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Original Article

Coinfections with Hepatitis B virus and Hepatitis C virus among tuberculosis patients in Jos, Nigeria

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ABSTRACT

Objectives: This study investigated the prevalence of hepatitis B virus (HBV) and hepatitis C virus (HCV) among tuberculosis (TB) patients in Jos, Nigeria.

Materials and Methods: Seventy-one (71) TB-positive individuals visiting anti-retroviral clinics (male and female between the ages of 15–55 years) were enrolled in the study. Questionnaires and consent forms were issued to these patients after obtaining ethical clearance for the study. Two milliliters of blood samples were obtained from each TB-positive individual by venipuncture and were analyzed using a hepatitis B and C rapid kit (Solid rapid test kit manufactured by Hangzhou Deangel Biological Engineering Co., Ltd. China). Analysis of data was performed with version 26 of SPSS software.

Results: Out of the seventy-one (71) TB patients recruited in the research, 4 (5.6%) and 2 (2.8%) patients had hepatitis B and C virus, respectively. In this study, HBV seroprevalence, 3 (13.1%) and 1 (11.1%) were recorded among two age groups: 26–30 and 36–40 years, respectively. HCV seroprevalence, 2 (9.1%) was reported within the age group 26–30 years only. The age group and the prevalence of HBV and HCV among the study subjects had no statistically significant relationship ($P > 0.05$). Of the 37 females examined, 2 (5.4%) were positive for HBV or HCV, respectively, while of the 34 males, 2 (5.9%) had only HBV. The variables which showed no significant relationship with hepatitis B and C virus were age ($P = 0.423$; $P = 0.436$), sex ($P = 0.660$; $P = 0.268$), newly diagnosed TB patients and those on treatment ($P = 0.416$; $P = 0.111$), blood transfusion ($P = 0.433$; $P = 0.330$), illegitimate sex ($P = 0.668$; $P = 0.239$), tattoo ($P = 0.298$; $P = 0.298$), human immunodeficiency virus status ($P = 0.542$; $P = 0.654$), use of sharp objects ($P = 0.409$; $P = 0.686$), and knowledge of the virus ($P = 0.702$; $P = 0.614$) as $P > 0.05$. In addition, variables that showed a significant relationship with HCV infection are those that have not been vaccinated with hepatitis B ($P = 0.015$) as $P < 0.05$.

Conclusion: TB patients attending the Faith Alive Foundation Hospital and Plateau Specialist State Hospital, Jos have a low seroprevalence of HBV and HCV and it is recommended that more sensitive and reliable diagnostic options such as enzyme-linked immunosorbent assay and polymerase chain reaction are employed in further studies. TB patients seropositive for HBV or HCV were referred to physicians for appropriate management to prevent complications and the likelihood of damage to the liver as a result of treatment with drugs against TB.

Keywords: Tuberculosis, Coinfection, Hepatitis, Patients, Prevalence

INTRODUCTION

The bacterium, *Mycobacterium tuberculosis,* is the etiologic agent of tuberculosis (TB) which mainly affects the lungs and remains a life-threatening disease in many parts of the globe.[1] Approximately 1.6 million died due to TB in 2021. TB has been listed as a disease of high public health importance in Africa and has remained a leading cause of disability and death.[2,3] Yearly global reports continue to rank Nigeria among the top burden countries for TB with Nigeria reporting second to the highest prevalence in Africa.[2,3] Coinfections of TB with hepatitis B virus (HBV) and hepatitis C virus (HCV) potentially lead to treatment failure and poor patient outcomes. TB cases are generally treatable; however, there are reports of complications due to hepatotoxicity as a result of viral hepatitis in some individuals.[4,5]

HBV and HCV have been suggested as key drivers of liver disease (Viral hepatitis) therefore, of public health concern globally.[4,6] Despite programmed HBV vaccination for neonates which began in 1992, there is still a recorded worldwide prevalence of 7.8% and 1.1% for hepatitis B surface antigen (HBsAg) and HCV, respectively, in which case about 93 million individuals reportedly may have

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life-long HBV infections. In Nigeria, however, the prevalence of HBsAg and HCV was 11.1% and 2.2%, respectively, in 2018.[6,7]

The seroprevalence of HBsAg and HCV infection among TB-positive individuals has been noted to vary across different regions. For HBsAg, a prevalence of 8.7–14.9% and 2.2–15.5% was reported in Northern and Southern Nigeria, respectively, in Pakistan, Sudan, and Brazil, a prevalence of 5.5%, 9.5%, and 26.5% was reported, respectively.[7,8] For HCV, a prevalence of 5.4–14.8% and 0.7–7.0% was reported in Northern and Southern Nigeria, respectively, and a prevalence of 3.5–10.0% in other countries.[7]

