ORIGINAL ARTICLE

Frequency of ATT Induced Hepatitis in Newly Diagnosed Pulmonary TB Patients

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ABSTRACT

Aim: To determine the frequency of ATT induced hepatitis in newly diagnosed pulmonary TB patients.
Methods: This descriptive, cross-sectional study was conducted at Department of Pulmonology Jinnah Hospital Lahore from August 2013 to February 2014. Total 95 newly diagnosed pulmonary TB patients were included in this study.
Baseline LFTs including ALT, AST, and bilirubin were done in every patient at time of induction and repeated at one month follow up. Data was analyzed by using SPSS 16.
Results: Mean age of the patients was 37.95 ± 14.46. Among the participants males were 51(53.7%) and females were 44(46.3%). Out of 95 patients, 34(35.8%) had ALT and AST derangements while 35(36.8%) had hyperbilirubinemia.
Conclusion: ATT induced hepatitis is a frequent complication in newly diagnosed cases of Pulmonary Tuberculosis. So, all patients put on ATT must be followed up for at least the initial month. The patients and the doctors have to be well-educated about the adverse effects of the ATT, its early recognition and management.
Keywords: Anti tubercular agents, Pulmonary tuberculosis, drug induced liver injury, hepatotoxicity

INTRODUCTION

Tuberculosis is a global health problem. Each year an estimated 8 million new cases and 2 million deaths occur due to TB worldwide[1.] Pakistan is ranked 7th most tuberculosis affected country in the world[2]. The disease prevalence in Pakistan is reported to be 263/100, 000 population[3]. WHO guidelines recommend use of 4 drugs including isoniazid, rifampicin, pyrazinamide and ethambutol for initial 2 months followed by 6 months of isoniazid and ethambutol only[4]. This drug regimen has high therapeutic efficacy and good patient acceptance. Hepatotoxicity is the most important side effect of anti tuberculous therapy (ATT)[5,6]. A recent study revealed the frequency of ATT induced hepatitis to be 19.67%. The severity ranges from alteration in liver enzymes, chronic active hepatitis and picture of acute hepatitis, occasionally complicated by acute liver failure carrying very high mortality unless transplanted[5].

The clinical risk factors for development of ATT induced hepatitis include old age, malnutrition, female gender, alcoholism, HIV infection, and chronic hepatitis B and C infections. Most of the hepatotoxic reactions are dose related, however some are caused by drug hypersensitivity.[7] Isoniazid and rifampicin induced damage may involve oxidative stress, lipid peroxidation, choline deficiency leading to lowering of phospholipids protein synthesis with alteration in cell wall configuration, reduced glutathione level and activation of CYP2E1[8]. The severity of ATT induced hepatitis ranges from asymptomatic alteration in liver enzymes to symptomatic acute hepatitis complicated by acute liver failure[9].

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METHODOLOGY

This cross sectional study was conducted at Department of Pulmonology, Jinnah Hospital Lahore from August 2013 to February 2014. Total 95 patients were included according to inclusion and exclusion criteria. An informed verbal consent was taken from every patient and approval was taken from institutional review committee. Newly diagnosed pulmonary TB patients of both genders, aged ≥ 16 years to ≤ 65 years with normal liver function test were included in this study.

Patients with previous history of jaundice, patients with abnormal LFTS, patients receiving higher dosage of ATT drugs, patients receiving other potentially hepatotoxic medications concurrent with ATT and patients with history of alcohol intake were excluded from the study. Baseline LFTs including ALT, AST, and bilirubin were done in every patient at time of induction. Patients were advised follow up for one month. At each follow up LFTs were sought. Data regarding age, gender, development of ATT

induced hepatitis and derangement of profile of LFTs was collected by attached Performa. All the collected data was entered in SPSS version 17 and analyzed. Mean and SD was calculated for numerical data. Frequencies and percentages were calculated for categorical data.

RESULTS

Mean age of the patients was 37.9±14.5, with age range from 16 years to 65 years. Out of 95 patients, males were 51(53.7%) and females were 44(46.3%). Out of 95, 35(36.8%) patients had ATT induced hepatitis (Fig 1), jaundice was found in 38(40%) patients. 34(35.8%) patients had deranged AST and ALT and 35(36.8%) patients had raised bilirubin. (Table 1).

