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Effect of body mass index on Disease progression in Chronic Hepatitis B Patients

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Abstract

Background and study aim: In recent years the burden of obesity and metabolic syndrome has been increasing. These diseases are associated with increased risk for chronic hepatitis B virus infection as well as worsened outcomes. The aim of this study was to investigate the association between obesity, defined according to body mass index, and hepatitis B viral load and fibrosis stage according to liver biopsy, among chronic hepatitis B Egyptian patients.

Methods: We performed a retrospective study on 50 patients with chronic hepatitis B virus infection at National Hepatology and Tropical Medicine Research Institute, Cairo, Egypt. The essential outcomes were laboratory tests, ultrasonography, and liver biopsy. Data analysis was used to reveal whether high BMI was a variable related to disease progression.

Results: A total of 50 HBsAg seropositive participants. All patients were classified into two groups according to BMI (non-obese, <30 kg/ m2; and obese, ≥30 kg/ m2). Obese patients ≥30 kg/m2 were at higher risk for elevated serum levels of ALT (P=0.5) and for lower serum levels of HBV DNA (P=0.08). Bright liver, liver cirrhosis, and splenomegaly were higher in obese patients than in non-obese. A1 was the commonest among obese and non-obese (74.1% and 91.3%) respectively. Also, F1 was the commonest among obese and non-obese (66.7% and 56.5%) respectively. No statistically significant difference was detected between obesity and fibrosis stage.

Conclusions: Subjects with body mass index ≥30 kg/m2 were at higher risk for elevated serum levels of ALT and for lower serum levels of HBV DNA and possible liver cirrhosis based on ultrasonographic findings. We did not find association between obesity and stage of fibrosis.

Keywords: Hepatitis B virus; Body mass index; Liver biopsy; Liver fibrosis; Chronic liver disease; Obesity; Fatty liver disease; Steatosis; Metabolic risk factors; Hepatitis B; Liver disease

Abbreviations: HBV: Hepatitis B Virus; CLD: Chronic Liver Disease; NAFLD: Non-Alcoholic Fatty Liver Disease; CBC: Complete Blood Picture; AST: Aspartate Aminotransferase; ALT: Alanine Aminotransferase; AFP: Alpha Fetoprotein; PCR: Polymerase Chain Reaction; BMI: Body Mass Index; SD: Standard Deviation; HCC: Hepatocellular Carcinoma; MS: Metabolic Syndrome

Introduction

Chronic hepatitis B virus (HBV) infection leads to progressive liver fibrosis and is the leading cause of chronic liver disease (CLD) [1,2]. Furthermore, as the incidence of obesity rises in the general population, non-alcoholic fatty liver disease (NAFLD) is also emerging as a disease of significant concern. NAFLD affecting more than 30% of adults in developed countries [3]. Coexistent steatosis is common in chronic hepatitis B infection and is also strongly associated with more advanced liver disease [4].

Obesity is one of metabolic risk factors associated with NAFLD that have recently emerged as potential cofactors in the development of fibrosis in cases of chronic HCV and HBV [5-7].

Consequently, the evaluation of hepatic fibrosis is highly important in the management of patients with CLD. In spite of certain limitations, histological assessment is the classic method to determine the extent of hepatic fibrosis [8]. As such, we used liver biopsy in the present study, to investigate the relationship between obesity and the risk of liver disease progression in chronic hepatitis B infection among this special patient group.

Aim of the work

To examine whether obesity according to body mass index was associated with higher hepatitis B viral load and more progressive disease in chronic hepatitis B Egyptian patients.

Patients and methods

Patients: This retrospective study included 50 patients with chronic hepatitis B presented to the out-patient clinics of the National Hepatology and Tropical Medicine Research Institute, Cairo, Egypt. Diagnosis of HBV was based on detection of HBsAg and quantitative HBV DNA by PCR. Patients with malignancy, decompensated liver disease, Patients with HIV infection

or hepatitis B and C co-infection and presence of absolute contraindication for liver biopsy were excluded from this study. An informed written consent was obtained from all patients in the study and according to the Declaration of Helsinki.

