

## THE PRACTICE OF HEPATOCELLULAR CANCER SURVEILLANCE IN NIGERIA

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### ABSTRACT

#### Background

Hepatocellular cancer is a disease of global and public health importance due to the widespread distribution of risk factors and associated high case fatality. Hepatocellular Cancer (HCC) in Sub-Saharan Africa is commonly seen among the younger age groups (<45 years) who present mostly in the terminal stage, when the disease is not amenable to any curative therapy.

Hepatocellular Carcinoma surveillance employs the use of simple, cheap and readily available investigations, to detect early curable cancer in individuals with risk factors for HCC.

#### Objectives

The aim of this study is to assess the practice of hepatocellular cancer screening among physicians.

#### Methodology

This is a nationwide online survey carried out among physicians who care for patients with HCC. A questionnaire was sent out via a web link to all consenting doctors in Nigeria. The responses were collated in a cloud-based application and data was analysed using Epi-info version 20.

#### Results

A total of 218 respondents, 142 were males (65.1 %) with a mean age of  $37.6 \pm 5.7$  years. The modal age group was 31–40 years 153 (69.5%). The main factors considered as a hindrance to surveillance were; the cost of the tests (57.7%), failure of return of patients (50.5%) and not being aware of a surveillance program (45.2 %). The majority of the respondents were Gastroenterologists and Family Physicians. 54% of the gastroenterologists and 64% of the family physicians have never offered HCC surveillance to their patients.

#### Conclusion

This survey highlights a knowledge gap in HCC surveillance among physicians. There is a need to make HCC surveillance a daily routine among patients at risk by all physicians.

**Keywords:** Surveillance, Hepatocellular Carcinoma, HBV, HCV, Cancer screening.

**Introduction**

Hepatocellular carcinoma (HCC) is a disease of public health significance. It is the fifth most common cancer and the second cause of cancer related death globally.(1)Fortunately, the most common causes of HCC are preventable. According to the GLOBOCAN in 2018, there were 781,631 deaths globally and Nigeria accounted for 68,716 deaths from HCC (2). HCC is an aggressive tumor with high mortality which is further confounded by late presentation when it is not curable. Conversely, earlier stages of HCC are mostly asymptomatic making early detection of the tumor difficult.

Sub-Saharan Africa and East Asia (especially China) together account for about 85% of all cases of HCC where hepatitis B, C are hyper-endemic.(1) In these regions, the incidence to mortality ratio is one.(3) Some of the identified reasons may be linked to myriad of factors that are considered to cause HCC such as high prevalence of hepatitis B which is 13.6% in Nigeria,(4) inadequate screening and appropriate treatment for viral hepatitis, poor utilization of screening protocol among patients at risk of HCC, limited resources for treating early HCC when detected. Moreover, the average survival from HCC in most sub-Saharan African countries is 2.5 months while in Nigeria it is 4 months. (5,6)

HCC surveillance offers the benefit of early detection of tumors and increases survival outcome in patients at risk.(7) It has been established to improve early tumor detection (odds ratio [OR] 2.08, 95% CI), curative treatment (OR 2.24, 95% CI) and survival (OR 1.90, 95% CI) (8). However, in Nigeria despite high endemicity of hepatitis B, C, and liver cirrhosis, HCC surveillance is not a common practice.(3) Globally, the uptake of surveillance is only about 20% even though in real life practice its importance cannot be

overemphasized.(9) In this study, we set out to identify the factors that affect the implementation of HCC surveillance in Nigeria.

**Objective**

The aim of this study is to assess the practice of HCC screening among Nigerian physicians.

**Methodology**

This was a nationwide online survey carried out among physicians who care for patients with viral hepatitis, liver cirrhosis, and HCC. Respondents were physicians who are practicing in any of the six geopolitical zones of the country.

