



ANTI TUBERCULOSIS INDUCED HEPATITIS

Arifa Khan, Umar Raza and Dr. Aftab Alem Jehangir*

Sheikh Zayed Hospital, Rahim Yar Khan.

*Corresponding Author: Dr. Aftab Alem Jehangir

Sheikh Zayed Hospital, Rahim Yar Khan.

Article Received on 12/08/2018

Article Revised on 03/09/2018

Article Accepted on 24/09/2018

ABSTRACT

Objective: To determine the frequency of Anti Tuberculosis induced hepatitis. **Methodology;** In this descriptive case series study which was carried out at Medical Unit II, Sheikh Zayed Hospital, Rahim Yar Khan during August 2017 to March 2018, the cases of both genders and age range of 15 to 50 years were included. The cases were selected irrespective of the site of the TB. Pulmonary TB (PTB) was labelled according to sputum examination and radiology while the extra pulmonary TB (EPTB) was labelled according to fluid analysis i.e. pleural, peritoneal or CSF or tissue biopsy like lymph nodes. ATT was given according to WHO dosage guided program. The hepatitis was labelled as yes when the enzymes were raised 3 times above their limit with signs and symptoms or 5 times without signs and symptoms where the final outcome was seen. **Results:** In this study there were total 150 cases with mean age 33.44 ± 10.11 years. There were 78 (52%) were males and 108 (72%) cases had PTB. ATT induced hepatitis was seen in 14 (9.33%) of the cases. ATT induced hepatitis was more seen in age group 15 to 31 affecting 10 (11.36%) of the cases with $p=0.04$. ATT induced hepatitis was also more common in cases with PTB affecting 12 (11.11%) of the cases as compared to 2 (4.76%) of cases in EPTB with p value of 0.01 **Conclusion:** ATT induced hepatitis is seen in every $1/10^{\text{th}}$ of the case and it is significantly high in age group 15 to 31 and those having PTB.

KEYWORDS: PTB, EPTB, Hepatitis.

INTRODUCTION

Tuberculosis (TB) is found till the ancient times and is one of the greatest killers of the human from the remote past to the recent times. It is one of the highest burden infectious diseases which are more prevalent in the under developing countries and certain group of cases in the developed ones like living in prisons, home cares, debilitated alcoholics and those having an immunocompromised state i.e. HIV. Its incidence in Pakistan is still high despite extensive measure taken and is 230 per 100000 population.^[1]

TB can affect any part of the body and can be broadly divided into two major types i.e. Pulmonary TB (PTB) and Extra Pulmonary TB (EPTB). The most common sites of extra pulmonary TB include pleura and lymph nodes. The diagnosis largely relies upon the site of involvement and in cases of PTB, it needs sputum smear supported by radiological investigations like X rays and CT scan chest. The other site involvement need specific tests like fluid analysis, biopsy etc.

Anti-tuberculosis therapy (ATT) is the standard care of treatment and world health organization (WHO) has done immense work to create a combination therapy and included drugs i.e. Isoniazid (H), Rifampicin (R),

Pyrazinamide (Z) and Ethambutol (E) where except of the last one all have the potential to be hepatotoxic. The data has revealed their toxicity in around 5 to 31%,^[3,4] and in the under developed countries data has shown it to be 5 to 11% only.^[5-8] There are multiple risk factors that can affect these and amongst them severity of the disease, co infection with other viruses and alcoholism are the salient ones.^[10,11]

OBJECTIVE

To determine the frequency of Anti Tuberculosis induced hepatitis.

