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ASSOCIATION OF SERUM ALBUMIN WITH ANTITUBERCULER THERAPY (ATT) INDUCED HEPATOXICITY

Pulmonary Medicine

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ABSTRACT

Background: Anti tuberculosis therapy (ATT) induced liver injury, a common serious adverse drug reaction, is one of the most challenging clinical problems, cause of hospitalization and life- threatening events. Various risk factors have been found to be associated with drug induced hepatitis (DIH) in general population. This study aimed to determine the risk factors, particularly low serum albumin associated with the DIH among the patients of pulmonary and extrapulmonary tuberculosis. **Method:** In this cross sectional study, 30 patients diagnosed with ATT induced hepatitis were included and their serum albumin levels were observed. Standard diagnostic criteria were applied for diagnosis of ATT induced hepatitis. Serum albumin levels along with age, gender and alcoholic status of patients with diagnosed DIH were noted. **Result:** Out of 30 patients studied, 7 were females and 23 were males. 19 (63.33%) were ≥ 35 years and 11(36.67%) were <35 years of age. 8 patients had extrapulmonary tuberculosis and 22 patients had pulmonary tuberculosis. Out of 22 patients with pulmonary tuberculosis, 14 (63.64%) patients and out of 8 patients of extrapulmonary tuberculosis, 4 (50%) patients had serum albumin level <3.5 g/dl. Conclusion: Low serum albumin is a risk factor for development of ATT drug induced hepatitis.

KEYWORDS

Anti tuberculosis therapy, Hepatitis, Serum albumin

INTRODUCTION:

Tuberculosis (TB) continues to be a major health problem in both developing and developed countries because of its resurgence among immunosuppressed patients. Anti tubercular therapy (ATT) comprising of isoniazid, rifampicin, and pyrazinamide has proven to be effective in treatment of TB and the most common cause of post marketing withdrawal of drugs is hepatotoxicity. The reported incidence of drug induced hepatitis (DIH) during TB treatment varies from 5 to 33%,.

The risk of hepatotoxicity is increased when the drugs are combined. Various risk factors for ATT induced hepatotoxicity have been proposed in different studies. Older age, poor nutritional status including baseline hypoalbuminaemia were independent predictors of occurrence of anti-TB DIH. Many authors have suggested management of ATT induced hepatotoxicity,. We report here the findings of a study done to assess the relation of serum albumin with hepatitis in patients receiving anti- TB treatment.

METHOD:

In this prospective observational study, we included patients diagnosed with ATT induced hepatitis and observed their serum albumin levels. In a cross sectional design consecutive 30 patients from March 2021 to July 2021 were included from a tertiary care center according to following criteria.

Diagnostic criteria for ATT induced hepatitis–
(Either 1 or 2 or 3 with 4 and 5)

1. A rise of 5 times the upper limit of normal levels (50 IU/L) of AST and/or ALT without symptoms of hepatitis.
2. A rise of AST and/or ALT above upper limit of normal with symptoms of right hypochondriac pain, anorexia, nausea, vomiting and/or jaundice.
3. A rise in the level of serum total bilirubin 1.5 mg/dl.
4. Absence of serological evidence of hepatitis A, B, C or E virus.
5. Improvement of LFT after withdrawal of ATT.

Inclusion criteria-
Diagnosed case of drug induced hepatotoxicity
Either sex , Age > 18 years

Exclusion Criteria:

1. History of previous liver diseases
2. Concomitant use of other hepatotoxic drugs (methotrexate, phenytoin, valproate, and fluconazole)
3. Pregnancy and breast feeding

Baseline characteristics like age, gender and history of alcoholism were also noted. Basic diagnosis of pulmonary or extrapulmonary TB was compared for incidence of ATT induced hepatitis. If a patient had disseminated TB involving lungs then he was included in the list of pulmonary TB.

For statistical analysis continuous variables were expressed using mean (±SD) and median (range). Categorical variables were expressed as frequency (n) and percentage.

RESULT:

Total 30 patients were studied based on inclusion criteria in which 7 were females and 23 were males. 19 (63.33%) were ≥ 35 years of age and 11(36.67%) were <35 years of age.8 patients had extrapulmonary tuberculosis and 22 patients had pulmonary tuberculosis. Out of 22 patients with pulmonary tuberculosis, 14 (63.64%) patients and out of 8 patients of extrapulmonary tuberculosis, 4 (50%) patients had serum albumin level <3.5 g/dl.

