Original Article

Prevalence of Drug Resistance in Pulmonary Tuberculosis

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ABSTRACT

OBJECTIVE: To determine the prevalence of primary and secondary drug resistance to first line anti-tuberculous drugs.

STUDY DESIGN: A hospital-based cross-sectional observational study.

PLACE AND DURATION: Department of Medicine Liaquat University Hospital Hyderabad/ Jamshoro & Institute of Chest Diseases Kotri from April 2005 to March 2007.

PATIENTS AND METHODS*:* Fifty cases of Pulmonary tuberculosis (TB) randomly selected from both institutes who fulfilled the following criteria 1) Sputa showed positive smear for Acid Fast bacilli on Zeil Nelson Stain.2) Chest x-ray showed shadow consistent with TB. A detailed history, contact with TB patients, previous use of anti-tuberculous drugs and Chest x-ray was done. Sputa of all patients were sent for detail report and culture sensitivity. Descriptive and inferential statistical analysis was performed using SPSS version 14.0.

RESULTS: Among 50 patients, 28(56%) were males and 22(44%) females, age ranged from 16-80 years (38.14 + 15.69). All 50 (100%) patients presented with fever and cough, haemoptysis in 36 (72%), chest pain in 9(18%) and dyspnea in 11(22%) cases, anemia in 39(78%) and lymphadenopathy in 12(24%). On chest x-ray examination, 19(38%) patients had multiple infiltrations, cavitations in 10(20%), fibrosis in 9(18%), consolidation in 5(10%), pneumothorax in 4(8%) and pleural effusion in 3(6%) cases. Sputum for AFB was positive in all cases. Twenty-one (42%) culture positive patients were of primary resistance and 29(58%) were of secondary resistance. Twenty (40%) were sensitive to five drugs, 9(18%) resistant to one drug, 11(22%) to two drugs, 7 (14%) to three drugs, 3(6%) to four drugs and none resistant to five drugs.

CONCLUSION*:* In our setting, the prevalence of resistance to anti-tuberculous drugs is high and alarming. Strategy should be made for proper treatment and compliance of patients to avoid the development of drug resistance.

KEY WORDS: Pulmonary tuberculosis, drug resistance, anti-tuberculous drugs.

INTRODUCTION

Tuberculosis (TB) is an infectious disease caused by Mycobacterium tuberculosis, most commonly affects lungs, but any organ of the body can be affected. Infection may be latent without significant symptoms or may result in active disease. TB is leading infectious cause of death world wide. Approximately one third of the world's population is infected with mycobacterium tuberculosis leading to 10 million new cases each year[1,2] as a primary public health threat[3] TB is most prevalent in persons of low socio-economic status. Population at highest risk includes homeless, alcoholics, drug abusers, prison inmates and poor living with unhygienic environment[2, 4] Health care workers in hospitals and long term care facilitators are also at increased risk, especially pulmonologist and respiratory therapists. Like other countries, TB is a major public health problem of Pakistan and is fourth leading cause of death.[5] According to World Health Organization (WHO) report of year 2000, Pakistan stands at 5th number behind China, India, Bangladesh and Indonesia and among 22 highest burden TB prevalent countries of the world.[6] The epidemiological pattern of TB is changing rapidly because of several factors including HIV epidemic, increased immigration from TB endemic countries, detoriation of infrastructure of TB treatment services, declining social situation and poor compliance of patients with treatment.[7,8] Drug resistant TB has increased in incidence and interferes with TB control programmes in developing countries with prevalence rate as high as 48%.[9] WHO estimated that some 50 million people might be infected with drug

resistant strains of mycobacterium TB world wide.[10] Drug resistant TB is an important problem of increasing significance for whole global community[11.] Major outbreaks of drug resistant TB have resulted in cluster of illness and death within shelter home and institutes, residential facilities and hospitals[12.] The synergy between TB, AIDS epidemic and surge of drug resistant clinical isolates of mycobacterium TB have reaffirmed TB as a primary public health threat.

