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Clinical Characteristics of Hepatocellular Carcinoma in Cirrhotic Patient

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Abstract

***Background*:** Hepatocellular carcinoma (HCC) is a major cause of cancer-related mortality globally, with a strong association with chronic liver disease, particularly cirrhosis. In cirrhotic patients, the overlapping clinical manifestations of HCC and underlying liver dysfunction complicate timely diagnosis and management. Understanding the clinical characteristics of HCC in this population is essential for improving outcomes. ***Objective*:** To evaluate the clinical characteristics of HCC in cirrhotic patients, focusing on differences in liver function, demographic profiles, and etiological factors. ***Methodology*:** A cross-sectional observational study was conducted at Bangabandhu Sheikh Mujib Medical University, Dhaka, Bangladesh, between December 2019 and August 2020. The study included 66 participants divided into two groups: cirrhotic patients with HCC (n=33) and cirrhotic patients without HCC (n=33). Data were collected through clinical, biochemical, and radiological assessments, with HCC diagnosis confirmed via fine-needle aspiration. Statistical analysis included t-tests, Chi-square tests, and ROC analysis. ***Results*:** The mean age of HCC patients was 49.85 ± 14.40 years, with 87.9% male predominance, similar to the cirrhosis group (mean age: 46.15 ± 11.06 years, 72.7% male). Significant differences were observed in prothrombin time (p=0.002), INR (p<0.001), and serum albumin (p=0.009), indicating relatively preserved liver function in HCC patients. HCC patients predominantly fell into Child-Pugh class B (54.5%), whereas cirrhotic patients were more commonly class C (39.4%, p=0.037). Hepatitis B virus (HBV) was the leading etiological factor in both groups, with HBsAg detected in 84.8% of HCC and 93.9% of cirrhotic patients. ***Conclusion*:** HCC in cirrhotic patients presents with distinct clinical and biochemical profiles, including better-preserved liver function and higher serum albumin levels compared to cirrhotic patients without HCC. The high prevalence of HBV in the region underscores the need for targeted surveillance and early intervention strategies. Further multicenter studies are recommended to validate these findings and enhance diagnostic and therapeutic approaches.

Keywords: Hepatocellular Carcinoma, Cirrhosis, Liver Function, Hepatitis B Virus, Child-Pugh Classification.

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INTRODUCTION

Hepatocellular carcinoma (HCC) is a primary malignancy of the liver and ranks among the most common causes of cancer-related mortality worldwide. Its prevalence is particularly high in patients with underlying chronic liver disease, especially cirrhosis. Cirrhosis not only serves as a critical risk factor but also creates a complex clinical landscape that influences the diagnosis, management, and prognosis of HCC [1-3]. Understanding the clinical characteristics of HCC in the

context of cirrhosis is vital for improving outcomes in this vulnerable patient population.

HCC typically develops as a consequence of chronic liver inflammation and fibrosis caused by hepatitis B or C infection, alcohol abuse, or non-alcoholic fatty liver disease (NAFLD). In cirrhotic patients, the tumor often arises within the fibrotic nodules characteristic of cirrhotic livers. The interplay between tumor biology and the altered hepatic microenvironment in cirrhosis makes the clinical presentation of HCC unique and challenging to discern in its early stages [4-6].

The clinical manifestations of HCC in cirrhotic patients can vary widely, ranging from asymptomatic cases detected incidentally during routine surveillance to symptomatic presentations with abdominal pain, weight loss, jaundice, or gastrointestinal bleeding. However, the symptoms of HCC often overlap with those of cirrhosis, such as ascites, encephalopathy, or portal hypertension, complicating the differentiation between tumor-related and liver disease-related symptoms [7-11].

Surveillance programs play a crucial role in the early detection of HCC in cirrhotic patients. Regular monitoring through imaging techniques like ultrasound, often combined with serum biomarkers such as alpha-fetoprotein (AFP), is recommended. Despite these efforts, the diagnosis may be delayed, especially in regions with limited access to healthcare resources, leading to advanced-stage detection and poorer prognoses.

The progression of HCC in cirrhotic livers is heavily influenced by the underlying liver function, assessed by scoring systems like the Child-Pugh classification or the Model for End-Stage Liver Disease (MELD) score [12]. These scores are pivotal in determining therapeutic strategies, ranging from curative options like liver transplantation or resection to palliative measures such as transarterial chemoembolization (TACE) or systemic therapy with agents like sorafenib.

