

**Research Article****Frequency of pre-diabetes in patients with chronic hepatitis C****<sup>1</sup>Tabinda Yasmin, <sup>2</sup>Ayesha Siddiqa****and <sup>3</sup>Fatima Khawar**<sup>1</sup>Consultant Pathologist, Department of Pathology, Civil Hospital, Bahawalpur<sup>2</sup>Consultant Pathologist, District Health Authority, T.H.Q. Hospital, Yazman, Bahawalpur.<sup>3</sup>Ex House Officer, Jinnah Hospital, Lahore

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**ABSTRACT****Objective:** To determine the frequency of prediabetes in patients of chronic hepatitis C infection.**Material and methods:** This cross sectional study was conducted at Department of Pathology, Civil Hospital, Bahawalpur from October 2017 to April 2018 over the period of six months. Total 182 patients with hepatitis C infection having age 30-60 years either male or female were selected from Department of Medicine Civil Hospital Bahawalpur. Prediabetes was assessed in selected patients.**Results:** Total 182 patients with hepatitis C were selected. Mean age of the patients was  $43.27 \pm 9.47$  years. Out 182 patients, prediabetes was found in 115 (57%) patients. Prediabetes was observed in 68 (63.55%) patients and 47 (62.67%) patients respectively in age group 30-45 years and age group 46-60 years. No association ( $P = 1.00$ ) of prediabetes with age groups was observed. Total 44 (42.31%) male patients and 71 (91.03%) female patients were found with prediabetes.**Conclusion:** Results of present study demonstrates a higher percentage of prediabetes in hepatitis C infected patients. No association of prediabetes was found with advancing age. Findings of present study also revealed that most of the females are victim of prediabetes as compared to males. Hypertension and obesity was significantly associated with development of prediabetes.**Keywords:** Hepatitis C, prediabetes, diabetes mellitus, IGT**INTRODUCTION:**

Hepatitis C virus (HCV) is a leading cause of chronic liver disease and hepatocellular carcinoma,<sup>1</sup> and epidemiologic studies have shown a strong association between HCV and type II diabetes mellitus (DM).<sup>2</sup> Pre-diabetes mellitus is defined as a state of abnormal glucose homeostasis in which deficiency or resistance to insulin is the hallmark. The pre-diabetic states, impaired fasting glucose (IFG) and impaired glucose tolerance (IGT), are exceedingly prevalent in the United States, with nearly 20% of the population suffering from IFG, 5% with IGT and 10% with combined IFG/IGT.<sup>3</sup> Impaired fasting glucose and IGT are manifestations of early derangements in glucose

homoeostasis that precede diabetes. IFG and IGT are thought to represent pathophysiologically distinct entities, characterized by higher degrees of hepatic insulin resistance in the former and higher degrees of peripheral (skeletal muscle) insulin resistance in the latter.<sup>4,5</sup>

Prediabetes mellitus precedes the development of overt type 2 diabetes mellitus (T2DM). It is associated with increased mortality and morbidity, and thus fits well with the criteria of a disease condition.<sup>6</sup> There are studies found that 30 to 70% people with HCV have insulin resistance or diabetes.<sup>2</sup> In one study by Ali et al<sup>7</sup>, pre-diabetes was found in 64.0% patients with

hepatitis C. The exact cause of diabetes in people with HCV is not completely understood, but it is believed that the hepatitis C virus may interfere with the way glucose is metabolized by the liver.<sup>8</sup> Due to the high rates of diabetes in the HCV population some experts believe that people with HCV should be routinely screened for diabetes.<sup>9</sup> There is mounting evidence that glucose abnormalities have a negative impact on the disease progression as well as antiviral therapy outcomes. Utilization of oral glucose tolerance testing has the potential to uncover previously undetected DM as well as impaired glucose tolerance or pre-diabetes in patients with chronic hepatitis C (CHC). Early detection of diabetes and prediabetes with oral glucose tolerance testing in CHC patients can lead to interventions, with significant positive impact on disease progression and antiviral therapy outcomes because insulin resistance impairs sustained response rate to PEG Interferon and Ribavirin Therapy and it is also a cause of steatosis and fibrosis progression in chronic hepatitis C<sup>10,11</sup>

The purpose of this study is to determine the frequency of pre-diabetes among hepatitis C patients in local population, so that we can determine the magnitude of the problem, because diabetes and insulin resistance are said to be associated with increased frequency of non-responders to hepatitis C treatment and a negative impact on the disease progression.<sup>12</sup> This study will also help us to design our routine practice guidelines and a public awareness program can be arranged for early recognition and management of this condition in order to reduce the mortality and morbidity of discussed population.

