

# CHRONIC VIRAL HEPATITIS C INFECTION;

## Frequency of impaired glucose tolerance in patients

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**ABSTRACT... Objective:** The objective of the study was to measure the frequency of impaired glucose tolerance (IGT) in patients having chronic hepatitis C at medical outpatient department (OPD) of Allied hospital Faisalabad. **Sample technique:** Non probability consecutive sampling. **Duration of study:** Duration of study was 6 months with first patient enrolled on 3.02.2010 and last patient enrolled on 07-08-2010. **Setting:** Medical (OPD) Outpatient Department of Allied Hospital, Faisalabad. **Subjects:** 375 patients with chronic hepatitis C, coming in Medical OPD of Allied hospital Faisalabad were enrolled. **Methods:** 375 patients diagnosed as having chronic hepatitis C coming in Medical OPD of Allied hospital Faisalabad, were included in the study. Fasting and two hours after glucose load blood sample were collected in sterilized syringes and was tested for fasting blood glucose (FBS) and random blood glucose level (RBS). **Results:** In this study 375 patients having HCV positive on Elisa were enrolled. Out of 375 patients with chronic hepatitis C, 143 (38.1%) were found to have IGT while 232 (61.9%) were having no IGT. There was significant association between chronic hepatitis C and development of IGT. **Conclusions:** It is concluded that there is close association in the development of IGT in patients with chronic hepatitis C.

**Key words:** Chronic hepatitis C, Type 2 Diabetes mellitus, insulin resistance.

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### INTRODUCTION

Impaired glucose tolerance (IGT) is defined as “fasting plasma glucose level between 101 mg/dl - 126 mg/dl and plasma glucose levels between 140 – 200 mg after 2 hours of 75 gram of oral glucose load”<sup>1</sup>. There are at least three hundred million people with IGT world wide<sup>2</sup>. Individuals with IGT are at 40% increased risk for developing type-2 diabetes mellitus over next five years<sup>3</sup>. It is also a risk factor for increased mortality and cardiovascular diseases<sup>4,5</sup>. IGT is categorized as a stage in the natural history of disordered carbohydrate metabolism and referred to a metabolic state intermediate between euglycemia and diabetes<sup>4,6</sup>. There is evidence that intensive life style changes in individuals with IGT prevented the development of type 2 diabetes mellitus by 58 % and also reduced the morbidity and mortality due to cardiovascular pathology<sup>3</sup>. Oral glucose tolerance test (OGTT) is one of excellent tools recommended by WHO to identify persons with IGT<sup>6</sup>. OGTT might play an excellent roll in screening of persons infected with hepatitis C virus for IGT<sup>6</sup>. The prevalence of Hepatitis C virus in Pakistan is 8-10% and to treat hepatitis C as per international

recommendations cost approximately 4 lacs per patient<sup>7</sup>. IGT is more common among patients suffering from chronic hepatitis C virus infection<sup>8,9</sup>. A comparative study done showed that prevalence of IGT was 30% among patients suffering from chronic hepatitis C virus infection, while it was 14% in those who were not suffering from chronic hepatitis C virus infection<sup>9</sup>. Another study showed that prevalence of IGT in chronic hepatitis C virus infected patients is 42.28%<sup>10</sup>. There is little local data available on this subject, thus this study will help to highlight the importance of screening of hepatitis C virus infected patients for IGT. Thus this will help to decrease the morbidity and mortality associated with IGT in chronic hepatitis C patients.

### MATERIAL AND METHODS

#### Settings

The study was conducted in the medical out patient department of Allied Hospital Faisalabad. Allied Hospital is a tertiary care teaching hospital having 1100 beds.

### Duration

The study was completed within 6 month after approval of synopsis. first patient was enrolled on 03-02-2010 and last patient was enrolled on 07-08-2010.

### Sample Size

Sample size was calculated by using WHO sample size calculator taking confidence level 95%, population proportion 42.28%,10 required precision .05. Sample size will be  $n=375$

### Sample Technique

By non probability consecutive sampling.

### Inclusion Criteria

All patients of either sex of age more than 25 years of age who had confirmed hepatitis C virus by ELISA technique at least 6 months back were included in the study.

### Exclusion Criteria

All patients who were known to have diabetes mellitus, pregnancy, patients taking drugs (diuretics, oral contraceptive pills, phenytoin and steroids), acute myocardial infraction. (History of chest pain, vomiting and sweating was taken to rule out this) , any recent surgery within one month, acute infection and fever , obesity. (Body mass index of more than 25 kg/m<sup>2</sup> was taken as obese). Both dyslipidemia and hypertension were included in the study.

### Study Design

Descriptive cross sectional study.

