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Anti tuberculosis Therapy (ATT) Induced Acute Liver Failure (ALF)

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Abstract: Background: Antituberculosis drug-induced acute liver failure (ALF) is quite common. However, factors predicting its development are still controversial. Objective: the aim of this study is to evaluate and investigate the anti tuberculosis therapy induced acute liver failure by going through the literature review. Methodology: we conducted our literature search for similar previous studies mainly in Medline (PubMed), the studies were included which are concerning the Antituberculosis drug-induced acute liver failure (ALF) up to December 2015. Result: studies it has been observed that the risk of ATT-induced acute liver failure ALF increases recently, with no significant correlation of age with ATT-induced hepatitis was found, although it has been reported that women are more prone to develop ATT-induced ALF. Conclusion: Standard antituberculous therapy including isoniazid, rifampin, ethambutol, and pyrazinamide is widely used for the treatment of active tuberculosis. Its most important side effect is acute liver failure.

Keywords: anti tuberculosis therapy, drug-induced, acute liver failure (ALF).

1. INTRODUCTION

Tuberculosis is becoming an increasingly important problem worldwide, especially with the alarming increase in the incidence of acquired immunodeficency syndrome (AIDS). (Davidson PT et al, 1992) Drug-induced acute liver faliure is a potentially serious adverse effect of the currently used antituberculosis chemotherapeutic regimens containing isoniazid, rifampicin and pyrazinamide.2-4 The underlying mechanisms of antituberculosis treatment (ATT)-induced hepatotoxicity and the factors predisposing to its development are not clearly understood. The age and sex of the patients, chronic alcoholism and chronic liver disease, (US Centers for Disease Control. 1985) hepatitis B virus carrier status, acetylator status, and nutritional status'0 have all been incriminated as possible predisposing factors in earlier studies. Liver function impairment during anti-TB therapy in patients with chronic viral hepatitis was due to mostly transient liver function impairment (TLI), with TLI occurring later than in controls. this paper is aim to evaluate the different studies discussing anti tuberculosis induced acute liver failure.

2. LITERATURE REVIEW

Tuberculosis continues to remain a significant infectious disease across much of the developing countires. It exacts a significant socioeconomic burden on the individual and society. The standard antitubercular treatment (ATT), which consists of isoniazid (INH), rifampicin (RIF), ethambutol, and pyrazinamide (PZA), is the best available treatment for tuberculosis (TB). However, the hepatotoxicity of INH and PZA can be severe, and even after drug withdrawal, patients may require liver transplantation (LT). In these cases, the strategy for the treatment of TB is poorly defined (Philippe Ichai et al, 2010).

(Durand F et al, 1995) stated in his study that the efficacy of this treatment is due to the combination of bactericidal drugs (INH, RIF, and PZA) and a bacteriostatic drug (ETH). Liver function abnormalities are the most commonly reported adverse effects of this standard regimen. Hepatotoxicity, mainly related to INH and PZA, has been widely reported. This hepatotoxicity ranges from liver function test abnormalities to acute liver failure (ALF). In most cases, ALF associated with INH and RIF occurs within 10 days of the initiation of the anti-TB regimen, whereas liver failure due to PZA develops after a longer period of treatment.

(D. Gude et al, 2011) conducted a study that is about Antitubercular therapy (ATT) induced acute heapatic faliure, and said although well known to clinicians, is often over looked and underrated. Given the low threshold of starting ATT, especially empirically, the adverse manifestations can take a considerable toll. A variety of associated risk factors compound the morbidity. We throw light on one such a case where ATT was detrimental to the patient and review the literature and possible preventive strategies.

Study done by (Hussain W et al, 1995) stated that three rare cases of tuberculosis per se causing ALF have been described with hyponatremia and hepatomegaly as the features at presentation. Usually widespread miliary tuberculosis (TB) underlies such cases although our case did not qualify for military TB owing to features like organ systems other than lung being spared, low ESR and the temporal association with ATT.

(Global tuberculosis Control, WHO report 2008) stated that there is the largest prospective study on ATT-ALF reported to date. ATT was the cause in 5.7% (n ¼ 70) of the ALF patients (n ¼ 1223) admitted to our hospital during the past 23 years. Although the proportion of ALF caused by ATT is small, it is substantial in absolute number and is a cause of concern because tuberculosis is highly prevalent in South Asia and Africa, where a large population reside. The estimated prevalence of tuberculosis in India is 283 per 100,000 populations.

(Black M, et al. 1957, Chan ED, et al. 2002) reported that the clinical presentation was similar in all ALF regardless of causes. During hospitalization, the frequency of complications such as gastrointestinal bleed, seizures, and renal failure were also similar among patients with ATT, HEV, and non-A non-E induced ALF. The liver failure rather than its cause resulted in complications. ATT-ALF has been shown to occur within first 2 months to 14 months after initiation of therapy.

In a recent study (Kumar R1 et al, 2010) they have found that approximately 63% of the patients with ATT-ALF consumed ATT empirically without objective evidence of tuberculosis, which could have been avoided. In the endemic region of tuberculosis, physicians often treat patients with pyrexia of unknown origin with ATT. The current study identified the risk associated with such therapy. Such information is important for health authorities and physicians dealing with the treatment of tuberculosis to prevent unwarranted deaths of ATT-ALF.

in study conducted by (Steele MA et al, 1991) Drug-induced liver disease is a well-known side effect of several drugs that are used for the treatment of active tuberculosis or latent tuberculosis infection. A meta-analysis has shown an incidence rate of liver toxicity of 2.6% with rifampin and INH co-administration, but only 1.1% with rifampin alone, and 1.6% with isoniazid alone.

