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Serological Profile of Hepatitis D Virus (Hepatitis Delta) in the Hepato-Gastro-Enterology Department of Chu Gabriel Toure

Sanra Déborah Sanogo[1*], Kadiatou Doumbia[2], Hourouma Sow[2], Moussa Younoussou Dicko[2], Youssouf Oumarou[3], Abdoulaye Berthé[2], Sabine Drabo[1], Luc Sidibé[1], Makan Siré Tounkara[2], Abdoulaye Maiga[1], Ouatou Mallé[1], Ganda Soumaré[1], Anselme Konaté[2], Moussa Tièmoko Diarra[2]

[1]Hepato-Gastroenterology Department, CHU Point G, Bamako, Mali
[2]Hepato-Gastroenterology Department, CHU Gabriel Touré, Bamako, Mali
[3]Department of Internal Medicine, Centre Hospitalier Universitaire Communautaire de Bangui, Bangui, Central African Republic
Email: *deborahsanra@yahoo.fr

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Abstract

Infection with the defective hepatitis D virus (HDV) co-infects or superinfects a patient carrying hepatitis B virus (HBV). Delta virus infection is relatively common. The seriousness of infection with the hepatitis D virus (HDV), a virus defective in a patient carrying the hepatitis B virus (HBV), lies in its aggravating effect on the associated viral hepatitis B. Our aim was to study the serological profile of HDV in HBsAg-positive patients. As this study was fragmentary, we initiated this study with the aim of investigating the serological profile of HDV in HBsAg-positive patients. This was a descriptive and analytical cross-sectional study that ran from March 2019 to February 2020, a 12-month period. It focused on the population of patients seen and screened positive for HBsAg. We obtained a frequency of 10%. The mean age of our patients was 41.8 ± 13.09 years. The sex ratio was 4.5. VHD RNA was detected in 50% of patients. In 100% of cases, the presence of VHD RNA was associated with advanced fibrosis according to the APRI score, but without any statistically significant link. All HBV-infected patients should be screened for anti-HDV Ac. HDV infection leads to rapid progression to complications of liver disease.

Keywords

HBsAg, VHD RNA, Liver Disease

1. Introduction

The seriousness of infection with the hepatitis D virus (HDV), a virus defective

in a patient carrying the hepatitis B virus (HBV), lies in its aggravating effect on the associated viral hepatitis B. In fact, this co-infection brings forward the onset of serious complications such as cirrhosis and hepatocellular carcinoma by around ten years, compared with HBV mono-infection. Indeed, this co-infection is thought to advance the onset of serious complications such as cirrhosis and hepatocellular carcinoma by around 10 years, compared with HBV monoinfection. Another drawback of this infection is the difficulty of treating it. Infection with the delta virus is relatively frequent, with a worldwide prevalence estimated at 5% among HBV carriers, *i.e.* 15 to 20 million people worldwide [1]. Prevalence ranging from 29.2% to 59% has been reported in Italy. The prevalence was 40%, 20% and 17% respectively in Kuwait, Saudi Arabia and Türkiye. South America is also a hotbed of Delta virus infection. Africa is also affected by this infection, with prevalence of 18.2% in Kenya and 29% in Niger [2].

In a study of 300 blood donors in Mali, anti-HDV antibodies were found in 2.7%, only one of whom carried genotype I Delta virus RNA (ribonucleic acid) [3]. As this study was fragmentary, we initiated this study with the aim of investigating the serological profile of HDV in HBsAg-positive patients.

