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FREQUENCY OF HEPATOCELLULAR CARCINOMA (HCC) IN PATIENTS WITH HEPATITIS C VIRUS

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Abstract

Objective: *To determine the frequency of Hepatocellular Carcinoma (HCC) in patients with hepatitis C virus at tertiary care hospital.*

Place and Duration of the Study: *The study was conducted at the Department of Medicine, Peoples University of Medical and Health Sciences for Women, Nawabshah, Pakistan from 15-June-2025 to 15-September-2025.*

Methodology: *A consecutive sample of 103 patients aged 18–70 years diagnosed with hepatitis C virus infection was recruited. Demographic and clinical details were recorded and alpha-fetoprotein, liver ultrasonography and biphasic computed tomography were performed to identify hepatocellular carcinoma. Data were processed using Statistical Package for the Social Sciences version 26. Stratification was carried out using Chi-square or Fisher exact test, whereas binary logistic regression was applied to determine potential predictors. A p-value <0.05 was taken as statistically significant.*

Results: *The mean age was 53.30 ± 8.66 years, mean body mass index was 25.52 ± 2.19 kg/m² and mean duration of hepatitis C virus was 116.42 ± 56.79 months. Males were 75 (72.8%) and rural residents were 69 (67.0%). Diabetes mellitus was present in 26 (25.2%), hypertension in 39 (37.9%) and obesity in 18 (17.5%). Hepatocellular carcinoma was found in 15 (14.6%) patients. Diabetes mellitus was the only significant regression predictor (odds ratio 7.060, 95% confidence interval 1.753–28.437, p=0.006). It was higher in diabetic patients, 10 (38.5%), than non-diabetic patients, 5 (6.5%) (p<0.001).*

Conclusion: *Hepatocellular carcinoma was found in a proportion of hepatitis C virus patients, with diabetes mellitus showing significant association.*

INTRODUCTION

Hepatitis C virus is an RNA virus that mostly infects the liver and is one of the most significant causes of chronic liver disease.[1] The infection is usually spread through blood, injection with an infected needle, through the use of contaminated needles and, in some cases, sexually or from mother to the child.[2] Patients who are infected by the virus may not exhibit any symptoms for a long time and may go unnoticed.[3] In some patients, the

infection gets cleared by the body's immune system whereas, in most other cases, it is chronic.[4] Hepatitis C virus infection over an extended period causes inflammation and damage to the liver.[5] When the liver continues to be damaged, there is gradual replacement of normal liver tissue with scar tissue, which could ultimately result in cirrhosis.[6] Hepatitis C virus infected individuals may suffer from reduced liver function, portal hypertension, ascites and jaundice among others.[7] There are certain variables that will influence the degree of liver damage such as length of infection, alcohol intake, metabolic problems and other liver infections.[8] Even after treating hepatitis C virus infection, individuals who have already suffered from advanced fibrosis or cirrhosis may still be prone to liver cancer.[9]

Hepatocellular carcinoma is the most prevalent form of cancer that originates in the liver and is usually associated with chronic liver diseases and cirrhosis.[10] One of the risk factors that can cause HCC is the hepatitis C virus; this is mostly due to liver inflammation, fibrosis and cirrhosis that occurs.[11] However, some people with HCC may not have cirrhosis. This type of cancer can be asymptomatic at an earlier stage and is usually detected when it is too late. The most common symptoms associated with this condition are loss of weight, abdominal pain, fatigue, jaundice and enlarged liver.[12]

It is necessary to evaluate hepatocellular carcinoma among patients infected with hepatitis C virus as chronic hepatitis C continues to be a significant source of hepatic disease that can result in major complications in the liver. Evaluation of the prevalence of hepatocellular carcinoma among the patients can assist in determining the burden of the condition and help identify high-risk patients. The evaluation will also be able to give valuable local information that can be useful in managing patients with chronic hepatitis C virus infections.

METHODOLOGY

This cross-sectional study was conducted in the Department of Medicine, Peoples University of Medical and Health Sciences for Women, Nawabshah from 15 June, 2025 to 15 September, 2025. A total of 103 patients with hepatitis C virus infection who fulfilled the predefined eligibility criteria were enrolled.

Sample size was determined using the World Health Organization sample size calculator, based on an expected hepatocellular carcinoma prevalence of 7.2%[13] among patients with hepatitis C virus infection, with a 95% confidence level and 5% margin of error, giving a required sample of 103 patients. Participants were selected through non-probability consecutive sampling.

