ORIGINAL RESEARCH ARTICLE

The Prevalence of Dual Human Immunodeficiency Virus/Hepatitis C Virus (HIV/HCV) Infection in Asymptomatic Pregnant Women in Benin City, Nigeria

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ABSTRACT

Concerted efforts have been made to combat HIV infection in Nigerian. By contrast, much less attention has been paid to hepatitis C viral (HCV) infection. These viruses have similar immuno-epidemiology. The objective of this study was to determine the prevalence of HCV/HIV dual infection among 269 antenatal attendees at the University of Benin Teaching Hospital in southern Nigeria. The study was prospective and cross-sectional and consisted of the analysis of the sera of the participants for anti-HCV and HIV antibodies using ELISA. The result showed that 1.86% samples were HCV antibodies positive while 8.30% were seropositive for HIV-1 antibodies. There were no cases of dual infections. The HIV positive women and their babies had antiretroviral therapy. We conclude that dual HCV/HIV infection in pregnancy in Nigeria may be uncommon but suggest multicenter studies to determine the national prevalence while initiating strategies for their prevention *(Afr J Reprod Health 2009; 13[2]:97-108).*

RÉSUMÉ

Prévalence du double virus immuno-déficitaire humain/l'infection hépatite virale C (VIH/HVC) chez les femmes enceintes asymptomatiques. On a fait des efforts concertés pour combattre l'infection du VIH au Nigéria. Par contre, on consacré beaucoup moins d'attention à l'hépatite virale C (HVC). Ces virus ont la même immuno-épidémiologie. Cette étude avait comme objectif de déterminer la prévalence de la double infection du HVC/VIH chez 269 femmes qui se présentaient pour des services prénatals à l'University of Benin Teaching Hospital au sud du Nigéria. Il s'agissait d'une étude prospective et transversale et consistait en analyses des sérums des participants pour l'anti HVC et les anti-corps du VIH à l'aide d'ELISA. Le résultat a montré que 1,86% des échantillons des anticorps du HVC ont été positifs alors que 8,3% ont été séropositifs à l'égard des anticorps du VIH-1. Il n'y avait pas de cas de double infection. Les femmes séropositives et leurs bébés ont subi une thérapie antirétrovirale. Nous concluons que la double infection du HVC/VIH dans la grossesse au Nigéria peut ne pas être commun, mais nous suggérons des études multicentrales pour déterminer la prévalence nationale tout en initiant des stratégies pour leur prévention *(Afr J Reprod Health 2009; 13[2]:97-108).*

KEYWORDS: Pregnancy; HCV; HIV; Coinfection; PMTCT; Nigeria

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Introduction

The human immunodeficiency Virus type-1 (HIV-1) and Hepatitis C virus (HCV) are two viruses with similar characteristics having in common diversities in numerous subtypes and capacities for mutation. Huge resources and technical inputs for preventive vaccines have remained largely futile in spite of decades of research in this area.[1-9]

The world marked with sober reflection December 1, 2006 as the 25th year since HIV/Acquired Immune deficiency syndrome (HIV/AIDS) was first recognized in 1981. More than 25 million people have suffered mortality and the lives of over 40 million (infected) people was by the end of 2005[10] hanging on the balance of possible future antiretroviral therapy (ART) to which many currently have no access. This was in spite of concerted efforts to curb the pandemic. In the recorded history of mankind, HIV/AIDS has remained the most destructive epidemic and Sub-Saharan Africa (SSA) has remained the hardest hit.[10] This sub-region only is home to 25.8 million (over 64% or about 2/3) of the globally infected population with women accounting for 77% of all the infections.[10,11] The implication of the feminization of this infection is increased vertical transmission (VT)that accounts for over 95% of under-5 pediatric HIV infections with associated high mortality.[10, 12] The VT of HIV is often worsened by maternal hepatitis B and C viral infections that damage or cross the placenta during the antenatal or intrapartum periods to infect the fetus or postnatally through breastfeeding.[13-15]

The incidence of obstetric HIV infection in this center in 1997/98 was reported to be 2.4% while Onakewhor et al reported 2.2% for hepatitis B in pregnancy.[16, 17] No co-infection was found in samples analyzed for HIV/HBV co-infections in this unit.[18] The increasing use of highly active antiretroviral therapy (HAART) for HIV has made HCV co-infection relevant and a prominent contributor to morbidity and mortality among HIV/AIDS sufferers. Liver disease progression and damage is more rapid in HIV seropositive individuals with CD4 count <200 cells/mL for whom the risk of end-stage liver disease is greatest.[19-23]

This small, enveloped, single-stranded RNA virus belongs to the Flaviviridae family and spreads primarily by contact with blood and blood products.[20] The incidence of HCV among blood donors in this center is 3%[24] while 0.5% has been reported for a neighboring Rivers State in Nigeria.[25] Generally, fewer women than men donate blood more so among women of reproductive age in our environment[24, 25] thus leading to paucity of information on HCV-seroprevalence among them. In the United States of America, 30% of HIV positive patients are reportedly co-infected with HCV with highest rates among intravenous drug users (IDUs).[20] This virus is ten times more infectious from needle stick injury than HIV[19] making this virus a nightmare for healthcare workers.

