



Impaired Glucose Regulation in Cirrhosis Liver – The Utility of Oral Glucose Tolerance Test

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Abstract

Background and Objectives: *Liver is one of the major organs to be involved in carbohydrate metabolism, and hence it is no surprise that chronic liver disease is associated with derangements in glucose metabolism. The objectives of this study is to find out the prevalence and clinical implications of the spectrum of glucose metabolism disorders (IGT/DM) in CLD and assess and compare the prognosis of the disease using the Child-Turcotte-Pugh scoring.*

Methods: *This study was conducted over a period of six months and included 50 patients. Detailed clinical examination along with biochemical and radiological investigations were carried out. OGTT was then performed in these individuals. Patients who were known diabetics, drugs causing hyperglycemia and pregnant women were excluded from the study.*

Results: *CLD was much more common in males. There was a significant percentage of IGT/DM diagnosed in these patients using OGTT. The results were, 36%-IGT and 28% DM. It was also proved that as the severity of disease worsened, which was assessed by CTP scoring, the degree of hyperglycemia also increase proportionately. The percentage of impaired glucose regulation in Child class A was 47% , class B 68% and class C 93%*

Keywords: *Chronic liver disease, oral glucose tolerance test, impaired glucose tolerance, diabetes mellitus.*

Introduction

Liver plays a central role in blood glucose regulation¹ and it is proved beyond doubt that chronic liver disease is associated with abnormalities of metabolism of carbohydrates. Advanced liver diseases manifest with metabolic derangements and this is regardless of the aetiology of the disease. To some extent, the abnormalities observed in the late stages of cirrhosis, regardless of the cause, are similar². The liver is responsible for the maintenance of the

blood sugar levels within normal limits by various mechanisms such as gluconeogenesis, glycogenesis and glycogenolysis. The blood glucose levels are very low in fulminant acute hepatitis; however this is in contrast with chronic liver disease where the incidence of diabetes and impaired glucose tolerance are of a significant percentage. The contribution to energy in fasting state is more by fats than the carbohydrates³. The incidence of diabetes is increased in patients with chronic hepatitis C^{4,5}, other metabolic

disorders like hemochromatosis and autoimmune hepatitis.

The degree of liver dysfunction⁶ directly correlates with the extent of carbohydrate metabolism disturbances. The metabolic changes in chronic liver diseases are complex and not fully understood^{6,7}.

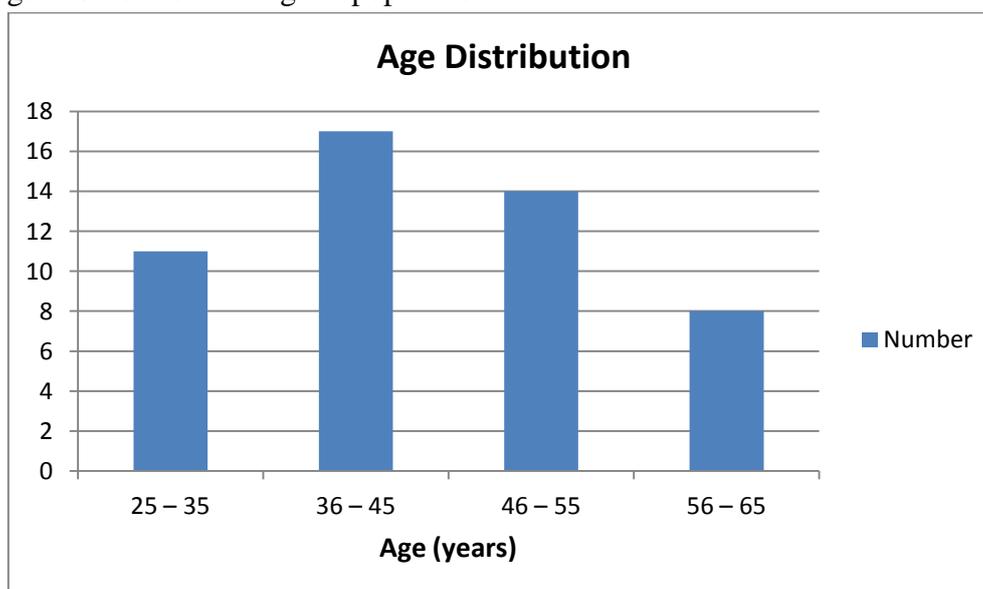
OGTT remains superior⁸ to the same test carried out through the intravenous route till date, because this gives an opportunity for the stimulation of secretion of insulin and other hormones normally.