#### **OPERATIONAL DEFINITION:**

**Hepatitis C:** Hepatitis C infection was determined by screening the person with anti-HCV antibody by ELISA third generation laboratory test and confirmed by PCR for HCV RNA.

**Pre-diabetes:** Patients were labeled as pre-diabetic when fasting plasma glucose level was 100 to 125 mg/dl (Impaired fasting glucose) or 2-hour Plasma Glucose on the 75-g Oral

Glucose Tolerance Test was 140–199 mg/dl (Impaired glucose tolerance).

#### **MATERIAL AND METHODS:**

This cross sectional study was conducted at Department of Pathology, Civil Hospital, Bahawalpur from October 2017 to April 2018 over the period of six months. Total 182 patients with hepatitis C infection having age 30-60 years either male or female were selected from Department of Medicine Civil Hospital Bahawalpur.

Patients with known Diabetes mellitus, any liver disease other than HCV (e.g. HBV, autoimmune hepatitis, hepatocellular carcinoma), family h/o Type II diabetes mellitus, H/o taking steroids and patients not willing to be included in the study were excluded.

An approval was taken from institutional review committee and written informed consent was taken from every patient.

Height was measured by measuring tape and weight was taken on digital weighing machine to calculate BMI. Blood pressure of all the selected patients was measured and history was taken regarding hypertension.

Blood sample of each patient was drawn and sent to the pathology laboratory of the hospital for analysis of blood glucose levels and findings were noted in term of pre-diabetes (present/absent) as per-operational definition. All this data was recorded on a predesigned proforma which was containing two parts i.e. 1<sup>st</sup> part was containing the patients bio-data while 2<sup>nd</sup> part was containing the study variables.

Statistical analysis was performed using SPSS version 20.0. Mean and standard deviation was calculated for age. Frequency and percentage was calculated for pre-diabetes (present / absent), gender, hypertension and obesity. Effect modifiers like age, gender, hypertension and obesity was controlled through stratifications. Post-stratification Chi square test was applied to see their effects on the pre-diabetes and p value  $\leq 0.05$  was considered as significant.

#### **RESULTS**

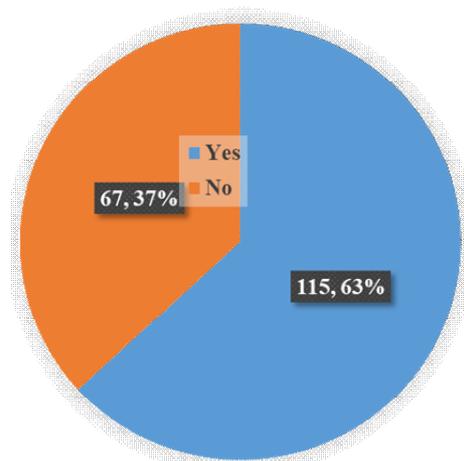
Total 182 patients with hepatitis C were selected. Mean age of the patients was  $43.27 \pm$

9.47 years. Out 182 patients, prediabetes was found in 115 (63%) patients. (Fig. 1)

Range of age was 30-60 years. Patients were divided into two age groups i.e. age group 30-45 years and 46-60 years. Total 107 (58.79%) patients belonged to age group 30-45 years and 75 (41.21%) patients belonged to age group 46-60 years. Prediabetes was observed in 68 (63.55%) patients and 47 (62.67%) patients respectively in age group 30-45 years and age group 46-60 years. No association (P = 1.00) of prediabetes with age groups was observed. (Table 1)

Out of 104 (57.14%) male patients, prediabetes was noted in 44 (42.31%) male patients. Among the 78 (42.86%) female patients, prediabetes was seen in 71 (91.03%) patients.

