CLINICAL AND EPIDEMIOLOGICAL ASSESSMENT OF THE PREVALENCE OF LIVER FIBROSIS ASSOCIATED WITH METABOLICALLY RELATED NECROINFLAMMATORY CHANGES IN PATIENTS WITH CHRONIC HEPATITIS.

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Abstract

Background

The coexistence of metabolic disorders with Chronic Hepatitis B has become an important clinical issue in hepatology. Increasing evidence suggests that metabolic abnormalities, including Hepatic steatosis and insulin resistance, may influence the progression of chronic viral liver disease and contribute to necro-inflammatory activity and the development of Liver Fibrosis. However, the extent to which viral or host-related metabolic factors contribute to hepatic steatosis in patients with chronic hepatitis B remains insufficiently clarified.

Objective

Aim of this study was to investigate the prevalence of metabolic disturbances and their association with necro-inflammatory changes and liver fibrosis in patients with viral hepatitis.

Methods

This study included 74 patients diagnosed with viral hepatitis. Clinical evaluation and laboratory investigations identified metabolic disturbances in 24 patients. Group 1 included patients with metabolic disturbances (n=24) and group 2 included those without metabolic disturbances (n=50). The groups were compared in terms of age, body mass index (BMI), viral load, and other biochemical parameters. Patients in group 1 were further categorized according to the severity of metabolic abnormalities.

Results

In group 1 (n=24), mean age, BMI, cholesterol, and HOMA-IR values were significantly higher compared with group 2 (n=50). There were no significant differences between the groups in viral load, HBeAg positivity, or other laboratory parameters. Logistic regression analysis identified HOMA-IR as the only independent predictor of metabolic disturbances in patients with viral hepatitis.

Conclusion

Metabolic disturbances in patients with viral hepatitis were primarily associated with host metabolic factors rather than viral characteristics. Early identification and management of these metabolic abnormalities may help prevent progression of liver injury.

Keywords

Viral Hepatitis, metabolic disturbances, BMI, liver function tests

Introduction

Hepatic steatosis (HS) and chronic viral hepatitis are both major contributors to chronic liver disease globally. Chronic hepatitis B (CHB) remains one of the leading causes of liver-related morbidity and mortality, with recent estimates indicating that approximately 350 million individuals worldwide are chronically infected with hepatitis B virus (HBV)[1]. Hepatic steatosis is characterized by excessive fat accumulation in hepatocytes, defined either as fat deposition exceeding 5% of the liver's total weight or involvement of more than 5% of hepatocytes on microscopic examination[2].

Multiple factors can induce HS, including medications, toxins, infections, and metabolic disturbances. Among these, non-alcoholic fatty liver disease (NAFLD) represents one of the most prevalent chronic liver disorders, affecting over a quarter of the general population. NAFLD is strongly associated with obesity, insulin resistance (IR), and metabolic syndrome, all of which contribute to hepatic lipid accumulation and progression of liver injury[3]. Importantly, metabolic dysfunction has been increasingly recognized as a critical determinant of liver disease progression, irrespective of viral etiology.

While the association between hepatitis C virus (HCV) infection and HS has been extensively documented, particularly in genotype 3 infection[4,5], the relationship between HBV infection and HS is less clear. Previous studies indicate that host metabolic factors and the direct cytopathic effects of HCV are significant contributors to hepatic fat accumulation[6]. In contrast, numerous large cohort studies have failed to demonstrate a strong association between HS and CHB[7,8]. Nonetheless, several reports suggest that metabolic factors, including obesity and insulin resistance, may exacerbate liver fat accumulation in patients with CHB[9–11], highlighting the complex interplay between host and viral determinants.

Given these considerations, understanding the prevalence and determinants of HS in CHB patients has become increasingly important. Investigating the contribution of metabolic abnormalities, including IR, alongside viral parameters, necroinflammatory activity, and fibrosis severity, can provide insights into disease progression and inform targeted clinical interventions.

The present study aimed to evaluate the prevalence of metabolic disturbances and hepatic fat accumulation in patients with viral hepatitis, examine their association with host metabolic factors and viral characteristics, and elucidate potential clinical and biochemical predictors of liver injury.

Materials and Methods

This cross-sectional study included 74 patients diagnosed with viral hepatitis. Among them, 24 patients were identified as having metabolic syndrome based on clinical evaluation and laboratory findings, while the remaining 50 patients did not exhibit metabolic abnormalities. Patients with a history of regular alcohol consumption, diabetes, known metabolic liver disease, autoimmune disease, or coinfection with HCV, HIV, or HDV were excluded from the study.

Demographic data, including age, sex, height, and weight, were recorded for all participants. Body mass index (BMI) was calculated as weight in kilograms divided by height in meters squared and categorized as normal (18.5–24.9), overweight (25–29.9), obese (30–34.9), or extremely obese (35–39.9). Laboratory assessments included liver function tests (ALT, AST, bilirubin, ALP), fasting glucose, cholesterol, triglycerides, insulin, C-peptide, ferritin, iron and iron-binding capacity, alpha-fetoprotein (AFP), and IGF-1 levels.

