

# Hepatocellular Carcinoma: A Cross-Sectional Analysis of Risk Factors

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## ABSTRACT

**Background** Hepatocellular carcinoma is the most prevalent primary liver cancer globally and the major cause of cancer-associated deaths.

**Method:** A cross-sectional study was carried out at CMH Multan's Department of Histopathology. The individuals with HCC presented to CMH Multan's OPD or indoor general medicine department were selected. Informed consent was obtained. On a standardised proforma, all information such as gender, age groups, residence status, family history, diabetes, smoking, hypertension, and obesity was entered and analysed using the latest version of the SPSS.

**Results:** 85 (67.5%) of the 126 study cases were male, whereas 41 (32.5%) were female. 72 (57.1%) were from metropolitan areas, while 54 (42.9%) were from rural areas. Smoking was found in 10 (7.9%), and diabetes was found in 43. (34.1%). Obesity was found in 18 (14.3%), and hypertension was present in 74 (58.7%). Only 5 (4%) of our study cases had a family history of HCC.

**Conclusion:** HCC is more common in male patients, older patients, urban patients, and patients with diabetes, hypertension, and obesity. Individuals with diabetes, hypertension, and obesity undergo screening for HCC regularly. Further research is necessary to recognise the environmental and genetic variables that could contribute to developing HCC in various environments and populations.

**Keywords:** Liver, Risk factors, Hepatocellular carcinoma, Liver neoplasms.

## INTRODUCTION

Hepatocellular Carcinoma (HCC) is a well-known health problem that results in an array of complications with the liver. It is the most common and primary type of liver cancer.<sup>(1)</sup> HCC, estimated to account for 5% of all malignant tumours worldwide, is the sixth most frequent malignancy and the third leading cause of cancer-related fatalities. HCC incidence is expected to have reached its highest by 2030.<sup>(2)</sup> HCC is an intricate condition with multiple related and associated risk factors. Significant developments in lifestyle have fundamentally transformed health objectives in the vast majority of the world over the last hundred years. Non-Alcoholic Fatty Liver Disease (NAFLD) prevalence varies significantly across Asia and the Pacific, as would be anticipated in a region with marked variation in socioeconomic, political, and educational growth rates, in addition to variations in dietary habits, lifestyle, and sedentary lifestyle.<sup>(3)</sup> The primary contributing factors to the increased malignancy burden among underprivileged communities include growing populations, ageing, social or economic-demographic variables, healthcare access, and viral illnesses.<sup>(4)</sup> The lifetime risk for individuals having hepatitis B virus (HBV) and hepatitis C virus (HCV) cirrhosis is estimated to vary between 10% and 37%. As a result, not all cirrhotic individuals, as well as not every individual with persistent HCV or HBV infection, will end up with HCC. Environment-related factors could contribute to how many individuals with cirrhosis develop HCC.<sup>(5)</sup> Chronic HCV or HBV infection, heavy alcohol use, cigarette smoking, and unusual genetic disorders are all risk factors for HCC in the United States of America. Recent research indicates that several metabolic illnesses, including obesity, diabetes, impaired glucose tolerance, NAFLD, and metabolic syndrome, are also significant risk factors for HCC.<sup>(6)</sup> Hepatobiliary tumours are among the most prevalent type of carcinoma in Pakistan, accounting for 10.7% of all malignancies. We have minimal knowledge concerning HCC in the Pakistani population, primarily collected from hep-B and hep-C patients. At the same time, we are oblivious to the natural history of non-hep-B or hep-C Hepatocellular carcinoma in our community.<sup>(7)</sup> Although HCC is a multi-faceted condition, it is primarily preventable. In Pakistan, a well-balanced strategy for mitigation, monitoring, and appropriate treatment may significantly enhance outcomes and decrease the prevalence of HCC. To reduce the overall burden of HCC, attention should be directed towards the risk factors that have the most detrimental effect on the disease.<sup>(8)</sup> To bring attention to this

