# Characterization and Outcomes of Hepatocellular Carcinoma in Chronic HCV or HBV Monoinfection

**Fatma Ali[1], Sherif Abbass [2], Mohamed Elgazzar [2], Manal Ebrahim Gomaa[3], Hassan Zaghla[2], Eman Abdelsameea[2], Nabil Omar [2]**

[1]*Hepatology and Gastroenterology Department, Shebin El-Kom Educational hospital, Egypt*
[2]*Hepatology and Gastroenterology Department, National Liver Institute, Menoufia University, Menoufia, Egypt*
[3]*Radiology department, National Liver Institute, Menoufia University,Egypt*

*Corresponding Author*
*Fatma Noaman Mohamed*
*Tel:0020482234586*
*E mail: fnim86@gmail.com*

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**Background and study aim:** Hepatocellular carcinoma (HCC) represents prevalent form of primary liver cancer and is among the frequently occurring malignancies globally due to hepatitis B virus (HBV) and /or hepatitis C virus (HCV) infection. We aimed to distinguish between HBV and HCV-caused HCC in characterization and outcomes.

**Patients and Methods**: One hundred and sixty HCC patients diagnosed by characteristic radiological pattern on multislice triphasic spiral computed tomography (CT) scan and /or dynamic magnetic resonance imaging (MRI) were included in the study. They were divided into 2 groups: 80 had HCV-related HCC patients and 80 had HBV-related HCC patients.

**Results:** Mean ± SD of age was 54.94±12.75, 59±7.95 years in HBV-related HCC and HCV-related HCC patients respectively with significant difference in age between two studied groups (P= 0.003). Male patients with HBV-related HCC represented 65% and they represented 64% in HCV-related HCC patients. All HCV-related HCC patients were cirrhotic while 2.5% of HBV-related HCC patients were not cirrhotic. Mean survival in HCV-related HCC compared to with HBV related HCC showed significant difference between both groups (6.7 and 4.84 respectively; P< 0.001). Age (p=0.037), PS (p=0.026) and creatinine (p=0.019) were associated with a negative impact on overall survival in HBV-related HCC patients. On the other hand, there was significant positive impact of increased albumin on survival (p=0.009).

**Conclusions:** HCC associated with HBV and HCV exhibits unique both pathological and clinical traits. Such distinctions underscore the need for tailored screening as well as management approaches that enhance surveillance of HCC, prompt identification and treatment efficacy.

## INTRODUCTION

Hepatocellular carcinoma (HCC) stands as the prevailing primary liver cancer across the globe. It holds the sixth position among the most frequently diagnosed malignancies and ranks as the second leading contributor to cancer-related deaths, accounting for roughly 1% of all global fatalities [1, 2]. Persistent viral hepatitis B and chronic hepatitis C represent significant risk factors for HCC development. However, the incidence of HCC demonstrates regional variation, influenced by the evolving natural progression of hepatitis C virus (HCV) and hepatitis B virus (HBV) infections within every geographical area [3-5]

In general, approximately 80% to 90% of HCC cases arise following the onset of liver cirrhosis, regardless of the underlying etiology.

Globally, approximately 80% of HCC cases are linked to HCV and HBV infections [3, 4]. HBV serves as a predominant reason for HCC in regions where the virus is endemic, such as certain parts of Africa and Asia. Conversely, in regions like Europe and the Middle East, HCV is the most prevalent cause [6]. Most of HCC cases related to HBV progress subsequent to liver cirrhosis, although some instances of HCC may arise without cirrhosis being present [7].

The annual incidence of HCC development is significantly higher in patients with HBV and cirrhosis and it can reach 3.16 per 100 person-years while patients without cirrhosis only report 0.1 per 100 person-years. Similarly, most HCC cases in patients with HCV infection emerge in the context of preexisting cirrhosis, or less commonly, significant fibrosis [8].

Globally, an estimated 71 million individuals suffer from chronic hepatitis C, a substantial portion of whom are expected to progress liver cirrhosis, hepatic failure, or HCC [9]. The prevalence of HCV has sparked significant international concerns due to its profound impact on morbidity and mortality [10]. Recently, the World Health Assembly adopted the Global Health Sector Strategy on viral hepatitis, aiming to eliminate viral hepatitis and establish global targets to reduce new infections and related deaths by 90% and 65%, respectively, by the year 2030 [11].

