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Original research article

Prevalence of Diabetes and Glucose Intolerance in Chronic Hepatitis B Patients at a Tertiary Care Centre in Bihar

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Abstract

Aim: The aim of the study was to compare the prevalence of glucose intolerance in chronic HBV infection.

Materials and Methods: It was a retrospective cohort study conducted in the Department of Medicine, Nalanda Medical College & Hospital, Patna, Bihar, India, during the period of one year. A total of 250 CHB-infected patients who either attended medicine out-patient department or admitted to medicine ward between October 2021 and March 2022 were studied. The diagnosis of CHB was based on the presence of hepatitis B surface antigen positivity for more than 6 months. In all the patients, fasting plasma glucose and postprandial plasma glucose samples were obtained. HbA1C, serum alanine aminotransferase, serum aspartate aminotransferase, and α-fetoprotein were done for all the patients. Hepatitis B e antigen status, HBV DNA, and genotype were determined by a commercially available assay. Fibroscan (transient elastography) is performed in all the patients.

Results: The present study included 250 patients. A majority of patients were in the age group of 21–30 years accounted for 32% and age group of 31– 40 years accounted for 24%. Among the others, 22% were between 11 and 20 years, 16% between 41 and 50 years, and 6% between 51 and 60 years. Gender-wise distribution of male and female was 56% and 44%, respectively. The number of patients with impaired and diabetic range of FBS was 18% and 26%, respectively. Similarly, for PPBS, 65 (26%) patients had impaired range and 95 (38%) patients with diabetic range. Glycated hemoglobin (HbA1C) value ≥5.7 were present in 165 (66%) patients. The number of patients with fibrosis ≥12.5 kPa was 70; all of them (100%) had FBS ≥110, PPBS ≥140, and HbA1C ≥5.7. The number of genotype C patients was 170, in which 80/170 had FBS ≥110, 115/170 had PPBS ≥140, and 105/170 had HbA1C ≥5.7. The number of patients with genotype D was 80, in which 30/80 had FBS ≥110, 40/80 had PPBS ≥140, and 60/80 had HbA1C ≥5.7.

Conclusion: The prevalence of glucose intolerance was increased in patients with CHB infection. HBV carriers with impaired glucose tolerance are at high risk for end-stage liver disease, and therefore HBV carriers should be considered for surveillance programs that closely monitor liver enzymes and lipid profile and detect changes in ALT and TG levels.
Keywords: Diabetes, glycated hemoglobin, lipid profile, fibroscan

Introduction

When it comes to carbohydrate metabolism, the liver plays an important role by ensuring that blood glucose levels stay within the usual range [1]. Besides lifestyle factors, such as obesity, that have been linked to an increased risk of type 2 diabetes, increased insulin resistance may play a role in the pathogenesis of glucose intolerance in individuals with liver disease [2]. Cirrhosis patients are more likely to have diabetes and impaired glucose tolerance (IGT) than the general population [3-6]. Several researches have looked at the frequency of diabetes in people with chronic hepatitis B (CHB) virus infection (HBV). There is no significant difference in the prevalence of cirrhosis between those who have it and those who do not [5].

Insulin resistance and glucose intolerance occur in the early stages of chronic liver disease in the majority of patients [7]. The natural history of diabetes caused by liver disease is distinct from the natural history of type 2 diabetes. Diabetes or insulin resistance in patients with liver disease is linked with a poor prognosis, including fast progression, medication resistance, and poor control of glucose levels [8,9]. This is due to the fact that diabetes or insulin resistance makes it harder to manage glucose levels.Previous research on the connection between cirrhosis of the liver and the onset of impaired glucose tolerance found that between sixty and eighty percent of patients with cirrhosis suffer from glucose intolerance, and between twenty and sixty percent of those also had diabetes [9].

Thus, the association of IGT and diabetes with CHB is open to question, as adjustment for confounding factors, like age, sex, degree of obesity etc, are rarely considered in most studies. It should be also noted that the criteria for the diagnosis of diabetes vary among studies, being fasting blood glucose, known diabetes or both and almost never diabetes based on oral glucose tolerance test (OGTT) as defined by the WHO criteria [10]. The diversity of the diagnostic criteria and the lack of adjustment for confounding factors render the proper comparison of the various results difficult if not impossible. The aim of the study was to compare the prevalence of glucose intolerance in chronic HBV infection.

Materials and Methods:

It was a retrospective cohort study conducted in the Department of Medicine, Nalanda Medical College & Hospital, Patna, Bihar, India, during the period of one year. A total of 250 CHB-infected patients who either attended medicine out-patient department or admitted to medicine ward between October 2021 and March 2022 were studied. The diagnosis of CHB was based on the presence of hepatitis B surface antigen positivity for more than 6 months.

Exclusion criteria were patients with prior antiviral treatment, established diabetes, concurrent HBV, and hepatitis C virus infection; patients receiving drugs or having conditions that cause fatty liver (tamoxifen, steroids, amiodarone, diltiazem, gastrointestinal bypass surgery, or severe recent weight loss), regular or excessive alcohol consumption; obese patients; pregnant and lactating women.

In the spectrum of glucose intolerance, the following were included: (i) IGT defined as fasting blood sugar (FBS) of 110–125 mg/dL and postprandial blood sugar (PPBS) of 140-199 mg/dL, (ii) diabetes detected for the first time defined as FBS ≥126 mg/dL and PPBS level ≥200 mg/dL. In all the patients, fasting plasma glucose and postprandial plasma glucose samples were obtained. HbA1C, serum alanine aminotransferase, serum aspartate aminotransferase, and α-fetoprotein were done for all the patients.

