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Assessment of Hepatocellular Carcinoma Patients Infected with Covid-19 Infection during the Pandemic

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Abstract

Hepatocellular carcinoma (HCC) patients are more susceptible to decompensation if they get Coronavirus disease 2019 (COVID-19) infection that leads to significant reduction in HCC related health services, reduction in surveillance activities and progression of HCC. On the other hand, symptoms of covid-19 infection are usually severe in HCC patients. Assessment of severity of covid-19 infection in HCC patients. And assessment of clinical course and outcome of HCC patients when they get infected by Covid-19. This is a retrospective case control study including 100 HCC patients (50 of them were infected by covid-19 while the other 50 were not infected). All patients were Egyptians presented to HCC clinic in national hepatology & tropical research institute (NHTMRI) from 1/2022 to 1/2023 assessed for covid-19 infection (by typical CT chest, covid swab and covid symptoms) and assessed for HCC staging (by Barcelona clinic liver cancer BCLC), clinical course over six months (by Child Pugh score) and mortality rates. Most of Covid-19 infected HCC patients had severe covid symptoms and progressive HCC course with mortality 72%, while low percentage of covid-19 HCC infected group were mild with stationary course. On the other hand, high percentage of non-infected HCC group have stationary HCC course with low mortality 24%. COVID-19 infection seems to have a significant effect on clinical course and outcome of HCC. Also, HCC patients are vulnerable to have more severe COVID-19 symptoms.

Keywords: Liver cirrhosis, Covid-19, Hepatocellular carcinoma

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1. Introduction

Hepatocellular carcinoma (HCC) considered a worldwide problem. Epidemiological data showed great variation from one country to another. Egypt considered the third in Africa and the 15th worldwide to suffer from HCC. It represents the most challenging health problem in Egypt as the number of patients increased nearly twofold in a decade [1]. The increased incidence may be explained by the improved screening programs [2], increasing incidence of hepatitis C virus [3] which is the most important risk factor in Egypt for developing liver cancer [4]. In addition to the increased survival rates of cirrhotic patients increasing the chance of developing HCC, Liver cirrhosis of different etiologies and hepatitis B virus infection considered the main risk factors worldwide, with an annual incidence reaching 1-6 % [5]. Hepatitis C viral infection with subsequent liver cirrhosis is the leading risk factor in Egypt [6]. Coronavirus disease 2019 (COVID-19) is a highly infectious disease caused by infection with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). The first Egyptian case discovered in February 2020 [7]. The first case was identified in China, in December 2019 [8]. Symptoms include cough, fatigue, and headache, loss of taste and smell, breathing difficulties [9]. *The aim of the current study is the* assessment of severity of covid-19 infection in HCC patients and assessment of clinical course and outcome of HCC patients when they got Covid-19 infection.

2. Materials and Methods

2.1. Population of study

The study included 100 HCC patients (50 of them infected by covid-19 while the other 50 were not infected). All patients were Egyptians presented to HCC clinic in national hepatology & tropical research institute from 1/2022 to 1/2023 assessed for covid-19 infection (by typical CT chest, covid swab and covid symptoms) and assessed for HCC staging by (BCLC), clinical course over six months (by Child Pugh score) and mortality rates.

2.2. Study design

Retrospective case control study.

2.3. Study location

Data collected from medical records of HCC clinic in the National Hepatology & Tropical Medicine Research Institute.

2.4. Inclusion criteria

HCC patients with confirmed COVID-19 infection (by typical CT chest "ground glass opacity", positive covid-19 swab and covid-19 symptoms as cough, dyspnea, fatigue, loss of taste and smell, fever after being in contact with covid-19 patient).

2.5. Exclusion criteria

Patients with underlying pulmonary disease or other co-morbidities as DM, HTN, CKD, IHD.

2.6. The Collected Patients' Data

- Birth date, gender, etiology of HCC, size and site of HCC and BCLC stage and Child Pugh score.
- Complete blood picture, full metabolic profile including liver function tests, Alpha-fetoprotein, Covid-19 PCR Swab.
- Abdominal ultrasound for assessment of HCC patients and CT chest for Covid-19 detection by presence of Ground glass opacity (GGO).
- COVID-19 disease severity using the Egyptian MOHP protocol:
  - Asymptomatic Infection: positive Covid-19 swab without symptoms.
  - Mild illness: symptoms of COVID-19 in absence of shortness of breath or abnormal chest imaging.
  - Moderate illness: symptoms or imaging suggestive of lower respiratory tract disease but with O2 saturation ≥ 94% on room air
  - Severe illness: oxygen saturation ≤ 94%, PaO2/FiO2 <300 with marked tachypnea >30 breaths/min or lung infiltrates >50%.
  - Critical illness: acute respiratory failure, septic shock, and/or multiple organ failure.