This study attempted to assess the notable clinical features and variations in outcomes among patients who developed HCC on top of hepatitis B virus (HBV) and hepatitis C virus (HCV) infection

## PATIENTS AND METHODS

This study was conducted on 160 patients with HCC, 80 patients (50%) had HCV- related HCC and 80 patients (50%) had HBV- related HCC from the outpatient clinic & HCC comittee, National Liver Institute, Menoufia University. The study was approved by the National Liver institute, Menoufia university Ethics Committee (IRB No: 00597/2024). The study protocol conforms to the ethical guidelines of the 1975 Declaration of Helsinki. The patients found to have focal lesion in the liver by abdominal ultrasound; diagnosis of HCC confirmed by characteristic radiological pattern detected by multislice triphasic spiral CT scan and /or MRI or liver biopsy if needed. Age < 18 years old, patients with benign hepatic tumors (eg.adenoma), patients with hepatic secondaries and patients with hepatocellular carcinoma who were negative for HCV, HBV infection were excluded. All patients were subjected to thorough history, co- morbidities [hypertension (HTN) and diabetes mellitus (DM)] and baseline laboratory tests; complete blood count (CBC), liver function tests (LFTs), renal function tests (RFTs), international normalized ratio (INR), and serum alpha-fetoprotein levels. Also, viral markers as HBsAg, HCV Ab, HCV RNA level and HBV DNA level were done. All patients were subjected to pelviabdominal U/S and triphasic CT abdomen and pelvis. Clinical classification of HCC based on Child Pugh score, MELD score, TNM staging system and Barcelona Clinic Liver Cancer staging systems. Then follow up of all studied patients was done for evaluation of treatment response, complications, survival and overall survival.

Statistical Analysis: Data were collected, tabulated and statistically analyzed using an IBM compatible personal computer with Statistical Package for the Social Sciences (SPSS) version 26 (SPSS Inc. Released 2018. Number (N) and percentage (%) were used to describe qualitative data. Median and interquartile ranges (IQR) were used to express quantitative data. Additionally, quantitative data were categorized using the mean for normally distributed data and the median for non-normally distributed data. Student's t-test (t) was employed to compare quantitative variables between two groups of normally distributed data, while Mann-Whitney's test (U) was utilized for comparison between two groups of non-normally distributed data. The Chi-square test ($\chi 2$) was applied to explore associations between qualitative variables. In cases where any expected cell count was less than five, Fischer's Exact test was employed. Survival analyses, including overall survival and disease-free survival, were conducted using Kaplan-Meier statistics. Uni- and multivariate analyses were employed to delineate prognostic indicators for survival. COX regression was utilized to evaluate the strength of association between independent risk factors and the dependent outcome, with risk estimated by Hazard ratio along with their 95% confidence interval. A significant difference was considered when $P < 0.05$.

## RESULTS

One hundred and sixty patients were included in the study; 80 patients had HCV- related HCC and 80 patients had HBV- related HCC. Patients with HBV-related HCC had a lower mean age at diagnosis than patients with HCV-related HCC, with a statistically significant age difference between the two groups (P=0.003). The gender distribution between the two groups under study did not differ statistically significantly (P=0.841). HCC predominantly occurred in males in both groups. Symptomatic cases often

manifested with jaundice (42.5% in HBV and 38.8% in HCV) and ascites (37.5% in HBV and 25% in HCV). No statistically significant difference was observed between the two groups in the presence of jaundice or ascites. For assessment of liver cirrhosis severity by the Child score, Child Class A & B patients were the majority of cases in both HCV and HBV (68.8 %, 30 %, 61.3 % and 37.5 % respectively). Between the two groups, no statistically significant difference was observed in the various Child classes (P=0.603). In both groups, the Mean MELD score was comparable (P=0.14). Compared to patients with HBV infection, those with HCV infection have a significantly increased chance of developing diabetes (P=0.008) as shown in Table 1.

Serum albumin levels were found to be lower in HCV-related HCC patients than in HBV patients (P = 0.564) , although this difference did not reach statistical significance. Further, the mean ALT, AST and hemoglobin levels were significantly lower in HCV-related HCCs than those with HBV-related HCC. In both groups, the prothrombin time and INR were comparable. In both groups, the average serum AFP level was elevated with no significant difference between two studied groups (P=0.123) Table 2.

Occurrence of cirrhosis in the liver was comparable between two groups. In HBV-related HCC, the non-cirrhotic liver rate was 2.5%, whereas in HCV-related HCC, it was 0% and the difference was not significant (P=0.497).

Mean survival in HCV-related HCC compared to with HBV related HCC showed significant difference between both groups (6.7 and 4.84 respectively; P< 0.001) as shown in Figure 1.

Univariate analyses for predictors of overall survival in HBV-related HCC patients showed that age, PS , BCLC , MELD, T Stage, albumin and creatinine, number of focal lesions were statistically associated with decreasing overall survival as shown in Table 3.

