

# Parallel and Overlapping Infection of Human Immunodeficiency Virus and Hepatitis B Virus Among Tuberculosis Patients Attending A Tuberculosis/Leprosy Referral Centre in Central Nigeria: A Cross-Sectional Study

Pennap GRI,  
Oti VB\*,  
Bako CA

Department of Microbiology, Nasarawa State University, Keffi, Nigeria

## Abstract

Tuberculosis (TB) is a global health problem. Coinfection with Human Immunodeficiency Virus (HIV) and Hepatitis B virus (HBV) among TB patients has paved way for the resurgence of *Mycobacterium tuberculosis* infection as well as increased risk of hepatotoxicity during tuberculosis therapy. There is paucity of published data on HIV/HBV infection in TB patients in Nigeria. This was a baseline study carried out to determine coinfection of HIV and HBV in Tuberculosis confirmed patients attending a TB/Leprosy referral healthcare Centre in Central Nigeria. Blood samples were collected from 400 confirmed TB patients and their sociodemograph information were obtained using a structured questionnaire. Samples were analyzed for anti-HIV and HbsAg using Enzyme Linked Immunosorbent Assay (J. Mitra and Co. Pvt. Ltd, India and Shantha Biotechnics Ltd, India respectively). Data were analyzed using SSP version 2.80. P value  $\leq 0.05$  was considered statistically significant. Of the 400 patients, 68(17.0%) tested positive for HIV and 48(12.0%) for HBV while 6 (1.5%) had HIV/HBV coinfection. Gender, history of STI, history of HBV vaccine and educational status were associated risk factors for the viral infection. Age, history of blood transfusion and scarification mark did not show any statistically significant association to the viral infections. The prevalence rates of HIV and HBV recorded in this population is a cause for alarm. There is therefore a need to introduce the monitoring of TB patients for therapy-related hepatotoxicity and performance of these viral infections.

## Keywords

HBV; HIV; Tuberculosis; Parallel and Overlapping; Nigeria

## Introduction

Human Immunodeficiency Virus (HIV) and Hepatitis B Virus (HBV) infection have emerged as a leading cause of morbidity and mortality due to liver disease in the world for the last two decades [1-3]. This overlapping infection is more common due to the similarity in their mode of transmission [1]. In coinfection, the presence of one virus results in a change in the natural history of the other [4]. For example, HIV enhances the natural course of HBV infection and accelerates progression of liver disease to liver cirrhosis and Hepatocellular Carcinoma (HCC). The progression of hepatic disease to liver cirrhosis in HIV patients is almost three-times faster when compared to those negative for HIV [5]. The World Health Organization (WHO) estimates approximately 240 million people worldwide are chronically infected with HBV [3]. Areas of high prevalence are similar to the global TB epidemiological "hotspots" which include sub-Saharan Africa and South Asia, where the prevalence is estimated to be between 8 and 20% [3,4].

Tuberculosis is still a leading global health problem caused by *Mycobacterium tuberculosis* complex. There are 9.6 million new cases of TB globally and 1.5 million deaths [6,7]. HIV infection which is recognized as a leading cause of death worldwide is central in escalating this situation. Sub-Saharan Africa is the most affected region, with 24.7 million people been infected with HIV which accounts for almost 70% of the global total of new HIV infections [6,8-9].

Several studies report an increased coinfection with HIV and/or HBV in TB patients [2,10-12]. However, there is paucity of published data on these viral infections among tuberculosis patients in Nigeria. In view of the aforementioned, this baseline study became imperative.

## Materials and Methods

### Study Area and Population

The study was designed to cover patients receiving treatment at the Tuberculosis/Leprosy unit of Evangelical Reformed Church of Christ (ERCC) Alushi, Nigeria. It is 134 Km from Abuja the Federal Capital and 62 Km from Lafia the state capital [13].