While up to 75% of cases of HCV acute infections may be asymptomatic, about 80% of acute HCV infected symptomatic individuals may become chronic carriers.[14] Liver transplantation is the only available treatment option for decompensated HCV-related cirrhosis and some early stages of hepatocellular carcinoma.[14] Fortunately, however, variable rates of spontaneous HCV clearance, that is less likely among HIV positive people with lower CD4 cell counts, have been reported.[26-34] Upon infection, HCV RNA is usually detectable within 2 weeks[35] while HCV antibodies usually develop 6 weeks to 6 months after infection.[19,36]

The symptoms of HCV infection are non-specific and include fever, fatigue, anorexia, nausea, and vomiting making a larger proportion of acute infections often undiagnosed.[37] These malaria-like symptoms in Nigeria make for suspicion of the later rather than the former except when the patient failed to respond to conventional anti-malarial treatment. Of clinical importance is the fact that in both cases, accurate diagnosis is important, as it offers an opportunity for improving treatment outcomes.

Mothers co-infected with HIV have increased risk of both sexual and VT of HCV during pregnancy or delivery than women with either mono-infection. Also, their babies have lower birth weights.[15,38, 39] The non-use of ART, poor virological control or high viral load during pregnancy, and vaginal delivery are other risk factors for increased VT especially for HIV.[3,40- 47]

Unlike HIV, and except there is high viral load[45] and HIV co-infection,[46,47] available evidence suggests that breast feeding is not a risk factor for VT of HCV. There is also no known intervention capable of interrupting VT of HCV.[3,38, 41] Fortunately, however, except for the variable reports of VT of 2.7% to 11.4% reported in some Italian studies,[45-48] various studies in the United States, Europe, Japan, Morocco, Egypt and Cameroon failed to detect VT of HCV.[6,48-57] The favorable outcomes have been attributed to partial endogenous production of interferon (alpha, beta, and gamma), in the placental environment.[6, 50-52]

In the United States, Federal guidelines recommend that all HIV positive persons be tested for HCV.[53-57] Though in principle we have provisions for screening for co-infections, apart from the traditional screening in pregnancy for syphilis and HIV, high cost of and lack of reagents and equipments have limited screening for other infections in Nigeria to only suspected cases. Consequently, there is dearth of information on the prevalence of HCV and HIV/HCV coinfection in the obstetric population. Screening for these infections opens a window of opportunity to provide patients education and behavioral modification through counseling. This was what informed the need for this study. This was the first such study in the Nigerian pregnant population.

The objective of this study was to determine the prevalence HIV and HCV dual infection in a cohort of booked

obstetric women attending for antenatal care services at a tertiary hospital in Benin City, Nigeria.

Methods

The setting and study design

This was a prospective cross-sectional study carried out at the Department of Obstetric and Gynecology and the Federal Government HIV laboratory in the Department of Pathology of the University of Benin Teaching Hospital (UBTH), Benin City, Nigeria.

Subjects

These were pregnant women booked for antenatal care and delivery in this hospital from June 1, 2005 December 31, 2005. Women who previously had blood transfusion, diagnosed HIV, hepatitis B or C positive were considered high risk women and were excluded from the study. Consecutive antenatal attendees were counseled and women that gave consent were enlisted for the study.

Procedure

Ten milliliter of blood was taken from the ante-cubital vein and sent to the laboratory in EDTA anticoagulant containing specimen bottles for serological test. Sera obtained after centrifugation were analyzed in the HIV laboratory for HIV and Hepatitis C antibodies. Specimen containers were coded to ensure confidentiality.

The HIV test: The screening for HIV-1 antibodies was done using the Capillus HIV-1/HIV-2 (Trinity Biotech PLC, Jamestown, New York, USA), and then the Genie1I HIV-1/HIV-2(Bio-Rad, Marnes La Coquette-France) test kits, while Determine HIV-1/2 (Abbott Laboratories, Illinois, USA) was used as a 'tie-breaker' for sero-discordant results according to the WHO double /triple Algorithm.[58]

The HCV test: The test was performed using a second generation Enzyme Linked immunosorbent assay (ELISA DOC INF 5125002) test kit (Human Diagnostica, Germany), according to the manufacturers instructions. All repeatedly reactive samples were then confirmed for anti-HCV antibodies using a commercial third generation ELISA (MONOLISA anti-HCV plus version 2, Biorad, Marnes-La-Coquette, France) in accordance with the manufacturers instructions.

