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SEROPREVALENCE OF HEPATITIS B (HBS AG) AND HEPATITIS C (ANTI-HCV) VIRUSES AMONG SUDANESE PATIENTS WITH HIV/TB CO-INFECTION

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Abstract

Background

Tuberculosis (TB) and hepatitis viruses infection are the two common co-infections in patients infected with human immunodeficiency virus (HIV). Hepatitis B and Hepatitis C infections are common in Sudan where TB is endemic and HIV is prevalent. Since anti-retroviral drugs and some of the anti-TB drugs are hepatotoxic, in HIV/TB co-infected patients, the management may be difficult, thus early detection of these viruses will influence the outcome of the disease. The objective of this study to determine the Seroprevalence of Hepatitis B (HBs Ag) and Hepatitis C (Anti-HCV) viruses among Sudanese patients with HIV/TB co-infection

Methodology

From November 2014 to March 2015, a cross-sectional hospital based study was conducted among HIV/TB co-infected patients attended at a reference centers in Khartoum State, Sudan. The participants were tested for serological markers of HBC infection and HBV antibodies.

Sera samples were collected from patients and tested for HBsAg and anti-HCV bodies using Enzyme-Linked ImmunoSorbent Assay (ELISA).

Results

Out of 53 HIV/TB co-infected patients recruited in the study, HBsAg was detected in 9.4% while anti-HCV antibodies was detected in 1.9% of patients using ELISA and there was no patient had both HBV and HCV co-infection.

Conclusion

HIV/TB infected patients have high probability of getting HBV and or HCV infection due to enhanced immunodeficiency by HIV. Shared route of transmission also plays significant role and is of epidemiological importance in our country. Thus routine screening of HIV/TB infected patients for concurrent infection with HBV and HCV should be made mandatory because co-infection with these hepatitis viruses will increase the risk of cirrhosis, liver deficiency and mortalities in comparison to when a person is infected with HIV and this may minimize the risk of hepatotoxicity occurring during treatment of such patient.

Keywords: HIV/TB Co-Infection, Hepatitis B (HBs Ag), Hepatitis C (Anti-HCV).

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INTRODUCTION

Tuberculosis and viral hepatitis are two of the commonest co-infections, seen among HIV-positive patients worldwide. Infection with hepatitis B (HBV) and hepatitis C viruses (HCV) are especially common and more significant in HIV patients. Hepatitis B virus (HBV) and hepatitis C Virus (HCV) are among the primary causes of morbidity and mortality in HIV patients. Coinfection of HBV and HCV with HIV has been associated with reduced survival, increased risk of progression to liver disease, and increased risk of hepatotoxicity, associated with antiretroviral therapy (Highleyman, 2010, Rosenthal *et al.*, 2003).

HBV and HCV share common pathways of transmission with HIV, including injection drug use, sexual intercourse, and mother-to-child transmission (Gonzalez and Keeffe, 2011). In the past few years, several guidelines and reviews have highlighted this problem and have provided recommendations about how to best manage patients coinfecting with HIV and HBV, HCV (Gonzalez and Keeffe, 2011, Ranjbar *et al.*, 2011). Human immunodeficiency virus (HIV) and Tuberculosis (TB) infection pose particular diagnostic and therapeutic importance and exert massive pressure on health care systems in African and Asian countries with large population of co-infected individuals; constitute the main problem of infectious disease in resource restricted countries (WHO, 2010, UNAIDS, 2010).

In 2013 of the estimated 9 million people who developed TB an estimated 1.1 million (13%) were HIV positive. There were also in 2013 360,000 deaths from HIV associated TB equivalent to 25% of all TB deaths, and around 25% of the estimated 1.5 million deaths from HIV/AIDS (WHO, Global Tuberculosis Control 2014). The HIV globally has dramatic association on epidemiology of TB in which prevalence of active TB increase by more than one third among 36 million estimated patients infected with HIV (Godfrey-Faussett *et al.*, 2002). This dramatically increases due to fact that of higher probability of either primary progression or reactivation of latent TB in HIV infected patient (Jon, 2004). With 1.3 million TB deaths (including TB deaths in HIV-positive individuals) in 2012 (WHO., 2013), TB and the human immunodeficiency virus (HIV) are the top causes of death from a single infectious agent worldwide (Lozano, 2012, Ortblad *et al.*, 2013). In Sudan the prevalence of tuberculosis are 209 cases per 100,000 of population and 50,000 incident cases during 2009 (Organization., 2010). Also the estimated prevalence of HIV among adults is 1.5% which remains lower than that of Southern Sudan and other African neighbors and report from 2002 suggest that 4% of TB patient are co-infected with HIV (El-Sony *et al.*, 2002). HIV with HBV or HCV co-infection began as a leading cause of morbidity due to liver disease throughout the world in the last two decades (Rockstroh, 2006, Stabinski *et al.*, 2015, Carrat and Perronne, 2005). HBV and HCV are more prevalent among HIV patients due to sharing the same route of transmission (Alter, 2006). The co-infection with hepatitis viruses increase risk of liver related mortality and morbidity due to hepatotoxicity result from antiretroviral medication in patient on protease inhibitors or risk of fatty liver disease due to taking nucleoside/nucleotide reverse transcriptase inhibitors (Sulkowski *et al.*, 2000, Barbaro *et al.*, 1999, Clausen *et al.*, 2014). And also HIV accelerates the natural course of HBV and HCV infection and facilitates faster progression of liver disease to cirrhosis and hepatocellular carcinoma. Disease progression to cirrhosis in HIV positive patients is almost three-times faster as compared to HIV negative patients (Mocroft *et al.*, 2003, Vallet-Pichard and Pol, 2006).