Data collection: All patients were subjected to basic laboratory tests including: Complete blood picture (CBC), Aspartate aminotransferase (AST), Alanine aminotransferase (ALT), serum albumin, total bilirubin, INR, Alpha fetoprotein (AFP), hepatitis seromarkers for HCV (anti HCV) and for hepatitis B virus (HBV); (HBsAg, anti HBc and anti HBs) using ELISA technique. HBV DNA was tested by quantitative polymerase chain reaction (PCR).

The following clinical parameters were recorded: age, sex, and body mass index (BMI). Ultrasound guided liver biopsies were performed. Fibrosis was staged according to the METAVIR scoring system from F0 to F4 as: F0 (no fibrosis), F1 (mild fibrosis without septa), F2 (moderate fibrosis with few septa), F3 (severe fibrosis with numerous septa without cirrhosis) and F4 (cirrhosis) [9]. All patients were classified into two BMI groupings (non-obese, <30 kg/m2; obese, ≥30 kg/ m2).

Statistical analysis

Numerical data were presented as means±standard deviation (S.D), while categorical data were presented as number (percent). The Mann-Whitney U test and the Chi-square test were used when appropriate. Statistical significance was considered if P value was less than or equal 0.05.

Results

The study was conducted on 50 chronic hepatitis B patients. They presented to the outpatient clinic of the National Hepatology and Tropical Medicine Research Institute, Cairo, Egypt.

The mean age of obese patients was 39.9+ 7.2 years, while the mean age of non-obese patients was 33.2+ 10.9 years, with a statistical significance (P=0.02). There was male predominance in both groups, without a statistical significance in relation to sex (P=0.3). Regarding the laboratory results, the significant difference was confined to hemoglobin which was significantly higher in obese than in non-obese patients (P=0.02). ALT level was elevated in obese patients compared with non-obese without a significant difference (P=0.5).

Table 1: Demographic feature and laboratory data of the studied patients in relation to BMI.

Variable	Obese BMI ≥ 30 kg/m² (n. 27)	Non-obese BMI < 30 kg/m² (n.23)	P value
Mean age ± SD	39.9+ 7.2	33.2+ 10.9	0.02
Gender			
Male	18 (66.7%)	18 (78.3%)	0.3
Female	9 (33.3%)	5 (21.7%)	
Hb	14.3+1.9	13.1±7.3	0.02
WBCs	5.8±1.3	6.1±1.5	0.08
Pls	190±48	201±71	0.5
Bilirubin	0.8±0.3	0.9±0.3	0.2
ALT (U/L)	85.2+ 37	52+ 83	0.5
AST (U/L)	38.7+ 25	37.1+ 19	0.8
Serum albumin	4.3±0.8	4.1±0.5	0.5
ALP	155.6±51	166±58	0.5
AFP	2.4±2	2.8±1.6	0.4
HBV DNA PCR	1300 (196-980000)	4030(268-2700000)	0.08

Obese patients (BMI ≥ 30 kg/m2) had lower HBV DNA PCR than in non-obese, however, did not show a statistical significance (P=0.08) (Table 1).

The ultrasound findings showed that bright liver, liver cirrhosis, and splenomegaly were higher in obese patients than in non-obese. There was not a statistical significance in abdominal ultrasonographic findings between both groups. A1 was the commonest among obese and non-obese (74.1% and 91.3%) respectively. Also, F1 was the commonest among obese and non-obese (66.7% and 56.5%) respectively. No statistically significant difference was detected between obesity and fibrosis stage (Table 2).

Table 2: Ultrasonographic findings and histopathological features of the studied patients in relation to BMI.