## Article Information

<b>DOI:</b>	10.31021/jtgch.20181102
<b>Article Type:</b>	Research Article
<b>Journal Type:</b>	Open Access
<b>Volume:</b>	1 <b>Issue:</b> 1
<b>Manuscript ID:</b>	JTGCH-1-102
<b>Publisher:</b>	Boffin Access Limited
<b>Received Date:</b>	February 22, 2018
<b>Accepted Date:</b>	March 06, 2018
<b>Published Date:</b>	March 13, 2018

### \*Corresponding author:

#### Victor B Oti

Department of Microbiology  
Nasarawa State University  
Keffi, Nigeria  
Tel. No: +2347069657739  
E-mail: Obabavictor1@gmail.com

**Citation:** Pennap GRI, Oti VB, Bako CA. Translational Pancreatology. Parallel and Overlapping Infection of Human Immunodeficiency Virus and Hepatitis B Virus Among Tuberculosis Patients Attending A Tuberculosis/Leprosy Referral Centre in Central Nigeria: A Cross-Sectional Study. J Transl Gastroenterol Clin Hepatol. 2018 Feb;1(1):102

**Copyright:** © 2018 Oti VB, et al. This is an open-access article distributed under the terms of the Creative Commons Attribution 4.0 international License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

A total of 400 tuberculosis patients attending the TB/ Leprosy referral Centres participated in this cross sectional Hospital-based study from May through August 2017. An informed consent was obtained from each participant or parents/guardians of participant below 18 years. A representative sample size was determined using the formula propounded by Naing, [14]. This study did not interfere with the normal management of the patients. Their socio-demographic and clinical information was obtained by administering a structured questionnaire.

### Sample Collection

Three ml of blood sample was collected from each patient by venipuncture into a labeled plain tube. This was allowed to clot at room temperature and spun for 5 minutes at 3,000 rpm. The resultant sera were harvested into well labeled cryovials and stored at -20°C until ready for use.

### Inclusion Criteria

Tuberculosis patients attending the TB/Leprosy Referral Centre were recruited for the study. Only those between the age of 15 and 65 years with active TB disease who indicated willingness to participate in the study and gave written informed consent were enrolled.

### Laboratory Assay

#### Anti-Human Immunodeficiency Virus (Anti-HIV) Detection

To detect anti-HIV, the anti-HIV 1/2 World Health Organization approved kit "DETERMINE" was used for the initial screening. All reactive samples were retested with a MicroELISA Kit (J. Mitra and Co. Pvt, Ltd, India). Both kits were used according to each manufacturer's specifications.

#### Hepatitis B Surface Antigen (HBsAg) Detection

A rapid in vitro qualitative sandwich immunoassay diagnostic kit was used for screening the sera for HBsAg. The test kit (HBsAg one step test strips, ACON Laboratories Inc, USA) utilizes a combination of monoclonal and polyclonal antibodies to detect HBsAg in serum.

All reactive samples were further confirmed using with Shantest™ HBsAg ELISA (Shantha Biotechnics Ltd, India). The test procedure and result interpretations were carried out according to the manufacturers' specifications.

### Statistical Analysis

The data obtained were subjected to descriptive statistical analysis using Smith's Statistical Package (SSP version 2.80, Claremont, California-USA). Chi-square statistical test was used to determine associations. Values obtained were considered statistically significant at  $P \leq 0.05$ .

### Results

A total of 400 Tuberculosis patients attending a TB/Leprosy Referral Centre participated in this study. Of them 68 (17.0%) were seropositive for anti-HIV and 48 (12.0%) for HBsAg while 6 (1.5%) were positive for both HIV and HBsAg infection surrogates. The prevalence of HIV/HBV coinfection among female TB patients was 3.6% ( $p < 0.05$ ). The prevalence for single infection was higher in males (17.2%) for HIV and females (14.3%) for HBV. The coinfection rate was 4.5%, 2.4%, 1.9% and 0.0% among patients aged <18 years, 33-39 years, >47 years and 19-25, 40-46 years respectively ( $P > 0.05$ ). Patients who had a history of STI (11.1%,  $P = 0.0000$ ), Presence of Scarification mark (2.9%,  $P = 0.2930$ ) and do not have any formal education (10.7%,  $P = 0.0000$ ) were more likely to be infected with HIV and HBV, while history of blood transfusion was more among those with no history of blood transfusion than those with a history of blood transfusion ( $P > 0.05$ ) (Table 1).

