INSIGHTS-JOURNAL OF
LIFE AND SOCIAL SCIENCES

INSIGHTS-JLSS
Insights-Journal of Life and Social Sciences

FREQUENCY OF TYPE 2 DIABETES MELLITUS IN HEPATITIS C PATIENTS IN A TERTIARY CARE HOSPITAL: A CROSS-SECTIONAL STUDY

Original Article

Karamat Shah[1]*, Shabnam Naveed[2], Sagar Kumar[1], Rumaisa[1], Muskan Ayub[1], Erum Dua Panhwar[1]

[1]Postgraduate Trainee, Ward 7, Unit 3, Department of General Medicine, Jinnah Postgraduate Medical Centre, Karachi, Pakistan.

[2]Professor and Head, Department of Medicine, Unit 3, Ward 7, Jinnah Postgraduate Medical Centre, Karachi, Pakistan.

Corresponding Author: Karamat Shah, Postgraduate Trainee, Ward 7, Unit 3, Department of General Medicine, Jinnah Postgraduate Medical Centre, Karachi, Pakistan, karamat2013@hotmail.com

Conflict of Interest: None

Grant Support & Financial Support: None

Acknowledgment: The authors gratefully acknowledge the support of the JPMC medical wards and laboratory staff in facilitating this study.

ABSTRACT

Background: Hepatitis C virus (HCV) infection is recognized not only for its hepatic complications but also for its metabolic impact, particularly its association with type 2 diabetes mellitus (T2DM). The viral-driven insulin resistance and beta-cell dysfunction significantly increase the risk of dysglycemia. While global estimates suggest a considerable burden of diabetes in HCV-infected individuals, local data in Pakistan remain limited. Understanding this comorbidity in high-burden settings is crucial to guide screening and integrated care strategies.

Objective: The study aimed to determine the prevalence of T2DM among adult HCV-positive in-patients and to examine its association with age, gender, body mass index (BMI), and family history of diabetes.

Methods: A descriptive cross-sectional study was conducted in the medical wards of Jinnah Postgraduate Medical Centre (JPMC), Karachi. A total of 320 adults (≥18 years) with confirmed HCV infection were consecutively enrolled. Demographic, anthropometric, and clinical details were collected, alongside biochemical assessment including fasting blood glucose (FBG) and glycated hemoglobin (HbA_1c). T2DM was defined by American Diabetes Association criteria. Univariate associations were assessed, and predictors were identified using multivariable logistic regression. Statistical significance was set at $p < 0.05$.

Results: Of the 320 participants, 96 (30.0%) were diagnosed with T2DM. Prevalence differed across age groups: 18.8% in those <40 years, 36.3% in 40–59 years, and 31.3% in ≥60 years ($p < 0.001$). Diabetes was more common among males (33.7%) than females (25.0%), though this was not significant ($p = 0.08$). T2DM prevalence rose with BMI: 7.8% in normal weight, 32.9% in overweight, and 76.9% in obese patients ($p < 0.001$). A positive family history was strongly associated, with T2DM in 50.0% versus 18.0% without ($p < 0.001$). In multivariate analysis, independent predictors included advancing age (OR 1.03, 95% CI 1.01–1.05; $p = 0.002$), higher BMI (OR 1.15 per unit, 95% CI 1.08–1.23; $p < 0.001$), and family history of diabetes (OR 3.10, 95% CI 1.85–5.20; $p < 0.001$).

Conclusion: Nearly one in three HCV-infected in-patients had T2DM, far exceeding general population rates. The strong influence of age, adiposity, and family predisposition underscores the need for routine diabetes screening and integrated care pathways in HCV management within Pakistan.

Keywords: Body Mass Index; Cross-Sectional Studies; Hepatitis C; Karachi; Prevalence; Risk Factors; Type 2 Diabetes Mellitus.