On multivariate cox regression analysis for predictors of overall survival in HBV-related HCC patients showed that age (HR=1.823, 95% CI: 1.036-3.208, p=0.037), PS (HR=2.243, 95% CI: 1.102-4.546, p=0.026), creatinine (HR=1.962, 95% CI: 1.119-3.443, p=0.019) were linked to a negative effect on survival. However, increasing albumin had statistically significant positive impact on survival (HR=0.318, 95% CI: 0.134-0.756, p=0.009) as shown in Table 4.

On the other hand, univariate analyses for predictors of overall survival in HCV-related HCC patients showed that age (p=0.043) and Child class (p=0.037) were statistically associated with decreasing overall survival, Table 5.

In cox regression analysis for predictors of overall survival in HCV-related HCC patients as regards age, it was not statistically significant independent factor affecting patients survival (p value =0.081) and hazard ratio (HR =1.662). Regarding Child class B&C, it was not statistically significant independent factor affecting patients survival with p value of 0.726 and 0.072 respectively. Regarding treatment with sorafenib, surgical, transarterial chemoembolization (TACE), thermal ablation, it was not statistically significant independent factor affecting patient's survival with p value of 0.342, 0.105, 0.830 and 0.576 respectively, Table 6.

**Table (1) Demographic and clinical data of studied groups:**

| **Variable** | | **Patients with HBV infection (n=80)** | | **Patients with HCV infection (n=80)** | | **Test of significance ($X^2$)** | **P value** |
|---|---|---|---|---|---|---|---|
| | | **No.** | **%** | **No.** | **%** | | |
| **Age (years)** | Mean ±SD | 54.94±12.75 | | 59±7.95 | | t=2.998 | 0.003* |


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| | | | | | | | |
|---|---|---|---|---|---|---|---|
| | Range | 20-83 | | 45 – 84 | | | |
| **Gender** | Male | 65 | 881.3 | 64 | 80.0 | 0.04 | 0.841 |
| | Female | 15 | 18.8 | 16 | 20.0 | | |
| **Special habit** | None | 43 | 53.8 | 36 | 45.0 | 2.954 | 0.399 |
| | Smoker | 20 | 25.0 | 28 | 35.0 | | |
| | Ex-smoker | 16 | 20.0 | 16 | 20.0 | | |
| **Clinical signs** | Jaundice | 34 | 42.5 | 31 | 38.8 | 0.233 | 0.629 |
| | Ascites | 30 | 37.5 | 20 | 25.0 | 2.909 | 0.088 |
| | Varices | 1 | 1.3 | 31 | 38.8 | 35.156 | <0.001** |
| | Ascites with encephalopathy | 21 | 26.3 | 15 | 18.8 | 1.290 | 0.256 |
| | Ascites with hepatorenal | 9 | 11.3 | 5 | 6.3 | 1.252 | 0.263 |
| **PS** | 0 | 61 | 76.2 | 34 | 42.5 | 19.472 | <0.001** |
| | 1 | 16 | 20.0 | 42 | 52.5 | | |
| | 2 | 3 | 3.8 | 4 | 5.0 | | |
| **Comorbidities** | DM | 15 | 18.8 | 30 | 37.5 | 6.957 | 0.008* |
| | HTN | 11 | 13.8 | 25 | 31.3 | 7.025 | 0.008* |
| **Child class** | A | 49 | 61.3 | 55 | 68.8 | 1.013 | 0.603 |
| | B | 30 | 37.5 | 24 | 30.0 | | |
| | C | 1 | 1.3 | 1 | 1.3 | | |
| **Child score** | Mean ±SD | 6.08±1.22 | | 6.07±1.17 | | t=0.066 | 0.947 |
| | Range | 5-10 | | 5 – 10 | | | |
| **BCLC** | 0 | 4 | 5.0 | 0 | 0.0 | 8.558 | 0.002* |
| | A | 34 | 42.5 | 56 | 70.0 | | |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| | B | 22 | 27.5 | 14 | 17.5 | | |
| | C | 20 | 25.0 | 10 | 12.5 | | |
| **MELD** | Mean ±SD | 8.2033±3.99 | | 8.96±3.81 | | U=1.476 | 0.140 |
| | Range | 1.13-20.22 | | 0.7-18.23 | | | |
| **T staging** | T1 | 41 | 51.2 | 51 | 63.7 | 5.108 | 0.164 |
| | T2 | 21 | 26.3 | 17 | 21.3 | | |
| | T3 | 4 | 5.0 | 6 | 7.5 | | |
| | T4 | 14 | 17.5 | 6 | 7.5 | | |
| **N staging** | N0 | 73 | 91.3 | 77 | 96.3 | 1.707 | 0.191 |
| | N1 | 7 | 8.8 | 3 | 3.8 | | |
| **M Staging** | M0 | 75 | 93.8 | 78 | 97.5 | 1.345 | |
| | M1 | 5 | 6.3 | 2 | 2.5 | | |

**PS**, performance status; BCLC, Barcelona Clinic Liver Cancer; MELD, Model for End-Stage Liver Disease; DM, Diabetes mellitus; HTN, Hypertension, SD, Standard deviation.