essential aspect, the World Gastroenterology Organization's World Digestive Health Day campaign on May 29, 2013, featured the slogan "Act today. Save your life tomorrow," since HCC is preventable with appropriate measures.<sup>(9)</sup> The vast majority of research in Pakistan has concentrated on viral infections such as hep-B and hep-C, as well as the risk of hepatocellular cancer. There is a paucity of research on additional risk factors such as hypertension, diabetes, obesity, and smoking. The aim of this descriptive cross-sectional study carried out at the CMH, Multan, Pakistan, was to fill this gap in the existing literature regarding potential risk factors that contribute to HCC other than hep-B and hep-C and to assist healthcare professionals and government agencies in developing targeted approaches for the high-risk population, thereby reducing disease burden.

## MATERIALS AND METHODS

Following ethics committee permission, a cross-sectional study was carried out at the CMH, Multan's Histopathology Department. The sample was selected from individuals with HCC who presented to the Combined Military Hospital Multan's outpatient department (OPD) or indoor general medicine department. Informed consent was obtained, and they were instructed on the study's aims, the integrity and availability of the information provided and the absence of any risk to the patient. On a standardised proforma, all information such as gender, age groups, residence status, family history, diabetes, smoking, hypertension, and obesity was entered and analysed using the latest version of the SPSS. The mean, as well as the standard deviation for patient age, were calculated using descriptive statistics. For categorical variables such as gender, age groups, residence status, cigarette smoking, family history, hypertension and diabetes, and obesity, frequencies and percentages were determined.

## RESULTS

There were 126 patients included in the study, of which 85 (67.5%) were male while 41 (32.5%) were females. The mean age was 54.18 ± 9.13. The minimum age was 39 years, while the maximum age was 70 years, as shown in Table 1.

The male patient's mean age was 53.88 ± 9.54 years, whereas the female patient's mean age was 54.80 ± 8.28 years (p=0.597). Most of the cases, 79 (62.7%), were over the age of 50 years. Of the 126 study cases, 54 (42.9%) were from rural, while 72 (57.1%) were from urban areas. Smoking was observed in 10

(7.9%) of our research cases. Diabetes was found in 43 (34.1%) of the patients. In our research, hypertension was present in 74 (58.7%) cases. The patients' mean Body Mass Index (BMI) was  $25.43 \pm 2.13 \text{ kg/m}^2$ , and obesity was observed in 18 (14.3%) participants. Only 5 (4%) people had a family history of HCC, as shown in Table 2.

Table 1: Age and Gender Distribution of Participants

Risk Factors		Frequency	Percentage
Age	Up to 50 years	18	37.3
	More than 50 years	108	62.7
Gender	Male	85	67.5
	Female	41	32.5

Table 2: Distribution of Factors Associated with Hepatocellular Carcinoma

Risk Factors		Frequency	Percentage
Hypertension	Yes	74	58.7
	No	52	41.3
Smoking	Yes	10	7.9
	No	116	92.1
Diabetes	Yes	43	34.1
	No	83	65.9
Obesity	Yes	18	14.3
	No	108	85.7
Residential Status	Urban	72	57.1
	Rural	54	42.9
Family History	Yes	5	4.0
	No	121	96.0

## DISCUSSION

Cancer is the leading cause of fatalities in the contemporary world, with HCC being the fifth most common malignancy and the third principal cause of malignancy-associated deaths worldwide.<sup>(10)</sup> African and Asian regions have been discovered to have the highest incidence of primary liver cancer, with eastern Asia having the highest age-standardised incidence rate (ASIR) and northern Europe having the lowest.<sup>(11)</sup> While the incidence of HCC is comparatively high in Asian and African regions, liver cancer fatalities are rising in more affluent countries, possibly due to changes in associated factors such as alcoholism, metabolic syndrome (MS), and obesity.<sup>(12)</sup> Chronic hepatitis C virus (HCV) or hepatitis B virus infection (HBV) or both have been identified as the aetiological factor in approximately three-quarters of all HCC cases.<sup>(13)</sup> Cirrhosis caused by alcoholism, smoking, arsenic, NAFLD, cirrhosis of any aetiologies, aflatoxin, oral contraceptive pills and tyrosinemia are also listed as risk factors.<sup>(14)</sup> In Pakistan, the ASIR for hepatocellular carcinoma is 7.6 for every 100,000 males and 2.8 for every 100,000 females annually.<sup>(7)</sup> The 5-year relative survival rate in the United States for HCC is only 14%, and it is even lower in developing countries.<sup>(15)</sup>