A questionnaire was designed on the survey monkey website. It consisted of 23 questions. This included the demographics of the respondents, setting of clinical practice, monthly average of viral hepatitis and HCC patients, and practice of HCC surveillance. A web link was subsequently generated and shared by investigators via online medium. Respondents were introduced to the purpose of the survey before proceeding to the survey proper.

Responses were collated in the cloud-based application and data was analyzed using Epi-info version 20 and Survey Monkey analyze data tool.

**Results**

Among the 218 respondents, 142 were males (65.1 %) with a mean age of 37.6 ± 5.7 years. The modal age group was 31-40 years 153 (69.5%), while 41-50, below 30 years and over 50 years constituted 17.75%, 9.1%, and 3.2% respectively.

Respondents were from all 6 geopolitical zones of Nigeria with modal distribution from North central 24.1 %. The distribution pattern is depicted in table 1 below:

**Table 1: Distribution of respondents by geopolitical zones.**

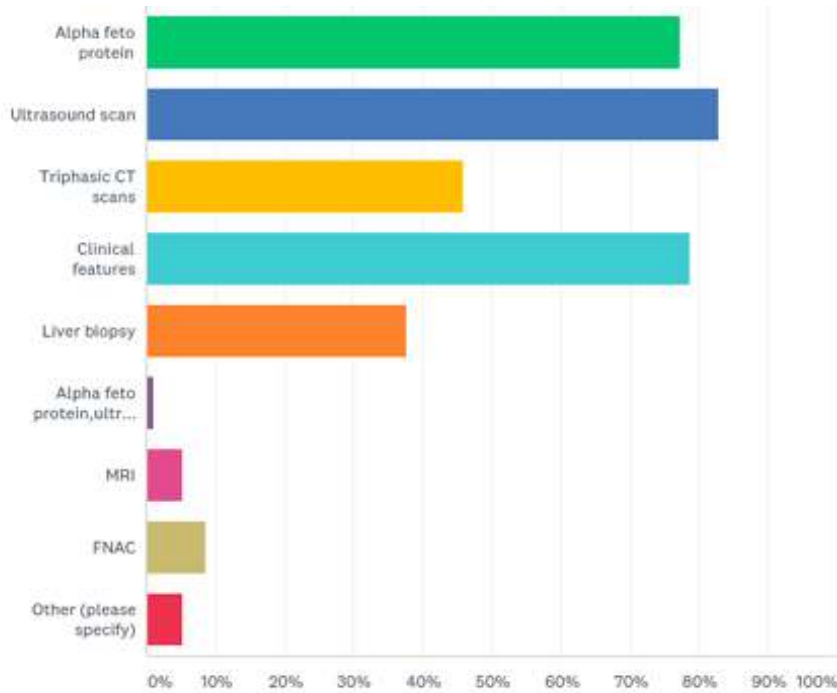
ANSWER CHOICES	RESPONSES	
North West	18.06%	39
North East	6.48%	14
North Central	24.07%	52
South South	23.15%	50
South East	11.11%	24
South West	17.13%	37
Total Respondents: 216		

Out of the 160 respondents (74.1%) who routinely manage hepatitis B patients only 28.7% were Gastroenterologists and trainee Gastroenterologists (GI specialists), while 15.6% were Family Physicians and trainee Family Physicians (Family Medicine specialists), and the rest cut across other specialties. Similarly, 144 respondents manage hepatitis C (66.7%) among which GI specialists accounted for 29.2%; Family Medicine specialists 15.3%; others specialties were 55.5%.

Over 50% and 78% of respondents that manage

hepatitis B and C have less than 10 a month respectively. Over 73% of respondents see on average less than 10 HCC patients a month while over 21% have 10-20 patients, 3.37% have between 20-30 with only 2(0.93 %) having more than 50 HCC per month.

Predominant diagnostic methods employed by respondents for HCC were ultrasound (82.86%), clinical (78.57%), other methods are shown in Figure 1.



