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Original Research Article

BLOOD GLUCOSE LEVEL IN ALCOHOLIC LIVER DISEASE - A HOSPITAL BASED CROSS SECTIONAL STUDY

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Abstract

Background: The spectrum of alcohol-related liver injuries varies from simple steatosis to cirrhosis. In the presence of hepatic disease, the metabolic homeostasis of glucose is impaired. The aim of this study was assess the alteration of blood glucose in alcoholic liver disease. **Materials and Methods:** A cross sectional study was conducted from October, 2014 to September, 2016 in the Department of Medicine, Regional Institute of Medical Sciences (RIMS) Hospital, Imphal, Manipur. Nondiabetic Patients with alcoholic liver disease admitted in ward during the study period were included in the study. Age and gender were the independent variable. Fasting blood sugar (FBS) and post prandial blood glucose (PPBS) were the dependent variable. Data collected were analyzed using SPSS-version-21. Mean, Standard deviations and proportions were used as descriptive data. **Result:** 106 patients were recruited for the study and 94.3% were males. The mean age of the patients was 49.79 ± 10.7 years. 45% and 46.2% of patients had normal fasting glucose and normal post prandial blood sugar, respectively. Similarly, 34% and 35.8% of the patients had impaired fasting glucose and impaired glucose tolerance, respectively. **Conclusion:** This study concludes that the prevalence of DM and IGT was found to be 23.6% and 40.6% respectively. So routine screening of patients with alcoholic liver disease for the presence of disorders of glucose metabolism is warranted.

INTRODUCTION

Alcohol is the world's third largest risk factor for disease and disability; causing at least 60 types of diseases and contributing to 200 others.[1] Globally, high-income countries of the developed world have the highest alcohol consumption, with 50.1% of the US population (adults over 18 years of age) being current regular drinkers.[2] In India alcohol users is around 61 million, of whom around 10 million have alcohol dependence.[3] In view of the magnitude of the problem, it becomes necessary for us to understand the effect of alcohol on various body systems. Indeed, alcohol affects almost all organs and systems of the human body.[4] The spectrum of alcohol-related liver injuries varies from simple steatosis to cirrhosis. These are not necessarily distinct stages of evolution of disease, but rather, multiple stages that may be present simultaneously in a given individual.[5] These are often grouped into three histological stages of ALD: fatty liver or simple steatosis, alcoholic hepatitis, and chronic hepatitis with hepatic fibrosis or cirrhosis.[6] These latter stages may also be associated with a number of histologic changes (which have varying degrees of specificity for ALD), including the presence of Mallory's hyaline, megamitochondria, or perivenular and perisinusoidal fibrosis.[7] The liver has an important role in carbohydrate metabolism since it is responsible for the balance of blood glucose levels, by means of glycogenogenesis and glycogenolysis. In the presence of hepatic disease, the metabolic homeostasis of glucose is impaired and resulting to disorders such as insulin resistance, glucose intolerance and diabetes. Insulin resistance occurs not only in muscular tissue, but also in adipose tissue, and this combined with hyperinsulinemia seem to be important pathophysiologic bases of diabetes in liver disease.[8]

Up to 96% of patients with cirrhosis may be glucose intolerant and 30% may be clinically diabetic.[9] Currently, it is a matter for debate weather Type 2

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diabetes mellitus , in the absence of other risk factors contributing to metabolic syndrome (obesity and hypertriglyceridemia), could be a risk factor for the development and progression of liver disease.[10] On the other hand, Diabetes which develops as a complication of cirrhosis is known as "hepatogenous diabetes" and is not recognized by the American Diabetes Association and the World Health Organisation as a specific independent entity.[11]

Depending on the etiology, the degree of liver damage and the diagnostic criteria, the reported incidence of glucose intolerance varies from 60 to 80% and that of diabetes between 20 and 60%.[12] It is known that from the early stages of chronic liver disease, insulin resistance and glucose intolerance may be found in most of these patients.[13] The diabetes manifests clinically as the liver function deteriorates, thus hepatogenous diabetes can be considered as an indicator of advanced liver disease.[14]

Patients with alcoholic liver disease have a high relative risk of suffering diabetes.[15] This risk is directly related to the amount of ingested alcohol, as it rises 2-fold in patients ingesting more than 270 g of alcohol per week compared with those ingesting less than 120 g/wk.[16] Acute alcohol ingestion produces a significant reduction in insulin-mediated glucose uptake. On the other hand, patients with chronic alcoholism frequently have chronic pancreatic damage and injury of pancreatic islet ß-cells resulting in DM.[9] Thus this study was conducted to evaluate the alteration in blood glucose in alcoholic liver disease in this part of the country.

