

**FREQUENCY OF TYPE 2 DIABETES MELLITUS IN HEPATITIS C VIRUS INFECTED POPULATION VISITING TERTIARY CARE HOSPITAL IN SINDH, PAKISTAN..**Sarmad Ali<sup>1</sup>, Muzafar Ali Shaikh<sup>2</sup>, Madiha Shah<sup>3</sup>, Fiza Shah<sup>4</sup>, Razia Bano<sup>5</sup>, Sadia Shaikh<sup>6</sup>.**ABSTRACT:**

**Background::** Hepatitis C virus (HCV) is a widely prevalent RNA virus, with a global prevalence estimated to be 2.5%, representing approximately 177.5 million people affected worldwide. Diabetes mellitus (DM) is a major cause of early morbidity and mortality worldwide, with a global prevalence of 9.3% affecting approximately 463 million people globally. There is not tending to screen Hepatitis C positive patients for Diabetes Mellitus in Pakistan. **Objective:** To determine frequency of Type 2 Diabetes Mellitus in patients who are seropositive for Hepatitis C. **Design:** Cross sectional descriptive **Study Setting:** Medicine ward of Liaquat University of Medical and Health Sciences, Jamshoro **Study Duration:** Six months from 01/06/2019 to 30/11/2019 **Methodology:** Utilizing non-probability consecutive sampling, patients with evidence of hepatitis C positive antibodies on Chromatography or ELISA, irrespective of liver cirrhosis and stage of disease were included in this study. Fasting blood glucose was done by taking venous sample after 8 hours of fasting. Structured proforma was used to collect data. Presence of Diabetes Mellitus was confirmed via Fasting blood sugar or HbA1c. **Results:** 327 patients were included in this study sample. Frequency of Type 2 Diabetes Mellitus in patients who are seropositive for Hepatitis C was observed in 37.9% within our study sample (124 out of 327 cases). The average age of the patients was 49.3±12.6 years. There was a significant association between occurrence of T2DM in HCV-seropositive patients and their age. There was no significant association between occurrence of T2DM in HCV-seropositive patients and their gender. **Conclusion:** A high prevalence of T2DM was noted in our study sample of HCV-infected patients in contrast to the unaffected population. Therefore, early intervention is needed to preemptively predict and avoid occurrence of T2DM. This would likely aid in limiting the coexistence of HCV infected patients with T2DM and associated psychosocial, financial, and resource implications.

**Key Words:** Hepatitis C virus, Type 2 Diabetes Mellitus, Hyderabad Sindh

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**INTRODUCTION**

Hepatitis C virus (HCV) is a widely prevalent RNA virus, with a global prevalence estimated to be 2.5%, representing approximately 177.5 million people affected worldwide<sup>1</sup>. Besides causing acute infection i.e. Acute Hepatitis C, it is also a significant cause of chronic liver disease with significant sequelae such as end stage fibrosis, liver cirrhosis and hepatic malignancy such as hepatocellular carcinoma<sup>2</sup>. HCV infection may also cause extra hepatic manifestations including glomerulonephritis, essential mixed cryoglobulinemia, sporadic porphyria, vasculitis, cutaneatarda, thyroid disease and B-cell non-Hodgkin lymphoma<sup>3</sup>. Diabetes mellitus (DM) is a major cause of early morbidity and mortality worldwide, with a worldwide prevalence of 9.3% affecting approximately 463 million people globally; and the figure is expected to rise up to 578 million by the year 2030 and 700 million by 2045<sup>4</sup>. Type 2 Diabetes Mellitus (T2DM) is a metabolic disease

characterized by hyperglycemia and insulin resistance, but also relative impairment in insulin secretion. It may lead to long-term macro and microvascular dysfunction of vital organs such as the eyes, kidneys, nerves, heart, and blood vessels, including retinopathy, end-stage renal disease, and stroke, myocardial infarction, and foot ulcers. Numerous other factors also contribute to the impact of DM on quality of life and socioeconomic nuances, particularly employment, absenteeism, and work productivity<sup>5</sup>. Multiple studies have attempted to establish the association between T2DM in HCV patients, with the hypothesis that T2DM is an extrahepatic manifestation of HCV; the most compelling evidence is a 2018 systematic review and meta analysis which reported a pooled prevalence of 19.7% T2DM among HCV patients, and further demonstrated a pooled prevalence of 20.7% in Asia<sup>6</sup>. The processes through which HCV is associated with T2DM include direct viral effects, insulin resistance,

