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Dr Zeeshan Zafar[1], Dr Zara Khatoon[2], Muhammad Asad Iqbal[3], Hafsa Ansar[4], Dr Muhammad Usman[5], Muhammad Nabeel Khan[6], Dr Bilal Khursheed[7]

A STUDY ON THE FREQUENCY OF ANTI-TUBERCULOUS THERAPY INDUCED HEPATITIS

[1]DHQ Hospital Mirpur, Email: zeeshanstar102@gmail.com
[2]DHQ Hospital Mirpur, Email: jabeenzara.1996@gmail.com
[3]DHQ Hospital Mirpur, Email: drasadpharma418@gmail.com
[4]DHQ Hospital Mirpur, Email: hafsaansar.3913@gmail.com
[5]DHQ Hospital Mirpur, Email: usmanchaudhary129@gmail.com
[6]DHQ Hospital Mirpur, Email: nabeelkhan3621@gmail.com
[7]DHQ Hospital Mirpur, Email: drbilalkhursheed@gmail.com

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Corresponding Author:Dr Zeeshan Zafar, DHQ Hospital Mirpur,
Email: zeeshanstar102@gmail.com

ABSTRACT

Objective: The aim of this study was to determine the frequency of anti-tuberculous therapy (ATT) induced hepatitis.

Methodology: The design of this study was a descriptive study. This study was conducted at DHQ Hospital Mirpur, and duration of this study was from May 2024 to December 2024. In this study the cases of known Tuberculosis were included. Anti-Tuberculosis Therapy included Isoniazid, Rifampicin Ethambutol and Pyrazinamide according to standard WHO recommended doses. The cases suffering from hepatitis B, C or HIV or those with derange liver functions were excluded from this study. The cases were followed weekly and Liver function tests (LFTs) were performed and hepatitis was labelled as yes where there was rise in liver enzymes three times upper limit with symptoms (nausea/vomiting/abdominal pain) or 5 times without any symptoms. The final outcome was seen at 4 weeks.

Results: In this study there were total 100 cases of TB out of which 70 (70%) were males and 30 (30%) females. The mean age of the subjects was 38.11± 11.45 years. There were 78 cases with pulmonary and 22 had EPTB. ATT induced hepatitis was observed in 6 (6%) of the cases. ATT induced hepatitis was significantly high in males affecting 5 (7.14%) cases with p value of 0.04. There was no significant difference in terms of weight groups with p= 0.68. Hepatotoxicity was more seen in cases having EPTB where 2 out of 22 cases had it; although this difference was statistically not significant with p=0.13.

Conclusion: ATT induced hepatitis is uncommon but is seen significantly high in male gender.

INTRODUCTION

Tuberculosis (TB) is a disease of ancient times and is one of the most common infectious diseases. It is more prevalence in developing countries but number is increasing in the developed ones due to emergence of Human Immunodeficiency Virus (HIV). The prevalence in Pakistan is 231 per 100,000 population[1]. It can involve any organ of the body and the treatment is the same and have combination of chemotherapeutic agents and include Isoniazid (H), Rifampicin (R), Pyrazinamide (Z), and Ethambutol (E) and among these first three agents are considered as hepatotoxic. Pyrazinamide is the most culprit drug and has this incidence rate of hepatitis in 9% of the cases while Isoniazid had this in 3% and Rifampicin in 1% of the cases[2]. There are different risk factors that can predispose to this and include male gender, previous viral hepatitis in the form of hepatitis B, C and HIV, alcoholism and concomitant use of hepatotoxic drugs. The frequency of hepatitis varies from 5 to 31% in different studues[3,4], while in Pakistan multiple studies show 5 to 11% only[5-10].