MATERIAL AND METHODS

Study design

Descriptive case series

Study Setting

Medical Unit II, Sheikh Zayed Hospital, Rahim Yar Khan

Duration

August 2017 to March 2018

Sampling technique

Non probability consecutive sampling

In this study the cases of both genders and age range of 15 to 50 years were included. The cases were selected irrespective of the site of the TB. Pulmonary TB was labelled according to sputum examination and radiology while the extra pulmonary TB was labelled according to fluid analysis i.e. pleural, peritoneal or CSF or tissue biopsy like lymph nodes. The case with hepatitis B and C infectivity were excluded. Then these cases were started with ATT according to WHO dosage guided program. Liver function tests were done every other day in 1st week and then twice a week for next 3 weeks and they were also assessed for nausea, vomiting and jaundice. The hepatitis was labelled as yes when the enzymes were raised 3 times above their limit with signs and symptoms or 5 times without signs and symptoms where the final outcome was seen.

Statistical analysis

The data entered and analyzed by using SPSS version 21.0. Post stratification chi square test was applied taking p value < 0.05 as significant.

RESULTS

In this study there were total 150 cases with mean age 33.44±10.11 years. There were 78 (52%) were males and 108 (72%) cases had PTB. ATT induced hepatitis was seen in 14 (9.33%) of the cases. There was no significant difference in terms of gender in both groups with p value of 0.11 as in table I. ATT induced hepatitis was more seen in age group 15 to 31 affecting 10 (11.36%) of the cases with p= 0.04 as in table II. ATT induced hepatitis was also more common in cases with PTB affecting 12 (11.11%) of the cases as compared to 2 (4.76%) of cases in EPTB with p value of 0.01 as shown in table III.

Table I: ATT induced hepatitis and gender.

ATT induced Hepatitis	Gender		Total	p value
	Male	Female		
Yes	9 (11.54%)	5 (6.94%)	14 (9.33%)	
No	69 (88.46%)	67 (93.06%)	136 (90.67%)	0.11
Total	78 (52%)	72 (48%)	150 (100%)	

Table II: ATT induced hepatitis and age.

ATT induced Hepatitis	AGE		Total	p value
	15-31	32-50		
Yes	10 (11.36%)	4 (6.45%)	14 (9.33%)	
No	78 (88.64%)	58 (93.55%)	136 (90.67%)	0.04
Total	88 (58.66%)	62 (41.34%)	150 (100%)	

Table III: ATT induced hepatitis and TB site.

ATT induced Hepatitis	TB site		Total	p value
	PTB	EPTB		
Yes	12 (11.11%)	2 (4.76%)	14 (9.33%)	
No	96 (88.89%)	40 (95.24%)	136 (90.67%)	0.01
Total	108 (72%)	42 (28%)	150 (100%)	

DISCUSSION

ATT induced hepatitis is a great concerning entity as holding the treatment can lead to progression of the disease and an irreversible damage and on the other had to continue with these drugs can further progress the damage or may warrant a change in treatment to other drugs that may not be as effective as these combination drugs or and can also raise the chances of drug resistance in such cases with incomplete treatments.

In the present study ATT induced hepatitis was seen in 14 (9.33%) of the cases. These results were in line with the findings of the past studies done in the same county where the prevalence was found to be around 1 to 11% of the cases.^[14,15] According to study done in Sindh

Province the ATT induced hepatitis was seen in 55 (11%) out of 500 cases. While in another study this was seen in 8% of the cases and ultimately 1% of the cases died due to this fulminant hepatic failure.^[8]

ATT induced hepatitis was also more common in cases with PTB affecting 12 (11.11%) of the cases as compared to 2 (4.76%) of cases in EPTB with p value of 0.01. The data in the past also revealed a strong association with the incidence of ATT induced hepatitis and the site of the disease where they also found it more in cases of PTB as compared to EPTB.^[3,7] In contrast to this few of these studies did not find any of the statistically significant difference.^[11,16] The reason of the cases with higher number in PTB can be due to hypoxic injuries to the liver. The extent of the disease was not studied in this study which was also

found to be significant marker in cases of PTB to denote the chances of drug induced hepatitis which was most common in cases suffering from advanced TB. According to a study done by Haq M et al it was seen that hepatotoxicity was seen more in cases of far advanced TB i.e. 16.66% in contrast to 7.14% cases suffering from Minimal and 2.17% having moderately advanced Pulmonary Tuberculosis.^[7]

CONCLUSION

ATT induced hepatitis is seen in every 1/10th of the case and it is significantly high in age group 15 to 31 and those having PTB.

