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ORIGINAL ARTICLE

Determination of Diabetes Mellitus among Hepatitis C Virus Associated Chronic Liver Disease

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ABSTRACT

Objective: Determination of diabetes mellitus among Hepatitis C Virus associated with chronic liver disease patients.

Patients and Methods: This cross sectional study was conducted in the central laboratory, department of Chemical Pathology, Allama Iqbal Medical College, Lahore, from 1stMay 2016 to 31stJanuary 2017. A total of 201 known cases of Chronic liver disease were included from medical wards of the Jinnah Hospital, Lahore. About 02 ml blood sample was collected from each individual for estimation of Fasting Blood Glucose and HbA1c. Patients were labeled as diabetic or non–diabetic according to the criteria for the diagnosis of diabetes mellitus described by American Diabetes Association 2017.

Results: Out of these 201 cases, 51% (n=103) were males and 49% (n=98) were females. Mean age of all participants was 55.2 + 10.6 years. Mean fasting blood glucose level was 201.9±111.0 mg/dl. Total 24.9% patients were found non-diabetic and remaining 75.1% were declared as diabetics.

Conclusion: High rate of diabetes mellitus was observed among hepatitis C virus associated chronic liver disease patients.

Key words: Chronic liver disease, Diabetes, Hepatitis C virus.

Author`s Contribution	Address of Correspondence	Article info.
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Introduction

Diabetes mellitus is one of the commonest diseases around the globe, and it is expected that by the year 2030 there will be 366 million people affected globally.[1] In the year 2000, global mortality due to diabetes was 2.9 million.[2] In Pakistan, It is estimated that 6.3 million persons have an age adjusted 7.9% prevalence of persons with diabetes (PWD) among adults, 20 years or older.[3] Pakistan, in 2030 will have an estimated 11.4 million persons with PWD and prevalence of 8.9% in the absence of major medications.[4]

There are many causes for Chronic Liver Disease (CLD), from which Hepatitis C Virus is most common. HCV was documented in 1989 as the primary agent of non-A, non-B hepatitis, which at the time accounted for almost 90

percent of all transfusion transmitted hepatitis cases in the United States.[5] Hepatitis C infection is one of the most alarming health problems globally, with an incidence of 200 million (3.3%) of the world's population.[6] Currently, about 4 million individuals in the United States are infected with HCV and 2.7 million of these people are acareers.[7] Nearly 30,000 new cases of HCV have been diagnosed annually, and more than two thirds appear to be related to parenteral route.[8] It is estimated that >10 million peoples are infected with HCV in Pakistan.[9]

HCV primarily affects the liver and ultimately causes cirrhosis,end-stage liver disease and hepatocellular carcinoma.[10] HCV-associated CLD is responsible for 8,000-10,000 mortalities per year and for 25 percent of all liver transplantations in the United States.[8,11]Association of DM and liver cirrhosis was first described by Bohan et al [12] and designated as hepatogenous diabetes in a study conducted by Megyesi et al[13] in which 57% of cirrhotic patients were found to have insulin resistance. Near about 80% of CLD patients may be glucose intolerant and between 10–20% may be clinically diabetic.[14] The liver is chiefly responsible for glucose homeostasis and store or release of glucose according to metabolic needs. In diabetes or insulin resistant states, impaired hepatic glucose release contributes considerably to the pathophysiology of those conditions. HCV infection is a known risk factor for hepatocellular carcinoma (HCC) and rising risk of HCC by 2–4 folds even after adjusting for other predisposing factors.[14] Acute or chronic liver disease can augment insulin resistance and effects of insulin on hepatocyte are disturbed.[15] In presence of hepatic disease, the metabolic homeostasis of glucose is deranged as a result of insulin resistance, glucose intolerance, and diabetes. Insulin resistance develops not only in muscle but also in adipose tissue which combined with hyperinsulinemia may seem as important pathophysiologic basis of diabetes in chronic liver disease.[16] Glucose absorbed from the intestinal tract is transported from portal vein to liver where most of the glucose is retained by the liver so that most of the rise in peripheral glucose concentration is a reflection of only a minor component of postprandial absorbed glucose. It is suggested that liver plays a more significant role than peripheral tissues in maintaining systemic blood glucose level following a meal.[14]

DM in patients of CLD may be subclinical hepatogenous diabetes is clinically different from type 2 DM since it is less frequently associated with microangiopathy and patients more often undergo complications of cirrhosis and increase the death rate is because of cirrhosis.[16] There are several international studies, that have reported association of diabetes with CLD, but very few such studies have been published from our region. The rationale behind this study was to ascertain the frequency of DM in patients of CLD.