Insulin resistance (IR) was estimated using the Homeostasis Model Assessment (HOMA-IR) according to the formula: HOMA-IR = (fasting insulin [μU/mL] × fasting glucose [mmol/L])/22.5. Viral markers, including HBsAg and HBeAg, were measured using macro ELISA, and HBV DNA levels were determined by TaqMan real-time polymerase chain reaction (PCR).

The patients were divided into two groups: group 1 with metabolic syndrome (n=24) and group 2 without metabolic syndrome (n=50). Comparative analyses between the groups were performed for age, BMI, HOMA-IR, viral load, and other laboratory parameters to identify clinical and biochemical predictors of metabolic disturbances in patients with viral hepatitis.

Statistical analyses were conducted using SPSS 15.0 for Windows. Continuous variables were expressed as mean ± standard deviation or median (range), and categorical variables as frequencies and percentages. Student's t-test was applied for parametric comparisons, chi-squared test for categorical variables, and Pearson's correlation coefficient for correlation analyses. A two-tailed p-value < 0.05 was considered statistically significant.

Results

The 74 patients included in the study were divided into two groups according to the presence of metabolic syndrome: group 1 (n=24) with metabolic syndrome and group 2 (n=50) without metabolic syndrome (Table 1). Among the 24 patients in group 1, 10 (42%) were classified as overweight, 9 (38%) as obese, and 5 (20%) as extremely obese based on BMI criteria.

Of the 74 patients, 48 were male and 26 were female, and the mean age was 32 ± 1.2 years. Among the patients, 16 (33%) of the males and 8 (31%) of the females had metabolic syndrome. Male gender was associated with a slightly higher prevalence of metabolic syndrome, although the difference was not statistically significant (p = 0.08).

Patients in group 1 had significantly higher mean BMI, fasting glucose, cholesterol, and HOMA-IR values compared with group 2. No significant differences were observed between the groups in viral load, HBsAg, HBeAg status, or other routine laboratory parameters. Logistic regression analysis identified HOMA-IR as the only independent predictor of metabolic syndrome in patienMean age, BMI, cholesterol, and average HOMA-IR levels in the metabolic syndrome group (n=24) were significantly higher than those in the group without metabolic syndrome (n=50). Among all patients, 28 were HBeAg positive, of whom 9 (32%) had metabolic syndrome. The remaining 46 patients were HBeAg negative, and 15 (33%) of them had metabolic syndrome. No significant differences in hepatitis serology (HBeAg positivity) were observed between patients with and without metabolic syndrome (P > 0.05).

Necroinflammatory activity and fibrosis stage were not associated with the presence of metabolic syndrome. Seventeen patients had received treatment for viral hepatitis, of whom 5 had metabolic syndrome, whereas 57 patients were untreated, of whom 19 had metabolic syndrome. The difference in prevalence of metabolic syndrome between treated and untreated patients was not statistically significant.

Logistic regression analysis including age, sex, BMI, cholesterol, and HOMA-IR as independent variables identified HOMA-IR (OR = 1.66, 95% CI: 1.0–2.7) as the only factor significantly and independently predictive of metabolic syndrome in patients with viral hepatitis.

Discussion

In the present study, the presence of metabolic syndrome in patients with viral hepatitis was not associated with differences in viral markers, including HBeAg status. Insulin resistance (IR), a well-known contributor to metabolic abnormalities, was identified as the only independent predictor of metabolic syndrome in these patients. Over recent years, IR has emerged as a key factor in the progression of chronic liver diseases and has been linked to complications such as cirrhosis and hepatocellular carcinoma, similar to those observed in chronic HBV and HCV infection15. IR has also been shown to predict poor response to antiviral therapy in patients with HCV16.

While HCV infection has a well-established relationship with both hepatic steatosis and IR17, the association between HBV and metabolic liver changes remains less clear. Previous studies on CHB patients have reported conflicting results, with some showing no significant association between HBV infection and hepatic fat accumulation18,19, while others suggest that host metabolic factors, including obesity, IR, and dyslipidemia, contribute to liver fat deposition20,21.

In our study, age, male gender, BMI, serum cholesterol, HOMA-IR, and hypertension were strongly associated with metabolic syndrome. Interestingly, male patients showed a slightly higher prevalence of metabolic abnormalities. No correlation was observed between viral load and the presence of metabolic syndrome, and HBeAg positivity was not a significant factor. Triglyceride levels were also not significantly associated with metabolic syndrome in this cohort.

Furthermore, metabolic syndrome was not correlated with the severity of liver fibrosis or necroinflammatory activity, consistent with prior reports9,22. Logistic regression analysis confirmed that HOMA-IR was the primary determinant of metabolic syndrome among patients with viral hepatitis. Treatment status did not significantly influence the prevalence of metabolic syndrome, aligning with previous findings23,24.

The main limitations of this study include the relatively small sample size and reliance on univariate analyses for most comparisons.

Conclusion

Metabolic syndrome was observed in 32% of patients with viral hepatitis. In these patients, metabolic abnormalities—including obesity, insulin resistance, and dyslipidemia—were primarily responsible for liver fat accumulation rather than viral factors. These findings highlight the importance of early identification and management of metabolic dysfunction in patients with chronic viral hepatitis. Further large-scale studies are warranted to evaluate the impact of metabolic syndrome on liver disease progression and the response to antiviral therapy.

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