

CO-INFECTION OF HEPATITIS B AND C IN TUBERCULOSIS PATIENTS AT SHEIKH ZAYED HOSPITAL, RAHIM YAR KHAN, PAKISTAN

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ABSTRACT

Background: Tuberculosis, HBV and HCV infections are common in our community, so chances of co-infections are high. Exact magnitude of this problem can help the Healthcare Professionals to plan a better and comprehensive care for both conditions.

Objective: To assess the frequency of co-infection of Hepatitis B and C in diagnosed patients of tuberculosis.

Methodology: A total of 846 consecutive patients having tuberculosis (pulmonary or extra-pulmonary) were included in this cross sectional study by non-probability consecutive sampling technique, from November 2017 to October 2018, at outpatients department of pulmonology, Sheikh Zayed Hospital, Rahim Yar Khan. ICT method was used to detect HBV and HCV. Sociodemographic data and site of disease (Pulmonary TB and Extra Pulmonary TB) recorded on a pre-designed Performa and results were analyzed with SPSS version 22.

Results: Out of 846 total patients of this study, 437 (51.7%) were males and 409 (48.3%) were females with mean age of 38.71±18.71 years. Total of 639 patients (75.5%) were suffering from Pulmonary TB and 207 (24.5%) were having extra pulmonary TB. Hepatitis B was present in 29 (3.4%) cases while Hepatitis C was present in 177 (20.9%) cases and both (B & C) were detected in 07 (0.83%) cases. HBV was found in 3.75% pulmonary TB cases and 2.41% Extra-pulmonary TB cases. ($p=0.357$). HCV was found in 22.5% pulmonary TB cases and 15.9% Extra-pulmonary TB cases. The difference was statistically significant ($p=0.043$).

Conclusion: Hepatitis C is very common finding in TB patients. Screening of all TB patients for HBV and HCV infection is needed to improve treatment outcome of TB patients and avoid spread of disease in community.

Keywords: Tuberculosis, Pulmonary tuberculosis, Extra-pulmonary tuberculosis, Hepatitis B, Hepatitis C

INTRODUCTION

The WHO Global Tuberculosis Annual Report 2018 shows that tuberculosis is among the top ten causes of death.¹ During 2017, TB caused an estimated 1.3 million deaths among HIV-negative people, with an additional 300,000 deaths from TB among HIV-positive people. Millions of people get sick with the disease each year. In 2017 alone, 10 million people developed TB disease globally, 5.8 million were men, 3.2 million women and 1 million children¹ It is important to consider that one third of world's population having latent TB infection is likely to develop active TB disease, anytime in their life due to conditions, which can compromise the immune system of host like Diabetes Mellitus and HIV. So TB is likely to remain a major public health problem in many developing countries and regions such as Africa and Asia.²

Global Hepatitis Report 2017 states that Hepatitis B is found highest in WHO Western Pacific Region and the WHO African Region. Approximately 257 million people are living with

hepatitis B virus infection worldwide.³ Hepatitis C is most prevalent in WHO Eastern Mediterranean and European Regions. An estimated 71 million people have chronic hepatitis C infection. The mortality among these patients is mostly due to complications like cirrhosis and hepatocellular carcinoma.³

Tuberculosis (TB) and Hepatitis B virus (HBV) co-infection is commonly found in the clinical practice among developing countries of South-east Asia.⁴ Chronic liver disease due to viral hepatitis raises a risk of hepatotoxicity during anti-tuberculous treatment up to 3-5 times more than TB patients, who do not have such infections. Therefore, co-infection of Hepatitis B and C with TB needs to be identified prior to the start of Anti-TB therapy and Liver Function Tests should be monitored carefully.⁵

Exact prevalence of co-infection is not known in most of the developing world. One study conducted in our institute previously showed the prevalence of HBV 3% and HCV 22% in TB patients.⁶ Prevalence of hepatitis, especially HCV was high compared to general population in Pakistan being reported between 3-6.6% in various studies.⁷⁻⁹ However, in

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that study only culture positive pulmonary TB cases were included. Secondly the sample size was small, only 100 cases were studied. We decided to conduct larger study with all the pulmonary TB (Both smear positive and negative cases) as well as extra pulmonary TB cases to validate the results of previous study. So this study was conducted to assess the frequency of Hepatitis B and C infections in tuberculosis patients.

METHODOLOGY

This cross-sectional study was carried out from November 2017 to October 2018 at Outpatient Department of Pulmonology, Sheikh Zayed Hospital, Rahim Yar Khan. Non probability consecutive sampling technique was used to enroll the patients. Patients between the ages of 15-70 years of either sex, diagnosed as any type of tuberculosis (pulmonary and extra-pulmonary TB) were included in this study. A Total of 865 patients who fulfilled the criteria were registered for this study. Informed consent was taken from patients for inclusion in this study and blood sampling.