The probability of liver damage while undergoing therapy for TB has been shown to increase when there are coinfections of HBV or HCV among TB-positive subjects.[6] Therefore, life-threatening liver damage can occur as a result of deferred treatment and subsequent poor treatment outcomes. The drugs (e.g., rifampicin, isoniazid, and pyrazinamide) used for TB therapy when there is coinfection with hepatitis B or C or both increase the risk of serious damage to the liver. Screening TB-positive subjects for hepatitis B and C will help identify those that are likely to develop hepatotoxicity so that they could be monitored closely and treated early if they develop drug-induced hepatotoxicity.[9,10] There is a need to carry out routine screening for hepatitis B and C viruses among TB patients for proper disease management and increased treatment success. Given the notable regional variation in the seroprevalence of HBsAg and HCV among TB-positive individuals, this study thus seeks to find out the seroprevalence of HBV and HCV among TB-positive subjects in Jos metropolis, Plateau State, North-Central Nigeria.

MATERIALS AND METHODS

Study design/population

This was a cross-sectional and descriptive study. The individuals recruited for the study included patients with GeneXpert *M. tuberculosis*/rifampicin (RIF) diagnosis for TB between 15 and 55 years attending Faith Alive Hospital and Plateau State Specialist Hospital, Jos, Plateau State between August and October 2018. A total of 71 participants were enrolled in the study.

Data collection

Consent was sought and obtained from each potential study participant that met our selection criteria. The eligible patients were approached by the research assistant to complete a structured questionnaire. Data on demographics, risk factors such as unprotected sex, blood transfusion, sharing of sharp objects, tattooing, immunization status, and knowledge of HBV and HCV infection were obtained using the questionnaire. A trained research scientist was responsible for interacting with the patients and collecting the data.

Ethical approval

Ethical clearance for the study was obtained from the Research and Ethics Committee of the Plateau State Specialist Hospital, Jos, and written consent was obtained from each participant before sample collection and administration of the questionnaire. Each participant was assigned a code to ensure the confidentiality of all information gathered in relation to the study.

Sample collection and analysis

Two milliliters of blood were obtained from each TB-positive individual (study participants comprised patients with RIF-resistant TB) in the study by venipuncture from the cubital vein with the use of sterile disposable syringes and needles. The blood samples were transferred into sterile anticoagulated tubes with screw caps and closed aseptically. The tubes were rolled and labeled. The blood samples were labeled and centrifuged for 5 min at 2000 revolutions per minute to separate the sera from the plasma. The test strip was kept on a clean air-dried surface; two drops of the sera sample were placed onto the sample pad. Then, one drop of the buffer is added to the sample well. The results were read after 10 min as described in the manufacturer's manual. The relative sensitivity, specificity, and accuracy of the HBV/HCV rapid kit are 97.8%, 97.7%, and 97.8%, respectively (Hepatitis B and C solid rapid test kit manufactured by Hangzhou Deangel Biological Engineering Co., Ltd, China).

Data analysis

Analysis of data was carried out using SPSS version 26. Descriptive (numbers and percentages) statistics were conducted, and data were presented using graphs, pie charts, tables, and comparisons. Statistical significance was determined using the Fisher's Exact Test (Test statistic is significant at 0.05 level).

RESULTS

Blood samples from 71 TB-positive individuals were screened for HBV and HCV surface antigens and 4 (5.6%) had HBV, while 2 (2.8%) had HCV. [Table 1] shows the prevalence of HBV and HCV among TB-positive subjects in relation to age and sex in Jos metropolis. Most of the study subjects, 22 (31%), were within the age range of 26–30 years, followed by 15 (21%) who were within ages 19–25 years. Most of the participants, 37 (52.1%), were female and 34 (47.9%) were male [Table 1]. In addition, [Table 1] shows that the seroprevalence of HBV and HCV was highest in the age group 26–30 years, 13.1% and 9.1%, respectively. Female subjects in this study had the same prevalence of HBV and HCV (5.4%), however, only HBV was reported among male subjects (5.9%).

[Table 2] shows the seroprevalence of hepatitis B and C virus among TB-positive individuals according to risk factors: Type

Table 1: The prevalence of HBsAg and HCV among TB patients according to age and gender in Jos Metropolis, Nigeria (*n*=71).