Of total 23 male patients with DIH, 15 (65.22%) showed low serum albumin level and out of total 7 females with DIH, 3 (42.86%) showed low serum albumin level. Out of 30 patients with DIH, 8 were alcoholic and 22 were nonalcoholic. All alcoholic patients were males. 3(37.5%) of alcoholic patients showed low serum albumin level.

Table1. Baseline characteristic of patients with drug induced hepatitis

Catagory	Number	Percentage
Males	23	76.67%
Age ≥ 35 yrs	19	63.33%
Alcoholic	8	26.67%
Pulmonary TB	22	73.33%
Extrapulmonary TB	8	26.67%
Serum albumin <3.5gm/dl	18	60%

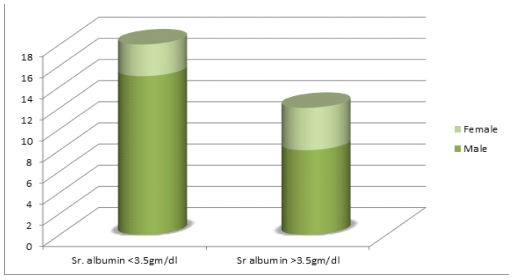

Fig1. Correlation of serum albumin with drug induced hepatitis in males and females

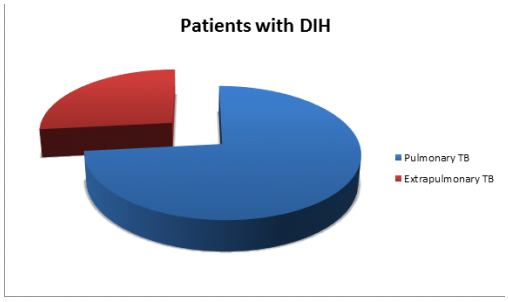

Fig2. Drug induced hepatitis in pulmonary and extrapulmonary tuberculosis

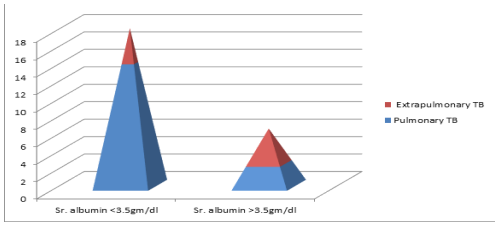

Fig3. Correlation of serum albumin with pulmonary and extra pulmonary tuberculosis

DISCUSSION:

The development of DIH during chemotherapy for TB is the most common reason leading to interruption of therapy(5). This is a potentially life-threatening condition but preventable. Early detection and interruption of therapy is of utmost importance as is monitoring of liver functions. Hypoalbuminaemia was recognized as a positive predictor of occurrence of DIH induced by short-course chemotherapy for TB in the developing countries(10).

In present study we found a higher incidence of DIH in patients above the age of 35 years as found by Naidoo et al in their study done in 2015 (11). Also Nihal Ali et al (2020) found increased incidence of DIH in age group 35 years but no association with gender and DILI in their study(12). Certain studies done in North India have found an association with female gender and DIH[–(13)].

In our study we found low serum albumin level as a risk factor for DIH similar to study done by Naidoo et al(11). However, low albumin level was not found to be a risk factor for the development of DIH in studies done by Latief M et al and Saha A et al[–(13)(14)].

Study done by saifun Nahar Faiz also found that the patients with history of high alcohol intake and with pre-treatment hypoalbuminemia have higher drug induced hepatotoxicity as compared to non-alcoholics and normal serum albumin level subjects as same as our study[–(15)(16)]. Also in one prospective hospital-based survey in Malaysia, the authors had found that those who developed anti-TB drug-induced hepatitis had lower mean BMI, lower serum albumin and higher serum globulin(17).

However, our study had some limitations like controls (patients on ATT without DIH) were not studied and due to study being cross sectional, longitudinal follow up was not done.

CONCLUSION: Low serum albumin is a risk factor for ATT induced hepatitis.

Conflict of interest – NIL
Source of support – NIL

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