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ORIGINAL RESEARCH ARTICLE

Prevalence of Primary Drug Resistant Tuberculosis in a Tertiary Care Hospital, Nepal

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ABSTRACT

Background & objectives: Tuberculosis is a transmissible disease mainly due to inhalation of infected droplet nuclei. The burden of drug resistant tuberculosis is very high in our neighboring countries India and China. Prevalence of primary drug resistant disease is difficult to estimate in our country because culture and sensitivity is not done routinely. This study was an attempt to find out the prevalence of drug resistant in newly diagnosed tuberculosis patients serving in the Nepalese Armed Forces. Medical records of patients serving in the Nepalese Armed Forces who had the provisional diagnosis of pulmonary tuberculosis for the first time from July 2012 to June 2014 were analyzed. They had their sputum subjected for both smear and culture with sensitivity testing. Out of 134 patients, 62 had culture positive for Mycobacterium tuberculosis and drug sensitivity was done for the first line 4 antitubercular drugs. Drug resistant strains were found in 5 cases (8.1%) of which 2 (3.2%) were resistant to 4 first line drugs - rifampicin, isoniazid, ethambutol and streptomycin. Prevalence of isoniazid resistance was the highest, found in 3 cases (4.8%). Primary drug resistant tuberculosis in newly diagnosed cases was high even in young healthy adults, and isoniazid resistant strains were the commonest.

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Key word: *Drug Resistant Tuberculosis, Nepal, Prevalence.*

INTRODUCTION

Tuberculosis is a transmissible airborne infection caused by Mycobacterium tuberculosis. It is transmitted by inhalation of infected droplet nuclei of 1-5 µm diameters that remain suspended in the environment when an infectious person coughs, sneezes, laughs or sings .[1] There were about 9 million new cases of tuberculosis in 2011 with 1.4 million deaths due to tuberculosis. The burden of tuberculosis is very high in our region, India and China combined accounting almost 40% of world cases.[2] Moreover, about 50% of world's multi-drug resistance tuberculosis (MDR-TB) cases are estimated to be in India and China.[3] With the advancement in diagnostic techniques it has been found that local epidemic of tuberculosis is mainly due to ongoing transmission rather than reactivation of dormant infection. Majority of transmission occurs before pulmonary tuberculosis is diagnosed and treated. Casual contact with infected environment may be sufficient for transmission.[4]

The principal pathways leading to development of drug-resistant tuberculosis are:

a. primary or initial and
b. acquired or secondary.

Primary drug resistance means that a person has been infected with drug-resistant TB strain. The acquired drug resistance is mainly due to inappropriate case management. Inadequate, incomplete or poor treatment quality which allows growth of bacteria with resistant mutations and that ultimately become dominant strain.[5] There are different methods to test drug susceptibility- phenotypic or conventional drug sensitivity testing (DST) evaluates the growth or metabolic activity in the presence of the drug and genotypic DST (molecular DST) detects TB DNA and mutations associated with specific drug resistance.[5,6]

The extent of drug resistant tuberculosis is difficult to estimate because culture sensitivity is not a routine test especially in newly diagnosed cases due to inadequate number of quality controlled laboratories in Nepal. This study is an effort to find out the prevalence of primary drug resistance in newly diagnosed tuberculosis patients serving in the Nepalese Armed Forces.

MATERIALS AND METHODS

This retrospective study was done in the Department of Chest Diseases of Shree Birendra Hospital, Chhauni, Kathmandu. Medical records of 134 serving soldiers of the Nepalese Armed Forces admitted with the provisional diagnosis of pulmonary tuberculosis from July 2012 to June 2014 were analyzed. All

the patients had their three samples of sputum (including two of early morning sputum) examined and culture and sensitivity done for acid and alcohol fast bacilli (AFB) in German Nepal Tuberculosis Project (GENETUP) laboratory. The GENETUP is accredited as the National Reference Laboratory by Supranational Reference Laboratory, Gauting, Germany for culture and drug sensitivity test for tuberculosis.

All sputum samples were examined by Ziehl- Neelsen method for AFB. Sputum samples were decontaminated with NAC-NaOH method and cultured in Lowenstein Jensen media for 8 weeks. The positive growth was identified by using paraminobenzoic acid. Drug susceptibility testing (DST) was performed by conventional 1 per cent proportion method against streptomycin (4µg/ml), isoniazid (0.2µg/ml), rifampicin (40µg/ml) and ethambutol (2µg /ml).

RESULTS

Out of 134 patients, 62 patients had culture positive for Mycobacteria tuberculosis. Of them 2 cases were smear negative. All 62 patients in this study were young. Of them 24 patients (39%) were in the age group 25-29 followed by 16 patients (26 %) in age group 30-34 years. (Table 1)

Table 1: Age group distribution

Age group	No	Percentage (%)
20-24	13	20
25-29	24	39
30-34	16	26
35-40	9	15
Total	**62**	**100**

Their sputum status is shown in table 2. Twenty six patients (43%) had at least one sputum sample showing 2+ whereas 22 patients (37%) had 3+ on sputum microscopy.

Table 2: Sputum AFB status

Sputum status	Number	Percentage
1+	12	20
2+	26	43
3+	22	37

Drug resistant strains were found in 5 cases (8.1%) of which 2 (3.322%) were resistant to all 4 drugs- rifampicin, isoniazid, ethambutol and streptomycin. Two drugs resistant cases were 2 (3.2%), one case resistant to rifampicin and isoniazid and another one to isoniazid and streptomycin. Single drug (ethambutol) resistance was found in a patient (1.6%). MDR resistant cases were 4.8%. (Table 3) Two smear negative cases were culture positive for MTB and strains were susceptible to first four drugs.