INTRODUCTION

Chronic infection with hepatitis C virus (HCV) and type 2 diabetes mellitus (T2DM) are two interlinked public health challenges that have generated a substantial global and local clinical burden. Both diseases carry profound implications for healthcare systems, economies, and patients' quality of life, and their co-occurrence demands greater attention in order to design integrated screening and management strategies (1). Understanding the extent of this association is particularly important in low- and middle-income countries (LMICs) such as Pakistan, where gaps in hospital-based prevalence data persist despite the known high burden of each disease individually. HCV remains a major global health concern. In 2019, it accounted for an estimated 6.2 million new infections, 540,000 deaths, and 15.3 million disability-adjusted life years (DALYs) lost—reflecting increases of more than 25% in incidence, nearly 60% in mortality, and over 40% in DALYs since 1990 (2). Worldwide, about 58 million individuals live with chronic HCV, yet only 21% are diagnosed and merely 13% have received treatment (3). A meta-analysis of 98 studies comprising 236,964 participants reported a global prevalence of 1.8% (95% CI: 1.4–2.3), with Africa bearing the heaviest burden at 7.1% (4). In Pakistan, the situation is even more critical. The National Hepatitis Registry records a viraemic prevalence of 4.2% (approximately 6.9 million chronically infected individuals), with genotype 3 as the dominant strain. Despite the scale of this burden, substantial gaps remain in diagnosis and treatment, hampering elimination efforts (5). Parallel to this, T2DM has reached epidemic proportions worldwide. In 2021, 537 million adults were living with diabetes, the majority with T2DM. Projections suggest these figures will rise to 643 million in 2030 and 783 million by 2045 (6,7). The economic impact is equally staggering, with diabetes-related health expenditure reported at USD 376 billion in 2010 and expected to reach USD 490 billion by 2030 (8). Pakistan is among the countries most severely affected, ranking third globally for the number of diabetic adults. According to the International Diabetes Federation, around 33 million adults in Pakistan live with diabetes, while an additional 11 million have impaired glucose tolerance (9).

Accumulating evidence suggests that chronic HCV infection plays a pathogenic role in the development of T2DM. Mechanistically, HCV induces insulin resistance through pro-inflammatory cytokines such as TNF-α and IL-6 and impairs insulin receptor signaling by downregulating insulin receptor substrate-1 (10). Improved insulin sensitivity and glycemic control following treatment with direct-acting antivirals further reinforce this causal link (11). Epidemiological studies confirm that non-diabetic individuals with chronic HCV have a 1.5–2.6-fold higher risk of developing T2DM compared with non-infected controls (12). Importantly, this association persists even after adjustment for conventional diabetes risk factors. The interaction between the two conditions appears bidirectional, as T2DM accelerates liver fibrosis and increases hepatocellular carcinoma risk in patients with chronic HCV (13). Despite the recognized association between HCV and T2DM worldwide, Pakistan lacks robust multicenter hospital-based prevalence data addressing this comorbidity. While the National Hepatitis Registry provides prevalence estimates and genotype distribution, it does not stratify patients by diabetic status (14). Similarly, national diabetes surveys highlight the burden of T2DM but offer no insight into coexistent HCV infection (15). Published studies prior to 2021 have been mostly single-center, cross-sectional, and based on heterogeneous diagnostic criteria, limiting their generalizability. This scarcity of reliable data in tertiary healthcare institutions underscores the need for targeted research in Pakistan to quantify the burden, improve patient outcomes, and inform integrated care models. Against this background, the present study aims to determine the prevalence of T2DM among adult patients with chronic HCV infection in a tertiary care hospital in Pakistan. Furthermore, it seeks to explore age-related and gender-based differences, while also examining the role of established risk factors such as body mass index, family history of diabetes, and other relevant clinical parameters. By addressing these objectives, the study intends to bridge a crucial knowledge gap and provide evidence to support more effective patient-centered management strategies.

METHODS

This study employed a descriptive, cross-sectional observational design to estimate the prevalence of type 2 diabetes mellitus (T2DM) among patients with chronic hepatitis C virus (HCV) infection. A cross-sectional design was considered appropriate because it allowed for the assessment of diabetes status at a single point in time within a defined HCV-infected cohort, without the requirement of intervention or follow-up. This approach also minimized recall bias and logistical constraints while providing a snapshot of the disease burden within a tertiary care setting. The study was conducted in the medical wards of Jinnah Postgraduate Medical Centre (JPMC), Karachi, a 1,650-bed tertiary care teaching hospital that serves a large and diverse patient population from urban and peri-urban areas. All adult patients aged 18 years and above, admitted with confirmed HCV infection during the six-month data collection period, were eligible for inclusion. Confirmation of HCV infection was based on documented anti-HCV antibody positivity, with or without polymerase chain reaction (PCR) confirmation for HCV RNA. Written informed consent was obtained in either Urdu or English,

