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Study of drug resistance in pulmonary tuberculosis cases in south coastal Karnataka

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Abstract The present cross-sectional study was conducted for the first time from the Udupi district of coastal Karnataka to know the prevalence of drug resistance and comparative analysis of MDR and non-MDR cases of pulmonary tuberculosis. Details of 862 smear positive cases of pulmonary tuberculosis with age $\geqslant$15 years from 12 designated microscopy centres of the Udupi district were studied. Initially 2 sputum samples trailed by one follow-up sample were collected from each patient and processed for culture and drug sensitivity on the Lowenstein-Jensen medium. A total resistance of 33.4% was observed that includes the mono-resistance of 22.5%, multidrug resistance (MDR) of 6.3% and extensive drug resistance (XDR) of 0.3%. Significant odds ratio (OR) was observed in category 2 cases (OR 3.9) for the development of MDR tuberculosis. A significant statistical association was observed using Fisher's exact test while comparing mortality rate (19.3% vs. 1.8%), treatment failure (8.8% vs. 3.8%) and cure rate (68.4% vs. 85.4%) between MDR and non-MDR cases ($p < 0.001$). Category 2 patients are important risk factors for the development of MDR in pulmonary tuberculosis. Due to high mortality and low cure rate in MDR

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cases it is imperative to know the drug sensitivity report before institution of anti-tubercular treatment.

1. Introduction

Tuberculosis (TB) a disease caused by *Mycobacterium tuberculosis* complex remains the cause of highest mortality in humans, leading to three million deaths annually, about five deaths every minute [1]. Pulmonary tuberculosis (PTB), the commonest form of TB is characterised by the involvement of lung parenchyma resulting in nodule formation in the lungs. India on an average accounts for nearly 25% of the global burden of tuberculosis and 29% of mortality due to tuberculosis [1].

Although the phenomenon of drug resistance in *M. tuberculosis* was observed as early as 50 years ago, the spread of multi-drug resistant tuberculosis (MDR) and emergence of extensively drug resistant tuberculosis (XDR) is threatening to destabilize global tuberculosis control [2]. India is also witnessing an increase in the number of MDR cases being reported from many parts of the country [3,4]. An updated report from WHO in 2013 estimated prevalence of 3.6% MDR tuberculosis in newly diagnosed cases and 20% in previously treated cases [5]. Though there is an increase in drug resistance, testing for MDR status is done in very few centres. Rowland has reported that fewer than 5% of new or retreatment cases are tested for drug sensitivity and an estimated 16% of the patients with MDR tuberculosis are receiving inappropriate treatment [6].

There are few well planned epidemiological studies from the states of Tamil Nadu, Maharashtra [7] and Gujarat [8]. However, studies available from the referral hospitals of Karnataka [9,10] show a much higher burden of MDR TB and it cannot be extrapolated to the community. The knowledge of drug resistance in PTB cases helps us to know the exact burden of MDR status in this area and assists in future to plan national control measures and the treatment strategies in the case of pulmonary tuberculosis.

Hence, a first community level study was undertaken to study the prevalence of drug resistance, comparison of MDR and non-MDR cases and to know the outcomes of treatment in PTB patients of the Udupi district in the south-western coastal area of Karnataka.

2. Methodology

2.1. Study settings

The cross-sectional study was carried out in the Department of Microbiology of a tertiary care centre of south-west coastal Karnataka in liaison with the district tuberculosis office during the period of September 2011—August 2014. Ethical clearance for the study was obtained from the institutional ethics committee.

2.2. Sample collection

A total number of 990 cases of smear positive PTB patients with ages $\geqslant$15 years from Designated Microscopy Centres of the Udupi district (including centres of three talukas and district tuberculosis centre), Karnataka were included in the study. Out of the 990 cases, cultures of samples from 28 cases had been contaminated, data could not be collected completely for 33 cases who denied participation, 37 cases were lost to follow up either due to mortality or switching over to private treatment and about 30 samples were culture negative after eight weeks of incubation. Hence the data for the remaining 862 cases as per the sample size calculation are presented in the study. Two sputum samples-one spot and one early morning sample were initially collected from each patient and the follow-up sample was collected after 3 months of the anti-tuberculosis therapy (ATT). The HIV status was determined for all the patients without failure under the revised national tuberculosis control programme with a spot test (Comb Aids, Span Diagnostics, India). The demographic data of all the cases were obtained by the interviewer through a predesigned questionnaire. No other forms of tuberculosis were evaluated in the study.

2.3. Sample processing

All the sputum samples were transported to our lab in the cold chain. Decontamination and concentration of the samples were done using the modified Petroff's method [11]. Samples were cultured on Lowenstein-Jensen media, incubated for 4—8 weeks and the growth was confirmed with the help of MPT 64 antigen detection kit as