Patients of either sex aged 18–70 years were eligible for participation. Hepatitis C virus infection was confirmed by detecting positive antibodies through the enzyme-linked immunosorbent assay method. Individuals with cirrhosis attributable to causes other than hepatitis C virus infection, such as hepatitis B virus infection, alcoholic liver disease, haemochromatosis, Wilson disease or end-stage liver disease, were excluded. Patients who declined to provide written informed consent were also excluded from the study.

Before collection of information, informed consent was obtained after explaining the study purpose, procedure and relevant information to each participant. Demographic and clinical details including age, gender, height, weight, body mass index (BMI), duration of HCV, residential status, diabetes mellitus and hypertension were recorded. Weight was measured in kilograms by using an electronic weighing scale and height was measured in centimetres with a wall mounted scale. Body mass index was calculated as weight in kg divided by height in metre^2. Diabetes mellitus was recorded as "Yes" in patients having documented history of diabetes mellitus and taking anti-diabetic medication for at least 6 months, while others were recorded as "No". Hypertension was recorded as "Yes" when there was documented history of hypertension with use of anti-hypertensive medication for at least 6 months, otherwise it was recorded as "No". Obesity was recorded as "Yes" when BMI was >27.5 kg/m^2 and as "No" when BMI was ≤27.5 kg/m^2.

At presentation, a detailed history was taken and complete physical examination was performed for each patient. Standard laboratory and radiological

assessment were then carried out. A 5-cc blood sample was collected by using a syringe and was sent to the pathology laboratory of the hospital for measurement of alpha-fetoprotein (AFP) level. Ultrasonography of liver was performed for assessment of focal liver lesions. For maintaining uniformity, all laboratory investigations were processed in the same hospital laboratory. Patients were further evaluated by biphasic CT scan for detection of hepatocellular carcinoma and the outcome variable hepatocellular carcinoma was recorded as Yes or No. Hepatocellular carcinoma was considered when CT liver showed arterial phase hyperenhancement with delayed washout in portal and venous phases or when ultrasound demonstrated a focal liver lesion with AFP level >300 ng/ml. All information was collected and recorded by the researcher himself.

The collected information was entered and analysed using IBM Statistical Package for the Social Sciences version 27. Continuous variables, including age, body mass index, duration of hepatitis C virus infection and alpha-fetoprotein level, were summarised as mean and standard deviation. Categorical variables such as gender, residential status, diabetes mellitus, hypertension, obesity and hepatocellular carcinoma were expressed as frequencies and percentages. Stratification was carried out according to age, body mass index, gender, residential status, diabetes mellitus, hypertension and obesity. Chi-square or Fisher exact test was used where appropriate. Binary logistic regression was performed to assess associations between age, body mass index, hepatitis C virus duration and comorbidities, including diabetes mellitus, with hepatocellular carcinoma. Odds ratios with 95% confidence intervals were calculated and $p<0.05$ was considered statistically significant.

RESULTS

A total of 103 patients with hepatitis C virus were included in the study. The mean age was 53.30±8.66 years, mean BMI was 25.52±2.19 kg/m² and mean duration of HCV was 116.42±56.79 months, while the mean alpha-fetoprotein level was 390.42±2078.46 ng/ml. Majority of the patients were male 75 (72.8%) and females were 28 (27.2%) and 69 (67.0%) patients belonged to rural area while 34 (33.0%) were from urban area. Diabetes mellitus was present in 26 (25.2%) patients, hypertension in 39 (37.9%) and obesity in 18 (17.5%) patients (Table-I).

Table I: Patient Demographics. n=103

Demographics	Mean ± SD
Age (years)	53.30±8.66
BMI (kg/m²)	25.52±2.19
Duration of HCV (months)	116.42±56.79
Alpha-fetoprotein (AFP) Level (ng/ml)	390.42±2078.46
Gender	
Male n (%)	75 (72.8%)
Female n (%)	28 (27.2%)
Residential Status	
Urban n (%)	34 (33.0%)
Rural n (%)	69 (67.0%)
Diabetes Mellitus	
Yes n (%)	26 (25.2%)
No n (%)	77 (74.8%)
Hypertension	
Yes n (%)	39 (37.9%)
No n (%)	64 (62.1%)
Obesity	

Yes n (%)	18 (17.5%)
No n (%)	85 (82.5%)

Frequency of hepatocellular carcinoma was found in 15 (14.6%) patients, whereas 88 (85.4%) patients had no hepatocellular carcinoma (Table-II).