On the other hand HCV and HBV infection complicate treatment of TB patient, in which the Hepatotoxicity is the major adverse effect of three of the first line anti-TB agents: isoniazid (INH), rifampin (RIF), and pyrazinamide (PZA) and the high risk of hepatotoxicity during anti-tuberculosis treatment reach up to five time more than TB patient without viral hepatitis (Steele *et al.*, 1991, Jeong *et al.*, 2015, Ramappa and Aithal, 2013). The risk of anti-TB hepatotoxicity increase to fourteen fold in HIV/HCV co-infected has been reported (Saukkonen *et al.*, 2006). Hepatitis B and Hepatitis C infections are common in Sudan where TB is endemic and HIV is prevalent. Since anti-retroviral drugs and some of the anti-TB drugs are hepatotoxic, in HIV/TB co-infected patients, the management may be difficult. This will be even worse if an HIV/TB patient is co-infected with HBV or HCV which will increase the rate of hepatotoxicity and complicate the management. Till now there is no data about seroprevalence of HBsAg or anti-HCV Abs among HIV/TB co-infected patients in Sudan.

Hence, this study will be carried out to high-light this point which may help in the management of the patients.

MATERIALS AND METHODS

This was Cross sectional- hospital based study conducted at Khartoum state in three HIV centers in the period from November 2014 to March 2015. 53 HIV positive patient (diagnose by ELISA and confirmed by a licensed western blot assay) co-infected with TB (by clinical diagnosis, Chest CT scan and positive AFB smear) were enrolled in this study. The demographic and clinical data were collected via questionnaires adopted for the study. Three ml of venous blood sample was collected from each patient; then serum was prepared and stored at -20 °C until analysis. Serum samples were tested for HBsAg and anti-HCV antibodies using enzyme-link immunosorbent assay (ELISA) (Fortress Diagnostics Limited, Unit 2C Antrim Technology Park, United Kingdom). The ELISA was performed as per manufacturer's instructions. The data was entered and analyzed using statistical Package for social sciences 16 (SPSS – 21). This study was approved by faculty of medical laboratory sciences, Al Neelain University, Khartoum, Sudan, and ethical clearance was obtained from ministry of health. Written consent was taken from selected subjects prior to questionnaire filling and blood sampling.

RESULTS

A total of 53 confirmed HIV/TB co-infected Sudanese patients were enrolled in this study. 20 (37.7%) were females and 33 (62.3%) were males; age range between 13 and 60 years. Sociodemographic characteristics of the study population are shown in Table 1. HBS Ag and anti-HCV antibodies were detected in 9.4% (5) and 1.9% (1) patients respectively and Co-infection of both hepatitis B and hepatitis C with HIV/TB was found to be 0%. The distribution of HBV and HCV co-infection in patients infected with HIV/TB is shown in Table 2. Four patients out of five infected with HBV the route of transmission of HIV was sexual intercourse and the rest with unknown route of transmission. The only one patient with HCV infection his route of transmission was sexual intercourse, the statistical analysis showed that there was in significant association between rout of transmission and HBV or HCV infection (P value:0.92 and 0.94 respectively).

The results of the present study showed that there was insignificant association between duration of the disease and HBV and HCV infection (P. Value: 0.63 and 0.9 respectively). The results list in Table No. 3 showed that three patients from the five patients positive for HBV were receiving antiretroviral treatment and the remaining two cases were free from that therapy and there was insignificant association between the antiretroviral therapy and HBV infection (P.value:0.37) whereas the single case positive for HCV was free from antiretroviral therapy with insignificant association also (P. value : 0.53). Univariate analysis of risk factors for HBV infection revealed that male gender and sexual transmission were associated with this infection. In a multivariate analysis, age ≥ 16 years and sexual transmission were independent risk factors associated with HBV infection (Table No. 1).

