

# CHRONIC HEPATITIS C VIRUS INFECTION; ASSOCIATION WITH TYPE 2 DIABETES MELLITUS

**DR. DILSHAD MUHAMMAD**FCPS (Medicine)  
MU-IV, DHQ Hospital, Faisalabad**DR. KHALID AMIN**FCPS (Medicine)  
Associate Professor of Medicine MU-IV  
DHQ Hospital, Faisalabad**DR. AMIN ANJUM**FCPS (Medicine)  
Senior Registrar MU-IV  
DHQ Hospital, Faisalabad**Dr. Masood Javed**FCPS (Medicine)  
MU-I, Allied Hospital, Faisalabad

**ABSTRACT... Objectives:** (1) To seek the association between chronic HCV infection and type 2 diabetes, mellitus. (2) To verify the effect of age, sex, socioeconomic status, obesity and presence of cirrhosis on the association of chronic HCV infection. **Design.** Case control study. **Setting:** DHQ Hospital, Faisalabad. **Subjects:** The subjects were divided into two groups. One was with positive anti-HCV antibody on ELISA method and other was without liver disease and negative for anti-HCV. Both the groups contained 500 subjects each and were selected according to the inclusion and exclusion criteria. **Intervention:** After a brief interview regarding age, residence, family history of diabetes, socioeconomic status, both the groups underwent weight and height measurements. The body mass was calculated according to the formulae. Ultrasonography of abdomen was done of all the patients of study groups to assess the liver status. **Main outcome measures:** Chi – square test was applied to see the association and then odds ratio was calculated to check the strength of association. **Results:** Diabetes mellitus was detected in 174 patients (34.8%) out of 500 patients in the group A as compared to 30 patients (6%) out of 500 patients in the group B. having chi-square value of 127.69 and significance of 0.000 with HCV +/ HCV- Odds ratio 0.120 and 95% CI 0.079-0.181. **Conclusions:** There is strong association between HCV infection and type 2 diabetes mellitus. Severity of Liver Disease was strong associated factor.

**Key words:** Chronic Liver Disease (CLD), Anti-Hepatitis C (Anti HCV) Cirrhosis of Liver, Diabetes Mellitus type-II (DM II) Insulin Resistance (IR), Body Mass Index (BMI)

## INTRODUCTION

Hepatitis C disease has become a worldwide growing problem. It is caused by an RNA virus belonging to flavivirus group in Pakistan prevalence is about 06-07%<sup>1</sup>. Chronic HCV infection may lead to cirrhosis and hepatocellular carcinoma.

It may also lead extra hepatic illnesses, including essential cryoglobulinemia, Porphyria cutanea tarda, membranous glomerulonephritis and bone marrow depression.

An increased prevalence of diabetes mellitus II in persons having HCV disease has been observed.

It was first reported by Allison et al<sup>2</sup>, in 1994 in a cross sectional survey in United States. Since then numerous studies has shown increased prevalence of diabetes in HCV patients than liver disease from other causes like alcohol and hepatitis B<sup>2</sup>.

Abnormalities of carbohydrates metabolism like hyperinsulinemia and insulin resistance are well recognized complications of cirrhosis. Diabetes can be explained on the basis of co-incidental pancreatic disease<sup>4</sup>.

One study suggests that cross re-activity of LKM auto antibodies with islets can lead to diabetes<sup>4</sup>.

In a Pakistani study at Larkana Hepatitis C has been shown strongly associated with type II diabetes mellitus. i.e. more than 77.7% of cirrhotic patients with diabetes were positive for HCV infection<sup>5</sup>.

In a recent research<sup>6</sup>, It is found that a) HCV infection leads to post receptor defect in IRS-I (insulin receptor substrate) associated with IR (insulin receptor) and b) insulin signaling defect in hepatic IRS-I tyrosine phosphorylation and P-13 kinase association / activation may contribute to insuline resistance which ultimately leads to diabetes development. Keeping in mind recent studies we carried out a study at DHQ Hospital,

Faisalabad to observe the association of Diabetes mellitus-II in HCV disease patient in our population and to verify the effect of other factors on this association.

## MATERIALS AND METHODS

### Setup

Study was carried out in outdoor and indoor of DHQ Hospital, Faisalabad from 1st July 2009 to 21st December 2009.

### Study Design

It was case control analytic study

### Procedure

The subjects were divided into two groups. In the study group five hundred patients with HCV infection were included. In the control group five hundred patients negative for anti-HCV were included. The patients under went anti-HCV testing via ellisa (enzyme linked immunosorbent assay, third generation).

All the patients with chronic liver disease due to HCV and control group under went fasting and random blood sugar testing they were categorized as diabetic when fasting blood sugar was greater than 7 mmol (126mg/dl) and random blood sugar greater than 11.1 mmol (200mg/dl) on more than one occasion. Patients on anti-diabetic were also categorized diabetic. All the investigations were performed from hospital laboratory.

