The Pathological Features of Primary Liver Cell Carcinomas in Nigerians: A Preliminary Study of Sixty- one Consecutive Cases from Ile-Ife, Nigeria

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Abstract

Aim: *To describe the pathological features of primary liver cell cancer as seen in a tertiary health care facility in Nigeria and compare these features with those recorded in other settings.*

Methods*: This is a retrospective study in which liver surgical biopsies and open biopsies specimens recorded over an 18 years' period were analysed with respect to age, sex and pathological features. Statistical analysis was performed using simple statistical methods.*

Results: *Sixty- one cases consisting 51 specimens obtained from needle biopsy, 5 open biopsies and 5 autopsy biopsies were analysed. There was a marked male preponderance with a male to female ratio of 2.1 : 1. The peak age of occurrence was the 6th decade of life (mean age was 32.8%) . The most common mode of presentation by these patients was abdominal swelling and most of the patients presented late. Hepatocellular carcinoma was the most common primary liver carcinoma and its shows strong association with hepatitis B virus but weak association with liver cirrhosis. Cholangiocarcinoma was the second most common and mostly seen in the females in this study. Majority of the tumours in this series were moderately differentiated.*

Conclusion: *This report show that the pathological features demonstrate certainm fundamental differences between primary liver cell carcinoma in Nigerian patients and those in other parts of the world.*

Keywords: Primary liver cell carcinoma, pathological features, Nigeria

Introduction

Primary liver cell carcinomas (PLCC) arise from the hepatocytes, intra-hepatic bile duct, endothelial cells and blood vessels. Primary liver cell carcinoma (PLCC) is one of the more common internal malignancies worldwide and is responsible for over 1 million deaths annually[1] Hepatocellular carcinoma (HCC) is a primary malignant tumour of the hepatocytes and does by far the commonest primary liver cell cancer, constituting more than 80% of primary liver cancers [2]. Hepatocellular

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carcinoma is second only to carcinoma of the pancreas in being the most lethal form of human cancer[3]. Aetiologically, high incidence PLCC differs fundamentally from the low-incidence type being strongly associated with the hepatitis B virus, and aflatoxin B1 to a lesser extent[4]. The clinical features of the high-incidence disease are equally as distinctive as the anecdotal reports would tend to suggest for its pathological features[5]

HCC is usually used interchangeably as PLCC in many Literatures and the international statistical classification of Diseases and Related Health Problems Code (ICD) in current use does not distinguish between HCC and the other primary liver cancers. In regions with a high incidence of HCC, including sub-Saharan Africa, this tumour accounts for 90-95% of all primary malignant tumours of the liver, whereas in regions with a low or intermediate incidence it account for 70 to 85% of these tumours [6] . The only exceptions to this geographical pattern of occurrence are in north eastern Thailand and parts of the Philippines, where the high incidence of cholangiocarcinoma as a result of endemic infestation of the liver with the Clonorchis sinensis or Opisthorchis viverini is responsible for this tumour being the most common hepatic malignancy [6]. Cholangiocarcinoma also occasionally arise in patients with cirrhosis due to chronic viral hepatitis or hereditary haematochromatosis. A good understanding of the pathological features of this disease has a strong correlation on cancer prevention and the type of treatment strategies to be administered to patient with the disease.

We present a preliminary report of the histopathological features of a cohort of 61 consecutive PLCC cases seen at Ile-Ife as part of an ongoing National Survey of the disease.

Materials and Methods

We retrospectively reviewed all cases of primary liver cell carcinoma seen in the department of Morbid Anatomy and Forensic Medicine, Obafemi Awolowo University Teaching Hospital Complex Ile-Ife, Nigeria. This hospital is a tertiary healthcare facility with 709 bed spaces located in Ife-Ijesha Senatorial district of Southwestern Nigeria and serves patients from Osun state, Ekiti state, Ondo state, Oyo state, Lagos state and part of Kwara state.

The surgical materials of patients diagnosed with primary liver cell carcinoma in the histopathology laboratory of the hospital between 1989 to 2007 were selected for the study.

The original request cards of the patients were carefully reviewed and the demographic data extracted and documented. The surgical pathology reports and autopsy findings of cases of PLCC were scrutinized age incidences, association with HBsAg, HCV, background liver cirrhosis, histological types, growth patterns and grading.

Statistical analysis was performed using simple statistical methods.

Results

There were 61 cases comprising of 51 needle biopsies, 5 open biopsies and 5 cases discovered during the autopsy.

Biodata of patients

There were 41 males (67.2%) and 20 females (32.8%) . The overall male to female ratio was 2.1: 1 . The mode was in the group between 51-60, the range was 62 years and the mean was 38.2 as shown in figure 1.