### Data Collection Procedure

The patients were selected from Medical OPD. The purpose of the research was explained to each patient. Those, who gave an informed consent, was included in the study. 375 patients who were Hepatitis C virus infected coming in medical out patients Department of Allied Hospital fulfilling the above mentioned inclusion criteria were included. The enrolled patients were

instructed to take unrestricted carbohydrate diet for three days, to avoid smoking, coffee and heavy exercise. After 8 hours over night fast venous blood sample was taken, which was labeled as fasting blood sugar (FBS) and sent to pathology laboratory of Allied Hospital, Faisalabad. Then 75 gm glucose in a glass of water was given to the patient to drink in less than five minutes. After 2 hours venous blood sample was taken, which was labeled as Random blood sugar (RBS) and sent to pathology laboratory of Allied Hospital, Faisalabad. Proforma had been developed to record the results.

### DATA ANALYSIS

The data was analyzed by using SPSS-10. The Descriptive statistics were calculated. The quantitative variables of the study were age , BMI, fasting blood sugar (FBS) and Random blood sugar (RBS) level. These variables were presented as Mean  $\pm$  SD. The qualitative variables were gender and impaired glucose tolerance. These were presented as frequency and percentage.

### ESULTS

In this study total 375 patients having chronic hepatitis C were included. Minimum age of the pt. was 25 and maximum 55 with a mean and STD of 42.95 and 7.05 respectively (table I). Out of total 375 patients, 187 (49.9%) were males and 188 (50.1%) were females .Among age distribution the study showed that out of total 375 patients 49 (13.1%) patients were having age from 25 to 35 years . Majority of them were among 36-55 years of age groups. 203 (54.1%) were having age from 36-45 years and 123 patients (32.8%) were having their ages between 46-55 years (Table II). Among 49 patients between 25-35 years of age 14 were having IGT +ve. Among 36-45 years 61 were having IGT +ve and among 46-55 years 68 patients were having IGT +ve. (GRAPH 1). In this study, out of 375 patients, minimum FBS was 66mg/dl and maximum was 126mg/dl .Mean FBS was 95.06 and Std.Deviation was 18.10 (table I)).Among 375

patients 143(38.1%) has FBS more than 100mg/dl and 232(61.9%) has FBS less than 100mg/dl (TABLE III). Minum RBS was 100mg/dl and maximum was 198mg/dl with .mean RBS was142.13and Std. Deviation was 22.68 (TABLE I) .143(38.1%) has RBS more than 140mg/dl and 232(61.9%) less than

140mg/dl (TABLE IV). Among 375 ,166(44.3%) were having BMI between 18-21.Among these 41 were having IGT +ve. 209(55.7%) were having BMI between 22-25. Among these 102 were having IGT +ve.(TABLE V-VI).

	N	Minimum	Maximum	Mean	Std. Deviation
Age	375	25	55	42.95	7.05
Body mass index	375	18	25	21.53	1.55
Fasting blood sugar	375	66	126	95.06	18.10
Random blood sugar	375	100	198	142.13	22.68
Valid N (list wise)	375				

Table-I. Descriptive statistics

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	25-35	49	13.1	13.1	13.1
	36-45	203	54.1	54.1	67.2
	46-55	123	32.8	32.8	100.0
	Total	375	100.0	100.0	

Table-II. Distribution of patients by age

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	for <100	232	61.9	61.9	61.9
	for >100	143	38.1	38.1	100.0
	Total	375	100.0	100.0	

Table-III. Fasting blood sugar of patients of chronic HCV

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	for <140	232	61.9	61.9	61.9
	for >140	143	38.1	38.1	100.0
	Total	375	100.0	100.0	

Table-IV. Random blood sugar of patients of chronic HCV

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	for 18-21	166	44.3	44.3	44.3
	for 22-25	209	55.7	55.7	100.0
	Total	375	100.0	100.0	

Table-V. Distribution of patients by body mass index

		Impaired glucose tolerance		Total
		IGT -ve	IGT +ve	
Body mass index	for 18-21	125	41	166
	for 22-25	107	102	209
Total		232	143	375

Table-VI. Distribution of patients of Impaired glucose tolerance by body mass index

