ORIGINAL ARTICLE

Isoniazid Resistance among New Cases of Sputum Smear Positive Pulmonary Tuberculosis

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ABSTRACT

Aim: To determine the frequency of primary drug resistance to isoniazid among new cases of sputum smear positive pulmonary tuberculosis.

Methods: One hundred and sixty nine newly diagnosed patients with sputum smear positive pulmonary tuberculosis from Jinnah Hospital and Lahore General Hospital were enrolled and sputum culture and sensitivity was tested by standard laboratory method. Patients with history of comorbid conditions and chronic steroid use were excluded.

Results: Mean age was 31.63±8.7 years and 82(48.5%) among included persons were male and 87 (51.5%) were female. Frequency of resistance to isoniazid came out about 20.1% while 79.9% persons were found sensitive to isoniazid. Thirteen patients (7.7%) were found resistant to rifampicin too. There is no effect of gender or age in both groups with and without resistance to isoniazid.

Conclusion: It was concluded that frequency of primary drug resistance to isoniazid is quite high (20%) so its reasons need to be identified.

Keywords: Sputum positive pulmonary tuberculosis, Isoniazid, Primary drug resistance in TB

INTRODUCTION

According to WHO Global tuberculosis report 2011, Pakistan ranks 5th of 22 high burden countries in tuberculosis (TB) and 4th among 27 high burden multidrug resistant (MDR) TB countries[1,2,3,4]. Drug resistant tuberculosis, particularly MDR represents a major global public health problem[1]. MDR-TB is increasing throughout the world both among new tuberculosis cases as well as among previously-treated ones[4,5]. Although previous treatment for TB is the strongest risk factor for development of MDR-TB, new patients are also at risk due to either spontaneous mutations or transmission of resistant strains[3]. The risk of transmission of resistant strains from close contacts is increasing day-by-day because of the growing burden of MDR-TB patients[6-11]

MDR-TB, defined as TB caused by organisms that are resistant to Isoniazid (INH) and Rifampicin (R) continues to threaten the progress Pakistan has made in controlling TB[1,4]. WHO has estimated 7100 MDR-TB cases among new pulmonary TB cases and 2300 among retreated pulmonary TB cases notified in 2010.The percentage of MDR-TB is 3.4 among new TB cases and 21 among retreated cases. A study published in IUALTD journal in 2008, although not representative for a specified annual cohort of notified smear positive new and retreatment cases shows 1.8% primary resistance[4].

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There are a few studies which have reported a high prevalence of MDR-TB among new TB cases.[10-13] Nation-wide representative data on prevalence of MDR-TB among new TB cases is an urgent need of hour to design effective empirical regimens, to monitor functioning and progress of national TB control programme and for continued surveillance of MDR-TB among new smear positive TB patients. This study will help us to achieve above said goals.

PATIENTS AND METHODS

A Cross-sectional survey to determine the frequency of primary drug resistance to isoniazid among new cases of sputum smear positive pulmonary tuberculosis was carried out in Jinnah Hospital and Lahore General Hospital using purposive non probability sampling. Primary drug resistance was defined as resistance of acid fast bacillus (AFB) to isoniazid (INH) in sputum cultures from patients of newly diagnosed sputum smear positive cases who never took INH as determined by history. Resistance was determined by proportion method i.e., growth of >100 colonies of AFB on Lowenstein Johnson medium containing 0.2g/ml concentration of INH after 6 weeks of incubation. Sputum positive pulmonary TB patients were those having two sputum smear positive for AFB by direct microscopy was labeled as sputum smear positive pulmonary tuberculosis patient. Taking prevalence of INH resistance 7.6% at 4% margin of error and 95% confidence level, estimated sample size was 169. Patients with history of chronic steroid use and comorbid conditions determined by history e.g. Diabetes mellitus were

excluded. After an informed consent 169 subjects those fulfilling the inclusion criteria were included in the study. A questionnaire was used as research instrument, containing background information i.e., age, sex, marital status, residential area. Sputum sample were collected in a sterile plastic container and transported to bacteriology department of institute of public health or a private lab within three hours. The outcome variable like frequency of primary drug resistance to isoniazid was recorded on proforma. Other variables like primary resistance to rifampicin and multidrug resistance was recorded additionally. Data collected was entered and analyzed using SPSS-17.

