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ROLE OF PRIMARY MULTIDRUG RESISTANT TUBERCULOSIS IN THE TUBERCULOSIS MENACE

KEY WORDS: Tuberculosis, Primary Multi drug resistant tuberculosis

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ABSTRACT

Background: The gains of newer diagnostic techniques and drug therapies in tuberculosis have been negated by the emergence of drug resistant bacteria. Non-adherence to prescribed regimen and poor management are believed to be chief causes, but increasingly, rise of person to person transmission of resistant organisms is being reported.
Methodology: This cross-sectional study evaluated the proportion of Primary Drug Resistant Tuberculosis (PMDR-TB) and risk factors associated with it in 61 patients having Multi Drug Resistant TB (MDR-TB).
Results: 24 of 61 patients had PMDR-TB (39.34%), 16 (26.23%) were Recurrent Tuberculosis and 21 (34.43%) Treatment Failures. 8 patients (33.33%) with PMDR-TB gave contact history within family member/s.
Conclusion: Proliferation of PMDR-TB is a disconcerting reality, fuelling a cycle of higher prevalence causing increase spread of drug resistant organisms. Rigorous contact tracing and stringent infection control measures are required to curb this menace.

INTRODUCTION:

Tuberculosis (TB) continues to be a vexing health problem globally with more than 10 million new cases and 1.5 million deaths each year[1]. India is the highest contributor to the global TB burden at 27%, adding 26.9 lakh TB cases in 2019 [2]. The real threat is the spread of drug resistant TB (DR-TB) worldwide; with the most populous countries like India, China and Russian Federation accounting for almost 50% of the combined total new cases of Rifampicin resistant (RR-TB) and Multi drug resistant tuberculosis (MDR-TB) in 2018[1].

MDR-TB refers to tuberculous infection caused by acid-fast bacterial organisms resistant to at least two drugs, isoniazid and rifampicin. Acquired MDR-TB (AMDR-TB) refers to resistance developed during or following chemotherapy in patients who had previously been regarded as having drug sensitive TB. Thus the resistance that develops in a patient who has received prior TB chemotherapy is defined as AMDR-TB. Primary MDR-TB (PMDR-TB) characterizes patients of MDR-TB who have no prior TB treatment history or treatment of <1 month[3].

WHO estimates that globally 3.4% of new TB cases and 18% of previously treated cases had MDR-TB or RR-TB[1]. The First Indian National Anti-Tuberculosis Drug Resistance Surveillance (2014 – 2016) reported that MDR-TB among new patients was 2.84%, among previously treated patients 11.62%, and among all patients 6.19% [4]. However, the survey may have underestimated the true burden of resistance as it had several limitations like inclusion of only smear positive Pulmonary TB and non-involvement of the private health care sector. The general consensus in early 2000 was that poor patient management, nonadherence to the prescribed regimen, a poor national program or some combination of these three were the main causes of MDR TB. However, in recent years there seems to be an increase in occurrence of MDR TB in persons who have never taken treatment before i.e PMDR TB.

Many studies have reported an increase in the trend of anti TB drug resistance in India[5,6]. A study using the dynamic Markov model has predicted that if India's TB management practices remain unchanged there will be a gradual transformation from the current drug sensitive epidemic of TB to a drug resistant epidemic and by 2032, an estimated 85% of MDR-TB will be Primary MDR-TB[7]. The 2008 Chinese DR-TB National Survey had also suggested that more than 80% of MDR-TB cases resulted from transmission of resistant strains[8]. Considering the above facts, in this study we estimated the proportion of PMDR-TB in patients diagnosed with MDR-TB by Gene Xpert and MGIT Liquid culture with drug sensitivity testing (DST) and ascertained whether contact history had a significant role in drug resistant TB.

MATERIALS AND METHODS:

This is a cross-sectional study done in an urban tertiary care hospital in Western India over a period of around two years, in which patients diagnosed as MDR TB on the basis of GeneXpert and MGIT with DST were selected and a detailed questionnaire on demographic, clinical characteristics, past history and treatment history was collected. Chest X-ray, CBC, ESR, LFT, RFT, RBS were done in all patients. Wherever required, special investigations like HRCT, MRI, USG were performed. Sputum sample of pulmonary TB patients and FNAC or pus in EPTB patients was sent for Acid Fast Bacilli, GeneXpert, MGIT Liquid culture and DST.

