Seroprevalence of other antibodies (herpes, CMV, rubella, varicella, hepatitis B and C, syphilis, chlamydia, mumps, toxoplasmosis) in HIV-positive patients

G.O. Ajayi[1], S.A Omilabu[2], D. Alamu[2], Y. Balogun[2], S. Badaru[3]

[1]Department of Obstetrics and Gynaecology [2]Prenatal Diagnosis and Therapy Centre
[3]Virology Unit, Department of Microbiology, College of Medicine, University of Lagos, Idi-Araba, Surulere/Lagos (Nigeria)

Summary

We attempted to determine the seropositivity of HIV-positive patients to other antibodies (herpes, CMV, rubella, varicella, hepatitis B, hepatitis C, syphilis, chlamydia, mumps, toxoplasmosis). The study was carried out at the Prenatal Diagnosis and Therapy Centre of a Tertiary Hospital in Lagos, Nigeria. A total of 70 patients (50 females and 20 males) attending the centre between June 1997 and December 2005 who were screened and found to be HIV-seropositive were further screened for herpes simplex IgG/IgM, CMV IgG/IgM, rubella IgG/IgM, varicella IgG/IgM, mumps IgG/IgM, toxoplasmosis IgG/IgM, chlamydia IgG/IgM, hepatitis B and hepatitis C IgG/IgM using ELISA kits and syphilis (THPA) using the HAE method. Our study showed that a large number of HIV-positive patients are carriers of other antibodies and should be screened for them before therapy.

Key words: HIV; Co-infection; Antibodies; Seroprevalence; Prepregnancy class.

Introduction

Human immunodeficiency virus (HIV) infection appears to influence the natural history of infections with certain pathogens. Interactions between HIV and co-infections may alter the natural history and therapy response of the diseases [1].

There is a high degree of epidermiological similarity between hepatitis B/C, herpes simplex, cytomegalovirus, syphillis, chlamydia and HIV in regard to high-risk groups, route of transmission, and the presence of virus in the body fluids [2] which may differ from others like rubella, mumps, varicella zoster, and toxoplasmosis. Transmission of some of them like syphilis, hepatitis, cytomegalovvirus and rubella through blood transfusion and intravenous drug abuse is well documented [3-7].

Co-infections of HIV with other viruses like hepatitis B/C are known to result in higher viral load of the virus and greater organ damage, like in the liver [1].

Studies of association of hepatitis B (HBV), hepatitis C (HCV), cytomegalovirus (CMV), rubella, herpes simplex, syphilis, chlamydia, and mumps in HIV cases are rare in Nigeria. Therefore, in this study we looked at the prevalence of these pathogens in our HIV-positive patients.

Materials and Methods

This study was carried out in the Prenatal Diagnosis and Therapy Centre, College of Medicine, University of Lagos, Nigeria between June 1997 and December 2005. A total of 70 (50 females and 20 males) attendees of the centre who were screened and found to be HIV-seropositive were further screened for herpes simplex IgG/IgM (Dia-Products Diagnostic Milano/Italy), rubella IgG/ IgM (Dia-Products Diagnostic Milano/Italy), varicella IgG/IgM (Orgenics Ltd, Israel), mumps IgG/IgM (Orgenics Ltd, Israel), toxoplasmosis IgG/IgM (Dia-Products Diagnostic Milano/Italy), chlamydia trachomatis IgG/IgM (Savyon Diagnostic Ltd/Israel), hepatitis (HBsAg) and hepatitis C (HCV) IgG/IgM (BioRad/France and Orgenics Ltd, Israel), using ELISA kits and syphilis (TPHA) (New Market Laboratories Ltd) using the HAE method. Samples positive for HBsAg and/or anti HCV antibody by the joint test were retested for confirmation of results.

Revised manuscript accepted for publication November 6, 2008

Results

The age group ranging from 26-35 years formed the largest group (53.43%) (Table 1).

Tables 2a and b show the prevalence of antibody positivity to different pathogens. Forty-one (82%) out of 50 females were positive for herpes IgG out of which 28 (68.3%) were positive for IgM. Twenty out of 12 (93.3%) were positive for herpes IgG out of which seven (63.6%) were positive for IgM. Thirty-seven (94.9%) out of 39 females were positive for CMV IgG out of which 21 (56.8%) were positive for IgM. Twelve (93.9%) out 13 males were positive for CMV IgG out of which seven (58.3%) were positive for CMV IgM. Thirty (76.9%) out of 39 females were positive for rubella IgG out of which nine (26.5%) were positive for rubella IgM. Eleven (91.7%) out of 12 males were positive for rubella IgG out

Table 1. — *Age distribution of HIV-seropositive patients between 1997 and 2005.*

