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Original Research Article

Low hepatitis D co-infection among hepatitis B virus surface antigen-positive blood donors in Kenya

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ABSTRACT

Background: Hepatitis delta virus (HDV) is a highly pathogenic virus, and causes rapid disease progression from fulminant hepatitis (FH) to development of hepatocellular carcinoma (HCC) in patients co-infected with hepatitis B virus (HBV). However, its exact global burden of HBV-HDV co-infections remains largely obscure, particularly in sub-Saharan Africa. The objective of this study was to determine the prevalence of anti-hepatitis delta virus (anti-HDV) in hepatitis B virus surface antigen (HBsAg)-positive blood donors from Kenya.
Methods: A total of 239 HBsAg-positive serum samples, obtained from healthy Kenyan blood donors from June 2014 to November 2017 were analyzed in this cross-sectional study. ELISA was done using the International Immunodiagnostics HDV Ab EIA kit, according to the instructions of the manufacturer, for anti-HDV immunoglobulin G (IgG) determination.
Results: Of the 239 HBsAg-positive blood donors, 187 (78.24%) were male, and 52 (21.76%) were female. The average age of the study participants was 24.11 years. Serological analysis revealed that 3/239 (1.26%) study participants were HDV seropositive.
Conclusions: Our data suggest that HDV infection is rare among blood donors in Kenya, with anti-HDV positivity rates being relatively lower compared to other countries. Nonetheless, ongoing surveillance is essential to track any potential changes in prevalence over time.

Keywords: Blood donors, Hepatitis B virus co-infection, Hepatitis D antibodies, Hepatitis D virus

INTRODUCTION

Hepatitis D virus (HDV), the causative agent of hepatitis delta, is a satellite virus that uses the hepatitis B virus (HBV) envelope for survival. HDV is a negative stranded RNA virus of 1.7 kilobases in size, and the only representative of the Deltaviridae family.[1,2]

Parenteral exposure to blood of infected individuals (needle-stick injuries, injection drug use, and transfusions) is the most efficient way of HDV transmission, particularly in HBsAg-positive individuals.[1,2] HDV appears only as a co-infection in patients harboring the HBV.[2,3] This means that HDV and HBV either simultaneously infect an individual, or HDV

infects the individual at the early stage after HBV infection. The essential diagnostic marker of this pattern is positive HBV surface antigen (HBsAg), a high titer of anti-hepatitis B core (HBc) immunoglobulin M (IgM) antibodies and anti-HDV antibodies.[4,5] Simultaneous acquisition of both viruses is often self-limiting in adults, and rarely leads to chronic HDV infection.[6,7] On the other hand, super-infection occurs when HDV infects the individual who has already established HBV infection or is a chronic HBV carrier. Anti-HBc IgM antibodies are absent in this pattern.[4]

In comparison to HBV infection alone, HBV-HDV co-infection is associated with increased progression to cirrhosis, hepatocellular carcinoma, end-stage liver disease, and death.[8-11] Moreover, hepatitis treatment regimens, including nucleoside and nucleotides, which normally decreases HBV viral loads do not impact HDV, while pegylated interferon alpha shows poor efficacy, with relapse common.[12,13] Additionally, HDV may lead to misclassification of HBV status.[14]

Globally, viral hepatitis causes approximately 1.34 million deaths annually, with 66% of the deaths attributed to HBV infection.[15] However, the fraction of this HBV-associated mortality that is linked to HDV confection remains uncertain, but is likely to be substantial given that approximately 48 to 60 million cases worldwide are co-infected.[4,15] There are also uncertainties about HDV epidemic patterns and its contribution to the development of cirrhosis and hepatocellular carcinoma (HCC) among HBsAg-positive people. Therefore, estimates of HDV prevalence including among general populations or specific population groups, is critical to guide clinical care, policy formulation and inform effective public health interventions and development of new medicines.[16] The extremely high burden associated with HDV-HBV co-infection, including severe disease, mortality, and attendant healthcare costs reinforce the need to improve and increase HDV screening and entry into care and treatment.[17] Also with the advent of new therapies for HDV, understanding the national epidemiology and prevalence of HDV is necessary to properly target and fund effective interventions.[18,19]

Kenya remains a sub-endemic area for HBV infection with about 1-5% prevalence of HBsAg carriers, although rates among specific high-risk populations (HIV co-infected, people who inject drugs (PWID) and jaundiced patients seeking medical care) are much higher.[20-23] Despite this situation, little is known about the exact HDV prevalence in Kenya patients.[24] We therefore, aimed to estimate the HBV-HDV co-infection among blood donors from Kenya.