MATERIALS AND METHODS

A cross sectional study was conducted between October 2014 and September 2016 in the Department of Medicine and in collaboration with the Department of Biochemistry, Regional Institute of Medical Sciences (RIMS). Alcoholic liver disease patients above 18 years admitted in medicine ward during the study period were included in the study population. Those who refused to participate, those with history of Hepatitis B, Hepatitis C, HIV infected patients, those who were diagnosed as diabetes mellitus before the onset of alcoholic liver disease and patients on anti-tubercular drugs were excluded from the study. Hundred and six patients who fulfilled the above criteria were enrolled into the study.

Variables like age, sex, liver function test, prothrombin time, INR and serum creatinine were analysed. Dependent variables were fasting blood sugar (FBS) and post prandial blood glucose (PPBS).

Working definition: Alcoholic Liver disease is diagnosed from significant alcoholic history, signs and symptoms of liver disease and derangement in liver function tests. Significant alcoholic history includes chronic alcohol intake of 40 to 80 gram of alcohol daily for men and 20 to 40 gram for women. Clinical features include jaundice, parotid enlargement, duputyren's contracture, spider naevi, abdominal distension and splenomegaly. Laboratory abnormalities include elevated liver enzymes (AST/ALT>1), elevated bilirubin and deranged prothrombin time and INR.[17]

Procedures: All patients who fulfilled the inclusion criteria were considered for the study. Patient particulars were noted and detailed history with particular importance to alcoholic history was taken. A complete general physical examination and detailed systemic examination was carried out in all the patients with due importance for signs of liver failure.[18] Fasting blood sugar, two hour post prandial blood sugar were measured by autoanalyser (Human Gesellschaft Für Biochemica und Diagnostica mbh, Germany) using glucose oxidase method.

Test principle (FBS, PPBS): In the Trinder reaction,[19,20] the glucose is oxidized to D-gluconate by the glucose oxidase (GOD) with the formation of hydrogen peroxide. In the presence of peroxidase (POD), a mixture of phenol and 4-aminoantipyrine (4-AA) is oxidized by hydrogen peroxide, to form a red quinoneimine dye proportional to the concentration of glucose in the sample. Ultrasound abdomen was done to check liver status. Routine investigations (complete blood count, liver function test, kidney function test, random blood sugar, urine routine examination), and other relevant investigations (PT, INR, HbsAg, anti HCV antibody, HIV antibody) were done. The collected data were entered and analyzed in SPSS (IBM) version 21. Summarization of data was carried out by using descriptive statistics such as mean, median, standard deviation and percentages. Either $\chi 2$ test or Fisher's exact test were used for categorical variables, and t-test or ANOVA for continuous variables. P-value < 0.05 was taken as statistically significant. Ethical approval was obtained from the ethical committee of the institute (IEC No. AC/112/EC/RIMS/2005) before the commencement of the study.

RESULTS

This study included 106 patients of alcoholic liver disease admitted in the Medicine wards, Regional Institute of Medical Sciences, Imphal from October 2014 to September 2016. Mean age of the patients was 49.79 ± 10.7 years and the most common age group was 41-50 years (33%) [Table 1]. Majority of the patients were male which accounted for 94.3% of cases [Table 2]. Nearly half of patients (45.2%) had normal fasting glucose, 34% had impaired fasting glucose and 20.8% had Diabetes [Table 3]. Similarly, 46.2% had normal post prandial blood sugar, 35.8% had impaired glucose tolerance and 17.9% had diabetes. Majority of the patients (98%) had raised bilirubin maximum being 1-10 (67.9%). Eighty nine percent of patients had raised SGOT (>40), 83% had raised SGPT (>30). All the patients had low albumin (<3.5) of which 62.3% had < 2.5. 88.7% of patients

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had reversal of A:G Ratio(<1) [Table 4]. Majority of the patients had coagulopathy with raised PT (>14) among 79.2% of patients and 92.5% of patients had raised INR (>1.2) [Table 5].

Nearly one-third of the patients (32.1%) had raised serum creatinine (>1.6) [Table 6]. The prevalence of impaired glucose tolerance (IGT) and diabetes mellitus (DM) among studied population was shown in [Table 7] where IGT was found in 43 patients (40.6%) and DM in 25 (23.6%) patients. [Table 8] shows out of six female patients four had IGT and two had normal glucose tolerance which is statistically insignificant (p=0.374).