Blood samples were taken and sent to the laboratory for detection of HBsAg and anti HCV antibodies by ICT (Immune Chromatographic Technique). Sociodemographic data was recorded on a predesigned performa. All the collected data was then analyzed with SPSS version 22.0. Mean \pm SD were computed for quantitative variables like age of TB patients. Qualitative variables like gender, type of TB (pulmonary or extra pulmonary) and HBV and HCV were presented as frequency and percentage. Ethical permission was taken from Institutional Review Board.

RESULTS

Out of 865 patients, samples of 846 patients were found adequate for performing the tests of HBV and HCV infections. Among them 437 (51.7%) were males and 409 (48.3%) were females. The mean age of patients was 38.71 ± 18.71 years. Out of 846 total patients of this study, 639 patients (75.5%) were suffering from Pulmonary TB and 207 (24.5%) were having extra pulmonary TB (Figure I). Further details of extra pulmonary TB is given in (Table I).

Figure I: Frequency of Pulmonary TB & Extra Pulmonary TB

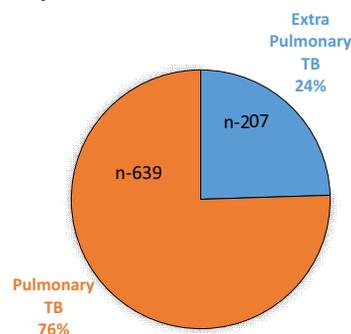


Table I: Type (location) of Tuberculosis

Type of TB	n	%age
Pulmonary Tuberculosis	639	75.5
Extra Pulmonary Tuberculosis	207	24.5
Pleural TB	80	9.5
Lymph nodes TB	44	5.2
Tuberculosis Meningitis	24	2.8
Abdominal TB	21	2.5
TB Spine	18	2.1
Miliary TB	6	0.7
Pericardial TB	4	0.5
TB Joints	3	0.4
Skin TB	2	0.2
Eye TB	1	0.1
Laryngeal TB	1	0.1
Pelvic TB	1	0.1
Testicular TB	1	0.1
Urogenital TB	1	0.1

Table II: Frequency Distribution of HBV and HCV in PTB and EPTB Patients

	Pulmonary TB n=639	Extra PTB n=207	Total n=846	P value
Hepatitis B	24 (3.75%)	05 (2.41%)	29 (3.42%)	0.357
Hepatitis C	144 (22.5%)	33 (15.9%)	177 (20.9%)	0.043
Both	07 (1.09%)	00 (00%)	07 (0.82%)	---

Hepatitis B was present in 29 (3.4%) cases while Hepatitis C was present in 177 (20.9%) cases and both (B & C) were detected in 07 (0.83%) cases. The frequency of Hepatitis B and C in pulmonary TB and extra-pulmonary TB cases is shown in (Table II)

DISCUSSION

In this study, HBV was detected in 3.4% and HCV was found in 20.9% of all types tuberculosis. The results of this study are comparable to our previous study published in 2013 that showed the prevalence of HBV and HCV was 3% and 22% respectively.⁶ Despite the inclusion of all types of TB cases, both pulmonary and extra pulmonary TB, increasing the number of patients investigated (846 vs 100) and a lapse of almost 6 years, figures have not changed much.

When we compared the results of this study for prevalence of HBV infection (3.4%) with those in general population of Pakistan and Rahim Yar Khan, there is not a big difference. A national survey conducted in 2007-2008 by PMRC showed the overall prevalence of HBV 2.5% in general population of Pakistan while in the district of Rahim Yar Khan, the prevalence of HBV was 4.7%.⁹ However, the prevalence of HCV infection in TB cases as revealed in this study (20.9%) and one of our previous study (22 %) is alarmingly high as compared with general population. PMRC survey of 2007-2008 revealed the overall prevalence of HCV 4.9% and 6.6 % in general population of Pakistan and people of Rahim Yar Khan respectively.

Another study published by Umar et al in 2010 showed frequency of HCV infection 3.0% and 4.7% in blood donors and general population respectively.⁷ Situation has not much changed since then. A recently published (2018) systemic review & meta-analysis by Al. Kanaani Z et al concluded that overall HCV prevalence was about 5 % in general population of Pakistan.⁸ Reasons for this higher prevalence needs to be studied further to take remedial steps. There is a sparse data on the prevalence of HBV and HCV in tuberculosis patients.

Review of literature has revealed some studies carried out in different parts of world which are tabulated for comparison with this study in Table III.