**Fig. 1:** Frequency of pre-diabetes



Prediabetes was significantly (P = 0.00) associated with gender. (Table 2)

Total 124 (68.13%) patients were hypertensive and prediabetes was found in 57 (45.97%) patients. All 58 non-hypertensive patients found with prediabetes. Statistically significant association between prediabetes and hypertension was observed with p value 0.000. (Table 3)

Total 104 (57.14%) patients were obese and 78 (42.86%) were non-obese. Prediabetes was noted in all (104) obese patients and in 11 (14.10%) non-obese patients. Prediabetes was significantly associated with obesity with p value 0.00. (Table 4)

**Table 1:** Stratification for age

Age group	Prediabetes		Total	P value
	Yes	No		
30-45	68 (63.55)	39 (36.45)	107 (58.79)	1.00
46-60	47 (62.67)	28 (37.33)	75 (41.21)	
<b>Total</b>	115 (63)	67 (36)	182	

**Table 2:** Stratification for gender

Gender	Prediabetes		Total	P value
	Yes	No		
Male	44 (42.31)	60 (57.69)	104 (57.14)	0.00
Female	71 (91.03)	7 (8.97)	78 (42.86)	
<b>Total</b>	115 (63)	67 (36)	182	

**Table 3:** Stratification for hypertension

Hypertension	Prediabetes		Total	P value
	Yes	No		
Yes	57 (45.97)	67 (54.03)	124 (68.13)	0.00
No	58 (100)	0	58 (31.87)	
<b>Total</b>	115 (63)	67 (36)	182	

**Table 4:** Stratification for obesity

Obesity	Prediabetes		Total	P value
	Yes	No		
Obese	104 (100)	0	104 (57.14)	0.00
Non-obese	11 (14.10)	67 (85.90)	78 (42.86)	
<b>Total</b>	115 (63)	67 (36)	182	

## DISCUSSION

Hepatitis C virus (HCV) infection is one the main causes of chronic liver disease worldwide. The number of chronically infected persons worldwide is estimated to be about 160 million, but most are unaware of their infection.<sup>12</sup> Since HCV has been discovered in late 1980, chronic hepatitis C (CHC) has become a complex multifaceted disease with several extra hepatic manifestations.<sup>13</sup>

Numbers of studies have demonstrated a strong association between HCV infection and insulin resistance (IR), providing possible link between this infection and diabetes mellitus.<sup>14</sup> IR is strongly connected with chronic hepatitis C (CHC) and IR can be developed early in the course of CHC.<sup>15</sup> Type II diabetes mellitus (T2DM) is more common in patients with chronic HCV than in the overall public and chronic hepatitis B patients.<sup>16</sup> IR has a major role in development of T2DM and it is the best predictor for the development of T2DM, and it assumes an essential part in development of T2DM.<sup>17</sup> HCV advances the progression of IR directly by affecting insulin signaling pathway at the cellular level. In addition, IR may play a role in the progression of the liver disease. In euglycemic individuals the estimation of HOMA-IR level helps to quantify IR. Diabetes can adversely affect the course of CHC.<sup>18</sup>

Present study was aimed to determine the frequency of prediabetes in cases of hepatitis C infection. Mean age of the patients was 43.27 ± 9.47 years. Out 182 patients, prediabetes was found in 115 (63%) patients.

In one study by Ali et al,<sup>19</sup> 38 men and 12 women having age ranged from 20-61 years were selected. All patients were infected with hepatitis C virus. Out of all, 64% of HCV patients were prediabetic which is in accordance with our findings. In another study by El-Kady,<sup>20</sup> total 60 hepatitis C infected

patients were selected. Prediabetes was found in 63.33% patients which is also comparable with our findings. Desouky et al<sup>21</sup> found total 63.8% patients with prediabetes. Delgado-Borrego et al<sup>22</sup> reported frequency of prediabetes in 62% patients. On the other hand in one Pakistani study, frequency of prediabetes among hepatitis C infected patients was 51%.<sup>23</sup> In our study, out of 104 (57.14%) male patients, prediabetes was noted in 44 (42.31%) male patients. Among the 78 (42.86%) female patients, prediabetes was seen in 71 (91.03%) patients. Prediabetes significantly (P = 0.00) associated with gender.

In one study, among the HCV infected patients, prevalence of prediabetes was 39% which is much lower than our study. In this study, 67% of HCV seropositive individuals were male and the rest, i.e 33% were females, which is in accordance with our study.<sup>24</sup>

In another study done by Singh P et al<sup>25</sup> in India, where 72.87% were males and 27.13% were females. One possible explanation for this may be the fact that males are more prone to harbor the risk factors for HCV infection, like injectable drug users as compared to females.

## CONCLUSION

Results of present study demonstrates a higher percentage of prediabetes in hepatitis C infected patients. No association of prediabetes was found with advancing age. Findings of present study also revealed that most of the females are victim of prediabetes as compared to males. Hypertension and obesity was significantly associated with development of prediabetes.

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