2.7. Ethical statement

This work had approved from the ethical committee, Cairo University

Table (1): The BCLC staging

Table (2): Child-Pugh score

Table (2): Child-Pugh score

2.8. Statistical design

The data analyzed by SPSS (statistical package for social science) version 26.0. Number (No), percentage (percentage), used were for qualitative data, while mean ± SD were used for quantitative data. P-value < 0.05 considered statistically significant.

3. Results and discussion

Table (3) shows the age & gender of the studied groups. The mean age of HCC infected group was 63.8 ± 7.9 with males representing 58% while in the non-infected group the mean age was 59 ± 5.6 with 52% males, which may points to the male predominance of HCC. Table (4) shows the tumor-related characteristics of the studied groups. Most of HCC lesions occurred in the right lobe with HCV being the most common etiology. The most vulnerable BCLC stage in the infected group is stage D that may explained by the poor general condition and altered immune response. Table (5) shows the baseline laboratory characteristics of the studied groups. The baseline laboratory data revealed very high levels of alfa feto-protein. Table (6) shows COVID-19 severity in the HCC infected group (N=50). Most of Covid-19 infected HCC group had severe Covid stage, which suggests that HCC renders the patient more vulnerable to more severe covid infection. Table (7) shows follow up within six months. The progression of HCC size is significantly higher in Covoid-19 infected group when compared to the non-infected group. Additionally, the patient decompensation and mortality rates are higher significantly in the Covid-19 infected group in comparison to the non-infected one (P value <0.001).

The expansion of the COVID-19 infection as a pandemic has rapidly become of great concern with unresolved questions. As from the start, many articles have published by several societies such as the European Association for the Study of the Liver (EASL) to provide guidance for management of patients with chronic liver diseases (CLD) infected with COVID-19. During COVID-19 course, 20–70% of patients got liver insult such as an increase in liver enzymes as well as bilirubin [10], which may attributed to direct cytotoxic damage or hypoxia of hepatocytes [11]. Additionally, therapeutic drugs used in COVID-19 as remdesivir, steroids, and azithromycin have cytopathic effect on the liver. Liver insult plays an important role in cytokine storm cascade and multi-organ failure. With the exception of cases of cytokine storm and rare drug related hepatopathies, liver insult is usually temporary and does not affect mortality [12]. HCC patients usually burdened with significant liver function impairment, which renders them susceptible to a more severe course of COVID-19 with high mortality rates. Patients in need for hospitalization and Intensive Care are especially at risk.

Some HCC patients may develop respiratory complications, but most of them develop acute on top of chronic liver failure with high mortality rates. Additionally, infection with COVID-19 may significantly delays oncological management, adversely affecting the outcome of the primary disease [11]. Since liver malignancy is the sixth most common cancer in the world and the fourth common cancer in Egypt, so studying the impact of COVID-19 on HCC patients needed. This study included 100 HCC patients (50 of them were infected with Covid-19 while the other 50 not infected) to assess the severity of covid-19 infection on HCC patients at (NHTMRI). The mean age of HCC infected group was 63.8 ± 7.9 with males representing 58% while in the non-infected group the mean age was 59 ± 5.6 with 52% males. Male predominance in HCC may explained by behavioural risk factors and compliance with antiviral treatment. Males are more vulnerable to get HBV and HCV with subsequent chronic hepatitis, cirrhosis and HCC. Males may have lower seroconversion after HBV vaccination compared to females, in addition to androgen induced up regulation of viral production and inflammation. In this study, 50 (50%) of the patients had COVID-19, among those 27 (54%) had severe infection, 15 (30%) had moderate infection, while 8 (16%) had mild infection.