Methodology

Hepatitis B e antigen status, HBV DNA, and genotype were determined by a commercially available assay. Fibroscan (transient elastography) is performed in all the patients. It is a noninvasive, rapid, and reproducible method, allowing evaluation of liver fibrosis by the measurement of liver stiffness. It is expressed in kilopascal (kPa). Data was collected and analyzed using paired t-test and $P < 0.05$ was considered statistically significant.

Results:

The present study included 250 patients. A majority of patients were in the age group of 21–30 years accounted for 32% and age group of 31–40 years accounted for 24%. Among the others, 22% were between 11 and 20 years, 16% between 41 and 50 years, and 6% between 51 and 60 years. Gender-wise distribution of male and female was 56% and 44%, respectively.

Table 1: Demographic details

Variables		Number	%
Age	11-20	55	22
	21-30	80	32
	31-40	60	24
	41-50	40	16
	51-60	15	6
Gender	Male	140	56
	Female	110	44

Table 12: Glucose parameters

Glucoseparameters		Number	%
FBS	<110	140	56
	110-125	45	18
	≥126	65	26
PPBS	<140	95	38
	140-199	65	26
	≥200	90	36
HbA1C	<5.7	85	34
	≥5.7	165	66

The number of patients with impaired and diabetic range of FBS was 18% and 26%, respectively. Similarly, for PPBS, 65 (26%) patients had impaired range and 95 (38%) patients with diabetic range. Glycated hemoglobin (HbA1C) value ≥5.7 were present in 165 (66%) patients. In the study, genotype of HBV observed was either type C or type D.

Table 3: Comparison between glucose intolerant patients and fibroscan, genotype, and hepatitis B virus

Number of patients	Fibroscan(kPa)		P-value	Genotype		P-value	HBVDNA(IU/ml)		P-value
	≤12.5	>12.5		C	D		<20,000	≥20,000	
FBS≥110 (N=110)	40	70	<0.001	80	30	0.645	0	110	0.177
PPBS≥140 (N=155)	85	70	<0.001	115	40	0.684	30	125	0.073
HbA1C≥5.7 (N=165)	95	70	<0.001	105	60	0.629	40	125	0.183

Comparison for association between patients having impaired and diabetic range of FBS, PPBS, and HbA1C with fibroscan value >12.5 kPa was found to be statistically significant. The number of patients with fibrosis ≥12.5 kPa was 70; all of them (100%) had FBS ≥110, PPBS ≥140, and HbA1C ≥5.7. The number of genotype C patients was 170, in which 80/170 had FBS ≥110, 115/170 had PPBS ≥140, and 105/170 had HbA1C ≥5.7. The number of patients with genotype D was 80, in which 30/80 had FBS ≥110, 40/80 had PPBS ≥140, and 60/80 had HbA1C ≥5.7.

Discussion:

A study that compared the risk for diabetes in patients with asymptomatic chronic HBV infection and non-carriers found no statistically significant difference between the groups [11]. These results, together with the finding that impaired glucose tolerance risk is increased in advanced liver diseases caused by HBV infections such as cirrhosis [8], suggest that HBV-related parenchymal damage, rather than HBV infection itself, causes impaired glucose tolerance [11]. Although previous studies have found a higher prevalence of diabetes in chronic HBV carriers than in non-carriers [12], we could not readily compare those results with ours given the heterogeneous population characteristics between the studies such as the stage of liver disease.

Maintaining good control of diabetes is difficult in patients with liver disease because pharmacological therapies are limited by hepatotoxicity and the risk of hypoglycemia [13]. However, we found that the proportions of HBV carriers with diabetes undergoing diabetes treatment (as defined by the prescription of insulin or oral anti diabetic agents) or meeting the criteria for well-controlled diabetes (HbA1c < 6.5%) were not significantly different from those of non carriers with diabetes.

In the study, the prevalence of glucose in tolerance in patients with CHB was significantly higher which is in accordance with the findings reported by Mavrogiannaki*et al* [14].Since a known diabetic patient was also excluded in the study, glucose intolerance was a new development in these patients. Therefore, glucose intolerance might be associated with CHB infection. In the absence of cirrhosis, prevalence varied from 1.9% to 14%, which is not different from that reported in the general population [15, 16]. However, in present study, the prevalence was found to be 65.5% considering postprandial plasma glucose.

According to the study conducted by Foucher *et al*. [17], a cut off of 7.2, 12.5, and 17.6 kPa was taken for the diagnosis of moderate fibrosis, severe fibrosis, and cirrhosis of the liver, respectively. In this study, the value of 12.5 kPa or more was taken which include patients having severe fibrosis as well as cirrhosis of the liver. Hence, patients with either severe fibrosis

or cirrhosis of the liver were observed to have significantly higher blood glucose level ranging from impaired to overt diabetes.

Genotype of the hepatitis B in this study was either genotype C or D. Genotype was compared with blood glucose level, but there was no significant association between them. Similarly, for HBV DNA level, comparison between levels of ≥20,000 IU/ml with blood glucose did not give a significant result.

Our study had several limitations. First, we measured only HBsAg and hepatitis B surface antibodies because total hepatitis B core antibodies were not included in the KNHANES protocol. Thus, we were only able to assess current HBV infections. Second, a previous study found a strong association between IFG and the hepatitis B e-antigen, a marker for HBV replication and infectivity [18], and an increase in γ-glutamyl transferase, which may reflect hepatic oxidative stress [18-20].

Conclusion:

The prevalence of glucose intolerance was increased in patients with CHB infection.HBV carriers with impaired glucose tolerance are at high risk for end-stage liver disease, and therefore HBV carriers should be considered for surveillance programs that closely monitor liver enzymes and lipid profile and detect changes in ALT and TG levels, so that elevations can be rapidly controlled to prevent impaired glucose tolerance in HBV carriers at an early stage.

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