PATIENTS AND METHODS

This cross-sectional observational study was conducted at department of Medicine Liaquat University hospital Hyderabad/Jamshoro and Institute of Chest Diseases Kotri. 50 cases of TB were randomly selected from both institutes between April 2005 and March 2007, who fulfilled the following criteria 1) Sputa showed positive smear for Acid Fast bacilli (AFB) on Zeil Nelson Stain.2) Chest x-ray showed shadow consistent with TB. A detailed history regarding age, sex, occupation, address, socioeconomic conditions, symptoms such as fever, cough, haemoptysis, dysponea, chest pain and weight loss were noted in a proforma. Patients were divided into groups by age (group-I 15-29 yrs, group-II 30-44 yrs, group-III 45-59 yrs, group-VI >60 yrs). History of contact with and previous use of anti-tuberculous drugs were also recorded. On physical examination general built, anemia, cyanosis, jaundice, edema, clubbing, and lymphadenopathy were examined. Chest examination was done for presence of signs of cavitations, fibrosis, pleural effusion, pneumothorax, consolidation of the lung. Abdomen, cardiovascular and nervous system were also examined for clue of military TB. Blood samples were sent for hemoglobin, ESR, and total leukocyte count. Chest x-ray was done on all patients. Primary drug resistance is defined as resistance to one of the drug in a patient undergoing anti-tuberculosis therapy for first time. Secondary drug resistance is documented as increasing level of resistance to one or more drugs in a patient who has received anti tuberculosis therapy earlier. First line anti-tuberculous drugs includes Isoniazid, Rifampicin, Streptomycin, Ethambutol and Pyrazinamide. The descriptive analyses of continuous variable were expressed as mean ± SD and categorical variable were expressed as proportion (%). The patient characteristics included age and gender. The P value < 0.05 was considered to be statistically significant. Statistical analysis was performed using SPSS version 14.

RESULTS

Among 50 patients, 28(56%) were males and 22(44%) were females, their age ranged from 16-80 years (38.14 + 15.69) and most of them belonged to poor socioeconomic status. Patients were divided into groups according to age (group-I 15-29 yrs, group-II 30-44 yrs, group-III 45-59 yrs, group-IV >60 yrs). Twenty seven (54%) belonged to urban and 23(46%) from rural areas, 38(76%) were smokers while 12 (24%) were non smokers. Clinically all 50(100%) patients presented with history of fever and cough, haemoptysis was present in 36(72%), chest pain in 9 (18%) and dyspnea in 11(22%) cases. On Physical examination anemia was present in 39(78%), cyanosis in 5(10%), edema in 6(12%), lymphadenopathy in 12(24%) and clubbing in 4(8%) patients. On X-ray chest, 19(38%) patients have multiple infiltrations, cavitations in 10(20%), fibrosis in 9(18%), consolidation in 5(10%), pneumothorax in 4(8%) and pleural effusion in 3(6%) cases. Sputum for AFB was positive in all cases. Twenty-one (42%) culture positive patients were those who have not taken anti-tuberculous drugs previously (Primary resistance) and 29(58%) culture positive were those who had taken anti-tuberculous drugs previously (secondary resistance) for at least 3 months. Among all culture positive cases, 20(40%) were sensitive to all five drugs, 9 (18%) resistant to one drug, 11(22%) resistant to two drugs, 7(14%) resistant to three drugs, 3(6%) resistant to four drugs and none of them was resistant to all five drugs. Total cases resistant to Isoniazid were 23(46%) with 9(18%) primary and 14(28%) having secondary resistance. Resistant cases to rifampcin were 13(26%) with 5(10%) primary and 8(16%) secondary resistance cases. Resistance to Ethambutol was observed in 15 (30%) cases, with primary resistance in 2(4%) and secondary in 13(26%) cases. Similarly cases resistant to Streptomycin were 9(18%) with primary in 2(4%) and secondary resistance in 7(14%) cases and resistance to Pyrazinamide was seen in 4(8%) cases, having primary in 1(2%) and secondary in 3(6%) cases.

