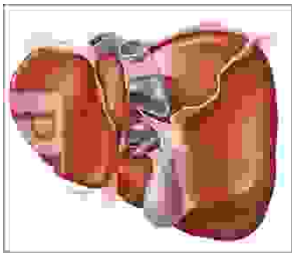
ORIGINAL PROF-766

CHRONIC HEPATITIS C INFECTION;

CORRELATION OF GLUCOSE TOLERANCE TEST, THE LEVELS OF FASTING BLOOD SUGAR (FBS) AND HEMOGLOBIN A1c (HbA1c)



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ABSTRACT... drirfan57@hotmail.com **Objectives:** To find out the possible effects of chronic hepatitis C on carbohydrate metabolism in liver. **Setting:** Independent Medical College and City Lab. Faisalabad. **Material & Methods:** A total of 42 male subjects between the age of 30-49 years having chronic hepatitis C were registered at random. For control group, 21 normal healthy males of same age group having normal liver function test. 5ml of fasting blood was taken and analyzed for blood sugar, GTT, HbA_1c, SGPT, Alkaline Phosphatase and Bilirubin. **Results:** The levels of SGPT were significantly raised, which shows liver cell injuries. The levels of Fasting blood glucose were towards the lower normal limit in patients having chronic hepatitis "C" while the levels of HbA_1c were higher in patients having chronic hepatitis "C". The glucose tolerance test showed a significant increase in the patients with Hepatitis C virus infection. **Conclusion:** The result showed that there is some disturbance in the regulation of glucose metabolism in patients having chronic hepatitis "C".

INTRODUCTION

The liver is essential for life, since it carries out a multiplicity of metabolic activities necessary for homeostasis, alimentation and defense[1]. The main function of the liver in carbohydrate metabolism is the maintenance of the blood glucose concentration. Hepatocytes are rich in membrane receptors for insulin and as a result the liver takes up half or more of glucose absorbed during feeding, thereby preventing marked hyperglycemia. The glucose taken up is stored as glycogen or metabolized as glycerol and fatty acids. Glucose derived from the breakdown of glycogen or from gluconeogenesis is released into the blood during fasting[2].

The reticuloendothelial system of the liver contains

many immunologically active cells. The liver acts as a 'sieve' for the bacterial and other antigens carried to it via the portal tract from the gastro-intestinal tract.

One or other of the hepatitis viruses almost always causes viral hepatitis. All these viruses give rise to illness which are similar in their clinical and pathological features and which are frequently anicteric or asymptomatic. The viruses identified until now have been named as A, B, C, D, E and G and each have worldwide distribution[3]. Chronic liver disease caused by hepatitis B and C is more prevalent in Pakistan and especially in Faisalabad district[4].

Chronic hepatitis is caused by hepatitis B and C viruses, which lead to chronic liver disease. The course of viral hepatitis is inflammation followed by fibrosis, which results in cirrhosis of liver[5]. Blood proteins are glycosylated and the degree of glycosylation is proportional to the levels of blood glucose.

Among the glycosylated proteins, glycosylated hemoglobin is the most important factor, which is measured to evaluate the long term control of diabetes mellitus. The formation of HbA_1c is non-enzymatic and is proportional to the concentration of glucose in blood. The concentration of HbA_1c shows the average glucose concentration over two or three months prior to the measurement[6].

Zayadi [7] studied the association of chronic hepatitis-C infection and diabetes mellitus. The aim of the study was to detect a possible etiological association between chronic hepatitis C-virus infection and diabetes mellitus. They concluded that chronic hepatitis C patients in Egypt are three times more likely to develop DM than HCV seronegative patients. Pancreatic beta-cells might be an extrahepatic target of HCV.

Caronia[8] further evidenced for an association between non-insulin dependent diabetes mellitus and chronic hepatitis C virus infection. This study confirms an association between HCV and non-insulin dependent diabetes mellitus.

Mason[9] studied the association of diabetes mellitus and chronic hepatitis C virus infection. They observed that patients with liver disease had a higher prevalence of glucose intolerance and hepatitis C virus (HCV) infection.

Konrad[10] observed that the HCV infected patients with normal glucose tolerance are insulin and glucose resistant. The impairment of glucose tolerance appears to be closely related with the severity of HCV induced liver damage.

Khokhar[11] has concluded that the patients with chronic hepatitis C virus infection and cirrhosis secondary to hepatitis C virus infection have strong association with diabetes mellitus and great majority of them are non-insulin dependent diabetics.

Qureshi[12] studied that diabetes is frequent in HCV related disease but is significantly more in those with chronic liver disease than in controls. The pancreatic damage secondary to extra hepatic viral replication appears to be the major cause. The prevalence of type II DM is higher in patients with HCV cirrhosis compared with a control group of patients with cirrhosis from other causes.

AIMS & OBJECTS

To find out the possible effect of chronic hepatitis C on carbohydrate metabolism in the liver, following parameters were studied.

