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ORIGINAL ARTICLE

Frequency of type 2 diabetes mellitus in patients with chronic hepatitis C virus infection presenting to a tertiary care hospital

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ABSTRACT

Background: Chronic Hepatitis C Virus (HCV) infection poses significant public health challenges, not only due to its hepatic-related complications but also its association with metabolic disorders including Type 2 Diabetes Mellitus (T2DM). Understanding the frequency and contributing factors of T2DM in HCV patients is crucial for improving diagnosis, treatment, and outcomes

Methods: This prospective study was conducted at the Medical Unit of Lady Reading Hospital, Peshawar Pakistan, from April to September 2021. A total of 200 HCV-seropositive patients aged 18–75 years were included. The diagnosis of HCV was confirmed through ELISA, and T2DM was determined based on HbA1c levels. Data on demographics, clinical parameters, and laboratory findings were collected. Statistical analysis was done which included univariate and multivariate logistic regression, to identify significant predictors of T2DM.

Results: The prevalence of T2DM among HCV-seropositive patients was 37%. Key risk factors for T2DM included cirrhosis (OR = 2.005, 95% CI: 1.15–3.43), age ≥40 years, obesity, male gender, and a family history of diabetes ($P < 0.05$). Patients with cirrhosis had a significantly higher prevalence of T2DM, especially those aged >60 years. Overall, 61% of participants were overweight, 19% were obese, and 20% had normal BMI. Multivariate analysis highlighted cirrhosis and metabolic factors as significant contributors to T2DM risk.

Conclusion: T2DM is highly prevalent among chronic HCV patients, particularly those with older age, having liver cirrhosis, obesity, and a family history of diabetes. Early screening and integrated management of metabolic and liver-related complications are essential for improving patient outcomes.

Keywords: Chronic Hepatitis C, Cirrhosis, Hepatitis C Virus, Insulin Resistance, Obesity, Type 2 Diabetes Mellitus

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Introduction

Infection with Chronic Hepatitis C Virus (HCV) is a major public health concern globally(1) affecting millions of individuals and leading to severe hepatic complications such as hepatocellular carcinoma and

cirrhosis(2). Despite the significant advances in the treatment of HCV through direct-acting antivirals, the long-term consequences of chronic infection continue to challenge healthcare systems worldwide(3). In addition to its well-documented liver-related effects, emerging evidence suggests a strong association between development of metabolic disorders and HCV infection particularly Type 2 Diabetes Mellitus (T2DM)(4).There are several mechanisms which explains a connection between chronic HCV infection and T2DM(5), including viral-liver injury by viruses, infection, inflammation, and the disruption of physiological metabolic processes(6). The key factor in the development of T2DM is Insulin resistance and is more prevalent in HCV-infected individuals, suggesting that these individuals are at higher risk of developing diabetes(7). The presence of diabetes exacerbate liver dysfunction and delayed antiviral therapy response is a significant challenge in patient management (8).

The prevalence of T2DM is steadily rising and is a global public health concern(9). As there is prominent interaction between these two conditions and both worsen each other's prognosis, it is necessary to better understand the frequency and impact of T2DM in patients with chronic HCV infection. The previous literature have indicated that patients with T2DM and HCV infection have experienced more severe damage to liver, increased risk of complications and poor treatment outcomes(10).

This study was conducted at Lady Reading Hospital Peshawar from April 2021 to September 2021, aims to determine the frequency of Type 2 Diabetes Mellitus in patients with chronic HCV infection presenting to the hospital. The findings from this study will enhance the understanding of relationship between HCV and T2DM, and will help the clinicians in early diagnosis, refining treatment approaches and improving the overall patient outcomes.

Methods

This cross-sectional observational study was conducted at the Medical Unit of Lady Reading Hospital, Peshawar Khyber Pakhtunkhwa, Pakistan. The hospital is largest tertiary care hospital in the region. The study protocol was approved by the Ethical Review Board of Lady Reading Hospital, having approval reference number Ref: No 80/LRH MTI dated 17-03-2021. The study cohort included patients of both genders aged between 18 and 75 years having confirmed HCV seropositivity through Enzyme-Linked Immunosorbent Assay (ELISA) and the diagnosis of Type 2 Diabetes Mellitus was based on HbA1c levels. The patient with and without chronic liver disease associated with HCV infection were included in the study. Data collection was done from the outpatient and in patient Medicine Department of Lady Reading Hospital. The data was collected by trained doctors using predesigned structure questionnaire. The exclusion criteria included liver cancer, Patients with Type 1 Diabetes Mellitus and those undergoing interferon therapies. The patients having co-existing viral infections such as Hepatitis B, Pregnant females and participants with end-stage liver disease were also excluded.

