

Insulin Resistance among Chronic Hepatitis C Patients in Bangladesh

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ABSTRACT

Background: Insulin resistance and diabetes mellitus have been detected in patients with chronic liver diseases (CLD); however, there is paucity of information regarding these comorbidities in liver disease patients of Bangladesh.

Materials and methods: Thirty patients with hepatitis B virus (HBV)-related CLD and 30 patients with hepatitis C virus (HCV)-related CLD were checked for existence of insulin resistance and diabetes mellitus.

Results: The mean fasting serum glucose in HBV-related CLD and in HCV-related CLD were 4.37 ± 0.58 and 4.6 ± 0.59 mmol/l, respectively ($p = 0.781$). The levels of fasting serum insulin levels were 7.06 ± 2.2 μ U/ml in HBV-related CLD and 9.08 ± 3.06 in HCV-related CLD ($p = 0.013$). The cutoff value of HOMA-IR was 1.73. The mean HOMA-IR of HBV- and HCV-related CLD were 1.35 ± 0.44 and 1.89 ± 0.71 respectively ($p = 0.001$).

Conclusion: It seems that insulin resistance is prevalent among HCV-related CLD patients in Bangladesh. This pilot study indicates that insulin resistance and diabetes mellitus should be checked in all patients of HCV-related CLD during their management.

Keywords: Insulin resistance, Chronic hepatitis B, Chronic hepatitis C.

How to cite this article: Ali MA, Al-Mahtab M, Yeasmin F, Akbar SMF, Rahman S. Insulin Resistance among Chronic Hepatitis C Patients in Bangladesh. *Euroasian J Hepato-Gastroenterol* 2013;3(2):117-119.

Source of support: Nil

Conflict of interest: None

INTRODUCTION

Circumstantial evidences indicate that metabolic anomalies are associated with chronic liver diseases (CLD),¹⁻³ however, it is elusive whether metabolic diseases are manifested as an outcome of liver diseases or these effect the course of liver-related comorbidities and complications. Among metabolic disorders, diabetes mellitus (DM) and insulin resistance (IR) are two predominant pathological conditions that prevail in higher percentage in patients chronically infected with hepatitis B virus (HBV) and hepatitis C virus (HCV). Most of the studies have shown that HCV-infected patients reveal higher prevalence of DM and IR than those with HBV-infected subjects.¹⁻³ However, Imazaki et al from Japan analyzed prevalence of DM and IR in 952 patients with HCV and HBV infection and concluded that HCV infection was not independently associated with development and IR by multivariate analysis in comparison with HBV infection.⁴

In this context, new controversy was pointed by Wang et al from Taiwan who assessed IR in 507 subjects and found no association of HBV infection and IR in their study.⁵

Taken together, it seems that HBV and HCV may be variably associated with DM and IR in different population. Bangladesh is a developing country with a population of more than 160 million. HBV infection is endemic in Bangladesh and epidemiological data indicates that about 8 to 10 million people of this country seem to be chronically infected with HBV.⁶ The prevalence of HCV is still a matter of controversy at Bangladesh because some investigators have reported very low prevalence of HCV, whereas, others have shown comparatively higher prevalence of HCV.⁷⁻⁹ The numbers of DM patients in Bangladesh is extremely high. Although there is lack of information about exact prevalence of DM among different group of population, a study among lean people has reported 8.4% prevalence of DM in rural Bangladesh.¹⁰

Being an endemic area of HBV, HCV and DM, almost nothing is known about the comorbidity of hepatitis virus and DM or IR in Bangladesh. The present study, a pilot study in nature, was undertaken to assess prevalence of DM and IR in patients with HBV and HCV infections at Bangladesh.

MATERIALS AND METHODS

The study was conducted on 60 patients with CLD. The patients attended the Department of Hepatology, Bangabandhu Sheikh Mujib Medical University, Dhaka, Bangladesh. The patients were included on a first come first basis. The patients were grouped into two; 30 patients with HBV-related CLD and 30 patients with HCV-related CLD. The diagnosis of CLD was done from clinical data and biochemical assessment of liver function test. The etiology was affirmed by evaluation of serological markers of HBV and HCV. Patients expressed hepatitis B surface antigen for more than 6 months or they expressed anti-HCV antibody in their sera. The age of patients ranged from 20 to 60 years. Patients with coinfection with HBV and HCV, history of taking antiviral drugs, history of alcoholism and metabolic syndrome were excluded from this study. Informed written consent was taken from each patient after explaining the nature and purpose of the present study. The study was approved by a departmental ethical committee.

