Study of Prevalence of MDR Tb among New and Previously Treated Cases with Smearpositive Follow up Results From Five Districts Of Andhra pradesh

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Abstract: Programmatic management of drug resistant TB under RNTCP is being implemented in Andhra Pradesh since 2011. During the initial years MDR TB cases were identified based on criteria-A. Since 2013 criteria B is implemented in identifying MDR cases in follow up sputum of new cases of pulmonary tuberculosis.

Keywords: Multidrug Resistance, Mycobacterium Tuberculosis, Retreatment cases, programmatic management of drug resistant tuberculosis.

I. Introduction

PMDT under RNTCP is being implemented in Andhra Pradesh in a phased manner since 2011. Before introduction of PMDT there was no consistent policy for treatment of MDR cases. Patients who were diagnosed as treatment failures and failed re-treatment regimens were either treated with cat-2 under RNTCP or second line drugs without any support from culture sensitivity. During the initial phase of PMDT, MDR suspects were diagnosed based on criteria-A till 2012. But by 2013, we implemented criteria B [1] and able to diagnose MDR among new cases under treatment of RNTCP whose follow up sputum samples were smear positive.

II. Objectives

The present study was undertaken to analyze the prevalence of resistance among strains of Mycobacteria obtained by the culture from patients under retreatment course who were smear positive from 3rd month in new cases and 4th month in retreatment cases under RNTCP Criteria-A and Criteria-B.

III. Materials And Methods

This is a retrospective study of patients attending 5 districts for screening based on drug sensitivity testing done on sputum samples of MDR suspects between 2013 January to 2015 January. Sensitivity for 1st line drugs that is Isoniazid, Rifampicin deduced by economic variant of proportion method. Sputum collected with aseptic containment measures were decontaminated and centrifuged and sediment inoculated on Lowenstein Jensen medium. Probable Mycobacterium Tuberculosis colonies identified by typical colony characteristics and Zeilneelson’s staining.

IV. Laboratory Methods

1.1. Sputum collection and decontamination:

One morning sample and one supervised spot sample (5-10 ml each) were collected at districts in sterile Mccortesy bottle containing 2 ml of equal volumes of 1% cetyl pyridium chloride cpc(wt/vol) and 2% sodium chloride(wt/vol)(cpc-nacl) in distilled water and transported to CS & DST lab within 7 days. The bottles were shaken until the samples were liquefied and kept at room temperature in walk-in incubator for 4 days maintaining adequate aseptic measures. After decontamination period of 4 days the bottles were filled with sterile distilled water up to the brim capped and then centrifuged at 3000g for 15 minutes using 50 ml
polypropylene tube adopters to minimize the chances of contamination. The mccortney tubes were then carefully removed from the centrifuge without shaking after discarding the supernatant fluid, 50 ml of sterile distilled water was added to the sediment and it was again centrifuged at 3000*g.

1.2. Culture And Sensitivity:
Inoculation was done for each sample from the sediment on two slopes of Lowenstein Jensen medium using sterile individually wrapped disposable 10 mm inoculation loops. The cultures were read weekly for 2 months. Probable Mycobacterium Tuberculosis colonies were identified by typical colony characteristics and Zeil Nelson staining for further confirmation of M. tuberculosis colonies were subjected to sensitivity testing along with an inoculation onto an LJ slope containing para nitrobenzoic acid to rule out the Non-tuberculous mycobacteria simulating the M. tuberculosis colonies. Sensitivity of the first line drugs were deduced by economic variant of proportion method.

2. Definitions: An MDR suspect in the present study was defined as patient suspected of drug resistant tuberculosis based on RNTCP criteria [1].

2.1. Criteria A
All failures of new TB cases
Smear positive previously treated cases who remain smear positive at 4th month onwards
All pulmonary TB cases who are contacts of known MDR TB case

2.2. Criteria B- in addition to criteria A
All smear positive previously treated pulmonary TB cases at diagnosis
Any smear positive follow up result in new or previously treated cases

2.3. Criteria C- in addition to criteria B
All smear negative previously treated pulmonary TB cases at diagnosis
HIV TB coinfection cases at diagnosis

MDR was defined as in vitro resistance to INH and Rifampicin with or without other Anti tubercular drugs. As Rifampicin resistance is quite rare without Isoniazid resistance, majority of DST results with rifampicin resistance are also considered to be Isoniazid resistant that is MDR TB under RNTCP and are managed as if they were MDR TB cases even if they do not formally qualify as MDR TB cases as per the above definition.