RESULTS:

61 patients were diagnosed with MDR TB at our centre on the basis of GeneXpert and MGIT culture reports of Sputum samples or FNAC of lymph node or affected site in patients having PTB and EPTB respectively. 51 patients had pulmonary TB while 10 had extra pulmonary TB (EPTB) of which 4 had lymph node, 4 bone/ spine TB while 2 had TB psoas abscess. Of the 61 patients, 21 were male and 40 female, age group ranging from 14 to 65 years, mean age 27 years. The study revealed that 16 of the 61 patients (26.23%) had recurrent TB i.e they had successfully completed treatment in the past but subsequently found to be microbiologically confirmed TB case, 21 (34.43%) were treatment failures at the end of their most recent course of treatment while 24 (39.34%) were PMDR-TB i.e those who had never received anti TB treatment ever or treatment naïve patients (Table 1). 8 patients (33.33%) with primary MDR TB gave history of contact of over 3 months to 3 years with family member/s who had MDR TB. A chi-square test of independence was performed to examine the correlation of contact history between the primary and acquired MDR-TB groups. However, the proportion of patients

who reported a contact history did not differ significantly between the two groups (p value .597).

Table 1: Causative Factors For MDR TB

Type	No. of cases	Percentage
Retreatment cases	16	26.23
Failure Cases	21	34.43
Primary MDR-TB	24	39.34

DISCUSSION:

Globally the large burden of drug resistant TB threatens to derail the entire fight against the elimination of TB. In India, which already has the highest absolute burden of TB in the world, many studies have highlighted the growing prevalence of DR and MDR-TB over the decades[5]. DR-TB is a serious public health problem because it is more expensive and difficult to treat requiring multiple toxic drugs for longer durations and is associated with higher morbidity and mortality. Compounding these problems are reports confirming that most new DR-TB cases are reflecting community transmission of resistant TB rather than acquisition during treatment.

Many studies from China have reported person-to-person transmission of resistant strains and attributed more than 80% of DR-TB cases to exogenous reinfection with a drug resistant strain[8,9]. Dheda et al[10] have stated that most MDR-TB is transmitted rather than acquired and based on molecular epidemiology data reported that an estimated 95.9% of MDR-TB in new TB cases and 61.3% in previously treated cases is due to transmission of the resistant strains. In India it appears that the reported prevalence of around 3% of PMDR-TB is an underestimation. Modelling studies[7] estimate that in 2032, an estimated 85% of MDR-TB will be PMDR-TB. Suen and colleagues[11] also projected that by 2035 over 60% of new MDR-TB cases will result from transmission rather than be acquired during treatment.

Our study revealed that the proportion of PMDR-TB cases was 39.34% (24/61 cases) while AMDR-TB was 60.66% (37/61 cases) of which treatment failure cases were 34.43% and retreatment were 26.23%. The proportion of PMDR-TB cases is much higher in our study compared to Global and Indian survey figures. This is possibly due to the study centre being located in a highly prevalent resistant TB area. In our study the proportion of failure cases is also high implying a high initial resistance to first line anti TB drugs in the community; probably indicating a need to evaluate drug resistance in all diagnosed TB cases at the first instance itself.

Traditionally poor patient management, inadequate or irregular treatment, non-adherence to prescribed regimen, poverty, social stigma, adverse effects, poor control programmes or a combination of these were considered the main causes of MDR-TB. However, evidence now suggests that other mechanisms including individual pharmacokinetics, variable penetration of drugs into lesions and spontaneous mutations may play an important role[10]. Another important factor is the transmission of drug resistant bacteria by contact with patients known to have DR-TB. In our study there was close contact history with family member/s having resistant TB in one third of patients with PMDR-TB and though this was not statistically significant, it is an important risk factor for MDR-TB.

Given the complexities of drug resistance and the alarming rise in transmission of resistant organisms, early diagnosis and effective treatment are no longer sufficient for curtailing this menace. PMDR- TB spread is a reality and the focus now must be on infection control measures such as contact tracing, rigorous family screening, using personal protection like masks, cultivating hygienic habits such as coughing/ sneezing with covering over mouth and not spitting in public places, having well ventilated rooms with adequate sunlight, admitting DR-TB patients in isolation wards or dedicated hospitals /sanatoriums till they are non-infectious, to halt the spread of drug resistant Tuberculosis.

CONCLUSION:

The rising prevalence of PMDR-TB indicates high levels of ongoing transmission of resistant TB organisms in the community. Interventions to break this vicious cycle need to expend equal emphasis on enhanced case detection and early treatment initiation along with stringent infection control measures and active family screening and contact tracing.

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