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FREQUENCY OF CHRONIC VIRAL HEPATITIS (B AND C) AMONG THE PATIENTS OF HCC PRESENTING IN SOCIAL SECURITY HOSPITAL FAISALABAD

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ABSTRACT

Hepatocellular carcinoma (HCC) is a leading cause of cancer-related mortality worldwide, with chronic viral hepatitis being a major etiological factor.

Objective:
This study was conducted to determine the frequency of viral hepatitis among patients diagnosed with HCC and to assess the proportion of patients with co-infection of hepatitis B and C.

Methods: *A cross-sectional study was carried out at Social Security Hospital Faisalabad over a period of six months.(December 24 to May 25) A total of 95 patients aged 18–70 years with confirmed HCC were included using non-probability consecutive sampling. Diagnosis of HCC was established through ultrasound findings, serum alpha-fetoprotein levels (>200 ng/ml), and confirmatory imaging with tri-phasic CT scan or MRI. Detection of Hepatitis B and Hepatitis C was performed using real-time PCR. Data were analyzed using SPSS version 26.0.*

Results: *Among the study population, hepatitis C was the most common etiology, observed in 50.5% of patients, followed by hepatitis B in 22.1%. Co-infection with both hepatitis B and C was identified in 17.9% of cases, while 9.5% of patients had non-B non-C HCC. Diabetes mellitus (60%), hypertension (34.7%), and smoking (42.1%) were frequently observed comorbidities. However, no statistically significant association was found between hepatitis status and these risk factors ($p > 0.05$).*

Conclusion: *Hepatitis C remains the predominant cause of HCC in this cohort, followed by hepatitis B and co-infection. A considerable proportion of non-viral HCC highlights the emerging role of metabolic risk factors. Integrated strategies focusing on early detection and management of viral hepatitis along with control of metabolic comorbidities are essential to reduce the burden of HCC.*

Keywords: Hepatocellular carcinoma, Hepatitis B, Hepatitis C, Co-infection, Risk factors

INTRODUCTION:

More than seventy million people worldwide suffer from chronic hepatitis virus infection, which if left untreated may culminate in end-stage liver cirrhosis and hepatocellular carcinoma. Hepatocellular carcinoma (HCC) is the most diagnosed cancer in individuals under the age of 60 years, and approximately 20% of HCC are attributable to HCV infection. With the significant increase in the number of cases with chronic hepatitis C (CHC) over the past 10 years, the incidence of HCC attributable to CHC is projected to increase (1, 2). Liver cirrhosis is an important risk factor for hepatocellular carcinoma. The reported annual incidence of HCC is about 8% in CHC cirrhotic patients. NAFLD together with viral hepatitis will be the predominant predisposing factors of hepatocellular carcinoma In the upcoming decades (1). Hepatitis virus infection is a major cause of advanced hepatic fibrosis and cirrhosis, with significantly increased risk for development of HCC. The morbidity and mortality of viral hepatitis-related HCC remains high, as rates of HCV cirrhosis continue to increase (3). The long-term goal of antiviral therapy for chronic HCV is to reduce complications from cirrhosis, including HCC. While the development of HCC in HCV patients who achieve disease sustained virologic response is reduced, these patients remain at risk for HCC, particularly those patients with advanced fibrosis and cirrhosis (4). Dominant risk factors for the development of cirrhosis include chronic infection with Hepatitis B Virus (HBV), Hepatitis C Virus (HCV), Hepatitis delta virus (HDV), non-alcoholic steatohepatitis (NASH), high intake of alcohol and exposure to aflatoxin B1, diabetes, obesity (5). , Elderly men with chronic hepatitis B, risky alcohol use, advanced liver fibrosis, metabolic syndrome and high HBV DNA levels should be monitored closely to detect the development of HCC (6, 7).

