

Variations in Parameters of Hepatotoxicity Induced by Anti TB Treatment with Comorbid Acute Viral Hepatitis

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ABSTRACT

Objectives & background: Drug-induced hepatotoxicity (DIH) is a common side effect of anti-TB drugs. Acute viral hepatitis (AVH) may be confounded with chronic alcoholic hepatitis clinically, biochemically, and histologically (CAH).

Place of Study: Rashid Latif Medical College Lahore

Duration of Study: March 2019 to January 2021

Methods: This prospective research examined the effect of acute viral hepatitis as a contributing and confounding factor in patients with normal baseline liver function who acquired acute hepatitis while taking short-course anti-TB medication. All acute hepatitis patients' blood was analysed for hepatitis A, B, C, and E markers.

Results: In 12 of 80 TB patients who developed viral hepatitis, the hepatitis E virus was present. Indicators of acute viral hepatitis included a delayed onset of acute hepatitis significant increases in aspartate aminotransferase (AST) and alanine aminotransferase (ALT), and a longer period for abnormal levels to normalise.

Conclusions: According to our statistics, 15% of anti-TB hepatotoxic patients had AVH. Before attributing the hepatotoxic impact of anti-TB medications to DIH patients, viral hepatitis should be evaluated and ruled out in all endemic-area patients.

INTRODUCTION

Isoniazid, rifampicin, and pyrazinamide are all critical first-line antituberculosis (anti-TB) drugs, and all three of them have the potential to induce hepatotoxicity. The phrase "drug induced hepatotoxicity" (abbreviated as "DIH") refers to an adverse effect that is commonly noticed during anti-TB therapy and frequently results in the treatment being halted. There has been a large amount of fluctuation in the occurrence of acute hepatitis among patients receiving short-course anti-TB therapy, and it may be based on the degree of transaminase elevation. On the other hand, what is widely considered to be drug-induced TB DIH might not necessarily be the case. Clinically, biochemically, and histologically, acute viral hepatitis can be misinterpreted for DIH⁵, making it a major condition that can create misunderstanding. Due to the limited quantity of evidence available, we decided to perform a prospective study to evaluate the possible contributing role of acute viral hepatitis as a confounding factor in patients with anti-TB DIH.

MATERIAL & METHODS

All patients' liver functions were normal before starting TB treatment. 80 individuals who got short-course anti-TB treatment and developed acute hepatitis were studied. HIV-positive individuals, those with chronic liver illness, chronic alcoholics, and those using hepatotoxic medicines were not permitted to participate. After getting signed informed consent from each patient, both institutes' Ethics Committees approved the research. Viral hepatitis indicators and HIV antibodies were sought for in all acute hepatitis patients' blood samples. During therapy, liver enzymes and bilirubin were measured every two weeks for the first two months, then once per month and if patients had acute hepatitis symptoms. Each patient had abdominal ultrasonography to rule out alternative liver ailment reasons. Both centers employed the same process and estimation approaches. According to the previous explanation, acute hepatitis requires at least one of the following:

(i) a rise in serum aspartate aminotransferase (AST) and/or alanine aminotransferase (ALT) five times the upper limit of normal levels (50 IU/l); (ii) a rise in serum total bilirubin greater than 1.5 mg/dl; (iii) any increase in AST and/or ALT above pre-treatment levels along with anorexia, nausea, Isoniazid, rifampicin These individuals were observed weekly until clinical and biochemical

liver damage signs normalised. Anti-tuberculosis drugs included ethambutol, streptomycin, and fluoroquinolones (ofloxacin, levofloxacin). These drugs weren't hepatotoxic. After the patient's liver levels normalised, first-line anti-tuberculosis drugs were resumed. The Fisher's exact test and the Student's t-test were used to compare demographic characteristics, the type of TB, the time for hepatotoxicity to develop, different laboratory parameters, and the time for liver function tests to normalise in patients with DIH and acute viral hepatitis. SPSS (23.0, SPSS Inc., Chicago, Illinois, USA) was used for analysis.

