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Factors Associated with Hepatic Steatosis in Black African Subjects with Chronic Viral Hepatitis B in Côte d'Ivoire

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Abstract

Context/Objectives: With the progression of the global epidemic of obesity and metabolic syndrome, the coexistence of hepatic steatosis in patients with chronic viral hepatitis B (VHB) is becoming significant. The aim of this work was to determine the factors associated with hepatic steatosis assessed by a Fibroscan with Controlled Attenuation Parameter (CAP) in patients with chronic viral hepatitis B in Côte d'Ivoire. **Methods:** This was a cross-sectional and analytical study. Data was collected from February 15 to July 31, 2020 in a private hospital structure in the city of Abidjan in Côte d'Ivoire. We included 83 patients with chronic viral hepatitis B. These were black patients, having performed a Fibroscan/CAP during the recruitment period and consenting to participate in the study. Patients with significant alcohol consumption, a secondary cause of hepatic steatosis, or other liver disease regardless of the etiology associated with hepatitis B were not included. **Results:** The frequency of hepatic steatosis in chronic VHB carriers assessed by the CAP in our study population was 48.19% including 24.10% severe steatosis. Obesity and high LDL cholesterol were statistically correlated with the presence of steatosis in our patients. Patients who had steatosis on ultrasound were 5 times more likely to have steatosis on CAP. Significant fibrosis was not significantly associated with steatosis. **Conclusion:** Obesity and LDL hypercholesterolemia are the main factors associated with hepatic steatosis detected by Fibroscan/CAP in patients with chronic viral hepatitis B.

Keywords

Non-Alcoholic Fatty Liver Disease, Chronic Viral Hepatitis B, Obesity,

Metabolic Syndrome, Fibroscan/CAP, Africa

1. Introduction

Several studies have shown a strong correlation between obesity, metabolic syndrome and non-alcoholic fatty liver disease (NAFLD) [1]. NAFLD, with an overall prevalence of 25.24%, is the leading cause of chronic liver disease in the United States of America and Europe [2]. Viral hepatitis B is also a public health issue. Indeed, 350 million people in the world are chronic carriers and 780,000 deaths are recorded annually due to its consequences, cirrhosis and hepatocellular carcinoma (HCC) [3].

These two liver pathologies can coexist in the same patient. The estimated frequency of fatty liver disease in patients with chronic viral hepatitis B worldwide varies between 27% and 51% depending on the study [4]. These two cofactors of chronic liver disease could therefore influence each other and even induce an acceleration of the progression of liver disease, in particular liver fibrosis. Indeed, several authors have indicated interactions between the hepatitis B virus and steatosis [5]. Côte d'Ivoire remains an area of high endemicity for viral hepatitis B with a prevalence of HBs antigen (HBsAg) estimated at 13% in the general population [6]. This suggests that the prevalence of the coexistence of these two pathologies could be significant in Côte d'Ivoire.

Liver biopsy is the "gold standard" for the exploration of hepatic pathologies, but its morbidity and mortality and its cost limit its performance to specific indications [7]. On the other hand, Fibroscan, an examination based on the exploration of the liver by impulse elastometry, is non-invasive and has a good indication for both chronic viral hepatitis B and steatosis [8] [9]. Little work has been done on the coexistence of viral hepatitis B and fatty liver disease in sub-Saharan Africa; which motivated this study with the aim of determining the factors associated with hepatic steatosis diagnosed by Fibroscan/CAP in black African subjects from Côte d'Ivoire, carriers of chronic viral hepatitis B.

2. Methods

This was a cross-sectional, descriptive and analytical study whose data was collected over the period from February 15, 2020 to July 31, 2020 in a hospital structure in the city of Abidjan (Ivory Coast). We recruited patients who came to perform a Fibroscan/CAP examination during the study period.

Black subjects with chronic viral hepatitis B who performed a Fibroscan/CAP during the recruitment period and who agreed to participate in the study by oral consent were included. Patients with significant alcohol consumption (greater than 30% for women and 40% for men), a secondary cause of hepatic steatosis, another hepatopathy whatever the etiology associated with hepatitis B were rejected.

The Fibroscan/CAP was performed in patients who had fasted for at least 2 hours before the examination. The examination was considered successful when there were 10 valid measurements, the success rate greater than 60% and IQR/med less than 30%. The examination was performed with the Fibroscan 530 Compact F81142 from Echosens. Sampling was consecutive and exhaustive non-probability. The statistical tests used were in univariate analysis: the Chi^2 test. They were significant when $p < 0.05$.