### Discussion

Tuberculosis is a serious public health challenge in most developing countries and it has jeopardy to the worldwide epidemic of HIV and HBV infections. This study investigated the parallel and overlapping infection of HIV and HBV infections among TB patients attending a TB/Leprosy Referral Centre in Central Nigeria. Such studies have been reported in a good number of nations, yet reports on these viral pathogens among TB patients are scarce in Nigeria. The

Risk Factor	No. Examined	No. Positive					
		HIV (%)	p value	HBV (%)	p value	HIV/HBV	p value
<b>Gender</b>							
Male	232	40 (17.2)	0.8987	24 (10.3)	0.2898	0 (0.0)	0.0043
Female	168	28 (16.7)		24 (14.3)		6 (3.6)	
<b>Age (Years)</b>							
< 18	44	4 (9.1)		8 (18.2)		2 (4.5)	
19-25	52	8 (15.4)		8 (15.4)		0 (0.0)	
26-32	84	14 (16.7)		6 (7.1)		2 (2.4)	
33-39	62	14 (22.6)	0.3955	8 (12.9)	0.5151	0 (0.0)	0.3397
40-46	54	14 (25.9)		4 (7.4)		0 (0.0)	
>47	104	14 (13.5)		14 (13.5)		2 (1.9)	
<b>History of Blood Transfusion</b>							
Yes	56	2 (3.6)	0.0104	6 (10.7)	0.7761	0 (0.0)	0.3235
No	344	66 (19.2)		42 (12.2)		6 (1.7)	
<b>History of STI</b>							
Yes	36	22 (61.1)	0	10 (27.8)	0.0106	4 (11.1)	0
No	364	46 (12.6)		38 (10.4)		2 (0.05)	
<b>Scarification Mark</b>							
Yes	68	16 (23.5)	0.1945	8 (11.8)	0.9536	2 (2.9)	0.293
No	332	52 (15.7)		40 (12.0)		4 (1.2)	
<b>Educational status</b>							
Non-formal Edu	56	26 (46.4)		24 (42.9)		6 (10.7)	
Primary	44	26 (59.1)		16 (36.4)		0 (0.0)	
Secondary	140	12 (8.6)	0	4 (2.9)	0	0 (0.0)	0
Tertiary	160	6 (3.8)		4 (2.5)		0 (0.0)	

**Table 1:** Parallel and Overlapping infection of HIV and HBV among tuberculosis patients attending TB/Leprosy Referral Centre in Central, Nigeria with respect to risk factors studied.

overall prevalence of HIV/HBV infection in this current study was 1.5% which is lower than findings from similar studies in the world. It was 12.7% among TB and HIV positive patients in Cameroun, 23.1% among tuberculosis patients in United Kingdom, 35.8% in TB patients in Brazil and 36.7% in HIV/AIDS and active tuberculosis patients in Brazil [2,10-12]. These differences might be as a result of different diagnostic methods, sample size and location of the study population.

The 17.0% prevalence of HIV infection among TB patients observed in this study is lower than the 44.2% and 19.8% reported by Pennap *et al.* in Nasarawa State and Okoh and Omuemu, in Benin, Nigeria respectively [15,16]. Several studies on the prevalence of anti-HIV among TB patients in different countries of the world have also shown different rates. For example, it was 32.8% in Cameroun, 13% in Ethiopia, 1.48% in India [2,4,17]. The observation in this study might not be unconnected with the fact that there is a relatively high prevalence of HIV circulating in the study area.

The prevalence of HBV infection among the study population in the present study was 12.0%. Similar findings have been reported in different studies [2,4,5,11,17-22]. Hepatitis B virus carrier might be at a higher risk of contracting TB. Infection of HBV in TB patients increases the risk of anti-TB treatment-induced hepatotoxicity and therefore, caution should be taken in checking patients for hepatotoxicity related to TB drugs [4].

The proportion of HIV and HBV infection was found to be higher in females (3.6%) than males (0.0%). Higher rate of HIV and HBV infections was discovered among male (17.2%) and female (14.3%) gender respectively. However, there was a statistically significant association among patients with respect to gender ( $p < 0.05$ ). This observation did not correspond with previous findings [2,4,5,12,15]. There is no obvious reason for such outcome but it is probably related to the higher incidence of HIV and HBV infections in females which might predispose them to TB as the formers are known to activate dormant TB. Women are more susceptible to HIV and HBV infections and are usually exposed to sexual activities earlier than men mainly due to economic challenges. Furthermore, most African women are so submissive to their husbands to the level that they have little or no say in sex related matters. The study was in a setting where early and polygamous marriage is common. It is therefore possible for one male to be a source of infection to several females [15].

