



“A PROSPECTIVE STUDY OF ANTITUBERCULAR DRUGS ON LIVER FUNCTION TESTS IN NEWLY DIAGNOSED TUBERCULOSIS PATIENTS”

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ABSTRACT

Background: This is a prospective study on tuberculosis and liver illness patients, it is necessary to determine the factors that put patients at risk for developing anti-tuberculosis drug-induced hepatotoxicity (anti-TB-DIH). In this study, both the prevalence of anti-TB-DIH and the factors that contribute to its development were studied. As a consequence of this, the purpose of the present study was to explore the abnormal liver function test in patients who were being treated for tuberculosis.

Aims and Objectives: (i) To investigation of liver dysfunction in antitubercular patients. (ii) To protect the liver from chemotherapy drug side effects through early detection. (iii) To understand drug-induced liver toxicity risk factors.

Materials and Methods: This is a prospective study of one hundred patients who were treated at the Department of Pulmonary Medicine and the Department of Biochemistry at the Sarojini Naidu Medical College, Agra. **Results:** Patients varying in age from 15 to 30 years comprised 21 (21%) of the study, 31–50 years comprised 31% of the study, 51–70 years comprised 38% of the study, and 71–80 years comprised 10% of the study, with 68 (68%) males and 32 (32%) females. When compared to the levels that were present before therapy, the levels of aspartate aminotransferase (AST), alanine aminotransferase (ALT), and alkaline phosphatase (ALP) exhibited a substantial increase after 2 months of treatment. A comparison of the patient's levels of AST, ALT, ALP, and gamma-glutamyl transpeptidase (GGT) before treatment and after treatment for 6 months demonstrated a considerable rise in all of these enzymes' activities.

Conclusion: In this study the majority of patients suffer hepatotoxicity within the first 14 days of beginning antituberculosis therapy (ATT) medication, it is imperative that the liver function of patients be monitored in the initial days in which treatment with ATT is being initiated.

KEY WORDS: Antitubercular Drugs; Newly Diagnosed Tuberculosis; Liver Function Test; Hepatotox

Introduction

TB is caused by bacteria (*Mycobacterium tuberculosis*) and it most often affects the lungs. TB is spread through the air when people with lung TB cough, sneeze or spit. A person needs to inhale only a few germs to become infected.

Every year, 10 million people fall ill with tuberculosis (TB). Despite being a preventable and curable disease, 1.5 million people die from TB each year making it the world's top infectious killer.

The number of people who contracted TB is expected to rise to 10.6 million in 2021, representing a 4.5% increase from the 10.1 million cases reported in 2020. The cumulative total number of people who have been diagnosed with TB and officially reported from 2018 to 2021 is 26 million.^[1]

ATT medication relies on early diagnosis and effective chemotherapy. Antituberculosis therapy (ATT's) hepatotoxic adverse effect has been extensively studied to determine its occurrence and outcome in individuals worldwide. In underdeveloped countries, short-course chemotherapy (SCC) for TB can lead to drug-induced hepatitis due to poor nutrition. It has been established that situations of protein energy malnutrition cause disruptions in the processes involved in drug metabolism, particularly the mechanisms involved in acetylation. It has been demonstrated that hypoalbuminemia can serve as a proxy sign for malnutrition. According to the findings of several research, it is associated with an increased risk of hepatitis.^[2,3]

Directly observed treatment is SCC. Isoniazid, rifampicin, and (RIF) (R), pyrazinamide (PZA) (Z), ethambutol, and streptomycin for 6–9 months. Revised National Tuberculosis Control Program treatment involves two phases: an intense phase and a continuing phase. Treatment lasts 6–9 months. Regular sputum microscopy tracks treatment response. The intensive phase lasts 2–4 months. Every dose of thrice-weekly treatment is observed. Depending on the treatment response, the continuation phase lasts 4–5 months. SCC's intensive phase and treatment medicines may differ.^[4]

The adverse effect of ATT that has the potential to cause substantial harm is hepatotoxicity. It can result in patients stopping their treatment; this can then lead to the development of drug resistance. To do this, it is necessary to have a solid understanding of the risk factors that are linked with the development of hepatitis. Primary care physicians need to be aware of the possibility for hepatotoxicity posed by ATT for the toxicity to be identified at an earlier stage. The majority of situations allow for the possibility of reintroduction. Only after all biochemical markers of liver injury have restored to normal levels is retreatment initiated.^[5,6] Both a biochemical test, in which the blood levels of alanine aminotransferase (ALT), Aspartate aminotransferase (AST), and alkaline phosphatase (ALP) were measured, and clinical monitoring of the patient's signs and symptoms were used to confirm the presence of anti-TB drug-induced hepatotoxicity (anti-TB-DIH) in the patients. After the hepatotoxicity has taken place, all of the medicines are stopped being administered, and retreatment is not begun until all of the biochemical indicators have returned to their normal levels.