1. The fasting blood glucose levels were analyzed to find out indirectly the adequate stores of glycogen in the liver and the process of gluconeogenesis.
2. HbA_1c was measured for true assessment of the regulation of blood glucose.
3. The action of liver by correlating the levels of FBS and HbA_1c.
4. Glucose tolerance test was performed to see the relationship of chronic hepatitis C with diabetes mellitus.

MATERIAL & METHODOLOGY

Selection of Subjects

A total of 42 male subjects between the age of 30-49 years having chronic hepatitis C at Independent Medical College, Faisalabad and City Lab faisalabad, were registered at random.

The patients did not have any other illness such as hypertension, tuberculosis or any malignancy. They were not taking any medication (oral or injectable) for diabetes mellitus.

For control group, 21 normal healthy male of same age group having normal liver function test and negative for hepatitis B and C virus were included in this project. Their normal liver status was further confirmed by ultrasound examination. Five ml of fasting blood was taken and analyzed for Blood Sugar, GTT, HbA_1c, SGPT, Alkaline Phosphatase and Bilirubin (Total, Direct and Indirect) in the City laboratory, Faisalabad. The protocol for oral GTT was followed in each subject to evaluate glucose tolerance to oral glucose load.

The results obtained were analyzed statistically by using student "t" test. The differences were considered statistically significant for values (P less than 0.05) and highly significant for values (P less than 0.001) and non-significant for values (P greater than 0.05).

RESULTS

The blood samples were analyzed, the data work tabulated and discussed as follow.

1. Fasting Blood Sugar

The comparison of average values of FBS showed a highly significant ($P < 0.001$) difference between control and chronic hepatitis C patients. The results showed that chronic hepatitis C had significant effect on FBS of the patients.

2. Glucose Tolerance Test

The comparison of average value of GTT showed a highly significant ($P<0.001$) difference between control and chronic hepatitis C patients. The results showed that chronic hepatitis C had significant effect on GTT of the patients.

3. Hemoglobin A_1c

Comparison of average HbA_1c levels revealed a highly significant ($P < 0.001$) difference between control and chronic hepatitis C patients. The results showed that the levels of hemoglobin A_1c in patients having chronic hepatitis C were higher than normal individuals.

Table-I. Levels of Fasting blood sugar in normal and hepatitis C patients.

Subjects	No. Of Subjects	Fasting Bloog Sugar (mg/dl) (X±S.D)
Normal	21	85.38±6.32
Hepatitis C Patients	42	74.45±7.87

4. Serum Glutamate Pyrurate Transaminase

Statistical analysis of the data showed that the average value of SGPT in control and patients having chronic hepatitis C and highly significant ($P < 0.001$) difference. The levels of SGPT were found to be markedly raised in patients of chronic hepatitis C as compared to control.

Table-II. Level of GTT in normal and hepatitis C patients.

Subjects	No. Of Subjects	Glucose Tolerance Test after 1 hr.	Glucose Tolerance Test after 2 hrs.
Normal	21	111.31±8.62	131.24±7.76
Hepatitis C patients	42	169.24±5.70	233.86±2.74

5. Serum Alkaline Phosphatase

The comparison of average values of serum alkaline phosphatase in control and patients having chronic hepatitis C showed a non-significant ($P > 0.05$) difference. The results indicated that the levels of alkaline phosphates were almost normal in chronic hepatitis C patients.

Table III. Levels of Haemoglobin A_1c in normal and hepatitis C patients.

Subjects	No. Of Subjects	Haemoglobin A_1c (%)(X± S.D)
Normal	21	4.94 ±0.55
Hepatitis C patients	42	7.18 ± 0.57

Table-IV. Levels of Serum glutamate Pyruvate transaminase (SGPT) in normal and hepatitis C patients.

Subjects	No. Of subjects	SGPT(U/ul)(X± S.D.)
Normal	21	24.66±5.33
Hepatitis C patients	42	170.04 ± 27.06

6. Serum Total Bilirubin

Statistical analysis showed a non significant ($P < 0.05$) difference between normal individuals and chronic hepatitis C patients. Total bilirubin level was therefore within normal limits in the patients under study.

Table-V. Levels of Serum alkaline phosphatase in normal and hepatitis C patients.

Subjects	No. Of subjects	S. Alk Phosphatase (U/ul) (X + S.D.)
Normal	21	216.38± 31.59
Hepatitis C patients	42	206.04± 31.00

7. Serum Indirect Bilirubin

Statistical analysis of the data showed a non significant ($P < 0.05$) difference. This showed that the indirect bilirubin levels were found to be normal in chronic hepatitis C patients.

8. Serum Direct Bilirubin

Statistical analysis showed a non-significant ($P < 0.05$) difference between normal and chronic hepatitis C patients. This showed that the direct bilirubin level was normal in the subject under study.

Table-VI. Levels of Serum total bilirubin in normal and hepatitis C patients.