depending on the preference of the participant. Exclusion criteria were strictly applied. Patients with a prior diagnosis of type 1 diabetes mellitus, those with incomplete medical or laboratory records that precluded reliable determination of diabetic status, and individuals with co-infections such as human immunodeficiency virus (HIV) or hepatitis B virus (HBV) were excluded. This ensured that the study sample specifically reflected HCV patients at risk of T2DM, without confounding from other significant comorbid infections or unclear diabetic history. Sample size was calculated using the World Health Organization (WHO) sample size calculator, assuming a 25% prevalence of T2DM among HCV patients, a 95% confidence interval, and 5% absolute precision. The minimum required sample size was 289 patients; however, to account for potential missing or incomplete data, the sample size was increased by 10%, yielding a final target enrollment of 320 patients. A non-probability consecutive sampling technique was used, whereby every eligible HCV-positive in-patient admitted during the study period was invited to participate until the required sample size was achieved.

Data were collected using a structured, pre-tested questionnaire alongside review of hospital records. Trained research assistants recorded demographic details (age, sex, body mass index, and place of residence), clinical information including duration and genotype of HCV infection, family history of diabetes, and comorbidities. Laboratory data were obtained from the JPMC central laboratory, which followed standard operating procedures. Investigations included fasting blood glucose measured by enzymatic methods, glycated hemoglobin (HbA1c) assessed using high-performance liquid chromatography (HPLC), and liver function tests including alanine aminotransferase (ALT), aspartate aminotransferase (AST), and bilirubin levels. These standardized laboratory methods ensured accuracy and reliability of results. Ethical approval for the study was obtained from the Institutional Review Board (IRB) of JPMC prior to initiation. Informed consent was taken in writing, in either Urdu or English, as per participant preference. Confidentiality was maintained by removing all personal identifiers from study records, and the data were stored securely on password-protected servers accessible only to the research team. Statistical analysis was performed using SPSS version 29. Continuous variables were summarized as means with standard deviations, or medians with interquartile ranges where appropriate. Categorical variables were described using frequencies and percentages, and prevalence of T2DM was calculated based on the American Diabetes Association (ADA) diagnostic criteria (fasting plasma glucose ≥126 mg/dL or HbA1c ≥6.5%) (12-14). Associations between categorical variables such as gender or family history and diabetes status were assessed using chi-square tests, while continuous variables such as age and body mass index were compared using independent sample t-tests or one-way ANOVA, depending on distribution. Variables found to be significant in univariate analyses at a p-value less than 0.10 were subsequently entered into a multivariate logistic regression model to identify independent predictors of T2DM, with statistical significance set at $p < 0.05$.

