

## Demographic Profile and Etiology of Hepatocellular Carcinoma in Zaria, Northern Nigeria

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### Abstract

**Background:** HCC is a common cancer worldwide and one of the leading causes of cancer death. This aim of this study is to determine the age and gender characteristics of the HCC patients in our center and to determine the contribution of viral hepatitis (B and C) and alcohol to the etiology of HCC among our patients.

**Methodology:** This is a retrospective study of HCC patients seen at the gastroenterology unit of ABUTH between April 2015 and September 2018. Data on age, gender, HBsAg, and HCV antibody status and alcohol consumption were recorded from the case files of all eligible patients.

**Results:** A total of 87 patients were included in the study. They consisted of 68 males (78.2%) and 19 females (21.8%) with male to female ratio of 4:1. The mean age of the study subjects was 46.7 years (SD ± 12.5), with a range of 22 and maximum age of 80 years. Majority of the patients were within the age group 40-49 (32.2%). HBsAg was present in 48 patients (55.2%), HCV antibody was positive in 14 patients (16.1%) and 3 patients (3.4%) were positive for both HBsAg and HCV antibody. Four (4.6%) had significant alcohol ingestion and in 18 patients (20.7%), the etiology was undetermined.

**Conclusion:** In our study, HCC was found predominantly among male patients in the age group 40-49 years. Viral hepatitis particularly HBV is the most important etiological factor for HCC among our patients.

**Keywords:** Age; Sex; Hepatitis B and C; Alcohol; Primary Liver Cell Carcinoma.

### Introduction

Primary liver cell carcinoma (PLCC) is a disease of public health concern with increasing incidence globally.<sup>[1]</sup> The most common form of PLCC is hepatocellular carcinoma (HCC) and the terms are commonly used interchangeably.<sup>[2]</sup> In 2020, PLCC was estimated to be 7<sup>th</sup> most commonly diagnosed cancer world-wide and the 3<sup>rd</sup> most common cause of cancer mortality.<sup>[1]</sup> Incidence of liver cancer varies around the world and traditionally more common in developing countries. It is estimated to be the 4<sup>th</sup> leading cancer in Africa and ranks highest among men in several West African countries.<sup>[1]</sup>

Hepatocellular carcinoma (HCC) is the 2<sup>nd</sup> commonest cause of cancer death among men, and 3<sup>rd</sup> among women in Africa.<sup>[5]</sup> The high rate of liver cancer in these countries reflects the prevalent causative factors of this carcinoma in these countries particularly chronic hepatitis B infection. In Nigeria, there is paucity of data on the incidence PLCC. According to WHO in 2018, it was

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estimated that 5,129 new cases with similar number of deaths will be recorded that year in Nigeria.<sup>[6]</sup> Fakunle et al reported more than 4 decades ago that Zaria has one of the highest burden of PLCC in the world.<sup>[7]</sup> Whether this is still the case is difficult to say as there is no recent report on PLCC from Zaria. Liver cancer is more common among males with male to female ratio of up to 4:1.<sup>[8,9]</sup> The age at which patient present varies across regions of the world. In Europe the median age of presentation is 65years while in sub-Saharan Africa, it is 45years.<sup>[5]</sup> This variation in age at presentation reflects the predominant risk factors for HCC across different regions of the world. In several parts of Africa and Asia where HBV is the predominant risk factor, the age at presentation is much lower compared to the developed countries where HCV and more recently NAFLD are the predominant risk factors for HCC.<sup>[10-12]</sup> Hepatocellular carcinoma(HCC) is the most common form of PLCC accounting for 70% to 85% of PLCC.<sup>[13]</sup> Most HCC occur on a background of liver cirrhosis.<sup>[13-15]</sup> Hepatitis B and C viruses are the most common risk factors for HCC with the most significant being HBV.<sup>[16-18]</sup> Cirrhosis from these viruses carries higher risk of HCC compared to other causes of cirrhosis.<sup>[13,19]</sup> Other etiological factors of HCC include alcohol, Non-Alcoholic Fatty Liver Disease(NAFLD), aflatoxin B1, and iron overload.<sup>[8,20-22]</sup> NAFLD is particularly important in that it is now assuming the most common cause of liver disease worldwide and has been associated with HCC even without cirrhosis.<sup>[24]</sup> Additionally, HCC hitherto classified as idiopathic in significant number of cases can be associated with NAFLD.<sup>[21]</sup>

This article sought to examine the demographic profile namely the age and gender distribution of HCC patients in our Centre, and then determine the contribution of viral hepatitis B and C and alcohol to the etiology of HCC among our patients.

### Methodology

This is a retrospective study of all adult patients seen at the gastroenterology unit of Ahmadu Bello University Teaching Hospital between April 2015 and September 2018 with diagnoses of HCC.

Data on age, sex, and presence or absence of HBsAg, HCV antibody and significant alcohol

consumption were recorded from the case file of all eligible patients. Alcohol consumption of at least 60g/day in males and 20g/day in female patients for at least 10 years is considered significant. Eligible patients are those with the clinical diagnosis of HCC and have at least one of the following: 1-imaging (ultrasound/CT scan) findings of HCC and 2-histologic features of HCC.

