BURDEN OF TUBERCULOSIS - COMBATING DRUG RESISTANCE

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Tuberculosis (TB) is a medical, social and economic disaster of immense magnitude and is a major global health concern. It is currently the leading cause of death among curable infections. World Health Organization (WHO) data show that approximately one third of the world's population is infected with TB. Approximately 8 million people become infected annually, resulting in more than 2 million deaths each year[1,2]. The emergence of multidrug resistant tuberculosis (MDR-TB) has made the problem more pronounced, and its increasing incidence has turned it into a global threat[1,3,4].

In 1959, Sir Crofton reported that "the right use of modern methods of chemotherapy now makes it possible to aim at 100% success in the treatment of pulmonary tuberculosis". 'But the greatest disaster that can happen to a TB patient is that his organisms become resistant to two or more of standard drugs'[5]. Despite the availability of effective Anti TB chemotherapy since the middle of last century, control of Tuberculosis (TB) still remains one of the most serious challenges to global health. TB is predominantly a disease of poverty with over 80% of cases occurring in Asia or Africa. Pakistan stands 8th among the highest disease burden countries with incidence of 181 cases per 100,000 population[6].

A potentially devastating threat to TB control is the emergence of strains that cannot be cured by standard anti-tuberculosis regimens. Drug resistance is a laboratory diagnosis and should not be just a clinical impression of treating doctors. If the patient is resistant to one drug it is called mono resistant, if two or more drugs it is poly resistant and if resistance to at least Rifampicin and INH it is Multi Drug Resistance or MDR-TB. Recently another type of Extreme drug resistance (XDR-TB) has been defined which includes MDR-TB plus resistance to an injectable aminoglycoside and a flouroquinolone[7]. The above mentioned resistances can be acquired or primary depending upon whether patient has received Anti TB treatment in the past or not. MDR-TB is essentially a man made problem and arises as a consequence of incomplete/inadequate treatment, leading to selection of drug resistant strains. It can also arise because of inadequate management of existing MDR-TB patients who are spreading the infection to their close contacts.

Control of drug resistant tuberculosis requires a strong health infrastructure to ensure the delivery of effective therapy coupled with surveillance and monitoring activities to enable timely intervention to limit transmission and spread of the disease[8]. Guidelines for programmatic management of drug-resistant TB have been developed by National TB programme and Pakistan Chest Society[9].

The treatment of MDR TB is to select the appropriate treatment regimen. Options available to the doctor would be either to select an Individualized Treatment Regimen (ITR) based on the drug sensitivity profile of the patient or to select a Standardized Treatment Regiment (STR) whereby patients would be treated with uniform drug regimen decided on the basis of the drug susceptibility pattern in the community. Pending availability of the laboratory results, the clinician may need to decide on a treatment in view of the deteriorating clinical condition of the patient with an "Empiric Regimen".

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. However according to WHO estimates there are about 15000 MDR TB cases in Pakistan and the incidence of primary and acquired MDR TB in the country is 3.2 & 28 % respectively. However a nationwide study found the primary drug resistance to be

1.8 %[8]. National MDR TB Guidelines recommend a standardized treatment regimen with an intensive phase of 6 months with Inj. Kanamycin, Cycloserine, Ethionamide, Ofloxacin, PAS and Pyrazinamide. During continuation phase atleast 4 drugs are given for atleast 18 months.

In addition to the treatment given to the patient it is also essential to prevent the transmission of MDR-TB especially in institution setting through the infection control measures like administrative controls which reduce the risk of exposure to infection and disease through policy and practice by isolating MDR-TB patients and by reducing period of hospitalization. The next step in Infection Control is Engineering Controls which reduce concentration of infectious bacilli in air in areas of likely contamination. This includes facilitating natural and artificial ventilation by fixing exhaust fans, room air cleaners and germicidal upper air ultra violet irradiation. Personal respiratory protection for individuals with the help of respirators is also recommended in environment contaminated with MDR-TB. Health education to the patients for cough hygiene is also useful to reduce the concentration of bacteria in the environment. This approach would be an effective interventional strategy for treating individual TB patients.

However, it was soon realized that for effective global management of MDR-TB, the emphasis has to shift from individual patient to a community based programme approach.

DOTS plus is a case management strategy under the aegis of DOTS to manage MDR-TB using second line drugs and infection control measures. As per definition it is clear that DOTS is a pre requisite to DOTS plus and hence can be considered only in situations where effective DOTS is being implemented[10]. Overall goals for the DOTS plus strategy are to reduce morbidity and mortality from MDR-TB and to cut the chain of transmission[11].

In order to ensure that DOTS plus strategy is implemented effectively, the WHO along with its international partners established a Green Light Committee in June 2000 to lay down the “Models of Good Practice” for MDR-TB patients. This committee ensures that benchmarks are met before DOTS plus is initiated at any site and also provides technical support for implementing DOTS plus protocols. One of the major hindrances in treating such patients is the cost of drugs and it was function of this committee to link up with drug manufacturers for assuring uninterrupted supply of quality drugs at reduced rates[12].

National TB programme has finalized the operational guidelines for implementing and pilot testing the DOTS Plus strategy in three sites in Pakistan. It plans to develop a central reference and provincial laboratories one in each province.

The challenges that we face for implementation of DOTS Plus strategies in the country are;

1. Laboratory: Quality assured laboratories for diagnosis and monitoring of MDR-TB patient is probably one of the major hurdles in starting and expanding DOTS plus in Pakistan where such a lab is still to be established.
2. Treatment: Providing daily treatment for a period of 2 years and strengthening defaulter retrieval mechanism would have to be addressed.
3. Logistic support: Availability of uninterrupted supply of quality assured drugs would be a challenge as the shelf life of some drugs is less than the treatment duration.

In conclusion, it can be said that DOTS Plus 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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