

Prevalence of diabetes in Hepatitis-C virus infected patients visiting a tertiary care hospital

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ABSTRACT

Background: Infection with the Hepatitis C virus (HCV) is a significant global public health concern, with chronic infection leading to severe complications such as liver cirrhosis and hepatocellular carcinoma. Recent studies have increasingly recognized the association between HCV infection and diabetes mellitus, particularly type 2 diabetes (T2D), highlighting the need for further investigation into this relationship.

Objective: This study aimed to determine the prevalence of diabetes among HCV-infected patients visiting a tertiary care hospital and to explore the potential association between HCV infection and the development of diabetes.

Methods: This retrospective cross-sectional study analyzed data from 130 individuals diagnosed with HCV infection. Demographic information, duration of HCV infection, presence of liver cirrhosis, and diabetes status were collected. Laboratory investigations included HbA1C levels to assess glycemic control and serological testing for HCV antibodies. Statistical analysis was performed to evaluate the association between HCV infection and diabetes, adjusting for potential confounding factors.

Results: The prevalence of diabetes among HCV-infected patients was 31.5%, with a mean HbA1C level of 6.04%, indicating suboptimal glycemic control in many patients. Liver cirrhosis was present in 25.4% of the study population. A significant association was observed between HCV infection and diabetes, with diabetic patients showing a higher likelihood of liver cirrhosis ($p = 0.0001$). Additionally, gender-based analysis revealed a statistically significant difference in diabetes prevalence, with females being more affected than males ($p = 0.04$).

Conclusion: Our findings underscore a strong association between HCV infection and diabetes, particularly in patients with advanced liver disease. The high prevalence of diabetes in this population highlights the need for routine screening and early intervention to mitigate complications and improve patient outcomes. These results advocate for integrated care approaches that address both HCV and diabetes, emphasizing the importance of early detection and management in improving the quality of life for affected individuals.

KEY WORDS: Hepatitis C Virus, Diabetes, Liver cirrhosis.

INTRODUCTION

Diabetes, a chronic illness, has emerged as a significant global health concern, affecting individuals and communities alike. As of 2021, an estimated 537 million adults were living with diabetes, a figure projected to rise to 784 million by 2045.¹ A staggering

81% of the diabetic population resides in low and middle-income countries. Diabetes, causing one death every five seconds, has led to a substantial increase in health expenditure, reaching approximately USD 966 billion in the USA. The disease impacts individuals physically, socially, economically, and leading to ocular,

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renal, neuropathic, cardiovascular, and cerebrovascular complications.²

Hepatitis C virus (HCV), an RNA virus from the Flaviviridae family, is a blood-borne viral illness primarily transmitted through HCV-contaminated blood products and equipment. Less common transmission modes include sexual and vertical transmission.³ Approximately 75-85% of patients develop chronic infection, which over 20-30 years, can lead to liver cirrhosis in 10-20% patients.⁴ Cirrhosis can result in hepatic decompensation, leading to ascites, upper gastrointestinal bleeding, hepatic encephalopathy, hepatorenal syndrome, and hepatocellular carcinoma.⁵

A 2018 meta-analysis, including 40 global studies, reported a pooled prevalence of Type II diabetes of 19.67% among HCV-infected patients. This prevalence is significantly higher than the 8.5% observed in the general population.⁶ There are multiple factors, such as direct viral impacts, insulin resistance, proinflammatory cytokines, chemokines, and other immune-related mechanisms, that are believed to play a role in the rise of this condition. A study experimentally demonstrated that the HCV core protein causes insulin resistance through modification of the insulin receptor substrate 1 signaling pathway.⁷

In the year 2019, a cross-sectional descriptive study was carried out at Liaquat University of Medical and Health Sciences, Jamshoro. The study involved 327 patients in order to ascertain the frequency of Type II diabetes among HCV patients. The study found that 37.9% of the HCV-infected patients had Type II diabetes.⁸

Currently, there is no trend to screen for diabetes in HCV-infected individuals in Pakistan. This oversight is due to the belief that liver cirrhosis carries a risk of hypoglycemia, and diabetes is sometimes overlooked, leading to complications. This study aims to emphasize the prevalence of diabetes among HCV-infected individuals, advocating for the introduction of diabetes screening in HCV patients at the earliest stage. This approach could potentially reduce diabetes-associated complications in HCV-infected patients.