METHODOLOGY

The design of this study was a descriptive study. This study was conducted at DHQ Hospital Mirpur, and duration of this study was from May 2024 to December 2024. In this study the cases of known Tuberculosis were included. Anti-Tuberculosis Therapy included Isoniazid, Rifampicin Ethambutol and Pyrazinamide according to standard WHO recommended doses. The cases suffering from hepatitis B, C or HIV or those with derange liver functions were excluded from this study. The cases were followed weekly and Liver function tests (LFTs) were performed and hepatitis was labelled as yes where there was rise in liver enzymes three times upper limit with symptoms (nausea/vomiting/abdominal pain) or 5 times without any symptoms. The final outcome was seen at 4 weeks. The data was analyzed by SPSS-Version 22. Effect modifier were stratified and post stratification Chi-Square test was applied taking P-value ≤ 0.05 as significant.

RESULTS

In this study there were total 100 cases of TB out of which 70 (70%) were males and 30 (30%) females. The mean age of the subjects was 38.11± 11.45 years. There were 78 cases with pulmonary and 22 had EPTB. ATT induced hepatitis was observed in 6 (6%) of the cases. ATT induced hepatitis was significantly high in males affecting 5 (7.14%) cases with p value of 0.04 as shown in table I. There was no significant difference in terms of weight groups with p= 0.68 (table II). Hepatotoxicity was more seen in cases having EPTB where 2 out of 22 cases had it; although this difference was statistically not significant with p=0.13 as in table III.

I: ATT Induced Hepatitis Vs Gender

Gender	ATT induced hepatitis		Total	p value
	Yes	No		
Male	5 (7.14%)	65 (92.86%)	70 (100%)	
Female	1 (3.33%)	29 (96.67%)	30 (100%)	0.04
Total	**6 (6%)**	**94 (94%)**	**100 (100%)**	

II: ATT Induced Hepatitis Vs Weight

Weight	ATT induced hepatitis		Total	p value
	Yes	No		
<40	4 (6.35%)	59 (93.65%)	63 (100%)	
>40	2 (5.12%)	35 (94.88%)	37 (100%)	0.68
Total	**6 (6%)**	**94 (94%)**	**100 (100%)**	

Table III: ATT Induced Hepatitis Vs Type of TB

Type of TB	ATT induced hepatitis		Total	p value
	Yes	No		
Pulmonary TB	4 (5.13%)	74 (94.87%)	78 (100%)	0.13
EPTB*	2 (9.09%)	20 (90.91%)	22 (100%)	
Total	**6 (6%)**	**94 (94%)**	**100 (100%)**	

***EPTB=** Extra pulmonary TB

DISCUSSION

Tuberculosis is itself a fatal condition as it can affect any organ of the body and need an intensive course of chemotherapeutic agents in the form of ATT which are not spare of side effect profiles. ATT induced hepatitis is a salient entity as it can alter the course of treatment and the choice of drugs to lesser effective drugs and ultimately can result in drug resistance emergence. In the present study, ATT induced hepatitis was seen in 6 (6%) of the cases. there is wide diversity in the prevalence of ATT induced hepatitis globally and it ranges from 1 to 61% [14,15]. This can be explained by multiple factors i.e. difference in the operational definitions, presence of viral hepatitis in the inclusion criteria, alcoholism and different acetylator status in different populations etc. But majority of the studies revoked this occurrence in 5 -11% of the cases.[5,8] ATT induced hepatitis was significantly high in males affecting 5 (7.14%) cases with p value of 0.04. This was also proved in the past that male gender is an independent risk factor to have drug induced hepatitis[16]. Various studies have shown that males have the highest number of cases with ATT induced hepatitis; few had signficnat[16] and others non-significant association with this[17-18]. Hepatotoxicity was more seen in cases having EPTB where 2 out of 22 cases had it; although this difference was statistically not significant with p=0.13. There were conflicting results and it was seen that this was more common in cases of pulmonary TB[3,7] while others revealed this more in cases with extra pulmonary TB[,19]. But none of these studies find any significant association with this.

CONCLUSION

ATT induced hepatitis is uncommon but is seen significantly high in male gender.

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