

Viral hepatitis B and C in HIV-infected patients in Saudi Arabia

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BACKGROUND AND OBJECTIVES: Hepatitis B and C are among the leading causes of death in human immunodeficiency virus (HIV)-infected patients. Prevalence data on viral hepatitis B and C in HIV-infected people in the region of Middle East and North Africa are scarce. We report the prevalence of viral hepatitis B and C in HIV-infected patients in Saudi Arabia.

DESIGN AND SETTINGS: Data on all HIV patients who attended HIV Program at King Faisal Specialist Hospital and Research Centre, Riyadh, Saudi Arabia, were kept longitudinally. For the purpose of this report, patients enrolled in the Program between January 1985 and December 2010 were included.

METHODS: Data on all HIV patients who received HIV care at age 18 and older between January 1985 and December 2010 were collected. Data were collected from patients' charts at our medical records department and electronically from the electronic health records and HIV database. We excluded patients who were deceased prior to completing work-up, lost follow-up, or acquired HIV perinatally.

RESULTS: Among 341 HIV-infected patients, hepatitis C infection was found in 41 (12%) patients. The commonest risk factor for hepatitis C virus and HIV acquisition was blood/blood product transfusion in 24 (60%) patients, of these 21 (88%) were hemophiliacs, followed by heterosexual transmission in 9 (22%) patients. The commonest genotype was genotype 1 observed in 18 patients (44%) followed by genotype 4 in 6 (15%) patients. Hepatitis B surface antigen was found in 11 (3%) patients. The commonest risk factor for hepatitis B virus and HIV acquisition was heterosexual transmission in 8 (73%) patients, followed by blood/blood product transfusion in 2 (18%) patients.

CONCLUSION: The prevalence of hepatitis C virus and hepatitis B virus infections are, respectively, 10 and 20 times higher among HIV-infected patients than in the general population.

Hepatitis B virus (HBV), hepatitis C virus (HCV), and human immunodeficiency virus (HIV) type 1 are among the top 10 leading causes of infectious disease deaths worldwide. HBV and HCV infections are common among HIV-infected individuals. The 3 viruses share similar modes of transmission. Both hepatitis viruses represent significant public health concerns in the HIV population.¹

According to the Joint United Nations Program on HIV/acquired immune deficiency syndrome (AIDS) (UNAIDS), about 34 million people are infected with HIV worldwide. An estimated 0.8% of adults aged 15 to 49 years worldwide are living with HIV, and the majority of them live in Asia and Africa.² The AIDS in Saudi Arabia (SA) was diagnosed and reported from Riyadh

in 1984.³ Epidemiological data on HIV infection in Saudi Arabia come mostly from point prevalence surveys, mandatory screening, facility-based surveillance, and surveys of high risk groups.⁴ There is paucity of general population HIV prevalence data within Saudi Arabia and the Eastern Mediterranean region. The estimate of UNAIDS of 2011 puts the general prevalence rate of less than 0.02%. For the period 1984 through 2009, a total of 15 157 cases with HIV infection were reported from Saudi Arabia: 4003 (26%) cases among Saudi citizens and 11 194 (74%) cases among expatriates.^{5,6}

Worldwide, HBV is the leading cause of chronic liver disease and a leading cause of death, accounting for up to half of all cases of cirrhosis and hepatocel-

lular carcinoma. An estimated 400 million people are infected with HBV with the majority of cases occurring in regions of Asia and Africa where the virus is endemic.⁷ Cross-community data released in 2007 revealed prevalence rates of HBV around 0.22% among adults in Saudi Arabia. The average reported prevalence was 0.15% with wide variations (ranging from 0.03% to 0.72%.) occurring between regions.^{8,9} The prevalence of HCV assessed in Saudi blood donors indicates HCV infection rates of 0.4% to 1.1%.^{8,10} A summary report compiled by the World Health Organization mentions 437 292 official reports of HCV infections among persons living in Saudi Arabia, giving an estimated prevalence of about 1.8%.¹¹

Co-infection of HBV and/or HCV with HIV is characterized by more rapid progression of liver disease including accelerated fibrosis, cirrhosis, and hepatocellular carcinoma.⁷ Approximately 10% of the HIV-infected population globally has concurrent chronic hepatitis B, with co-infection more common in areas of high prevalence for both viruses. In countries where the viruses are highly endemic, the rate can be as high as 25%.¹² In areas where HBV is less endemic (North America, Europe, and Australia), HBV and HIV are most often acquired during adolescence or adulthood through sexual transmission or injection drug use. The prevalence of HIV-HBV co-infection in these regions is generally less than 10% in the HIV-infected population.¹² However, up to half of injection drug users infected with HIV are co-infected with HBV. The majority of HBV infections in settings where the virus is highly endemic occurs through perinatal transmission (predominant in East and Southeast Asia) or in young children, transmitted through close household contact or through medical or traditional scarification procedures (predominant in Africa).⁷ The risk of perinatal transmission is lower in Africa than in Asia, a disparity that could be due to a lower prevalence of hepatitis B e antigen (HBeAg) and other differences in the pathogenic characteristics of circulating HBV genotypes.⁷ Among HIV-positive persons studied from Western Europe and the USA, the overall chronic HBV infection has been found in 6% to 14%, including 4% to 6% of HIV-positive heterosexuals, 9% to 17% of HIV-positive men who have sex with men, and 7% to 10% of injection drug users.¹³