Variable	No. tested	HBsAg positive	HCV-positive	*P*-value[a]	*P*-value[a]
		n (%)	*n* (%)	HBsAg	HCV
Age (years)					
<18	5	0 (0)	0 (0)		
19–25	15	0 (0)	0 (0)		
26–30	22	3 (13.1)	2 (9.1)	0.42	0.43
31–35	12	0 (0)	0 (0)		
36–40	9	1 (11.1)	0 (0)		
>41	8	0 (0)	0 (0)		
Gender					
Female	37	2 (5.4)	2 (5.4)		
Male	34	2 (5.9)	0 (0.0)	0.66	0.27
Overall prevalence	*n*=71	4 (5.6)	2 (2.8)		

n: Number of participants, %: Percentage, [a]Fisher's exact test, Test statistic is significant at 0.05 level, HBsAg: Hepatitis B surface antigen, HCV: Hepatitis C virus, TB: Tuberculosis

Table 2: The prevalence of HBsAg and HCV among TB patients in relation to risk factors in Jos Metropolis, Nigeria (*n*=71).

Risk factors	No. tested	HBsAg positive	HCV-positive	*P*-value[a]	*P*-value[a]
		n (%)	*n* (%)	HBsAg	HCV
Type of TB patients					
Newly diagnosed	24	2 (8.3)	2 (8.3)	0.42	0.11
On treatment	47	2 (4.2)	0 (0.0)		
Sex (Sexual intercourse)					
Safe	35	2 (5.7)	2 (5.7)	**0.67**	**0.23**
Unsafe	36	2 (5.6)	0 (0.0)		
Blood transfusion					
Yes	46	3 (6.5)	2 (4.3)	**0.43**	**0.33**
No	25	0 (0.0)	0 (0.0)		
Tattoos					
Yes	32	1 (3.1)	2 (6.3)	**0.29**	**0.3**
No	39	3 (7.6)	0 (0.0)		
Vaccination (three doses of Hep B vaccine)					
Yes	21	1 (4.8)	0 (0.0)	**0.39**	**0.01**
No	50	3 (6.0)	2 (4.0)		
HIV status					
Positive	29	2 (6.9)	1 (3.4)	**0.52**	**0.65**
Negative	42	2 (4.8)	1 (2.4)		
Use of sharp objects					
Yes	29	1 (3.4)	1 (3.4)	**0.4**	**0.69**
No	40	3 (4.2)	1 (1.4)		
Heard of HBV/HCV					
Yes	39	2 (5.1)	0 (0.0)	**0.7**	**0.61**
No	32	2 (6.3)	2 (6.3)		

n: Number of participants, %: Percentage, [a]Fisher's Exact Test, *P*-values (in bold), Test statistic is significant at 0.05 level, Sex: Sexual intercourse, Safe: Used Condom, HBsAg: Hepatitis B surface antigen, HCV: Hepatitis C virus, TB: Tuberculosis, HBV: Hepatitis B virus, HIV: Human immunodeficiency virus

of TB patients (newly diagnosed and those on treatment); newly diagnosed patients had a higher prevalence of 4.2% and 0.0% respectively. Similarly, both HBV and HCV prevalence (5.7%) was higher among those who had safe sexual intercourse (used condom) than among those who had unsafe sex with HBV and HCV prevalence of 5.7% and 0.0% respectively. In relation to blood transfusion, both hepatitis B and C had a high prevalence rate of 6.5% and 4.2%, respectively, among those who have engaged in blood transfusion. Based on Tattooing, HBV had a high prevalence of 7.6% among those who had never received a tattoo before while for hepatitis C, the prevalence was higher, 6.3% among those who received tattoos in the past.

For vaccination, both HBV and HCV had a high prevalence rate of 6.0% and 4.0%, respectively, among those who have never been vaccinated. The prevalence rate of HBV and HCV was higher among HIV-positive subjects with 6.9% and 3.4% prevalence respectively. HBV prevalence (7.5%) was higher among those who do not use sharp objects while HCV had a higher prevalence rate (3.4%) among those who use sharp objects than those who do not (2.5%). There was a prevalence of HCV (6.3) among those who have not heard about the virus and none among subjects who have heard about HCV. HBV had a higher prevalence (6.3%) among those who have not heard about the virus compared to 5.1% among those who have not heard about HBV. The result showed that there is no significant association ($P > 0.05$) between the variables [Table 1].

[Table 2] shows the proportion of participants who had positive HBsAg and HCV in relation to risk factors. A greater proportion of participants who had positive HBsAg and HCV results had a history of blood transfusion and had not received any vaccination. The proportion of participants with positive HBsAg and HCV results was equal despite the HIV status. No statistically significant association was observed between the HBsAg and HCV results and the occurrence of any risk factors.

