

Full Length Research Paper

Exploratory study of hepatitis D virus infection in HBsAg carriers in Abidjan, Côte D'ivoire in 2016

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In sub-Saharan Africa, the prevalence of co-infection with hepatitis D (HDV) and hepatitis B viruses (HBV) is poorly known. Chronic infection with HBV is currently treated by nucleoside analogs whereas interferon is used to inhibit HDV. Nevertheless, Hepatitis Delta is not routinely diagnosed in Côte d'Ivoire. This study aims to estimate the current prevalence of Hepatitis D infection among HBV-infected patients in Abidjan to determine whether it is necessary to implement its routine practice in the country. A cross-sectional analytical study was conducted from January 2016 to June 2016 at the Pasteur Institute of Côte d'Ivoire (Abidjan). Patients were screened for Hepatitis D Virus infection through detection of anti-HDV antibodies. A total of 87 patients between 17 and 70 years, including 12 anti-HIV positive, were recruited. A subset of 16 (18.4%) have acute hepatitis B while 71 (81.6%) were chronically infected with HBV. Concerning viral loads, 37 patients (42.5%) displayed values > 1.0 E+05 UI/mL; 22 (25.3%) range between 20 and 1.0 E+05 UI/mL and 28 (32.2%) were undetectable for HBV DNA. Out of these, 20 (22.9%) was positive for anti-HDV. Infection with HDV was not associated with any clinico-pathological variables such as age, gender, disease stage or even HBV DNA loads. The current seroprevalence of anti-Delta antibodies among HBV carriers is high in Abidjan. The study provides important information pledging for the introduction of systemic anti-Delta testing in HBV-infected patients in Côte d'Ivoire.

Key words: Hepatitis D virus, frequency, hepatitis B carriers, Abidjan-Côte d'Ivoire.

INTRODUCTION

Hepatitis D virus (HDV) is a defective virus which requires helper functions of hepatitis B virus (HBV) for its propagation. Similar to many RNA viruses, HDV exhibits high genetic heterogeneity. RNA recombination may reflect the template-switching activities of host RNA

polymerases (Lin et al., 2017). This can be a source of therapeutic failure. It is known that co-infection of HDV/HBV tends to accelerate the progression of infection towards cirrhosis and hepatocellular carcinoma. It is also estimated that up to 80% of all chronic patients

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with hepatitis D will develop cirrhosis (Amanullah et al., 2014; Wedemeyer, 2010). According to the World Health Organization (Wedemeyer, 2010), among 240 million chronic HBV carriers reported worldwide, approximately 15 to 20 million individuals are also infected with HDV. In Africa, approximately one fourth of the 65 million of HBsAg-positive individuals is suspected to be dually infected with HDV. In western Africa, prevalence of the HDV infection is estimated to range between 1.3 and 50% (Andernach et al., 2014). Nevertheless, the anti-HDV antibody prevalence in HBsAg carriers was reported only in few countries including Cameroun (17.6%), Gabon (15.6 to 70.6%) (Makuwa et al., 2009), Ghana (11.3 %) (Asmah et al., 2014).

The aim of this study was to determine the prevalence of HDV in HBsAg carriers in Abidjan.

METHODS

The study was conducted in HBsAg carriers coming for biological investigations to the Institute Pasteur within the framework of their follow-up from January 2016 to June 2016. All participants gave written informed consent. Ethical approval was obtained from the National Committee of Ethics and Research (NCER).

A case report form was used to collect the socio-demographic data (sex, age), clinical data (clinical information) and biological data (viral load and HBsAg) of the patients. Viral load, serological HIV and HBsAg were collected from the patient registry of the Pasteur Institute of Côte d'Ivoire.

Serum samples were collected for subsequent anti-HDV antibodies detection. The presence of anti-Delta IgG was qualitatively determined using a commercially available ELISA kit (ETI-AB-DELTA-2, DiaSorin, Italy) based on a competitive assay. All samples were tested and confirmed following the manufacturer's instructions.

Data analysis was performed using Epi-info version 3.5.4 software (July 30, 2012). Anti-HDV prevalence was described with a 95% confidence interval.

RESULTS

Epidemiological data

A total of 87 patients positive for HBsAg were included during a six months period (January to June 2016) of this study. The median age of the patients was 42 years (range 17-70). Gender proportions were balanced (51.7% males and 48.3% females). Acute hepatitis B (IgM anti-HBc-positive) was found in 16 patients (18.4%) while 81.6% were affected from a persistent infection.

Biological data

The viral load and HIV results were obtained from Institut Pasteur registry of patients. Concerning viral loads, 37 patients (42.5 %) displayed values above 1.0 E+05 UI/mL; 22 (25.3%) range between 20 and 1.0 E+05 UI/mL and 28 (32.2%) were undetectable for HBV DNA.

HBV DNA loads do not depend on age ($p = 0.22$); sex ($p = 0.27$) and clinical status ($p = 0.64$, Table 1).

Among the patients, 12 (13.8%) were anti-HIV positive. HIV status was not related to age ($p = 0.07$), sex ($p = 0.54$) nor the clinical status ($p = 0.61$) of the patients. It was detected that among these we noted the presence of anti-HDV Ab in 2 patients, thus the existence of triple infection. The latter have a chronic clinical stage, evidence of an acceleration of complications of associated liver diseases.

