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Research Article

Hepatocellular Carcinoma: Clinical, Biological and Imaging Aspects in Yaounde (Cameroon)

Carcinome hépatocellulaire : aspects cliniques, biologiques et morphologiques à Yaoundé, Cameroun

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ABSTRACT

Introduction. Sub-Saharan Africa is a high-risk area for hepatocellular carcinoma, mainly because of hepatitis B and C virus infections. Patients are younger than in other regions of the World. Data on hepatocellular carcinoma in Cameroon mostly concern epidemiology. The aim of this study was to describe clinical, biological and morphological aspects of HCC in a group of patients in Cameroon. **Methods.** It was a cross-sectional study. Clinical records of patients diagnosed with hepatocellular carcinoma between January 1st, 2013 and April 30th, 2016 were reviewed using R® software for Windows version 4.2.1. Patients were divided into two groups for analysis: HBV-related hepatocellular carcinoma vs hepatocellular carcinoma from other causes. **Results.** We obtained medical records for 55 patients. The median age (25th-75th percentiles) was 58.0 years (IQR 38.5-65.5). Hepatitis B and C were the main causes of hepatocellular carcinoma. There was a statistical difference ($p < 0.0001$) between the median age of those having HBV-related hepatocellular and other patients, 39.0 (IQR 35.0-43.0) and 63.0 (IQR 54.0-73.0) respectively. Abdominal pain (> 70 %), weight loss (> 40%) and abdominal mass (27 %) were the most common clinical manifestations. There was a predominance of multinodular form of hepatocellular carcinoma in both groups, with the largest tumour size of > 60 mm. **Conclusion.** Hepatocellular carcinoma patients presented late with an extremely low possibility to undergo curative treatment. This highlights the importance of primary prevention by HBV immunization and early diagnosis and management of viral hepatitis.

RÉSUMÉ

Introduction. Les données sur le CHC au Cameroun concernent surtout l'épidémiologie. Nous voulions décrire les aspects cliniques, biologiques et morphologiques du CHC chez un groupe de patients. **Méthodologie**. Il s'agissait d'une étude transversale. Les dossiers cliniques de 55 patients diagnostiqués avec un carcinome hépatocellulaire entre le 1er janvier 2013 et le 30 avril 2016 au CHU de Yaoundé ont été analysés à l'aide du logiciel R® pour Windows version 4.2.1. Les patients ont été divisés en deux groupes : ceux ayant un carcinome hépatocellulaire lié au VHB vs ceux avec d'autres causes de CHC. **Résultats**. L'âge médian (25e-75e percentiles) était de 58,0 ans (IQR 38,5-65,5). Les hépatites B et C étaient les principales étiologies. Il y avait une différence statistique (p < 0,0001) entre l'âge médian de ceux ayant un CHC secondaire au VHB et d'autres patients, 39,0 (IQR 35,0-43,0) et 63,0 (IQR 54,0-73,0) respectivement. La douleur abdominale (> 70 %), la perte de poids (> 40 %) et une masse abdominale (27 %) étaient les manifestations cliniques les plus fréquentes. La forme multinodulaire du carcinome hépatocellulaire prédominait dans les deux groupes, avec la plus volumineuse tumeur mesurant plus de 60 mm. **Conclusion**. En définitive, les patients atteints de CHC se sont présentés tardivement avec une possibilité extrêmement faible d'avoir un traitement curatif. Cela souligne l'importance de la prévention primaire par la vaccination contre le VHB et le diagnostic et la prise en charge précoces des hépatites virales.

HIGHLIGHTS OF THE STUDY

What this study adds to our knowledge

1. The median age was 58.0 years and the sex ratio was 1.89
2. Hepatitis B and C were the main causes of hepatocellular carcinoma.
3. Patients presented late with an extremely low possibility to undergo curative treatment**.**
4. Abdominal pain and weight loss were the most common clinical manifestations, far ahead of the presence of abdominal mass, even in cases of large or multinodular tumors.

How this is relevant to practice, policy or further research.

