SURVEILLANCE OF ANTI-TUBERCULAR DRUG RESISTANCE

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ABSTRACT

Tuberculosis is the leading cause of death in Nepal. Failure in early detection and drug resistance are two most important problems in treatment and cure of the tuberculosis. The objective of the study was to assess the drug resistance pattern in *Mycobacterium tuberculosis* isolated in Tribhuvan University teaching Hospital. More than 85% of isolates were sensitive to all the four drugs and 5.5% of isolates were multidrug resistant. The drug resistant isolates were obtained more frequently from previously treated patients. More extensive studies should be carried out by independent organizations to collect more representative data on drug resistance tuberculosis.

Key Words: Tuberculosis, drug resistance and surveillance.

INTRODUCTION

Tuberculosis is a global emergency. Presently, 8 million new cases occur each year and 3 million die with tuberculosis in the world.¹ Nearly 38% of the global burden of TB exists in the SAARC member countries. Three of the SAARC member countries, Bangladesh, Pakistan and India are among the 22 high burden countries in the world. Thirty seven percent of the global TB cases occur in these three countries. At present there are 80,000 tuberculosis patients including 44000 new

tuberculosis cases in Nepal and 9,000 cases die of tuberculosis each year.² The prevalence of tuberculosis has been found to be high in the productive age group of the population.^{3,4} Resistance of *M. tuberculosis* to antibiotics is a man made amplification of spontaneous mutations in the genes of tubercle bacilli.⁵ Although tuberculosis is a curable and preventable disease, unfortunately, it does not happen. The increasing number of resistant cases to anti-tuberculosis treatment in developing countries has alarmed the patients and the physician's equally.⁶ Drug resistance

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complicates tuberculosis treatment.⁷ Multi drug resistance (MDR) is defined as resistance to at least isoniazid and Rifampicin, the two most potent drugs and the mainstays of anti-tuberculosis treatment.⁸ MDR tuberculosis (TB) is the public health threat requiring sound epidemiological data. Resistant to both Isoniazid (H) and rifampicin ®, MDR TB is difficult to treat.⁹

The objectives of the study were to assess the level of drug resistance in isolates obtained from out patients and inpatients and help physicians to review the treatment in those patients not responding to therapy due to various reasons.

MATERIALS AND METHODS

Seventy new and 4 isolates obtained from previously treated cases were studied over a period of one year from January to December 2000 at Tribhuvan University Teaching Hospital (TUTH). Sputum samples were collected from the suspected pulmonary tuberculosis where as variety of sample according to the site such as pleural fluid, ascitic fluid, urine, etc were collected from suspected extra-pulmonary tuberculosis. Those specimens were processed according to the modified Petroff Method (WHO/TB/98.258) and then inoculated in Ogawa media and incubated at 37°C for 6-8 weeks. Typical cream colored buff and rough colonies against the green egg based medium were observed. Those colonies were identified by biochemicals and Niacin test. After that those culture were subjected for anti-tubercular drug sensitivity test.

The sensitivity test was done by the "Absolute concentration method". For the anti-tuberculosis drug sensitivity test 1% ogawa medium was used with anti-tuberculosis drugs in the following concentrations: isoniazid (INH) 0.1 µg/ml, 1µg/ml, 5µg/ml, Rifampicin (RMP) 10µg/ml, 50µg/ml, Streptomycin (SM) 20µg/ml, 200 µg/ml,

Ethambutol (EMB) 2.5 µg/ml, 5 µg/ml. The tubes were incubated at 37°C for 6 weeks.

RESULTS

Of the 74 isolates tested for antimicrobial sensitivity four were from previously treated patients. During the study period four patients were documented with pervious drug exposure. All the four isolates from the previously treated patients were resistant to two or more anti tuberculosis antibiotics.

Among the 70 untreated patients, 63 (90%) of isolates were sensitive to all four antibiotics but the remaining was resistant to two or more antibiotics. Therefore primary drug resistance (PDR) was seen in 1(1.4%) to EMB, 3(4.3%) to two drugs, 2(2.8%) to three drugs and 1(1.4%) of the isolates to four drugs as shown in Table.1. The overall proportion of PDR to any of the first line drugs was 9.8% and multi drug resistance (RMP+INH) in untreated patients was 8.6%.

Table No. I
Resistance pattern of all the isolates

S. No.	Drug Susceptibility testing results	No. of culture positive patients tested for drug susceptibility				Total
		Untreated		Treated		
		No	%	No	%	
1	Total tested	70		4		74
2	Sensitive	63	90.0	0	0	63
3	Resistance to 1 drug EMB	1	1.4			1
4	Resistance to 2 drugs RMP+INH	3	4.3	1	25.0	4
5	Resistance to 3 drugs RMP+INH+EMB	2	2.8	2	50.0	4
6	Resistance to 4 drugs RMP+INH+SM+EMB	1	1.4	1	25.0	2
7	Multi drug resistance RMP+INH	6	8.6	4	100	

DISCUSSION

The objectives of this study were to ascertain the level of antimicrobial resistance in patients diagnosed at hospital. The study revealed that the 90% of isolates were sensitive to all four drugs and 10% of the isolates had primary resistance to one or more drugs tested against it and 8.6% of the isolates were multidrug resistances (MDR). Of the

74 isolates four strains were isolated from previously treated cases and all isolates were multi drug resistant. It is very rare to have past history of treatment and only 4 (5.4%) patients had given past history of treatment with anti-tubercular drugs. Similar study in German Nepal tuberculosis project demonstrated that the level of MDR resistance in untreated cases was 5.7% and 1.6% in 1987-1990 and 1991-1994, respectively. The study also showed that the level of MDR was 30% of the isolates in 1987-1990 and around 10% in 1990-1994 study period.¹⁰ In comparison to these studies, the WHO/IUALTD global project on anti-tuberculosis drug resistance surveillance conducted in 1994-1997 showed monoresistance in 5.7% and multidrug resistance in 1.1%.⁵ And the recent anti-tuberculosis drug resistance by WHO/IUALTD showed that mono resistance was in 4.8% and Multidrug resistance in 1% of new cases and monoresistance in 7.4% and multidrug resistance in 7.4% among previously treated cases.¹¹

CONCLUSIONS

The present study showed relatively high level of monoresistance and also MDR in new cases. Almost all other studies and present study in Nepal revealed high level of MDR in previously treated cases. The study shows that the burden of MDR-TB is high in the community. Poor case management may have led to acquired resistance in patients who then infected their contacts with primary resistant strains of tuberculosis. This study shows an urgent need to establish effective TB control activities.

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