Aims and Objectives

1. To study the various clinical, biochemical and radiological manifestations of Chronic Liver Disease.
2. To determine the prevalence and clinical implications of the spectrum of glucose metabolism disorders (Impaired Glucose Tolerance/ Diabetes Mellitus) in patients with chronic liver disease.
3. To correlate the glycemic levels with the class of Child Turcotte Pugh Scoring System, in assessing the prognosis of the disease.

Age Distribution

Chart No 1 - Age Distribution among the population1



Materials and Methods

This is an observational study conducted in Govt sivagangai Medical College, sivagangai over a period of six months duration.

The study population included 50 patients who attended the Department of Medicine, both as outpatient or inpatient, and were diagnosed to have chronic liver disease. The individuals were taken up for the study after getting their informed consent.

Study Design: Cross sectional study

Period of Study: Six Months (Feb 2019 – July 2019)

Ethical Committee Approval: Approved

This study was approved by the Ethical Committee, Sivagangai Medical College.

Statistical Analysis:

The significance testing was done using the Chi Square Test. The results were considered significant if the 'p' value was below 0.05.

Observations & Results

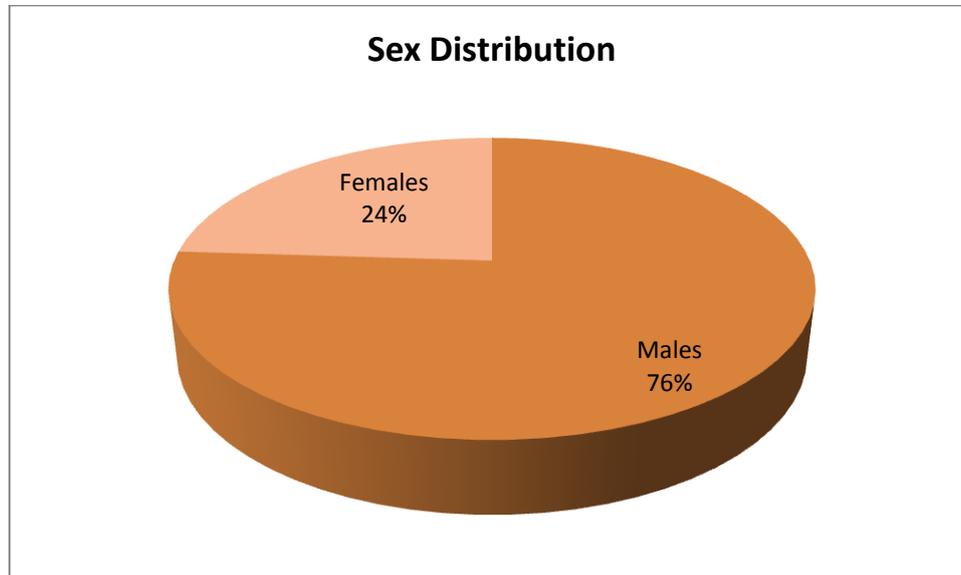
During the 6 month study period, a total number of 50 patients were studied for finding out the prevalence of impaired glucose tolerance and diabetes mellitus in patients with cirrhosis liver, and its relation to other selected variables.