RESULTS

A total of 362 hepatitis C virus (HCV)–positive in-patients were screened; 320 met eligibility criteria and were included in the analysis. The mean age was 45.3 ± 11.8 years; 96/320 (30.0%) were aged <40 years, 160/320 (50.0%) were 40–59 years, and 64/320 (20.0%) were ≥60 years. Males comprised 184/320 (57.5%) and females 136/320 (42.5%). Mean body mass index (BMI) was 26.9 ± 4.2 kg/m²; BMI categories were normal in 128/320 (40.0%), overweight in 140/320 (43.8%), and obese in 52/320 (16.2%). A family history of diabetes was reported by 120/320 (37.5%). Mean duration of HCV infection was 2.1 ± 1.4 years. The prevalence of type 2 diabetes mellitus (T2DM) was 96/320 (30.0%; 95% CI, 25.2–35.2), and 224/320 (70.0%) had no diabetes. In univariate analyses, T2DM varied by age group (18.8% for <40 years, 36.3% for 40–59 years, 31.3% for ≥60 years; $p < 0.001$), showed a non-significant difference by gender (33.7% male vs 25.0% female; $p = 0.08$), and increased stepwise across BMI categories (7.8% normal, 32.9% overweight, 76.9% obese; $p < 0.001$). T2DM was more frequent with a positive family history (50.0% vs 18.0%; $p < 0.001$). In multivariable logistic regression, higher age and BMI, and a positive family history independently predicted T2DM: age (per year) OR 1.03 (95% CI 1.01–1.05; $p = 0.002$), BMI (per 1 kg/m²) OR 1.15 (95% CI 1.08–1.23; $p < 0.001$), and family history (yes vs no) OR 3.10 (95% CI 1.85–5.20; $p < 0.001$). Male sex was not an independent predictor (OR 1.45; 95% CI 0.88–2.39; $p = 0.14$). Laboratory parameters differed by diabetes status. Mean fasting blood glucose (FBG) was 148 ± 25 mg/dL in T2DM and 92 ± 10 mg/dL without T2DM ($p < 0.001$). Mean HbA_{1c} was 8.2 ± 1.5% in T2DM and 5.6 ± 0.4% without T2DM ($p < 0.001$). Liver enzymes were higher in T2DM: ALT 65 ± 20 vs 55 ± 18 U/L ($p = 0.002$) and AST 60 ± 15 vs 50 ± 14 U/L ($p = 0.005$). Total bilirubin was 1.2 ± 0.4 vs 1.0 ± 0.3 mg/dL ($p = 0.010$). Genotype distribution was genotype 3 in 240/320 (75.0%), genotype 1 in 64/320 (20.0%), and genotype 2 in 16/320 (5.0). T2DM prevalence within genotypes was 25.0% (60/240) for genotype 3, 46.9% (30/64) for genotype 1, and 37.5% (6/16) for genotype 2, with a significant association between genotype and T2DM ($p = 0.010$). Duration of infection was associated with T2DM: <1 year 10.0% (8/80), 1–3 years 25.0% (40/160), and >3 years 60.0% (48/80) ($p = 0.001$). Comorbidities were more frequent in T2DM: hypertension 41.7% (40/96) vs 22.3% (50/224) ($p < 0.001$), dyslipidemia 31.2% (30/96) vs 17.8% (40/224) ($p = 0.005$), and obesity (BMI ≥30 kg/m²) 41.7% (40/96)

vs 5.4% (12/224) ($p < 0.001$). Correlation analysis showed positive associations of age with FBG ($r = 0.30$, $p < 0.01$) and HbA_1c ($r = 0.28$, $p < 0.01$); BMI with FBG ($r = 0.40$, $p < 0.01$) and HbA_1c ($r = 0.45$, $p < 0.01$); duration with FBG ($r = 0.20$, $p < 0.05$) and HbA_1c ($r = 0.22$, $p < 0.05$). FBG and HbA_1c were strongly correlated ($r = 0.85$, $p < 0.01$).

Table 1: Characteristics of HCV-Infected In-Patients (n = 320)

Characteristic	Value
Age (years)	45.3 ± 11.8
Age groups, n (%)	
< 40	96 (30.0)
40–59	160 (50.0)
≥ 60	64 (20.0)
Gender, n (%)	
Male	184 (57.5)
Female	136 (42.5)
BMI (kg/m²)	26.9 ± 4.2
BMI categories, n (%)	
Normal (< 25)	128 (40.0)
Overweight (25–29.9)	140 (43.8)
Obese (≥ 30)	52 (16.2)
Family history of diabetes, n (%)	120 (37.5)
Duration of HCV (years)	2.1 ± 1.4

Table 2: Prevalence of Type 2 Diabetes Mellitus and Associated Comorbidities among HCV-Infected Patients

Variable / Comorbidity	Category / Status	n (%)	p-value
Diabetes Status	Type 2 diabetes mellitus	96 (30.0)	—
	No diabetes	224 (70.0)	—
Hypertension	T2DM (n = 96)	40 (41.7)	< 0.001
	No T2DM (n = 224)	50 (22.3)	
Dyslipidemia	T2DM (n = 96)	30 (31.2)	0.005
	No T2DM (n = 224)	40 (17.8)	
Obesity (BMI ≥ 30)	T2DM (n = 96)	40 (41.7)	< 0.001
	No T2DM (n = 224)	12 (5.4)	