The present study reported a highest infection of HIV and HBV among patients aged  $< 18$  years with a prevalence of 4.5% and a highest prevalence of single infection of HIV and HBV among those aged 33-39 years and  $< 18$  years respectively. There were no statistically significant associations between the prevalence of the viral infections and age ( $p > 0.05$ ). This observation corresponds with report from similar studies [10,12,15,16]. This indicates that being young is a possible risk factor for contracting these viruses.

This study did not demonstrate any association of HIV and HBV infection with history of blood transfusion ( $p > 0.05$ ) but there was an association statistically between HBV prevalence and history of blood transfusion ( $p < 0.05$ ). Patients with no history of blood transfusion had a higher prevalence than those with a history of blood transfusion for both single and multiple infections. This reflects the effectiveness of the measures taken by our blood banks. Similar outcome was reported in a study conducted in Sudan [5].

Similarly, the viral parallel and overlapping infections were associated with history of Sexually Transmitted Infections (STIs). The infections with anti-HIV (61.1%), HBsAg (27.8%) and HIV and HBV (11.1%) were higher among those with a history of STIs. This agrees with a similar study in Ethiopia [17]. The presence of an STI is an obvious risk factor for the acquisition of the viral pathogens and other opportunistic parasites.

With reference to scarification mark, patients with a scar had a 2.9% HIV/HBV coinfection rate. Those with no scarification mark had a 12.0% HBV prevalence and patients with a history of scarification mark had 23.5% HIV prevalence. No statistical association between scarification mark and the viral infections was recorded ( $p > 0.05$ ).

However, this may not be a perfect conclusion because the marks are actually given early in life, and considering the mean age of the subjects, those who might have contracted infections through such means should have died especially of HIV. In a related development, educational status appeared to be a risk factor for both single and dual infections. Obviously, infection was highest among those with no formal education for HIV (46.4%), HBV (42.9%) and HIV/HBV (10.7%). Education has been acknowledged to be of advantage in various facets of life. It helps in making informed decision and also sourcing for useful information regarding health status on possible ways of avoiding infectious agents [23]. This report is consistent with reports of Okoh and Omuemu, and Hussain *et al.* which asserted that educational status has a statistically significant association with on HIV and HBV positivity [4,16].

## Conclusion

The 1.5%, 12.0% and 17.0% prevalence of HIV/HBV, HBV and HIV among TB patients is a cause for alarm and it is suggestive to more careful screening for these viral agents in TB patients. Although, some risk factors identified in this study, such as gender, history of STI and educational status can be said to have contributed to infections in the area. Coinfection of these viruses increases the risk of hepatotoxicity particularly during treatment of TB. Therefore, adopting strategies such as integrating HIV testing, target screening, counselling and referral services into the existing system for HIV/ HBV/TB prevention and/or treatment services is recommended in the study area.

## Limitations

HBV DNA by Polymerase Chain Reaction (PCR) was not done due to availability of the technology. This may have increased the prevalence of HBV in our study as it would allow early diagnosis of these viral agents before HBsAg were detectable in serum. Limited availability of funds prevented viral loads studies as well as measurement of other viral serological markers among the patients.

## Ethical Approval

In line with the Helsinki Declaration, clearance for this study was obtained from the Health Research Ethics Committee of Nasarawa State Ministry of Health.

## References

1. Tahziba H, Kulshreshtha KK, Yadav VS, Kiran K. HIV and VHB coinfections among patients with active tuberculosis disease attending a Primary Health Care Centre in a Rural Area of North India. *Egyptian Journal of Chest Diseases and Tuberculosis*. 2016;65(1):227-232
2. Sama LF, Djinou OIN, Wam EC, Bamou R, Ali IM, et al. Seroprevalence of Hepatitis B and C virus and High risk of Hepatotoxicity among TB/HIV positive and HIV negative population in Western Cameroon. *Global Journal of Infectious Diseases and Clinical Research*. 2017;3(1):001-008.
3. World Health Organization. *Global Hepatitis Report 2017*. Geneva
4. Hussain T, Kulshreshtha KK, Yadav VS, Katoch K. Human Immunodeficiency virus and Hepatitis B virus coinfections among tuberculosis patients attending a Model Rural Health Research Unit in Ghatampur, North India. *Indian J Med Microbiol*. 2015;33(4):496-502.
5. Nail AM, Nazar EA, Mohammed OE. Seroprevalence of hepatitis B and C viruses among tuberculosis patients. *Sudan Journal of Medical Sciences*. 2013;8(1):17-22
6. World Health Organization Media Center/HIV/AIDS (2014) June 3, 2015.
7. World Health Organization. *Global Tuberculosis Report 2015*. Geneva
8. Abdallah TM, Idriss MI, Ahmed AM, Ali AA, Saeed OK. Seroprevalence of hepatitis B and hepatitis C viruses among Tuberculosis patients in Kassala, Eastern Sudan. *Global Journal of Infectious Diseases of Clinical Research*. 2015;1:001-003

