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Original article

Prevalence of drug resistant tuberculosis in Arsi Zone, Ethiopia

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Abstact

Background: Wide spread of occurrence of multi-drug resistance tuberculosis is becoming a major challenge to effective tuberculosis control. Thus, it is imperative to monitor the sensitivity of anti-TB drugs regularly.

Objective: To determine the prevalence resistance to anti-TB drugs in a well established control program area in Arsi zone.

Methods: A health institution based cross-sectional study was designed in Arsi zone Oromia Region, Ethiopia. Patients who have never been treated and previously treated with anti-tuberculosis treatment: isoniazid, streptomycin, thiacetazone, rifampicin and ethambutol were included in the study. Culture positive specimens were tested for susceptibility testing to the anti–tuberculosis drugs using a proportion method with Loweinsten – Jensen medium.

Results: The over all resistance to one or more of the anti–tuberculosis drugs was 19.5% (38/195). Primary and acquired resistance were 18.2% (32/172) and 31.6% (6/19), respectively. Multi drug resistance tuberculosis (isoniazid and rifampicin) was absolutely nil in both cases.

Conclusion: A wider use of Directly Observed Treatment Short course in the area may contribute to the control of the incidence of drug resistance. [Ethiop. J. Health Dev. 2001;15(1):11-16]

Introduction

Tuberculosis (TB) continues to be an important public health problem world –wide, in terms of both mortality among the adult population and the appearance of micro epidemics of Tuberculosis due to multi drug resistant strain (1). Worldwide, infection with Mycobacterium tuberculosis is estimated at 1.7 billion at any given time and the global TB burden to be 9 million new cases in 1995 (2,3). Of the people infected with Mycobacterium tuberculosis, 5-10% usually develop clinical tuberculosis in the course of their lives, mainly through endogenous exacerbation of latent bacilli and 3 million patients die from the disease annually (2).

Ethiopia has a high rate of tuberculosis infection and the disease is one of the major public health problems in the country. Studies from hospital-based records indicate the disease to be among the leading cause of death (4). Although there are as yet no reliable national prevalence figures, the annual incidence of new cases is estimated to be 169/100,000 and prevalence of 338/100,000 (5).

Poor management of tuberculosis control causes resistance to anti-tuberculosis drugs. Wide spread of occurrence of multi drug resistance Tuberculosis (MDR-TB) would constitute a major threat to tuberculosis control in resource poor country (6). The human immune deficiency virus (HIV) infection, MDR-TB, poverty, migration, ethnic conflicts and substance abuse is an increasing problem and has become an additional challenge to TB control efforts (7-9). The HIV epidemic is a main reason for the reversal of the steep decline in the prevalence of Tuberculosis in places with effective functioning Tuberculosis Control Program (10-12). In Ethiopia the periodic drug resistance survey is lacking. Few studies have reported the level of resistance to one or more drugs to be in the order of 15% to 37% (13 -15).

Arsi is located in the eastern part of Oromia region, Ethiopia. The estimated population is around 2.4 million. Two hospitals, seven health centers and clinics are under Arsi zone health bureau. Arsi is the first in the region where directly observed treatment short course (DOTS) has been implemented in 1992. Recent data shows the number of case finding (smear positive) was about 40 percent (Data from National Control Program).

Since there is an increasing tendency to apply DOTS, throughout the country, properly designed drug resistance surveillance is needed. The objective of this study was therefore to estimate the prevalence of drug resistance tuberculosis and to see the performance of the control program in Arsi zone, Ethiopia.

Methods

A health institution based cross-sectional study was designed. The study was conducted in Arsi Zone of Oromia Region, Ethiopia. Diagnosis of tuberculosis in the program depends on sputum smear examination. The study was conducted in the two hospitals and six health centers that are under Arsi Zone Health Bureau.

All previously treated with anti-tuberculosis drugs (isoniazid, streptomycin, thiacetazone, rifampicin and ethambutol) and all previously untreated smear positive tuberculosis patients who visited the health institutions between June 1997 and June 1998 were included in the study.

Patients were interviewed by a TB-coordinator to obtain information on age, sex, occupation and history of previous treatment. Immediately after collection of sputum for culture, patients were put on treatment. Resistance of tubercle bacilli was reported as primary or acquired. Primary resistance defined as the presence of resistant strain of M. tuberculosis in a patient with no history of prior treatment. Acquired resistance is that which is found in a patient who has received at least one month of prior anti-tuberculosis treatment (16).

A sputum sample was collected from each eligible patient using standard container and were kept in refrigerator at 40C. Using cold boxes all the collected sputa were transported to mycobacteriology laboratory in the Ethiopian Health and Nutrition Research Institute, Addis Ababa. Samples were decontaminated and further homogenized according to petroff's method with 4% sodium hydroxide (17,18). The decontaminated samples were inoculated onto two Loweinstein - Jenson (LJ) media containing tubes and were incubated at 370C for 8 weeks and examined weekly for the growth of mycobacterium. Species identification was performed using standard biochemical tests including: niacin production, nitrate reduction and 680C labile Catalase test (18).

Isoniazid (INH, Sigma Chemicals Co. St. Louis, MO, USA), Streptmycin (SM, Sigma Chemicals Co. St, Louis, MO, USA), Thiacetazone (THA Sigma chemicals Co. St. Louis, MO, USA), Rifampicin (RIF, Sigma Chemicals Co. England) and Ethambutol (EMB Sigma Chemicals Co. St. Louis, MO, USA) were tested on 195 M. tuberculosis isolates. A stock solution of each drug was prepared in a proper solvent (19). Multi-drug resistance was defined as resistance at least to both isoniazid and rifampicin (20).

