

MULTIDRUG-RESISTANT TUBERCULOSIS: CURRENT SITUATION IN PAKISTAN

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Multidrug-resistant tuberculosis (MDR-TB) is a form of tuberculosis (TB) infection which is resistant to at least two of the most effective first-line anti-TB drugs, namely isoniazid and rifampicin. Globally, in 2015, an estimated 480,000 new MDR-TB and an additional 100,000 rifampicin-resistant TB (RR-TB) cases were eligible for MDR-TB treatment and around 250 000 died during this period. MDR-TB, or rifampicin-resistant TB, occurs in 3.9% of new TB cases and 21% of previously treated TB cases. Six countries accounted for 60% of the new cases; India, Indonesia, China, Nigeria, Pakistan and South Africa.¹

The MDR-TB detection and its treatment remains a huge challenge. In 2015, of the estimated 580,000 people newly eligible for MDR-TB treatment, only 125,000 (20%) were enrolled. Five countries accounted for more than 60% of the gap; India, China, the Russian Federation, Indonesia and Nigeria. Globally, the MDR-TB treatment success rate is quoted to be 52%.

The WHO 2016 global report on country profiles for the 30 high-burden countries for tuberculosis showed Pakistan among the highest burden countries. In 2015, with the estimated population of 189 million, the incidence rate for TB (including HIV+TB) was 270 cases per 100 000. Furthermore, the incidence rate for MDR-TB was 14 cases per 100, 000 and the TB treatment coverage (notified/estimated incidence) was 63% (44-98). In 2015, the Pakistan national TB budget was US\$ 62 millions, of which 1% was domestic funded, 65% was funded by international donors whereas 35% were unfunded or by someone else.²

According to 2015 global report, an estimated

MDR/RR-TB cases in Pakistan were 14000, 4.2% new cases and 16% among previously treated cases. Out of these only 2553 (18.2%) MDR/RR-TB and 68 (0.4%) XDR-TB patients were enrolled for treatment.

Due to seriousness of the situation and difficult treatment regimen of MDR-TB, National TB control programme (NTP) planned to control the disease through programmatic management of drug resistant TB (PMDT) throughout the country. The magnitude of the MDR-TB problem in Pakistan is difficult to estimate. Different reports from across the country are not comparable because the protocol for the studies were neither standardized nor were the laboratories having quality assured culture sensitivity.

A survey from all over the country showed that 24.3% of the previously treated cases were MDR-TB. Among MDR-TB isolates, 47.0% were ofloxacin (OFX) resistant. Extensively drug-resistant TB was found in two (0.4%) isolates.³ Risk factors for MDR-TB are contact of TB/DR-TB, prior history of TB medication, age, gender, low socioeconomic status and low education status.⁴ A survey conducted in Punjab showed that older age and previous history of treatment are the main factors responsible for MDR-TB.⁵ A study from Khyber Pakhtunkhwa explained previous history of tuberculosis, low socioeconomic status, lack of education and Poor compliance in tuberculosis treatment were the factors responsible for occurrence of MDR-TB.⁶

Study by Khan et al., (2015) concluded that treatment success rate among 2008-2011 cohort of MDR-TB patients was 63%.⁷ Another study from Khyber Pakhtunkhwa (2012-13 cohort) showed the success rate of MDR-TB patient was 78.7%.⁸ A study from Rawalpindi showed that 10% patients successfully

completed their treatment.⁹ A study from Karachi showed 39.2% of success rate of the disease.¹⁰ In another study from Khyber Pakhtunkhwa, success rate of 74.3% has been reported.¹¹

Different studies have quoted predictors responsible for poor outcomes of MDR-TB, for example a study from Lady Reading Hospital (LRH), Khyber Pakhtunkhwa found that age, rural residence, lung cavitation, previous use of SLD's, resistance to SLD and resistance to ofloxacin were the predictors for unsuccessful treatment outcome.⁸ Another study also from Khyber Pakhtunkhwa also mentioned the factors associated with poor outcomes were age, lung cavitation, resistance to second line drugs (SLD), and resistance to ofloxacin.¹¹

As MDR-TB is transmitted from one person to another hence with the treatment prescribed to the patients, it is essential to prevent the transmission of MDR-TB. To find out transmission level of this disease a study was carried out on contacts of 209 MDR-TB index cases. A total of 1467 household contacts were identified and screened, 95 of them children < 5 years. Of total contacts, 56 (3.8%) were diagnosed with TB, among them 54 (96%) with MDR-TB and 2(4%) with drug-susceptible TB.¹² Another study for the same purpose was conducted in Lady Reading Hospital Peshawar, Khyber Pakhtunkhwa. In this study 610 contacts of 200 MDR-TB index case were investigated. Results of this study point out that 17.4% were diagnosed with MDR-TB and 4.2% with drug susceptible TB.¹³

In fact SLDs used for the treatment of MDR-TB are highly toxic with many adverse side effects. A study conducted in LRH, KPK pointed out that among study cohort 72.4% experienced at least one adverse drug reaction (ADR). Gastrointestinal disturbance was the most commonly observed adverse event (42%), followed by psychiatric disturbance (29.3%), arthralgia (24.3%) and toxicity (21%). Due to ADRs, treatment regimen was modified in 20 (11%) patients.¹⁴

These studies suggest that MDR TB is a serious disease with relatively poor outcome treated in countries like Pakistan with conventional over 20 months of toxic drugs with multiple adverse drug reactions. In Pakistan its outcome is below the target of WHO which is 80%.

We are aware that MDR-TB is man-made. Factors responsible for this disease are; Poor adherence with TB treatment, wrong treatment (wrong dose, regimen or time of treatment), Irregular anti-TB drug supply at health facilities and failure to follow DOTS in letter and spirit.

Obviously to reduce the incidence of MDR-TB, it is imperative that TB is treated correctly the first time. It is these man-made factors that result in the emergence of MDR-TB. WHO has recently recommended a shorter regimen for MDR-TB treatment, comprising 4-6 months of Kanamycin (KM), Moxifloxacin (MXF), Prothionamide (PTH), Clofazimine (CFZ), Pyrazinamide (PZA), High-dose Isoniazid (INH) and Ethambutol (EMB), followed by 5 months of MXF, CFZ, PZA and EMB.³ This regimen has a high success rate (>80%) as compared with this conventional treatment. Due to high Quinolone resistance less than 50% of MDR-TB would be eligible for this regimen which is caused of concern.^{15,16}

Healthcare providers need to be better trained throughout the country for proper management of TB. In addition, patients need more motivation and education to appreciate the importance of adherence to their initial treatment. The problem with irregular drug supplies can be addressed by proper drug stock planning. It is time to come to use the proper trained staff under proper guidelines for proper implementation of DOTS/PMDT programme successfully and hence reduce the incidence of MDR-TB.

In conclusion, it can be said that PMDT intervention requires concerted, sustained and planned activities and meeting the challenge would be a gradual process. Even though the government has embarked on the journey to tackle MDR-TB problem but the highest priority would still be to prevent MDR through effective DOTS.

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