Risk factors such as age, sex, social economic status, family history of diabetes, obesity and presence of cirrhosis were noted, weight and height of each patient was noted to calculate body mass index with following formula.

Body mass index (BMI) = wt (kg)/Height (Meter<sup>2</sup>).

They were categorize as normal with BMI 21-25 kg/m<sup>2</sup>, Over weight with BMI 26-30 kg/m<sup>2</sup> and obese if BMI more than 31. Social economic status was determined from monthly income. Low social economic group if

monthly income was less the 8000 per month. Abdominal ultrasound was done to see the status of Liver disease in anti-HCV positive patients.

## STATISTICAL ANALYSIS

Following statistical tests were applied for the data analysis of two groups.

Pearson Chi-square statistics were used. Odds ratio was calculated and 95% confidential interval presented. Interactions were considered for age, sex, socio economic status, BMI, Presence of cirrhosis and family history of diabetes mellitus. All statistical analysis were performed by using the SPSS software, version 10 (USA).

## RESULTS

In this study, a total of 1000 patients were included. There were two groups, One was anti- HCV positive (Group A) and other was anti-HCV negative (group B). Both groups contained 500 patients each.

In group A patients 174 patients (34.8%) were diabetics while in group B only 30 patients (6%) were diabetic.

Patients were having ages between 30 yrs to 80 years and the major bulk was between 41-70 years of age. Patients distribution according to the age is given to the figure-I.

Association between HCV status of patients (%age) according to the age is given in Table-I. There were 280 (56%) males and 220 (44%) female in group A while group B showed 296 (59.2%) male and 204 (41.8%) female. Most of subjects belonged to urban areas in both groups (Group A 60% and group B 58.4%).

Regarding the socio-economic status most of the patients belonged to the lower status. In the group A patients 294 (58.8%) [180 male, 114 female] had cirrhotic and 206 (41.2%) were non cirrhotic (Chronic hepatitis 106 male and 100 female).

Chi-square test was applied to see the association of risk factors with DM-II. Odd ratios were calculated and 95% confidential interval presented. There was chi-square value of 127.69 and significant of 0.000 with HCV positive / HCV negative patients. Odds ratios 0.20 and 95% of C1 0.079/0.181.

Lower social economic status was significantly associated with DM-II in HCV positive patients (sig = 0.01). There was significant association between BMI of patients and type-II DM in both groups but in group A (HCV positive) association was much more highly significant (sig 0.000) as compared to group B (HCV negative) (sig = 0.008). Regarding the liver status, out of 294 cirrhotic 132 were detected as diabetics while in 206 non cirrhotics only 42 had diabetes. So presence of cirrhosis was strong risk factor for development of DM-II (sig 0.000) with odds ratio 3.182 and 95% as C1 2.113 - 4.792.

Various interactions of factors like age, BMI, Status of Liver Diseases and socio economic status within both groups are given the following tables and figures.

**DISCUSSION**

Allison et al published the first report of link of DM-II and HCV disease. They conducted their study on liver transplant awaiting patients and found DM-II five times more prevalent in HCV related cirrhosis than cirrhosis unrelated to HCV infection.

This study demonstrated that 34.8% of patient with chronic HCV infection had DM-II. Although our figure varied from other studies i.e. 18.7% in Pakistan<sup>7</sup>, 21-23%

in USA<sup>8,9</sup>, 29% in Canada<sup>10</sup>, 20.9% in Japan<sup>11</sup> and 25.4% in Egypt but our findings are in consistent with the above mentioned studies. An Italian study reported 39% HCV patients had DM-II<sup>12</sup>. In our study group-B showed percentage of DM-II 6%. National survey in Pakistan Healthy population has revealed prevalence of diabetes about 4.5-11%<sup>13,14</sup>. So this finding in the group-B goes consistent with these studies in non-HCV patients.

Increasing age was significantly associated with DM-II (Chi-square value of 19.25 and sig=0.002).Sex did not appear to be a risk factor. This is in contrast to a study by caronia s et al where male sex was a major variable associated with DM-II (09). Lower socio economic status and DM-II association is significant in group A (Chi-square value 9.16 and sig = 0.01) as compared to group B where (sig = 0.08 with chi-square value of 4.98). There

Table-I.					
HCV Status	Diabetes		Non Diabetes		P-value
	n	%	n	%	
HCV +	174	34.8	326	65.2	<0.001
HCV -	30	6.0	470	94.0	
Total	204	20.4	796	79.6	
<i>Chi square = 127.697      df = 1      Sig = 0.000**</i> <i>Minimum expected count = 102.00</i>					
Risk Estimate					
	Odds ration		95% confidential interval		
			Lowe	Upper	
HCV + / HCV -	0.120		0.079	0.181	

Table-II. Association between HCV status of patients (%) according to age						
HCV Status	Age (year)					
	31-40	41-50	51-60	61-70	71-80	>80
HCV +	16.4	27.2	30.4	16.0	6.8	3.2
HCV -	15.6	24.4	31.4	19.8	6.4	2.4
Total	16.0	25.8	30.9	17.9	6.6	2.8
<i>Chi-square = 3.589      df = 5      sig = 0.610 NS</i> <i>Minimum expected count = 14.00</i>						