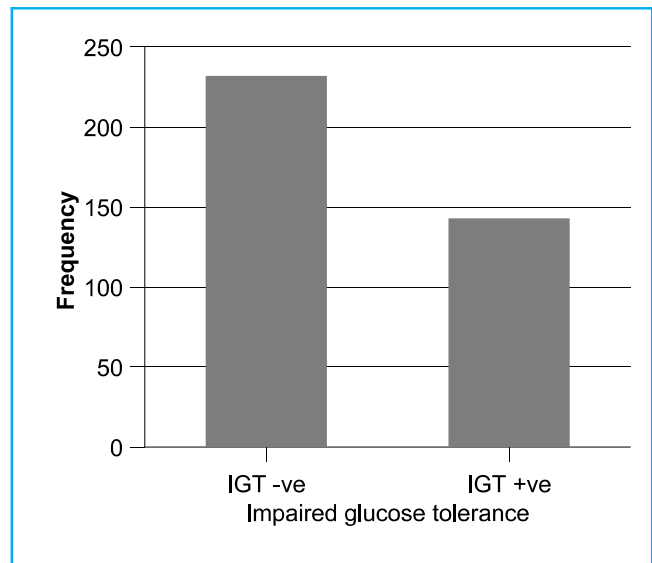


Fig-2. Frequency of IGT in chronic HCV

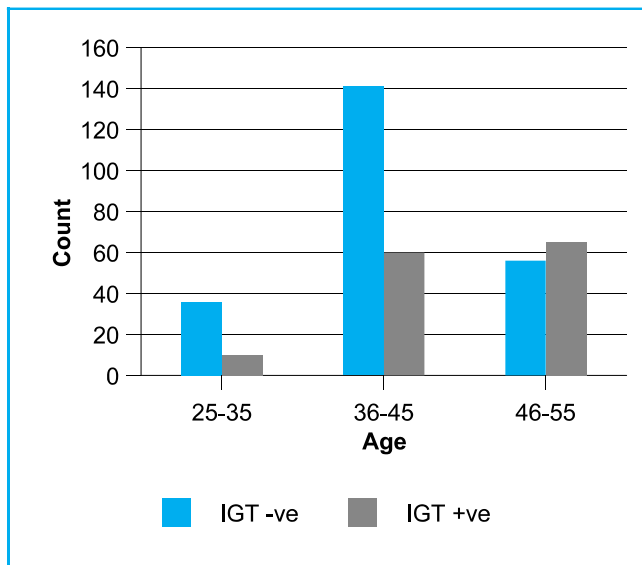


Fig-1. Distribution of patients of IGT By Age

Out of 375 patients with CHC 143 (38.1%) were found to have IGT while 232(61.9%) were having no IGT. (Fig- 2). Most patients presented with IGT having age group 36-55. (Fig-1).

**DISCUSSION**

Hepatitis C virus (HCV) infects approximately 170 million individuals worldwide. Chronic HCV infection has been estimated to be responsible for approximately 250 000 to 350 000 deaths per year. Whereas the hepatic manifestations of hepatitis C are well described the extrahepatic manifestations, though common, are less well appreciated. IGT is more common among patients suffering from chronic hepatitis C virus infection<sup>11</sup>. There is well established relation between cirrhosis of liver and development of IGT and diabetes mellitus as its extra hepatic complication. 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<sup>12</sup>. The first observation that

cirrhotic patients infected with HCV may present with T2D more often than patients with cirrhosis of other etiology was reported in 1994 by Allison et al<sup>13</sup>. In our study out of 375 patients with CHC, 143 (38.1%) were found to have IGT while 232 (61.9%) were having no IGT. Out of total 375 patients majority of them were among 36-55 years of age and. Slight male dominance was found in our patients. Khokhar N<sup>14</sup> also reported the same pattern in a study conducted in Islamabad. An other study by Afzal M et al<sup>15</sup> in 2004 showed that the levels of fasting blood glucose were towards the lower normal limit in patients having chronic hepatitis C while the levels of HbA1c were higher in patients having chronic hepatitis C. The glucose tolerance test showed a significant increase in the patients with IGT in Hepatitis C virus infection. Mehta SH et al<sup>16</sup> in the United States, in a cross sectional study observed increased prevalence of type 2 diabetes and IGT occurs more often in persons with HCV infection who are older than 40 years of age. Suliman MI et al<sup>17</sup> in 2004 conducted a Comparative study to establish a potential relationship between chronic hepatitis C virus infection and diabetes mellitus in Bahawalpur. This study is comparable to our study. Ryu JK et al<sup>18</sup> and Shah IA et al<sup>19</sup> found highly significant association between IGT and HCV was found. P<.01. The incidence of type II DM and IGT among HCV infected patients with chronic disease has been reported variously from 23% to 62%<sup>19</sup>. A recent, large meta-analysis, the first of this kind, has reached the same conclusion<sup>20</sup>. Insulin resistance and T2DM have important effects on the hepatitis C progression and response to antiviral therapy<sup>21</sup>, which warrants specific and effective measures to correct such metabolic anomalies. The control of glucose abnormalities in CHC not only improves response to anti viral therapy but also decrease incidence of hepatocellular carcinoma<sup>22</sup>. However, as hyperglycemia and diabetes are independent risk factors for the response to treatment in patients with chronic HCV infection, early diagnosis and control of DM in these patients could result in better care and outcome of HCV patients. So, early

screening of patients with chronic HCV infection for detection of IGT and glucose metabolism disorders is recommended to improve patients' outcome although better control of HCV could prevent development of IGT and DM in these patients.

## CONCLUSIONS

Considering the disease burden and high economic cost of chronic hepatitis C treatment, early detection of D.M will not only reduce the cost of treatment failure but will also help in identifying the patients who require early management of type 2 diabetes mellitus. The specific mechanisms by which HCV leads to IGT and type 2 diabetes are not fully understood, but it seems that an increase of insulin resistance associated with both steatosis and the overproduction of proinflammatory cytokines could play a crucial role. These mechanisms are initiated in the early stages of hepatic disease. The knowledge of the pathogenic mechanisms involved in IGT and diabetes associated with HCV infection will enable us not only to further identify those patients at high risk of developing diabetes but also to select the best therapeutic option and decrease the burden of complications related to CHC and hepatogenous Diabetes Mellitus.

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the recipient to become independent of it.*

*John D. Rockefeller*