2.1. Parameters Studied

Sociodemographic and clinical parameters:

- age, gender, profession
- history: high blood pressure, diabetes, familial liver disease
- Alcohol consumption; regular exercise; the usual intake of traditional therapy
- weight (kg); height (cm); waist circumference (cm)
- body mass index BMI (kg/m^2): defined by weight/height squared

18 - 24.5 = normal; 25 - 29.9 = overweight; 30 - 34.9 = obesity grade I; 35 - 39.9 = obesity grade II; ≥40 = grade III or morbid obesity

Biochemical and hematological parameters:

- Fasting venous blood sugar (g/l); hemoglobin level (g/dl); the mean corpuscular volume (Fl); platelet count: 10^9/l; transaminases: ALAT (IU/l) and ASAT (IU/l); total and conjugated bilirubin level (mg/l); the level of HDL cholesterol (g/l), LDL cholesterol (g/l), triglycerides (g/l), total cholesterol (g/l), uric acid (g/l), lipidemia (g/l); serum albumin (g/l); the dosage of gamma glutamyl transpeptidases (IU/l) and alkaline phosphatases (IU/l).

Tests to assess hepatic steatosis:

- Fatty Liver Index (FLI): BMI, waist circumference, GGT, triglycerides (MDCalc application).

Steatosis present if FLI > 60; Steatosis absent if FLI < 30; Steatosis indeterminate value between 30 and 60.

- Liver ultrasound: steatosis if increased echogenicity of the liver parenchyma compared to that of the right renal cortex.

2.2. Measurement of Liver Fibrosis

F0 - F1: fibrosis absents or not significant if elastometry < 7.2 Kpa

≥F2 or significant fibrosis if elastometry ≥ 7.2 Kpa and < 9.4 Kpa

≥F3 or severe fibrosis if elastometry ≥ 9.4 Kpa and <12.2 Kpa

F4 or cirrhosis if elastometry ≥ 12.2 Kpa.

Measurement of steatosis by CAP with Fibroscan®:

S0 or absence of steatosis if CAP < 222 dB/m

S1or minimal steatosis if CAP ≥ 222 dB/m and <247 dB/m

S2 or moderate steatosis if CAP ≥ 247 dB/m and <274 dB/m

S3 or severe steatosis if CAP ≥ 274 dB/m.

Little work has been done on the coexistence of viral hepatitis B and fatty liver in sub-Saharan Africa; which motivated this study with the objectives of evaluating the frequency of hepatic steatosis by Fibroscan/CAP in black African subjects from Côte d'Ivoire, carriers of chronic viral hepatitis B and to highlight the factors associated with this fatty liver.

3. Results

3.1. General Characteristics of the Study Population

We included 83 patients with chronic viral hepatitis B in our study. The average age of our patients was 43.14 ± 9.46 years, with extremes of 29 and 82 years. There was a clear male predominance in our study population; men represented 71.08% of the total number, *i.e.* a sex ratio of 2.46.

3.2. Descriptive Study

Arterial hypertension was the predominant antecedent in our study population with a frequency of 15.66%. The body mass index was normal in 25% of our patients and 50% had a high waist circumference (Table 1).

Transaminases were elevated in 43.24% and 44.59% of our patients for ALT and AST respectively; 36.61% had hypercholesterolemia, with 21.73% having normal HDL cholesterol levels. Triglycerides were elevated in 30% of patients; hyperglycemia was present in 4.41% of patients. Quantitative HBsAg was greater than 1000 IU/ml in more than 85% of patients and almost 50% had DNA greater than 2000 IU/ml. No patient had HBe Antigen (Ag) positive or HBe antibody negative (Table 2). Quantitative HBs Antigen (QHBsAg) greater than 1000 IU/ml and DNA less than 2000 IU/ml were not factors statistically associated with steatosis.

On Fibroscan/CAP, more than half of the patients had F1 fibrosis and less than 5% had F4 fibrosis. Half of the patients had S0 steatosis, *i.e.* a frequency of CAP steatosis of 51.81%. Grade 3 steatosis was present in 24.10% of patients (Table 3).

Steatosis was present on ultrasound in 31.08% of cases and more than half of the patients had a normal-appearing liver on ultrasound; 1 patient had a fibrotic liver.