**Table (2) Laboratory data of studied groups**

| **Variable** | **Patients with HBV infection (n=80)** | **Patients with HCV infection (n=80)** | **Test of significance** | **P value** |
|---|---|---|---|---|
| | Mean ±SD | Mean ±SD | | |
| **Bilirubin [mg/dL]** | 1.47±1.2 | 1.25±0.73 | U=0.941 | 0.347 |
| **Albumin [g/dL]** | 3.57±0.67 | 3.51±0.6 | t=0.578 | 0.564 |
| **INR** | 1.25±0.25 | 1.24±0.25 | t=0.143 | 0.886 |
| **AST [U/L]** | 61.36±48.28 | 44.93±28.88 | U=2.596 | 0.009* |
| **ALT [U/L]** | 65.44±49.5 | 57.14±50.67 | U=2.447 | 0.014* |
| **AFP [ng/mL]** | 1630±9146 | 8511±65686 | U=1.544 | 0.123 |

| | | | | |
|---|---|---|---|---|
| **Hb [g/dL]** | 12.59±2 | 11.72±1.56 | t=3.008 | 0.003* |
| **TLC[ /mm$^3$]** | 5.59±2.25 | 7.52±5.5 | U=1.301 | 0.193 |
| **Platelet [×10$^3$/mm$^3$]** | 152.74±71.7 | 138±84 | U=1.886 | 0.059 |
| **Creatinine [mg/dL]** | 0.92±0.21 | 0.96±0.23 | t=1.054 | 0.293 |

INR: international normalized ratio; AST: aspartate aminotransferase; ALT: alanine aminotransferase; AFP: alpha-fetoprotein; Hb: hemoglobin; TLC: total leucocyte count.

**Table(3):Univariate overall survival analysis of risk factors associated with HCC in HBV patients**

| **Parameters** | | **HBV Patients** | | **Test of sig.** | **P value** |
|---|---|---|---|---|---|
| | | **Mean (95% CI)** | **Median (95% CI)** | | |
| **Gender(No, %)** | **Male** | 3.351(2.52 – 4.18) | 3(1.99 -4.01) | 2.459 | 0.117 |
| | **Female** | 4.12(3.1 – 5.12) | 5(3.21 – 6.79) | | |
| **Age** | **<55 years** | 4.64(3.46 – 5.83) | 3(1.89 -4.1) | 5.703 | 0.017* |
| | **>55years** | 2.63(2.1 – 3.24) | 2(0.67 – 3.32) | | |
| **PS** | 0 | 4.24(3.35 – 5.14) | 4(3.1 – 4.89) | 14.64 | 0.001* |
| | 1 | 1.96(1.18 – 2.75) | 1(0.817 – 1.18) | | |
| | 2 | 1.33(0.68 – 1.99) | 1 | | |
| **Child score** | A | 3.99(2.86 – 5.12) | 3(1.72 – 4.28) | 1.75 | 0.417 |
| | B | 2.81(2.18-3.45) | 3(2.08 – 3.95) | | |
| | C | 6(6-6) | 6(6-6) | | |
| **BCLC** | **0** | 4(1.92-6.08) | 3 | 14.929 | 0.002* |
| | A | 3.7(3.04-4.43) | 4(3.1-4.89) | | |
| | B | 3.66(2.29-5.03) | 3(1.4-4.5) | | |