In a study of Egypt, 514 HCV patients were enrolled, 108/514 patients (21%) had focal lesion detected by US, 17.3% had elevated AFP >200, overall HCC diagnosis was confirmed in 20%. Occurrence of HCC was significantly higher in smokers, diabetics, patients with decompensated liver and those with positive family history of HCC. Only 19.4% of HCC patients were diagnosed in the early stage rendering them candidate for curative treatment. It was concluded that, a national surveillance program for HCC in cirrhotic viral hepatitis patients by combining ultrasound examination and AFP is highly recommended. Co-infection with HBV was significantly higher in HCC compared to HCV along groups (11.7% versus 4.6%). Zampino et al. stated that HBV and HCV co-infection is associated with more rapid progression to HCC (8). HCC was more frequent in HBV-HCV group (14%) compared with HBV (2%, p = 0.006) and HCV monoinfected (4%, p = 0.006) (9).

Understanding the prevalence and impact of these co-infections is crucial because the presence of both HBV and HCV infections is known to significantly increase the risk of developing HCC. By establishing the frequency of such co-infections among HCC patients, this study seeks to highlight the importance of early diagnosis and management of HCC in patients with chronic viral hepatitis. Early detection can lead to timely and more effective treatments, ultimately reducing the morbidity and mortality associated with HCC. This study will provide valuable local data that can inform healthcare strategies and policies aimed at better managing and preventing HCC in patients with chronic viral hepatitis in this region. Additionally, the insights gained can guide healthcare planning, resource allocation, and educational programs, ultimately contributing to reduced morbidity and mortality associated with HCC in the region.

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METHODOLOGY:

The objective of the study was to determine the frequency of viral hepatitis among the patients of HCC presenting in Social Security Hospital Faisalabad and to determine the frequency of patients of HCC with both B and C viral hepatitis among those presenting in Social Security Hospital Faisalabad.

Any individuals with solid focal lesion seen on ultrasound examination of the liver, and/or serum AFP level >200 ng/ml were examined by tri-phasic CT, and/or MRI to confirm or rule out the diagnosis of HCC, will be include.

Exclusion creteria: Any patient with history of disturbance of liver or inflammation of liver diagnosed for more than 6 months was labeled as chronic hepatitis. HBV was defined as any patient positive for viral markers of HBV and confirmed on PCR for HBV DNA. HCV was defined as any patient positive for viral markers of HCV and confirmed on PCR for HBV RNA.

The study was conducted at Social Security Hospital Faisalabad. It was a cross sectional study done after proper approval of synopsis. Non probability consecutive sampling technique was used. Sample size was calculated using WHO sample size calculator. Expected frequency of viral hepatitis among the patients of HCC was taken as 14% with a confidence level of 95% and absolute precision of 7%, yielding a sample size of 95.

All patients of either gender aged 18 to 70 years, admitted with diagnosis of HCC as per the operational definition were enrolled in the study. Patients having HIV were excluded.After the approval to carry out this study from the Ethical Review Committee, subjects meeting the operational definitions and inclusion criteria were enrolled after informed consent. All adult patients diagnosed with HCC were included and status of viral hepatitis was noted for both HBV and HCV. Blood samples were taken in all cases of HCC (confirmed on radiology and raised AFP level), as diagnosed by a consultant, and Hepatitis B Virus (HBV) and HCV detection and quantification by Real-Time PCR was performed. Individuals with solid focal lesion in ultrasound examination, and/or serum AFP level >200 ng/ml were examined by tri-phasic CT, and/or MRI to confirm or rule out the diagnosis of HCC.

Data regarding the patients such as age, gender, family history, alcohol consumption and results of PCR for viral hepatitis (HBV and HCV) were recorded on the data collection sheet. Data analysis was done using SPSS version 26.0 (IBM Corp, Armonk, NY, USA). Quantitative variables were expressed as mean ± SD including age. Qualitative variables were expressed as numbers and percentages including gender, history of alcohol consumption, smoking, alcohol, Diabetes, hypertension, family history of liver disease, and status of HBV and HCV. Data was stratified for age and gender, and post stratification chi square test was applied to see the effect of these effect modifiers on the outcome. A p value of <0.05 was considered statistically significant.

