

## Monoresistance to Rifampicin: An Uncharted Territory in The Management of Drug-Resistant Tuberculosis

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Tuberculosis (TB) disease caused by the bacilli *Mycobacterium tuberculosis* (MTB) is a chronic disease, mostly involving the lungs but can also involve other parts of the body, which if left untreated may lead to severe illness which can be fatal. Worldwide, TB is the 13th leading cause of death. TB occurs in every part of the world but its distribution is heterogenous. As per WHO global TB report, the biggest quantum of cases occurs in the South and South-Eastern Asian region (46%). Africa contributes to 23% with Western pacific taking 18% of the burden of TB [1].

Multidrug-resistant TB (MDR-TB) which is resistance to both first line drugs Rifampicin, (R) and Isoniazid (H) as well as R(R) TB (Rifampicin resistance with or without H resistance) with incident cases of about 465000 MDR-TB and R(R) TB in 2019, drug-resistant tuberculosis (DR-TB) remains a public health crisis [2]. The cartridge based nucleic acid amplification Test (CBNAAT) can detect *Mycobacterium TB* and can also provide information on the sensitivity or resistance of Rifampicin.

Since this test does not require much manpower and can be rapidly done in a peripheral setup with the result coming in hours, the information on R resistance (present or absent) in MTB detected is easily obtained. Since R resistance in India is almost always associated with H resistance, the R (R) patient is treated on the same regime as MDR-TB. However, this is not invariably true as Rifampicin monoresistance (hereby referred to RMR) is also present in some cases. The Line Probe Assay (LPA) gives the information on both R and H resistance. RMR, if present, gives the advantage of adding H to the treatment regime. Being one of the highly potent bactericidal drug against TB drug with comparatively lesser side effects, it would improve the outcome of these patients.

RMR is uncommon in India but not rare. A recent study from India conducted by Palani et al. showed 11% of RMR in R(R) TB [3]. Hence all R(R) TB diagnosed as per CBNAAT may be also subjected to LPA (especially smear positive cases) and liquid cultures as far as possible depending on feasibility and availability. RMR is much more common in certain parts of the globe especially South Africa which is a high TB burden country. Almost 38% of patients have RMR in South Africa in the R(R) group and this appears to be associated with Human Immuno-deficiency Virus (HIV) co-infection [4]. A reasonably high level of RMR was also

seen in Korea with 30 % RMR among R(R) in a study by Bai et al. This study also demonstrated a progressive rise in RMR from 17% to 30% over 10 years (1994 – 2004) [5].

Twenty one percent (21%) of MDR patients were reported in a German study to be harbouring RMR [6]. A study from China which accounts for the second highest MDR TB Burden country after India, revealed 18% RMR in R(R)TB [7]. A meta-analysis from Iran by Nasiri MJ et al revealed 33.3% and 14.8% of RMR cases in newly diagnosed and previously treated TB patients who had R(R) resistance as diagnosed by GeneXpert [8].

The outcome of treatment of RMR TB is much worse compared to Drug-Sensitive TB and hence all efforts may be done to know about RMR. However, in countries like India, provision of LPA to all R (R) patients may not be currently possible because of the constraints of resources, infrastructure and manpower. The laboratory services are being enhanced and are being spread over whole of India under the ambitious National Tuberculosis Elimination Programme (NTEP). Though the HIV test is performed on all diagnosed TB patients in India, we can study the prevalence of HIV in the Indian RMR patients which may demonstrate its analogy with the African RMR TB population.

To conclude, the most important advantage in knowing the status of RMR is the clinical benefit of the bactericidal action of H being used in the treatment regime which may significantly improve the outcome of these patients and also determine the risk factors (such as HIV) associated with RMR.

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