3. OBJECTIVES

The number of cases of tuberculosis (TB) has increased considerably over the past decade; this is especially true for cases involving resistant strains. This has led to the use of newer therapeutic agents in multiple-drug combinations, and these therapies may lead to destruction of the liver (acute liver failure) of TB infected patients. Therefore, the purpose of this paper is to evaluate the Anti tuberculosis therapy induced acute liver failure, and to high light the most important outcomes from the literature review about this topic to increase the strength of evidence about this matter

4. METHODOLOGY

A literature search was carried out on Databases including MEDLINE (PubMed), EMBASE, Cochrane Database of Systematic Reviews and Database of Abstracts and full research. Reviews search was performed for studies published up to 2015. Studies were selected depending on Anti tuberculosis therapy (ATT) induced acute liver failure (ALF), using the terms ‘anti tuberculosis ’, ‘acute liver failure’, ‘drug induced liver failure’, ‘liver injure’, All studies were included that was discussing about anti tuberculosis therapy that induce Acute liver failure. The strength of this paper comes from review many study in the literature and depending on the analysis of different population from all over the world.

5. RESULTS AND DISCUSSION

(Kumar R1 et al, 2010) found Antituberculosis therapy (ATT)-associated acute liver failure (ATT-ALF) is the commonest drug-induced ALF in South Asia. Prospective studies on ATT-ALF are lacking. The current study prospectively evaluated the magnitude, clinical course, outcome, and prognostic factors in ATT-ALF. From January 1986 to January 2009, 1223 consecutive ALF patients were evaluated: ATT alone was the cause in 70 (5.7%) patients. Another 15 (1.2%) had ATT and simultaneous hepatitis virus infection. In 44 (62.8%) patients, ATT was recommended experimentally without

complete proof of tuberculosis. ATT-ALF patients were more youthful (32.87 [+/ - 15.8] years), and 49 (70%) of them were ladies. Most had hyperacute presentation; the middle icterus encephalopathy interim was 4.5 (0-30) days. The middle length of time of ATT before ALF was 30 (7-350) days. At presentation, propelled encephalopathy and cerebral edema were available in 51 (76%) and 29 (41.4%) patients, separately. Gastrointestinal drain, seizures, contamination, and intense renal disappointment were recorded in seven (10%), five (7.1%), 26 (37.1%), and seven (10%) patients, individually. Contrasted and hepatitis E infection (HEV) and non-A non-E-impelled ALF, ATT-ALF patients had almost comparable presentations with the exception of more established age and less height of liver chemicals. The death rate among patients with ATT-ALF was high (67.1%, n = 47), and just 23 (32.9%) patients recouped with restorative treatment. In multivariate investigation, three variables freely anticipated mortality: serum bilirubin (>or=10.8 mg/dL), prothrombin time (PT) prolongation (>or=26 seconds), and grade III/IV encephalopathy at presentation.

(Steele MA et al, 1991) The exact utilization of ATT ought not be likened to their improper and aimless use. The undesirable remedy of ATT is not safe on account of its inclination to causing so as to bring about serious hepatotoxicity and even demise intense liver disappointment (ALF). The reported rates of ATT affected hepatotoxicity fluctuate from 2.3% to 28% and are higher among the Indian populace (11.5%) than the Western populace (4.3%).

A few studies (Wong WM et al, 2000, Fernandez-Villar An et al, 2004, Ungo JR et al, 1998) about ATT-ALF were connected with a poor result. The death rate was 67.1%, essentially higher than that of HEV-ALF (46%) (P ¼ 0.001). Just 32.9% patients made due with concentrated therapeutic treatment. The unconstrained survival of ALF from particular medication responses, including those from ATT, in the United States is 20% to 30%, and on the off chance that we accept around 15% of patients who experience liver transplantation would really have made due with therapeutic treatment alone, then the survival of ALF from ATT in the United States would be roughly 35% to 45%, which is very near the survival depicted here. This proposes the emergency unit results of ATT-ALF just unassumingly. Three-fourths (76%) of ATT-ALF patients kicked the bucket within 5 days of hospitalization; henceforth, liver transplantation ought to be considered at the soonest. The explanation behind high mortality among ATT-ALF patients is hazy. The conceivable clarification could be diminished hepatocyte recovery in view of greasy invasion and quirky harm connected with ATT. Another striking finding in our study was a high (80%) rate of mortality among the ALF patients with joined ATT and viral cause. Be that as it may, it was not fundamentally higher than that of ATT-ALF (P ¼ 0.53), which might be inferable from littler number of patients in the previous gathering. A few studies have demonstrated that hepatitis B or hepatitis C infection co-contamination builds the danger of ATT-affected hepatotoxicity.

There is wide uniqueness in the reported rate of ATT-affected intense liver disappointment in various studies, the rate being much higher in studies from India (8-39%) (Parthasarathy R et al, 1989). Than in those from Western natio (2-3%).Why only some patients who receive ATT develop acute liver failure is not clear. Whether some host factors, genetic predisposition, environmental factors, or some interaction among various factors is responsible is not known (Rao NK et al,1982).

6. CONCLUSION

Roughly 20% of the worldwide populations with tuberculosis (3.32 million) live in India. Thusly, number of patients with ATT hepatotoxicity in India might be significant. A forthcoming study reported that seven (9.72%) of 72 patients analyzed as ATT hepatotoxicity created ALF (ATT-ALF) and had a death rate of 85.7%. Along these lines, ATT-ALF might have a more forceful normal course than in hepatitis infection (related ALF, the incessant reason for ALF in South Asia. ATT is the commonest medication prompted ALF in south Asia, where tuberculosis is endemic. Though clinical profile, characteristic course, prognostic model, and helpful techniques have been very much depicted for paracetamol-affected ALF, data on ATT-ALF in the English writing is meager and comprises of reports of just couple of patients.

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