

# Association of Glycemic Control and Chronic Hepatitis C Virus Infection in Patients of Type 2 Diabetes Mellitus

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<sup>1</sup> Write the manuscript and data collection

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## Introduction

Diabetes mellitus has highest and sharply increasing incidence rate in the world. It is estimated that it will be increased about 69% by 2030 as compared with 2010 in the developing countries and about 20% increase is expected in industrialized countries. According to different estimates 18 to 24 million diabetic patients are expected in Africa till the

## ABSTRACT

**Objectives:** To determine the association of glycemic control with HCV infection among the patients of type 2 diabetes mellitus.

**Study Design:** Descriptive Cross Sectional

**Duration and Setting:** This study was conducted from June 2016 to January 2017 in OPD's of General Medicine, Pakistan Institute of Medical Sciences Islamabad, and Mohtarma Benazir Bhutto Medical College Mirpur.

**Methodology:** This cross-sectional study was started after taking approval form hospital ethical committee. In this study a total of 108 patients of type 2 diabetes mellitus were included. Type 2 Diabetic patients fulfilling the inclusion and exclusion criteria were selected for the study and were advised anti HCV antibodies by 3rd generation ELISA. The samples were sent for anti HCV antibodies, blood sugar and HbA1c. The type 2 diabetic patients were considered of having good glycemic control with the help of HbA1c  $\leq$  6.5 % and patient with  $>$  6.5 % HbA1c value were considered as having poor glycemic control.

**Results:** The mean age of the patients was 43.5 years with standard deviation of 6.8 years. There were 49 (45.37%) male and 59 (54.63%) female patients in the study. The HCV infection was present in 15 (13.89%) patients of type 2 diabetes A large number of patients 77 (71.29%) had poor glycemic control on the basis of HbA1c level and only 31 (28.70%) patients had good glycemic control. The rate of HCV infections was considerably higher 33.77% in poor glycemic control patients as compared with the 22.58% patients whose glycemic control was good, but the result was not statistically significant having p-value of 0.2536.

**Conclusion:** The frequency of HCV infection among type 2 diabetic patients having poor glycemic control is substantially high as compared to patients of good glycemic control group.

**Key Words:** Type 2 Diabetes, HCV, Glycemic Control, HbA1c

year 2030. This very high incidence is extremely alarming because the diabetes increases the risk of many carcinomas like breast, kidney, colorectal and pancreas. <sup>1</sup>

This disease is spreading dramatically, in 2014 more than 287 million people diagnosed with diabetes throughout the globe and it is expected that this figure will rise up to 592

million people in the year 2035. Another major health problem in the world is rapidly increasing disease of hepatitis C virus infection, which affecting more than 170 million people in the world. Among these cases of HCV more than 80% case have chronic infection. HCV is major of morbidity and mortality in the world, because it can cause acute hepatitis and chronic liver disease which further complications to chronic kidney disease, cirrhosis and liver cancer.<sup>2</sup> Many reports are being published indicating the relationship between hepatitis C virus infection and type 2 diabetes mellitus. According to different studies the patients of HCV have increased risk of getting type 2 diabetes as compared to non-HCV patients. Similarly, the risk of HCV infection increases at least 2 times in the patient having diabetes mellitus.<sup>3</sup>

One of the main causes of serious conditions like cirrhosis and liver cancer is considered hepatitis C virus infection. The recent statistics shows that the prevalence of HCV infection is approximately 3% worldwide and it affects more than 170 million people in the world. The main effect of hepatitis C infection is on liver but it can result in many extra hepatic expressions like sialadenitis, cryoglobulinemia and porphyria cutanea tarda.<sup>4,5</sup>

Many studies have proven a substantial relationship between type 2 diabetes and HCV infection. But some studies also have given contradictory results to this situation demonstrating no difference between HCV infections rate in type 2 diabetics and non-diabetics. According to the results of a study conducted in Taiwan for observing association of type 2 diabetes with HCV, it was observed that the HCV seropositivity increased by 2.8 times in patients of type 2 diabetes as compared with non-diabetic controls.<sup>6</sup> Similar results were noted from a study conducted in Italy in which it was observed that the prevalence rate of HCV in type 2 diabetics was more than 3 times higher (7.6%) as compared with non-diabetics having 2.3% prevalence rate of HCV infection.<sup>7</sup> Similar trend has been observed in Pakistani studies have an odd ratio of 3.03 of getting HCV infection among the patients of type 2 diabetes mellitus.<sup>8</sup>

The glycemic control become difficult in patients of type 2 diabetes having HCV infection because HCV increases the insulin resistance. So the results from this study will help in formation of effective screening programme among the patients of type 2 diabetes, because early detection and better management of HCV infection will help in better prognosis of the patients reducing morbidity and mortality due to complication of HCV in type 2 diabetic patients.