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| Parameters | | HBV Patients | | Test of sig. | P value |
|---|---|---|---|---|---|
| | | Mean (95% CI) | Median (95% CI) | | |
| | C | 1.8(1.155-2.57) | 1(0.96-1.04) | | |
| **MELD** | <8 | 4.71(3.45-5.96) | 4(2.41-5.59) | 7.92 | 0.005* |
| | >8 | 2.538(2.02-3.05) | 2(1.03-2.97) | | |
| **T Stage (No, %)** | **T1** | 3.87(3.26-4.49) | 4(3.127-4.828) | 17.9 | <0.001** |
| | **T2** | 3.38(2.03-4.7) | 2(0.013-3.99) | | |
| | **T3** | 1.33(0.68-1.97) | 1 | | |
| | **T4** | 1.58(1.03-2.12) | 1(0.951-1.05) | | |
| **N Stage (No, %)** | **N0** | 3.69(2.94-4.5) | 0.541(2.12-3.88) | 0.792 | 0.374 |
| | **N1** | 1.833(1.15-2.55) | 1 | | |
| **M Stage (No, %)** | **M0** | 3.71(2.95-4.47) | 3(2.06-3.9) | 2.233 | 0.135 |
| | **M1** | 1.93(0.95-2.92) | 2(0-4.15) | | |
| **Number of focal lesions** | **Single** | 3.61(3.07-4.17) | 4(2.99-5.1) | 7.431 | 0.006* |
| | **Multiple** | 2.43(1.41-3.49) | 1(0.585-1.41) | | |
| **Lobe** | **Right lobe** | 3.22(2.65-3.79) | 3(1.98-4.02) | 1.857 | 0.395 |
| | **Left lobe** | 3.75(3.15-4.35) | 4 | | |
| | **Bilobular** | 2.98(1.65-4.3) | 2(1.39-2.61) | | |
| **focal lesion size (Cm)** | **<5cm** | 3.74(2.9-4.57) | 3(1.9-4.9) | 0.349 | 0.554 |
| | **>5cm** | 2.6(1.93-3.34) | 3(1.5-4.49) | | |
| **Albumin** | **<4** | 2.7(2.25-3.2) | 2(1018-2.82) | 10.406 | 0.001** |
| | **>4** | 6.17(4.19-8.15) | 6(3.17-8.8) | | |

| Parameters | | HBV Patients | | Test of sig. | P value |
|---|---|---|---|---|---|
| | | Mean (95% CI) | Median (95% CI) | | |
| **Hb** | **<11** | 2.77(1.84- 3.69) | 2(0.21-3.79) | 0.932 | 0.334 |
| | **>11** | 3.82(2.9-4.69) | 3(2.03-3.97) | | |
| **Creatinine** | <0.9 | 4.39(3.34-5.44) | 4(2.63-5.36) | 8.522 | 0.004* |
| | >0.9 | 2.34(1.7-2.95) | 2(1.6-2.39) | | |
| **Treatment** | Sorafenib | 3.59(2.06-5.14) | 3(1.38-4.61) | | 0.753 |
| | TACE | 2.98(2.3-3.62) | 3(1.76-4.23) | | |
| | Thermal ablation | 3.76(2.29-5.2) | 3(0.218-5.78) | | |
| | Ethanol injection | 3.07(2.06-4.08) | 3(1.41-4.59) | | |

**PS**, performance status; BCLC, Barcelona Clinic Liver Cancer; MELD, Model for End-Stage Liver Disease; Hb, hemoglobin.

**Table (4): Cox regression analysis for predictors of overall survival in HCC patients due to HBV infection**

| | Predictors (Independent variables) | Hazard Ratio | P value | 95% CI (lower-upper) |
|---|---|---|---|---|
| **Age** | **> 55years** | 1.823 | 0.037* | 1.036-3.208 |
| **PS** | **1** | 2.243 | 0.026* | 1.102-4.546 |
| | **2** | 2.712 | 0.122 | 0.767-9.597 |
| **BCLC** | **A** | 1.354 | 0.691 | 0.304-6.038 |
| | **B** | 1.93 | 0.393 | 0.427-8.720 |
| | **C** | 3.535 | 0.107 | 0.760-16.453 |

| | | | | |
|---|---|---|---|---|
| **MELD** | **>8** | 1.468 | 0.230 | 0.784-2.750 |
| **T Stage (No, %)** | **T2** | 1.3 | 0.551 | 0.549-3.078 |
| | **T3** | 3.278 | 0.113 | 0.756-14.223 |
| | **T4** | 3.111 | 0.015* | 1.248-7.756 |
| **Number of focal lesions** | **Multiple** | 1.285 | 0.549 | 0.566-2.920 |
| **Albumin** | **>4** | 0.318 | 0.009* | 0.134-0.756 |
| **Creatinine** | **>0.9** | 1.962 | 0.019* | 1.119-3.443 |

CI, Confidence interval, PS, performance status; BCLC, Barcelona Clinic Liver Cancer; MELD, Model for End-Stage Liver Disease.