Table 3: Univariate Associations with T2DM

Variable	Category	T2DM n/N (%)	p-value
Age group	< 40 (n = 96)	18/96 (18.8)	< 0.001
	40–59 (n = 160)	58/160 (36.3)	
	≥ 60 (n = 64)	20/64 (31.3)	
Gender	Male (n = 184)	62/184 (33.7)	0.08
	Female (n = 136)	34/136 (25.0)	
BMI category	Normal (n = 128)	10/128 (7.8)	< 0.001
	Overweight (n = 140)	46/140 (32.9)	
	Obese (n = 52)	40/52 (76.9)	
Family history	Yes (n = 120)	60/120 (50.0)	< 0.001
	No (n = 200)	36/200 (18.0)	

Table 4: Multivariate Predictors of T2DM

Predictor	OR (95% CI)	p-value
Age (per year)	1.03 (1.01–1.05)	0.002
Gender (male vs. female)	1.45 (0.88–2.39)	0.14
BMI (per 1 kg/m² increase)	1.15 (1.08–1.23)	< 0.001
Family history (yes vs. no)	3.10 (1.85–5.20)	< 0.001

Table 5: Laboratory Parameters by Diabetes Status

Parameter	T2DM (n = 96) mean ± SD	No T2DM (n = 224) mean ± SD	p-value
Fasting blood glucose (mg/dL)	148 ± 25	92 ± 10	< 0.001
HbA_{1c} (%)	8.2 ± 1.5	5.6 ± 0.4	< 0.001
ALT (U/L)	65 ± 20	55 ± 18	0.002
AST (U/L)	60 ± 15	50 ± 14	0.005
Total bilirubin (mg/dL)	1.2 ± 0.4	1.0 ± 0.3	0.010

Table 6: HCV Genotype, Duration of Infection, and Prevalence of Type 2 Diabetes Mellitus

Variable	Category	n (%)	T2DM n (%)	p-value
Genotype	Genotype 3	240 (75.0)	60 (25.0)	0.010
	Genotype 1	64 (20.0)	30 (46.9)	
	Genotype 2	16 (5.0)	6 (37.5)	
Duration of Infection	< 1 year	80 (25.0)	8 (10.0)	0.001
	1–3 years	160 (50.0)	40 (25.0)	
	> 3 years	80 (25.0)	48 (60.0)	

Table 7: Correlation Matrix of Continuous Variables

	Age	BMI	Duration	FBG	HbA_{1c}
Age	1.00	0.15†	0.10†	0.30**	0.28**
BMI	0.15†	1.00	0.05	0.40**	0.45**
Duration	0.10†	0.05	1.00	0.20*	0.22*
FBG	0.30**	0.40**	0.20*	1.00	0.85**
HbA_{1c}	0.28**	0.45**	0.22*	0.85**	1.00