HCV infect about 30% of the HIV-positive individuals in the USA and Europe.⁴ The majority of liver-related deaths in HIV-positive patients occur in people with chronic hepatitis C virus infection.¹⁴ A meta-analysis by Chen et al showed that HCV-HIV co-infection was more frequent than HBV-HIV co-infection, indi-

cating that patients with HIV seemed to have a higher risk of HCV infection.¹⁶ This outcome might be due to sex, age, ethnicity, occupation, marital status, and injection drug use.¹⁵ A recent meta-analysis showed that the overall mortality risk ratio for HIV-HCV co-infected patients compared with HIV mono-infected patients is increased by 35%.¹⁶

Co-infections of HIV and HBV and/or HCV represent a major global public health threat and raise several challenging issues for the treating clinician. Because each virus affects the other's natural history and response to therapy, HIV-HBV/HCV co-infection requires dedicated research. No previously published studies indicating the prevalence of viral hepatitis in HIV-infected patients are available in Saudi Arabia. We therefore, executed this epidemiological study to estimate the prevalence of viral hepatitis B and C in HIV patients.

METHODS

Data on all HIV patients who attended HIV Program at King Faisal Specialist Hospital and Research Centre, Riyadh, Saudi Arabia, were kept longitudinally. For the purpose of this report, patients enrolled in the Program between January 1985 and December 2010 were included. Data were collected from patients' charts at our medical records department, electronically from the electronic health records, and from the HIV database. We excluded patients who were deceased prior to completing workup, lost follow-up, or acquired HIV perinatally. An HIV-infected patient was confirmed using AxSYM® HIV1/2 gO MEIA (Abbott Laboratories, Abbott Park, IL, USA). Positive serum samples were confirmed using Western Blot or CHIRON® RIBA® HIV-1/HIV-2 SIA (Chiron Corp, Emeryville, CA, USA). For the purpose of this study, HBV was defined as present in patients who were positive for hepatitis B surface antigen or HBeAg or who had detectable HBV DNA during the study period. HCV infection was defined as present in patients who were seropositive for HCV antibody and had test results positive for HCV RNA.

Data were statistically analyzed using the software package SAS version 9.3 (Statistical Analysis System, SAS Institute Inc., Cary, NC, USA). Descriptive statistics for the continuous variables were reported as mean (standard deviation) and categorical variables were summarized as frequencies and percentages. All continuous values were compared by using independent *t* test, whereas categorical variables were compared by Chi-square test and Fisher exact test. The level of statistical significance was set at $P < .05$. The project was

approved by the Institutional Review Board (RAC # 2111 042). As the study was observational and no patient identifiers were used, a consent form was waived.

RESULTS

A total of 472 patients with HIV infection at King Faisal Specialist Hospital and Research Centre were included in the study. Those excluded comprise 131 patients because either they died before completing all viral hepatitis studies (32 patients), or had their care transferred, or were no-show after initial diagnosis (80 patients), or acquired HIV perinatally (19 patients). The remaining 341 patients represented the cohort for this report. Their baseline characteristics are shown in **Table 1**.

Hepatitis C infection was found in 41 (12%) patients. The commonest risk factor for hepatitis C virus and HIV acquisition was blood/blood product transfusion in 29 (71%) patients, of those, 21 (88%) were hemophiliacs, followed by heterosexual transmission in 9 (22%) patients. The commonest genotype was genotype 1 observed in 18 (44%) patients followed by genotype 4 in 6 (15%) patients. HCV treatment was given to 14 (35%) patients, of whom only 5 (36%) sustained virological response, whereas 7 (50%) patients failed treatment. HIV viral load RNA was undetectable in 15 (36.5%) patients. CD4 count was >200 in 10 (24.3%) patients. Liver biopsy was performed in 10 (24.3%) patients. Eight out of 10 patients had stage 1 and 2 liver disease. Normal liver function was noted in 29 (70.7%) patients. Out of 41 HCV-HIV patients, 7 (17%) patients died, and cirrhosis was the main cause of death.