*P value of < 0.05: statistically significant

**Table(5):Univariate overall survival analysis of risk factors associated with HCC in HCV patients**

| **Parameters** | | **HBV Patients** | | **Test of sig.** | **P value** |
|---|---|---|---|---|---|
| | | **Mean (95% CI)** | **Median (95% CI)** | | |
| **Gender(No, %)** | **Male** | 4.98(4.24-5.7) | 4(3.36-4.64) | 2.019 | 0.155 |
| | **Female** | 3.69(2.64-4.74) | 3(2.55-3.46) | | |
| **Age** | **>60 years** | 4.05(3.22-4.88) | 3(2.54-3.45) | 4.115 | 0.043* |
| | **<60years** | 5.39(4.46-6.33) | 4(1.71-7.36) | | |
| **PS** | 0 | 4.61(3.62-5.59) | 3(2.48-3.52) | 0.319 | 0.852 |
| | 1 | 4.76(3.88-5.63) | 3(2.23-3.67) | | |
| | 2 | 4.25(2.5-6) | 3 | | |
| **Child score** | A | 4.29(3.57-5.01) | 3(2.64-3.36) | 6.609 | 0.037* |
| | B | 5.72(4.52-6.9) | 7(5.37-8.63) | | |

| Parameters | | HBV Patients | | Test of sig. | P value |
|---|---|---|---|---|---|
| | | Mean (95% CI) | Median (95% CI) | | |
| | C | 2(2-2) | 2 | | |
| **BCLC** | **A** | 4.84(4.07-5.61) | 3(2.44-3.56) | 2.63 | 0.268 |
| | **B** | 7.07(2.46-3.68) | 3(2.17-3.82) | | |
| | **C** | 4.6(3.32-5.88) | 4(2.48-5.51) | | |
| **MELD** | <8 | 4.41(3.62-5.2) | 3(2.49) | 0.921 | 0.337 |
| | >8 | 5(4.01-5.99) | 4(3.35-4.65) | | |
| **T Stage (No, %)** | **T1** | 4.72(3.9-5.52) | 3(2.36-3.64) | 3.120 | 0.374 |
| | **T2** | 3.88(2.71-5.05) | 3(2.23-2.77) | | |
| | **T3** | 3.83(2.86-4.8) | 3 | | |
| | **T4** | 5.17(3.67-6.66) | 4 | | |
| **N Stage (No, %)** | **N0** | 4.76(4.08-5.38) | 3(2.49-3.5) | 0.005 | 0.945 |
| | **N1** | 4(1.56-6.45) | 3(1.4-4.6) | | |
| **M Stage (No, %)** | **M0** | 4.68(4.03-5.33) | 3(2.49-3.5) | 0.675 | 0.411 |
| | **M1** | 5.5(3.42-7.58) | 4 | | |
| **Number of focal lesions** | **Single** | 4.87(4.17-5.57) | 3(2.46-3.54) | 1.513 | 0.219 |
| | **Multiple** | 3.182(2.52-3.84) | 3(1.96-4) | | |
| **Lobe** | **Right lobe** | 4.62(3.85-5.39) | 3(2.38-3.62) | 1.456 | 0.483 |
| | **Left lobe** | 5.19(3.86-6.49) | 3(2.03-3.99) | | |
| | **Bilobular** | 3.17(2.31-4.02) | 3(1.87-4.13) | | |
| **focal lesion size (Cm)** | **<5cm** | 4.043(3.2-4.88) | 3(2.49-3.51) | 0.09 | 0.765 |
| | **>5cm** | 4.79(4.03-5.55) | 4(3.41-4.59) | | |

| Parameters | | HBV Patients | | Test of sig. | P value |
|---|---|---|---|---|---|
| | | Mean (95% CI) | Median (95% CI) | | |
| **Albumin** | **<4** | 4.78(3.36-6.17) | 4(2.81-5.19) | 0.001 | 0.970 |
| | **>4** | 4.73(4-5.45) | 3(2.46-3.54) | | |
| **Hb** | **<11** | 4.82(3.99-5.64) | 4(3.38-4.62) | 0.136 | 0.712 |
| | **>11** | 4.58(3.56-5.6) | 3(2.51-3.49) | | |
| **Creatinine** | <0.9 | 4.69(3.84-5.55) | 3(2.35-3.64) | 0.011 | 0.916 |
| | >0.9 | 4.77(3.79-5.73) | 3(2.22-3.78) | | |
| **Treatment** | Sorafenib | 3.67(2.39-4.93) | 3(2.31-3.69) | 10.08 | 0.039* |
| | Surgical | 2.87(2.13-3.6) | 3(2.39-3.61) | | |
| | TACE | 5.69(4.59-6.77) | 7(2.54-11.45) | | |
| | Thermal ablation | 4.4(3.2-5.59) | 3(2.31-3.69) | | |
| | Ethanol injection | 4.36(3.2-5.7) | 4(3.37-4.63) | | |

PS, performance status; BCLC, Barcelona Clinic Liver Cancer; MELD, Model for End-Stage Liver Disease; Hb, hemoglobin; TACE, transarterial chemoembolization.