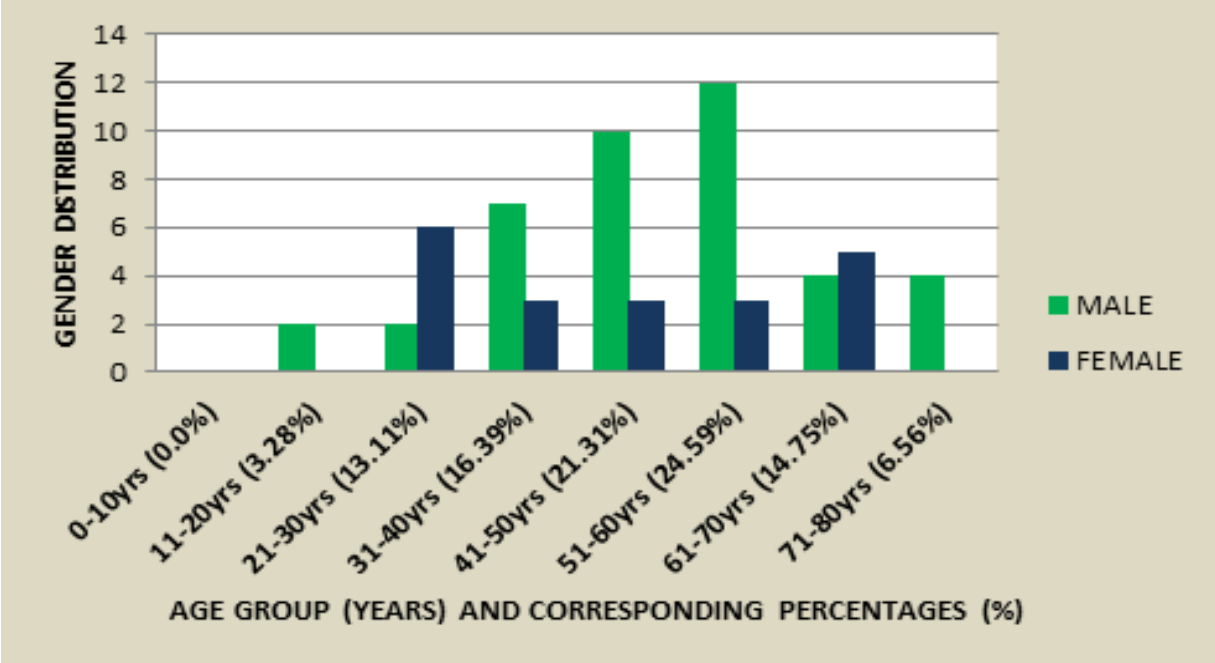

Fig. 1: Age- sex distribution

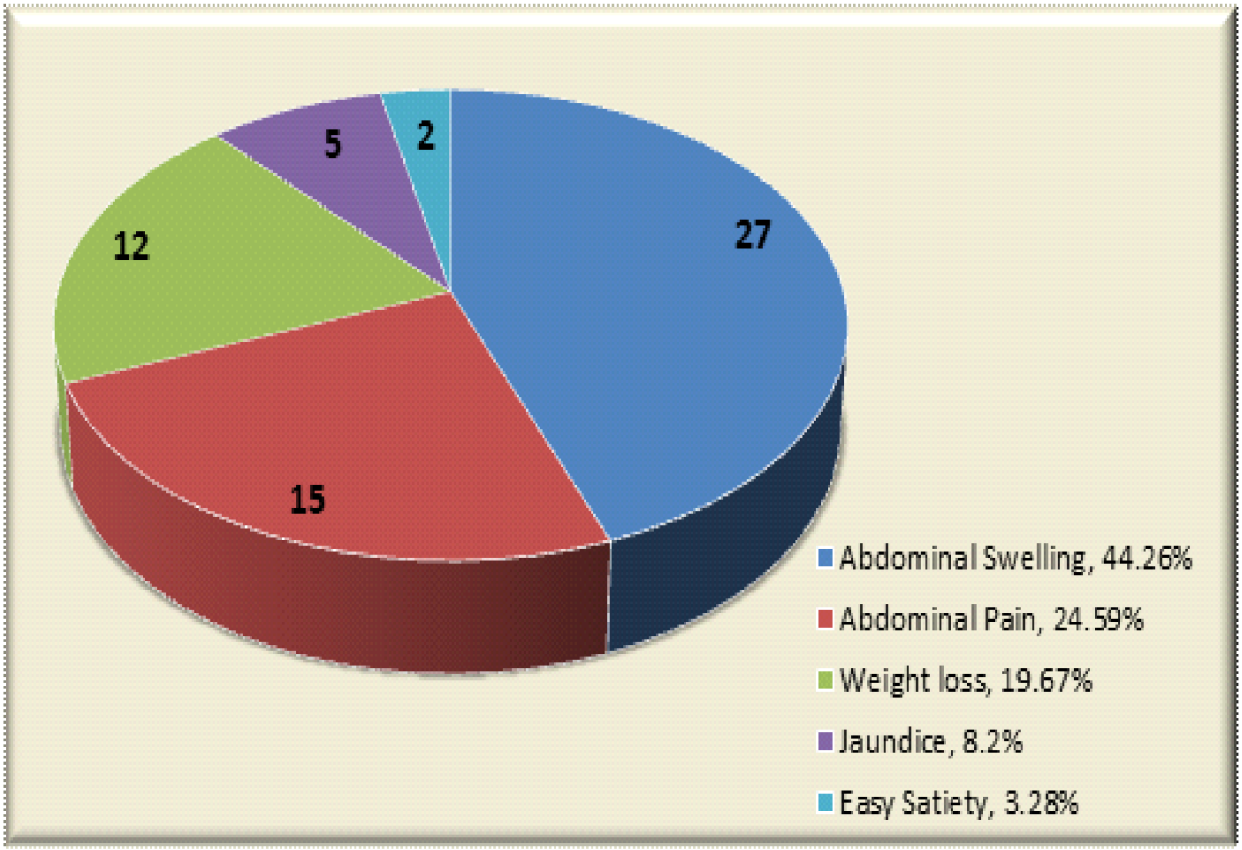

Fig. 2 : Common presenting symptoms

Table 1

AGE GROUP (YEARS)	HbsAg				HCV			
	POSITIVE		NEGATIVE		POSITIVE		NEGATIVE	
	Male	Female	Male	Female	Male	Female	Male	Female
0-10								
11.-20	2							
21-30	2	2	2		1		1	
31-40	3	2	1	1			1	1
41-50	3							
51-60	3	1		2				
61-70			1	1			1	1
71-80	2		2		1			
TOTAL	**15**	**5**	**6**	**4**	**2**	**0**	**3**	**2**

Common presenting symptoms

The most common symptom presented to the hospital with by these patients in our study was abdominal swelling and this constituent 44.26% of the common presenting symptoms as shown in figure 2.

Association with HBsAg and HCV

Twenty of the cases (32.79%) were positive for HBsAg , 10 of the cases(16.39%) were negative for HBsAg while the HBsAg status of the remaining 31cases (50.82%) were unknown in this study while 1 case (1.64%) was positive for HCV and 5 of the patients (8.20%) were HCV negative (Table 1).

Types of specimens

Fifty-one of the cases (83.6%) had needle biopsy done, five of them (8.20%) had open

Table 2: Age –sex with background cirrhosis

Age Group (Years)	Cases with Cirrhotic Background			
	Male	Female	Total	Percentage
0-10				
11-20	1	1	2	28.57
21-30				
31-40		1	1	14.29
41-50				
51-60	2		2	28.57
61-70	1	1	2	28.57
71-80				25
	4	3	7	100

Table 3: Growth patterns

Age Group (Years)	Growth Patterns					
	Trabecular		Pseudo glandular		Fibrolamellar	
	M	F	M	F	M	F
0-10						
11.-20						1
21-30		1				
31-40	2			1		
41-50	1			2		
51-60	2	1	2			
61-70	2	1				
71-80				1		
TOTAL	7	3	2	5		1

Table 4: Age-sex grading

Age Group	Grading						