Variable	Obese BMI ≥ 30 kg/m² (n. 27)	Non-obese BMI < 30 kg/m² (n.23)	P value
Liver			
Normal	9 (33.3%)	11 (47.8%)	0.5
Bright	7 (25.9%)	4 (17.4%)	
Cirrhotic	11(40.7%)	8 (34.8%)	

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Spleen			
Average	16 (59.3%)	17 (73.9%)	0.3
Enlarged	11 (40.7%)	6 (26.1%)	
Activity			
A1	20 (74.1%)	21 (91.3%)	0.07
A2	7 (25.9%)	1 (4.3%)	
A3	0	1 (4.3%)	
Fibrosis			
F1	18 (66.7%)	13 (56.5%)	0.6
F2	6 (22.2%)	8 (34.8%)	
F3	3 (11.1%)	2 (8.7%)	

Discussion

Chronic hepatitis B virus (HBV) infection is a challenging disease worldwide [10]. It is well-known that HBV infection is a main risk factor for hepatic fibrosis, cirrhosis and hepatocellular carcinoma (HCC) [11-14]. It is significant to exactly predict the stage of liver fibrosis progression in chronic viral hepatitis patients, which has significant implications for prognosis and treatment [15].

Metabolic syndrome (MS) involves three characteristics of the following: dyslipidemia, an impaired fasting glucose metabolism, hypertension or central obesity [15,16].

It is vastly known that hepatitis C virus infection might increase the risk of metabolic syndrome and diabetes mellitus [17,18]. HBV and its relationship with metabolic syndrome have also become a focus of research [19]. In the current study, we investigated whether obesity, according to body mass index, was associated with higher hepatitis B viral load and more progressive disease in chronic hepatitis B Egyptian patients.

There are only few studies regarding the relationships of chronic hepatitis B infection with obesity. In the present study we did not find any association between chronic hepatitis B infection and obesity, as Obese patients (BMI ≥ 30 kg/m2) had lower HBV DNA PCR than in non-obese, however, it did not show a statistical significance (P=0.08). This is consistent with previous studies [20,21] which found that extreme obesity was associated with low HBV viral load and was a significant predictor of HBsAg seroclearance in chronic hepatitis B patients. This may be a reason why HBV patients with higher BMI had less fatty liver. Jinjuvadia et al, [22] observed among patients with chronic HBV infection, a lower odd of having central obesity.

The relationship between chronic HBV infection, and abnormal liver function, is complex. Patients with chronic HBV infection have a higher risk of abnormal liver function, such as elevated ALT levels [10]. Previous studies have also confirmed the predictive role of an elevated ALT level with an increased incidence of metabolic syndrome [23,24], and it is consistent with the present study as ALT level was elevated in obese patients compared with non-obese without a significant difference (P=0.5).

High BMI is involved in the transition from HBV carrier state to hepatocellular carcinoma (HCC) and liver-related mortality [25,26]. Similarly, in the present study the ultrasound findings showed that bright liver, liver cirrhosis, and splenomegaly were higher in obese patients than in non-obese.

In a study including 850 HBV patients, the prevalence of MS was found to be 5%. The extent of liver fibrosis was found more serious in patients accompanying metabolic syndrome. Body mass index (BMI) was one of the factors that showed association with advanced fibrosis (fibrosis stages 3 to 4). In multivariate analysis, metabolic syndrome was found to be independently associated with liver fibrosis [27].

In a recent prospective cohort study of 663 CHB patients, obesity was found to be associated with liver fibrosis progression [7]. Even the effect of such coincident, metabolic syndrome was most apparent in the immune tolerant phase. Its effect was independent of the change in viral load and ALT level [7]. This is supported by the observation from a survey in general population that CHB is associated with a lower prevalence of fatty liver, hypertriglyceridemia and metabolic syndrome [7].

These studies are consistent with the current study in which obese subjects with BMI ≥ 30 kg/m2 were not associated with advanced fibrosis as shown in histologic examination.

Conclusion

Subjects with body mass index ≥30 kg/m2 were at higher risk for elevated serum levels of ALT and for lower serum levels of HBV DNA and possible liver cirrhosis based on ultrasonographic findings. We did not find association between obesity and stage of fibrosis.

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