The age of the patients range from 29 to 65 years. The majority of the patients were within the age group of 36 to 45 years (34%). This was followed

closely by patients within the age group of 46 to 55 years (28%). The mean age group was 45.42 years.

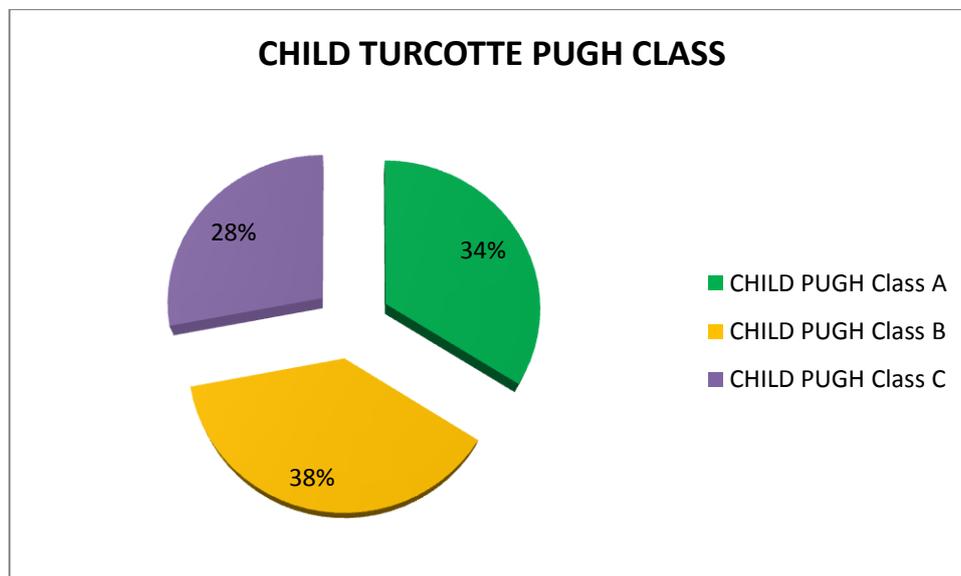
Sex Distribution

Chart No 2 – Sex Distribution among the study population



Child Turcotte Pugh Classification

Chart No 3 - Distribution of cases within the CTP Class



Of the 50 patients under this study, the number of cases in the various classes of the CTP classification were as follows – Class A: 17 (34%), Class B: 19 (38%), Class C: 14 (28%). The maximum number of patients were within the class B.

Oral Glucose Tolerance Test

50 patients in this were subjected to the oral glucose tolerance test, by administration of 75 g of glucose in 300 ml of water and measuring the plasma glucose levels at 0, ½, 1, 1 ½ and 2 hrs. The results of the test are as follows.