Fig.1: ATT induced hepatitis

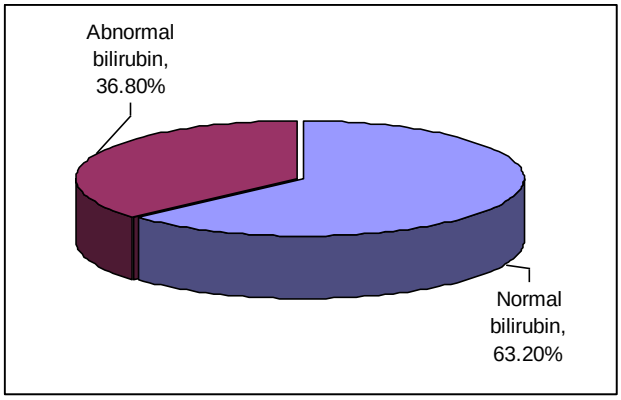

Table 1: Frequency of deranged LFTs during ATT

LFTs	Normal	Abnormal
AST	61 (64.2%)	34 (35.8%)
ALT	61 (64.2%)	34 (35.8%)
Bilirubin	60 (63.2%)	35 (36.8%)

DISCUSSION

The study reveals high degree of hepatotoxicity induced due to Antituberculous therapy. Thirty five (36.8%) patients had ATT induced hepatitis. This is a high striking rate. Tuberculosis is a major cause of preventable infectious disease and death in the world[10,11]. Timely diagnosis and proper chemotherapy are the mainstays of treatment[12]. The hepatotoxic side effect of ATT has been under extensive discussion and studies to confirm their frequency and outcome in patients, all over the world[13,14].

Surprisingly most of the research work has been done in the west and in the more developed nations of the world, while studies to the effect have practically never, if ever been done in Pakistan so commonly. A study was conducted at the Medical Unit, Ayub Teaching Hospital, Abbottabad[15], where 500 diagnosed cases of tuberculosis were treated with first-line standard anti-tuberculous drugs. Most of them were treated with Isoniazid (INH), Rifampicin, Pyrazinamide (PZA) and Ethambutol. Therapy was initiated with 4 drug regimen. A comprehensive history and examination of every patient was taken to exclude any hepato-toxicity predisposing factors. Raised transaminases were noted in 19(3.8%) patients, and 21(4.2%) patients developed overt hepatitis. These values can be compared with our study i.e., 35(36.8%) had ATT induced hepatitis.

A secular change in the incidence rate of drug-induced hepatitis (DIH) due to anti-tuberculosis chemotherapy including isoniazid (INH) and rifampicin (RFP), but not including pyrazinamide (PZA), the researchers retrospectively studied the incidence rates of DIH in patients treated with chemotherapy including INH and RFP in four periods 1980-83, 1987-88, 1991-92, and 1998-2000. The incidence rates of DIH were 10/111 (9%), 23/131 (17.6%), 26/123 (21.1%) and 32/117(27.4%) respectively. This secular increase of the incidence rate of DIH was statistically significant ($p=0.01$)[16]. ATT-induced hepatitis was detected in 70% of the patients using Antituberculous therapy with Pyrizinamide being used in addition to INH and Rifampicin in New Dehli India, which is a much higher than the rate of hepatotoxicity found in our study. But our study is a descriptive cross-sectional study and there is no control group for comparison in contrast with the aforementioned study which was a case-control study[17].

But another study which carried out at the National TB referral center Iran in 2006-2008 where 99 (13%) patients out of 761 patients, developed DIH during anti-TB treatment, which is less than our study. There was no difference in sex, nationality, smoking, or opium use history between the hepatitis group and the control group ($P > 0.05$).

CONCLUSION

ATT induced hepatitis is a frequent complication of newly diagnosed cases of Pulmonary Tuberculosis. So, all patients put on ATT must be followed up for at least the initial month. The patients and the doctors have to be well-educated about the adverse effects of the ATT, its early recognition and management.

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