Using strict aseptic techniques About 5 mL of venous blood sample was collected from each patient. The diagnosis of diabetes was confirmed through HbA1c levels According to the guidelines of UK diabetic association and the diagnosis of Hepatitis was confirmed via detection of Hepatitis C Virus (HCV)

using Enzyme-Linked Immunosorbent Assay (ELISA). Additional relevant laboratory tests were performed, including serum cholesterol, serum albumin, complete blood count, bilirubin and prothrombin time. The presence of liver cirrhosis was confirmed using abdominal ultrasonography, and patients' previous laboratory reports were also reviewed to ensure diagnostic accuracy.

The latest version of SPSS (version 29) was used for statistical analysis. The student t-test was applied for the comparison of participants with and without Type 2 Diabetes Mellitus. Categorical variables were presented as frequencies and percentages, while the Chi-square test was employed for the analysis of nominal categorical variables. The prevalence of Type 2 Diabetes Mellitus among HCV seropositive patients was calculated and expressed as a percentage. Factors associate with Type 2 Diabetes Mellitus were identified via the application of multiple logistic regression model, the dependent variables included gender, age, weight, BMI, HCV seropositivity and family history of diabetes. To identify significant predictors, variables having a p-value < 0.25 in univariate analysis were included in the multivariate analysis.

Results

A total of 200 patients with chronic Hepatitis C virus (HCV) infection were included in this study. The age of the participants ranged from 18 to 75 years. In the study 63% were male, and 37% were female. The body mass index (BMI) distribution indicated that 61% of the participants were overweight, 19% were obese, and the remaining 20% had a normal BMI.

Table 1: Demographic Features of the Research Population

Variables	Total (n=200)
Age in years	Mean: 45.1 ± 11.6 (Range: 18-75)
Gender	-
Male	63%
Female	37%
Body Mass Index (BMI)	-
Normal BMI	20%
Overweight (BMI 25-29.9)	61%
Obese (BMI ≥30)	19%

The overall prevalence of Type 2 Diabetes Mellitus (T2DM) among HCV-seropositive patients was 37%. Notably, a statistically significant proportion of patients with cirrhosis, especially those older than 60 years, had a higher prevalence of T2DM ($P \leq 0.001$).Further analysis revealed significant associations between T2DM and factors including male gender, obesity, and cirrhosis ($P < 0.05$). As illustrated in Table2, the comparison of mean values between diabetic and non-diabetic HCV-seropositive patients demonstrated significant differences in the cirrhotic subgroup ($P = 0.001$). In the multivariate analysis, cirrhosis was associated with a twofold increased risk of developing T2DM compared to non-cirrhotic patients (OR = 2.005, 95% CI: 1.15, 3.43).

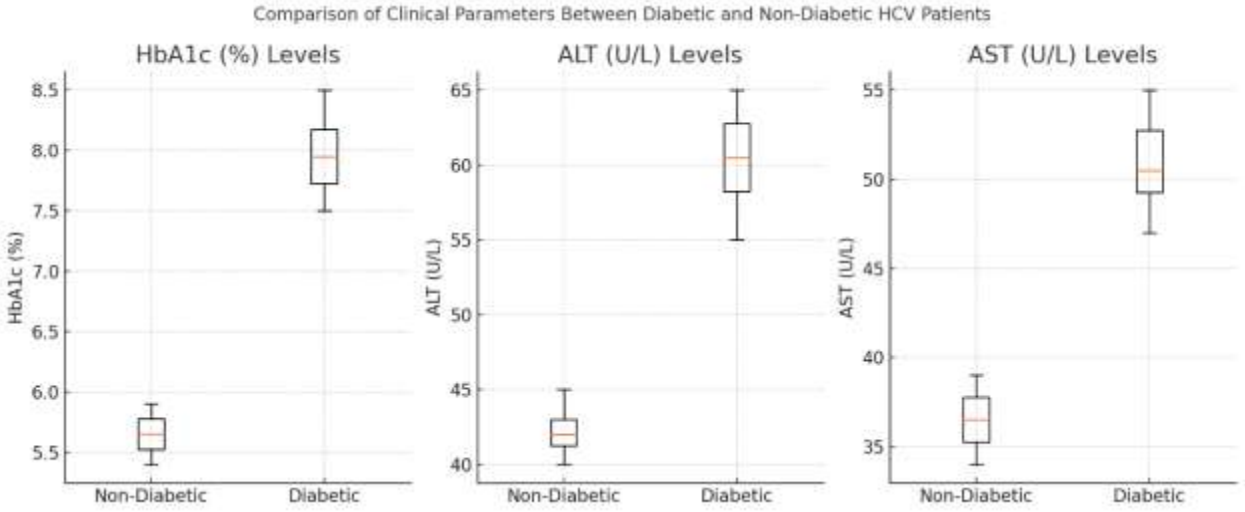
Table 2: Logistic Regression Analysis of Risk Factors

