ORIGINAL RESEARCH ARTICLE

Tanaffos (2003) 2(7), 47-51

Pattern of Drug Resistance in Pulmonary TB Patients

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ABSTRACT

Background: *Tuberculosis is a common infectious disease these days; it has the highest mortality rate among all infectious causes only after HIV/AIDS. The emergence of tuberculous bacillus species resistant to multiple drugs has become a serious global threat to the human health. Drug resistance is either acquired with the initial infection (from a host harboring resistant tubercle bacilli) or develops during treatment with antituberculous chemotherapeutic agents because of poor patients compliance or inadequate/ inappropriate treatment regimens. This study has been done to evaluate drug resistance and to determine the type of resistance in drug resistant tuberculosis patients.*

Materials and Methods: *The files of patients hospitalized during the past 2.5 years in Massih-Daneshvari clinical mycobacteriology ward due to suspected drug resistant tuberculosis were evaluated. Those who had a sputum antibiogram indicating resistance at least to one anti-TB drug were included in the study. Data, including demographic data, radiologic findings, sputum smear, sputum culture, and antibiogram were recorded in a specified questionnaire. Analysis was done for central indices using the SPSS software.*

Results: *Forty-three cases met the inclusion criteria. Twenty-seven (63%) were male and 16(37%) were female with the age range of 16-80 years (mean ±SD, 36.9 ±16.76). Twenty-five cases (58%) were Afghan and 13(30%) were Iranian (Other nationalities had not been recorded). Antibiograms of 38 patients (88%) showed resistance at least to isoniazid and rifampicin; these patients were considered as multidrug resistant (MDR) cases. In 24 cases (56%), the Mycobacterium tuberculosis was resistant to all four-drug isoniazid (INH), rifampicin (RIF), streptomycin (STM), and ethambutol (EMB). Thirty-six patients (85%) had resistance at least to STM, and 26 patients (60%) were resistant at least to EMB. Bacillus drug susceptibility to pirazinamide (PZA) was not specified.*

Conclusion: *Most drug-resistant cases of TB were seen among Afghan emigrants. Ninety-five percent of cases had a history of treatment at least once, and the resistance was secondary (acquired). Despite discontinuation of streptomycin usage as an anti-TB drug in Iran in the recent years, the most common type of resistance was related to this drug, occurring in 85% of cases. Confirming different studies in other countries, the lowest resistance to the first line anti-TB drugs was for EMB, detected in 56% of cases.* ***(Tanaffos 2003; 2(7): 47-51)***

Key Words: *Tuberculosis, Pulmonary Tuberculosis, Multi-drug resistance*

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INTRODUCTION

Tuberculosis (TB) is the most common cause of death due to infectious diseases globally after AIDS (1). Approximately, 2 billion people in the world are infected with mycobacterium tuberculosis, and 8.8 million new cases of tuberculosis occur annually, with over 50000 attributable deaths each week (2). The presence of multidrug-resistant tuberculosis (MDR-TB) is a strong global threat to human health. Drug resistance is either primary (initial), in which TB bacilli are initially drug-resistant or secondary (acquired). The latter develops during treatment by patient's inappropriate consumption of drug or inadequate and inappropriate treatment regimens.

Tuberculous bacilli resistance is divided in to three categories including monoresistance, combined resistance, and multi-drug resistance (MDR). MDR is determined by resistance of bacilli at least to isoniazid and rifampicin. This study was performed for the evaluation of drug resistance of tuberculous bacilli in hospitalized patients with pulmonary TB in Massih Daneshvari Hospital.

MATERIALS AND METHODS

Between the year 2000 and 2002, we reviewed the files of hospitalized patients in TB ward of Massih-Daneshvari hospital and selected those who had been treated with suspicion of MDR TB. Among these, the files of patients whose antibiogram had confirmed drug resistance were selected. Demographic, paraclinical and radiologic data along with antibiogram and the kind of treatment given were obtained from records. Then data were analyzed by SPSS software.

