

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

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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 ≤ 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].

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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
Gender							
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)	
Age (Years)							
< 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)	
History of Blood Transfusion							
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)	
History of STI							
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)	
Scarification Mark							
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)	
Educational status							
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.

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