Objective

This study aims to explore the distinct clinical characteristics of HCC in patients with cirrhosis, highlighting the importance of an integrated approach to diagnosis and management.

METHODOLOGY

Study Design

The study was designed as a cross-sectional observational study to evaluate specific outcomes within a defined population.

Study Setting

The research was conducted in the Department of Hepatology at Bangabandhu Sheikh Mujib Medical University (BSMMU), located in Dhaka, Bangladesh.

Study Duration

The study spanned from December 2019 to August 2020, covering a period of approximately nine months.

Study Population

The study included suspected cases of hepatocellular carcinoma (HCC) among patients attending the Hepatology outpatient department (OPD) or admitted to the inpatient department. Cirrhotic patients without evidence of HCC served as the control group, ensuring a comparative framework.

Sample Size

The sample size was determined using power analysis for a single proportion, assuming a hypothesized sensitivity of 90% for serum Alpha-L-Fucosidase (AFU). Based on an expected sensitivity of 70% (per Montaser *et al*., 2012), with 85% power and a 5% alpha error, the calculated sample size was 36 per group. Adjusting for a 10% attrition rate, the target was set at 40 per group. However, due to COVID-19 constraints, 33 patients were enrolled in each group.

Sampling Technique: Consecutive convenient sampling was employed to select study participants.

Inclusion Criteria: Participants were eligible if they met the following criteria:

- **Cirrhosis with HCC**:

Diagnosed based on clinical stigmata, laboratory features (e.g., prolonged prothrombin time, low serum albumin), ultrasound evidence, or endoscopic signs of esophageal varices. HCC diagnosis was confirmed via fine-needle aspiration (FNA) from hepatic lesions.

- **Control group**: Cirrhotic patients without HCC.
- Aged 18 years or older.

Exclusion Criteria

Exclusions Included:

- Patients undergoing or with prior treatment for HCC.
- Evidence of other malignancies.
- Presence of inflammatory/septic conditions, diabetes mellitus, or thyroid disorders.
- Co-morbidities rendering FNA unfeasible.
- Acute viral hepatitis, alcoholic hepatitis, or pregnancy.

Grouping

Participants were divided into two groups:

- **Group I**: Cirrhotic patients with HCC (n=33).
- **Group II**: Cirrhotic patients without HCC (n=33).

Data Collection

Both quantitative and qualitative data were collected using a pre-designed questionnaire, developed through literature review and expert consultation.

Data Collection Procedure

Eligible participants were identified from the Hepatology OPD and inpatient wards based on clinical, biochemical, and radiological evaluations. Inflammatory, infectious, and other malignancies were excluded through clinical assessments and additional tests (e.g., CRP, serum CEA, CA 19.9, CA 125). Fine-needle aspiration (FNA) was performed for HCC confirmation, and informed consent was obtained from all participants.

All patients underwent imaging studies, including abdominal ultrasound and triphasic CT scans, to document liver cirrhosis and focal lesions. Laboratory tests, including liver function tests and viral markers (HBsAg, Anti-HBc, Anti-HCV), were performed in BSMMU's pathology and biochemistry departments.

Study Variables

The Study Evaluated:

- **Independent Variables**: Cirrhosis with or without HCC.
- **Outcome Variables**: Liver function (e.g., ALT, bilirubin, INR), viral markers, Child-Pugh class, tumor characteristics (size, number), and biomarkers (AFU, AFP).
- **Demographic Variables**: Age and sex.

Statistical Analysis

Data were analyzed using SPSS (version 25). Quantitative variables were presented as means ± standard deviations or medians with interquartile ranges. Comparisons were made using t-tests or Mann-Whitney U tests. Categorical variables were analyzed using Chi-Square or Fisher's exact tests. Receiver operating characteristic (ROC) analysis was performed to assess AFU sensitivity and specificity. Correlations between AFU and AFP were determined using Spearman's correlation coefficient, with a p-value <0.05 considered statistically significant.