**Figure 1. Methods of diagnosis of HCC among survey participants.**

Most of the respondents see their HCC patients in advanced stage as shown in table 2 below:

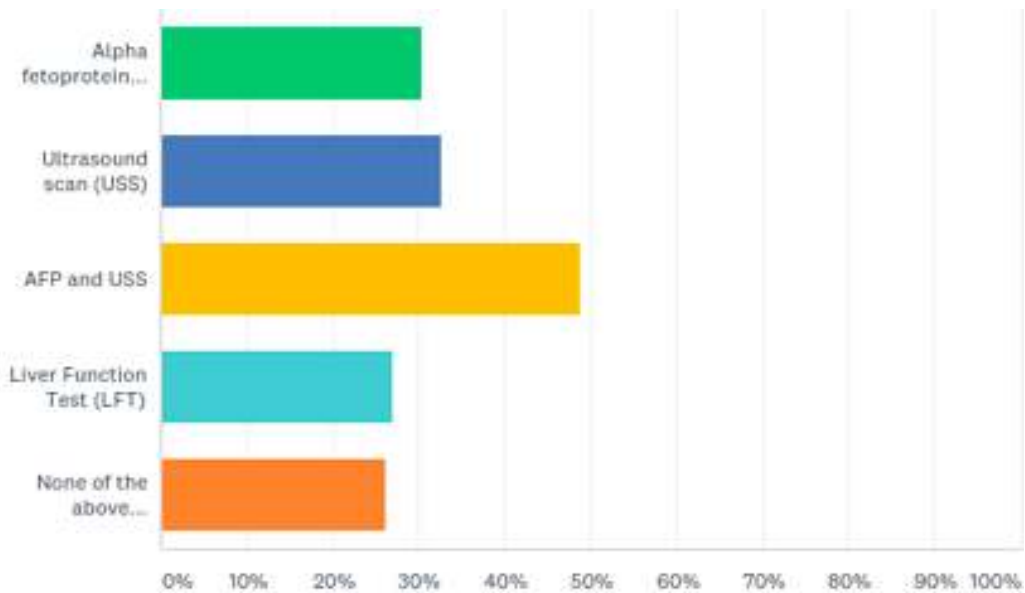
**Table 2. Distribution of BCLC STAGE at presentation of HCC patients**

BCLC stage	Percentage	Frequency
0	2.35	5
A	4.69	10
B	12.68	27
C	30.99	66
D	27.23	50
I DON'T KNOW	59.62	127
TOTAL		213

Over 51% of 213 respondents do not know about HCC surveillance including GI specialists 25.2%, and Family Medicine specialist 13.6%. Similarly, 69.59% of respondents do not know about Nigerian guidelines for HCC surveillance. Only 24.65% of respondents offer routine surveillance to their patients, however, over 44% of respondents never offer such services among which majority see fewer cases per month. 22.6% of Gastroenterology specialist offer surveillance always while 33.3%

said to have never offered it. On the other hand, 11.3% of family medicine specialist offer surveillance always and 17.7% of them said to have never offered it.

Most respondents prefer abdominal ultrasound scan (USS) and serum alpha fetoprotein (AFP) as the preferred surveillance modality for all participants as shown in figure 2 below:



**Fig.2 Surveillance method used by study participants**

Majority of the respondents agree that surveillance should be offered to all cirrhotics (93.4%) and that the Society for Gastroenterology and Hepatology in Nigeria (SOGHIN) should enforce a surveillance program for HCC among patients at risk (79.3%).

