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. Carcinoma

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## ABSTRACT

**Objective:** To determine the outcome of COVID-19 among hepatocellular carcinoma patients at tertiary care hospital.

Study Design: descriptive case series study

**Place and Duration of Study:** This study was conducted at the Department of Medicine, Nishtar Hospital Multan from December, 2020 to December, 2021.

**Materials and Methods:** All patients of hepatocellular carcinoma diagnosed with COVID–19 of either sex aged more than 20 years were included in this study. Collected Data was entered into SPSS version 22 and was analyzed through its statistical package.

**Results:** A total of 62 patients with hepatocellular carcinoma presenting with COVID–19 were included, of which 69.4% (n = 43) were male while 30.6 % (n = 19) were female patients. Mean age of these patients was  $59.60 \pm 8.94$  years (range; 42–78 years). Mean duration of hospitalization in these patients was  $11.37 \pm 6.18$  days and 58.1 % (n = 36) were hospitalized for more than 1 week. Admission to intensive care unit (ICU) was noted in 25.8% (n = 16) of these patients. In–hospital mortality in HCC patients having COVID–19 was noted in 27.4 % (n = 17).

**Conclusion:** High frequency of in-hospital mortality was noted in hepatocellular carcinoma patients infected with COVID-19 in our study.

Key Words: Hepatocellular Carcinoma, mortality, COVID-19

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#### INTRODUCTION

The world is facing the challenges of pandemic COVID-19 which not only affect the healthcare system but almost every field by disturbing planning and creating psycho-socio-economic crises globally. Pakistan is also affected by this infectious viral disease and facing the multiple crises especially morbidity and mortality by Coronavirus Disease 2019. Current outbreak of SARS-CoV-2 noval Coronavirus (2019nCoV) was first reported from a local seafood market in Wuhan, a city of China, on 31st December 2019. Later, it was named as Corona Virus Disease - 2019 (COVID-19) by World Health Organization on 11th February 2020. This epidemic of COVD-19 become a global issue and declared as pandemic by WHO.

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The morbidity and mortality rates varying from 1 % to as high as 11 % from  $Italy^{1-3}$ .

The initial group of researchers in Wuhan, China, reported following clinical features of COVID–19, Symptoms at onset: fever, fatigue & myalgia, dry cough, sputum production, headache, haemoptysis, diarrhea. Subsequent symptoms: dyspnoea<sup>4</sup>. A study published in The Lancet, revealed person to person transmission in a familial cluster of pneumonia associated with the 2019 novel coronavirus<sup>5</sup>. COVID–19 with average incubation period of 5.2 days has very transmissibility rate of 4.02, indicating that each patient will infect approximately 4 persons. Human to human transmission of the virus has been reported through respiratory droplets, body secretions and aerosols transmission has also been documented<sup>6-8</sup>.

Mortality rates are being reported from different countries which indicate higher proportions of deaths in patients with underlying illnesses such as diabetes, hypertension, coronary heart disease, chronic obstructive pulmonary disease (COPD), asthma, chronic lung injury, advanced age, gender and cancers<sup>9-11</sup>. COVID-19 has been proven to be highly contagious and soon after its initial outbreak, number of patients and rate of mortality surpassed the numbers of SARS outbreak in 2003. Different reports have shown that patients having various comorbidities such as hypertension, followed by diabetes and coronary heart

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disease and regression analysis revealed increasing odds of in-hospital mortalities being related with increasing age, Sequential Organ Failure Assessment (SOFA), increased blood d-Dimer levels >1 µg/mL are risk factors for poor prognosis and in-hospital mortality in patients with COVID-19<sup>12</sup>. Cancer patients have been declared as high risk group under the circumstances of ongoing COVID–19 pandemic as these patients are usually highly susceptible to various types of infections as a results of their immunodeficient condition as a result of underlying malignant condition and also due to use of anti–cancer treatment modalities that may include systemic therapy and radiotherapy.

Results of this study will help researchers and healthcare policy makers to formulate guidelines regarding specific clinical course and medication to control this pandemic by reducing mortality rate to cope with this deadly disease. It will also contribute in scientific and research fields for the awareness, outcome prediction and impact assessment of interventions, plan of action for preventive measures and effective treatment. The results of this proposed study will also highlight importance of clinical course, medication, its effectiveness and control which will ultimately lead to lower burden of morbidities, decreased mortalities and less healthcare expenditures. This will not only relieve extra pressure from healthcare authorities but will also improve quality of life targeted population, relive psychosocial stress, enhance their physical activity and productivity .

