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RESEARCH ARTICLE

First line anti-tubercular drug resistance among patients visiting German Nepal Tuberculosis Project, Nepal

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ABSTRACT

INTRODUCTION: Tuberculosis is one of the commonest causes of death in the world. It remains a major public health problem in developing countries including Nepal. Despite the reduction in incidence of tuberculosis by the implementation of anti-tuberculosis drugs regimen, TB remains pandemic due to emergence of drug resistant strain of M. tuberculosis. The aim of this study was to evaluate the first line anti-tubercular drug resistance among patients visiting German Nepal Tuberculosis Project, Nepal.

MATERIALS AND METHODS: Anti-tubercular drug susceptibility test for first line drugs (Rifampicin, Isonizid, Ethambutol, and Streptomycin) was performed by proportion method (n=141) for new sputum smear positive patients attending German Nepal Tuberculosis Project, Kathmandu, Nepal.

RESULTS: 78.1% (n=110.) were sensitive to all 4 drugs. Eight isolates (5.6%), 4(2.8%), 10(7.1%) and 31(21.9%) were resistant to any 4, 3, 2 and 1 drug respectively. Proportion of drug resistant (PDR) to one drug was 12.6%, two drugs 7.6%, three drugs (6.3%) and four drugs was 5.6%. Our result indicates the PDR to the first line drug was 21.9% and multidrug resistant (MDR) was 12 (8.5%).

CONCLUSIONS: Drugs resistant cases of tuberculosis in increasing. Surveillance and monitoring of the drug resistant tuberculosis is necessary to prevent emergence of MDR, extensively drug resistant and so-called totally drug resistant tuberculosis.

KEY WORDS: Tuberculosis; Anti-tubercular drugs; Multi-drug resistant

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INTRODUCTION

Tuberculosis (TB) is a public problem. The 1990's have witnessed a resurgence of TB. Re-emergent TB is fuelled by the pandemic HIV and AIDS and by single and multi drug resistance.[1] Treatment with anti-tubercular drugs is the only effective method to cure active TB disease. Highly effective medications for tuberculosis have been available for nearly 50 years. Bactericidal anti-tuberculosis drugs like, rifampicin, isoniazid, pyrazinamide, streptomycin and bacteriostatic like, ethambutol, ethionamide, thiacetozone, para-aminosalicylic acid and cycloserine are in practice.[2]

Drug susceptibility testing is designed to show that the great majority of bacilli in culture are as susceptible to a given drug as one or more known susceptible strains. It is also of value in the surveillance of tuberculosis in order to detect and monitor emergence of drug resistance. There has, however, been considerable debate whether a susceptibility test is essential for the management of individual patients or not. In some countries, a fear of litigation leads to a regular use of susceptibility testing and it is highly desirable in regions where drug and multi-drug resistant is common.[3]

TB drug resistance is a major problem that threatens the success of DOTS. WHO has recommended treatment strategy for detection and cure of TB as well as global tuberculosis control. Drug resistance arises due to the improper use of drugs in the treatment of TB patients. This improper use is a result of a number of actions, including administration of improper treatment regimens by health care providers and failure to ensure the completion of whole course of treatment. Essentially, drug-resistance arises in areas with poor TB control program.

Unfortunately, owing to poor prescribing practices, inadequately formulated drugs, intermittent supplies of drugs, poor compliance and a lack of supervision of therapy, drug resistance is a serious and increasing problem in many regions.4 The objective of the study is to determine the first line anti-tubercular resistance in patients visiting German Nepal Tuberculosis Project.

MATERIALS AND METHODS

This study was conducted in German-Nepal Tuberculosis Project (GENETUP) Kalimati, Kathmandu, Nepal from October 28, 2007 to September 01, 2008. This work is the continuation study of Regmi S., et al, 2008.[5] Anti-tubercular drug susceptibility test was performed using proportion method.