9. Khalid H Idris, Bahaeldin K Elamin. Seroprevalence of hepatitis b (HbsAg) and hepatitis C (anti-VHC) viruses among Sudanese patients with HIV/TB coinfection. *International Journal of Information Research and Review*. 2015;2(6):765-768
10. Blal CA, Passos SR, Horn C, Georg I, Bonecini-Almeida, et al. High Prevalence of hepatitis B virus infection among Tuberculosis patients with and without HIV in Rio de Janeiro, Brazil. *European Journal of Clinical Microbiology Infectious Disease*. 2005;24(1):41-43
11. Bushnell G, Stennis NL, Drobniak AM, Proops DC, Ahuja SD, et al. Characteristics and Tuberculosis treatment outcomes in TB patients with viral hepatitis, New York City, 2000-2010. *Epidemiology Infection*. 2015;143(9):1972-1981
12. Araujo-Mariz C, Lopes EP, Ximenes RA, Lacerda HR, Miranda-Filho DB, et al. Serologic markers of hepatitis B and C in patients with HIV/AIDS and active tuberculosis. *Journal of Medical Virology*. 2016;88(6):996-1002
13. Binbol NL, Marcus ND. Geography of Nasarawa State: A study of flora and fauna. 2010;pp.4-12
14. Naing NN. Determination of sample size. *Malaysian Journal of Medical Sciences*. 2003;10:84-86
15. Pennap G, Makpa S, Ogbu S. The prevalence of HIV/AIDS among Tuberculosis patients in a Tuberculosis/Leprosy Referral Centre in Alushi, Nasarawa State, Nigeria. *The Internet Journal of Epidemiology*. 2009;8(1):1-6
16. Okoh, A, Omuemu. Prevalence of HIV/AIDS and TB co-infection among patients in Benin city, Nigeria. *Geneva, Health Forum*. 2012;Paper ID: NOV
17. Woreta A, Hunegnaw A, Yimam Y, Genet A, Belay G. Assessment of triple infections of HIV, TB and hepatitis (B and C); and associated risk factors in selected district of North Wollo Zone, Ethiopia. *Journal of Viral Hepatitis*. Poster Session. 2014;P42
18. Aires RS, Matos MA, Lopes CL, Teles SA, Kozlowski AG, et al. Prevalence of hepatitis B virus infection among tuberculosis patients with or without HIV in Goiania City, Brazil. *Journal of Clinical Virology*. 2012;54(4):327-331
19. Salami TA, Babatope IO, Ademiyi GM, Samuel SO, Echekwube PO. Hepatitis B and HIV coinfection- Experience in a rural/urban health center in Nigeria. *Journal of Microbiology and Biotechnology Research*. 2012;2(6):841-844
20. Okeke TC, Anyaehie BU. HIV coinfection with hepatotropic viruses and mycobacterial tuberculosis. *Journal of AIDS Clinical Research*. 2013;4:1-8
21. Nooredinwand HA, Connell DW, Asgheddi M, Abdullah M, O Donghne M, et al. Viral hepatitis prevalence in patients with active and latent tuberculosis. *World Journal of Gastroenterology*. 2015;21(9):8920-8926
22. Merza MA, Haji SM, Alsharafani AM, Mohammed SU. 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):313-317
23. Oti VB, Usman BA, Pennap GR, Eno-Ibanga CK. Seroprevalence of Herpes Simplex Virus type 2 (HSV-2) among pregnant women accessing antenatal care in a tertiary healthcare facility in Central, Nigeria. *Asian Journal of Research in Medicine and Pharmaceutical Sciences*. 2017;1(4):1-6