#### MATERIALS AND METHODS

This descriptive case series study was done T Department of Medicine, Nishtar Hospital, Multan, from 06–December–2020 to 05–December–2021 using non–probability purposive sampling technique. All patients of hepatocellular carcinoma (n=62) diagnosed with COVID–19 of either sex aged more than 20 years were included in this study. Sample size was 62 HCC patients with, sample size has been calculated using P 1 = 20 %<sup>12</sup> at 95 % CI, d = 10 % and 80 % power of test (5% margin of error) using Epi–info software of CDC.

Patients having chronic Kidney disease, liver transplantation, malignancies, COPD and those who were not willing to be included were excluded from our study.

After approval from the ethical review committee, 62 HCC patients with COVID-19 patients fulfilling the inclusion criteria was selected from COVID– wards of Nishtar Hospital Multan. After taking informed written consent after describing them objectives of this study, ensuring them confidentiality of the information given to us in this study and fact that there will not be any risk involved to the patient while taking part in this study. These COVID patients was taken and followed till discharge to ascertain outcome (mortality which was confirmed by a straight line on ECG, absence of pulse and blood pressure) of COVID–19 and all information was recorded in the proforma.

Collected data was entered into SPSS version 22 and was analyzed through its statistical package. Descriptive statistics was used to analyze the data. Mean  $\pm$ S.D was calculated for age of the patients, duration of stay and BMI. Frequencies and percentages were calculated for qualitative variables like gender, diabetes, hypertension, IHD, age groups, obesity, mortality and residential status. Effect modifiers like age, diabetes, hypertension, IHD, gender, obesity, duration of stay and level of education were controlled by stratification and their effect on outcome was seen applying Chi square test taken  $p \leq 0.05$  as significant.

#### RESULTS

A total of 62 patients with hepatocellular carcinoma presenting with COVID–19 were included, of which 69.4% (n=43) were male while 30.6% (n=19) were female patients.

Table No.1: Stratification	of outcome	with regards
to study variables		

Study	Mortality					
Variables	Yes	No	P value			
Gender						
Male (n=43)	08	35	0.020			
Female (n=19)	09	10	0.030			
Age groups						
Up to 50 Years (n=35)	10	25	- 0.998			
> 50 Years (n=27)	07	20				
	Residential	status	•			
Rural (n=21)	08	13	0.222			
Urban (n=41)	09	32	0.232			
	Hospital	stay	•			
Up to 7 days (n=26)	03	23	0.022			
> 7 days (n=36)	14	22				
• • •	Diabet	es	•			
Yes (n=25)	15	10	0.001			
No (n=37)	02	35	0.001			
Hypertension						
Yes (n=38)	14	24	0.044			
No (n=24)	03	21	0.044			
Obesity						
Yes (n=19)	06	13	0.759			
No (n=43)	11	32				
	ICU admi	ssion				
Yes (n=38)	12	04	0.001			
No (n=24)	05	41	0.001			
Se	ocioeconom	ic status	-			
Poor (n=20)	06	14				
Middle Income (n=42)	11	31	0.768			

Mean age of these patients was 59.60±8.94 years (range; 42-78 years). Mean age of male patients was 57.88±9.14 years while 63.47±7.26 years for females and 56.5% (n=35) were aged up to 60 years. Sixty six percent (n=41) were from rural areas and 67.7% (n=42) had middle income family background. History of diabetes was noted in 40.3% (n=25), hypertension in 61.3 % (n=38) and 30.6% (n=19) were obese (Mean Mean BMI=26.31±1.86  $kg/m^2$ ). duration of hospitalization in these patients was 11.37±6.18 days and 58.1% (n=36) were hospitalized for more than 1 week. Admission to intensive care unit (ICU) was noted in 25.8% (n=16) of these patients. In-hospital mortality in HCC patients having COVID-19 was noted in 27.4% (n=17), while impact of confounders on mortality has been shown in Table 1.