V. Results
Of all the MDR suspects whose sputum was examined were under cat-1 are 32% & under cat2 are 68%. Among them the prevalence is more among males 74% when compared to females 26%. The age group frequently affected are among 20-39 yrs 61%. In our sample there are 3 co infected cases with HIV, deaths 8, and two were defaulted from treatment. In our Study the prevalence of MDR detection among cat-1 follow up samples is 0.75-4.5% and in cat-2 is 1.7 to 11.1%.

VI. Discussion
In 2011, 6.2 million cases of TB were notified by National TB control program and reported to WHO. 5.8 million individuals newly diagnosed in 2011 and 0.4 million were previously diagnosed TB patients whose treatment regimen was changed. India and China accounted for 39% of notified cases of TB worldwide in 2011 [2]. Emerging spread of drug resistant M tuberculosis is a serious threat to tuberculosis control program because patients with DR bacilli respond less readily to therapy than those with sensitive bacilli in the community. Resistance to two or three drugs is difficult to treat and that often results in treatment failure. A major concern and one of the greatest biological interest in our study was to detect MDR cases early in the stage of initiation of treatment for the first time when the patients treated under category 1.

<table>
<thead>
<tr>
<th>Specimen</th>
<th>TOTAL SAMPLES</th>
<th>SPUTUM</th>
<th>CAT-1</th>
<th>CAT-2</th>
<th>TOTAL</th>
</tr>
</thead>
<tbody>
<tr>
<td>SKLM</td>
<td>173</td>
<td>3(1.7%)</td>
<td>3(1.7%)</td>
<td>6</td>
<td></td>
</tr>
<tr>
<td>VZM</td>
<td>337</td>
<td>5(1.5%)</td>
<td>8(2.4%)</td>
<td>13</td>
<td></td>
</tr>
<tr>
<td>EG</td>
<td>431</td>
<td>18(4.6%)</td>
<td>46(11.1%)</td>
<td>64</td>
<td></td>
</tr>
<tr>
<td>WG</td>
<td>671</td>
<td>51(7.5%)</td>
<td>12(1.8%)</td>
<td>18</td>
<td></td>
</tr>
<tr>
<td>VSKP</td>
<td>540</td>
<td>12(1.2%)</td>
<td>21(3.97%)</td>
<td>31</td>
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</tbody>
</table>
The highest proportion of initial MDR TB has been documented in 4.6% in present study. This rate is highly alarming in new cases and higher than the studies reported by RNTCP and Indian national figures in WHO global surveys. Data from studies conducted by NIRT, Chennai and National TB Institute, Bangalore have found MDR TB levels <1-3% in new cases. A retrospective analysis of various randomized clinical trials conducted by the NIRT, Chennai with various rifampicin containing regimens in the initial intensive phase and with or without rifampicin. In the continuation phase reveal an overall emergence of resistance to rifampicin in only 2% of patients despite high level(18%) of initial resistance to isoniazid either alone or in combination with other anti TB drugs. In 2008, in 27 high MDR TB burden countries 2.3% (1.8-2.8%) MDR was estimated in new cases [3]. WHO in 2011, 2.1% was reported (1.5-2.7%) of new TB cases with MDR TB in India [4].

In the present study high incidence of initial MDR was seen in countries with low prevalence of initial multi drug resistance, the current standardized treatment regimens for new cases appear to be adequate. However in countries where the prevalence of initial MDR exceeds 3% it is necessary to implement criteria B i.e., DST in every new case of TB or to reexamine these standardized regimens given the unacceptably high rates of failure and relapses. Urgent reassessment is needed because of very poor treatment outcomes in all countries, but particularly in the countries with high prevalence of MDR.

VII. Conclusion

This study reveals high rate of MDR among the new sputum smear positive pulmonary tuberculosis patients. This high prevalence indicates the standard of TB treatment and reflects dissemination of MDR cases with in the community. High initial MDR TB will ultimately lead to very desperate situation of TB management.

A supervised standardized treatment, careful use of drugs, focused clinical, radiological and bacteriological follow up from accredited laboratories are key factors in the successful management of MDR TB. Over the counter availability of anti TB drugs should be banned by government. As the TB is a notifiable disease, the treatment should be initiated with the prescription of a trained doctor. Misuse of quinolones and macrolides should be discouraged. Government should see that no doctor is left without training under PMDT. Community training awareness programs should be organized to decrease drug default by patient. Community involvement in detecting and intimating cases, containment measures for disease spread and fully supervised treatment for MDR cases will decrease the prevalence of Multi drug resistant tuberculosis in future.

References