as one of the global epicentre of TB including the drug resistant one and many patients are being treated with second line anti-TB drugs. However, there is limited data on psychiatric disorders from the second line anti-TB drugs on the Indian patients. Indian patients are different from their global counterparts both by genetic structure and phenotype; hence prone to differ in anti TB drug action and pharmacokinetics also. Therefore, there is need for more data from the Indian patients related to second line anti-TB drugs including the psychiatric disorders. Hence, the present study was been planned to systemically generate and analyze the psychiatric disorders of the second line anti TB drugs on Eastern Indian patients.

METHODS

This cross sectional study was designed to include all patients

receiving treatment for Drug Resistant TB over a period of one year. So there was no prespecified sample size for this study. This study was conducted at DR-TB centre, Burdwan Medical College and Hospital. Permission of Institutional Ethics Committee was obtained for the study. Written informed consents were obtained from all participating patients. 75 patients were included in the study. They were followed every month for 6 (9) months in intensive phase after the start of 2nd line drugs and adverse drug reactions were recorded, as the maximum adverse reactions usually occur in this period. Treatment was given as per guidelines by Revised National TB Control Program PMDT (Programmatic management of drug-resistant TB) (Erstwhile DOTS Plus).[5]

Inclusion Criteria

1. Patient of age >18 years.
2. Both sexes.
3. Patients with proved drug resistant tuberculosis.

Exclusion Criteria

1. Patient admitted <7 days in DR-TB Centre.

Parameters studied include:

1. HB%, TC, DC, ESR
2. Blood urea, serum creatinine
3. Liver function test
4. FBS/PPBS
5. Sputum for AFB stain and gram stain
6. Line probe assay
7. Urine albumin, sugar and microscopy
8. Chest X-RAY PA view.

After selection of each patient on the basis of inclusion and exclusion criteria a written informed consent was taken. Data was collected using a pretested pro forma meeting the objectives of the study. Detailed history, physical examination and necessary investigations were undertaken. The purpose of the study was explained to the patient and informed consent obtained.

At the end of the study the data was complied, tabulated for analysis.

All the collected data were analysed by using SPSS version 16 statistical software. Descriptive statistics were applied to the data. All data were presented as number and percent. Chi Square Test and Fisher exact test were applied wherever applicable to find out statistical differences and p value <0.05 were considered statistically significant.

RESULTS

In our study among the 76 cases, most of them were pulmonary Tuberculosis (96%) whereas only 4% were Extra Pulmonary Tuberculosis. Majority were from age group 21-30 (44%), that is, the most productive age group of life. Majority 64% either studied upto 5th standard or are illiterate (Fig 1). Majority (95%) live in a Kuchcha house. 32% of patients were farmers, 23% were housewives and 12% were labourers. Most of them (84.2%) had no co morbidities but among the rest a significant number of patients (6.6%) had Diabetes Mellitus. Majority 67 out of 76 had a history of incomplete ATD intake (88.2%).

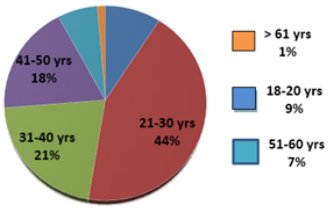

Figure 1. Distribution of Age Group in MDR and XDR TB Patients

Table 1: Psychiatric Disorders in Patients receiving treatment for DR TB

ADRs	Frequency(%)	Time interval after CAT IV/V regimen Month(m)
		Month(m)
Psychosis	8(10.5)	3.9%< 3 m,
Hallucination	1(1.3)	6.5%- 7 m
Suicidal attempt	3(3.9)	
Paranoia	1(1.3)	
Depression	3(3.9)	

Table 2: Action taken for Patients having psychiatric disorders after receiving DR TB treatment

Name of the ADRs	Action taken	Outcome	Suspected Drug(s)	WHO-UMC causality Assessment Scale
Psychosis	For 5(6.6%) pts Cs was replaced with PAS and ref to Psychiatrist.One pt replaced wth PAS no ref.2(2.6%) pt ref.to Specialist,in one pt reintroduce of Cs after 6 m symptoms reappeared.Cs replaced with PAS	6(7.9%) pts recovered fully,1(1.3%) pts partially recovered,1 pt outcome unknown as refusd treatment after 6 m	Cs,H,Mfx-1(1.3), Cs,Eto-1(1.3), Cs-6(7.9)	Cs-Certain-1 Cs-Probable-5 Cs-Possible-2 H-Possible Mfx-Possible Eto-Possible

DISCUSSION

The present study has found that the second line anti-TB drugs are prone to produce adverse drug reactions in almost every patient. In the later phase many patients suffered from psychiatric disorders. In our study psychosis was detected in some patients whereas in the study by Hire et al[6] psychosis was reported in fewer patients and in the study by Dela AI[7] psychosis was reported in more patients.

Table 2: Comparison of Various Studies Related to ADRs of 2nd Line Anti Tubercular Drugs

Names of ADRs	Our Study (n=76) (%)	Rohan Hire et al (Central India, n=110)[7] %	Dela AI (Gujarat, India n=72)[8] %
Psychosis	10.5	4.5	14.38

Cycloserine was replaced with PAS in a number of patients. There are several possible explanations for the differences in the number of patients requiring drugs to be replaced from the regimen. These include genetic and phenotypic differences of the patients of Eastern India as well as variation in ability of the health care workers to detect ADRs and provide management.

The major strength of the study was complete follow up of the patients for a long duration. The study also utilized the standard tools like WHO-Uppsala Monitoring Center tool for causality assessment which is simple and widely used worldwide. However, there were few weaknesses in the study. These include limited sample size, no formal sample size pre-estimation and possibility of under-reporting of psychiatric disorders.

CONCLUSIONS

Adverse Drug Reactions are common findings with second line anti TB drugs. Almost all major systems are affected by the ADRs due to these drugs though the large proportion is non-serious and self limiting. Psychiatric disorders usually cluster around later phase of treatment. Patients with low BMI are more prone to develop psychiatric disorders. On replacement

of Cycloserine with PAS most of the patients overcame the psychiatric disorders. However, there is need for further studies to explore the serious psychiatric disorders and validation of the present findings in larger sample population.

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