Drug Resistant TB

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One third of the world population is infected with TB bacillus. Since 1985 there has been a renewed epidemic of TB that was previously thought to be in check[1]. There is evidence to believe the main factor for this resurgence has been the human immunodeficiency virus (HIV). In Pakistan the prevalence of TB, according to WHO estimate, is around 200/100 000 population[2]. A recent study from a Pakistani rural area had shown that these WHO figures may be an under estimate. In the village studies the prevalence of smear positive and smear negative cases were found to be 544 and 1949/100 000 respectively[3]. One major area of concern during this TB epidemic is the growing rate of drug resistance. The WHO in 1997 estimated that some 50 million people might be infected with drug resistant strains worldwide[4]. The hardest hit areas were Russia, Central Africa, India, Pakistan, Thailand and the Philippines.

Drug resistant IB is entirely a man made problem and results from inadequate chemotherapy. In community it is the chronic cases, resulting from poor treatment, that are the reservoir of deadly drug resistant strains of TB. The only way to prevent TB entirely is to effectively treat the active cases so as to stop the transmission of this infection in the community. Countries like Pakistan, that do not have an active National TB Program, are transforming an eminently treatable infection into a life threatening disease. Despite the availability of effective anti-TB drugs the severity of drug resistant TB has continued to increase worldwide and TB killed more people each year at the end of this century than it did in the beginning.

In dnig resistant TB. the bacilli are resistant to one or more anti-TB drugs. Multi drug resistant (MDR) TB is the most severe form of TB as the bacilli are resistant to both isonaizid and rifampicin, irrespective of resistance to other drugs. Resistance has been encountered against all anti-TB drugs and it arises by chromosomal mutation in a small proportion of bacilli in any wild strain. These resistant strains are selected by mono-therapy in conditions where the bacterial population is sufficiently large, as in cavitatory pulmonary disease. Mono-therapy may be given because of the administration of an inadequate regimen or because of initial drug resistance. Trials done in 1940's have shown that mono-therapy with Streptomycin was effective but the response did not last long as resistance developed to the drug[5]. Furthermore, response to two drugs was better than to single drug treatment and that combined chemotherapy prevented the emergence of drug resistance bacteria[6].

There are two types of drug resistance. Primary (initial) resistance occurs in persons who have not received any anti-TB therapy and they are initially infected with drug resistant strains. Secondary (acquired) resistance occurs in patients who have previously received anti-TB therapy and resistance develops as a result of inadequate regimen. It is relevant to differentiate primary from secondary resistance since primary resistance is less severe, often to one drug and with lower level of resistance (MIC) to individual drugs. Secondary resistance, on the other hand, is more severe and often to 2 or more drugs. Once drug resistance develops, TB bacilli become more difficult to kill, the treatment regimen is up to 100 times more expensive and the duration of therapy has to be extended up to two years.

Study from USA has shown that the main risk factors associated with drug resistant TB are history of recurrent TB (O.R. 4.5, 95% C.I. 2.6-7.6) and presence of HIV infection (O.R. 3.6, 95% C.l. I .5-8.8). Drug resistance was found to be significantly associated with homelessness, injecting drugs and excess alcohol use[7]. In HIV patients exposure to MDR-TB during their hospital stay is associated with a very high risk of acquiring infection (O.R. 39.3. $p<0.001$) and has resulted in outbreaks of MDR-TB in hospitals[8]. TB is reported to be running rampant in Russian prisons, where drug-resistant varieties are

rapidly spreading and up to 30 percent of infections are caused by MDR-TB strains. A treatment program with I)OTS- Plus is being implemented in which patients follow a regimen of "second-line" TB drugs for as long as two years, versus six months in standard treatment[9]. Health care workers are also at an increased risk of contracting TB and a number of health care workers have succumbed to it. Delayed diagnosis, substandard room ventilation and inferior chemotherapy are the important factors that predispose to such infections. A recent study reported that 12 of 3 10 (4%) of nurses developed active TB over a 2-v ear period at a hospital in Malawi, a risk 40 times that in general public[10].

A critical strategy for successful elimination of TB is an effective and complete treatment of all active cases. Management of MDR-TB in a low income country is a nightmare. Even with the availability of second line expensive drugs the problem connot be addressed without the ability to detect drug resistance in all new patients. The best way of managing MDR TB is to prevent it from emerging. When dealing with patients with TB, physicians should ensure that they always use anti-TB therapy in correct doses, in correct combination and for the full duration. Therapy should be supervised and a single anti-TB drug should never be added to a failing regimen. Drug formulations of doubtful efficacy should be avoided. Lack of National TB Program in the country is a big drawback in ensuring uniformity of treatment and documentation of success.

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