Chart No 4 – Results of OGTT

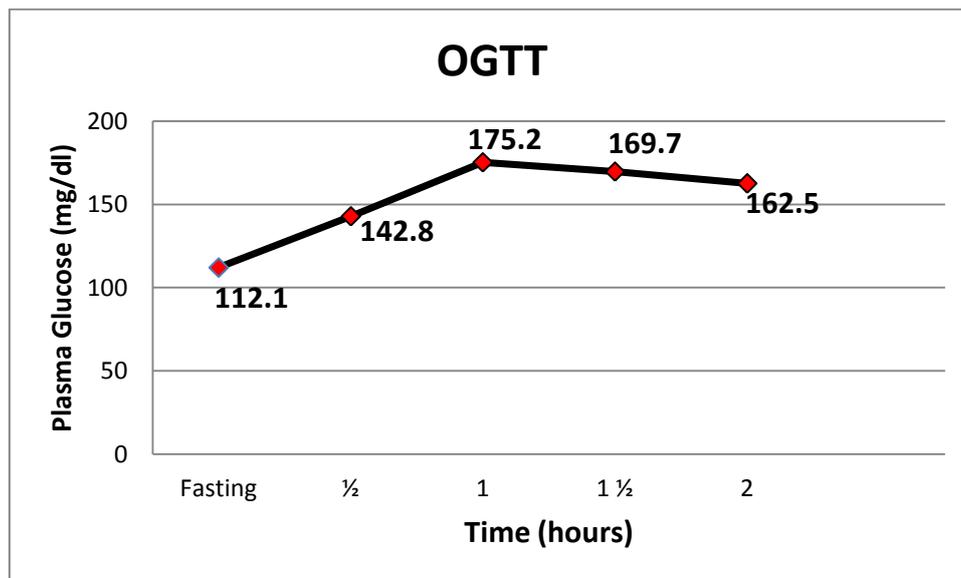
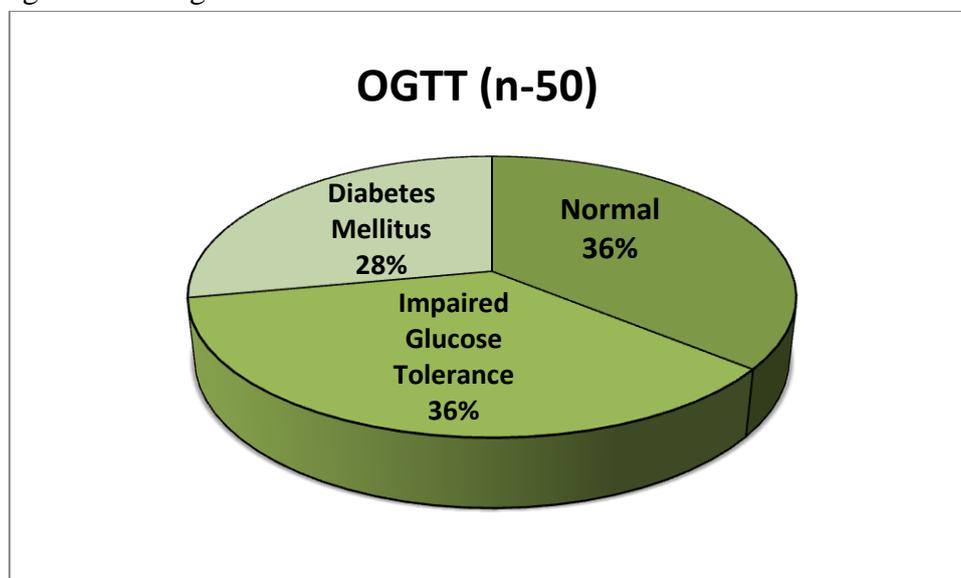


Chart No 5 – Diagram showing Distribution of Results of OGTT



The mean of the oral glucose tolerance test performed in all the 50 patients were as follows: fasting- 112.1, ½ hr- 142.8, 1 hr- 175.2, 1 ½ hrs – 169.7 and 2 hrs – 162.5 mg/dl. The results of the OGTT in these 50 patients were as follows: 18(36%) of them had normal results, 18 (36%) of them had impaired glucose tolerance and the remaining 14 (28%) of them had diabetes mellitus.

other studies like the Naik B K, Mishra et al, Anklesari et al and Sarkar, the most common symptom was abdominal distension. Jaundice was present in 36% of the patients in this study, which was comparable with that done by Anklesari, where the % was also 36. In our patients, fever was a manifestation in 28% of them which was comparable with Naik B K study.

Discussion

The commonest symptom in our study was anorexia, which was around 80%. In this study the % of abdomen distension was 60, which was the second commonest symptom. However in all the

Table No 6 - Comparing OGTT results with previous studies

OGTT	Present study (%)	Nishida T et al ¹⁷ (%)	Hagel S ¹⁵ (%)	Müller MJ et al ¹⁸ (%)	Hagel S ¹⁶ (%)
Diabetes	28	21	34	37	-
IGT	36	23	37	36	37
Normal	36	39	29	27	33

The results of the oral glucose tolerance test in this study, showed glucose metabolism disorders ie impaired glucose tolerance and diabetes in 64% of the cases. The number of patients with normal OGTT were 18 (36%); 18(36%) of them had impaired glucose tolerance and the remaining 14 (28%) of them had diabetes mellitus.