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RESULTS: A total of 95 patients diagnosed with hepatocellular carcinoma (HCC) were included in the analysis. The cohort was predominantly male (71.6%), with females comprising 28.4%. The mean age was within the middle to older age range (data summarized in Table 1). Among viral causes, Hepatitis C was the most frequent etiology, identified in 48 patients (50.5%), followed by Hepatitis B in 21 patients (22.1%). Co-infection with both hepatitis B and C was observed in 17 patients (17.9%), while non-B non-C HCC accounted for 9 cases (9.5%) (Table 2). No statistically significant association was observed between hepatitis status and any of the evaluated risk factors. Cramér's V test was used to determine the strength of association. These findings indicate weak or negligible correlations between hepatitis status and associated risk factors. A multinomial/logistic regression model was constructed to assess independent predictors of non-B non-C HCC versus viral HCC.Risk factors were stratified according to hepatitis status (Table 3). Diabetes mellitus was the most prevalent comorbidity across all groups, particularly among hepatitis B (66.7%) and hepatitis C (60.4%) patients. Hypertension was more frequently observed in hepatitis C-related HCC (39.6%). Smoking prevalence was relatively uniform across all categories. A positive family history of HCC was slightly higher in hepatitis B and co-infection groups. Chi-square test was applied to evaluate associations between hepatitis status and risk factors. Hepatitis C remains the predominant etiology of hepatocellular carcinoma in this cohort, followed by hepatitis B and co-infection. A substantial proportion of patients demonstrated metabolic risk factors, particularly diabetes mellitus. However, no statistically significant association or strong correlation was identified between hepatitis status and diabetes, hypertension, smoking, or family history. Multivariate analysis further confirmed the absence of independent predictors for non-viral HCC, suggesting that metabolic risk factors are broadly distributed across all etiological categories.

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Table 1: Baseline Characteristics of Study Population (n = 95)

Variable	Frequency (n)	Percentage (%)
Male	68	71.6
Female	27	28.4
Diabetes Mellitus	57	60.0
Hypertension	33	34.7
Smoking	40	42.1
Family History HCC	19	20.0

Table 2: Distribution of Viral Hepatitis Status in HCC Patients

Hepatitis Status	Frequency (n)	Percentage (%)
Hepatitis C	48	50.5
Hepatitis B	21	22.1
HBV + HCV	17	17.9
Non-B Non-C	9	9.5

Table 3: Stratification of Risk Factors by Hepatitis Status

Variable	HCV (n=48)	HBV (n=21)	HBV+HCV (n=17)	Non-B Non-C (n=9)
Diabetes	29 (60.4%)	14 (66.7%)	9 (52.9%)	5 (55.6%)
Hypertension	19 (39.6%)	6 (28.6%)	5 (29.4%)	3 (33.3%)
Smoking	20 (41.7%)	9 (42.9%)	7 (41.2%)	4 (44.4%)
Family History	9 (18.8%)	5 (23.8%)	4 (23.5%)	1 (11.1%)

Table 4: Association Between Hepatitis Status and Risk Factors

Variable	Chi-square (χ^2)	p-value	Significance
Diabetes	1.02	>0.05	Not significant
Hypertension	1.34	>0.05	Not significant
Smoking	0.08	>0.05	Not significant
Family History	0.94	>0.05	Not significant

Table 5: Correlation Between Hepatitis Status and Risk Factors

Variable	Cramér's V	Interpretation
Diabetes	0.10	Weak
Hypertension	0.12	Weak
Smoking	0.03	Negligible
Family History	0.09	Weak

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DISCUSSION:

Hepatocellular carcinoma (HCC) remains a major global health burden and is strongly associated with chronic viral hepatitis, particularly Hepatitis B and Hepatitis C. The present study evaluated the frequency of viral hepatitis among patients with HCC in a tertiary care setting and explored the distribution of co-infection along with associated risk factors. The findings demonstrated that hepatitis C was the predominant etiology, followed by hepatitis B and co-infection, while a smaller proportion of patients had non-B non-C HCC.10,11

The predominance of hepatitis C in this cohort aligns with regional epidemiological patterns observed in Pakistan, where HCV infection is highly prevalent and constitutes a major risk factor for chronic liver disease and subsequent malignant transformation. Previous studies have reported that HCV accounts for up to 50–70% of HCC cases in South Asia, which is consistent with the findings of the current study10,11. Chronic HCV infection leads to persistent inflammation, fibrosis, and cirrhosis, ultimately predisposing to hepatocarcinogenesis through both direct and indirect molecular mechanisms12.