RESULTS

The age of the patients with hepatocelluoar carcinoma ranged from 27 to 72 years with the mean age of 49.85 ± 14.40 years; whereas the age of the patients with cirrho- sis ranged from 25 to 68 years with the mean age of 46.15 ± 11.06 years; difference was not significant (t=1.169; p=0.247). Among the patient with hepatocelluoar carcinoma, 16 (48.5%) patients were in the age group of above 50 years and 17 (51.5%) patients were in the age group of up to 50 years; it was 10 (32.3%) and 23 (67.7%) patients respectively in cirrhosis group. Difference was not significant (χ2=2.285; p=0.131)

Table 1: Age distribution of the study group

Age group	Hepatocellular carcinoma (n=33)	Cirrhosis (n=33)	P value
≤ 50 years	17 (51.5%)	23 (67.7%)	p=0.131ns
> 50 years	16 (48.5%)	10 (32.3%)	
Mean age ± SD in years	49.85 ± 14.40	46.15 ± 11.06	p=0.247NS

There were 29 (87.9%) male and 4 (12.1%) female in patients with hepatocellular car- cinoma; whereas 24 (72.7%) male and 9 (27.3%) female in cirrhosis group. There was no significant difference of sex between two groups (χ2=2.395; p=0.122)

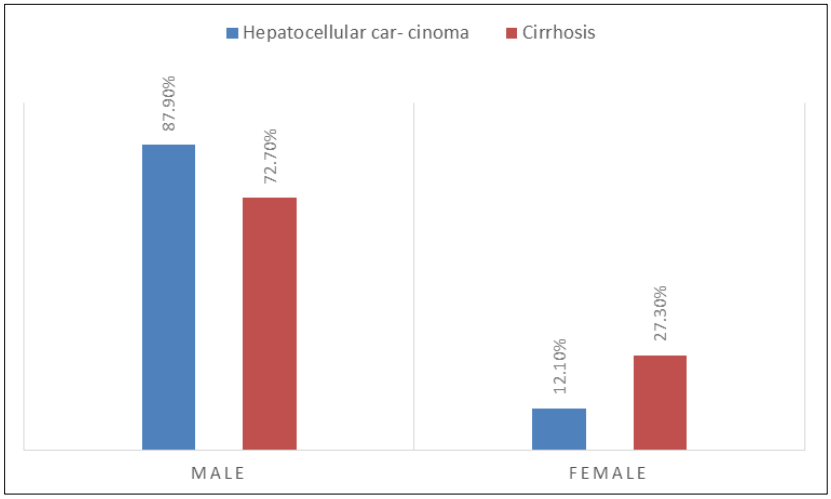

Figure 1: Gender Distribution of the study Group

The mean serum bilirubin (mg/dl) in HCC group and cirrhosis group were 1.90 ± 0.63 and 2.04 ± 0.58 respectively; difference was not significant (t=-0.920; p=0.361). The mean serum ALT (U/L) in HCC group and cirrhosis group were 68.42 ± 33.87and 59.21 ± 35.71 respectively; difference was not significant

(t=1.075; p=0.286). The mean prothrombin time (second) in HCC group and cirrhosis group were 14.88 ± 3.46 and 18.38 ± 5.10 respectively; difference was significant (t=-3.262; p=0.002). The mean INR in HCC group and cirrhosis group were 1.24 ±0.32 and 1 .60 ± 0.39 respectively; difference was significant (t=4.044; p<0.001). The mean serum albumin (g/dl) in HCC group and cirrhosis group were 2.87 ± 0.60 and 2.43 ± 0.72 respectively; difference was significant (t=2.682; p=0.009).

Table 2: Clinical characteristics of the study group

Clinical characteristics	Hepatocellular car-cinoma (n=33)	Cirrhosis (n=33)	P value
Serum ALT	68.42 ± 33.87	59.21 ± 35.71	p=0.286ns
Serum Bilirubin	1.90 ± 0.63	2.04 ± 0.58	p=0.361ns
Prothrombin time	14.88 ± 3.46	18.38 ± 5.10	p=0.002s
INR	1.24 ±0.32	1 .60 ± 0.39	p<0.001s
Serum Albumin	2.87 ± 0.60	2.43 ± 0.72	p=0.009s

Regarding etiological profiles, 28 (84.8%) patients in HCC group and 31 (93.9%) patients in cirrhosis group were expressing HBsAg in their sera (p=0.523). Anti HCV was detected in 1(3.0%) patient in HCC group and none in cirrhosis group (p=1.000). Non B and non-C etiology was found 4 (12.1%) patients in HCC group and 2 (6.1%) patients in cirrhosis group (p=672).