For the proportion method, a suspension of bacteria equivalent to McFarland No. 1 was made. To a sterile glass tube containing glass beads, few drops of normal saline was added. About 1mg of colonies was transferred to the glass tube with sterile loop from the culture tube. The colonies were homogenized by placing the tube in vertex (rotator). After complete homogenization, the suspension was made as McFarland std. 1 by adding normal saline. The standard suspension was diluted as 10^{-1}, 10^{-2} and 10^{-3}. The dilution 10^{-1} was taken as test solution and 10^{-3} was used for control. For anti-tuberculosis drug susceptibility test, LJ media with different drug in different concentration was used. The concentration of INH, EMB, SM and RMP in LJ medium was (0.025, 0.05, 0.1 and 0.2 µg/ml), (0.125, 0.25, 0.5 and 2 µg/ml), (0.5, 1, 2, and 4 µg/ml) and (2.5, 5, 10 and 40 µg/ml) respectively in 4 tube sets. The incubation and reading and interpretation was done as per the standards for LJ proportion method.

Quality control was done by maintaining strict aseptic condition during handling and processing of the bacilli. The sterility of each batch of test medium was confirmed by incubating 5% un-inoculated tubes with the inoculated tubes as control.

RESLUTS

Among the 141 *M. tuberculosis* isolates, 19 (13.4%) were resistant to INH, 11 (7.8%) were resistant to EMB, 24 (17.1%) were resistant to SM and 17 (12.1%) were resistant to RMP. Among the 4 drugs, EMB was most sensitive (n=130, 92.2%) followed by RMP (n=124, 87.9%), INH (n=122, 86.5%). Among 4 drugs, SM appeared to be least sensitive of all drugs. The resistant to all 4 drugs were 8 isolates, any 3 drugs were 4 isolates, any 2 drugs were 10 isolates and any one of the drugs were 31 isolates. The multi-drugs resistant isolates were 12 (8.5%). Proportion of drug resistant

Table 1. Resistance Pattern of all isolates

Characteristics		Resistant	
		n	%
Total, n=141		31	21.9
Mono resistance	RMP	17	12.1
	INH	19	13.4
	EMB	11	7.8
	SM	24	17.1
Poly resistance	RMP + INH	12	8.5
	RMP+SM	13	9.2
	RMP+EMB	10	7.1
	INH+EMB	8	5.6
	INH+SM	12	8.5
	SM+EMB	10	7.1
	RMP + INH+SM	10	7.1
	RMP+SM+EMB	10	7.1
	INH+SM+EMB	8	5.6
	RMP+INH+EMB	8	5.6
	RMP+INH+SM+EMB	8	5.6
MDR		12	8.5

(PDR) to one drug was 12.6%, two drugs 7.6%, three drugs (6.3%) and four drugs was 5.6%.

DISCUSSION

Drug-resistant TB is a serious public health issue in many developing countries, as its treatment is longer and requires more expensive drugs.[6] Recurrence of TB cases should be treated only after performing antibiotics sensitivity tests.[7]

Drug resistance reports available from Nepal have shown the emergence of multi-drug resistance (MDR). In Nepal, acquired resistance to one or more drugs arising during the course of treatment is around 65% to isonizid and around 30% to rifampicin.[8] Initial drug resistance in Nepal has been reported to be 5-24%.[9] Shrestha *et al*. (1996) reported the initial resistance for each specific drug as RMP in 4.5%, INH in 9.4%, SM in 18.3% and EMB in 7.3% and RMP+INH in 3.6% in a study carried out for 8 years at Urban TB clinic in Kathmandu valley.[9] In our study, resistant to individual drug like, isonizid was 13.5%, ethambutol was 7.8%, streptomycin was 17.1% and rifampicin was 12.1%. Combined INH+RMP resistance was 8.5%. In our study, drug resistant to one drug was found to be 12.6%, 2 drugs was 7.6%, 3 drugs was 6.3% and to 4 drugs 5.6% and MDR (RMP+INH) was 8.5%. Proportional study shows the drugs resistant pattern is similar so the implementation of DOTS program should be made more effective in order to reduce the MDR-TB cases.

CONCLUSION

The drug resistance is emerging in Nepal including the rise of MDR TB. National Tuberculosis control program should ensure that the defaulters in DOTS are reduced and prevent emergence of MDR TB. The program should also monitor the first line drug resistance continuously.

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