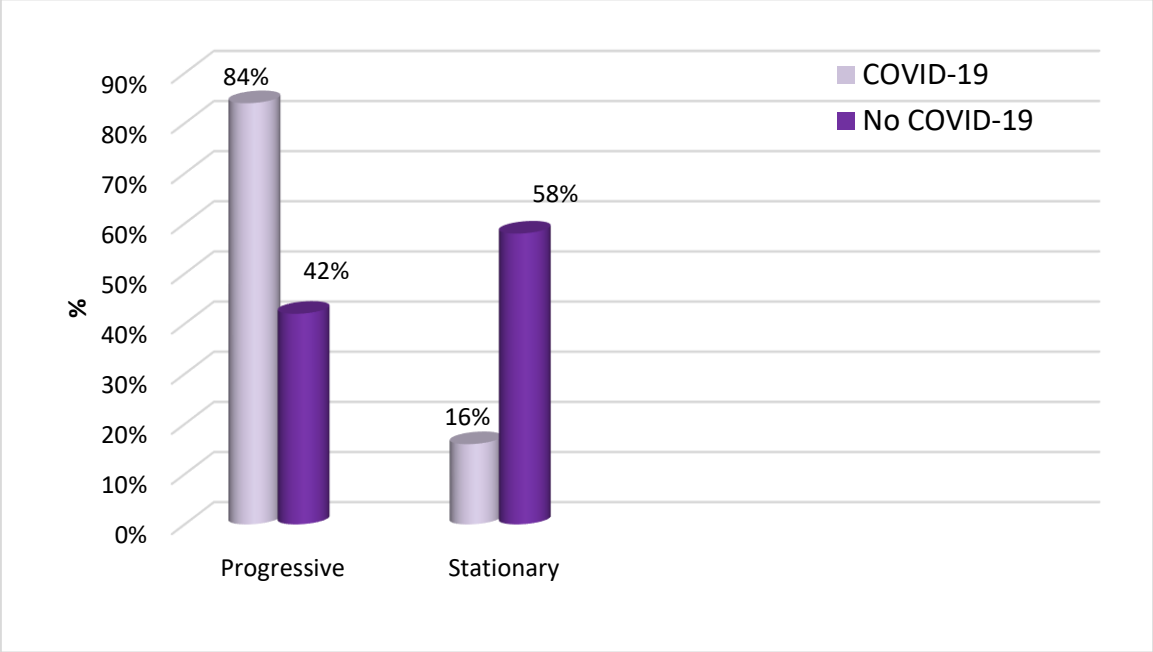

Figure (1): Bar chart displaying the relation of COVID-19 infection with HCC status on follow up

Table (1): The BCLC staging

BCLC staging	
Stage 0…..very early	Child Pugh score A; single nodule <2 cm; performance state 0–1.
Stage A… early	Child Pugh score A-B; 1 nodule or 2–3 nodules <3 cm; Performance state 0–1.
Stage B….intermediate	Child Pugh score A-B; multinodular; Performance state 0–1.
Stage C….advanced	Child Pugh score A-B; Portal vein thrombosis or extra hepatic spread or N I or M I; Performance state 0–2.
Stage D….terminal	Child Pugh score C, any T, N or M, PS >2.

N I stand for lymph node involvement, M I stands for metastasis, and T stands for tumor size.

Table (2): Child-Pugh score

	(1) point	(2) points	(3) points
Bilirubin (µmolL)	<35	35 – 50	>50
Albumin (gm/L)	>35	28 – 35	<28
INR	< 1.7	1.71 – 2.30	> 2.30
Ascites	None	Mild	severe
Encephalopathy	None	Mild	Severe
Scores:	**Class A**	**Class B**	**Class C**
	5–6 points	7–9 points	10–15 points
	100%; 1-year survival	80%: 1-year survival	45%: 1-year survival

Table (3): Age & gender of the studied groups

		HCC group infected with covid-19 N =50	**Non infected HCC group N = 50**
Age (years)	**Mean ± SD**	63.8 ± 7.9	59 ± 5.6
Sex	**Male** **Female**	29 (58 %) 21 (42 %)	26 (52%) 24 (48%)