Subjects	No. Of Subjects	Serum total bilirubin(mg /dl) (X± S.D.)
Normal	21	0.41±.007
Hepatitis C patients	42	0.82± 0.09

Table-VII. Levels of Serum indirect bilirubin in normal and hepatitis C Patients.

Subjects	No. Of Subject	S. Indirect bilirubin(mg /dl)(X± S.D.)
Normal	21	0.83± 0.08
Hepatitis C patients	42	0.43± 0.05

Table-VIII. Levels of Serum direct bilirubin in normal and hepatitis C patients.

Subjects	**No. Of subjects**	**S. Direct Bilirubin (mg/dl)(X±S.D.)**
Normal	21	0.43 ± 0.06
Hepatitis C patients	42	0.44± 0.06

DISCUSSION

The levels of serum total conjugated (direct) and unconjugated (indirect) bilirubin were normal in control and study (hepatitis C) subjects. On comparison the levels of total and fractions of serum bilirubin in both control and study subjects the results were non significant ($P > 0.05$). Bilirubin is formed from the iron free porphyrin portion of heme in the reticuloendothelial cells of the liver, spleen and bone marrow. Bilirubin is transported in blood tightly bound to albumin and then is taken up by hepatocyte by facilitated transport system and conjugated with glucuronic acid and excreted through the bile.

Albumin bound bilirubin is called unconjugated or indirect bilirubin while glucuronic acid conjugated billirubin is called conjugated or direct bilirubin[13]. In chronic viral hepatitis prior to onset of cirrhosis or

intrahepatic biliary obstruction the levels of total direct and indirect bilirubin remains normal[14]. The patients of chronic hepatitis C registered in this study were suffering from initial phase of chronic hepatitis C. There was no development of cirrhosis or other complications.

The levels of serum alkaline phosphatase in study subjects and controls were in normal limits. There was no statistical difference ($P > 0.05$) in the levels of alkaline phosphatase among the two groups.

Alkaline phosphatase is hepatocyte membrane bound enzyme. It's serum levels are raised when there is intra or extra hepatic biliary obstruction or in hepatic malignancy. The increased biliary pressure results in the induction of one of the enzyme involved in the hepatocyte synthesis of alkaline phosphatase which is secreted to the plasma in obstructive liver disease 2-4 times of normal[15].

In the study subjects of chronic hepatitis C the disease was in the stage of uncomplicated chronic hepatitis. There is neither acute severe inflammation nor obstructive billiary disease. So the levels of alkaline phosphatase were not significantly raised in the patients as compared to control.

The levels of serum GPT were markedly raised in patients of chronic hepatitis C as compared to control. The hepatitis C virus in chronic infections cause injuries to the liver parenchyma. Due to viral injuries the hepatocytes are broken down at a much higher rate than the physiological wear and tear of the liver. SGPT is the mitochondrial enzyme. When there is lysis of the hepatocyte, the lysosomal enzymes destroy the intra-cellular organelles e.g. mitochondria. The enzymes transaminases e.g. SGPT due to higher rate of liver cell damage, are raised in plasma. Elevated activity of SGPT is reported in various studies on chronic hepatitis[16].

Fasting blood glucose levels in patients having chronic hepatitis were in normal range, but these levels were significantly lower ($P < 0.05$) in patients as compared to control. Liver is the glucose buffering organ of the body. In well fed state the liver store glucose in the form of glycogen and at the fasting conditions liver supply glucose by the process of glycogenolysis and gluconeogensis. The normal level of fasting blood glucose ranges from 60-110 mg/dl. The levels of fasting blood glucose in patients of chronic hepatitis were at the lower side of normal limits. The lower levels of fasting blood glucose in patients of chronic hepatitis as compared to control might be due to decreased stores of glycogen in the liver of patients and decreased activity of gluconeogenesis in liver.

The levels of HbA_1c in patients having chronic hepatitis were higher than the normal range (4.2 – 6.2%). The levels of HbA_1c provides a retrospective index of the integrated plasma glucose values over and extended period and is not subject to the wide fluctuations observed when blood glucose levels are assayed. In Patients having chronic hepatitis the blood glucose level is towards the lower side of normal limits and the raised levels of HbA_1c shows the higher levels of blood glucose might be at the post prandial state. Ultimately these results reflect some disorders in the regulation of blood glucose levels in the patients having chronic hepatitis.

The levels of HbA_1c in patients having hepatitis C are higher[17], which shows the association of hyperglycemia and diabetes mellitus with chronic hepatitis C Infection. Various other workers reported higher incidence of diabetes mellitus in patients having chronic hepatitis C[18].

The glucose tolerance test showed a significant derangement in the patients with Hepatitis C virus infection. This intolerance to glucose is caused by partial loss of glycogen synthetic function by the liver resulting from a decrease in the number of functionally active cells. It could also be concluded that the patients having normal glucose tolerance have glucose resistance and the impairment of glucose tolerance is directly proportional to the severity of liver damage[10,20].

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