**Table-III. Distribution (%) according to association between body mass index of patients and type-II diabetes mellitus.**

HCV Status	BNI Status	Diabetes Mellitus		Total
		Diabetic	Non Diabetic	
HCV +	<20	13.9	86.1	14.4
	21-25	27.1	72.9	47.2
	25-30	56.0	44.0	30.0
	30-35	38.1	61.9	8.4
HCV -	<20	-	100	23.6
	21-25	6.3	93.7	41.2
	25-30	9.7	90.3	28.8
	30-35	9.4	90.6	6.4

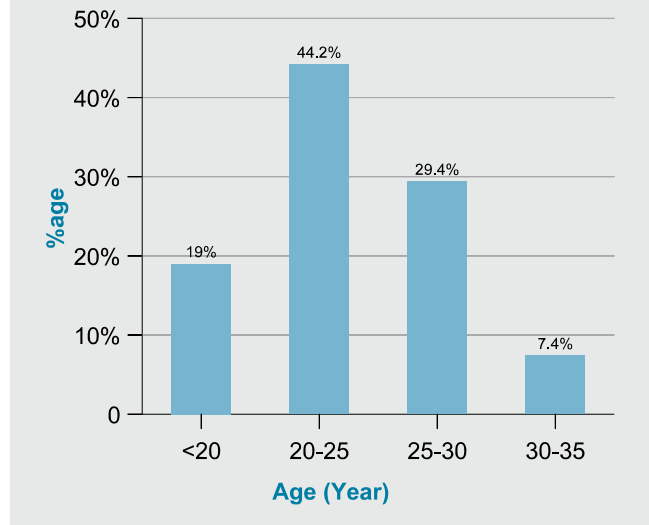
HCV+

*Chi Square = 49.92 df = 3 sig = 0.000\*\*\* Minimum expected count = 14.62*

HCV -

*Chi Square = 11.75 df = 3 sig = 0.008\*\* Minimum expected count = 2.28*

**Fig-1. Distribution of patients according to their body mass index**



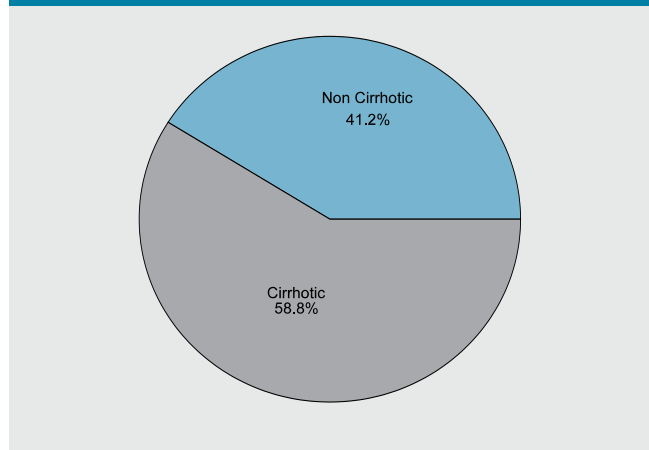
**Table-IV. Distribution of HCV + patients according to association of liver status and type II diabetes mellitus**

HCV Status	Diabetic		Non Diabetic	
	n	%	n	%
Cirrhosis	132	44.9	162	55.1
Chronic hepatitis	42	20.4	164	79.6
Total	174	34.8	326	65.2

*Chi Square = 32.169 df = 1 sig 0.000\*\*\* Minimum expected count = 71.69*

	Odds ratio	95% confidence interval	
		Lower	Upper
Cirrhosis / Chronic hepatitis	Odds ration 3.182	2.113	4.792

**Distribution of hepatitis patients according to their liver status in group: A**



was significant association between BMI of the patients of DM-II in both groups.

In our study, out of 294 cirrhotic patients of group A (HCV Positive) 132 were (44.9%) diabetics. This proves the presence of cirrhosis has a significant association with DM-II.

This is consistent with the first ever study by Alison et al and other studies (08-09-11). Claudia in a study in 2005 had showed that DM-II and impaired fasting glucose (IFG) prevalence was high among HCV infected patients

with advanced liver disease versus those with early histological disease. ( $P=0.0004$ ). In this study obesity was also ruled out as a risk factor in these HCV patients<sup>15</sup>.

## CONCLUSION

In the light of this study HCV infection was found to be strongly associated with DM-II development than liver disease due to other causes like HBV and alcoholic liver diseases. Moreover it is more common in more advanced disease and advanced age. This again signifies the importance of early treatment of HCV infected patients.

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**Correspondence Address:**

Dr. Dilshad Muhammad  
MU IV, DHQ Hospital,  
Faisalabad.  
dilshadoctor@yahoo.com

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