Each seropositive woman had liver enzyme assay (liver function test) done. All the women were post test counseled. The HIV seropositive women had highly active antiretroviral therapy (HAART) consisting of three drugs in the antenatal period, during labor and in the puerperium. They also had counseling on appropriate infant feeding options and drug adherence. Both seropositive and seronegative women continued with their antenatal care and delivery in this unit. Upon delivery the babies had Nevirapine syrup and were enlist into the Pediatric ARV program for follow-up management

while the women were referred to and linked with the adult antiretroviral (ARV) Program for follow up management and the hospital's Social Group.

Data analysis

The data were analyzed using the GraphPad Instat™ software version 2.05a, using Students T tests for continuous variables. The data are presented as proportions of HIV-1 and HCV–antibody seropositive and seronegative cases.

Results

A total of 275 women were counseled, 4 of which met the exclusion criteria and two dropped out of the study for personal reasons before vene-puncture. All 6 women were excluded from the study leaving 269 women for HIV- and HCV-antibodies screening. The mean age of the women was 30.3 ± 4.8 years and a mean parity of 2. While 23(8.30%) samples were confirmed seropositive for HIV-1 antibodies, 5(1.86%) were seropositive for HCV antibodies. There were no cases of dual HCV/ HIV-1 infection.

Discussion

Hepatitis C viral infection is not rare in the Nigerian obstetric population while HIV seroprevalence was on the increase. The seroprevalence of anti-HCV and HIV-1 antibodies in our antenatal women was 1.86% and 8.30% respectively.

The HCV prevalence in this study is higher than the 0.5% reported for blood donors in a neighboring Rivers State in the same geopolitical zone,[25] the 0.8% and 1% respectively for HIV-1 sero-negative and positive women in neighboring West African country, Cote d'Ivoire[5] and the 0.69% reported for Japanese parturients.[59] The HCV prevalence of 1.86% in this study was comparable with the 1.8% reported for Cameroonian women,[2] the 1.86% for the general American population[15] and the 1.2% to 1.7% reported for Italian pregnant women.[60,61] It is within the 0.1% to 4.5% reported for pregnant Canadian population.[40] The prevalence is lower than the 3.0% reported for blood donors in this center,[24] the 5% in Tanzanian obstetric population,[62] and the 13.0% for Egyptian women.[63] Our HCV prevalence is also lower than the 40% prevalence reported for HCV/HIV and the 8% HBsAg/HIV co-infected European patients.[64] The prevalence of HCV was marginally lower when compared with the 2.2% of anti- HBV antibodies reported for pregnant women in this center some four years previously.[17]

The anti-HIV-1 antibodies seroprevalence rate of 8.3% in this study is almost four times the 2.4% reported for this centre in 1997/98.[16] The HIV prevalence is greater than the highest Nigerian national seroprevalence rate of 5.8% in 2001 and the current rate of 4.4%.[65] This higher rate may not be unconnected with the reference nature of the hospital even though women with known risk factors were excluded from the study. In a similar analysis of the data from the

initial 11 pilot sites(all tertiary health facilities) in Nigeria, in September 2004 after about 27 months PMTCT services, 19,895 women were tested and HIV seroprevalence rate of 8.5% was reported.[66] Similar rates have been reported in the same West African sub-region; prevalence of 6.7% and 9.0% HIV-seropositivity respectively in women of neighboring countries of Cameroon[2] and Cote d'Ivoire.[6] In Tanzanian, the prevalence rate of 6.7% has also been reported. [62]