In the current investigation, patients exhibited signs of moderate hepatotoxicity when given lower dosages initially; however, these doses gradually increased over the following days while the patients' clinical and biochemical states were monitored daily. Throughout the entirety of the treatment, every patient was kept under close surveillance.^[7,8]

The term "liver function tests" is a misnomer as many of the tests do not comment on the function of the liver but rather pinpoint the source of the damage. Elevations in ALT and AST in out of proportion to ALP, and bilirubin denotes a hepatocellular disease. An elevation in ALP and bilirubin in disproportion to ALT and AST would characterize a cholestatic pattern. A mixed injury pattern is defined as an elevation of alkaline phosphatase and AST/ALT levels. Isolated hyperbilirubinemia is defined as an elevation of bilirubin with normal alkaline phosphatase and AST/ALT levels.^[9] The R ratio has been used to assess whether the pattern of liver injury is hepatocellular, cholestatic, or mixed.

Treatment

Isoniazid, Rifampicin, Pyrazinamide, and Ethambutol were administered during the initial phase, which lasted for 2 months. Isoniazid and rifampicin-based treatment during the continuation phase for a period of 4 months.

Aims and Objectives

The objectives of the study are as follows:

- To investigate toxicity of liver in antitubercular patients
- To protect the liver from chemotherapy drug side effects through early detection
- To understand drug-induced liver toxicity risk factors.

Inclusion Criteria

Patients are included

1. Seriously ill persons with new presumptive TB admitted in SN medical college.
2. Patients diagnosed with TB through sputum microscopy.

Patients below the age of 12 year and recurrent cases are excluded in this study.

MATERIALS AND METHODS

This is a prospective study of 50 patients who were treated at the Department of Pulmonary Medicine and the Department of Biochemistry and Microbiology between June 2023 and January 2024.

Patients diagnosed with TB through sputum microscopy and chest X-ray

Methodology-5ml blood was collected aseptically in plain vials. Sample were analyzed for LFT on a fully automated analyzer Selectra pro-M

Statistical Analysis

Data were entered into Microsoft Excel (Windows 7; Version 2007), and analyses were performed using the Statistical Package for the Social Sciences (SPSS) for Windows software (version 22.0; SPSS). Descriptive statistics such as mean and standard deviation for continuous variables, frequencies, and percentages were calculated for categorical variables were determined.

RESULT

In this study, about 15–30 years 20 (20%), 31–50 years 30 (30%), 51–70 years 38 (38%), and 71–80 years 12 (12%) aged patients were found where 68 (68%) are males and 32 (32%) are females. The distribution of patients based on abnormal LFT is presented in Table 1. Based on biochemical derangement, all patients had mild hepatotoxicity according to WHO adverse medication reaction categorization. AST 58.5 ± 5.6 , ALT 45.6 ± 5.21 , and ALP 135 ± 5.23 increased significantly after 2 months of treatment ($P < 0.05^*$). The tabulation of the results is shown in Table 2. In the current investigation, patients who were getting antitubercular treatment were followed for abnormal LFTs values, which suggested that these patients were experiencing mild hepatotoxicity. In this study, aberrant LFTs showed mild hepatotoxicity in antitubercular drug-treated patients.

Table 1: Distribution based on altered liver functions test

Total bilirubin	11
Direct bilirubin	11
AST	35
ALT	15
ALP	15
Serum GGT	8

AST-Serum aspartate transaminase ALT Serum alanine transaminase ALP-Serum alkaline phosphatase GGT-Gamma glutamyl transferase

LFT	AST	ALT	ALP	GGT	TB	DB
Before treatment	45.2±3.14	31.5±2.51	115±7.5	42.5±3.5	0.7±0.6	0.5±0.1
After 2 months	58.5±5.6*	45.6±5.21*	135±5.23*	52.5±4.12	2.5±0.5	0.7±0.2
After 6 months	65.3±2.95*	61.5±3.75*	145.6±2.63*	62.3±2.5*	2.0±0.5	0.8±0.4

DISCUSSION

In this study among 100 patients, about 15–30 years 20 (20%), 31–50 years 30 (30%), 51–70 years 38 (38%), and 71–80 years 12 (12%) aged patients were found where 68 (68%) are males and 32 (32%) are females.

In this study, all patients had mild hepatotoxicity according to WHO adverse medication reaction categorization. AST 58.5 ± 5.6 , ALT 45.6 ± 5.21 , and ALP 135 ± 5.23 increased significantly after 2 months of treatment ($P < 0.05^*$). Abnormal LFTs parameters were monitored and revealed mild hepatotoxicity in patients receiving antitubercular therapy. This is correlated with other studies Vijayalakshmi *et al.*, Sailendra *et al.*, Molla *et al.* [9]

TB patients were carried out by Sailendra *et al.* It was revealed that there was a 3% incidence of drug-induced hepatotoxicity. It was shown that 16% of patients had an asymptomatic rise in serum enzyme levels and that 9% of patients had an incidence of high serum bilirubin level. Antituberculosis treatment has been shown to induce hepatic impairment, as described by Vijayalakshmi *et al.* [10]

Molla *et al.*, studied patients with first-line TB therapy-induced hepatotoxicity and ALT/AST levels at least 3 times ULN were managed. Hepatotoxic patients were treated according to WHO and IUTB recommendations. [11]

CONCLUSION

This study suggests that monitoring tuberculosis patients during the first 2 months of ATT should identify most drug induce liver injury earlier, potentially lowering treatment interruption and mortality.

DECLARATIONS:

Conflicts of interest: There is no conflict of interest associated with this study

Consent to participate: There is consent to participate.

Consent for publication: There is consent for the publication of this paper.

Authors' contributions: All authors equally contributed to the work.

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