Hepatitis B was identified as the second most common etiology. Although its proportion was lower than HCV in this study, HBV remains a well-established oncogenic virus with the ability to induce HCC even in the absence of cirrhosis. This is primarily due to viral DNA integration into the host genome and activation of oncogenic pathways13. The observed frequency of HBV-related HCC in this study is comparable to other local and regional studies, although global trends suggest higher HBV prevalence in East Asia and Sub-Saharan Africa14.

An important finding of this study was the presence of HBV and HCV co-infection in a notable proportion of patients. Co-infected individuals are known to have a more aggressive disease course with

accelerated progression to cirrhosis and higher risk of HCC compared to mono-infection15. The synergistic interaction between HBV and HCV may enhance viral replication and increase hepatic injury, thereby promoting carcinogenesis. This highlights the need for early detection and aggressive management strategies in co-infected patients.

The proportion of non-B non-C HCC cases, although relatively small, is clinically significant. This group likely represents patients with metabolic or cryptogenic liver disease, including non-alcoholic fatty liver disease (NAFLD). The rising trend of non-viral HCC has been increasingly reported worldwide and is attributed to the growing burden of metabolic syndrome, diabetes mellitus, and obesity16. In the present study, a substantial proportion of patients had diabetes, supporting the hypothesis that metabolic factors contribute to hepatocarcinogenesis even in the absence of viral hepatitis.

Despite the high prevalence of diabetes, hypertension, and smoking among the study population, no statistically significant association was found between these risk factors and hepatitis status. This suggests that these factors are broadly distributed across different etiological groups rather than being confined to a specific viral category. Similar observations have been reported in previous studies where metabolic risk factors were found to independently contribute to HCC risk irrespective of viral status17.

Smoking was present in a considerable proportion of patients, although it did not show a significant association with hepatitis status. Tobacco use has been implicated as an independent risk factor for HCC, possibly through oxidative stress, DNA damage, and synergistic interaction with other carcinogens18. The lack of significant association in this study may be due to sample size limitations or uniform distribution of smoking habits across groups.

Family history of HCC was observed in a subset of patients, indicating a possible genetic or shared environmental predisposition. Although no significant association was demonstrated, familial clustering of HCC has been reported in the literature and may be related to genetic susceptibility, viral transmission patterns, or common lifestyle factors19.

The absence of statistically significant associations in stratified and multivariate analyses suggests that while viral hepatitis remains the primary etiological driver of HCC, metabolic and lifestyle factors contribute in a more generalized manner. This underscores the multifactorial nature of hepatocarcinogenesis and the need for a comprehensive risk assessment approach. From a clinical perspective, the findings emphasize the importance of screening and early detection of viral hepatitis, particularly HCV, in high-risk populations. In addition, the growing contribution of non-viral factors highlights the need for targeted interventions addressing diabetes, obesity, and lifestyle modifications.

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CONCLUSIONS:

Hepatitis C remains the leading cause of HCC in this cohort, followed by hepatitis B and co-infection. Non-B non-C cases, although fewer, demonstrate the emerging role of metabolic risk factors. The findings highlight the need for integrated preventive strategies targeting both viral hepatitis and metabolic syndrome to reduce the burden of HCC.

LIMITATIONS:

Limitations of the study include its single-center design, relatively small sample size, and lack of detailed assessment of other potential risk factors such as obesity and NAFLD. Furthermore, the cross-sectional nature of the study limits causal inference. Future studies with larger sample sizes and longitudinal follow-up are recommended to better understand the interaction between viral and metabolic factors in HCC development.

CONFLICT OFF INTEREST:

Nil

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