HCC screening techniques include both radiographic tests and serological indicators. Ultrasonography (US), computed tomography (CT), and magnetic resonance imaging (MRI) with contrast are all typical diagnostic procedures used for surveillance.<sup>(16)</sup>

Our study included 126 participants who met the study's inclusion criteria. There were 85 (67.5%) male and 41 (32.5%) female patients among the total 126 study cases. A survey from Lahore by Nadeem et al.<sup>(17)</sup> observed male gender preponderance in 68% of patients, which is comparable to our findings. Farooqi et al.<sup>(18)</sup> additionally observed that male gender pervasiveness in HCC is consistent with our results. Alam et al.<sup>(19)</sup> kept a 64% male gender dominance in HCC, which concurs with our findings.

The mean age of our research cases was  $54.18 \pm 9.13$  years, with a minimum age of 39 years and a maximum age of 70 years. Male patients had a mean age of  $53.88 \pm 9.54$  years, while female patients had a mean age of  $54.80 \pm 8.28$  years. According to our findings, 79 (62.7%) of our research cases were over 50 years old. Nadeem et al.<sup>(17)</sup> found similar results in a study conducted in Lahore. Naheed et al.<sup>(20)</sup> also, in a study conducted in Lahore, reported a mean age of  $45 \pm 10.95$  years for the

individuals they studied, which is consistent with our findings. Farooqi et al.<sup>(18)</sup> also reported a mean age of  $47.4 \pm 4.2$  years, comparable to our results. Alam et al.<sup>(19)</sup> also observed that 64% of the participants were between 45 and 60, which aligns with our findings.

54 (42.9%) of the 126 research cases were from rural, whereas 72 (57.1%) were from metropolitan regions. Smoking was found in 10 (7.9%) cases in our investigation. The more significant percentage of patients in urban areas can be ascribed to increased exposure to environmental toxins. The mean BMI was  $25.43 \pm 2.13 \text{ kg/m}^2$ , and obesity was observed in 18 (14.3%) of our study cases, which is in accordance with a local study.<sup>(21)</sup>

Only 5 (4%) of the research's individuals had a family history of HCC. Diabetes was identified in 43 (34.1%) of the individuals in our research. A study conducted in the Netherlands by Wlazlo et al.<sup>(22)</sup> revealed 37% diabetes, comparable to our observations. A survey carried out by Zein et al.<sup>(23)</sup> from the United States reported 25% diabetes, which correlates to our findings. In the study we conducted, hypertension was present in 74 (58.7%) of the cases. Almani et al.<sup>(24)</sup> reported 42% hypertension, which is in accordance with our findings.

## CONCLUSION

HCC is more common in male patients, older patients, urban patients, and patients with diabetes, hypertension, and obesity, according to our findings. In our research populace, smoking and a family history of HCC were less prevalent risk factors. Based on the results we obtained, we recommend that individuals with diabetes, hypertension, and obesity undergo screening for HCC on a regular schedule, especially if they are over the age of fifty and male. We also argue that these individuals should be encouraged to quit smoking and lose weight to decrease their likelihood of HCC and other challenges. More research is needed to understand the environmental and genetic factors that may play a role in developing HCC in various environments and populations. Additionally, regular screening and early detection can improve the prognosis of HCC. Therefore, healthcare providers should prioritise screening and monitoring for individuals at high risk of developing HCC.

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