## DISCUSSION

COVID–19 related healthcare limitation confronted with treatment modalities for the patients having various chronic illnesses and cancers; particularly among patients having hepatocellular carcinoma. Hepatocellular remains one of the commonest causes of the cancer related mortalities in Pakistan and other parts of the world <sup>13, 14</sup>. Cancer patients have been declared as high risk group under the circumstances of ongoing COVID–19 pandemic as these patients are usually highly susceptible to various types of infections as a results of their immunodeficient condition as a result of underlying malignant condition and also due to use of anti–cancer treatment modalities that may include systemic therapy and radiotherapy <sup>15, 16</sup>.

A total of 62 patients with hepatocellular carcinoma presenting with COVID-19 were included, of which 69.4% (n=43) were male while 30.6% (n=19) were female patients. Amaddeo et al<sup>12</sup> from France has also reported 83.6% male patients with hepatocellular carcinoma having COVID-19, similar to our results. Pomej et al<sup>17</sup> from Austria has also reported 83 % male patients with hepatocellular having COVID-19, similar to our findings. Guler-Margaritis et al<sup>18</sup> from Romania has also reported 63% male gender preponderance in HCC patients infected with COVID-19, same as our findings. Ribaldone et al<sup>19</sup> from Italy has also reported 80.6% male gender predominance in HCC patients infected with COVID-19, similar to our results. Zhang et al<sup>20</sup> from China has also reported 60.7% male patients with malignancy predominating HCC infected with COVID-19, similar to that of our study results.

Mean age of these patients was  $59.60\pm8.94$  years (range; 42 - 78 years). Mean age of male patients was  $57.88\pm9.14$  years while  $63.47\pm7.26$  years for females and 56.5% (n = 35) were aged up to 60 years. Amaddeo et al<sup>12</sup> from France has also reported 67 years mean age among patients with hepatocellular carcinoma having COVID–19, similar to our results. Pomej et al<sup>17</sup> from Austria has also reported  $66\pm11$  years mean age of the

patients with hepatocellular having COVID–19, similar to our findings. Guler-Margaritis et al<sup>18</sup> from Romania has also reported 53.83±17.45 years mean age in HCC patients infected with COVID–19, same as our findings. Ribaldone et al<sup>19</sup> from Italy has also reported 64.0 years mean age in HCC patients infected with COVID–19, similar to our results. Zhang et al<sup>20</sup> from China has also reported 65 years mean age among patients with malignancy predominating HCC infected with COVID–19, similar to that of our study results

Sixty six percent (n=41) were from rural areas and 67.7% (n=42) had middle income family background. History of diabetes was noted in 40.3% (n=25), hypertension in 61.3% (n=38) and 30.6% (n=19) were obese (Mean BMI=26.31 $\pm$ 1.86 kg/m<sup>2</sup>). Pomej et al<sup>17</sup> from Austria has also reported 37% diabetes and 57% hypertension among patients with hepatocellular having COVID–19, similar to our findings. Ribaldone et al<sup>19</sup> from Italy has also reported mean BMI was 26.1 kg/m<sup>2</sup> in HCC patients infected with COVID–19, similar to our results. Zhang et al<sup>20</sup> from China has reported 15% diabetes with malignancy predominating HCC infected with COVID–19 which is lower than our study results.

Mean duration of hospitalization in these patients was  $11.37\pm6.18$  days and 58.1% (n=36) were hospitalized for more than 1 week. Admission to intensive care unit (ICU) was noted in 25.8% (n=16) of these patients. Amaddeo et al<sup>12</sup> from France has also reported similar results. Zhang et al<sup>20</sup> from China has also reported 21.4% ICU admission rate in patients with malignancy predominating HCC infected with COVID–19, similar to that of our study results.

In-hospital mortality in HCC patients having COVID-19 was noted in 27.4% (n=17). Amaddeo et al<sup>12</sup> from France has also reported 19.1% mortality rate in hepatocellular carcinoma having COVID-19, similar to our results.

# CONCLUSION

High frequency of in-hospital mortality was noted in hepatocellular carcinoma patients infected with COVID-19 in our study. In-hospital mortality was associated with female gender, prolonged duration of hospitalization, ICU admission, diabetes and hypertension. Hepatocellular carcinoma patients should be aggressively managed followed by diagnosis to improve their prognosis as these patients are more prone to adverse events of COVID-19.

#### **Author's Contribution:**

Concept & Design of Study:	Ali Raza
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Data Analysis:	Muhammad Ali Wadhak,
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**Conflict of Interest:** The study has no conflict of interest to declare by any author.

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