Age	1997	1998	1999	2000	2001	2002	2003	2004	2005	Total	%
≤ 20											
21-25				3		1	2		1	7	10.0
26-30				4		4	5	3	1	17	24.3
31-35	2		2	3	2	2	1	6	1	19	27.1
36-40				1		2		3		6	8.6
41-45				1	1			2		4	5.7
46-50								1		1	1.4
> 50				1		1				2	2.8
Unknown age	1		4	1	4	2	1	1		14	20.0
Total	3	0	6	14	7	12	9	16	3	70	100

Table 2a. — *Prevalence of antibody positivity to different pathogens in females (n = 50).*

		HSV		CMV		RUB.		MUMPS		TOXO.		CHL.		VAR.				
Type of pathogen	HIV	IgG	IgM	IgG	IgM	IgG	IgM	IgG	IgM	IgG	IgM	IgG	IgM	IgG	IgM	HepB	HepC	Total
Total screened	50	41	39	39	37	39	34	38	32	40	35	43	36	24	24	38	37	39
Positive			28	37	21	30	9	25	17	27	15	31	22	14	5			4
Negative			11	2	16	9	25	13	15	13	20	12	14	10	19	38	37	37
Percentage %		82%	63.3	94.9	56.8	76.9	26.5	65.8	53.1	67.5	42.9	72.1	61.1	58.3	20.8	0	0	10.3

HSV: herpes simplex virus; CMV: cytomegalovirus; RUB: rubella; Toxo: toxoplasmosis; CHL: chlamydia; VAR: variable.

Table 2b. — *Prevalence of antibody positivity to different pathogens in males (n = 20).*

		HSV		CMV		RUB.		MUMPS		TOXO.		CHL.		VAR.				
Type of pathogen	HIV	IgG	IgM	IgG	IgM	IgG	IgM	IgG	IgM	IgG	IgM	IgG	IgM	IgG	IgM	HepB	HepC	Total
Total screened	20	13	11	13	12	12	13	13	12	13	10	14	5	11	8	12	11	11
Positive		12	7	12	7	11	12	12	6	2	2	8	2	8	1	2	3	3
Negative		1	4	5	1	1	1	6	1	8	6	3	3	7	10	1	8	8
Percentage %		93.3	63.6	93.3	58.3	91.7	93.3	93.3	50	93.3	20	57.1	40	72.7	12.5	16.7	27.3	27.3

HSV: herpes simplex virus; CMV: cytomegalovirus; RUB: rubella; Toxo: toxoplasmosis; CHL: chlamydia; VAR: variable.

of which ten (93.9%) were positive for IgM. Fourteen (58.3%) out of 24 females were positive for varicella IgG out of which five (20.8%) were positive for varicella IgM. Eight (72.7%) out of 11 males were positive for varicella IgG and one (12.5%) was positive for varicella IgM. Twenty-five (65.8%) out of 38 females were positive for mumps IgG out of which 17 (53.1%) were positive for IgM. Twelve (93.3%) out of 13 males were positive for mumps IgG out of which six (50%) were positive for IgM. Twenty-seven (67.5%) out of 40 females were positive for toxoplasmosis IgG out of which 15 (42.9%) were positive for IgM. Twelve (93.3%) out of 13 females tested positive and two (50%) out of ten IgG-positive cases tested positive for IGM. Thirty-one (72.1%) out of 43 females tested positive for chlamydia IgG out of which 22 (61.1%) were positive for IgM. Eight (57.4%) out of 14 males were positive for chlamydia IgG, two (40%) out five IgG-positive tested positive for IgM. None (0%) of the 38 females tested positive for HBV and HCV. Two (16.7%) out of 12 males were positive for hepatitis and none were positive for HCV. Four (10.3%) out of 39 females were positive for syphilis, while three (27.3%) out of 11 males were positive for syphilis. The difference was highly significant showing increased incidence of association and co-infection by these pathogens. Thirty-seven of 50 (74%) of these female patients had multiple co-infections with 5/50 (10%) females having five different pathogens and 13/20 (65%) males having multiple co-infections with three of 20 (15%) males having five or six different pathogens. The prevalence of pathogen IgM antibodies were in the female herpes simplex type 2 IgM – 28/50 (56%), chlamydia – IgM 23/50 (46%), mumps IgM – 17/50 (34%), CMV IgM 14/50 (28%), rubella IgM – 9/50 (18%), varicella IgM – 4/50 (8%) and syphilis – 4/50 (8%). In the males, the prevalence of herpes simplex type 2 IgM was 11/20 (55%), CMV IgM – 7/20 (35%), syphilis and HCV each 3/20 (15%), toxoplasmosis IgM and hepatitis surface antigen each 2/20 (10%), chlamydia IgM – 2/20 (10%), and varicella zoster IgM – 1/20 (5%).

