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Original research article

Evaluation of Random Blood Sugar in Chronic Liver Disease Patient of Bihar

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Abstract

Background: Liver is one of the important target organ for insulin and its counter regulatory hormones, such as glucagon. Chronic liver disease (CLD) is often associated with glucose intolerance and diabetes. Glucose intolerance and frank diabetes are seen in a lot number of patients with chronic liver disease. The number of CLD patients continues to increase in INDIA because of alcohol (ethanol) consumption and epidemics of obesity and non-alcoholic fatty liver diseases (NAFLD).

Methods: This is a observational, study (descriptive study) of 60 patients admitted in the wards of, Department of General Medicine, Jawaharlal Nehru Medical College and Hospital, Bhagalpur. Study period of June 2020 to Sep 2021 who matched the inclusion criteria. Data was collected after obtaining informed/written consent from patient. Detailed history, clinical examination, general physical and systemic examination and relevant laboratory investigations were done.

Conclusion: The occurrence of glucose metabolism disorder in chronic liver disease was high. OGTT helped in unmasking diabetes in many patients. The number of impaired glucose tolerance and diabetics were more in Child Pugh B and C compared to Child Pugh A**.**

Keyword: Glucose tolerance, CLD, NAFLD.

Introduction

The liver is the largest organ in the human the body, which plays a major in various important functions which are essential for the human body. Liver is involved in synthesis of carrier proteins and metabolism of various hormones. In another key function and an important role is in the metabolism of gonadal hormones and synthesisof sex hormone binding globulin. Liver is one of the important target organ for insulin and its counter regulatory hormones, such as glucagon. Chronic liver disease (CLD) is often associated with glucose intolerance and diabetes. Glucose intolerance is seen in upto 80% of patients with CLD, and frank diabetes is present in 30%-60%. Depending on aetiology, CLD, hasa significant impact on hepatic glucose metabolism. The number of CLD patients continues to increase in INDIA because of alcohol(ethanol)consumption and epidemics of obesity and non alcoholic fatty liver diseases (NAFLD). in some sub population such as morbidly obese the prevalence of NAFLD is high.The association of NAFLD with concurrent diabetes increases general mortality. Diabetes developed as a complication of cirrhosis is known as hepatogenous diabetes (HD). Around 30% to 60% of cirrhotic patients suffer from this metabolic disorder. Insulin resistance in

muscular, hepatic and adipose tissues as well as hyperinsulinemia, seem to be pathophysiologic bases for HD. An impaired response of the islet ss-cells of the pancreas and the hepatic insulin resistance are also contributing factors. These limitations must be understood to avoid misinterpretation of results. A1c levels in CLD are frequently falsely low limiting the utility of A1c in these patients. Non-alcoholic fatty liver disease (NAFLD), alcoholic cirrhosis, chronic hepatitis C (CHC), and hemochromatosis are more frequently associated with HD. HD inearly cirrhosis stages may be sub clinical. Only insulin resistance and glucose intolerancemay be observed. About 30% of patients with cirrhosis have diabetes mellitus (DM). Insulin resistance in muscular and adipose tissues and hyperinsulinemia seem to be the pathophysiologic bases of diabetes in liver disease. Non-alcoholic fatty liver disease, alcoholic cirrhosis, chronic hepatitis C (CHC) and hemochromatosis are more frequently associated with DM. Insulin resistance increases the failure of the response to treatment in patients with CHC and enhances progression of fibrosis. Hepatogenous diabetes is clinically different from that of type 2 DM, since it is less frequently associated with microangiopathy and patients more frequently suffer complications of cirrhosis. DM increases the mortality of cirrhotic patients. Due to the persistent glucose intolerance in patient with chronic liver disease especially cirrhosis, more studies related to this problem are needed. Hence we decided to undertake the study to assay the severity of glucose intolerance in patients with the various class of chronic liver disease.

Objectives

To study the relationship between chronic liver disease and impaired glucosetolerance and diabetes based on OGTT, To study the risk factors associated with impaired glucose tolerance in CLD.