2. Material and Methods

This was a descriptive and analytical cross-sectional study that took place from March 2019 to February 2020, a 12-month period. It took place in the Hepato-Gastro-Enterology Department of the Gabriel Touré University Hospital in Bamako and focused on the population of patients seen and screened positive for HBsAg. Our sample size was estimated at N = 110. We included all HBsAg-positive patients over 18 years of age seen in consultation during the study period, who had undergone Ac-anti VHD testing, and patients who had given verbal consent. We excluded HBsAg-positive patients who did not receive an HDV antibody test, as well as non-consenting patients. We used quantitative RT-PCR for confirmation of viral hepatitis D, and these molecular analyses (RT-PCR) and ELISA were performed at the Mérieux laboratory. The parameters studied were: sex, age, prothrombin rate (PT), transaminases, blood count, protein electrophoresis, total bilirubinemia. Immunochromatographic (VIRUCHECK AgHBs® with 95.6% sensitivity and 98.2% specificity) and enzyme immunoassay (AgHbs MEDIFF®) techniques were used in our study for hepatitis B screening. Quantification of HBV viral load, anti-HDV Ac testing and RNA assay were performed using ELISA and RT-PCR techniques respectively. For the diagnosis of hepatitis D, we used the DiaSorin total anti-HDV antibody ELISA kit (IgM and IgG anti-HD), with a sensitivity of 99.99% and a specificity of 98.99%. Quantitative RT-PCR was used for confirmation of viral hepatitis D. HIV co-infection (HIV serology) and HIV antibody testing was also performed.

The APRI score was performed in all included patients to assess hepatic impact, which was significant for a value ≥ 0.66.

All patients were informed of the nature of the study and their verbal consents

were required for inclusion. We have obtained the approval of the FMOS Ethics Committee. Data were collected on a survey form and analyzed on Epi-Info version 7.2 software. The Fisher p-test was used to compare data, which was significant for a value ≤ 0.05.

3. Results

From March 2019 to February 2020 we collected 11 patients with Ac-anti VHD out of 110 HBsAg-positive patients, a frequency of 10%.

Men represented 81.8% of the sample, with a sex ratio of 4.5 (Figure 1). The mean age of our patients was 41.8 ± 13.09 years, with extremes of 20 and 67 years (Figure 2). HBsAg was detected during screening in 45.5% of cases.

Jaundice, hepatomegaly, splenomegaly and weight loss were found at identical frequencies of 18.2%.

We found thrombocytopenia in 36.4% of patients, Albuminemia < 35 g/l in 45.5% TP < 50% in 9.1% and Bilirubinemia > 35 mg/l in 4/5 of patients or 80%.

The presence of RNA was statistically associated with elevated bilirubinemia > 35 mg/l and decreased platelet count < 150 × 10^3 (Table 1). HDV RNA was detected in 50% of the 8 patients tested. HBV/HDV/HIV co-infection was found in one patient. In 100% of cases, the presence of VHD RNA was associated with advanced fibrosis according to the APRI score, but without any statistically significant link. A dysmorphic liver was found in 36.3% of patients. In 36.4% of

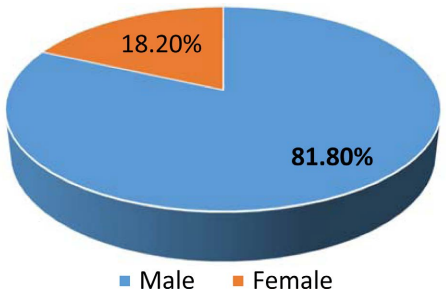

Figure 1. Sex.

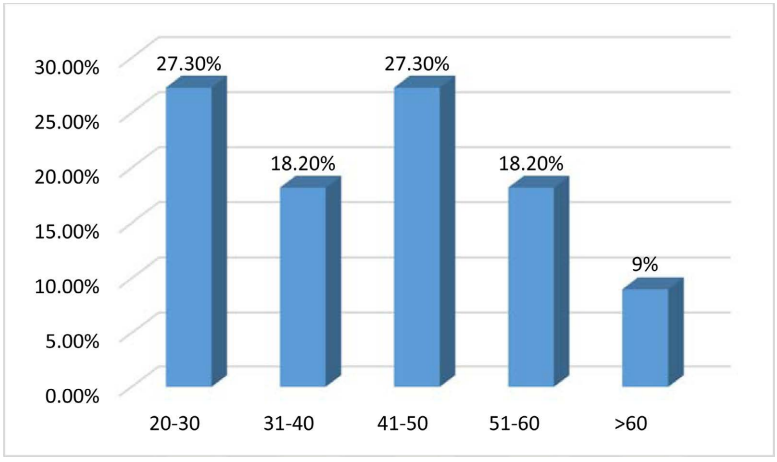

Figure 2. Age range (Years old).