Discussion

HIV shares a common route of infection with HBV, HCV, and CMV, herpes simplex type II, syphillis and chlamydia [2, 5-8]. HIV, HBV, herpes simplex type II, syphillis and chlamydia are known to be sexually transmitted. CMV can also be sexually transmitted whereas others can not. However sexual transmission of HCV has been documented [9]. Nonetheless in this study none of the patients were HCV seropositive and only two were HBV positive. In cases of herpes simplex virus (HSV) 82% of the females and 93.3% of the males were IgG-positive but 63.3% of the females and 63.6% of the males were herpes simplex IgM-positive. The incidence of co-infection was equally high in both males and females for CMV, rubella, mumps, toxoplasmosis, chlamydia and varicella.

This confirmation has had a pronounced effect on the natural history of these infections. Although the effect of these viruses on HIV infection is still uncertain, HIV appears to have a marked influence on the natural history of these pathogens. Although most of these pathogens are not directly cytopathic to liver cells, hepatic necrosis is being mediated by Th1 lymphocyte-induced cytotoxic T lymphocytes (CTL). Therefore, any process which affects quantity and quality of CTL response will have a bearing on the outcome of liver damage, e.g. in HBV infections. Further, in HIV-HBV co-infections, there is an increase in persistence of HBV [10], increase in HBV viral load [11, 12], and increase in the incidence of HBV reactivation and re-infection [13]. However, despite an increase in HBV-DNA load, hepatic necrosis is lower and the activity and number of CTL are reduced by the presence of HIV [1]. Until recently, the effect of HIV on HCV infection has not been investigated; patients with HIV died long before their liver disease became problematic. With successful therapy of HIV, it is becoming clear that HCV may lead to an onset of advanced liver disease [8]. It is known that HCV disease is associated with the development and persistence of studying various specific responses by Th1 lymphocyte-induced cytotoxic T lym-

phocytes. The loss of these cells has been limited to the re-emergence of viremia [14].

Sexually transmitted infections (STIs) are markers of high-risk sexual behavior in an individual/spouse/sexual partner. Infections due to HSV are extremely common. While most infections are asymptomatic or mild, some can be transmitted to neonates and are associated with other STIs and cervical neoplasms in females [15]. IgM antibodies to HSV-2 are increased to four times the normal value two to four weeks after infection and the enzyme linked immunosorbent assay (ELISA) is a specific sensitive and simple test which confirms the infection by HSV. HSV-2 may contribute more to HIV infection because of its higher frequency than other STIs. Thus because of the recurrence of genital herpes, high prevalence of genital herpes in populations at risk for HIV infections and a large number of herpes-infected persons who continue their sexual activities despite being infectious, genital herpes is a risk factor for acquisition of HIV-1 infection [16].

HSV-2 infection is also significantly associated with syphilis. In our study, out of the four HIV-positive female patients who were TPHA positive, three were HSV 2 IgM sero-positive and one HSV IgG sero-positive, whereas the three HIV-positive males were all HVS IgG/IgM sero-positive. HSV-2 antibodies are a much more reliable notification of risky behavior than Treponema pallidum antibodies [17]. However, a large number of genital infections are also caused by HSV-1.

HSV is one of the TORCH organisms like CMV, toxoplasmosis, varicella and chlamydia infection in pregnancy accounts for half of the morbidity and mortality among neonates [18]. It may also lead to abortion/prematurity, intrauterine growth retardation and disseminated infection of neonates [19, 20]. HSV predisposes to other STIs as it causes mucosal erosions and may increase the concentration of HIV and other STIs in semen and vaginal fluids. Asymptomatic shedding can infect neonates and they themselves are at more risk of developing cervical cancer [21] and therefore it is important to screen them. Our result further shows that multiple pathogen co-infection is high in HIV-positive patients. It is thus clear that apart from other infections, HIV-infected individuals have a high probability of getting no infection with other pathogens with herpes simplex HIV disease progression and enhanced immunosupression has a direct bearing on the natural history and pathogens of these infectiosn. Sexual transfusion of TORCH pathogen appears to be significant and is of epidemiological importance in the light of heterosexual transfusion of HIV apart from blood transfusion in Nigeria. Monitoring HIV- infected patients for concurrent infection with torch pathogen is therefore necessary.

References

[1] Brendon M.: "Thyagarajan virus SP HIV and hepartotropic viruses interactions and treatment". *Indian J. Med. Microbiol.*, 1998, *16*, 4.

[2] Rustgi V.K., Hoofnagle J.H., Gerin J.L., Gelmann E.P., Reichert C.M., Cooper J.N., Macher A.M.: "Hepatitis B virus infection in the acquired immunodeficiency syndrome". *Ann. Intern. Med.*, 1984, *101*, 795.

[3] Alter M.J., Hadler S.C., Judson F.N., Mares A., Alexander W.J., Hu P.Y. *et al.*: "Risk factors for acute non-A non-B hepatitis in the United States and association with hepatitis C virus infection". *JAMA*, 1990, *264*, 2231.