RESULTS

One hundred and sixty nine patients with mean age 31.63±8.7 years were included in the study. 82 included persons (48.5%) were male and 87(51.5%) were female. Frequency of resistance to isoniazid came out about 20.1% while 79.9% persons were found sensitive to isoniazid. 156 patients among 169 (92.3%) were sensitive to rifampicin while multidrug resistance was found in 12 patients (7.1%). To determine the effect of gender and age distribution on presence of resistance to isoniazid, rifampicin and both (multidrug), we cross tabulated and stratified data into two groups male and female and above and below 30 years. Gender distribution was same in both groups with and without resistance to isoniazid (p value = 0.565), rifampicin (p value = 0.25) and multidrug (p value= 0.275). Similarly age distribution was equal in both groups with and without resistance to isoniazid (p value= 0.25), rifampicin (p value= 0.49) and multidrug (p value= 0.36).

DISCUSSION

More than 2 billion people (about one-third of the world population) are estimated to be infected with Mycobacterium tuberculosis. The global incidence of tuberculosis (TB) peaked around 2003 and appears to be declining slowly[10,11,12,13]. According to the WHO, in 2010, 8.8 million individuals became ill with TB and 1.4 million died. But situation seems different in Pakistan.[4] To achieve millennium development goals, drug resistance has to be addressed. Progress has been made in achieving the first MDG target (to halt and reverse rising trends in the incidence of TB).[4] This goal has been wholly or partially achieved in most regions of the world.[11] there has been less success in achieving the second MDG target (to halve the prevalence and death rates due to TB present in 1990 by the year 2015). However, some progress has been achieved. For example, if the rate of improvement seen from 2001-2006 in prevalence and death rates in the Americas, eastern Mediterranean, Southeast Asia and western Pacific regions continues during the period 2006 and 2014, the second MDG goal will be achieved. Unfortunately, this goal will not be achieved by 2015 in the African and European regions at the current rates of improvement[1].

One difficulty in achieving the goals described is that a dramatic TB resurgence occurred in some areas during the 1990s. Drug susceptibility test (DST) of mycobacterium tuberculosis remains a significant part of monitoring process of TB resistance to drugs.[3] In Africa, this resurgence was largely due to the HIV epidemic, but it was also compounded by poor access to health services[2,8]. In Eastern Europe, this resurgence can be attributed to widespread economic decline, secondary declines in the overall quality of health services, poor living conditions, alcoholism, and the emergence of infection due to MDR strains of M. tuberculosis. A study conducted in New Delhi, India in 2011 showed 1.1% primary multidrug resistance. A study conducted in Burkina Faso involving 323 newly diagnosed tuberculosis patients showed 3.2% primary MDR[2]. A study conducted in Addis Ababa, Ethiopia involving 173 newly diagnosed smear positive tuberculosis patients showed 13.3% primary resistance to INH, 1.2% primary resistance to Rif and 0.6% primary MDR[8].

Mean age was 32 years showing that the most vulnerable group to pulmonary tuberculosis is young working adults. This will not only lead to increased morbidity and mortality in our population but also loss of man power. A young adult if affected in his productive live spam by tuberculosis mean that a Family has lost its economic support. In our sampled population there was almost equal distribution of gender in patient affected with pulmonary tuberculosis. Woman living in confines of their house are found to have this contagious disease. An infected woman will spread the disease to children and other household members if not detected early rising trends of pulmonary tuberculosis in women may change the trends in epidemiology of tuberculosis. More young teenagers and school children will be affected.

Isoniazid is a drug used as first line therapy against pulmonary tuberculosis in combination with other drugs its resistance may produce very huge negative effects on treatment strategy. In our study 25% of the patients were found resistant to isoniazid. Our study results were different as reported by Sheikh MA et al[10]. In previous study primary resistance came out about 42% but the sample size is quite low similarly in another African study 13.3% patients were resistant to isoniazid[2]. Our results are

similar to by Iqbal R et al. showing resistance to isoniazid 24.1%[11]. But a study performed in KPK showed very low prevalence of isoniazid resistance about 8.4%[12].

Rifampicin is the most effective anti-tuberculosis drug in combination therapy. We additionally calculated resistant to rifampicin in our sample. It came out about 8%. All the individuals with isoniazid resistant were also resistant to rifampicin except one. The results of our study are comparable that were reported by Sheikh MA et al. but it significantly different from Iqbal R et al. as they have shown rifampicin resistance in sampled population about 26.4%[11] Multidrug resistance i.e., resistance to rifampicin and isoniazid was present in 12 patients (7%). It is lower as compared with Iqbal R et al. [11] who showed it about 12.3% and higher than found in KPK study by Javed et al.[12]

CONCLUSION

It is concluded that primary resistance to isoniazid is quite high in new patients with sputum smear positive pulmonary tuberculosis along with resistance to rifampicin and both drugs combined. Strategies are needed to address the issue and get a real picture of isoniazid resistance in our population

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