There was no statistically significant association between steatosis and the presence of fibrosis, nor between the stage of fibrosis and steatosis (Table 4).

Table 1. Distribution of patients according to anthropometric measurements.

Anthropometric measurements	Number (n = 83)	Percentage
BMI (kg/m^2)		
Normal (18 - 24.5)	21	25.30
Overweight (25 - 29.9)	**46**	**55.42**
Obese (≥30)	**16**	**19.28**
High waistline	**42**	**50.60**

Table 2. Distribution of patients according to virological parameters.

Virology	Number	Percentage
Quantitative HBsAg ≥ 1000	61 (n = 71)	85.91
VHB DNA ≥ 2000	33 (n = 71)	46.47
HBeAg Negative	67 (n = 67)	100
HBe antibody Positive	64 (n = 64)	100

Table 3. Distribution of patients according to the degree of steatosis and fibrosis.

Variable	Number	Percentage
Degree of fibrosis	(n = 83)	
F1	**59**	**71.08**
F2	10	12.05
F3	10	12.05
F4	**4**	**4.82**
Degree of steatosis	(n = 83)	
S0	**43**	**51.81**
S1	15	18.07
S2	5	6.02
S3	**20**	**24.10**

Table 4. Correlation between steatosis and fibrosis.

Fibrosis	Steatosis			
	Present n (%)	Absent n (%)	OR (IC à 95%)	p-value
F1	25 (62.5)	34 (79.1)	/	/
F2	5 (12.5)	5 (11.6)	1.4 (0.4 - 5.2)	0.74
F3	7 (17.5)	3 (7.0)	3.2 (0.7 - 13.4)	0.17
F4	3 (7.5)	1 (2.3)	4.0 (0.4 - 41.6)	0.32
Total	40 (100)	43 (100)		

Obese patients were 5 times more likely to have steatosis than those with a normal BMI with a statistically significant difference. Overweight and waist circumference were not statistically associated with steatosis (Table 5).

Quantitative HBsAg greater than 1000 IU/ml and DNA less than 2000 IU/ml were not factors statistically associated with steatosis (Table 6).

4. Discussion

4.1. Frequency of Hepatic Steatosis in the Study Population

The frequency of hepatic steatosis assessed by Fibroscan/CAP in our study was 48.19%. This frequency was very high given the risk of hepatic and extra-hepatic

complications of this condition. Ben Slama *et al.* in Tunisia had found a prevalence of steatosis assessed by histology of 38.3%, in a population of patients with chronic viral hepatitis B [10]. This difference could be due to sampling fluctuations related to biopsy collection. Seto *et al.* in a population of chronic carriers of HBV, in whom steatosis was assessed by Fibroscan, found a prevalence of steatosis of 40.8% [11]. This difference would be related to the fact that in our study the thresholds defined to make the diagnosis of steatosis with CAP were lower than in those defined in the Seto study. Indeed, some authors had found the presence of steatosis in patients with chronic viral hepatitis B for lower CAP values than in the other study populations (NAFD alone, HCV) [12]. Asim *et al.* found a higher prevalence of steatosis assessed by CAP in their patients, *i.e.* 72.2% [13]. This difference with our study could be explained by the fact that in this study, nearly 70% of the patients had a BMI greater than 30 and the effect of obesity on the presence of hepatic steatosis is well known in the literature [1].

Table 5. Correlation between steatosis and anthropometric constants.

Anthropometric measurements	Steatosis			
	Present n (%)	Absent n (%)	OR (IC à 95%)	p-value
BMI (kg/m^2)				
Normal	6 (15.0)	15 (34.9)	/	/
Overweight	23 (57.5)	23 (53.5)	2.5 (0.8 - 10)	0.10
Obesity	11 (27.5)	5 (11.6)	5 (1.25 - 10)	0.02
Total	40 (100)	43 (100)	/	/
Waist size				
High	24 (60.0)	20 (46.5)	1.7 (0.7 - 4.1)	0.22
Normal	16 (40.0)	23 (53.5)		
Total	40 (100)	43 (100)		

Table 6. Correlation between steatosis and virology.