chemokines, cytokine signal suppression and other immune mediated mechanisms<sup>5</sup>. Several cross-sectional studies have attempted to investigate whether there is a trend of higher HCV antibodies prevalence in T2DM patients than expected in the general population. At present, there is no trend to screen Hepatitis C positive patients for Diabetes Mellitus in Pakistan.

**MATERIALS& METHODS**

This was a hospital-based, cross sectional descriptive study to obtain the frequency of HCV infection among patients diagnosed with T2DM, over a six-month period from 01/06/2019 to 30/11/2019 in Department of Medicine, Liaquat University Hospital Hyderabad/Jamshoro. Non-probability consecutive sampling was utilized for sample collection. Following informed consent, the data was noted on pre-determined proforma. Inclusion criteria were: Patients of both genders, between age 20 to 70 years, diagnosed with Type 2 Diabetes mellitus i.e. the serum fasting sugar level above 126 mg/dL or HbA1c levels above 6.5% was considered as Diabetes mellitus, who had evidence of Hepatitis C antibodies on Chromatography or ELISA, irrespective of liver cirrhosis or disease stage who were agreeable to participate in the study. Exclusion criteria were pregnant women, patients with hepatocellular carcinoma or patients with co-existing hepatitis B infection. Fasting blood glucose was done by taking venous sample after 8 hours of fasting. The demographic characteristics of the patients and

laboratory investigations including Fasting Blood Sugar, HbA1c, complete blood counts, prothrombin time, serum albumin, bilirubin, serum creatinine were obtained. Presence of Diabetes mellitus was confirmed via Fasting blood sugar and HbA1c. The composed dataset was entered in SPSS (version 20.0) and analyzed accordingly. The frequency and percentage was calculated for gender and age. Quantitative data i.e. Age in years, Fasting Blood sugar, HbA1c, creatinine, total bilirubin, albumin, platelets, and prothrombin time, hemoglobin, were described using mean ± standard deviation with 95% confidence interval. Outcome was calculated and stratified by age and gender by chi-square test. P was considered significant at p≤0.05.

**RESULTS**

327 subjects were recruited in this study, with evidence of Anti-HCV antibodies on Chromatography or ELISA, irrespective of liver cirrhosis and stage of disease. The average age of the subjects was 49.3±12.6 years. There were 158 (48.3%) male and 169(51.7%) female patients. Frequency of T2DM in study sample was 37.9% (124 out of 327 cases). The mean fasting blood sugar was 113.2 mg/dL (±19.9) and mean HbA1c was 6.2(±0.6). Occurrence of T2DM in the study's HCV seropositive patients was significantly high in above 40 years of age patients (p=0.0005). Frequency of T2DM in HCV seropositive patients was not significantly associated with whether the patient was male or female (p=0.662).

**Table 1: Summary of outcome variables among study sample**

Variable	Mean	Standard Deviation	95% CI	
			Lower limit	Upper limit
Age in years	49.3	12.6	47.9	50.7
Fasting Blood Sugar	113.2	19.9	111.0	115.4
Hba1c	6.184	0.6	6.12	6.2
Bilirubin	0.2	0.03	0.2	0.2
Albumin	3.8	0.4	3.7	3.8
Prothrombin Time	16.1	2.1	15.9	13.4
International Normalized Ratio	1.5	0.8	1.4	1.6
Creatinine	1.3	0.1	1.2	1.3
Hemoglobin	11.4	0.9	11.3	11.5
White Cell Count	5.6	1.4	5.4	5.7
Platelets	324,938.8	80,193.4	316,214.6	333,663.1