	I		II		III		IV
	M	F	M	F	M	F	
0-10							
11-20							
21-30			1	1		1	
31-40			2				
41-50			1	1	2		
51-60				1	2	1	
61-70			1			1	
71-80							

biopsy and five (8.20%) was diagnosed at autopsy.

Background Liver Cirrhosis

Seven (11.48%) had associated liver cirrhosis with the peak occurrence in the age groups 11-20, 51-60 and 61-70 (Table 2).

Growth patterns

The trabecular pattern was the most common in this study 10 (16.39%), the pseudo glandular pattern was 7 (11.48%), fibro lamellar 1(1.64%) were seen (Table3).

Histological grading

Most of the histology types of PLCC seen were grade II (13.11%) and 11.48% of the patients had grade III tumor (Table 4).

Discussion

The incidence and aetiological factors of hepatocellular carcinoma vary dramatically around the world [7-9]. Our findings are essentially similar to other reports in high incidence area with primary liver carcinoma[10-17]. The age range and sex distribution observed in this study are similar to those previously reported in Nigeria and other nations in sub-Saharan Africa [18-20]. The median peak age incidence in this survey was 38 years. This agrees with results from same centre previously reported [21] and other studies from high incidence areas [22- 24] which indicated that the tumour tends to occur at a younger age. The

young age at which HCC occurs in the sub-Saharan Africa is most striking in Mozambique where more than 50% of the patients with HCC were less than 30 years at first presentation [22]. This contrasts reports from developed countries with low or intermediate incidences of HCC , where patients with HCC usually present with median age of approximately 65 years [7, 25-26].