For example, information on HDV prevalence in Kenya is lacking, although one study described anti-HDV positivity rates, where a low prevalence in most parts was observed, except northern Kenya, which recorded 31% among HBsAg-positive asymptomatic patients.[24]

Against this background, this study determined the sero-prevalence of HDV among blood donors from Kenya.

METHODS

Study settings

Blood samples were obtained from regional blood transfusion centres in Eldoret, Kisumu, Nakuru, Kisii (western Kenya region), Embu and Machakos (Eastern Kenya region), Garissa, Lodwar (Nothern Kenya), Mombasa and Voi (Coastal region) Nairobi and Nyeri (Central Kenya region). These regional blood transfusion banks collect blood from volunteer donors who are identified through regular blood donation campaigns.

Study design

This was a cross-sectional study in which anonymized blood samples were obtained from regional blood banks from June 2014 to November 2017.

Sample size determination

The minimum sample size was calculated using Fisher et al, formula, with an estimated overall HBV prevalence of 8% in Kenya and a 5% margin of error.

$$n = \frac{Z^2 P(1-P)}{E^2}$$

Where n represents the required sample size,

Z is the Z-value corresponding to the desired confidence level (1.96 for a 95% confidence level),

P denotes the estimated proportion expressed as a decimal (0.08), and E indicates the margin of error (0.05).

This gave a minimum sample size of 113, however a total of 239 HBsAg-positive blood donors were recruited to enhance the validity of the study.

Inclusion criteria

All apparently healthy blood donors, at the NBTS sites, aged between 18 and 60 years, with hemoglobin level of not less than 12.5 gm/dl and a pulse of between 50 and 100 beats per minute with no irregularities were included in this study. In addition, only those participants willing give consent and to give a blood sample for both serological and molecular analysis were included.

Exclusion criteria

Participants aged <18 and >60 years, with hemoglobin level less than 12.5 gm/dl, a pulse of <50 and >100 beats per minute and/or with irregularities and those not-consenting were excluded from the study.

Data collection tool for socio-demographics

A standardized questionnaire was used to record demographic data of the study population. The data collected included age and gender. This data was entered into a password-protected excel spread sheet without any identifiers to maintain the confidentiality of the participants.

Blood sample collection

Five (5 ml) of peripheral venous blood was collected from all the study subjects under aseptic condition using sterile disposable syringe. The samples were then transported to the laboratory as soon as possible.

Screening for HBV and HDV

To screen for HBV and HDV, sera were separated from whole blood at room temperature and stored at -20°C in screw-capped vials. Hepatitis B surface antigen (HBsAg) was detected using the Murex HBsAg version 3 kit, a qualitative enzyme-linked immunosorbent assay (ELISA) specifically designed for HBsAg detection. A total of 239 de-identified positive samples were transported from the regional NBTS to the Kenya Medical Research Institute (KEMRI) in Nairobi, where they were stored at -80°C. Subsequently, the samples were sent to the National Microbiology Laboratory (NML) of the Public Health Agency of Canada for HDV screening. HDV IgG antibodies were identified using HDV IgG testing kits (Wantai BioPharm, Beijing, China). The ELISA procedures followed the manufacturer's guidelines, with samples showing an OD/COV ratio >1.5 considered seropositive for anti-HDV antibodies 25.

RESULTS

Demographics and regional distribution of HBsAg-positive study participants

The study enrolled 239 HBsAg-positive blood donors, with the majority being male (187, 78.24%) and 52 (21.76%) females, and a mean age of 24.11 years. Serological testing for HDV revealed that 3 out of 239 samples (1.25%) were positive for HDV. Regional distribution of the HBsAg-positive samples indicated that 42.26% were from Western Kenya, 23.01% from central, 20.92% from eastern, 8.37% from northern, and 5.43% from the coastal region (Table 1).

Sero-prevalence of HDV among HBsAg-positive asymptomatic blood donors

Screening for HDV IgG antibodies using an indirect anti-HDAg ELISA identified that only 3 (1.26%) out of 239 HBsAg-positive asymptomatic blood donors were seropositive for HDV. Among these three seropositive cases, two were from Eastern Kenya, and one was from Northern Kenya (Table 2). All three HBV-HDV co-infected donors were males, aged 23, 36, and 42 years. Two blood donors from eastern Kenya exhibited anti-HDV titers of 0.862 and 0.619, respectively, while the donor from northern Kenya had a titer of 1.876.