Hepatitis B surface antigen was found in 11 (3%)

patients. The commonest risk factor for hepatitis B virus and HIV acquisition was heterosexual transmission in 8 (73%) patients, followed by blood/blood product transfusion in 2 (18%) patients. Only 2 (18%) patients had HBcAb; the rest 9 (82%) had no HBcAb. Seven of hepatitis B virus patients (70%) had undetectable HIV viral load and 8 (80%) had CD4 count >350. Out of 330 patients without hepatitis B surface antigen, 109 (33%) had immunity, whereas others remained non-immune. Alanine aminotransferase elevation was noted in 32 (16%) hepatitis C patients and 5 (2.5%) hepatitis B surface antigen patients.

DISCUSSION

Our study involves a representative number of HIV-infected patients in Saudi Arabia. The prevalence rates of hepatitis B surface antigen and hepatitis C infection among Saudi HIV-infected patients are not known. We demonstrated that hepatitis C virus infection is 10 times higher among HIV-infected patients than in the general population. The most common risk for acquisition of hepatitis C virus was blood/blood product transfusion. The prevalence of HCV among our HIV patients may be higher than the prevalence among the total number of HIV-infected patients in Saudi Arabia. This is related to the composition of our HIV population, as we were the facility where majority of hemophiliacs received care after HIV infection. This initial high rate of HCV among HIV hemophiliacs was also noted in other countries.¹⁷ Our HCV rate among HIV patients is not as high as in developed countries because we have a smaller proportion of our HIV patients who acquired HIV as intravenous drug abusers. Because

Table 1. Basic data on all patients in the cohort and groups based on type of virus infection.^a

Criteria	All patients n=341 (%)	No viral hepatitis n=290 (85%)	Hepatitis C virus n=41 (12%) ^b	Hepatitis B virus N=11 (3%) ^b
Median age, y (range)	43 (16-83)	43 (16-77)	43.5 (28-83)	47 (32-71)
Median CD4 + T lymphocytes (range)	531 (5-1550)	542 (5-1394)	430 (6-1550)	366 (7-1222)
Median HIV viral load (range)	Undetectable (0-1 521 775)	Undetectable (0-1 521 775)	Undetectable (0-133 596)	Undetectable (0-67 399)
Risk for HIV infection				
Heterosexual	234 (69)	217 (75)	9 (22)	8 (73)
Blood and blood products	68 (20)	38 (13)	29 (71)	2 (18)
Homosexual and bisexual	12 (3.5)	12 (4)	0	0
Intravenous drug abuse	2 (0.6)	1 (0.3)	1 (2.4)	0
Organ transplantation	2 (0.6)	1 (0.3)	1 (2.4)	0
Unknown	23 (6.5)	21 (6.9)	1 (2.4)	1 (9)

^aAll significance testing between the two groups revealed no difference.

^bOne patient was infected with both HBV and HCV

HIV: Human immunodeficiency virus, HBV: hepatitis B virus.

HCV is not transmitted as effectively as HIV through the sexual route, HCV remains low among our HIV population in whom more than 50% acquired HIV through the sexual route.¹⁸ The predominant HCV genotype in Saudi Arabia has been^{4,19} but in our study only 15% had genotype 4 and 44% had genotype 1. This is the predominant genotype in developed countries,²⁰ which points to the fact that majority of our HIV/HCV co-infected patients received blood and blood products that used to be imported prior to HIV era.

The response to therapy is also notably lower among our patients. One-third of patients had a sustained virologic response (SVR) to hepatitis C virus treatment in comparison to almost 90% SVR in other populations.²¹ HCV-related liver cirrhosis was a leading cause of death in almost 30% of patients with HIV infection. Mortality among our HIV patients co-infected with HCV was because of HCV and liver failure.

Although the rates of hepatitis B surface antigen positivity are lower than the rates of HCV infection in our HIV cohort, these rates are still several times higher than the rates of the general population. If compared with the younger population, HBV infection is 20 times higher in HIV-infected patients. The national hepatitis B vaccination program has significantly re-

duced the rates in the young population. Almost 20% of patients with hepatitis B infection had a low CD4 count (<200) and a high viral load. Our reported data (3%) of hepatitis B infection and HIV is less than what is reported internationally (6%-14%). This is again related to different risk factors of acquisition of both viruses in our report compared to international data,¹³ referral bias, and regional diversity as mentioned by Chen et al.¹⁵ Our study also points to the low rates of vaccination for HBV in our HIV-infected patients. This again was noted elsewhere, as patients who started the vaccination did not take the 3 doses that they were supposed to take.¹³

The limitations of our study include limited number of patients from overall population, referral bias being a tertiary care center. As data are scarce not only from Saudi Arabia but from the whole region, our data on prevalence of HCV/HBV and HIV co-infection indicate rates that are lower than other countries where injection drug use remains high among HIV patients. The importance of viral hepatitis therapy in HIV-infected patients mandates HIV programs in the region to adopt a screening and prevention program in people living with HIV and adjusting antiretroviral therapy according to viral hepatitis status.

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