RESULTS

The patients under study were 43 (27 men (63%) and 16 women (37%) with age range of 16-80 years). Among them, 25 cases (58%) were Afghan and 13(30%) were Iranian; the nationality of the remaining had not been recorded. Sputum smear was 1+, 2+, and 3+ in 14 (32.5%); 14 (32.5%); and 13 (30.1%) cases, respectively. Two patients (4.9%) had negative sputum smear but positive sputum culture. The sputum cultures of all patients were positive ranging from 1+ to 4+. Also, 14 (33%), 13 (30%) and 12 (28%) cases had 1+, 4+, and 3+ sputum cultures, respectively. Only 4(9%) patients had 2+ sputum culture. Around 95% of 43 cases had received anti-tuberculosis treatment for at least once. Meanwhile, the history of 1, 2, 3, and 4 times of treatment was obtained from 25(58%), 12 (28%), 3(7%), and 1 cases respectively. Antibiogram was carried out for all patients in which bacilli were resistance to at least isoniazid and rifampicin (MDR-bacilli) in 38 (88%) cases.

The status of TB bacilli resistance was as follows: there was resistance to isoniazid (INH), rifampicin (RIF), and streptomycin (STM) in 24 (56%) cases and the bacilli were only sensitive to ethambutol (EMB). In 4 (9%) and 2 (5%) cases, they were resistant to INH, RIF and INH as well as STM, respectively.

Interestingly, TB bacilli were resistant at least to STM in 36 (85%) cases. Only 35 out of 43 cases had radiologic data (including chest X-ray and CT Scan), among whom 27 (63%) cases had cavitary lesions in their lungs, and the remaining 8 had other pulmonary lesions. Regarding treatment, 31 (72%) patients had received four-drug standard regimen plus ofloxacin and amikacin or only ofloxacin, so that the first drug regimen was used in 19 (44%) patients and the second in 12 (30%) patients. Other drug regimens were determined on the kind of antibiotic used including INH, pirazinamide (PZA), EMB, cycloserin, amikacin, ciprofloxacin, and ofloxacin.

DISCUSSION

In the United States 1997, about 8% of isolated Mycobacterium tuberculosis had primary resistant to INH, out of which 1.3% were resistant at least to INH and RIF (3). Estonia, Iran, China, India and some part of Russia were reported to be the most endemic regions of drug resistant and multidrug-resistant tuberculosis in the world. The rate of primary resistance in Japan was as high as the median of the world, but the rate of acquired (secondary) resistance was almost twice of the median (4). In the year 2000, the World Health Organization (WHO) registered 273000 cases of MDR-TB worldwide (5).

Drug resistance has clinical and paraclinical determinations; however, there is no single definition for it. In our center, a MDR bacilli should have the following three criteria:

1. Persistent positive sputum smear in spite of "Directory Observed Treatment Short Course" (DOTS).
2. Unchanged or progressive radiologic features.
3. Confirmed resistance at least to INH and RIF by paraclinical report.

In our study, the number of cases having MDR-bacilli criteria was 38 (88%). Twenty-six (56%) patients were resistant to INH, RIF, STM, and EMB. This rate is more than that of other world medical centers which is probably due to referring patients to our center. In fact, those patients with clinical suspicion of MDR-tuberculosis had been referred to this hospital. The performed studies have shown that the majority of Mycobacterium tuberculosis strains resistant to INH and RIF are also resistant to other anti-TB drugs. Similarly in the present study, 38 cases were resistant at least to INH and RIF; 4 cases of them were resistant only to these two drugs, and the remaining had simultaneous resistance at least to one other drug.

In a study by Liu et al. (6), single drug resistance to INH and STM was most common, respectively. The present study also showed that 41 (95%) and 36 (85%) cases had resistance at least to INH and STM, respectively. In a study conducted by Liu et al. (6) and other performed studies including in Ethiopia (7), single drug resistance to EMB has been very low. Similarly, minimum resistance to EMB was obtained in 26 patients (60%) in our study which is the least in comparison with other drugs.

Regarding the high prevalence of resistance to STM, adding this drug in MDR-tuberculosis suspects is probably inappropriate and may induce more resistance to other concurrently prescribed drugs. Low prevalence of resistance to EMB causes its consumption as a low-cost drug in suspicion of MDR-TB suspects. In the present study, the majority of the study patients had TB with acquired drug resistance. Ninety-five percent of them had at least a single history of treatment, and most of them had responded to the standard drug regimen whom had once again in the form of MDR.

As a conclusion, a single definition for MDR-TB is very necessary for control and appropriate treatment of this disease.

One of the reasons for inadequate treatment is the delay in reporting drug resistance from the laboratory which is due to applying traditional methods for culture and antibiogram. Therefore, we recommend the application of new methods for culture and rapid testing of drug susceptibility such as BACTEC system and gene analysis (PCR) in order to achieve more rapid paraclinical diagnosis of MDR- bacilli resulting in more precise and faster treatment of the disease.

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