Risk Factor	Univariate Analysis OR (95% CI)	P-value	Multivariate Analysis OR (95% CI)	P-value
Age ≥ 40 years	1.78 (1.10 – 2.89)	0.015	1.65 (1.05 – 2.74)	0.032
Male Gender	1.52 (1.02 – 2.26)	0.042	1.49 (1.01 – 2.20)	0.048
Obesity (BMI ≥30)	1.65 (1.08 – 2.55)	0.027	1.58 (1.02 – 2.46)	0.039
Family History of DM	1.89 (1.20 – 2.98)	0.012	1.85 (1.18 – 2.90)	0.015
Cirrhosis	2.005 (1.15 – 3.43)	<0.001	1.98 (1.12 – 3.35)	0.001

The multivariate binomial analysis further identified significant risk factors for T2DM among HCV-infected patients. These included age ≥40 years, body weight ≥70 kg, a family history of diabetes, ($P < 0.05$). All of these factors are associated with the diagnosis of Type 2 Diabetes Mellitus.

Additionally, cirrhosis was a key determinant in the likelihood of developing T2DM, with cirrhotic patients showing a significant increase in the risk of T2DM in both univariate and multivariate analyses. The odds of developing T2DM were approximately two times higher in cirrhotic HCV-seropositive patients compared to non-cirrhotic individuals (OR = 2.005, 95% CI: 1.15, 3.43).

Figure 1: Comparison of Clinical Parameters between Diabetic and Non-diabetic patients



In summary, the prevalence of Type 2 Diabetes Mellitus among chronic Hepatitis C patients was notably higher in those with cirrhosis, particularly in individuals over 60 years of age, with male gender, obesity, and a family history of diabetes also significantly contributing to the development of diabetes in this population.

Table 3: Comparison of Mean Values between Diabetic and Non-Diabetic HCV-Seropositive Patients, with Focus on Cirrhotic Subgroup

Parameter	Diabetic Patients (n = 74)	Non-Diabetic Patients (n = 126)	P-Value
Age (Mean ± SD)	48.2 ± 10.1	42.8 ± 12.2	0.015
BMI (Mean ± SD)	30.1 ± 4.9	27.3 ± 4.5	0.021
Weight (Mean ± SD)	80.4 ± 10.5	72.6 ± 9.8	0.004
Proportion of Cirrhotic Patients (%)	45%	25%	0.001

For the comparison of categorical variables Chi-square analysis was used, and the logistic regression analysis was performed to identify significant risk factors associated with T2DM in HCV patients. Variables having a p-value <0.25 in univariate analysis were included in the multivariate logistic regression model to assess independent predictors of T2DM.

Discussion

In our study, the prevalence of Type 2 Diabetes Mellitus (T2DM) among chronic Hepatitis C virus (HCV)-seropositive patients was 37%, which is higher than the 31.5% prevalence reported in a similar study

involving 361 HCV-infected individuals(11). In both of these studies there was significant prevalence of T2DM in patients with diabetes mellitus as compared to non-infected population group, demonstrating an increased risk in HCV infected group. This supports the hypothesis that infection with HCV is a prevalent independent risk factor for the development of T2DM. we also observed that cirrhosis is a key determinant in the development of T2DM as cirrhotic patients exhibited a twofold increased risk of developing T2DM (OR = 2.005, 95% CI: 1.15, 3.43) These observations are in agreement with previous studies suggesting that liver disease severity exacerbates the risk of diabetes, we also noticed that there was a significant association between T2DM development with advanced age (≥40 years), male gender and family history of diabetes(12,13).