Note: p < 0.10; * p < 0.05; ** p < 0.01

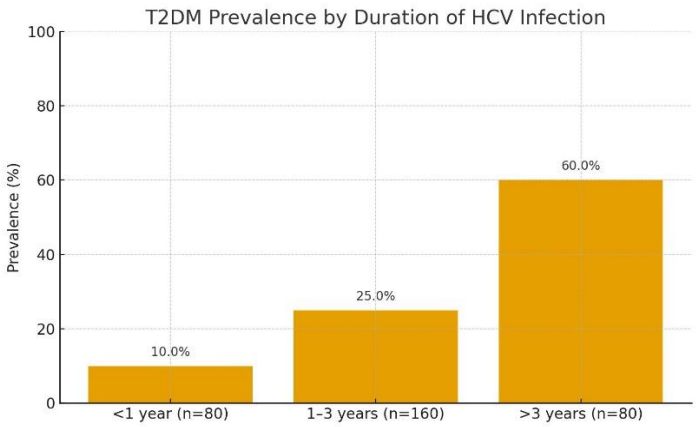

Figure 2 T2DM Prevalence by Duration of HCV Infection

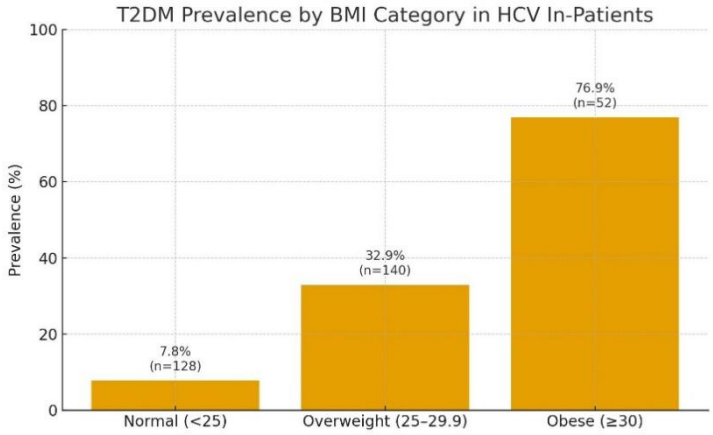

Figure 2 T2DM Prevalence by BMI Category in HCV In-patients

DISCUSSION

The study identified a 30.0% prevalence of type 2 diabetes mellitus (T2DM) among hospitalized adults with chronic hepatitis C virus (HCV) infection, a figure that exceeded many tertiary-care estimates reported globally and supported the notion that chronic HCV may amplify metabolic risk beyond background population levels. This magnitude aligned with hospital-based ranges typically between 20–40% in HCV cohorts and remained consistent with epidemiological evidence that HCV infection increases the odds of T2DM after accounting for conventional risk factors (16,17). The observed pattern also resonated with mechanistic work showing that HCV-related

inflammatory signaling impairs insulin receptor pathways and promotes insulin resistance, and that successful antiviral therapy improves glycemic indices, thereby supporting a biologically plausible link between chronic infection and dysglycaemia (18). Independent associations with age, body mass index (BMI), and family history strengthened the clinical relevance of routine metabolic screening in HCV clinics. Each additional year of age was associated with a modest rise in the odds of T2DM, consistent with age-related cumulative metabolic burden. BMI showed the largest effect size on a continuous scale, indicating that excess adiposity likely acts as a catalyst that tips insulin-resistant individuals into overt diabetes, a pattern that mirrored the steep univariate gradient from normal weight to obesity (19). A positive family history tripled the odds of T2DM, suggesting an additive or synergistic contribution of genetic predisposition and shared environments on top of virus-related mechanisms. Male sex did not retain significance in multivariable analysis, implying that sex differences observed in univariate comparisons were largely explained by age, adiposity, and familial risk (20).

Genotype-specific patterns suggested that T2DM was more common in genotype 1 than genotype 3, although genotype was not incorporated in the final multivariable model due to sample-size constraints for some strata. This left open the possibility that viral genetic factors may influence metabolic risk either directly or through linkage with unmeasured host or environmental characteristics, and it justified larger, genotype-balanced analyses (21,22). The strong duration gradient—rising from 10.0% in those with <1 year of infection to 60.0% beyond three years—supported the concept that prolonged inflammatory exposure may progressively erode insulin signaling and glycemic control. Concordant laboratory differences, with higher fasting glucose, HbA_{1c}, and liver enzymes in those with T2DM, pointed to a two-way interplay in which metabolic dysfunction and hepatic injury coexist and may aggravate one another (23). The findings carried immediate clinical implications. In high-burden settings, routine screening for dysglycaemia in HCV services appeared justified, with particular attention to older individuals, those with higher BMI, and those reporting a family history of diabetes. Early detection offered an opportunity to implement lifestyle modification and pharmacotherapy that may mitigate hepatic disease progression, cardiovascular risk, and downstream health-care utilization. From a health-system perspective, embedding diabetes prevention and control within HCV care pathways promised efficiency, especially in resource-constrained environments where co-management could reduce morbidity and costs (24).