Table III: Prevalence of HBV and HCV in tuberculosis patients.

Place of study	Hepatitis B	Hepatitis C	Type of patient	No. of patients
Thailand ¹⁰	09%	31%	HIV + TB	752
India ¹¹	6.4%	2.1%	HIV + TB	951
Georgia ¹²	4.3%	12%	TB	300
Duhok ¹³	1.8%	0.9%	TB	214
Taiwan ¹⁴	5.7%	6.5%	TB	261
Sudan ¹⁵	15.3%	01%	TB	98
Pakistan, RYK ⁶	03%	22%	TB	100
This Study	3.4%	20.9%	TB	846

In these studies, conducted in different countries, results widely varied. Prevalence of HBV ranged from 1.8% to 15.3% and that of HCV from 0.9% to 31%. Higher prevalence of both HBV (9%) and HCV (31%) found in the study conducted in Thailand may be explained by inclusion of patients having both TB and HIV infection. However, it cannot be the sole explanation. HIV infection is not significant in Pakistan and particularly in this area of Rahim Yar Khan. A study from Lahore reported only 0.28% (3 out of 1074) TB patients were tested positive for HIV infection.¹⁶ None of the 49 TB patients tested at Multan were infected with HIV.¹⁷ Similarly, none of the 100 tested at Rahim Yar Khan revealed HIV infection.¹⁸ Therefore, this very high prevalence of HCV cannot be explained on this basis. In addition to the inclusion criteria, background prevalence of HBV and HCV in general population as well as the prevailing infection control practices may be responsible for these variable results. There must be many other risk factors for HCV that needs to be studied in different geographical areas.

In our previous study,⁶ only culture positive pulmonary TB cases were included. In this study, we intended to see if the inclusion of all TB cases both pulmonary (smear/culture positive or negative) as well as extra-pulmonary TB cases have any impact on prevalence of HBV or HCV. As far as overall prevalence of HBV or HCV is concerned, it is almost same (Table III). However, on further sub analysis, HBV was found in 24 out of total 639 pulmonary TB cases (3.75%) cases while it was there in 5 out of 207 Extra-pulmonary TB cases (2.41%). The difference was not statistically significant ($p = 0.357$). On the other hand, HCV was found in 144 out of total 639 pulmonary TB cases (22.5%) cases while it was there in 33 out of 207 Extra-pulmonary TB cases (15.9 %). The difference was statistically significant (p

=0.043). Further studies are needed to see whether the site of TB disease have any impact on prevalence of hepatitis.

According to results of this study, every fourth TB patient is infected with either HBV or HCV. Without strict infection control measures, fellow patients and health care workers are at a risk of acquiring hepatitis. Furthermore, HBV and HCV co-infection is an independent risk factors for ATT induced hepatotoxicity. Wan Soo Kim et al found that the incidence of ATT induced hepatotoxicity during standard anti-TB therapy varies from 2-28%¹⁹ Further studies are needed to see the impact of this high prevalence in our patients.

This study has certain limitations. We did not study the risk factors for HBV and HCV in our patients. Secondly, due to financial constraints, we used the ICT method to detect HBV and HCV which is less accurate than ELISA and PCR. However, study done in 2013 by Akhtar J et al showed almost comparable results of HBV and HCV detection by ICT and ELISA with only one false positive result by ICT.²⁰ Therefore, in resource limited countries, it may be an acceptable answer.

CONCLUSION

In our study the frequency of HCV is very common in TB patients. Almost one in every four TB cases is infected with either HCV or HBV which can endanger the treatment outcome of patients and spread of infection in community. Therefore, in such high burden geographical regions, the screening for HBV and HCV in all TB patients should be mandatory and strict infection control measures should be enforced to reduce burden of disease.

Authors Contribution; IB: Study Designed and planned research work, Abstract writing, Sample Collection and Data Analysis. **HSN:** Data Analysis, Literature Review. Interpretation of Results and Write up. **MR:** Sample Collection, Data Analysis and interpretation of Results. **MUH:** Study designed and planned research work. Writing conclusion and recommendation.