## Methodology

This cross-sectional study was started after taking approval from hospital ethical committee. In this study a sample of 108 type 2 diabetes mellitus patients were enrolled from the OPD's of General Medicine, Pakistan Institute of Medical Sciences Islamabad, and Mohtarma Benazir Bhutto Medical College Mirpur. This study was conducted in a time period of approximately 6 months from June 2016 to January 2017. WHO sample size calculator was utilizing for calculation of sample size by using parameters like 95% confidence level, Anticipated population proportion (Prevalence of HCV in Type 2 diabetics) 7.6%, and absolute precision of 5%. These patients were selected by non-probability consecutive sampling after taking informed written consent to be included in the study.

All the patients of both genders having type 2 diabetes, between 20 to 60 years of age and patients diagnosed/treated for type 2 DM for less than 15 years were included in the study. Patients with history or presentation of ketoacidosis or diabetic coma or type 1 DM, Impaired liver functions (ALT > twice normal range) or positive Hepatitis B serology, history of abnormal lipid metabolism, intravenous drug users, having history of blood transfusion, or organ transplant and history of body tattooing were excluded from the study.

Diabetes mellitus type 2 was diagnosed on the basis of Fasting Plasma Glucose at or above 126 mg/dl (7.0 mmol/L), or random plasma glucose concentration  $\geq$  200 mg/dL (11.1 mmol/L) in the presence of symptoms. Type 2 Diabetic patients fulfilling the inclusion and exclusion criteria were selected for the study and were advised anti HCV antibodies by 3rd generation ELISA. The samples were sent for anti HCV antibodies, blood sugar and HbA1c. The type 2 diabetic patients were considered of having good glycemic control with the help of HbA1c  $\leq$  6.5 % and patient with > 6.5 % HbA1c value were considered as having poor glycemic control. All the information was collected on a predesigned performa. SPSS v. 21 was used for data entry and analysis. Quantitative variables were described with the help of Mean and standard deviation and qualitative variables were presented in the form of frequency and percentages. The rate of HCV infection was compared by applying Chi-square test between patients having good and poor glycemic control. P-value < 0.05 was considered significant.

## Results

In this present study a total of 108 patients of type 2 diabetes mellitus were selected to investigate the association between diabetes and Hepatitis C infection. Majority 42 (39%) of the patients in the study had age between 41-50 years followed by the group having age in the interval of 51-60 years and 24 (22%) patients had age between 31-40 years. The mean age of the patients was 43.5 years with standard deviation of 6.8 years. There were 49 (45.37%) male and 59 (54.63%) female patients in the study.

The HCV infection was present in 15 (13.89%) patients of type 2 diabetes and in 93 (84.26%) patients, the results of anti HCV were negative for HCV infection. In the study sample the glycaemic control was not considerably good among the patients of type 2 diabetes. A large number of patients 77 (71.29%) had poor glycaemic control on the basis of HbA1c level and only 31 (28.70%) patients had good glycaemic control as elaborated in table I.

Characteristics	Number	Percentage
<b>Age of patients (Year)</b>		
20-30	9	8%
31-40	24	22%
41-50	42	39%
51-60	34	31%
<b>Mean <math>\pm</math> SD</b>	43.5 $\pm$ 6.8	
<b>Gender of Patients</b>		
Male	49	45.37%
Female	59	54.63%
<b>HCV infection</b>		
Present	15	13.89%
Absent	93	84.26%
<b>Glycemic control</b>		
Good	31	28.70%
Poor	77	71.29%

According to the results of the study it is obvious that the rate of HCV infections is considerably higher in poor glycaemic control patients in the incidence of HCV infection rate is 33.77% as compared with the patients whose glycaemic control was good on the basis of HbA1c. In patients of good glycaemic control group, the rate of HCV infection was 22.58%. Although the incidence rate of HCV infection was noted substantially high in poorly controlled diabetes group in comparison to well controlled diabetes group but the result was not statistically significant having p-value of 0.2536 as elaborated in table II.