RESULTS

The 36 patients with acute hepatitis had a mean age of 32.1+ 11.3 years, 22.6% had pulmonary TB, 49.3% had extrapulmonary TB, and 24.1% had disseminated or military TB. 80 people got acute hepatitis; patients with acute hepatitis had anorexia, nausea, and vomiting. 29 individuals had clinically evident jaundice. Only 98% of 80 people with high liver enzymes reported symptoms. Hepatitis E was the most common viral hepatitis, and serological evidence showed acute viral hepatitis Anti-HAV IgM antibody 7.2 HBsAg, Anti-HBc IgM antibody 12.9 Anti-HCV IgM antibody 19 Anti-HEV IgM antibody 51.1 Anti-HCV and Anti-HEV IgM antibody 7.1. Acute viral hepatitis started later than DIH (P < 0.03). Acute viral hepatitis increased AST (P < 0.02) and ALT (P < 0.001) more than DIH. Acute viral hepatitis patients took longer to recover than DIH patients (P < 0.03). Acute viral hepatitis and DIH had similar abdominal ultrasonography findings.

| Positive viral marker | % |
|------------------------------------|------|
| Anti-HAV IgM antibody | 7.2 |
| HBsAg, Anti-HBc IgM antibody | 12.9 |
| Anti-HCV IgM antibody | 19 |
| Anti-HEV IgM antibody | 51.1 |
| Anti-HCV and Anti-HEV IgM antibody | 7.1 |

Table 1 Positive viral hepatitis serological markers in anti-TB patients with acute hepatitis

DISCUSSION

During TB treatment, hepatotoxic reactions vary widely. Despite using the same methods, the figures are far higher in poor countries. Poor food, growing age, widespread parasitism, persistent infections, intoxication, indiscriminate medicine usage,

ethnic considerations, sickness severity, or genetic susceptibility may contribute to this condition.

Metanat M et al. identified another component 18 of 38 children with acute hepatitis while on anti-TB drugs had acute viral hepatitis A or B. This represents 39.5% of afflicted children. Saukkonen JJ et al. found hepatitis B and C in 12 of 60 TB patients with acute hepatitis. 17.5% of patients. These studies lacked serological testing for viruses other than A and B5 and hepatitis E7. In 14.7% of individuals with acute hepatitis, hepatitis E was the most common etiology. Current study revealed this. This isn't surprising considering Pakistan's high hepatitis E prevalence. In tuberculosis-prevalent countries, persons who develop acute viral hepatitis while taking anti-TB treatment may be misdiagnosed with DIH if sufficient serological testing is not conducted. A delayed start of acute hepatitis, substantial increases in hepatic transaminases, and a longer time to normalize are all markers of acute viral hepatitis rather than DIH, and these features may prompt doctors to consider viral hepatitis. Acute viral hepatitis is more likely than DIH to produce acute hepatitis, according to our observations. Longer normalisation times (during which a less effective modified treatment regimen with nonhepatotoxic medications is utilised) can further enhance disease transmission and drug resistance, especially in individuals with a high bacillary burden. It's vital to recognize acute viral hepatitis in tuberculosis patients with a positive sputum smear (TB). In Pakistan and other impoverished nations, National TB Control Programs do not include routine liver function tests and serological testing for viral hepatitis. Even though most patients are treated in these settings. Patients with HIV and TB co infection who are treated with hepatotoxic antiretrovirals may exacerbate their status. Experts have not yet produced guidelines for treating TB in people with abnormal liver functions from DIH or acute viral hepatitis.

Once acute hepatitis is diagnosed, all potentially hepatotoxic medicines must be stopped until clinical and biochemical hepatotoxicity is resolved. This must be done when acute hepatitis is detected. In the meanwhile, nonhepatotoxic drugs such as ethambutol, streptomycin, and quinolones like ofloxacin can be provided following renal function and visual acuity examinations. After transaminitis clears up, you can start using antituberculosis drugs again. National TB Control Programs in low-resource countries should include treatment guidelines for DIH and acute viral hepatitis. These criteria may include the provision of alternative, non-hepatotoxic drugs and/or the discontinuation of therapy, followed by the cautious, deliberate reintroduction of first-line hepatotoxic therapies.

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