Table (4): Tumor-related characteristics of the studied groups

		HCC group infected with covid-19 N =50	Non infected HCC group N= 50
Site of HCC	**Right lobe** **Left lobe**	43 (86 %) 7 (14 %)	32 (64%) 18 (36%)
Size of HCC (cm) in case of single lesion (n=88)	**Mean ± SD**	7.6 ± 4.5	5.6 ± 2.3
Total tumor size (cm) in case of multiple lesions (n=12)	**Mean ± SD**	10.2 ± 3.8	11.3 ± 2.1
Underlying liver disease	**HCV** **HBV** **Alcoholic** **NAFLD**	34 (68 %) 16 (32 %) No one No one	30 (60%) 20 (40%) No one No one
BCLC stage	**A** **B** **C** **D**	12 (24 %) 6 (12 %) 12 (24 %) 20 (40%)	28 (56 %) 8 (16 %) 9 (18 %) 5 (10%)

Table (5): Baseline laboratory characteristics of the studied groups

			HCC group infected with covid-19 N =50	Non infected HCC group N= 50
CBC	**Hb**	**Mean ± SD**	11.7 ± 2.1	12.7 ± 1.1
	WBCs	**Mean ± SD**	6.0 ± 2.6	4.0 ± 2.2
	PLts	**Mean± SD**	125.1 ± 63.6	145.1 ± 22.6
Liver functions	**Albumin**	**Mean± SD**	3.2 ± 0.9	3.23 ± 0.6
	Total bilirubin	**Mean± SD**	5.2 ± 7.3	2.2 ± 6.3
	Direct bilirubin	**Mean± SD**	3.3 ± 5.9	1.3 ± 0.9
	ALT	**Mean± SD**	49.5 ± 43.0	35 ± 2.3
	AST	**Mean± SD**	43.2 ± 24.6	37 ± 0.5
AFP		**Mean± SD**	4849.0± 17316.2	4549.0 ± 16216
Creatinine		**Mean± SD**	1.2 ± 0.3	1.1 ± 0.3
INR		**Mean± SD**	1.5 ± 0.5	1.3 ± 0.4

Table (6): COVID-19 severity in the HCC infected group (N=50)

COVID-19 severity (n=50)	**Mild** **Moderate** **Severe**	8 (16 %) 15 (30 %) 27 (54%)

Table (7): Follow up within six months

		HCC infected with COVID-19 (n=50)	HCC not infected with COVID-19 (n=50)	P value
Follow-up of HCC within 6 months	**Progressive in size** **Stationary**	42 (84 %) 8 (16 %)	21 (42 %) 29 (58 %)	**<0.001**
Follow-up of the patient status (by Child Pugh score) within 6 months	**Compensated** **Decompensated** **Died**	6 (12 %) 8 (16%) 36 (72%)	22 (44 %) 16 (32%) 12 (24 %)	**<0.001**

Most patients in the infected HCC group had severe Covid-19 infection, which suggests that HCC renders the patient vulnerable to more severe covid-19 stage. Guan et al. [13] reported that most patients had mild and moderate infection (42.85% & 33.33%), while 19% got severe infection. 50% of patients with infiltrative HCC had severe pneumonia. In the current study, 6 (12%) of the HCC infected group were alive and compensated, 8 (16%) were alive with decompensation, while 36 (72%) died. The decompensation and mortality rates are significantly higher (p value < 0.001) compared to the non-infected HCC group. A significant relationship was found between COVID-19 infection and BCLC stage of the HCC patients, the commonest stage in COVID-19 infected patients was stage D, 20 (40%) which may be explained by the poor general condition and altered immune response, while the commonest stage in COVID-19 non-infected patients was stage A, 28 (56%). On contrary, Geh et al. [14], revealed that there was no relation between COVID-19 infection and BCLC stage of HCC cases, the commonest stage in COVID-19 infected patients was stage C, 62 (52%), also the commonest stage in COVID-19 non-infected patients was stage C, 89 (47%). The rate of HCC progression was higher significantly among COVID-19 infected patients, 84% vs. 42% in the non-infected group (p value < 0.001). Additionally, a significant relationship seen between COVID19 infection and the fate of the HCC patients, the commonest fate in COVID-19 infected patients was death (72%), while the commonest fate in COVID-19 non-infected patients was stationary course with compensation (44%) (P value < 0.001). In view of the above results, our study may highlight that Covid-19 infection may influence the clinical course of HCC; additionally it shows that HCC renders the patients susceptible to more severe Covid-19 infection.

4. Conclusion

Infection by COVID-19 seems to have a significant effect on clinical course and outcome of HCC. In addition, HCC patients are more vulnerable to have more severe COVID-19 symptoms.

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