This can be compared to the study carried out by Nishida T et al where the results of OGTT were as follows: 22 (39%) of them were normal, 13(23%) of them had IGT and the remaining 21(38%) had diabetes mellitus. This study also proved that diabetes mellitus and serum albumin were important independent negative predictors of survival. This also correlated with the study carried out by Hagel S which showed normal values in 23(29%), IGT in 29 (37%) and DM 27(34%). It was also proved beyond doubt that independent risk factors that lead to the development of carcinoma was diabetes mellitus along with older age and advanced liver fibrosis.

Conclusion

Cirrhosis liver is a very common disease in our country, with some of the major risk factors being alcohol, viral infection, carcinomas etc. The prognosis of chronic liver disease is varied and depends on a large number of parameters, including the stage of diagnosis of the disease. It is usually believed that chronic liver disease is associated with low blood sugar levels. However hypoglycaemia is most common in fulminant hepatic failure. Chronic liver disease, in contrast, presents with a significant percentage of glucose metabolism disorder (Impaired Glucose Tolerance/Diabetes Mellitus), and this is more evident with the later stages of the disease. The diabetes that occurs secondary to cirrhosis liver is given the term 'Hepatogenous Diabetes'. The

degree of hyperglycaemia is an important prognostic factor in assessing the long term survival; and hence early detection by comprehensive diagnostic approach is mandatory. In normal individuals 80 % of glucose is contributed by glycogenolysis after a prolonged fasting state. The hepatic glycogen is decreased in patients with chronic liver disease, which affects glycogenolysis adversely. Amino acids and lipids, the precursor of gluconeogenesis although are utilised prematurely to maintain the blood glucose levels, the fasting low blood sugar levels are not corrected. This is one reason for the utilisation of the oral glucose tolerance test (OGTT) in screening for diabetes in CLD, over fasting plasma glucose. The main mechanism for the carbohydrate intolerance in CLD includes insulin resistance and impaired secretion of insulin from the pancreatic cells.

The results in our study also showed significant percentage of patients with glucose metabolism disorders and this correlated well with the severity of the disease. That is, as the disease progressed (assessed by the Child Turcotte Pugh Scoring System) the degree of hyperglycaemia also worsened. The association of Diabetes Mellitus and cirrhosis liver leads to a more aggressive disease, with regard to the morbidity and mortality of the patient. The diagnosis of diabetes has hence very significant prognostic implications in the course of the disease.

These individuals are usually asymptomatic for diabetes till the end stage of the liver disease as true with any other diabetic patient. Hence screening of patients diagnosed with liver disease is of utmost importance at the earlier stages itself. This enables for the quicker and effective treatment of diabetes in these patients. But all said and done, there are few restrictions and

contraindications for the treatment of diabetes in cirrhosis. However, with the recent development in the various therapeutic option, the outlook of the life of the patients has improved.

In conclusion, screening for diabetes with either fasting plasma glucose /OGTT should be done at

the onset of the diagnosis of liver disease and at regular intervals; this is to enable the early diagnosis and efficient management of impaired glucose regulation in cirrhotics, and to improve the quality of life of these patients.

FACTORS LEADING TO HYPERGLYCEMIA:

- Reduced hepatic glucose uptake
- Reduced hepatic glycogen synthesis
- Insulin resistance in liver
- Porto- venous glucose shunting
- Insulin resistance in muscle and adipose tissue
- Increased counter regulatory hormones

FACTORS LEADING TO HYPOGLYCEMIA:

- Reduced synthesis of glucose
- Reduced hepatic glycogen content
- Glucagon resistance in liver
- Reduced oral intake
- Increased insulin secondary to porto venous shunting

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