DISCUSSION

Viral hepatitis in TB patients has been demonstrated to potentiate the risk of hepatotoxicity induced by therapy against TB.[6,9,11,12] The seroprevalence rate of HBV and HCV among the 71 TB patients (aged 15–55 years) studied was 5.6% and 2.8%, respectively. The prevalence of viral hepatitis varies across regions in Nigeria and beyond. Most of the participants, 22 (31%), were in the age category of 26–30 years, and mostly females, 37 (52.1%). The overall seroprevalence of HBsAg and HCV infection among TB patients in our sample population was 5.6% and 2.8%, respectively. This finding differed from that of a similar study conducted in Sokoto State (both in Northern Nigeria) which showed a much higher prevalence of HBsAg and HCV of 14.9% and 5.4%, respectively.[7] Similarly, another study in Kano, Northern Nigeria, which used sputum smears showed a higher prevalence of 8.7% for HBsAg and 14.8% HCV among TB patients compared to our study.[13] In southern Nigeria, a prevalence of 2.2–15.5% and 0.7–7.0% has been reported for TB coinfection with HBsAg and HCV, respectively.[7] Furthermore, studies in other countries such as Pakistan, Sudan, and Brazil showed a prevalence of HbsAg among TB patients of 5.5–26.5%, respectively;[14-16] and a prevalence of HCV of 3.5–10.0%.[15,16] These regional variations in prevalence can be attributed to different environmental and hygienic conditions. Elsewhere, Akhtar *et al.* reported a 5.5% and 10.0% prevalence of HBV and HCV, respectively, in Pakistan.[17] Nail *et al*. and Kuniholm *et al*. documented 9.5% and 4.3% of HBV and 3.5% and 12.0% of HCV in Sudan and Thailand, respectively.[18,19]

The variations in the prevalence rate of HBV and HCV among TB patients observed in our study compared to these reports could be attributed to the differences in screening methods, different sample sizes, geographical location, economic, and hygiene status of the studied populations.

Patients aged 26–30 years had the highest seroprevalence of HBV and HCV infection of 13.6% and 9.1%, respectively, which agrees with the previous reports.[7,8] The high prevalence of HBV and HCV recorded in this study could be due to high sexual activity among people of this age category. In relation to sex, males had the highest HBV prevalence of 5.9% with females recording higher HCV infections of 5.4%. This may be due to the assertion that women are more exposed to sexual activity than men due to economic challenge.[20] This is in concordance with the related prevalence reported by Imoru *et al*. with the prevalence of HBV and HCV being 15.9% and 7.5% among females and 14.01% and 3.8% among males, respectively.[7]

TB patients who had a previous history of blood transfusion had a higher prevalence of HBV and HCV which are 6.5% and 4.3%, respectively. This was in line with the earlier reported prevalence by Muayad *et al*. which was 16% for HBV and 4% for HCV, respectively.[21] This may be due to the fact that the blood being transfused to these patients was not properly screened for HCV and HBV before being transfused to them in the past.[21]

Knowledge of HBV and HCV reports indicates that there was good knowledge of the virus which was 54.9%. However, 5.1% of these patients who claimed knowledge of HBV were positive for HBV. This may be due to the fact that these patients were reluctant to take preventive measure against HBV and HCV infections.[20]

In this study, 70.4% of study subjects were not vaccinated with HBV vaccine (based on the information obtained from the questionnaires administered to study participants) and there was seroprevalence of HBV and HCV among the study subjects not vaccinated; 6.0% and 4.0%, respectively. This may be due to the fact that there is less coverage of vaccination by primary healthcare services. This agrees with a previous study carried out in Brazil.[14]

HBV had a higher prevalence rate (7.5%) among those that do not share sharp objects while HCV had a similar prevalence rate among those who shared sharp object and those who do not share sharp objects. This may be due to the fact that these same patients were involved in one or more risk factors like receiving blood transfusion in the past or having unprotected sex. However, this disagrees with the reported prevalence of HBV and HCV which were 5.1 and 1.8%, respectively by Imoru *et al*. in Sokoto, Nigeria.[7] Although HBV and HCV seropositivity in this study was lower compared to other studies in Nigeria, the individuals seropositive for HBV

and/or HCV were referred to physicians for appropriate management given the complications envisaged due to TB coinfection and treatment with anti-TB drugs. It is recommended that HBV and HCV screening tests should be carried out among diagnosed TB patients to guide therapeutic decisions. This will help improve public health education on the transmission of these viral infections and assist in reducing the complications and mortality rate among TB patients.

CONCLUSION

From this study, it was observed that the prevalence of HBV and HCV infection among TB patients in Jos Metropolis was 5.2% and 2.8%, respectively. This suggests that there is a low seroprevalence of HBV and HCV in the population studied. HBsAg and HCV rapid tests can misdiagnose some patients due to the low sensitivity of rapid test kits compared to enzyme-linked immunosorbent assay (ELISA) or polymerase chain reaction (PCR). Therefore, it is recommended that HBV/HCV ELISA/PCR should be used in further studies rather than rapid tests. In addition, TB patients seropositive for HBV or HCV were referred to physicians for appropriate management to prevent complications and the risk of anti-tuberculous drug-induced liver damage.

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Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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