Table 3: Drug resistance pattern

Resistant Drugs	No	Percentage
Rifampicin, INH, Ethambutol, streptomycin	2	3.22
Rifampicin, INH	1	1.6
Ethambutol	1	1.6
Streptomycin, INH	1	1.6

It was seen that isoniazid resistance was highest with 3 cases (4.8%). Strains resistant to rifampicin were found in 3.2 % cases.

All the drug resistant cases were smear negative at the time of writing this paper except one who was tested positive for HIV and second line drug therapy was recently started.

DISCUSSION

Emergence of drug resistance strain of Mycobacterium tuberculosis due to the genetic mutation in the bacilli is a major challenge for the Millennium Development Goals (MDG).[5] WHO estimation of MDR-TB burden in new cases for Nepal and India for 2013 was 2.2% which was lower than our findings though we had smaller sample size. China has reported that 5.7% were MDR-TB among new cases in her national survey. Former Soviet Union region has top 10 locations for primary MDR tuberculosis. Of them Kyrgyzstan has the highest (26%). Two surveys were carried out in Nepal by National Tuberculosis Program (NTP) and GENETUP in 2010 for primary drug resistance tuberculosis. The prevalence of MDR-TB in new cases was same on both surveys (2.2%). The global incidence of MDR-TB in new cases is not changing in recent years and was 3.5% in 2013 though the study done in King George's Medical University, Lucknow, Uttar Pradesh by Jain A et al found a decline in number of MDR strains from 35.6% in 2009 to 22.8% in 2012.[7]

The prevalence of primary drug resistant tuberculosis of 8.1% in our study was lower than reported in two studies from North India. The prevalence of 4 drugs resistant strain and the strain resistant to isoniazid and other three drugs were higher in their studies.[10,11] Isoniazid resistance without rifampicin resistance in new cases was lower in our study than Global estimation.[3] Isoniazid resistance has been reported 41% in a study by Maurya A K et al.[9] Study by Malhotra B et al from Jaipur, India found that primary drug resistance to isoniazid was 13.6%, and to rifampicin 6.8%, both were higher than our findings.[10] Resistance to isoniazid and rifampicin in previously treated patients was much higher- 62.22% and 57.22% respectively.[13,14] Abouyannis M et al in their study in Malawi found only 0.4% of the 1196 new cases were MDR-TB and mono-drug resistance or any combination of drug resistance excluding MDR cases were 6.3%. They have attributed the success to Malawi's tuberculosis programme.[15]

Difference of prevalence of drug resistance among countries may be due to difference in the use of antituberculosis drugs and their combinations and use of these drugs to treat other bacterial infections and effectiveness of national programme.[16]

CONCLUSION

Primary drug resistant tuberculosis in newly diagnosed cases was quite common even in young healthy adults of the Nepalese Armed Forces. Isoniazid resistant strains were the commonest.

REFERENCES

1. Dharmadhikari AS, Nardell EA. Transmission of mycobacterium tuberculosis. In: Tuberculosis, A comprehensive clinical references. Editors Schaaf HS, Zumla AI. 2009: 8-15.
2. Global Tuberculosis report 2012. WHO/HTM/TB/2012.6 WHO/HTM/TB/2012.6:3-4.
3. Multidrug and extensively drug-resistant TB (M/XDR-TB): 2010 Global report on survellence and response.
4. Van der Spuy GD, warren RM, Richard MJ, Beyers N, Behr MA, Helden PD. Use of Genetic Distance as a measure of ongoing transmission of Mycobacterium tuberculosis. Clin Microbioll 2003;41(12):5640-5644.
5. Companion handbook to the WHO guidelines for the programmatic management of drug-resistant tuberculosis. © World Health Organization 2014.
6. National Tuberculosis Programme Nepal. General Manual, 3rd Edition 2012:44-45.
7. Jain A, Diwakar P, Singh U. Declining trend of resistance to first-line anti-tubercular drugs in clinical isolates of Mycobacterium tuberculosis in a tertiary care north Indian hospital after implementation of revised national Tuberculosis control programme. Indian J Med Microbio. 2014 Oct-Dec;32(4):430-3.
8. Partner of the month: Highlighting the work of the Nepal Anti-Tuberculosis Association (NATA) on MDR-TB. http://www.stoptb.org/news/stories/2014/ns14_062.asp
9. National Tuberculosis Programme Nepal, Annual report Fy2012/13.
10. Maurya AK, Singh AK, Kumar M, Umrao J, Kant S, Nag VL, Kushwaha RAS, Dhole TN. Changing patterns and trends of multidrug resistant tuberculosis at referral centre in Northern India: A 4-year experience. Indian J Med Microbiol 2013;31:40-6.
11. Malhotra B, Pathak S, Vyas L, Katoch VM, Srivastava K, Chauhan DS, Singh D, Sharma VD, Das R, singh HB. Drug susceptibility profiles of mycobacterium tuberculosis isolates at Jaipur. Indian J Med Microbiol 2002;20:76-8.
12. http://www.who.int/tb/country/data/profiles/en/
13. Global tuberculosis report 2014. http://www.who.int/tb/publications/global_report/en/
14. Rawat J, Sindhwani G, Dua RJ. Five-year trend of acquired antitubercular drug resistance in patients attending a tertiary care hospital at Dehradun (Uttarakhand). Lung India 2009;26:106-8.
15. Abouyannis M, Dacombe R, Dambe I, Mpunga J, Faragher B, Gausi F. Drug resistance of Mycobacterium tuberculosisin Malawi: a cross-sectional survey Bull World Health Organ2014;92:798–806.
16. Hoffner S. Unexpected high levels of multidrug-resistant tuberculosis present new challenges for tuberculosis control. The Lancet 2012;380:1367-1369.