Table II: Frequency of Hepatocellular Carcinoma Among Patients with Hepatitis C Virus. n=103

Hepatocellular Carcinoma	Frequency	% age
Yes	15	14.60%
No	88	85.40%
Total	103	100%

On binary logistic regression analysis, diabetes mellitus was found the only significant predictor of hepatocellular carcinoma (B=1.954, S.E.=0.711, Wald=7.559, OR=7.060, 95% C.I.: 1.753-28.437, p=0.006), meaning that diabetic patients had about seven times more odds of developing hepatocellular carcinoma. Age (OR=0.932, p=0.271), BMI (OR=0.941, p=0.730) and duration of HCV (OR=0.982, p=0.067) were not significantly associated with hepatocellular carcinoma (Table-III).

Table III: Binary Logistic Regression Analysis for Predictors of Hepatocellular Carcinoma. n=103

Variable	B	S.E.	Wald	OR (Exp B)	p-value	95% C.I. for EXP(B)	
						Lower	Upper
Age (years)	-0.071	0.064	1.213	0.932	0.271	0.821	1.057
BMI (kg/m²)	-0.060	0.174	0.12	0.941	0.730	0.669	1.325
Duration of HCV (months)	-0.018	0.010	3.346	0.982	0.067	0.963	1.001
Diabetes Mellitus (Yes)	1.954	0.711	7.559	7.060	0.006	1.753	28.437

OR = Odds Ratio; S.E. = Standard Error; B = Regression Coefficient; C.I. = Confidence Interval

On stratification, hepatocellular carcinoma was significantly more frequent in diabetic patients 10 (38.5%) as compared to non-diabetic 5 (6.5%) patients (p<0.001). No significant association was found with age group (p=0.070), BMI (p=0.575), gender (p=0.745), residential status (p=0.224), hypertension (p=0.780) and obesity (p=0.460). All 15 cases of hepatocellular carcinoma were seen in patients aged above 45 years, 15 (18.1%), but this difference was statistically not significant (Table-IV).

Table IV: Association of Hepatocellular Carcinoma with Demographic and Clinical Factors. n=103

Factors	Sub Groups	Hepatocellular Carcinoma		p-value
		Yes n(%)	No n(%)	
Age (years)	≤45	0 (0.0%)	20 (100.0%)	0.070**
	>45	15 (18.1%)	68 (81.9%)	
BMI (Kg/m²)	≤25	5 (11.4%)	39 (88.6%)	0.575**

	>25	10 (16.9%)	49 (83.1%)	
Gender	Male	10 (13.3%)	65 (86.7%)	0.745**
	Female	5 (17.9%)	23 (82.1%)	
Residential Status	Urban	7 (20.6%)	27 (79.4%)	0.224*
	Rural	8 (11.6%)	61 (88.4%)	
Diabetes Mellitus	Yes	10 (38.5%)	16 (61.5%)	<0.001**
	No	5 (6.5%)	72 (93.5%)	
Hypertension	Yes	5 (12.8%)	34 (87.2%)	0.780**
	No	10 (15.6%)	54 (84.4%)	
Obesity	Yes	4 (22.2%)	14 (77.8%)	0.460**
	No	11 (12.9%)	74 (87.1%)	

**Chi-Square Test; **Fisher Exact Test*

DISCUSSION

In the present study, hepatocellular carcinoma was found in 15 (14.6%) patients with hepatitis C virus. This is quite high frequency and it may be due to continuous inflammation and liver cell injury by the virus, which cause fibrosis, cirrhosis and abnormal regeneration of hepatocytes over the years, so the risk of malignant change is increased.

Diabetes mellitus was the most important factor in this study. Hepatocellular carcinoma was seen in 10 (38.5%) diabetic patients as compared to 5 (6.5%) non-diabetic patients (p<0.001) and diabetic patients had about seven times more odds of hepatocellular carcinoma (OR=7.060, p=0.006). The possible reason is insulin resistance and high insulin level in diabetes, which stimulate liver cell growth and increase oxidative stress and fat deposition in the liver. Hepatitis C virus itself also worsen insulin resistance, so both conditions together make the liver more prone to cancer.