REFERENCES

1. WHO. Global TB report [internet]. 2013 [cited 2014 Jun 05]. Available from: <http://www.who.int/tb/publications/global-report/en/>
2. Steele M, Burk RF, Desprez RM. Toxic hepatitis with isoniazid and rifampin: a meta-analysis. *Chest*, 1991; 99(2): 465-71.
3. Khalil H, Dashti-Khavidaki S, Rasoolinejad M, Rezaie L, Etminani M. Anti-tuberculosis drugs related hepatotoxicity: incidence, risk factors, pattern of changes in liver enzymes and outcome. *Daru J Pharm Sci.*, 2009; 17(3): 163-67.
4. Singh MK, Mamatha S, Jain R, Jha AK, Nigam SK. Incidence and risk factors for hepatitis in patients receiving anti tuberculosis treatment. *J Evo Med and Dent Sci.*, 2013; 02(1): 01-08.
5. Tariq S, Khan TS, Malik S, Anwar MS, Rashid A. Frequency of anti-tuberculous therapy-induced hepatotoxicity in patients and their outcome. *J Ayub Med coll Abbott*, 2009; 21(4): 50-52.
6. Haq MU, Rasul S, Khan SU, Saeed S, Tahir TM. Anti Tuberculosis drug induced hepatitis. *Pak J Chest Med*, 2001; 7(5): 41-45.
7. Haq MU, Rasul S, Iqbal ZH, Chaudhary MK, Bhatti AH, Anwar N, et al. Incidence of Hepatitis in patients taking antituberculosis treatment. *Ann King Edward Med Coll*, 1996; 2(3): 49-51.
8. Shaikh MA, Yakta DE, Shaikh D. Frequency of Hepatotoxicity during anti-tuberculosis treatment at Medical Unit of LUHMS Sindh. *Med Chann*, 2012; 18(1): 20-23.
9. Anand AC, Seth AK, Paul M, Puri P. Risk Factors of hepatotoxicity during anti-tuberculosis treatment. *Med J Armed Forces Ind*, 2006; 62(1): 45-49.
10. Crofton J, Seaton A, Seaton D, Leitch AG. *Crofton and Douglas's Respiratory Diseases*. 5th ed. Oxford: Blackwell, 2000.
11. Singla R, Sharma SK, Mohan A, Makharia G, Sreenivas V, Jha B, et al. Evaluation of risk factors for antituberculosis treatment induced hepatotoxicity. *Ind J Med Res.*, 2010; 132(7): 81-86.
12. WHO. *Treatment of tuberculosis: Guidelines for national tuberculosis control program*. 4th ed. Geneva: World Health Organization, 2008.
13. McPherson RA, Pincus MR. *Henry's Clinical Diagnosis and Management by Laboratory Methods*. 22nd ed. Philadelphia: Elsevier Saunders, 2011.
14. Centers for Disease Control and Prevention (CDC); American Thoracic Society. Update: adverse event data and revised American Thoracic Society/CDC recommendations against the use of rifampin and pyrazinamide for treatment of latent tuberculosis infection—United States, 2003. *MMWR Morb Mortal Wkly Rep.*, 2003; 52: 735–9.
15. Singh J, Garg PK, Tandon RK. Hepatotoxicity due to antituberculosis therapy; clinical profile and reintroduction of therapy. *J Clin Gastroenterol*, 1996; 22(3): 211-4.
16. Ansari S, Bawany MA, Hayat AS, Munir A, Khahro AA, Naz F. drug induced hepatitis; does hepatitis B and hepatitis C co-infection increases the risk during anti tuberculous chemotherapy. *Professional Med J.*, 2014; 21(1): 49-54.