**Table (6): Cox regression analysis for predictors of overall survival in HCC patients due to HCV infection**

| Predictors (Independent variables) | | Hazard Ratio | P value | 95% CI (lower-upper) |
|---|---|---|---|---|
| **Age** | **>60years** | **1.662** | **0.081** | **0.940-2.904** |
| **Child score** | **B** | **0.850** | **0.726** | **0.342-2.113** |
| | **C** | **7.342** | **0.072** | **0.835-64.522** |
| **Treatment** | **Sorafenib** | **1.695** | **0.342** | **0.571-5.035** |
| | **Surgical** | **2.103** | **0.105** | **0.857-5.160** |

| Predictors (Independent variables) | | Hazard Ratio | P value | 95% CI (lower-upper) |
|---|---|---|---|---|
| | **TACE** | **0.889** | **0.830** | **0.306-2.584** |
| | **Thermal ablation** | **1.297** | **0.576** | **0.522-3.224** |

CI, Confidence interval; TACE, transarterial chemoembolization.

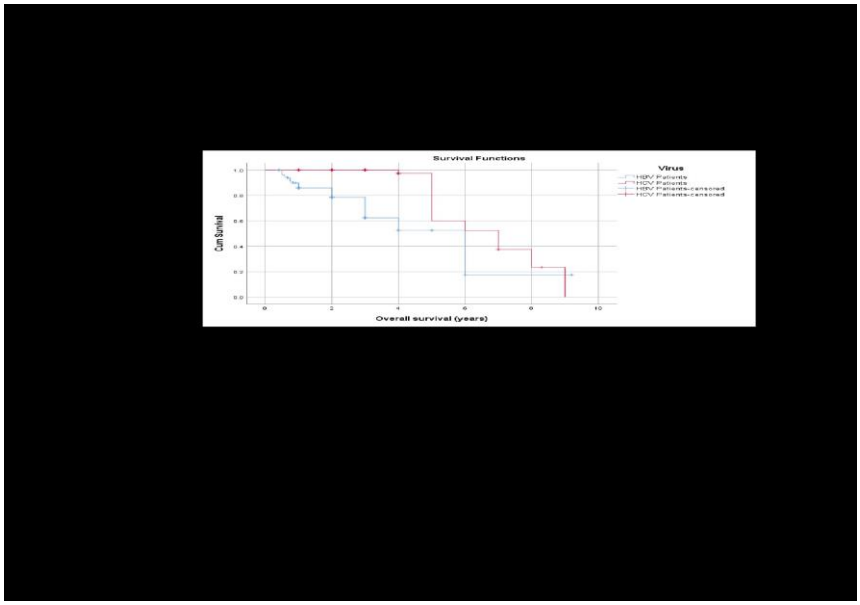


Figure 1: Kaplan meier estimation of overall survival.

## DISCUSSION

Most of studies about hepatocellular carcinoma focused on HCV-related hepatocellular carcinoma regarding clinical and pathological characteristics. So the aim of this work was to focus on hepatocellular carcinoma on top of HBV. In our trial, while HBV- and HCV-related HCC share certain characteristics, they tend to display distinct differences in clinical characteristics and presentation. Upon initial diagnosis, the majority of patients exhibited good synthetic function. The mean ± SD of albumin was 3.57±0.67 g/dL in HBV- related HCC patients and mean ± SD of albumin was 3.51±0.6 g/dL in HCV- related HCC patients. Both groups had high mean serum AFP levels and the difference was not significant.

Significantly, in our study, a greater proportion of patients had a solitary lesion diagnosis of hepatocellular carcinoma (HCC). Notably, solitary lesions were more frequently observed in patients with HCV-related HCC (86.3%) compared to those with HBV-related HCC (65.0%). We noticed a significant difference in the prevalence of solitary lesions between HCV-related and HBV-related HCC (P = 0.002). Patients with HCV-related HCC more frequently exhibited tumor sizes exceeding 5 centimeters compared to those with HBV-related HCC. Barazani et al.'s study revealed that tumors in cirrhotic HBV patients were larger in their maximum diameter and more often > 5 cm or bilobar, but not different as regards number of tumors, grade or frequency of metastases. Also, further analysis of OLT recipients revealed that 56% of HBV patients and 18% of HCV patients, respectively, had tumors bigger than 5 cm and were not eligible for liver transplantation due to the Milan criteria (P = 0.005) [12]. Moreover, patients with HBV-related HCC had a higher incidence of macrovascular invasion and metastases, with no statistically significant difference was noted between the two groups.