This highlights the importance of primary prevention by HBV immunization and early diagnosis and management of viral hepatitis

INTRODUCTION

Primary liver cancer is the sixth most commonly diagnosed cancer and the third leading cause of cancer death worldwide in 2020, with approximately 906,000 new cases and 830,000 deaths. Hepatocellular Carcinoma (HCC) is the main type of primary liver cancers representing 75%-85% of cases (1). Sub-Saharan Africa is among the most high-risk areas for HCC, mainly due to hepatitis B virus (HBV) and hepatitis C virus (HCV) infections and Aflatoxin exposure (1–4). Previous studies showed that HCC occurs at a younger ages in Sub-Saharan Africa patients than in other regions of the World, and patients present with advanced or terminal disease and thus there is no possibility for curative-intended treatment to be implemented (5). Yet, data on hepatocellular carcinoma in Cameroon mostly concern epidemiology. The aim of this study was to describe clinical, biological and morphological aspects of HCC in a group of patients in Cameroon.

METHODS

Study design and patients

We did a cross-sectional retrospective study. Clinical information for patients diagnosed with hepatocellular carcinoma between January 1, 2013 and April 30, 2016 were extracted from medical records at the University Teaching Hospital of Yaounde (UTHY). The Review Board of the UTHY approved the study. The extracted clinical information consisted of: patient demographic characteristics (age and gender of the patients), clinical symptoms at the first visit, and physical signs at the time of diagnosis of HCC, alcohol intake, viral hepatitis test results, alpha-fetoprotein level, and tumour characteristics on imaging. The diagnosis of HCC was based either on cross-sectional 4-phases contrast CT-scan or the combination of liver ultrasound describing liver masses with high level of alpha-fetoprotein (cut-off > 200 ng/ml). HBV was confirmed when the HBsAg test was positive, whereas HCV was confirmed by the detection of Anti-HCV antibodies with or without HCV-RNA detection. Alcohol intake was considered risky when the daily intake was more than 40 g for men and 30 g for women, for more than 10 years. The tumour characteristics assessed were the number of masses (single mass or multinodular) and the size of the largest tumour (in millimetres).

Statistical analysis

Statistical analyses were done using R® software for Windows version 4.2.1 (6). Because HCC in Sub-Saharan Africa is mainly due to HBV infection, we divided patients into two groups for analysis (HBV-related HCC vs HCC from other causes). Variables were described as mean (± standard deviation) or median (interquartile range, IQR) if quantitative or as count (percentage) if categorical. We used the Chi-square test or Fisher's exact test where necessary for comparison between proportions and student t test to compare means between groups or Man-Whitney test when necessary. The threshold for significance was set at the level of 5%.

Ethics

The Review Board of the UTHY approved the study.

RESULTS

We obtained information for 55 patients diagnosed with hepatocellular carcinoma during the study period. The median age of patients was 58.0 years (IQR 38.5-65.5) with extremes of 20 and 81 years and almost two-thirds were male. Almost a half of patients was aged 60 years or above and one-fourth was below 40 years (Table 1). The two main causes of HCC in our patients were viral hepatitis B and C, which are associated with alcohol consumption in some cases. In 16 patients (29 % of cases), the cause of the hepatocellular carcinoma was not identified. There was a statistical difference ($p < 0.0001$) between the median age of those having HBV-related HCC and those having HCC of other causes, 39.0 (IQR 35.0-43.0) and 63.0 (IQR 54.0-73.0) respectively. There was no gender difference between the two groups.

Table I: Demographic characteristics of patients.

Variables	N	%	Cumulative %
Age groups			
19-29	7	12.7	12.7
30-39	7	12.7	25.4
40-49	8	14.5	39.9
50-59	6	11	50.9
≥ 60	27	49.1	100
Gender			
Male	36	65.5	65.5
Female	19	34.5	100
Etiology			
HBV	16	29.1	29.1
HCV	11	20	49.1
Alcohol	1	1.8	50.9
HBV and alcohol	2	3.6	54.5
HCV and alcohol	6	11	65.5
Unknown	16	29.1	94.6
HCV and HIV	3	5.4	100

HBV: hepatitis B virus; HCV: hepatitis C virus; HIV: human immunodeficiency virus.

The most common clinical manifestations in order of decreasing frequency were abdominal pain (in 13/18 [72.2 %] patients with HBV-related HCC and 25/36 [69.4 %] of patients with HCC due to other causes respectively),

weight loss (in 8/18 [44.4 %] and 16/37 [43.2 %] cases respectively) and abdominal mass (in 5/18 [27.8 %] and 10/37 [27.0 %] cases respectively). There was no difference in all clinically relevant characteristics except for ascites which was more prevalent in hepatocellular carcinoma of other causes than chronic HBV (Table 2). In both groups of patients there was a predominance of multinodular form of HCC.

Table II: Clinical and paraclinical characteristics of patients with HCC according to etiology.