The samples were screened for IgG directed against HDV and 23.0% of them were positive. Anti-HDV was more prevalent in females than in males (31% vs 15%) but this difference is not statistically significant ($p = 0.14$). Regarding age of the patients, the prevalence of HDV antibody was higher between 31 and 45 years with 29.7%. However, the difference with anti-HDV negative subjects is not statistically significant ($p = 0.43$).

Prevalence of anti-HDV was different between patients with acute hepatitis B (12.5%) and chronic carriers (33.9%) of HBV albeit without reaching the level of significance ($p = 0.40$). In patients with HIV, 16.7% were carriers of anti-HDV antibodies but this figure was not statistically different in anti-HIV negative patients ($p = 0.72$). The distribution of anti-HDV according to the different variables is shown in Table 1.

DISCUSSION

The prevalence of HDV infection in this study was 23.0%, a figure considerably higher than the estimated worldwide prevalence of 5% (Rizzetto and Ciancio, 2012). This result is lower than the results of other studies conducted in Bangladesh (24.4%) and those conducted by Seetlani et al. (2009). It is higher than the results of Nwokediuko and Ijeoma (2009) and Opaleye et al. (2016) with 12.5% in Nigeria and similar to Darwish et al. (1992), with 23.53%. This high prevalence rate was found again; the HDV virus being an RNA virus, with its great capacity of heterogeneity during these replications, as shown by the works of Lin et al. (2017) in Taiwan could explain the therapeutic failures observed in patients on ARVs. But in a lot of countries such as Italy, this high frequency of HDV infection has declined where the prevalence has dropped from 22% in 1987 to 8.2% in 1997 (Gaeta et al., 2000). There are several factors such as improvement in socioeconomic status of the population, proper vaccination against HBV (Lin et al. 2015) in Taiwan, better guidance and education regarding safety measures and systematic screening of the general population (Gaeta et al. (2001). This is not the case of Côte d'Ivoire that is still in the exploratory phase concerning HDV.

The prevalence of HDV virus infection is higher in patients with chronic hepatitis B in Côte d'Ivoire while it is higher in patients with acute hepatitis B in Pakistan (Amanullah et al., 2014). This situation might be

Table 1. Relationship of HDV antibody with different variables.

Variable	Total patients (n = 87)	Anti-HDV Ab positive (n = 20)	Anti-HDV Ab negative (n = 67)	P-Value
Age (years)				
< 15	1	0	1	0.43
16-30	25	6	19	
31-45	37	11	26	
> 45	24	3	21	
Gender				
Female	42	13	29	0.14
Male	45	7	38	
Clinical stage				
Acute hepatitis	16	2	14	0.40
Patient on treatment	4	0	4	
Patient with liver disease	6	2	4	
Chronic hepatitis	61	16	45	
Viral load (UI/ML)				
Undetectable	28	6	22	0.71
20 to 100000	22	4	18	
>100000	37	10	27	
Anti-HIV g				
Positive	12	2	10	0.72
Negative	75	18	57	

explained by the high frequency of co-infection HDV/HBV in both populations. Patients between 30 and 40 years were most concerned about HDV infection in Nigeria but differ with the findings observed in Pakistan (Khan et al., 2011). This difference could be explained by the characteristics of the populations in different study particularly differences in proportions of the various categories of HBV and/or different study population profiles.

Analysis of the sex revealed that females (31.0%) were more often infected than males (15.6%). In a similar study, Roshandel et al. (2008) found female predominance (9.9%) in Northeast Iran. However, Nwokediuko in Nigeria found males were most infected than females by 12.8 and 7.1% respectively (Nwokediuko and Ijeoma, 2009). This situation could be explained by the different proportion of male and female in different study.

According to HIV status, this study has shown the existence of triple infection, a source of accelerated liver complications, such as the work of Lee et al. in Taiwan in 2013 (Lee et al., 2015). Also, future works require more investigations.

According to the viral load, the study showed that HDV antibodies were frequently presented in patients with high viral load (> 100000 UI/ML). This result is different from

the outcome of Iris and colleague, 2014 (Lorenc et al., 2017). The study also revealed the presence of HDV antibodies in 21.4% of HBV undetectable viral load. Hence, it is important to look for HDV even at a low viral load, as highlighted by the work of Beata Lorenc and colleagues in Poland in 2016 (Mumtaz et al., 2005).

Limitation of the study

The main limitation of this study is the small size of the population studied. This situation enabled the proposal of only reasonable speculations regarding age, sex, acute or chronic HBV infection and viral loads of the patients.

Conclusion

The prevalence of HDV antibodies among HBsAg-positive patients in this study was high with 23% despite the decreasing trend affecting HDV infection prevalence worldwide. This study is crucial both for public health, that is, to improve the future control of HDV and for clinical practice as it means that antiviral nucleosides are not relevant around one fourth of the HBsAg-positive patients in Côte d'Ivoire.

Future studies of HDV infection to determine genotypes are necessary to improve surveillance. A prospective study supported by Ivorian authorities should be urgently implemented to define more accurately the actual prevalence of HDV infection in HBV carriers throughout Côte d'Ivoire.

CONFLICT OF INTERESTS

The authors have not declared any conflict of interests.

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