Susceptibility testing was determined using the simplified variant proportion method. A 10-2 mg/ml and 10-4 mg/ml diluted bacterial suspension from the primary culture was used and 0.01 ml was inoculated on two slopes of 6 ml of control and drug containing media. Resistance is expressed as the percentage of colonies on drug containing media in comparison to the growth on drug free media at the critical concentrations of the drugs, i.e., 0.2 g/m INH, 4 g/ml SM, 2 g/ml THA, 40 g/ml RIF and 2

g/ml EMB. The critical proportion for resistance was 1% to all drugs(19). Each new batch of drug – containing medium was checked with a reference strain (H37 Rv) from American Type Culture Collection ATCC, for drug activity in order to disclose errors in the amount of drugs dispensed or heating.

Results

A total of 203 smears positive patients were obtained during the study period among these, sputum cultures were positive for 195 (96.1%) patients, the rest 8 sputum were either contaminated or did not grow tubercle bacilli. Of the 195 there were 99 men and 96 women, with a mean age of 37 years. Eighty-two (42.1%) of the 195 patients were farmers, 58(29.7%) were housewives and 43 (22.1%) were students. Among 195 patients, 176(90.2%) never had prior treatment to anti-tuberculosis drugs and 19 (9.7%) had had prior treatment to anti-tuberculosis drugs for a mean duration of one month.

Of all patients 176 never received any anti-tuberculosis treatment before. The overall resistance level to one or more anti- tuberculosis drugs was 38/195 (19.5%). Of which 32/176 (18.2%) was primary resistance and 6/19 (31.6%) was acquired resistance (Table 2). Primary resistance to isoniazid and streptomycin were 2.3% and 11.4%, respectively. Of the 19 patients who had had prior treatment, resistance to isoniazid was 5.3% and 10.5% to streptomycin. The rates of primary and acquired MDR-TB were nil as was mono resistance to rifampicin and ethambutol. There was no association between drug resistance and the demographic variables.

Discussion

In this study the overall rate of drug resistance at 19.5% is lower than previous study done in Harar which was 37.3% (15). The low rate of drug resistance in our study is thought to be due to relatively well-organized control program in the area.

Acquired drug resistance in this study is 31.6%. Since this study was conducted in area where DOTS were implemented, and the control program was relatively efficient, it may have an indication of the low rate of resistance comparing to the previous studies done in Ethiopia (15,21,22). In some African countries with efficient national control program such as Tanzania, relatively low levels of acquired drug resistance have been reported (23).

Primary drug resistance in our finding is 18.2% whereas previous study in Harar showed 32.5% (15) As observed in Arsi, the accessibility of anti-tuberculosis drugs, supervised treatment and the wide practice of treating tuberculosis patients in the health institutions with the recommended diagnosis, treatment and follow up procedures, may contribute to the low rate of primary drug resistance. Primary drug resistance rate observed to isoniazid in this study (2.3%) was lower than the previous two studies done in TB centers, which showed 12%, 21.4% in 1984 and in 1997 respectively (14,15). This may reflect that patients coming to the health institutions are more likely to have not received prior anti-tuberculosis treatment as compared to the patients coming to tuberculosis centers. Single drug resistance to streptomycin was highest in this study. Overall the tendency of drug resistance to streptomycin seems increasing in recent years (5,14,15). This is thought to be related to the past wide spread use of streptomycin as antibiotic in the treatment of infectious disease other than tuberculosis. The absence of resistance to rifampicin alone and in combination with isoniazid in this study may probably indicate that these drugs are properly used in the study area.

One limitation of this study is that patients classification in acquired drug resistance group were defaulters, relapse cases, treatment failures and chronic execrators. Since this study is cross-sectional it was difficult to observe either patients were re-infected with exogenous resistant bacilli or not. Another limitation of the study is that it had small number of samples particularly in acquired resistance group. Thus, further study is needed to elucidate the finding.

In conclusion, the findings suggest that the introduction of DOTS may have contributed to the low prevalence of drug resistance in this area. Therefore, a wider use of DOTS, periodic drug-surveillance system and further study including HIV status are recommended.

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Tables

Table 1: **The over all resistance to one or more anti-tuberculosis drugs by socio demographic factors**

Characteristics	**Total population**	**Number of drug resistance detected**	**Percent**	**P-value**
Age year				
7-20	79	20	25.3	0.23
21-41	88	14	15.9	
>41	28	4	14.3	
Sex				
Female	96	15	15.6	0.25
Male	99	23	32.2	
Occupation		15		
Farmers	82	8	53.6	0.05

Student		9		
Housewives	43	6	18.6	
Other	58		15.5	
	12		50.0	
Previously treated	176 19			
Yes		32	18.2	0.27
No		6	31.6	
Total	195	38	19.5	

Table 2: **Anti-tuberculosis drug resistance in Arsi zone, Ethiopia**

Drug	Primary resistance (%) (n=176)	Acquired resistance (N=19)
Isoniazed	4 (2.3)	1 (5.3)
Streptomycin	20 (11.4)	2 (10.5)
Thiacetazone	2 (1.1)	0
Rifampicin	0	0
Ethambutol	0	0
Isoniazid + Streptomycin	5 (2.8)	3 (15.7)
Isoniazid + Rifampicin	0	0
Isoniazid + Rifampicin + Thiacetazone	1 (0.5)	0
Any drug	32 (18.2)	6 (31.6)

Figures

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