Table 1: Age distribution of patients (N = 106)

Age in years	No. of patients	Percentages	Mean ± SD
30-40	25	23.6	49.7 ± 10.78 years
41-50	35	33.0	
51-60	31	29.2	
61-70	10	9.4	
71-80	4	3.8	
>80	1	0.9	
Total	106	100.0	

Table 2: Distribution of the patients by gender (N=106)

Gender	No. of patients	Percentages
Female	6	5.7
Male	100	94.3
Total	106	100.0

Table 3: Distribution of the patients by blood sugar levels (N=106)

Blood sugar level (mg/dl)		No. of patients	Percentages
FBS (mg/dl)	< 100	48	45.2
	100-125	36	34.0
	≥ 126	22	20.8
PPBS (mg/dl)	<140	49	46.2
	140-199	38	35.8
	≥ 200	19	17.9

Table 4: Distribution of the patients by liver function test parameters (N=106)

Liver function tests		No. of patients	Percentages
Total Bilirubin	<1	2	1.9
	1-5	44	41.5
	5-10	28	26.4
	>10	32	30.2
SGOT	5-40	12	11.3
	40-120	70	66.0
	>120	24	22.6
SGPT	5-30	18	17.0
	30-90	78	73.6
	>90	10	9.4
Albumin	<2.5	66	62.3
	2.5-3.5	40	37.7
	>3.5	0	0.0
A:G Ratio	<1	94	88.7
	>1	12	11.3

Table 5: Distribution PT/INR among the patients (N=106)

Coagulation profile		No. of patients	Percentages
PT	<11	2	1.9
	11-14	20	18.9
	>14	84	79.2
INR	0.8-1.2	8	7.5
	1.2-2	64	60.4
	>2	34	32.1

Table 6: Serum Creatinine (mg/dl) distribution in patients studied

Serum Creatinine (mg/dl)	No. of patients (n=106)	Percentages
<1.6	72	67.9
>1.6	34	32.1
Total	106	100.0

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Table 7: Prevalence of IGT/DM in patients studied

IGT/DM	No. of patients	Percentages
Normal	38	35.8
IGT	43	40.6
DM	25	23.6
Total	100	100.0

Table 8: Gender distribution of patients studied in relation to ICGT and DM

Gender	IGT/DM, n(%)			Total, n(%)
	Normal	IGT	DM	
Female	2(5.3%)	4(9.3%)	0(0%)	6(5.7%)
Male	36(94.7%)	39(90.7%)	25(100%)	100(94.3%)
Total	38(100%)	43(100%)	25(100%)	106(100 %)

P=0.374, Not significant, Fisher test

DISCUSSION

In this study, the mean age of alcoholic liver disease patients was 49.79±10.78. This is agreeable with observation made in other studies.[21] Majority of the patients 100 (94.3%) were male. This may be because alcohol consumption is less prevalent among females in this part of the world.

Liver function tests assessed among the patients shows, total bilirubin was raised with mean of 8.02±6.55, SGOT was raised with mean 112.40±96.86, SGPT was raised with mean 56.63±39.33, 100% of the patients had low albumin (<3.5) with mean 2.35±0.48. Mean PT was raised with mean 19.25±5.25, INR was raised with mean 2.02±0.89. All the parameters were consistent with the alcoholic liver disease.[17] Majority of the patients 94 (88.7%) had reversal of A:G ratio which is indicative of chronicity of the disease. USG abdomen shows features of liver parenchymal disease (cirrhosis) in 98 (92.5%) and remaining had hepatomegaly with ascites.

This study is done exclusively on alcoholic liver disease. As we excluded the patients who were diagnosed to have DM before the onset of liver disease, the prevalence of DM which is observed in this study can be considered as HD. Mean fasting blood sugar (FBS) of patients was 105±29.47 mg/dl and mean post prandial blood sugar (PPBS) was 155.38±49.97 mg/dl. Both the parameters were in impaired glucose tolerance range. ADA guidelines were used to define IGT and DM. In this study the prevalence of IGT and DM in alcoholic liver disease was as follows: DM in 25 patients (23.6%) and IGT in 43 patients (40.6%). The results were consistent with a similar study by Garcia-Compean D et al,[22] done on cirrhosis of liver, which showed prevalence of HD in 28 patients (21.5%) and IGT in 36 patients (38.5%).

CONCLUSION

This study concludes that the prevalence of DM and IGT was found to be 23.6% and 40.6% respectively. So routine screening of patients with alcoholic liver disease for the presence of disorders of glucose metabolism is warranted.

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