



Drug Resistant Tuberculosis in Children- Risk Factors and Therapeutic Response

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ABSTRACT

33 children less than 18 years of age (mean age 15.6 years) were resistant to both isoniazid and rifampicin from 2010 January to March 2015. Of these, 6 died within 2 months, 25 patients were on treatment with category 4 antitubercular drugs for mean duration of 12.72 months. Contact (mostly household) with drug resistant tuberculosis (DRTB) cases was found in 9 (36%) subjects. Treatment outcome in these 25 (75.6%) subjects showed clinical and microbiological improvement. To conclude, contact with DR TB case is important risk factor for DR TB in children. Moreover, good treatment outcomes of cases can be obtained in DR TB cases in children if timely initiated.

KEYWORDS : Drug resistant, Tuberculosis, Children, Contacts, Outcome

Introduction

Tuberculosis (TB) remains a major health problem in India accounting for 24% of the global cases (1). Rapid emergence of drug resistance (DR) in recent years is a major challenge in the management of TB. Globally, an estimated 4,80,000 people developed MDR-TB in 2013 (1). According to WHO data from drug resistance surveys, 3.6% of newly diagnosed TB cases and 20% of those previously treated for TB had MDR-TB in 2012(1). There is an increase in MDR –TB cases in India from 21,498 to 35,385 between 2012 and 2013(1). There is scarce data on DR and therapeutic response of second line antituberculosis drugs in children from India (2). Hence this retrospective study was undertaken to study the profile of drug resistant Tuberculosis (DR-TB) children and also to see the therapeutic response in children.

Methods

This retrospective study was done in Pediatrics and Tuberculosis and chest department of the institute after approval from the ethical committee. Records of subjects less than 18 years of age from January 2011 to February 2015 diagnosed to have drug resistant TB were obtained. Children were diagnosed as DRTB based on drug susceptibility testing on culture of sputum in case of pulmonary TB or other appropriate samples for extra pulmonary forms of TB. Patients were classified DR TB as per WHO classification (3). These patients were started on second line anti tuberculosis drugs according to Revised National Tuberculosis Control Program.

Clinico-demographic details of the study subjects were obtained from records. These patients were followed up for clinical assessment (subsidence of symptoms, any side effects to drugs etc) and microbiological assessment (sputum microscopy and culture) for a minimum duration of 6 months. Repeat chest X-ray was done where possible. Treatment compliance to second line anti tubercular therapy was also noted.

Results

Records of 33 patients <18 years with DR-TB were noted. All these subjects were resistant to both Isoniazid and Rifampicin and were classified as MDR-TB. Additional drug resistance was seen to streptomycin and ethambutol in one subject each. Mean age was 15.06 years with mostly female subjects. Of these 33 subjects, 6 died (within 2 months of therapy), 1 was transferred to other centre and 1 was lost to follow up. Baseline profile of these patients is shown in Table 1.

None of the subjects were co-infected with HIV infection. Remaining 25 subjects were followed up. History of contact with DR tuberculosis patients was present in (9/25) 36% subjects and (3/25)12% had been previously treated for tuberculosis. Mean duration of treatment received in these patients was 12.72 months (range 6- 24 months). Clinical improvement was seen in all the patients in the form of decline of symptoms, improved appetite and general well being. Sputum conversion was seen in the 25 subjects within 6 months of therapy. Radiological clearance occurred in 6 out of 12 patients in whom chest X-rays were repeated. Patients were compliant to the treatment. Side effects observed were hearing loss and joint pain in one subject each.

Discussion

Drug resistance to anti tubercular treatment is a public health challenge of growing concern. In our study only 33 patients with MDR TB were registered during the study period taken. The probable reason for less number of cases is low yield of culture proven drug resistant TB in children. Median age of MDR TB cases (15.06 years) in our study was much higher than other studies. In another Indian study median age of DR-TB was found to be 7 years (2). However, in a study from South Africa median age was reported to be 2.5 years (5). The reason for higher age in our study is probably due to difficulty in getting positive sputum and other tissue cultures in younger children.

In our study all the patients were MDR with resistance to both INH and RMP. These findings are similar to study by Ira shah et al who also noted MDR in 97.1% of cases (2). It is in sharp contrast to study by Alrajhi et al (6) who noted polyresistance in 5% cases only.

The most important risk factor identified in our study was contact with resistant cases. Previous studies (7, 8) have also shown that DR-TB infection occurs in childhood contacts with resistant index cases. We found past history of ATT intake as less important risk factor for DR-TB, this is in contrast to another study (6) which showed that history of previous ATT was the only risk factor associated with DR-TB with odds ratio 19.9 ($P < 0.001$).

Response to therapy showed sputum conversion in (75.6%) patients. Clinical improvement was also seen these patients. A recent meta-analysis by Ettehad D et al showed treatment success in 81.67% for MDR-TB among children (9). Mortality in our study (18.2%) was much higher than reported in the meta analysis showing it to be 5.9% (9)

probably due to delayed initiation of therapy as most of the mortality occurred within 2 months of therapy.

Our study has limitation of small number of patients. However, we may have missed out on some patients who may have had DR-TB as only culture proven cases were registered. It is thus required to widen the definition of MDR TB.

To conclude contact with MDR TB cases is the major risk factor for MDR TB in children .Although treatment of paediatric MDR TB has been neglected, but good treatment outcomes can be achieved if timely initiated.

Table 1 - Profile of Drug Resistant Tuberculosis in children (n=33)

Variable	Frequency (%)	
Gender (n=33)	Male	12(36.4%)
	Female	21(63.6%)
Age (n=33)	<10 yr	2(6.5%)
	≥10 yr	31(93.5%)
Symptoms (n=25)	Fever	25(100%)
	Cough	23(92%)
	Hemoptysis	3(12%)
	Weight Loss	25(100%)
	Abdominal Distension	1(4%)
Type of TB(n=33)	Pulmonary	32(97%)
	Extrapulmonary	1(3%)
Risk factor(n=25)	Contact with DR case	9(36%)
	H/O previous antitubercular treatment	3(12%)

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