MATERIAL AND METHODS

Study design: The study is a descriptive cross-sectional analysis.

Duration of Study: From October 6, 2022, to April 6, 2023

Sample Size: Utilizing the WHO sample size calculator, a confidence level of 95%, a population proportion of 37.95%, and an absolute precision of 8.5% were inputted. Sample Size (n): 130

Ethical Approval and Informed Consent: For availing ethical review committee approval Pakistan Atomic Energy Commission (PAEC) General Hospital was consulted. All the documents required for research were according to the guidelines of ethical review committee of the PAEC General Hospital. This study was approved by the Ethical Review Committee of PAEC General Hospital (IRB No. PGHI-IRB (DMe)-RCD-06-044).

For proper recruitment of patients for the research each patient was provided comprehensive details

about the goal, methods and possible hazards, and advantages of the study. This enabled them to take well informed decision about their participation in the research study. An official consent form was willingly filled by involving participants for the research study.

Recruitment and Selection Criteria for Participants: The study participants were sourced from patients diagnosed with Hepatitis C Virus (HCV) infection receiving treatment at PAEC General Hospital in Islamabad.

Those patients having a diagnosis of Hepatitis C Virus (HCV) infection arriving at PAEC General Hospital Islamabad were informed

Inclusion criteria:

- Patients between the ages of 20 and 80, regardless of gender.
- All patients with positive Anti-HCV antibodies on ELISA with or without the presence of cirrhosis.

Exclusion criteria:

- Patients already having diabetes.
- Patients having Hepatocellular carcinoma.
- Patients having Hepatitis B infection.
- Pregnant Females.
- Patient using steroids.

Procedures for Data Collection: After taking informed consent from the patients recruited for the study. Participants went through an interview for taking their demographic data, such as age, gender, health issues and their socioeconomic status. Clinical history was also recorded for knowing HCV viral loads, their length of infection and the treatment or therapy they were given. Height, Body mass index (BMI) and weight were also recorded as part of medical History.

Laboratory Studies: For performing biochemical analysis finding the linkage between HCV infection and diabetes mellitus, patients who were recruited for the study went through different laboratory procedures. Hemoglobin A1C (HbA1C) test was performed. Serological testing for anti-HCV antibodies using Enzyme-Linked Immunosorbent Assay (ELISA) was performed. All the procedures were carried out according to proper standard operating procedures (SOP's) ensuring standards.

Table-I: Demographics and Baseline Characteristics.

S. No 1	Liver cirrhosis	Frequency	Percentage
	Yes	33	25.4
	No	97	74.6
	Total	130	100.0
S. No 2	Diabetes	Frequency	Percentage
	Yes	41	31.5
	No	89	68.5
	Total	130	100.0

Table-II: Frequency of liver cirrhosis and Frequency of diabetes.

		Age distribution				Total	P value
		20 to 35 years	36 to 50 years	51 to 65 years	66 to 80 years		
Diabetes	Yes	5	12	13	11	41	0.50
		12.2%	29.3%	31.7%	26.8%	100.0%	
	No	20	19	28	22	89	
		22.5%	21.3%	31.5%	24.7%	100.0%	
Total		25	31	41	33	130	
		19.2%	23.8%	31.5%	25.4%	100.0%	

Data Analysis: The data after being gathered was placed in a database and quickly analyzed statistically through SPSS software programs (SPSS, version 20). The descriptive statistics were applied to compile the population clinical data and also demographic makeup. Whereas inferential statistic were applied to perform the regression analysis and also correlation testing to study the relationship between Diabetes and HCV infection which may account for any confounding factors. A p-value of less than 0.05 was deemed to be statistically significant.

Ethical Considerations: To protect the rights and welfare of participant's standard ethical procedure for research

were strictly followed. Patient confidentiality was assured and data anonymization was guaranteed to assure patient data privacy. Patient's complaints were promptly addressed and handled through proper procedures.