Review of Literature

The liver is the largest organ of the body, weighing 1–1.5 kg and representing 1.5– 2.5% of the lean body mass. The size and shape of the liver vary and generally match the general body shape—long and lean or squat and square. This organ is located in the right upper quadrant of the abdomen under the right lower rib cage against the diaphragm and projects for a variable extent into the left upper quadrant. It is held in place by ligamentous attachments to the diaphragm, peritoneum, great vessels, and upper gastrointestinal organs. The liver receives a dual blood supply; ~20% of the blood flow is oxygen-rich blood from the hepatic artery, and 80% is nutrient-rich blood from the portal vein arising from the stomach, intestines, pancreas, and spleen(1).

The majority of cells in the liver are hepatocytes, which constitute two-thirds of the organ‘s mass. The remaining cell types are Kupffer cells (members of the reticuloendothelial system), stellate (Ito or fatstoring) cells, endothelial and blood vessel cells, bile ductular cells, and cells of supporting structures. Viewed by light microscopy, the liver appears to be organized in lobules, with portal areas at the periphery and central veins in the center of each lobule. However, from a functional point of view, the liver is organized into acini, with both hepatic arterial and portal venous blood entering the acinus from the portal areas (zone 1) and then flowing through the sinusoids to the terminal hepatic veins (zone 3); the intervening hepatocytes constitute zone 2. Blood flowing into the portal areas is distributed through the sinusoids, passing fromzone 1 to zone 3 of the acinus and draining into the terminal hepatic veins (―centralveins‖). Secreted bile flows in the opposite direction—i.e., in a counter-currentpattern from zone 3 to zone 1. The sinusoids are lined by unique endothelial cells that have prominent fenestrae of variable sizes, allowing the free flow of plasma but not ofcellular elements. The plasma is thus in direct contact with hepatocytes in thesubendothelial space of Disse. Hepatocytes have distinct polarity. The basolateral sideof the hepatocyte lines the

space of Disse and is richly lined with microvilli; itexhibits endocytotic and pinocytotic activity, with passive and active uptake ofnutrients, proteins, and other molecules. The apical pole of the hepatocyte forms thecanalicular membranes through which bile components are secreted. The canaliculi of hepatocytes form a fine network, which fuses into the bile ductular elements near the portal areas. Kupffer cells usually lie within the sinusoidal vascular space and represent the largest group of fixed macrophages in the body. The stellate cells are located in the space of Disse but are not usually prominent unless activated, whenthey produce collagen and matrix. Red blood cells stay in the sinusoidal space asblood flows through the lobules, but white blood cells can migrate through or aroundendothelial cells into the space of Disse and from there to portal areas, where they canreturn to the circulation through lymphatics. Hepatocytes perform numerous and vital roles in maintaining homeostasis and health. production of bile and its carriers (bile acids,cholesterol, lecithin, phospholipids), the regulation of nutrients (glucose, glycogen, lipids, cholesterol, amino acids), and the metabolism and conjugation of lipophilic compounds (bilirubin, anions, cations, drugs) for excretion in the bile or urine. Measurement of these activities to assess liver function is complicated by the multiplicity and variability of these functions. Evaluation of patients with liver disease should be directed at (1) establishing the etiologic diagnosis, (2) estimating disease severity (grading), and (3) establishing the disease stage (staging). Diagnosis should focus on the category of disease(hepatocellular, cholestatic, or mixed injury) as well as on the specific etiologic diagnosis. Grading refers to assessment of the severity or activity of disease—activeor inactive as well as mild, moderate, or severe. The natural history of cirrhosis is characterized by an asymptomatic phase, referred toas –compensated cirrhosis, followed by a progressive phase marked by the development of complications of portal hypertension and/or liver dysfunction, designated –decompensated cirrhosis. In the compensated phase portal pressure may be normal or below the threshold of clinically significant portal hypertension although esophageal varices may appear still in the compensated phase of the disease. Decompensation is defined by the development of ascites, portal hypertensive gastrointestinal (GI) bleeding, encephalopathy, or jaundice. SAGT disorders were associated with reduced long term survival in patients with compensated LC and normal FPG. Additionally, SAGT, Child-Pugh B, and high Child-Pugh and MELD scores were independent negative predictors of survival.These findings suggest that SAGT may give rise to morbid conditions that increase mortality of patients.