Patients and Methods

This cross sectional study was conducted in Department of Chemical Pathology, Allama Iqbal Medical College, Lahore, from 1st May 2015 to 31st January 2016. Study was approved by ethical review board of the Institute. Total 201 patients of HCV associated chronic liver diseases of either gender were inducted from medical wards of the Jinnah Hospital, Lahore. Diagnosis of CLD was made by clinician of the ward on the basis of laboratory investigations and ultrasonography.[18] Patients with acute stage of liver disease, renal failure, known for Diabetes, HBV or any other virus career and those who refused to become the part of the study were excluded from the study. All participants were requested for overnight (10–12 hours) fast. Next morning 01 ml blood sample in sodium fluoride tube was collected from each individual for estimation of FBG. Similarly, 01 ml blood was taken in EDTA tube for HbA1c analysis. All specimens were transported to the lab under standardized conditions. Centrifugation was done at 2500 rpm for 5-7 minutes. Blood glucose was estimated by endpoint enzymatic (Glucose Oxidase – PAP) method, using diagnostic reagents on semi-automated chemistry analyzer (MicroLab-300) manufactured by Merck. HbA1c was analyzed by Beck-man coulter Access 2 automatic special chemistry analyzer by using immunoassay technique. Based on the findings of FBG and HbA1c, patients were labeled as diabetic or non–diabetic according to the criteria for the diagnosis of DM as described by American Diabetes Association 2017. SPSS 21.0 was used for statistical analysis. Frequency and percentages were calculated

Results

Among 201 cases, 51% participants (n=103) were males and 49% (n=98) were females. Mean age of all patients was 55.2 ± 10.6 years. Mean FBG was 201.9±111.0 mg/L. Total 24.9% individuals were found non-diabetic and remaining 75.1% were declared as diabetics (Table 1). Thus diabetic population was 75 % (151/201) of the whole study population. Among 75 % of diabetic population, 49% (74/151) were female and 51% (77/151) were male.

Table 1: Fasting Glucose and Glycated Hemoglobin in CLD patients

Groups	Frequency	Percentage
Non-Diabetic (Glucose < 100 mg/dl), HbA1c (<6.5%)	50	24.9
Diabetic (Glucose ≥ 126 mg/dl), HbA1c (≥6.5%)	151	75.1
Total	201	100

Discussion

Hyperglycemia is seen in patients of CLD, after ingestion of oral glucose, resulting in hyperglycemia in central circulation and leading to impairment of glucose uptake by peripheral tissues due to insulin resistance.[8] In our study, 250 cases of CLD have been evaluated for the prevalence of DM. We found that 75% of our study population was diabetic. Multiple researchers have reported the prevalence of DM (12.9 – 23.2%) from different regions of the globe.[19-21] In Pakistan, the previously reported prevalence of DM is 18.7 – 34.8%.[22-24] This rate is low as compared to our study. The basic reason for this higher prevalence is still unknown but few researchers have reported that persons of old age 40 years or above with hepatitis C infections are more likely to have diabetes.[25] Our findings are in agreement with this. Another reason for this highest prevalence may be due to the population difference as previous researches has been done in different areas of Pakistan but our study population was patients admitted in Jinnah Hospital, Lahore which one of the major referral/teaching hospital of the province. Among 75 % (151/201) of diabetic population, 49% (74/151) were female and 51% (77/151) were male. The gender difference was not a significant factor in our study as both genders were almost equally enrolled. However, in a previous study, it was found that DM was dominant in males.[26]

Many researchers have also reported the association of chronic liver disease and impaired glucose tolerance. A study conducted in Larkana, Pakistan reported 78% prevalence of DM in a population of cirrhosis.[27] The exact pathophysiology underlying the association of chronic hepatitis C with DM is still unknown. A detailed knowledge of the underlying cause of HCV associated glucose metabolism disturbance is warranted, in order to improve clinical management of chronic hepatitis C patients.[28,29] Accumulation of fat in liver cells is also a factor for the development of insulin resistance as described by many researchers. Steatosis in HCV positive cases is also closely related to expression of HCV core protein and possibly, it is related to change metabolic profile.[30] All patients who are suspected for CLD should be screened for DM from time to time. If management of high blood glucose level is addressed in patients of CLD, this will reduce the risk of complications associated with diabetes in these patients. This study was a single center cross sectional study with small sample size. Multicenter Cohort studies should be conducted on a large sample size so the exact phenomena for the development of DM in chronic liver disease cases may be described.

Conclusion

The frequency of diabetes mellitus in patients suffering from chronic liver disease was high. This can be controlled and managed by the early detection of blood glucose level in chronic liver disease cases. Early detection of DM may avoid micro or macro angiopathic complications of DM and life expectancy of such patients can be improved.

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