**Table 2: Frequency of HCV-seropositive patients with T2DM by age group**

Age group	Type 2 Diabetes Mellitus		Total	P-value
	Yes	No		
<30 years	3 (11.5%)	23 (88.5)	26 (7.9%)	0.0005
31 to 40 years	8 (11.9%)	59 (88.1%)	67 (20.5%)	
41 to 50 years	51 (58.0%)	37 (42.0%)	88 (26.9%)	
51 to 60 years	21 (23.3%)	44 (67.7%)	65 (19.9%)	
61 to 70 years	41 (50.6%)	40 (49.4%)	81 (24.8%)	

**Table 1: Frequency of HCV-seropositive patients with T2DM by gender**

Gender	Type 2 Diabetes Mellitus		Total	P value
	Yes	No		
Male	58 (36.7%)	100(63.3%)	158	0.662
Female	66 (39.1%)	103(60.9%)	169	

## DISCUSSION

Hepatitis C virus (HCV) can be life threatening, with various morbidities and mortalities, and chronic liver disease is one of its most significant complications, represented by a 2.5% global prevalence (1, 2). The occurrence of HCV infection in T2DM patients is an ongoing public health dilemma. HCV is nearly endemic in Pakistan; a recent systematic review in 2018 estimated an average HCV prevalence of 6.2% within the national population, reported as high as 34.5% in the high-risk groups and 55.9% in people with hepatic co-morbidities, with about one in 20 Pakistanis being affected (7). Prior studies suggest that nearly 10 million people within Pakistan are living with HCV (8). Diabetes mellitus (DM) is another major concern involving the developed and developing countries. A 2017 study in Khyber Pakhtunkhwa, Pakistan, reported a prevalence of 26.4% prevalence of T2DM in HCV (14), while another study in Hyderabad, Sindh revealed a 31.5% T2DM prevalence in HCV patients (15). The data from our study sample revealed a T2DM prevalence of 37.92% (124 out of 327) cases HCV seropositive patient, which was higher than other regional studies. In our study there were 48.3% males and 51.7% females with a near equal ratio, and there was no significant association found between gender and occurrence of HCV infection in the study sample. It is, however, in disagreement with another study showing female to male ratio reported as 1:16.5 (9). In our study the average subject age was 49.3±12.6 years. These results are concordant with prior research on this population group, particularly 2 studies carried out in Lahore city revealing marginally increased risk of HCV prevalence in middle aged groups (9, 10). This increased prevalence can be correlated to risk factors such as exposure, blood product transfusions, syringe re-use, and a trend of non-allopathic non-sterile traditional practices, however such inference needs further robust investigation to prove significant association. A systematic review by White et al reported an increased risk of T2DM when compared between HCV infected patients and an uninfected control group (11). A point to be noted is that recent data points towards a three-fold increased T2DM prevalence in HCV seropositive patients (12). Cumulatively, this data suggests a

significant association between HCV and T2DM. One of the hypothesized rationales is that the pathophysiology of T2DM secondary to HCV consists of dysregulation in insulin production, surge of liver TNF- $\alpha$ , augmented hepatic gluconeogenesis, and resistance to insulin, because the HCV virus may likely induce insulin resistance through complex molecular mechanisms (13). All these data support our suggestion that HCV is the stimulus rather than the consequence of Diabetes Mellitus among the population studied.

## CONCLUSION

Despite significant variation in study methodologies and global applicability of available studies in some countries, particularly those without a centralized data collection protocol, the results of the study may be utilized in improving health care policy making. The conclusive data from our study suggested a remarkable prevalence of T2DM among HCV-afflicted individuals in contrast with non-affected population. This clearly suggests that timely prevention plus medical management for HCV should be initiated to avoid potential risk of T2DM occurrence and concurrent complications. Furthermore, relevant decision makers will need to ensure prioritizing preemptive strategies and policy changes for decreasing the concurrent T2DM-HCV disease burden.

**ETHICS APPROVAL:** The ERC gave ethical review approval

**CONSENT TO PARTICIPATE:** written and verbal consent was taken from subjects and next of kin.

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**CONFLICT OF INTEREST:** No competing interest declared.

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