Table 1. Biological profile and VHD RNA.

Biological signs	Patients	RNA (+)		RNA (−)		*p Fisher*
		Numbers	%	Numbers	%	
ASAT >30 UI/l (n = 4)		3	75	1	25	0.242
ALAT > 30 UI/l (n = 4)		2	50	3	75	0.500
Prothrombin level < 50% (n = 4)		1	25	0	0	0.500
Bilirubinemia (n = 4) > 35 mg/l		3	75	0	0	0.02
Albuminemia < 35 g/l (n = 4)		2	50	1	25	0.500
Platelets (n = 4)	<150 × 10^3	3	75	0	0	0.02
	>150 × 10^3	1	25	4	100	0.02
Hemoglobin (n = 4)	<12 g/dl	2	50	0	0	0.214
	>12 g/dl	2	50	4	100	0.214

cases, patients had at least one sign of endoscopic portal hypertension.

4. Comments and Discussion

The limitations of the study are essentially due to the limited resources of our patients. From March 2019 to February 2020, 110 patients with HBsAg were tested for HDV. This sample was limited by the cost of the investigations required. However, the size of the sample made it possible to assess the prevalence of HDV infection. This work demonstrated that the prevalence of HDV is not negligible, since we obtained a prevalence of 10%. This rate is significantly higher than those reported by Gordien in France (5.5%) [4], Komas *et al.* in Central Africa (4.03%) [5] and Sawadogo *et al.* (3.38%) in Burkina Faso [6]. These differences may be explained by the large sample size in our study compared with other studies, except the one carried out in Burkina Faso in a blood donor population.

In our study, Delta viral replication was found in 3.7% of patients who benefited from VHD RNA testing, higher than that reported by reported by Sawadogo *et al.* [6] in Burkina Faso, which was 2.27%. However, it was lower than those carried out in Cameroon at 34.2% by Emily *et al.* [7], Gish *et al.* in the USA at 8% [8].

Men were more represented in our study, the same finding was made by Mansour in Mauritania [9] and by Gordien*et al.* in France [4]. The mean age of our patients was 41.8 ± 13.09 years, comparable to those reported by Mansour in Mauritania [9] and by Kpossou in Benin [10] which was 36 years for both author. This could be explained by the youth of the African population. The discovery of HBsAg was incidental in the majority of cases (45.5%).

Jaundice, hepatomegaly, splenomegaly and weight loss were predominant in our study. Lunel-fabiani *et al.* in 2009 in Mauritania found that hepatomegaly, signs of hepatocellular insufficiency and portal hypertension were more frequent

in patients with HDV ($p < 0.001$) [11]. HBV/HDV and HIV co-infection was found in one patient in our study. Sawadogo *et al.* also found a single HBV/HDV and HIV co-infection [7].

In our study, Delta viral replication was found in 3.7% of patients tested for HDV RNA, higher than the 2.27% reported by Sawadogo *et al.* [6] in Burkina Faso. It is lower than those carried out in Cameroon at 34.2% by Emily *et al.* [7], and Gish *et al.* in the USA at 8% [8].

The presence of HDV infection was indicative of impaired hepatocellular function in our RNA-positive patients. In 75% of cases, RNA-positive patients had hepatic dysmorphia on ultrasound and endoscopic signs of portal hypertension. Advanced fibrosis according to APRI score is in 100% of these cases. The study by Safer *et al.*, carried out in Tunisia, found VHD positive in 61.5% of cirrhotic patients [12].

5. Conclusion

All HBV-infected patients should be screened for anti-HDV Ac. HDV infection leads to rapid progression of liver disease complications. Accompanying measures for hepatitis B patients are needed to ensure better follow-up.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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