Several limitations tempered inference. The single-center, cross-sectional design limited generalizability and prevented causal interpretation. Consecutive non-probability sampling introduced potential selection bias and may have over-represented clinically complex in-patients. Unmeasured confounding persisted, including antiviral treatment status, dietary intake, physical activity, socioeconomic position, and medication use beyond antidiabetic agents. The reliance on anti-HCV antibody positivity "with or without" RNA confirmation at inclusion risked misclassification of chronic infection; confirmed RNA status for all participants would have improved internal validity. Genotype 2 was infrequent, constraining precision for genotype-specific estimates, and the multivariable model did not report calibration, discrimination, or checks for multicollinearity, which would have strengthened the methodological transparency. Despite these constraints, internally consistent gradients across age, BMI, family history, and duration, alongside strong biochemical differences, supported the robustness of the overall pattern. The study had notable strengths. It applied standardized laboratory methods within a large tertiary hospital, used clear diagnostic thresholds for T2DM, and evaluated a prespecified set of clinical and biochemical covariates that reflected routine practice. The presentation of both univariate gradients and adjusted associations improved interpretability for bedside decision-making. Future research should prioritize multicenter designs with probability sampling to enhance representativeness, universal HCV RNA confirmation to minimize misclassification, and detailed capture of antiviral exposure and virological response. Longitudinal cohorts are needed to quantify incident diabetes risk post–direct-acting antiviral therapy, evaluate whether sustained virological response attenuates dysglycaemia, and delineate the temporal interplay between improving liver health and metabolic trajectories. Interventional studies targeting weight reduction and cardiometabolic risk in high-risk HCV populations should test whether structured lifestyle programs and modern antidiabetic agents can prevent progression from insulin resistance to overt diabetes. Inclusion of non-HCV comparison groups will clarify the extent to which the virus independently contributes to diabetes risk beyond shared demographic and lifestyle determinants. An integrated framework that couples viral eradication, proactive metabolic screening, and tailored lifestyle support appears most likely to generate durable benefits in this high-risk population.

CONCLUSION

This study demonstrated that type 2 diabetes mellitus was notably prevalent among patients with chronic hepatitis C infection, far exceeding rates in the general population. Advancing age, increased body mass index, and a family history of diabetes emerged as key predictors, underscoring the combined influence of viral, genetic, and lifestyle factors in shaping metabolic risk. The findings reinforce mechanistic evidence that chronic HCV contributes to insulin resistance and progressive beta-cell dysfunction, highlighting the need for

routine metabolic screening in HCV care pathways. Integrating diabetes prevention and management into hepatitis C services has the potential to improve patient outcomes, reduce complications, and lessen the overall healthcare burden in high-risk populations.

AUTHOR CONTRIBUTION

Author	Contribution
Karamat Shah*	Substantial Contribution to study design, analysis, acquisition of Data Manuscript Writing Has given Final Approval of the version to be published
Shabnam Naveed	Substantial Contribution to study design, acquisition and interpretation of Data Critical Review and Manuscript Writing Has given Final Approval of the version to be published
Sagar Kumar	Substantial Contribution to acquisition and interpretation of Data Has given Final Approval of the version to be published
Rumaisa	Contributed to Data Collection and Analysis Has given Final Approval of the version to be published
Muskan Ayub	Contributed to Data Collection and Analysis Has given Final Approval of the version to be published
Erum Dua Panhwar	Substantial Contribution to study design and Data Analysis Has given Final Approval of the version to be published

REFERENCES

1. Sallam, M., & Khalil, R. (2024). Contemporary insights into hepatitis C virus: A comprehensive review. Microorganisms, 12(6), 1035.

2. Stasi, C., Milli, C., Voller, F., & Silvestri, C. (2023). The epidemiology of chronic hepatitis C: Where we are now. Livers, 4(2), 13.

3. Yang, J., Qi, J. L., Wang, X. X., Li, X. H., Jin, R., Liu, B. Y., Liu, H. X., & Rao, H. Y. (2023). The burden of hepatitis C virus in the world, China, India, and the United States from 1990 to 2019. Frontiers in Public Health, 11, 1041201.

4. Grigoriev, P., Hernandez, M., & Wilson, L. (2024). Diabetes and infection: Review of the epidemiology, mechanisms and principles of treatment. Diabetologia, 67(5), 789–805.

5. Ciardullo, S., Mantovani, A., Ciaccio, A., Carbone, M., Invernizzi, P., & Perseghin, G. (2022). Hepatitis C virus infection and diabetes: A complex bidirectional relationship. Diabetes Research and Clinical Practice, 187, 109870.

6. Zhou, M., Wang, H., Zheng, Y., et al. (2023). Global, regional, and national burden of diabetes from 1990 to 2021: A systematic analysis for the Global Burden of Disease Study. The Lancet, 401(10363), 183–208.

7. Chen, J., Li, X., Patel, S., et al. (2025). Global burden of type 2 diabetes mellitus from 1990 to 2021, with projections to 2030 and 2045: A systematic analysis of the Global Burden of Disease Study. BMC Medicine, 23(1), 90.