[4] Matee M.I., Lyamuya E.F., Mbena E.C., Magessa P.M., Sufi J., Marwa G.J. *et al.*: "Prevalence of tranfusion-associated viral infections and syphilis among blood donors in Muhimbili Medical Centre, Dar es Salaam, Tanzania". *East Afr. Med. J.*, 1999, *76*, 1670.

[5] Matee M.I.N., Magesa P.M., Lyamuya E.F.: "Seroprevalence of HIV, hepatitis B and C viruses and syphilis infections among blood donors at the Muhimbili National Hospital in Dar Es Salaam, Tanzania". *BMC Public Health*, 2006, *6*, 21.

[6] Oronsaye F.E., Oronsaye J.I.: "Prevalence of HIV-positives and Hepatitis B surface antigen-positive among donors in the University of Benin Teaching Hospital". *Nigeria Trop. Doct.*, 2004, *34*, 159.

[7] Pultoo A., Meetoo G., Pyndiah M.N., Khittoo G.: "Seroprevalence of cytomegalovirus infection in mauuritrain volunteer blood donor". *Indian J. Med. Sci.*, 2001, *55*, 73.

[8] Cropley I., Main J.: "Hepatitis C virus infection: co-infection with HIV and HBV". *Baillieres Best Pract. Res. Clin. Gastroenterol.*, 2000, *14*, 265.

[9] Fainboim H., González J., Fassio E., Martinez A., Otegui L., Eposto M. *et al.*: "Prevalence of hepatitis viruses in an anti-human immunodeficiency virus positive population from Agentina. A multicentric study". *J. Viral Hepat.*, 1999, *6*, 53.

[10] Bosworth M.J., Cooper D.A., Donovan B.: "The influence of human immunodeficiency virus type 1 infection on the development of the hepatitis B virus carrier state". *J. Infect. Dis.*, 1991, *163*, 1138.

[11] Krogsgaard K., Lindhardt B.O., Nielson J.O., Andersson P., Kryger P., Aldershvile J. *et al.*: "The influence of HTLV-III infection on the natural history of hepatitis B infection in male homosexual HBsAg carriers". *Hepatology*, 1987, *7*, 37.

[12] Bodsworth N., Donovan B., Nightengale B.N.: "The effect of concurrent human immunodeficiency virur infection on chronic hepatitis B. A study of 150 homosexual men". *J. Infect. Dis.*, 1989, *160*, 577.

[13] Levy P., Marcellin P., Martinot-Peignoux M., Degott C., Nataf J., Benhamou J.P.: "Clinical course of spontaneous reactivation of hepatitis B virus infection in patient with chronic hepatitis B". *Hepatology*, 1990, *12*, 570.

[14] Lauer G.M., Walker B.D.: "Hepatitis C virus infection". *N. Engl. J. Med.*, 2001, *345*, 41.

[15] Venkitaraman A.R., Seigneurin J.M., Lenoir G.M., John T.J.: "Infections due to the human herpes viruses in southern India". *A Seroepidemiological Survey. Int. J. Epidem.*, 1986, *15*, 561.

[16] Hook E.W. 3rd, Cannon R.O., Nahmias A.J., Lee F.F., Campbell C.H. Jr., Glasser D., Quinn T.C.: "Herpes simplex virus infection as a role factor human immunodeficiency virus infection in heterosexual". *J. Infect. Dis.*, 1992, *165*, 251.

[17] Bogaerts J., Ahmed J., Akhter N., Begum N., Rahman M., Nahar S. *et al.*: "Sexually transmitted infection among married women in Dhaka Bangladesh: unespected high prevalence of herpes simplex type 2 infection". *Sex Transm. Inf.*, 2001, *77*, 114.

[18] Turbadkar D., Mathur M., Rele M.: "Seroprevalence of torch infection in bad obstetric history". *Indian J. Med. Micribiol.*, 2003, *21*, 108.

[19] Mookherjee N., Gogate A.: "Incidence of HSV infection in bad obstetrics history (BOH) cases". *Indian J. Med. Microbiol.*, 1994, *12*, 60.

[20] Kumar A., Gupta N., Sharma J.B.: "Genital herpes. A reappraisal". *Obstetrics Gynaecol. Today*, 2006, *5*, 426.

[21] Shukla A., Das K. *et al.*: "Herpes simplex virus type 2 in carcinoma of cervix: A controlled serological study". *J. Obstet. Gynaecol. India*, 1984, *34*, 315.

Address reprint requests to:
G.O. AJAYI, M.D.
Department of Obstetrics and Gynecology
College of Medicine/University of Lagos
P.M.B. 12003 Idi-Araba Surulere, Lagos (Nigeria)
e-mail: prenataldiagnosiscentre@hotmail.com