The predominant obstacle for HCC surveillance among respondents was non-awareness of such program. Similarly, cost and noncompliant patients also play a significant role. Other factors are shown in table 3 below:

**Table 3. Factors affecting HCC surveillance implementation.**

Answer choices	Responses %	Number
No time	8.65	18
Busy schedule	28.85	60
Don't trust results	12.98	27
Never detected early tumors	9.31	19
Not aware of surveillance program	45.19	94
No structured program	42.31	88
Cost of test	57.69	120
Failure of patients return	50.48	105
Unsure of cirrhotic state	9.13	19
Surveillance doesn't help	0.96	2
Others	4.81	10
Total		208

About 50% of respondents use the recommended screening modality for HCC which are USS and AFP 6 monthly. Although (32.7%) use only USS which is also recommended by the AASLD

	Don't trust results	Surveillance does not help	Unsure of cirrhotic status	Failure of return of patients	Cost of test	No structured program	No time	Not aware of surveillance	Busy schedule	Never detected a tumor in the past
Gastroenterologist	30.2	28.6	29.0	30.7	28.3	34.4	28.9	27.2	28.9	29.0
Family Medicine	16.1	15.7	16.5	16.7	18.2	13.0	15.9	13.6	17.1	18.0
General Practice	9.4	10.6	10.0	6.1	9.1	6.9	10.4	8.8	9.4	9.5
Internal Medicine	26.4	26.7	26.0	26.3	25.3	25.2	27.4	28.0	27.7	26.5
Paediatrics	2.6	2.3	2.5	3.5	3.0	1.5	2.5	4.0	1.9	2.5
Other specialties	15.1	15.7	15.5	16.7	16.2	19.1	14.4	17.6	14.5	14.0

**Table 4: Factors affecting HCC surveillance by specialty (%)**

**Discussion**

This nationwide survey involved mainly physicians at their youthful age and has clearly demonstrated the inadequacy of HCC surveillance program in Nigeria with less than a quarter of respondents offering recommended surveillance. This is similar to findings in other studies.(10) Considering lack of awareness as one of the major factors preventing HCC surveillance practice, there is a need for creating awareness among physicians about it and various modalities available. It is evident that the management of chronic viral hepatitis, liver cirrhosis, and HCC is not limited only to Gastroenterologists, but rather it cuts across various specialties, hence there is need for regular step down training and retraining of all physicians on the current local and universal protocol for managing these diseases, and capacity building on HCC screening methods across all centers because patients who were offered surveillance live longer, have better survival and better opportunities of receiving curative therapies.(11) To this end, there is a need for a structured screening program for HCC nationwide, this we suggest should be championed by SOGHIN as seen in cases of EASL, AASLD and APASL.(12–14)

Ultrasonography and AFP were considered to be the preferred HCC surveillance tools in this survey. Both are not sensitive or specific for this purpose.(15) European Association for the Study of Liver 2018 HCC guideline strongly recommends surveillance to be performed by experienced personnel in all high-risk populations using abdominal USS every six months.(12) A study done in the Middle East concluded that AFP has very poor screening and diagnostic value.(16) The EASL, AASLD and APASL guidelines currently do not recommend the use of AFP as a diagnostic tool in HCC.(12–14,17). But the AASLD recommends both Triphasic CT scan and Liver biopsy as a preferred diagnostic tool for HCC.(18,19) The main factors considered to hindering the practice of HCC surveillance were cost and failure of patients to return for follow-ups. The average cost of USS across the country is 3000 Naira (10 US dollars) while AFP is 5000 Naira (18 US dollars ) this may seem small, but when you consider the over 80% of the population of Nigeria pays for healthcare out of pocket and the percentage living on less than 2 dollars a day (20,21), it will immediately be clear that the second reason which is the failure of patients to return may not be unrelated to funds and indirectly, cost of the test.

Studies elsewhere have also identified cost as a limiting factor to the uptake of surveillance for HCC.(11) But further analysis has demonstrated that HCC screening is, in the long run, more cost effective. Implementation of HCC surveillance has been demonstrated to aid detection of early tumor. (7–9)From the survey, over half of the participants see patients who present with the advanced disease (BCLC C or D) both of which are not amenable to early cure treatment options. This further buttresses the need for a structured program to tackle the menace of HCC.(22,23)(JULES LEVIN AASLD 2018).34% of Gastroenterologists consider the lack of a structured screening to be responsible for the poor implementation of an HCC surveillance program.

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