8. Tariq, I., Ullah, Z., Kakar, A. A., et al. (2023). National Hepatitis Registry in Pakistan: Prevalence, genotype distribution, and elimination planning. Tropical Medicine and Health, 51(1), 150.

9. Sun, H., Saeedi, P., Karuranga, S., Pinkepank, M., Ogurtsova, K., Duncan, B. B., et al. (2022). IDF Diabetes Atlas: Global, regional and country-level diabetes prevalence estimates for 2021 and projections for 2045. Diabetes Research and Clinical Practice, 183, 109119.

10. Fasil A, Geremew D, Bewket G, Kiflie A, Abebe M, Biadgo B. Seroprevalence of HBV and HCV Among Diabetes Mellitus Patients Attending University of Gondar Hospital, Northwest Ethiopia. Clin Lab. 2022;68(9).

11. Coelho MPP, de Castro P, de Vries TP, Colosimo EA, Bezerra JMT, Rocha GA, et al. Sarcopenia in chronic viral hepatitis: From concept to clinical relevance. World J Hepatol. 2023;15(5):649-65.

12. Ye Y, Shrestha S, Burkholder G, Bansal A, Erdmann N, Wiener H, et al. Rates and Correlates of Incident Type 2 Diabetes Mellitus Among Persons Living With HIV-1 Infection. Front Endocrinol (Lausanne). 2020;11:555401.

13. Younossi ZM, de Avila L, Racila A, Nader F, Paik J, Henry L, et al. Prevalence and predictors of cirrhosis and portal hypertension in the United States. Hepatology. 2025.

14. Landis D, Sutter A, Khemka S, Songtanin B, Nichols J, Nugent K. Metformin as adjuvant treatment in hepatitis C virus infections and associated complications. Am J Med Sci. 2024;368(2):90-8.

15. Popescu MS, Firu DM, Mitruț R, Mărgăritescu DN, Kamal AM, Pădureanu V, et al. Metabolic Impact of Diabetes Mellitus Type 2 in Hepatitis C Virus Infected Patients. Curr Health Sci J. 2021;47(3):405-11.

16. Huo J, Xu Y, Chen X, Yu J, Zhao L. Inverse association between type 2 diabetes and hepatocellular carcinoma in East Asian populations. Front Endocrinol (Lausanne). 2023;14:1308561.

17. Duseja A, Singh SP, De A, Madan K, Rao PN, Shukla A, et al. Indian National Association for Study of the Liver (INASL) Guidance Paper on Nomenclature, Diagnosis and Treatment of Nonalcoholic Fatty Liver Disease (NAFLD). J Clin Exp Hepatol. 2023;13(2):273-302.

18. Boukaira S, Madihi S, Bouafi H, Rchiad Z, Belkadi B, Benani A. Hepatitis C in North Africa: A Comprehensive Review of Epidemiology, Genotypic Diversity, and Hepatocellular Carcinoma. Adv Virol. 2025;2025:9927410.

19. Singh SP, Madke T, Chand P. Global Epidemiology of Hepatocellular Carcinoma. J Clin Exp Hepatol. 2025;15(2):102446.

20. Makvandi M, Azaran A, Jalilian S, Nahad MP, Azizolahi B, Neisi N. Frequency and genotype distribution of hepatitis C virus infection in patients with diabetes type 2 in Ahvaz, Iran. Iran J Microbiol. 2021;13(5):703-11.

21. Rajsfus BF, Mohana-Borges R, Allonso D. Diabetogenic viruses: linking viruses to diabetes mellitus. Heliyon. 2023;9(4):e15021.

22. Kim DY. Changing etiology and epidemiology of hepatocellular carcinoma: Asia and worldwide. J Liver Cancer. 2024;24(1):62-70.

23. Younossi Z, Aggarwal P, Shrestha I, Fernandes J, Johansen P, Augusto M, et al. The burden of non-alcoholic steatohepatitis: A systematic review of health-related quality of life and patient-reported outcomes. JHEP Rep. 2022;4(9):100525.

24. Usmani MA, Rahman AS, Jamal Q, Siddiqui M. Association of Type 2 Diabetes and Hepatic Encephalopathy in Chronic Liver Disease Patients. Cureus. 2021;13(8):e17061.