Such findings are corresponding with those reported by Aljumah et al [13].

In our present study, we observed generally poor survival rates of 63.7% among patients with HBV-related HCC and 70% among those with HCV-related HCC, and the difference was not significant in survival. These findings align with those reported by Aljumah et al [13].

Upon further stratification poor outcomes were linked to the HCV group's viral status, metastasis, increased AFP levels (>400), and non-transplant treatment.. The overall poor survival observed in the study remained significant ($P < 0.001$). In line with our results, Kitisin and Packiam [14], revealed that the proportion of patients who could benefit from curative treatments was just 29.5%.

Globally, hepatitis C virus (HCV) infection stands as the primary cause of cirrhosis, accounting for 93% of cases [15], thus serving as a significant risk factor for hepatocellular carcinoma (HCC) [8].

The incidence and complications of HCV have been on the rise, making it the most significant risk factor for developing liver cancer, including hepatocellular carcinoma (HCC) in Egypt. On a global scale, hepatitis B virus (HBV) represents one of the infectious risk factors for HCC, accounting for 88% of cirrhosis-related cases [16]. However, in Egypt, there has been a decline in the prevalence of HBV infection over the past two decades, attributed to the success of a nationwide vaccination strategy [17]. A notable reduction has been observed in the prevalence of HBV-related HCC in this study [18].

In Egypt, both HBV and HCV infections are transmission in the horizontal direction. However, unlike HBV, HCV exposure primarily occurs later in life due to contact with contact with bodily fluids contaminated in high-risk groups [19]. Our study revealed that patients with HBV received their diagnosis earlier than those with HCV, with a statistically significant age difference between the two groups ($P = 0.003$). This finding aligns with observations from Japanese studies. Interestingly, HBV infection patients, especially younger ones with comparatively intact hepatic reserves, might develop HCC even in the absence of cirrhosis [20].

Numerous researches indicated that those with HCC who get it earlier in life may have been overlooked in HCC surveillance programs, leading to diagnosis at an advanced cancer stage [21].

Diabetes and alpha-fetoprotein production are associated with a distinguishing factor in the advancement of HCC in patients with HBV versus HCV. Compared to individuals infected with HBV, patients infected with the hepatitis C virus (HCV) are much more likely to acquire diabetes. Additionally, some findings suggest that diabetes and HCV co-increase hepatocellular carcinoma risk. In our study, both groups had higher mean serum alpha-fetoprotein (AFP) levels and the difference was not significant [22].

Patients without severe fibrosis may develop HCC, which could indicate the presence of yet-to-be-identified additional elements in the pathogenic process of HBV [23]. Numerous research studies have reported a notable decrease in the risk of hepatocellular carcinoma in patients who had interferon therapy and sustained viral clearance. In contrary, the progression of HCC in cirrhosis patients remained unaffected by direct-acting antivirals. Preliminary research have even suggested a potential raise in the development of de novo HCC or recurrence of treated HCC following direct-acting antiviral therapy [24]. The global burden of HCC continues to rise, primarily propelled by the populations infected with HBV and HCV. Nonetheless, the widespread use of the HBV vaccination and the use of novel and very effective antiviral therapies for HCV are anticipated to attenuate the progression into cirrhosis, thereby reducing the subsequent of HCC development [25].

**Conclusion:** Hepatocellular carcinoma associated with hepatitis B virus and hepatitis C virus exhibit distinct clinical and pathological characteristics. Such disparities underscore the need for tailored treatment policies to enhance surveillance of HCC , facilitate early detection, and optimize strategies for management.

Author contribution: We declare that all listed authors have made substantial contributions to all of the following three parts of the manuscript:

-Research design, or acquisition, analysis or interpretation of data.

-Drafting the paper or revising it critically.

-Approving the submitted version.

We also declare that no-one who qualifies for authorship has been excluded from the list of authors.

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All data are available on request

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The study is approved by the ethics committee of National Liver Institute, Menoufia University and conducted in accordance with Helsinki standards.

**Patient consent statement:**

An informed consent from each participant

**RESEARCH HIGHLIGHTS:**

- Hepatocellular carcinoma occupies a prominent place among the most frequently diagnosed worldwide malignancies.
- Identifying clinical and pathological characteristics between hepatitis B virus hepatitis C virus related hepatocellular carcinoma are needed.
- These differences highlight the requirement for adequate screening polices that facilitate early detection and optimize management strategies.

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