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Research Article

An assessment of ATT induced hepatitis in cases of pulmonary TB patients

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ABSTRACT

Objective: To assess the ATT induced hepatitis in cases of pulmonary TB patients presenting at Lahore General Hospital, Lahore.

Material and methods: This cross sectional study was conducted at Department of Pulmonology, Lahore General Hospital Lahore from February 2018 to August 2018 over the period of 6 months. Total 95 patients of pulmonary TB taking ATT were selected and ATT induced hepatitis as assessed in selected patients.

Results: Mean age of the patients was 37.95 ± 14.46 years. Out of 95 patients of pulmonary TB taking ATT, male patients were 51(53.7%) and female patients were 44(46.3%). ATT induced hepatitis was found in 35(36.8%) patients.Raised AST derangement was noted in 34 (35.8%) patients, ALT derangement was noted in34 (35.8%) patients and bilirubin derangement was noted in35 (36.8%) patients.

Conclusion: Results of present study showed a higher percentage of ATT induced hepatitis in cases of pulmonary TB. Raised AST derangement, ALT derangement and bilirubin derangement levels were observed.

Keywords: ATT, TB , drug induced liver injury, hepatotoxicity

INTRODUCTION

Tuberculosis is a global health problem.[1] Each year an estimated 8 million new cases and 2 million deaths occur due to TB worldwide[1.2,3] Pakistan is ranked 7th most tuberculosis affected country in the world.[4] The disease prevalence in Pakistan is reported to be 263/100, 000 population.[5]

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.[6] This drug regimen has high therapeutic efficacy and good patient acceptance.[7] Hepatotoxicity is the most important side effect of antituberculous therapy (ATT).[7, 8] A recent study revealed the frequency of ATT induced hepatitis to be 19.67 %.[7]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.[7]

Most of the hepatotoxic reactions are dose related, however some are caused by drug hypersensitivity.[9]

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.[10]

The severity of ATT induced hepatitis ranges from asymptomatic alteration in liver enzymes to symptomatic acute hepatitis complicated by acute liver failure.[11]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.[9]

Early identification and modification of treatment regimen are required for patients who are at increased risk of anti tuberculous induced hepatotoxicity.

The current study would be indeed helpful in identifying hepatotoxicity developed during the course of ATT, thus helping early detection and effective management of this serious side effect. This will help in better monitoring of symptoms and liver function tests after starting ATT and would also stimulate the physicians to better educate the patients and their caregivers regarding the symptoms and signs of hepatotoxicity related to ATT and hence reducing morbidity and mortality.

MATERIAL AND METHODS

This cross sectional study was conducted at Department of Pulmonology, Bahawal Victoria Hospital, Bahawalpur. Total 95 patientswere 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 gender, 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 baseline 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. A patient complaining of jaundice and/or anorexia, abdominal pain additionally had LFTs checked at the hospital laboratory. Data regarding age, gender, developmentof ATT induced hepatitis and derangement of profile of LFTs was collected by attached proforma.

All the collected data were entered in SPSS version 17 and analyzed. Mean and SD was calculated for numerical data. Frequencies and percentages were calculated for categorical data.

RESULTS

Total number of participants was 95, which included patients both from the in- and out-patient(OPD), recruited consecutively over a 6 month period. Mean age of the patients was 37.95±14.46, with age range from 16 years to 65 years. Among the patients 35(36.8%) had ATT induced hepatitis (Figure No.1)

Out of 95 patients male were 51(53.7%) and female were 44(46.3%). Fig. 2

Jaundice was found in 38(40%) patients. Among the patients, 34(35.8%) had deranged AST 61(64.2%) had normal AST and 61(64.2%) had normal ALT and 34(35.8%) had deranged ALT. Sixty (63.2%) had normal bilirubin and 35(36.8%) had raised bilirubin. (Table No.1)

Fig. 1: Frequency ATT induced of hepatitis

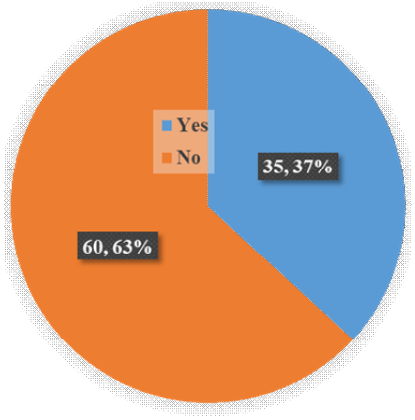

Fig. 2: Gender Distribution

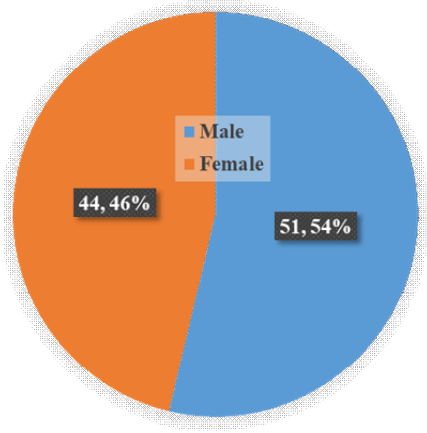

Table No.1

Liver Function Tests	Normal N (%)	Raised N (%)
AST DERANGEMENT	61 (64.2)	34 (35.8)
ALT DERANGEMENT	61 (64.2)	34 (35.8)
BILIRUBIN DERANGEMENT	60 (63.2)	35 (36.8)

DISCUSSION

In present study higher (36.8%) rate of ATT induced hepatitis was noticed in pulmonary TB patients. This is a high striking rate. Tuberculosis is a major cause of preventable infectious disease and death in the world.[12,13] Timely diagnosis and proper chemotherapy are the mainstays of treatment.[14] 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.[15,16] Surprisinglymost 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 [17] was conducted at the Medical Unit, Ayub Teaching Hospital, Abbottabad, 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 (7 males and 14 females), out of whom one (0.2%) male died of Acute Fulminant Hepatitisthese values can compare with our study i.e 35(36.8%) had ATT induced hepatitis.

A high degree of hepatotoxicity as compared to the aforementioned study, although this may due to not exactly been able to categorize the hepatotoxicity for example in the aforementioned study like overt hepatitis and acute fulminant hepatic failure have been described.

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, 87-88, 91-92, and 1998-2000.

The incidence rates of DIH were 10/111 (9.0%), 23/131 (17.6%), 26/123 (21.1%) and 32/117 (27.4%) in 1980-83, 87-88, 91-92, and 1998-2000, respectively. This secular increase of the incidence rate of DIH was statistically significant ($p = 0.01$).[18]However these rates were a bit lower than what our study found.

ATT-induced hepatitis was detected in 70% of the patients using Anti-tuberculous therapy with Pyrizinamide being used in addition to INH and Rifampicin in New DehliIndia, 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.[19]

But another study which carried out at the national TB referral center Iran, 2006-2008 where99 (13.0%) 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 ($P > 0.05$). DIH was significantly higher in patients older than 65 years ($P = 0.019$).[20]

CONCLUSION

Results of present study showed a higher percentage of ATT induced hepatitis in cases of pulmonary TB. Raised AST derangement, ALT derangement and bilirubin derangement levels were observed.

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