The levels of triglycerides, hHDL cholesterol, and glucose were estimated using commercial kit, according to

the instruction of the manufacturer. Measurement of fasting serum insulin was done by AxSYM Hormone Analyzer (Abbott AXSYM System^R, USA) by microparticle enzyme immunoassay (MEIA) method (name of company, city, state, country). Fasting serum glucose was also measured in all patients. IR was calculated using the homeostasis model assessment (HOMA-IR) method using the following equation: $IR (HOMA-IR) = \text{fasting serum insulin } (\mu\text{U/ml}) \times \text{fasting serum glucose (m mol/l)} / 22.5$. A HOMA-IR > 1.73 was considered indicative of IR.

STATISTICAL ANALYSES

Statistical analyses were performed using SPSS software version 10.0 for Windows (SPSS Inc., Chicago, IL, USA). Comparisons between the two groups were made using Chi-square test for categorical variables and the Student's t-test and Pearson's correlation test for continuous variables. All p-values were based on a two-sided test of statistical significance. A p-value of <0.05 was considered statistically significant.

RESULTS

The age of the patients of HCV-related CLD (42.3 ± 12.3 years, $n = 30$) was higher than that of the HBV-related CLD (35.4 ± 10.0 years, $n = 30$), but the difference was not statistically significant ($p = 0.06$). The major bulk of patients were male among HBV-related CLD (83% vs 17%). Among HCV-related CLD patients, 60% were male and 40% were female. The levels of alanine aminotransferase (ALT) were 49.9 ± 20.7 IU/l in 30 patients with HBV-related CLD, whereas, these were 68.2 ± 31.5 U/l in HCV-related CLD. However, the differences were not statistically significant ($p > 0.05$). The levels of serum triglycerides did not show any significant difference between HBV-related and HCV-related CLD (138.8 ± 29.8 vs 120.4 ± 21.4 U/l, $n = 60$, $p < 0.05$). However, the levels of HDL cholesterol was higher in HBV-related CLD compared to HCV-related CLD (39.43 ± 4.51 vs 36.73 ± 9.79 mg /dl, $n = 60$, $p < 0.05$).

Fasting serum glucose was almost similar in both in HBV- and HCV-related CLD patients. The levels of serum glucose in HBV- and HCV-related CLD were 4.37 ± 0.58 and 4.6 ± 0.59 mmol/l, respectively ($p = 0.781$).

Fasting serum insulin was measured and compared in patients with HBV-related CLD and HCV-related CLD. Fasting serum insulin mean (\pm SD) were $7.06 (\pm 2.2)$ $\mu\text{U/ml}$ in HBV-related CLD and $9.08 (\pm 3.06)$ in HCV-related CLD groups. The difference was significant between the two groups ($p = 0.013$).

Finally, we compared the levels of HOMA-IR between two groups of patients. HOMA-IR in HCV-related CLD

was higher than that in HBV-related CLD (1.89 ± 0.71 vs 1.35 ± 0.44) ($p = 0.001$). IR was found in 14 patients with HCV-related CLD.

To explore the clinical, biochemical and virological indicators associated with IR in HBV- and HCV-related CLD, correlations between several parameters including age, waist circumference, ALT, HBV DNA, HCV RNA, high density lipoprotein, triglycerides, fasting serum insulin were compared with HOMA-IR. Among these only fasting serum insulin strongly correlated with HOMA-IR in patients with CLD groups ($r = 0.924$, $p = 0.000$ and $r = 0.861$, $p = 0.000$ respectively).

DISCUSSION

The study presented from different parts of the world have shown that DM and IR were present in variable numbers of patients with HBV-related and HCV-related CLD.¹⁻⁵ Also, a higher prevalence of DM and IR has been shown in HCV-related CLD compared to HBV-related CLD.¹⁻³ The study presented here about DM and IR in Bangladeshi patients have supported what that have been reported by most investigators regarding prevalence of DM and IR in CLD patients. Nevertheless, this is a pilot study and the outcome of this study is not enough to draw a firm conclusion about these diverse factors and CLD in Bangladesh. In spite of these facts, this is the first study about DM and IR in Bangladesh, a country that harbor millions of patients with CLD and also large population of DM. A well-planned study about DM and IR in CLD patients should be undertaken in this country.

Although prevalence of HCV seems to be low in Bangladesh, but, some studies have pointed a high prevalence of this virus in this country.⁷⁻⁹ Out of 30 HCV-related CLD patients, 14 have IR. This is extremely important issue for managing these patients. At present, HCV-infected patients are treated by antiviral agents. It would be important to assess if these drugs alter IR in these patients at Bangladesh.

In conclusion, although preliminary, this study has shown that IR seems to be associated with HCV-related CLD at Bangladesh. Further large-scale studies would be needed to confirm these results.

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