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REFERENCES

1. WHO. Global tuberculosis report 2018. 2018 [cited 2018]; Available from: http://www.who.int/tb/publications/global_report/en/.
2. Badawi A, Sayegh S, Sallam M, Sadoun E, Al-Thani M, Alam MW, et al. The global relationship between the prevalence of diabetes mellitus and incidence of tuberculosis: 2000-2012. *Global journal of health science* 2014;7(2):183-91.
3. WHO. Global hepatitis Report 2017. Available from: <https://www.who.int/hepatitis/publications/global-hepatitis-report2017/en/>
4. Patel N, Singh S. Antituberculosis therapy in patients with hepatitis B viral infection. *Hepatitis B Annual* 2012;9(1):16-48
5. Agha MA, El-Mahalawy II, Seleem HM, Helwa MA. Prevalence of hepatitis C virus in patients with tuberculosis and its impact in the incidence of anti-tuberculosis drugs induced hepatotoxicity. *Egyptian Journal of Chest Diseases and Tuberculosis* 2015;64(1):91-6.
6. Masood-Ul-Haq, Arshad A S, Hakim A, Mehmood I, Ali S, Rasheed S. High prevalence of hepatitis B & C in TB patients – will it be the next threat to tuberculosis control? *JSZMC*; Apr - Jun, 2013 : 04 (02) :427-31.
7. Umar M, Hamama-tul-Bushra, Ahmad M, Khurram M, Usman S, Arif M, Adam T, et al. hepatitis C in Pakistan: A Review of Available Data. *Hepat Mon* 2010; 10(3):205-14.
8. Al Kanaani Z, Mahmud S, Kouyoumjian SP, Abu-Raddad LJ. 2018 The epidemiology of hepatitis C virus in Pakistan: systematic review and meta-analyses. *R. Soc. Open Sci.* 2018 5: 180257.
9. Hepatitis B and C survey Pakistan - Pakistan Health Research Council. Available from: <http://phrc.org.pk/assets/hepatitis-national-survey.pdf>.
10. Sirinak C, Kittikraisak W, Pinjeesekikul D, Charusuntornsri P, Luanloed P, Srisuwanvilai L-o, et al. Viral hepatitis and HIV-associated tuberculosis: Risk factors and TB treatment outcomes in Thailand. *BMC Public Health* 2008;8(1):245-9
11. Padmapriyadarsini C, Chandrabose J, Victor L, Hanna LE, Arunkumar N, Swaminathan S. Hepatitis B or hepatitis C co-infection in individuals infected with human immunodeficiency virus and effect of anti-tuberculosis drugs on liver function. *Journal of Postgraduate Medicine* 2006;52(2):92-6.
12. Kuniholm MH, Mark J, Aladashvili M, Shubladze N, Khechinashvili G, Tsertsvadze T, et al. Risk factors and algorithms to identify hepatitis C, hepatitis B, and HIV among Georgian tuberculosis patients. *International journal of infectious diseases* 2008;12(1):51-6.
13. Merza M, Haji S, Alsharafani A, Muhammed S. Low prevalence of hepatitis B and C among tuberculosis patients in Duhok Province, Kurdistan: Are HBsAg and anti-HCV prerequisite screening parameters in tuberculosis control program? *International Journal of Mycobacteriology* 2016;5(3):313-7.
14. Sun HY, Chen YJ, Gau CS, Chang SC, Luh KT. A prospective study of hepatitis during antituberculous treatment in Taiwanese patients and a review of the

- literature. Journal of the Formosan Medical Association, Taiwan yi zhi 2009;108(2):102-11.
15. Abdallah TM, idriss MI, Ahmed AM, Ali AA, Saeed OK. sero-prevalence of hepatitis b and hepatitis C viruses among tuberculosis patients in kasala eastern sudan. Glob J Infect Dis Clin Res 1 (1): 001-003 DOI: 10.17352/2455-5363.000001.
 16. Ch. MK, Syed ZA, Younas M. Prevalence of Human Immunodeficiency Virus (HIV) infection in patients with pulmonary tuberculosis. PJCM; 2009, Vol 15 No.3:18-21-5
 17. Syed ZA, Khan MI, Aslam M, Tasir IH. Frequency of HIV infection in patients with pulmonary tuberculosis and various cancers at Nishtar Hospital Multan. Pak. J. Med. Res. Oct-Dec 2003;42(4):149-51.
 18. Masood-Ul-Haq, Arshad A S, Hakim A, Mehmood I, Rasheed S, Ali S, Sohail I. Universal HIV testing for TB patient; is it really applicable universally? JSZMC; Oct – Dec, 2012, Vol 03 No. 04:371-74.
 19. Kim WS, Lee SS, Lee CM, Kim HJ, Ha CY, Kim HJ, et al. Hepatitis C and not Hepatitis B virus is a risk factor for anti-tuberculosis drug induced liver injury. BMC Infectious Diseases 2016;16(1):50.
 20. Akhtar J, Qamar MU, Haleem A, Waheed A, Sarwar F, Anwar J. Sero-prevalence of HBV and HCV in tuberculosis patients at Sheikh Zayed Hospital Rahim Yar Khan, Pakistan. Biomedica; Apr-Jun, 2013 : 29: 69-72.

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