Material and methods

This is a observational, study (descriptive study) of 60 patients admitted in the wards of, Department of General Medicine, Jawaharlal Nehru Medical College and Hospital, Bhagalpur, Bihar. Study period of June 2020 to Sep 2021 who matched the inclusion criteria. Datawas collected after obtaining informed/written consent from patient. Detailed history, clinical examination, general physical and systemic examination and relevant laboratory investigations were done. study was conducted on the patients admitted in the wards of, JLNMCH, Bhagalpur. will be taken for study considering the inclusion and exclusion criteria.
All patients were interviewed as per the proforma and a complete clinicalexamination will be done.

Diagnosis of chronic liver disease was based on thorough clinical evaluation,biochemical investigations and USG abdomen.

Inclusion criteria

All patients of chronic liver disease, who do not have the history of diabetes, admitted in medical wards JLNMCH, Bhagalpur, Bihar.

Exclusion criteria

Age <18years, Known cases of diabetes mellitus**,** Patients receiving insulin, oral hypoglycemics, drugs like corticosteroids,Thiazides , Patients with chronic pancreatitis.

Chronic liver disease in the clinical context is a disease process of the liver that involves a process of progressive destruction and regeneration of the liverparenchyma leading to fibrosis and cirrhosis. It refers to disease of the liver which lasts over a period of 6 months. It consists of a wide range of liver pathologies which include inflammation (chronic hepatitis), liver cirrhosis.

Results

Table 1: Gender distribution of subjects studied

Gender	No. of subjects	%
Female	13	21.7
Male	47	78.3
Total	60	100.0

The total number of subjects studied are 60. The number of males were 47(78.3%)and the number of females were 13(21.7%).

Table 2: Age distribution of subjects studied

Age in years	No. of subjects	%
<30	1	1.7
30-40	18	30.0
41-50	14	23.3
51-60	19	31.7
61-70	8	13.3
Total	60	100.0

Mean ± SD: 48.32±11.07

The mean age group of the subjects studied was 48.32±11.07 years. The majority ofthe subjects were belonging to the age group 51-60 years and 41-50 years.

Table 3: Hemoglobin (g/dl) distribution of subjects studied

Hemoglobin (g/dl)	No. of subjects	%
<12	30	50.0
12-16	29	48.3
>16	1	1.7
Total	60	100.0

Mean ± SD: 11.29±2.85

The mean of the hemoglobin distributed among the subjects was 11.29±2.85 g/dl. Majority of the subjects were anemic. The number of subjects with hemoglobin lessthen 12g/dl were 30(50%).

Table 4: Total Bilirubin (µmol/L) distribution of subjects studied

Total Bilirubin (µmol/L)	No. of subjects	%
<2	28	46.7
2-3	17	28.3
>3	15	25.0
Total	60	100.0

Mean ± SD: 2.52±1.95

The mean distribution of total bilirubin among the subjects studied is 2.52±1.95µmol/L. The number of subjects with total bilirubin <2 was 28(46.7%), 2-3 was 17(28.3%), >3 was 15(25%).

Table 5: Total Protein distribution of subjects studied

Total Protein	No. of subjects	%
<5	5	8.3
5-7	49	81.7
>7	6	10.0
Total	60	100.0

Mean ± SD: 6.05±0.82

The mean of the total protein among the subjects was 6.05±0.82. Number of subjectswith protein <5 were 5(8.3%), 5-7 were 49(81.7%), >7 were 6(10%).

Table 6: Serum Albumin (mg/dl) distribution of subjects studied

Serum Albumin(mg/dl)	No. of patients	%
<2.8	21	35.0
2.8-3.5	29	48.3
>3.5	10	16.7
Total	60	100.0

Mean ± SD: 2.92±0.53

The mean of the serum albumin distributed among the patient was 2.92±0.53mg/dl. The number of subjects with albumin<2.8 were 21(35%), 2.8-3.5 were 29(48.3%) and>3.5 were 10(16.7%).