Variable	Steatosis			
	Present n (%)	Absent n (%)	OR (IC à 95%)	p-value
	QHBsAg			
QHBsAg >1000	31 (91.2)	30 (81.1)	2.4 (0.6 - 10.2)	0.31
QHBsAg < 1000	3 (8.8)	7 (18.9)		
Total	34 (100)	37 (100)		
	DNA			
DNA < 2000	16 (48.5)	17 (44.7)	1.2 (0.5 - 2.9)	0.81
DNA ≥ 2000	17 (51.5)	21 (55.3)		
Total	33 (100)	38 (100)		

Wang *et al.* in 2014 [14] found in patients assessed by biopsy, 36.6% of patients at stage S0, 36.36% at stage S1, 19.05% at stage S2 and 9.09% at stage S3. In our study, 51.81% of patients were at stage S0, 18.07% at stage S1, 6.02% at stage S2 and 24.10% at stage S3. Sasso *et al.* [15] stated that CAP values were significantly different from one grade of steatosis to another except for grades S2 and S3 for which the difference was not significant. Seto *et al.* in 2018 [11], had found values close to ours in terms of grade S3 steatosis, *i.e.* 22.6% of their study population.

The prevalence of non-alcoholic fatty liver disease was as high as 46% depending on the diagnostic method, age, sex and ethnicity [16]. It was correlated with that of the metabolic syndrome and its components that increased the risk of severe liver disease. But steatosis could be present in 7% of people with normal weight [17]. This high proportion of patients with steatosis in our study raised questions about the best way to manage these patients in order to slow the progression of liver disease in view of these two cofactors.

4.2. Factors Associated with Fatty Liver in the Study Population

In our study, obesity and the presence of steatosis on ultrasound were correlated with the presence of CAP steatosis. Host factors, in this case metabolic syndrome, have been shown to be related to the presence of fatty liver even in patients with chronic viral hepatitis B [18]. Sun *et al.* in China in 2019 found that high weight and high blood pressure were associated with the presence of steatosis [19]. Asim *et al.* found that weight, insulin resistance and high transaminase levels were related to higher grades of steatosis [13]. Altiparmak *et al.* found in their patients in whom steatosis had been diagnosed by pathological examination, that they had an average age, a BMI, higher cholesterol and triglyceride levels than patients without steatosis [20]. The prevalence of the metabolic syndrome in our study was 12% but this was not statistically linked to the presence of hepatic steatosis. Our study did not find a significant link between DNA levels, quantitative HBsAg and steatosis. In our study, there was no statistically significant association between steatosis and fibrosis. Seto *et al.* in 2017 found that severe steatosis was correlated with severe fibrosis in both patients on treatment and those without treatment for hepatitis B [11]. But high CAP was an independent factor significantly associated with severe fibrosis. Thus, increasing the CAP value by 10 dB represented a risk of severe fibrosis of 15%. In our study, nearly 5% of our patients had F4 fibrosis while 12% had severe fibrosis (F3). Seto *et al.* [11] had found a prevalence of F3 and F4 fibrosis of 27.1% and 11.2% respectively in their population under HBV treatment and lower rates of 4.4% and 2% respectively in their untreated patients. This could be explained by the fact that the presence of fibrosis greater than or equal to F2 was one of the major criteria for initiating HBV treatment.

4.3. Limits and Strength of the Study

The limits of our study were essentially the small size of our sample linked to the

cost of the Fibroscan/CAP examination and the difficulties of including patients who rarely visited hospital structures during this period due to the Coronavirus Covid-19 pandemic. The strength is due to the original character of our study.

5. Conclusion

It appears from our study that the frequency of steatosis detected by Fibroscan/CAP in black African patients chronically carrying HBV in Ivory Coast was 48.19%. Non-alcoholic fatty liver disease therefore represents a public health issue which is beginning to become a reality in our countries in sub-Saharan Africa. Its coexistence with hepatitis B, which itself has a serious health impact, would promote the more rapid occurrence of complications such as liver cirrhosis or even hepatocellular carcinoma, hence the need to screen for it in any patient carrying the hepatitis B virus.

Authors Contribution

Kouamé Hatrydt Guillaume Dimitri wrote the article, made conception and design, data acquisition, Kissi Anzouan-Kacou Henriette Ya made data analysis and interpretation. Gogan Patricia and Bangoura Aboubacar Demba filled and analyzed the database. Mahassadi Kouamé Alassane and Yao Bathaix Fulgence Mamert made the critical revision of the article. Attia Koffi Alain motivated the study.

Conflicts of Interest

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

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