Data was analyzed using statistical software IBM SPSS Version 23. Results from categorical data were expressed as frequencies and percentages, while quantitative data were expressed as mean and standard deviation and presented as tables.

## Results

### Demographic characteristics

A total of 87 patients were eligible and included in the study. They consisted of 68 males (78.2%) and 19 females (21.8%) with male to female ratio of 4:1. The mean age of the study subjects was 46.7 years (SD  $\pm$  12.5), ranging from a minimum age of 22 to a maximum age of 80. Majority of the patients were within the age group 40-49 years (32.2%) with only 4 patients aged 70 and above. (Table 1)

### Etiology of HCC

HBsAg only was present in 48 patients (55.2%), HCV antibody was positive in 14 patients (16.1%) and 3 patients (3.4%) were positive for both HBsAg and HCV antibody. Four (4.6%) had significant alcohol ingestion and 18 patients (20.7%) had none of these three etiological factors. (Table 2).

**Table 1:** Age and gender distribution of patients

AGE GROUP	GENDER		TOTAL(n)
	MALE (n)	FEMALE (n)	
20-29	4	1	5
30-39	16	3	19
40-49	23	5	28
50-59	12	6	18
60-69	11	2	13
>70	2	2	4
TOTAL	68	19	87

**Table 2:** Etiological factors of HCC

	FREQUENCY	PERCENTAGE
HBV	48	55.2
HCV	14	16.1
HBV+HCV	3	3.4
ALCOHOL	4	4.6
UNDETERMINED	18	20.7
<b>TOTAL</b>	<b>87</b>	<b>100.0</b>

## Discussion

HCC is a common malignancy and one of the leading causes of cancer mortality worldwide. Majority of our patients are males with a male to female ratio of 4:1. This is consistent with other findings in Nigeria and other countries.<sup>[25-27]</sup> Most of our patients fall within the age group of 40-49 years with the mean age of presentation being 46.7±12.5 similar to findings by others in Nigeria.<sup>[25,26,28]</sup> Prevalence peaked at age 40-49 years and decreases with advancing age among our patients. Kew et al reported decreasing incidence with increasing age among rural black population with HCC, however, incidence generally increases with increasing age.<sup>[26,29]</sup>

HBV is the single most important risk factor for HCC.<sup>[30]</sup> It is hyperendemic in most parts of Africa and in Nigeria pooled prevalence was 9.5% in a systematic review and metanalysis by Ajuwon et al.<sup>[32]</sup> In our study, 55.2% of the patients were positive for HBsAg. This frequency of HBsAg seropositivity among our patients is in agreement with findings by Nwokediuko et al in Enugu and Mustapha et al in Gombe.<sup>[28,33]</sup> Similar finding was also reported by Chin'ombe et al in Zimbabwe and Umoh et al in The Gambia.<sup>[35]</sup> This finding indicate that HBV is the most important risk factor for HCC in our patients. HCV antibody on the other hand was found in 16.1% of our patient. This is similar to findings by other authors in Nigeria and The Gambia.<sup>[25,28,35-37]</sup> Both HBV and HCV constituted about 75% of the risk factors for HCC among our patients which is in consonance with the report of 75-80% of HCC worldwide are attributable to chronic HBV and HCV infections.<sup>[16,35,38]</sup> Co-infection with these viruses was not common among our patients and found in only 3.4% of the patients similar to finding by Krik et al in The Gambia and Ayoola et al in Saudi Arabia.<sup>[37,39]</sup> However, dual infection confers increased risk of HCC development on the patients.<sup>[37]</sup> The contribution of alcohol to the etiology of HCC among our patient is substantially less as significant alcohol ingestion was found in only 4.6% of the patients. This is consistent with the fact that alcohol play a minor role in the etiology of HCC compared to viral hepatitis particularly in intermediate and high incidence areas such as ours.<sup>[27,40,41]</sup>

Significant number of our patients (20.7%) don't have evidence of viral hepatitis B and C or history of significant alcohol ingestion. Other etiological factors of HCC may be responsible in these category of patients. Though exposure to aflatoxin was not tested for among our patients, it is possible that these patients with undetermined risk factors have aflatoxin as their major risk. Aflatoxin exposure is an important risk factor for HCC in regions of the world where HBV is endemic such as sub-Saharan Africa.<sup>[29,42]</sup> Aflatoxin is a hepatocarcinogen found in many staple food products in parts of the world such as sub-Saharan Africa where poor food storage practice, high humidity and temperature allows the growth of the fungus *Aspergillus* spp.<sup>[43-46]</sup> NAFLD has become the most common cause of liver disease worldwide and is associated with obesity and metabolic syndrome.<sup>[47-50]</sup> And because of our increasing rate of adoption of western lifestyle, it is expected that NAFLD will also increase among our populace with the attendant consequences such as cirrhosis and HCC. Therefore, NAFLD may be a contributing factor to etiology of HCC among our patients. Further studies are needed to elucidate the actual contributions of these other factors to the etiology of HCC among patients.

In conclusion, PLCC among our patients commonly affect male patients in the age group 40-49 years. Viral hepatitis particularly HBV is the most important etiological factor and together with alcohol accounted for about 80% of the causes of PLCC among our patients.

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