Our study found a 37% prevalence of Type 2 Diabetes Mellitus (T2DM) among chronic Hepatitis C virus (HCV) seropositive patient, which aligns with previous studies which showed an increased risk of diabetes among HCV-infected individuals as compared to noninfected controls while data from recent studies showed prevalence up to three times higher in HCV-seropositive patients. (14)

Our study identified a significant association between male gender and the prevalence of Type 2 Diabetes Mellitus (T2DM) among HCV-seropositive patients; however, contrasting findings have been reported in other studies(15). For instance, Elhawary et al. (2011) observed no significant relationship between gender, education level, marital status, and T2DM prevalence in HCV-positive individuals, a finding attributed to similar patient distributions within their hospital-based sample(16). Despite this, the insignificant association in such studies cannot be overlooked, as T2DM is generally more prevalent in males within the broader population, as supported by other research(17). These inconsistencies highlight the need for larger-scale studies to further investigate gender-related differences and other sociodemographic factors influencing the risk of T2DM in HCV-seropositive patients.

The relationship between cirrhosis and the higher prevalence of T2DM in HCV-infected individuals is consistent with previous studies. Our study found that cirrhotic HCV patients had an odds ratio (OR) of 2.005 for developing T2DM, which aligns with the results of a similar study that reported an identical OR of 2.005 for the increased likelihood of T2DM among cirrhotic HCV patients(18). These findings are in agreement with the previous research which showed that liver cirrhosis significantly increases the risk of development of T2DM and the prevalent rate ranging from 19.5% to 50% in patients having advanced liver disease(19). These studies emphasize that liver cirrhosis may lead to a higher susceptibility to T2DM as liver function declines; the underlying mechanism may be due to changes in insulin resistance and metabolism.

Our study's results are in line with previous research which suggested that advanced liver disease such as cirrhosis, plays a pivotal role in the pathogenesis of T2DM among HCV-infected patients. Given the increasing prevalence of both HCV and T2DM worldwide, the implications of our findings are helpful for clinical practice. HCV patients, particularly those with liver cirrhosis and other identified risk factors, should be regularly assessed for T2DM to optimize management strategies and prevent the long-term complications associated with both conditions.

Conclusion

This study highlights a significant association between chronic Hepatitis C virus (HCV) infection and Type 2 Diabetes Mellitus (T2DM).The findings underscore the impact of cirrhosis, advancing age, male gender, obesity, and a family history of diabetes as key risk factors for T2DM in this population. These results emphasize the need for early screening and proactive management of metabolic and liver-related complications in chronic HCV patients, particularly those at higher risk. Given the increasing burden of both HCV and diabetes, integrated healthcare strategies focusing on lifestyle modifications, weight management, and close monitoring of glycemic status should be prioritized. Future research should explore targeted interventions to mitigate diabetes risk and improve long-term outcomes in this vulnerable patient population.

Limitations

This study has several limitations, firstly, the limited sample size of 200 patients, may not fully capture the diversity of the broader HCV-infected population, and a larger sample size would be beneficial for applying generalizability of the results.

Our study was single centered thus limiting the external validity of the findings, as it may not be fully reflecting the HCV-infected populations in other regions, particularly in community-based or rural contexts.

The inclusion of only HCV-seropositive patients limits the ability to generalize the results, thereby limiting the assessment of the true incidence of Type 2 Diabetes Mellitus (T2DM).

Our study was cross-sectional which limits the establishment of causal relationships between chronic HCV infection, cirrhosis, and the development of T2DM.

Potential confounding factors, such as socioeconomic status, lifestyle factors, and medications, were not comprehensively controlled for in this study, which could also contribute to the development of T2DM.

Lastly, the reliance on clinical diagnoses of cirrhosis and T2DM introduces the possibility of misclassification, particularly in patients with early-stage liver disease or undiagnosed diabetes. More precise diagnostic criteria, such as liver biopsy or advanced imaging, along with standardized blood glucose measurements, would enhance the accuracy of the findings.

Future Recommendation

Based on the findings of this study, future research should focus on multi-centered, large-scale population and longitudinal studies are suggested for establishing the causal relationships between chronic Hepatitis C virus (HCV) infection, cirrhosis, and the development of Type 2 Diabetes Mellitus (T2DM).

for early detection of T2DM there should be Targeted screening protocols should be developed particularly in HCV-infected patients having cirrhosis and other associated risk factors. Additionally, the underlying mechanisms of insulin resistance and liver dysfunction should be investigated in the cohort which can offer valuable insights for therapeutic strategies.

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Data acquisition, analysis and interpretation	BA, GR, WA
Manuscript writing and approval	BA, MI, JA
All the authors agree to take responsibility for every facet of the work, making sure that any concerns about its integrity or veracity are thoroughly examined and addressed.	