Table 3: Etiological profile of hepatocellular carcinoma and cirrhosis

Viral Marker	Hepatocellular car- cinoma (n=33)	Cirrhosis (n=33)	P value
HBsAg			
Positive	28 (84.8%)	31 (93.9%)	p=0.523ns
Negative	5 (15.2%)	2 (6.1%)	
Anti-HCV			
Positive	1 (3.0%)	0 (72.7%)	p=1.000ns
Negative	32 (97.0%)	33 (100.0%)	
Non-B, Non C	4 (12.1%)	2 (6.1%)	†p=0.672ns

Regarding Child Pugh classification, 10 (30.3%), 18 (54.5%), and 5 (15.2%) patients with HCC were in class A, B, and C, respectively; while 11 (33.3%), 9(27.3%), and 13 (39.4%) patients with cirrhosis were in Child Pugh class A, B and C respectively. There was a significant difference between the two groups ($\chi 2$=6.603; p=0.037).

Table 4: Distribution of patients according to Child-Pugh classification

Child-Pugh	Hepatocellular car- cinoma (n=33)	Cirrhosis (n=33)	P value
Class A	10 (30.3%)	11 (33.3%)	p=0.037s
Class B	18 (54.5%)	9 (27.3%)	
Class C	5 (15.2%)	13 (39.4%)	
Total	33 (100.0%)	33 (100.0%)	

DISCUSSION

The mean age of HCC patients in this study (49.85 ± 14.40 years) is consistent with several studies conducted in Asian populations, which often report a mean age between 50 and 55 years. However, the prevalence of younger patients in the study (51.5% were ≤ 50 years) contrasts with data from Western populations [12], where HCC is predominantly observed in older age groups due to the longer latency period of risk factors like hepatitis C and non-alcoholic fatty liver disease (NAFLD). Regarding gender distribution, the higher proportion of males in the HCC group (87.9%) aligns with global trends that report a male predominance, likely attributed to sex-specific hormonal and environmental factors influencing liver carcinogenesis [13].

The study found significantly lower prothrombin time and INR levels in the HCC group compared to the cirrhosis group, suggesting better coagulation function in the former. This is consistent with findings in other studies, which attribute relatively preserved liver function in HCC patients to their often being diagnosed in earlier stages of liver disease. Additionally, higher serum albumin levels in the HCC group indicate a better nutritional and synthetic liver function compared to the cirrhotic group, which is supported by prior research emphasizing albumin as a prognostic marker in liver diseases [14].

A notable similarity with other studies conducted in South Asia is the high prevalence of hepatitis B virus (HBV) infection among both HCC (84.8%) and cirrhotic patients (93.9%) [15]. This is in line with the endemic nature of HBV in the region.

However, the low prevalence of hepatitis C virus (HCV) infection in the study (3% in HCC group) is a striking difference from Western studies, where HCV is a leading cause of HCC. This discrepancy highlights the geographic variation in the etiological spectrum of liver diseases.

Significant differences in Child-Pugh classification between the two groups (p=0.037) highlight the advanced liver dysfunction in cirrhotic patients compared to those with HCC. The predominance of Child-Pugh class B in the HCC group and class C in the cirrhotic group aligns with studies that suggest patients with cirrhosis alone often have more decompensated liver disease [11]. This further emphasizes the role of HCC screening in identifying patients with relatively preserved liver function who may benefit from early therapeutic interventions.

Although specific biomarker analysis was not detailed here, the findings are likely to align with prior research showing that HCC patients often exhibit elevated levels of alpha-fetoprotein (AFP) and other tumor markers compared to cirrhotic patients. Future comparisons involving biomarkers like Alpha-L-Fucosidase (AFU) may provide additional insights into diagnostic accuracy and disease progression.

The observed differences in liver function parameters and Child-Pugh classification between the groups underscore the importance of individualized management strategies. However, the absence of significant differences in age and gender distribution limits the generalizability of these findings to broader populations. Furthermore, the low sample size and regional focus restrict direct comparisons with larger, multicenter studies.

CONCLUSION

The study highlights significant clinical differences between hepatocellular carcinoma (HCC) and cirrhotic patients, particularly in liver function parameters, with HCC patients showing better-preserved prothrombin time, INR, and serum albumin levels. The predominance of hepatitis B virus as the primary etiological factor underscores its role in HCC development in the region, emphasizing the need for targeted prevention and surveillance programs. Differences in Child-Pugh classifications suggest that HCC is often diagnosed in patients with relatively compensated liver function, providing an opportunity for early therapeutic intervention. These findings reinforce the importance of tailored management strategies for cirrhotic patients at risk of HCC to improve outcomes.

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