The occurrence of glucose metabolism disorder in our study is 53.3% which was diagnosed with the help of OGTT; out of which 38.3% had impaired glucose tolerance; 5% had impaired fasting glucose and 10% had diabetes mellitus. Among the subjects in child pugh class A 71.4% had normal glucose tolerance and 28.6% hadglucose metabolism disorder. In child pugh class B, 41.4% had normal glucose tolerance and 28.6% had glucose metabolism disorder. In child pugh class C, 35.3% had normal glucose tolerance and 64.7% had glucose metabolism disorder. Among the subjects in child class A 28.6% had impaired glucose tolerance and none had impaired fasting glucose or diabetes mellitus. In child class B 41.2% had impaired glucose tolerance, 11.8% had impaired fasting glucose and 13.8% had diabetes mellitus.

Discussion

Liver plays a major role in glucose metabolism. In CLD, the homeostasis of glucose metabolism is impaired as a result of which insulin resistance, glucose intolerance anddiabetes mellitus occurs. Diabetes which develops as a complication of liver disease is known as ‗hepatogenous diabetes‖. The natural history of hepatogenous diabetes is different from that of hereditary type 2 diabetes mellitus. Patients with hepatogenous diabetes suffer more from the complication of cirrhosis. Diabetes in patients with liver cirrhosis maybe subclinical as the fasting glucose levelsmaybe normal; hence OGTT is preferred to detect the impairment of glucose metabolism. Our study is relevant because it prospectively assessed overt and subclinical glucose metabolism disorders. The occurrence of glucose metabolism disorder in our study is 53.3% which was diagnosed with the help of OGTT; out of which 38.3% had impaired glucose tolerance; 5% had impaired fasting glucose and 10% had diabetes mellitus. This implies that the patients with chronic liver disease are at high risk for glucose metabolism disorder. In Rym ennaifer et al. study of glucose metabolism disorders in cirrhosis of liver in the tunisisan population, 68.8% had glucose metabolism disorders; 42.8% were diabetics and 6% had impaired glucose tolerance, which is times more than the general population (9.9% vs 42.8%), indicating that patients with cirrhosis are at high risk for glucose metabolism disorders. a study by Diego Gracia et al. of the included patients 30 had normal glucose tolerance and 70 had subclinical abnormal glucose tolerance(SAGT); found that in liver cirrhosis patients who had SAGT the long term survival was reduced. Additionally, high Child Pugh scores were independent negative predictorsof survival. In our the number of patients with glucose metabolism disorders were more in Child Pugh class B and C were 58.6% and 64.7% respectively when compared to child A 28.6%.(61) In Majumder et al study, in the year 1967, 57% was the incidence of glucose intolerance in the cirrhotics(62). In Vij J C et al study in the year 1976, 42.5% was theincidence of glucose intolerance in the cirrhotics(62). In Saini J S et al study in the year 1992, 44% was the incidence of glucose intolerance in the cirrhotics(63). In Muller MJ et al study in the year 1994, the incidence of glucose intolerance is 73%. In a study carried out in japan, with 58 cirrhotics without overt diabetes who underwent OGTT; they found that albumin and abnormal OGTT were independent predictors of survival(64) In our study also significant number patients had hypoalbuminemia. About 83.3% had serum albumin <3.5g/dl. Despite of the similarities in results in both the studies, ours differs in the following points – 74% of the Gracia et al. study had alcoholic and cryptogenic cirrhosis, 78.5% of patients in Japanese study had viral etiology(HBV and HCV).

Conclusion

we can say that majority of the patients with chronic liver disease have glucose metabolism disorder. Some patients were found to have frank diabetes and some had impaired glucose tolerance and impaired fasting glucose. In our study majority of the patients with chronic liver disease were males. One of the main cause for chronic liver disease was alcoholic liver disease. In our study majority of patients had anemia and hypoalbuminemia, showing their significance in chronic liver disease.

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