RESULTS

This result shows 130 patients presenting with Hepatitis C Virus. The mean age of the patients was 52.35 ± 16.94 years. The mean HbA1C was $6.04 \pm 1.12\%$. The mean BMI was 27.06 ± 3.11 kg/m² and the mean HCV duration as 1.97 ± 0.72 months (Table-I). Regarding age distribution there were 25 (19.2%) patients in the age group of 20 to 35 years, there were

Table-III: Stratification of Diabetes with Age.

S. No. 1		Gender		Total	P value
		Male	Female		
Diabetes	Yes	18	23	41	0.04
		43.9%	56.1%	100.0%	
	No	56	33	89	
		62.9%	37.1%	100.0%	
Total		74	56	130	
		56.9%	43.1%	100.0%	

S. No. 2		Liver cirrhosis		Total	P value
		Yes	No		
Diabetes	Yes	22	19	41	0.0001
		53.7%	46.3%	89	
	No	11	78	100.0%	
		12.4%	87.6%	130	
Total		33	97	130	
				100.0%	

31 (23.8%) patients in the age group of 36 to 50 years, there were 41 (31.5%) patients in the age group of 51 to 65 years and there were 33 (25.4%) patients in the age group of 66 to 80 years. Regarding gender distribution there were 74 (56.9%) males while 56 (43.1%) female patients in our study as shown in Table-I. In our study the frequency of liver cirrhosis was 33 (25.4%) while the frequency of diabetes was 41 (31.5%) as seen in Table-II below. Among the 41 diabetic participants, 13 (31.7%) were aged 51–65 years, 12 (29.3%) were aged 36–50 years, 11 (26.8%) were aged 66–80 years, and 5 (12.2%) were aged 20–35 years. Among the 89 non-diabetic participants, 28 (31.5%) were aged 51–65 years, 22 (24.7%) were aged 66–80 years, 20 (22.5%) were aged 20–35 years, and 19 (21.3%) were aged 36–50 years. The association between diabetes and age distribution was not statistically significant ($p = 0.50$). The stratification of diabetes by age groups can be seen in Table-III below. For gender, among 41 diabetic participants, 18 (43.9%) were male, and 23 (56.1%) were female. Among the 89 non-diabetic participants, 56 (62.9%) were male, and 33 (37.1%) were female. The difference in diabetes prevalence between males and females was statistically significant ($p = 0.04$). For liver cirrhosis, 22 (53.7%) of the 41 diabetic participants had liver cirrhosis, while 19 (46.3%) did not. Among the 89 non-diabetic participants, 11 (12.4%) had liver cirrhosis, while 78 (87.6%) did not. The association between diabetes and liver cirrhosis was highly significant ($p = 0.0001$). The distribution of diabetes based on gender and liver cirrhosis status, along with the p-values indicating statistical significance can be seen in Table-IV below.

DISCUSSION

Hepatitis C and type 2 diabetes (T2D) are both widespread conditions in the world. Hepatitis C virus (HCV) is close to being widespread in Pakistan, as indicated by a comprehensive analysis conducted in 2018 which approximated that the general population has an average HCV prevalence of 6.2%. The frequency was even greater among high-risk populations, reaching as much as 34.5%, and in individuals with hepatic comorbidities, the prevalence was reported as 55.9%. It was found that approximately one out of every 20 Pakistanis is impacted by this virus.⁹ Studies have shown that over 33% of individuals suffering from chronic HCV infection are likely to encounter a minimum of one extrahepatic symptom.¹⁰ Therefore, our investigation was centered on determining the occurrence of diabetes in individuals with HCV infection at a tertiary care hospital in Pakistan.