Co-infection with HIV/HCV is associated not only with increased progression to liver cirrhosis but also increased mother-to child transmission of both HIV and HCV. Studies from Tanzania revealed a HIV/HCV co–infection rate of 1.51% [62] while 1.2% has been reported for women in Abidjan, Cote d'Ivoire.[6] A much higher HIV/HCV coinfected rates of 30% and 63.4%, which were strongly related to illicit drug use, were reported respectively for American[20] and Spanish[38] women. In Cameroon, Njouom et al[2] reported a HIV/ HCV coinfection rate of 6.7%. We found no case of dual HIV/HCV infection in this study. The lack of co-infection may be a chance finding due possibly to the small sample size even though none of the women studied admitted to intravenous drug use. Hepatitis C virus co-infection with HIV-1 is reported to increase the risk of both sexual and maternal–fetal transmission of HCV.[15] While no appropriate inter-vention to prevent mother-to–child transmission for HCV is known,[3, 38, 41] the HIV positive women in this study had highly active anti-retroviral therapy (HAART) to interrupt the transmission and reduce the risk of fetal and infant infection, even though we had no facilities to monitor the viral load for both infections. We did not, however, determine the vertical transmission rate for babies of HCV seropositive mothers in this study as we lacked facilities for HCV RNA studies at the time of the study and this was considered one limitation of the study. After delivery, the infants and mothers were referred to the pediatricians and physicians for follow-up.

In the absence of facilities for viral DNA and RNA studies, determination of the vertical transmission rate for babies of the HIV positive mothers require longer follow-up of about 15 months[67] and this was being collated and analyzed as part of the general population of women that benefited from the Prevention of Mother-to-Child trans-mission (PMTCT) Program of HIV in this center. A report from neighboring country of Cameroon[2] however showed no vertical transmission among the babies born to HCV positive mothers. Similar findings from various part of the world have been reported by other wokers.[45,49,61,63,68] Apart from coinfec-tion, the vertical transmission rate of HCV is however said to be influenced by other risk factors among which is chronic liver disease[6, 14, 25] It has been reported that up to 75% of cases of acute HCV infection are asymptomatic even as 80% of acute HCV infected symptomatic individuals become chronic carriers.[69] None of the women that tested positive

for either HCV or HIV had symptoms or clinical signs of hepatitis. There was also no case of HIV/HCV co-infection in this study.

The measurement of alanine aminotransferase (ALT) level is an important non-specific laboratory test in HCV-infected persons. It is also a means of identifying hepatic disease and the best test for monitoring HCV infection and the efficacy of therapy in the intervals between molecular testing.[15,70] The results of the liver enzymes assayed were essentially normal in the HCV and HIV antibody seropositive subjects. Hepatitis C virus carriers with normal and persistently normal ALT levels have also been reported by Persico et al.[71] Also, less than 10% of HCV infected persons are said to have elevated transaminases.[14]

We found no adverse effects of seropositivity of HCV or HIV on the course of the pregnancies in the women studied. Floreani et al[60] also reported non-increase in adverse pregnancy outcome in HCV infected pregnant women in their study.

The treatment for HCV is expensive and complex requiring rigorous monitoring which could not be provided for these women during pregnancy. Apart from cost and availability of anti-HCV drugs, safety concerns in pregnancy precluded treatment at the time of the study especially when the women were asymptomatic. Information on treatment modality of HCV in pregnancy in the literature was scarce. No data were available to determine whether interferon therapy or other antiviral agents can reduce the risk of vertical transmission of HCV infection.[34] Moreover, most of the currently available anti-HCV drugs (interferon alfa or combination of interferon alfa with ribavirin and or amantadine)[72,73] are contra-indicated in pregnancy. Consequently, apart from the antiretroviral prophylaxis provided the HIV-infected women to prevent vertical transmission, those with HCV infection were not subjected to treatment.

Unlike HIV infection, breastfeeding has not been shown to increase the rate of transmission of hepatitis C[15,74] even though available data do not exclude the possibility of a low transmission rate for HCV.[40] The women were therefore counseled along these lines and about the non-likelihood of their offspring posing danger to other sibs or friends in daycare or other public places. Hepatitis C virus is not contagious and such children have been reported to pose no risk for their surroundings.[40]

Conclusion

This study has provided the evidence that HCV was not an uncommon infection in the Nigerian pregnant population and the fourfold increase in prevalence of obstetric HIV a major concern for neonatal infection in our country.

While we acknowledge the small sample size of our study population, dual HIV/HCV infection may not be very common. We suggest a more elaborate study, especially multi-centre studies, to determine the national prevalence of HCV and HCV/HIV co-infection to enable formulation of guidelines for

management and establishment of preventive programs. Facilities should be upgraded in tertiary health centers for easy diagnosis, viral typing, viral load and neonatal or infant diagnosis of these viruses to prevent a loss to follow-up which is often a common problem in our country. We call on policy makers and health care providers to put in place preventive and control measures including public enlightenments at national or regional levels about HCV and HIV infections. Hepatitis C viral-induced liver disease, often worsened by HIV coinfection, remains the major indication for liver transplant for which our present levels of economy and health infrastructures can least support. With no vaccines or cure in sight for the two infections, it will be a calamity to be complacent about the existence of these infections in the Nigerian population.

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