Table 1. Incident HIV/AIDS cases by selected characteristics

			HBS Ag	Anti HCV
Gender	MALE	33(62.2%)	5 (15.2%)	1 (3.0%)
	FEMALE	20(37.7%)	0 (0 %)	0 (0 %)
			P value : 0.08	P value :0.60
Age group	0-15 Years	1 (3.0%)	0	0
	16-30 Years	15 (28.3%)	3(20 %)	1(6.6%)
	31-45 Years	31 (58.4%)	2(6.4%)	0
	>45 Years	6 (11.3%)	0	0
			P value :0.90	P value : 1.00
HIV Transmission	Sexual	38(71.6%)	4 (10.5%)	
	Blood transfusion	3 (5.6 %)	0 (0.0%)	
	Vertical	1 (1.8 %)	0 (0.0%)	
	Unknown	11 (20.7%)	1 (9.0%)	
			P value: 0.92	P value : 0.94

Table 2. ELISA result status of study population (n= 53)

HBS Ag	Anti HCV Antibodies	ELISA Results
5 (9.4%)	1 (1.9%)	Positive
48 (90.6%)	52 (98.1%)	Negative

Table 3. antiretroviral and TB treatments among study group with Hepatitis infections

	NO	HBS Ag	Anti HCV
ART Taking treatment	23(43.3%)	3(13.0%)	0 (0.0%)
No ART Tasking treatment	30(56.6%)	2(6.6%)	1(3.3%)
		P value : 0.60	P value : 0.53
Anti TB Taking treatment	30(56.6%)	4(3.3%)	0(0.0%)
No Anti TB Taking treatment	23(43.3%)	1(4.3%)	1(4.3%)
		P value : 0.37	P value : 0.43

DISCUSSION

The present study represents- to the best of our knowledge-the first study in Sudan about the seroprevalence of hepatitis B and C virus among HIV/TB patients. Our study is the first to indicate that infection with HBV and HCV is a significant problem among patients with HIV/TB in Sudan. The co-infection of Hepatitis B or Hepatitis C virus with HIV/TB patients accelerates disease progression and may complicate the management of patients infected with HIV. Overall, the prevalence of hepatitis B, hepatitis C, or both, with HIV/TB Coinfection, is 11.3%. Among these, HBV/HIV is 9.4%, HCV/HIV is 1.9%. We did not assess prevalence of other hepatitis viruses in the HIV positive population, such as hepatitis A, hepatitis D, and hepatitis E. Different prevalence rates of hepatitis and HIV Coinfection have been reported by study by country, as well as by hepatitis subtype(Gupta and Singh, 2006, Rebbani *et al.*, 2013, Tremeau-Bravard *et al.*, 2012, Rao *et al.*, 2015). The prevalence of HBV is similar to the finding of 6.6% in Nigeria (Soriano *et al.*, 2002). However, the prevalence of HIV/HBV co-infection in this study is lower to the findings of 11.9% in Ibadan (Otegbayo *et al.*, 2008) and 11.5% in Abuja (Adewole *et al.*, 2009), both in Nigeria. The differences in prevalence in these studies could be attributed to differences in patient selection. In this study the seroprevalence of HCV among HIV/TB patients was 1.9% and this was similar to that study carried TB patients in Gezira area (2.2%) (Mudawi *et al.*, 2007) and Kassala State (1%) (Abdallah, 2015) and lower than that carried among tuberculosis patients (19.4%) reported in high epidemic country in which it was attributed to high risk factors such as intravenous drug abuse (Hajek, 2010).

The prevalence of HBV among general population was reported as 6.8 % and 8.2 % in central and eastern Sudan respectively (Abdallah, 2015, Hajek, 2010, Abdlah, 2011). In this study among HBV infected individuals, 38(71.6%) HIV/TB patients had history of sexual transmission, 3 (5.6 %) of blood transfusion, 1 (1.8 %) vertical and 11 (20.7%) of unknown causes. In case of HCV infected persons, 4 (10.5%) HIV/ TB infected individuals had history sexual transmission, 1 % with no history of injecting drug user and surgery. According to our knowledge a very limited data is available regarding co-infection of HIV/ TB and hepatitis at national and international history. In a study, Kuniholm *et al* reported that history of blood transfusion; injection of drug and prison were significant risk factors for HBV and HCV among Georgian TB patients (Kuniholm *et al.*, 2008). The spread of both HBV and HCV are mainly linked by poor knowledge, socioeconomic status, use of contaminated needles and syringes by quacks, barbers and drug users.

Conclusion

It is thus clear that apart from other infections like TB, HIV infected patients have high probability of getting HBV/HCV infection due to enhanced immunodeficiency by HIV. Shared route of transmission also plays significant role and is of epidemiological importance in our country. Thus routine screening of HIV/TB infected patients for concurrent infection with HBV and HCV should be made mandatory because co-infection with these hepatitis viruses will increase the risk of cirrhosis, liver deficiency and mortalities in comparison to when a person is infected with only one of these viruses (Mohammadi *et al.*, 2009).

Furthermore, those found to be negative should be immunized with HBV vaccine to improve the prognosis of their HIV status. There is also an urgent need to conduct detailed studies on the interplay of HIV/TB and hepatotropic viruses in the Sudan community with a plethora of multipronged approaches to investigate the real crisis of HIV/hepatotropic viral infection pattern at the earliest to efficiently control and manage the situation.

Disclosure of conflict of interest

We certify that there is no conflict of interest with any financial organization regarding the material discussed in the manuscript.

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