In most geographical regions of the world, men have a higher incidence of HCC than the women [27-28] . In this study, the male to female ratio is 2.3: 1 , this shows a significant male preponderance and comparable with studies from other parts of the sub-Saharan Africa including Nigeria, which reported that HCC occurs at least twice as likely in the male population when compared with the female population [29-31]. The increased risk of HCC occurrence in the male could be attributable to the higher rate of chronic HBV infection which is approximately twice that of the female [32.] Furthermore, dietary iron overload is more common among the males than the females especially in the sub- Saharan Africa. The males consume more far larger volumes of the iron – rich home – brewed alcohol and they do not menstruate hereby increasing the concentration of iron storage in the liver. Recent evidence suggests that increased body iron has been associated with the incidence of HCC in sub-Saharan Africa [33.] .

HCC usually presents in most patients with typical symptoms and signs such as upper abdominal pain, generalized abdominal swelling, weakness, loss of weight and jaundice especially when the tumour has reached the advanced stage [34-35]. However, a significant number of patients present in a variety of unusual ways such as acute abdominal crisis resulting from rupture of a nodule [4, 36-37] during the clinical course the disease. In this study, abdominal swelling was the most common symptom but this was second to abdominal pain. Weight loss, jaundice and weakness were some of the typical symptoms and signs seen in this study. Unusual clinical presentation such as haemoperitoneum which resulted from tumour rupture was also recorded in this study. Majority of the patients presented late to this hospital and this might be due to lack of resources to settle hospital bills and lack of effective screening programme for primary liver cell carcinoma in our environment.

Our study shows a strong association between HBsAg and primary liver cell carcinoma. Serology screening was done for HBsAg in only 49% of the all the cases studied, out of which 67% tested positive for HBsAg. This is consistent with the finding by some authors which shown that majority of patients with HCC in high incidence areas are HBsAg positive [38- 41]. Hepatitis C virus (HCV) antibody was positive in 1.64% of patients and this is consistent with the general view that HCV contributes less than HBV to the high incidence of HCC in sub-Saharan Africa and Southeast Asia [39, 42-43].

Primary liver cell carcinoma and cirrhosis frequently coexist in population with a low incidence; the tumour often arises as a complication of long standing symptomatic cirrhosis [44].

We observed an expected weak association between primary liver cell carcinoma and liver cirrhosis in this study.

Majority of our histological types were primary liver cell carcinoma with only 8.2% was cholangiocarcinoma. In this study, the females were more affected by cholangiocarcinoma than the males, with female to male ratio of 4:1. This contradicts most studies were a higher male incidence were reported [45-47]

The gross and histologic growth patterns of HCC may be influenced both by the aetiology of the tumour and the presence and nature of any co-existing liver pathology. Despite this, many of the pathological features of the tumour in patients in sub-Saharan Africa are similar to those in other populations, although there are

a number of important differences in the tumour size and association with cirrhosis [48-51]. The growth patterns of HCC in Black African patients and South Eastern Asia patients are often massive (expanding) in nature, but are less common in North American patients [52]. There are differences in the frequency with which the different histological types are present. In a series in Zaire, well- differentiated HCC was present in only 1.3% of patients and moderately differentiated tumours in 12% [50]. The remaining tumours were poorly differentiated. This, however, contrasts with our study conducted also in high incidence area with most of our sampled was moderately differentiated. The criteria used for the grading include: nuclear chromatism; nuclear/ cytoplasm ratio; cell cohesiveness; cell function (bile production) and histological architecture. Particular attention was paid to the cell-type and classification.

In our local study, the trabecular histological type was by far the most common. Other histological types seen were the pseudoglandular and the fibro lamellar pattern. This report contradicts the findings from Zaire which reported mixed histological type as the commonest histological cell type in their series [50].

Conclusion

In conclusion, hepatocellular carcinoma is the most common type of primary liver cell carcinoma in our environment. Chronic infection with HBV remains the major aetiological factor of HCC in our environment. The clinical outlook of this disease is poor due to late presentation and lack of effective screening programme for primary liver cell carcinoma in our locality.

Limitation of the Study

This is a retrospective study and some of the information retrieved from the request cards, surgical registers and the histopathology reports were not comprehensive enough. Many of the histopathology reports did not capture all the parameters that could have helped us in the evaluation of the growth pattern and the grading in this study. We were only able to present the growth pattern and grading in eighteen and fifteen of the cases respectively. We made some efforts in overcoming these challenges, but our efforts were not successful, as the slides and tissue blocks of the cases with inadequate histopathology reports were not seen in the archival store in the Department.

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