Characteristics	HBV-related HCC	HCC of other causes	*p-value*
Median age (years)	39.0 (35.0-43.0)	63.0(54.0-73.0)	< 0.0001
Gender			
Male	12 (66.7 %)	24 (64.9 %)	0.8951
Female	6 (33.3 %)	13 (35.1 %)	1.000
Clinical signs			
Abdominal pain	13/18 (72.2 %)	25/36 (69.4 %)	1.000
Jaundice	3/18 (16.7 %)	1/37 (2.7 %)	0.188
Weight loss	8/18 (44.4 %)	16/37 (43.2 %)	1.000
Abdominal mass	5/18 (27.8 %)	10/37 (27.0 %)	1.000
Ascites	1/18 (5.5 %)	13/37 (35.1 %)	0.042
Biology			
Alpha-fetoprotein (mean ± sd, ng/ml)	521708.36 (±1266341.94)	183956.53 (±705023.77)	0.266
Radiological tumor characteristics			
Multinodular	12/18 (66.7 %)	22/37(61.1 %)	0.894
Size of largest tumor (mm)	89.84 (±45.49)	68.59 (±39.36)	0.138

HBV: hepatitis B virus; HCC: hepatocellular carcinoma; sd: standard deviation.

DISCUSSION

Cameroon is in a highly endemic zone for hepatitis B virus infection which is the major cause of HCC in sub-Saharan Africa (7). The median age of patients in our study was 58.0 years (IQR 38.5-65.5) with almost 50 % of patients being aged 60 years old or above. Yet those who had HBV-related hepatocellular carcinoma were younger [median age: 39.0 (IQR 35.0-43.0)] than those with HCC of other causes. This result was in consistence with those of previous studies on HCC in Africa (2,3,8,9). There was a high proportion of HCC of unknown causes, as stipulated by other studies from Africa (3,9). This might be due to poor means for aetiological research, either economically or technically (screening for alpha1-antitrypsin deficit, Wilson's disease or other rare causes of cirrhosis which might end up in hepatocellular carcinoma). But, it is possible that these were HCC secondary to chronic HBV infection, which might have been confirmed by systematic screening for HBV-DNA and total hepatitis B core antibody (HBc-antibody). In fact, in highly endemic zones for HBV infection, there may be a certain proportion of isolated HBc-antibody due to either previous HBV exposure, an HBsAg mutation or "occult" hepatitis B infection. All of these situation may lead to HCC even though the HBsAg is not detected (10–13). The clinical manifestations are globally consistent with those in the literature, with the exception of ascites which was less prevalent for patients with HBV-related HCC (14–16). Yet we have not found a scientific explanation to this difference in ascites occurrence in the two groups. There was no difference between the two groups regarding the median alpha-fetoprotein levels and the frequency of multinodular tumours as well as in the size of the largest tumour. This can be regarded as a similarity in poor outcome for the two groups of patients. In fact, although less sensitive and mildly specific for HCC detection, increase in alpha-fetoprotein levels predicts advanced stage of the disease and hence, a poor outcome (17). Moreover, a largest tumour size of > 38 mm is also usually associated to poor survival rates whether in the presence or absence of cirrhosis (18).

There were some limitations to this study, notably its retrospective and monocentric nature as well as the lack of the Child-Turcotte-Pugh classification which is important in the Barcelona Clinic Liver Cancer (BCLC) classification of the patients. But patients in our settings used to come at advanced level of the disease and therefore performing laboratory analyses for BCLC classification with the purpose of staging and treatment choice may seem needless or simply as a wasting of resources without benefit for patients since most of them do not have social insurance.

CONCLUSION

Chronic viral hepatitis were the major causes of hepatocellular carcinoma in our study. Abdominal pain and weight loss were the most common clinical manifestations, far ahead of the presence of abdominal mass, even in cases of large or multinodular tumours. Patients presented late in our settings with an extremely low possibility to undergo curative-intended treatment, highlighting the urgent need for more intensive primary prevention and an effective implementation of surveillance in patients at risk in order to diagnose HCC at earlier stages. HBV immunization coupled with early diagnosis and management of viral hepatitis should therefore still be the cornerstone of our strategy against HCC.

DECLARATIONS

Authors' contribution: MAG, NDGR, FNC and KMP conceived the study. MAG and FNC collected the data. MAG, TNMJA and NDGR analysed the data and drafted the manuscript. MAG, NDGR, FNC, TNMJA, KMP and ON proofread and corrected the manuscript. All authors agreed with the final manuscript to be submitted for publication.

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