Numerous studies indicate that individuals who have chronic HCV infection have a higher likelihood of developing T2D. Although T2D and insulin resistance (IR) are the two consequences of HCV infection that are more frequently described, HCV is also known to be linked to a number of autoimmune manifestations, including type 1 diabetes (T1D).¹¹ Most studies provide strong evidence in favor of this connection, despite a few studies that were

unable to show it when liver dysfunction was not present. Moreover, studies have linked T2D to an increased risk of contracting HCV.¹²

Diabetes can also be brought on by HCV treatment, particularly interferon alpha (IFN). IFN's immunomodulatory action can cause or make autoimmune disorders worse. Interferon-induced thyroiditis (IIT) stands out as the most commonly reported autoimmune side effect of IFN therapy. However, various other autoimmune diseases such as T1D, systemic lupus erythematosus, rheumatoid arthritis, pernicious anemia, optic neuritis, and autoimmune hemolytic anemia have also been associated with IFN therapy.¹³

A high occurrence of Type 2 Diabetes Mellitus (T2DM) has been observed in patients with Hepatitis C infection in a study carried out at Lady Reading Hospital in Peshawar, Pakistan, with an incidence of 26.42%.¹⁴ The mean HbA1C level was 6.04%, which is slightly above the normal range, suggesting that many patients may have undiagnosed diabetes or prediabetes. The mean BMI was 27.06 kg/m², indicating that many patients were overweight or obese, a known risk factor for diabetes. The gender distribution shows a slight male preponderance,

Table-IV: Stratification of Diabetes with Gender and Liver Cirrhosis.

<i>Descriptive statistics (n = 130)</i>		
<i>Variable</i>	<i>Mean</i>	<i>SD</i>
Age (Years)	52.35	16.947
HbA1C %	6.0470	1.12938
BMI (kg/m ²)	27.0656	3.11886
HCV duration	1.97	0.725
<i>Age distribution</i>		
<i>Age distribution</i>	<i>Frequency</i>	<i>Percent</i>
20 to 35 years	25	19.2
36 to 50 years	31	23.8
51 to 65 years	41	31.5
66 to 80 years	33	25.4
Total	130	100.0
<i>Gender distribution</i>		
<i>Gender</i>	<i>Frequency</i>	<i>Percentage</i>
Male	74	56.9
Female	56	43.1
Total	130	100.0

with 56.9% male patients. This was in agreement with one of the study done at Lady Reading Hospital, Peshawar.¹⁴

The mean age of the patients was 52.35 years, indicating that the majority of patients were middle-aged or older. The findings align with previous studies conducted on this demographic, indicating a slightly elevated susceptibility to HCV prevalence among individuals in the middle age bracket.¹⁵

The frequency of liver cirrhosis was 25.4%, indicating that many patients had advanced liver disease. Multiple studies revalidate our findings of higher risk of liver cirrhosis in patients HCV having diabetes as compared to non-diabetics.¹⁶ Therefore, routine screening for diabetes among HCV-infected patients and early detection of both conditions are crucial to prevent complications and improve patient outcomes.

These findings have important implications for clinical practice, highlighting the need for routine screening for diabetes among HCV-infected patients and vice versa. The significant occurrence of diabetes and liver cirrhosis highlights the necessity of timely identification and management of these conditions to avoid complications and enhance patient prognosis.

There were few limitations of this study such as the sample size was small, with only 130 patients, which may limit the generalizability of the findings. It was a single-center study, including only patients from one tertiary care hospital, and had a retrospective design, relying on existing data. The demographic representation was limited, as the study included patients from a single region. Additionally, there was no control group to compare patients with HCV infection to those without, and the follow-up period was short, not allowing for assessment of long-term outcomes. Finally, measurement limitations, such as the potential inaccuracy of HbA1c levels in reflecting glucose control, may have impacted the results

CONCLUSION

Our findings underscore a strong association between HCV infection and diabetes, particularly in patients with advanced liver disease. The high prevalence of diabetes in this population highlights the need for routine screening and early intervention to mitigate complications and improve patient outcomes. These results advocate for integrated care approaches that address both HCV and diabetes, emphasizing the importance of early detection and management in improving the quality of life for affected individuals.

Further research is needed to explore the causal relationship between HCV infection and diabetes and to identify effective strategies for prevention and management.

Conflict of Interest: The authors have verified that there are no conflicts of interest associated with this study.

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Abbreviations: SD: standard deviation; HbA1C: glycated hemoglobin; BMI: body mass index; HCV: hepatitis C virus.

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