TABLE I:
BASIC SOCIO-DEMOGRAPHIC AND CLINICAL CHARACTERISTICS OF PATIENTS (n=50)

Age (in years) Mean + SD (Range)	38.14+15.69 (16-80)
Age group: 15-29 30-44 45-59 60 and above	n (%) 23(46) 16(32) 7(14) 4(8)
Gender Male Female	 28(56) 22(44)
Locality Rural Urban	 27(54) 23(46)
Income Groups Poor Middle	 43(86) 07(14)
Smoking status Smoker Non-smoker	 38(76) 12(24)
H/O contact with TB patients Contact +ve Contact -ve	 9(18) 41(82)
Presenting Symptoms Cough Fever Haemoptysis Weight loss Chest pain Dyspnea	 50(100) 50(100) 36(72) 27(54) 09(18) 11(22)
Radiological Findings TB cavitations Multiple infiltrations Fibrosis Consolidation Pneumothorax. Pleural effusion	 10(20) 19(38) 09(18) 05(10) 04(8) 03(6)

TABLE II:
MICROSCOPY (ZN STAINING) RESULT IN RELATION TO SEX (n = 50)

	Few AFB seen n(%)	Moderate AFB seen n(%)	Numerous AFB seen n(%)
Male	4(28.6)	08(47)	10(52.6)
Female	10(71.4)	09(53)	09(47.4)
Total	14(28)	17(34)	19(38)

TABLE III:
DRUG RESISTANT CASES IN RELATION TO AGE AND SEX (n = 50)

	Group-I (15-29 yrs) n(%)	Group-II (30-44 yrs) n(%)	Group-III (45-59 yrs) n(%)	Group-IV (>60 yrs) n(%)
Resis-tance in Males	05 (45.5)	07(53.8)	03(60)	01(100)
Resis-tance in Females	06 (54.5)	06(46.2)	02(40)	0
Total	11(22)	13(26)	05(10)	01(02)

TABLE-IV:
RESISTANT PATTERN OF ONE OR MORE DRUGS (n =50)

Sensitivity Pat-tern	Primary cases n (%)	Secondary cases N(%)	Total n(%)
Culture positive	21(42)	29(58)	50(100)
Sensitive to all drugs	12(24)	8(16)	20(40)
Resistant to one drug	2(4)	7(14)	9(18)
Resistant to two drugs	4(8)	7(14)	11(22)
Resistant to three drugs	3(6)	4(8)	7(14)
Resistant to four drugs	0(0)	3(6)	3(6)

DISCUSSION

The problem of emergence of drug resistant strains of tubercle bacilli is interesting and serious to clinicians in their effort to prevent and treat TB. The mutant strains which are resistant to one anti-tuberculous drug were sensitive to others and this is basis of poly chemotherapy for treating TB which prevent selection of resistant mutants and leads to sterilization of the lesion. Today poly chemotherapy is matter of great concern due to emergence of resistant strains to multiple anti-tuberculous drugs. The results of our study shows that prevalence of drug resistance in mycobacterium TB is significantly greater in Sindh as compared to other parts of Pakistan. Bhatti et al[13] conducted his study at Institute of TB and chest disease,

and PMRC Tuberculosis research centre Lahore showed that resistance to Isoniazid was 34%, Streptomycin 40.6%, Ethambutol 3.8% and Rifampicin 4.5%, whereas our study shows the resistance as 46%, 18%, 30% and 26% respectively. Similar study conducted at Mayo hospital Lahore in 1999, showed Isoniazid resistance in 25%, Streptomycin 19%, Rifampicin 15%, Pyrazinamide 32% and Ethambutol 12%. Khan J et al conducted study in Karachi in 1992 observed primary resistance to one or more anti-tuberculous drugs in 17% and secondary resistance in 36%[14] whereas our study shows primary resistance in 30% and secondary resistance in 70% cases. In the Unites States, primary resistance to one or more drugs was 8% and secondary resistance 23% during 1982-86 and in1993 primary resistance was present in 33% and secondary resistance in 44%.[15, 16] Similarly in Canada primary drug resistance is found in 62% and secondary resistance in 38% cases.[17] These studies show high primary drug resistance in United States and Canada than in our study. The methods which can be tried to prevent the development of drug resistant TB are firstly proper health education and counseling of TB patients to develop compliance with treatment. Patient must know the course of disease, proper dose of each and every drug, the duration for which patient has to take the drug, how he is dangerous for his close contact if the disease is not properly treated. Secondly government agencies should take proper energetic efforts to supply anti-tuberculous drugs to the patients in adequate amount free of cost. Thirdly quarantine of patients with treatment failure in their homes or tuberculous sanatoria is to be tried because confinement of these patients may protect others and may accelerate their treatment and cure.

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