Table 1: Demographics and regional distribution of HBsAg-positive blood donors.

Characteristic	N (%)
Age years, mean (range)	24.11 (16-78)
Gender	
Male	187 (78.24)
Female	52 (21.76)
Regions	
Western Kenya	101 (42.26)
Central Kenya	55 (23.01)
Eastern Kenya	50 (20.92)
Northern Kenya	20 (8.37)
Coastal Kenya	13 (5.43)

Table 2: Seroprevalence of hepatitis delta virus infection among asymptomatic blood donors in Kenya, based on regions.

Regions	HBsAg-positive cases (N)	Anti-HDV-positive cases N (%)
Western Kenya	101	0 (0)
Central Kenya	55	0 (0)
Eastern Kenya	50	2 (4)
Northern Kenya	20	1 (5)
Coastal Kenya	13	0 (0)
Total	239	3 (1.26)

DISCUSSION

Despite the high burden of HDV infection among chronic carriers of HBsAg worldwide, little is known about the sero-prevalence of HDV antibodies in Kenya.[17,26,27] In this study, we demonstrate that the sero-prevalence of HDV is relatively low (1.26%) among HBsAg-positive asymptomatic blood donors from multiple towns across five regions in Kenya. This is consistent with a previous study, which reported low HDV prevalence in most parts of Kenya, except in northern Kenya, where HDV was reported among 31% of HBsAg-positive asymptomatic patients.[24] The result is also consistent with another previous study, which did not find HDV infection among patients presenting with jaundice in Kenyan liver clinics.[22]

An earlier Kenyan study suggested that delta infection seem to be mainly clustered around three specific ethnic groups, the Turkana, the Rendille and the Samburu people, living in Northern Kenya.[24] Our findings partially align with this observation, as one of the three HDV-positive cases identified in our study was from Lodwar, located in northern Kenya, predominantly inhabited by the Turkana ethnic group. However, it is noteworthy that

the other two HDV-positive cases were recorded in Machakos and Embu, situated in the Eastern region of Kenya. Machakos is primarily inhabited by the Kamba ethnic group, while Embu is home to the Embu and Mbeere communities. These findings suggest a more complex clustering pattern than previously understood.

Studies conducted in Bobo-Dioulasso, a city in Burkina Faso, reported prevalence of 3.38% among blood donors.[28] In a Mauritanian study, HDVAb was found in 20% of HBsAg positive blood donors.[29] Furthermore, results from a Sudan study showed the prevalence of HDV IgG and IgM antibodies to be 4.5% (8/178) and 2.8% (5/178), respectively, in the blood donors' group.[30] In Egypt, an HDV prevalence of 4.7% (8/170) was reported among HBsAg positive blood donors.[31] In comparison with our study, the HDV prevalence reported in these previous studies from other parts of the African continent is substantially high. The prevalence of HDV is partially dependent on the local prevalence of HBV. The predominant mode of HDV transmission in specific regions is also an important determinant of its local prevalence.[32] Therefore, the high prevalence of HDV among blood donors in North and West Africa countries compared to Kenya might reflect differences in the local HBV prevalence and/or different modes of HDV transmission.

The findings of the current study align with previous studies, which observed that the prevalence of HDV is not necessarily proportional to that of HBV in asymptomatic populations, a phenomenon that remains poorly understood.[33-35]

High and low anti-HDV antibodies titers in HBsAg chronic carriers are termed super-infection and co-infection, respectively.[5] Therefore, the two cases from Eastern Kenya, which had optical density (OD) values of less than 1, can partly be attributed to co-infection, while the one case from Northern Kenya was probably a case of super-infection, since anti-HDV antibody titer was high. Importantly, acute coinfection is followed by clearance of both viruses in approximately 95% of people, whereas HDV superinfection results in chronic HDV-HBV infection course in more than 90% of patients.[6]

Our study has some limitations. We used a convenient sample of HBV-infected individuals that we could access. Furthermore, we were unable to perform HDV RNA to confirm current hepatitis delta infection, and hence this study's positive case was probably based on HDV exposure and not necessarily current infection.

CONCLUSION

In conclusion, HBV-HDV coinfection rate is low among Kenyan blood donors. Generally, these findings are useful for future studies, since there is little information available about HDV infection in Kenya.

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Conflict of interest: None declared
Ethical approval: The study was approved by the Kenya Medical Research Institute's National Ethical Review Committee (Approval No. SSC-2209)

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