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Drug Resistance of *Mycobacterium tuberculosis* Strains Isolated from Patients with Pulmonary Tuberculosis in South Eastern of Iran

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In the present research, we decided to study the drug resistance rate of isolated strains to the first line of anti mycobacterium drugs: isoniazid, rifampine, ethambutol and streptomycin. All tuberculosis patient who referred to Bou-Ali hospital (the only center for training and treatment of Infectious disease in Sistan and Baluchestan province) during March 2001-July 2003 whose sputum sample smear by ZNCF staining were found positive, were included in our study. After primary culture and subsequent passages, the strains of *Mycobacterium tuberculosis* were identified and isolated according to the growth rate, pigmentation and biochemical tests. Subsequently, drug sensitivity test of isolated was carried out by proportional standard method. In this study on 84 isolated strains of *Mycobacterium tuberculosis* from patients who referred to Zahedan Bou Ali hospital during March 2001-July 2003 demonstrated drug resistance to Rifampin, Isoniazid, Streptomycin and Ethambutol was 55.9, 39.2, 33.3 and 27.3%, respectively. Present findings indicated that the prevalence of drug resistance against first line of anti TB drugs will gradually became a serious problem and targeted programs for reduction of these resistance rates is essential.

Key words: *Mycobacterium tuberculosis*, drug resistance, Rifampin, Streptomycin

INTRODUCTION

Tuberculosis is a bacterial disease that may contaminate people for all of their life (CDC, 1997). Prolonged required time for treatment, presence of primary resistant strains, changing or discontinuation of anti TB drugs before completion of therapy, presence of the underlying disease, changes in the life conditions and the incidence of abnormal behavior such as alcoholism, homelessness, addiction, grate migration, migration around big cities and AIDS, have caused the incidence and dissemination of drug resistance strains to be a serious and dangerous problem (CDC, 1997; Raviglione *et al.*, 1997; Cole and Telenti 1995).

Although in the last few years there was not much reports on increasing drug resistance in *Mycobacterium tuerculosis*, the pattern of resistance has been changed (i.e. poly resistant strains increased and mono resistant ones decreased) (Gorokhova, 1997; Cole, 1995).

Sistan and Baluchestan province (the biggest province in the south east of Iran) regarding to its special cultural and economical conditions, is at a special risk for endemic situation of Tuberculosis. So, this study was done for determination of drug resistance of isolated strains to the first line of anti TB drugs (Isoniazid, Rifampin, Ethambutol and Streptomycin) in *Mycobacterium tuberculosis* strains isolated from Tuberculosis patients referring to Bou-Ali Hospital.

MATERIALS AND METHODS

In this study, prevalence rate of drug resistance rate to first line anti tuberculosis drugs in *Mycobacterium tuberculosis* strains isolated from newly and previously diagnosed patients referring to Bou-Ali Hospital of Zahedan in March 2001-July 2003 was determined. Samples of all patients referring to Bou-Ali Hospital during this time that had a positive smear results with ZNCF staining methods were collected.

After primary culture and necessary subculturing on Lowenstein-Johnsen medium and based on the growth rate, pigmentation and biochemical tests, 84 *Mycobacterium tuberculosis* strains were identified and entered to the study. Drug sensitivity testes of isolated strains to Isoniazid, Rifampin, Ethambutol and Streptomycin was done by standard proportional method (Sommer and Good, 1985; Vossler, 2000).

RESULTS AND DISCUSSION

Study on the 84 *Mycobacterium tuberculosis* strains isolated from patients showed that resistance rate to Rifampin(RIM), Isoniazid (INH), Streptomycin (STM) and Ethambutol (EMB) was 47(55.9%), 33(39.2%), 28(33.3%) and 23(27.3%), respectively (Table 1) and the prevalence of isolation of multiple drug resistant (MDR) and polyresistant strains was 14 (Table 2) and 32(28.09%) (Table 3), respectively.

With spreading of Human Immunodeficiency Virus (HIV) and AIDS in the world, changing in the life styles of individuals, increasing population of developing countries and spreading resistant strins of *Mycobacterium tuberculosis* in the communities, Tuberculosis has been changed to a world's important problem. In this study we performed drug sensitivity tests on 84 isolated strains of *M. tuberculosis* and it was determined that the most prevalent drug resistivity between isolated strains was Rifampin 47(55.9%), Isoniazid 33(39.2%), Streptomycin 28(33.3%) and Ethambutol 23(27.3%), respectively.

The order of observed resistance pattern in this study was similar with the results that was reported by Tehran training, treatment and research center or Tuberculosis and Lung Disease (Bastar *et al.*, 2001) but was different from some other published researches in which resistance rate to Isoniazid (Lu *et al.*, 2003, Naudziunas and Andriuskeviciene, 2003; Liu *et al.*, 2002) or Streptomycin (Kart *et al.*, 2002; Wang *et al.*, 2002a;

Table 1: The frequency of resistant strains of *M. tuberculosis* to the first line of anti-T. B drugs

No. of strains	Resistant to 4 drugs	Resistant to 3 drugs	Resistant to 2 drugs	Frequency of resistance to each of the drugs				Without any resistance
				Isoniazid	Rifampin	Ethambutol	Streptomycin	
84	7 8.3%	7 8.3%	18 21.4%	33 39.2%	47 55.9%	23 27.3%	28 33.3%	6 7.1%

Table 2: The frequency of MDR strains isolated from *M. tuberculosis* samples

No. of samples	Resistant to 4 drugs (HRES)	Resistant to 3 drugs (HRE)	Resistant to 3 drugs (HRS)	Resistant to 2 drugs (HR)	No. of MDR strains
84	7 cases (8.3%)	3 cases (3.5%)	3 cases (3.5%)	1 case (1.2%)	14 cases (16.6%)

Isoniazid (H), Rifampin (R), Ethambutol (E) and Streptomycin (S)

Table 3: The frequency of polyresistant strains within isolated strains of *M. tuberculosis*

No. of samples	Resistant to 4 drugs (HRES)	Resistant to 3 drugs			Resistant to 2 drugs					Total number of polyresistant strains	
		RES	HRS	HRE	HR	RS	HS	RE	HE		Es
84	7	1	3	3	1	4	4	3	4	2	32 (38.09%)
			7					18			

Isoniazid (H), Rifampin (R), Ethambutol (E) and Streptomycin (S)

Al-Hajjai *et al.*, 2001) was the most frequent ones. Also in Wang study (Wang *et al.*, 2002b) that the most observed resistance rate was to Rifampin, the second prevalent observed resistance rate was to Streptomycin, which is different with this study. Similar with the most previous studies (Bruchfeld *et al.*, 2002; Ding *et al.*, 2000), the least observed resistance rate was to Ethambutol. This study showed that MDR and polyresistant strains constitute 14(16.6%) and 32(38.1%) of isolated strains respectively. So, targeted programs for reduction of these rates is essential. In polyresistant strains, the most common observed resistivity was to two drugs followed by three and four anti-tuberculosis drugs which in order was similar with the results of Alrajhi *et al.* (2002) and Tsogt *et al.* (2002).

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