**Table 2: Association of Hepatitis C infection with Glycemic Control**

Hepatitis C virus	Good Glycemic Control (n= 31)		Poor Glycemic Control (n= 77)		P-Value
	Frequency	Percentage	Frequency	Percentage	
Present	7	22.58 %	26	33.77 %	0.2536 *
Absent	24	77.42 %	51	66.23 %	
Total	31	100	77	100	

\* Association is not significant at 5% level of significance

## Discussion

The etiology and pathogenesis of type 2 diabetes mellitus among the HCV positive patients is not clear. Although the function and relationship of insulin resistance with fibrosis score cannot be ignored. Type 2 diabetes mellitus is an abruptly emerging problem worldwide. The main causes for its rapid increase are increasing sedentary lifestyle, obesity, positive family history of diabetes mellitus, aging and HIV co-infection etc. <sup>9, 10</sup>

Abnormal glucose homeostasis is a condition of metabolism which occur in patients of diabetes mellitus. According to different estimates, diabetes have affected more than 171 million people worldwide and this figure is increasing horribly day by day. Same status of diabetes evolution has been observed in Pakistan, with an average burden of 3% to 7.2% in general population. The prevalence of diabetes has been estimated 4 to 6 fold more prevalent in south Asian countries as compared with European countries.<sup>11, 12</sup>

The results of this present study shows that HCV infection was more prevalent in patients of older age as compared with younger age groups, which is also supported by the literature. <sup>13</sup>

Due to more parenteral exposure which increases the chances of infection, the older age patients are more prone to HCV infection as compared with younger age patients.

The comparison of HCV infection rate on the basis of gender showed that the infection rate was significantly higher in male patients as compared to female patients of type 2 diabetes mellitus.

Analysis of HCV infection rate with respect to gender revealed that males had higher HCV infection rate. Out of 15 HCV positive cases 9 (60%) were male while 6 (40%) were female type 2 diabetic patients. Similar results to this study were noted by Caronia et al, who found that male patients

have significantly higher rate of HCV infection as compared to female patients.<sup>14</sup>

Many previous studies and this present study found a convincing connection between type 2 diabetes mellitus and HCV infection. This relationship can be explained on the basis of several reasons like defect in insulin secretion have relationship with HCV pathophysiology causing T2D. This cause excessive production of hepatic glucose and insulin resistance which is consequential of the core-encoding region of HCV, who is sufficient to induce insulin resistance via direct or indirect way. The other foremost important risk factors for HCV are positive family history and advancing age in patients of type 2 diabetes.

The results of this present study showed that the HCV infection was present in (13.89%) patients of type 2 diabetes and in 93 (84.26%) patients, the HCV status was negative. These results are in agreement with previous studies who also found the prevalence rate around this value.<sup>15, 16, 17</sup> But some studies have shown very higher rate of HCV among the patients of type 2 diabetics. Many studies conducted on anti-HCV sero-prevalence, have found the relationship between HCV infection and type 2 diabetes mellitus. In a research on type 2 diabetic patients it was found that black cast had higher rate of HCV positive patients (28% vs. 12%) as compared with white patients of type 2 diabetes.<sup>18</sup>

According to the results of this present study it was noted that a large number of patients had (71.29%) poor glycemic control on the basis of HbA1c level and only (28.70%) patients had good glycemic control. The rate of HCV infections was considerably higher in poor glycemic control patients in which the incidence of HCV infection was noted 33.77% as compared with the patients whose glycemic control was good having the rate of HCV infection as 22.58%. But this difference was not statistically significant. But some studies have shown the increased prevalence of glucose abnormalities and diabetes mellitus among patients with chronic hepatitis C virus (HCV) infection.<sup>25</sup> Some studies in the literature have shown no association of HCV with glycemic control status as found in the present study whereas some researched found increased risk of HCV with good control<sup>19</sup> and with poor control in others studies.<sup>20</sup>

Morbidity and mortality related to diabetes can be minimized by improving the access and quality of healthcare system and with effective control and timely management of diabetes mellitus. The establishment of the facilities for lab

tests like blood glucose and HbA1c tests to monitor the status of diabetes and provision of insulin injections will help considerably in reducing diabetes and its related complications, especially among poor patients of our population.<sup>21</sup> Although many studies have shown link between diabetes mellitus and HCV infection, but this association has yet not been illuminated. Similarly, the results of the present study also did not show any statistically significant association between type 2 diabetes and HCV infection.

## Conclusion

The study results prove the underline glucose intolerance in HCV patients because the prevalence of HCV was considerably high in type 2 diabetic patients with poor glycemic control. The main etiology of type 2 diabetes is complex and its main pathophysiology is deficiency in insulin secretion or insulin action with increase in hepatic glucose production. All these factors are major contributors for development of overt hyperglycemia. So the pathogenic relationship of HCV infection with type 2 diabetes or relationship of type 2 diabetes with development of HCV infection require further investigations.

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