International Journal of Advanced Biotechnology and Research (IJBR)
ISSN 0976-2612, Online ISSN 2278–599X,
Vol-9, Issue-2, 2018, pp564-568
http://www.bipublication.com

Research Article

A cross sectional study on ATT induced hepatitis in pulmonary TB cases

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ABSTRACT

Objective: To study ATT induced hepatitis in pulmonary TB cases.
Material and methods: This cross sectional consisted on 95 pulmonary TB cases.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 male patients were 51(53.7%) and female patients were 44(46.3%). Out of 95 patients 35(36.8%) had ATT induced hepatitis.
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: Antitubercular agents, Pulmonary tuberculosis, drug induced liver injury, hepatotoxicity

INTRODUCTION

Tuberculosis (TB) continues to remain a significant infectious disease across much of the world.[1-2]It poses a formidable socioeconomic burden on the individual and on the society.[3] There were 8.6 million newer TB cases and an estimated 1.3 million deaths that occurred worldwide in 2012. New cases of TB-infected individuals are treated by a combination of four drugs: isoniazid (INH), rifampin (RIF), pyrazinamide (PZA), and ethambutol. However, a variety of adverse reactions of these drugs have been reported; one of the well-known toxic effects is hepatotoxicity.[4-6]

A recent study revealed the frequency of ATT induced hepatitis to be 19.67 %.[7]Most of the hepatotoxic reactions are dose related, however some are caused by drug hypersensitivity.[8-9] 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

Total 95 newly diagnosed patients of pulmonary TB either male or female age range from 16-65 years with normal liver function were selected from selected from Medicare Hospital Multan during January 2017 to June 2017. 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. 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, development of 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. Out of 95 patients male were 51(53.7%) and female were 44(46.3%).

Among the patients 35(36.8%) had ATT induced hepatitis (Figure No.1), 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)

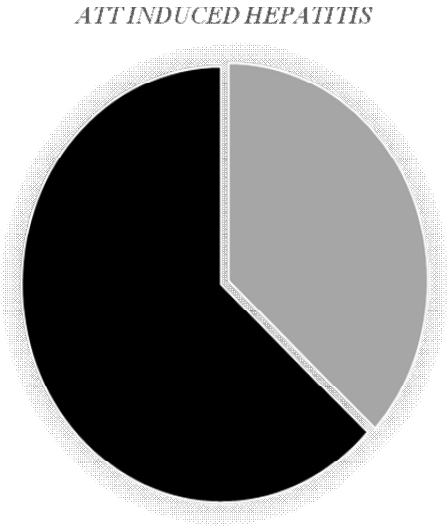

Table No.1

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

The study reveals high degree of hepatotoxicity induced due to Anti-tuberculous 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.[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 ith 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]

LIMITATIONS

- As sample size was small, so the results cannot be generalized to the entire population.
- The study did not include a control group for comparison.
- The study did not probe into or investigate the relevant risk factors for ATT induced hepatotoxicity like age, gender, alcohol use etc.
- The study did not focus on the treatment of ATT induced hepatitis.

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.

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