All 15 (18.1%) cases of hepatocellular carcinoma were seen in patients above 45 years of age, although the difference was not statistically significant (p=0.070). This may be because of longer exposure to the virus and gradual liver damage with increasing age, while the small number of younger patients (n=20) may be the reason for no significance. Other factors like BMI, gender, residential status, hypertension and obesity were not significantly associated with hepatocellular carcinoma, which could be due to the small sample size and few cases of the disease in the study.

In the present study, hepatocellular carcinoma was found in 15 (14.6%) patients with chronic hepatitis C virus infection. Bartosch *et al.* [14] and Liang *et al.* [15] described that HCC develop after long standing infection with inflammation, fibrosis and cirrhosis, usually after 2 to 4 decades, with yearly incidence about 1 to 5% and this support the present finding. Soomro *et al.* [16] found lower frequency, 22 (8.3%) and Mujtaba *et al.* [17] reported 8 (6.67%) in 2 years follow-up. The reason may be younger patients (mean age 42.3±7.5 years) in Soomro *et al.* [16] and inclusion of HBV patients with short follow-up in Mujtaba *et al.* [17] Dandachi *et al.* [18] reported 26 (15%) HCC as second primary malignancy, which look similar to the present frequency, but the outcome measure was different, so direct comparison should be done carefully.

Diabetes mellitus was the only significant predictor in this study, as HCC was seen in 10 (38.5%) diabetic against 5 (6.5%) non-diabetic patients (p<0.001; OR=7.060, p=0.006). Rosa *et al.* [19] found diabetes in 59 (45.0%) of veterans with HCC, which is in line with the present result and Bartosch *et al.* [14] explained that insulin resistance, steatosis and oxidative stress increase the risk of malignant change. In contrast, Soomro *et al.* [16] did not find significant association (p=0.937) and the reason may be that only cirrhotic patients were included with few HCC cases, so the effect of diabetes was diluted.

All 15 (18.1%) HCC cases were seen in patients above 45 years, but the difference was not significant (p=0.070). Sargsyan *et al.* [20] reported

mean age 56.23±1.45 years with advanced fibrosis (F4, 80.0%) in HCC group and Rosa *et al.* [19] reported mean age 62.2±7.9 years, so older age with longer liver damage is common in these studies. Soomro *et al.* [16] found significant age association (p=0.008), while the present study did not, possibly because of smaller sample and only 20 patients in the younger group. Abara *et al.* [21] also noted that most patients were ≥60 years (68.5%), which support the role of advanced liver disease in older age.

Male patients were 75 (72.8%) in the present study, similar to Soomro *et al.* [16] (74.6%), Dandachi *et al.* [18] (78%) and Rosa *et al.* [19] (all male), but gender was not significantly associated (p=0.745), same as Soomro *et al.* [16] (p=0.831). Rural residence was seen in 69 (67.0%) patients, near to 70 (58.33%) in Mujtaba *et al.* [17] and it was also not significant (p=0.224). Hypertension was present in 39 (37.9%) patients without significant association (p=0.780), which agree with Soomro *et al.*[16] (p=0.853). The mean AFP level was 390.42±2078.46 ng/ml with very high SD, showing that few patients had very high values. Rosa *et al.* [19] found AFP <250 in 77.8% and Mujtaba *et al.* [17] found <150 in 7 (87.5%) HCC cases and Sargsyan *et al.* [20] noted AFP remain elevated in only 40.0% of HCC patients, so AFP alone is not reliable for detection. Abara *et al.* [21] reported that only 320 (10.9%) patients had regular 6-monthly surveillance and Rosa *et al.* [19] found 95.4% cases diagnosed incidentally, so regular screening is needed. D'Aleo *et al.* [22] described higher HCC burden in HCV/HIV coinfection, but HIV status was not assessed in the present study, so comparison is not possible.

The current study has some limitations. This was a single-center study with small number of patients and hence the findings cannot be generalized to other populations. This study has been conducted using cross-sectional design; hence, causation cannot be determined. The number of HCC patients is very low; thus, confidence intervals are wide and some of the variables may fail to reach statistical significance. Some key variables such as viral load, genotype, cirrhosis stage, alcohol consumption and co-infection have not been considered in the study.

CONCLUSION

The research has concluded that the disease hepatocellular carcinoma is very common amongst patients infected with the hepatitis C virus. The most important risk factor in the development of this condition is diabetes mellitus; other factors were not found significant. The importance of routine screening and control of diabetes in such patients cannot be underestimated.

Patients' Consent

All participants provided written informed consent before being enrolled in the study.

Competing Interests

The author declared that there were no competing interests associated with this research.

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