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Epidemiological, Diagnostic and Therapeutic Aspects of Hepatocellular Carcinoma at the Regional Teaching Hospital of Ouahigouya in Burkina Faso

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Abstract

Objective: The aim of the study was to clarify the epidemiological, diagnostic and therapeutic aspects of hepatocellular carcinoma at Regional Teaching Hospital of Ouahigouya in Burkina Faso. **Patients and Methods:** This study was a retrospective, single-center, descriptive study of patients with hepatocellular carcinoma hospitalized in the Hepato-Gastroenterology Department of Regional Teaching Hospital of Ouahigouya from February 22, 2014, to December 13, 2022. Diagnosis was based on the presence of hepatic nodules on liver cirrhosis on ultrasound or abdominal CT scan. An alpha-fetoprotein level ≥ 200 ng/mL was considered significant. Histological diagnosis was not possible in our practice setting. **Results:** Three hundred and twenty-two patients were hospitalized during the study period with a mean age of 48.07 ± 15.1 years. The sex ratio, male-female ratio, was 2.42. The reason for hospitalization was deterioration of general condition (94.1%), abdominal pain predominantly in the right hypochondrium (85.2%), abdominal distension (62.1%), jaundice (54.3%), and digestive hemorrhage (8%). Hepatomegaly predominated (76.1%), followed by ascites (71.1%), jaundice (54.3%), collateral venous circulation (25.7%), splenomegaly (21.1%), and encephalopathy (15.8%). Alpha fetoprotein was greater than 200 ng/mL in 56.9% of cases. HBs antigen was positive in 73.9% of cases, total anti-HBc antibodies in 89.1% of cases, and anti-HCV antibodies in 6.1% of cases. Ultrasound (99.3%) and abdominal CT scan (25.7%) showed more than multiple nodules in 50.4% of cases. Treatment was most often palliative, based on support-

ive care in 99.3% of cases. **Conclusion:** The diagnosis of hepatocellular carcinoma is always made at an advanced stage when the possibilities of curative treatment are exceeded. Biology and radiology were the main diagnostic criteria used, and treatment was symptomatic in almost all cases.

Keywords

Hepatocellular Carcinoma, Ouahigouya, Burkina Faso

1. Introduction

Hepatocellular carcinoma (HCC) is the most common primary malignant liver tumor. It ranks third among cancers and represents the second leading cause of cancer-related death worldwide [1]. It occurs mainly and with increasing frequency in developing countries, where it affects increasingly younger people [2] [3]. The etiology of HCC is dominated by hepatitis B virus (HBV) and hepatitis C virus (HCV), heavy alcohol consumption and non-alcoholic steatohepatitis. In Burkina Faso, according to Globocan 2022 [1], liver cancer comes first among all cancers for all sexes combined, with an overall incidence of 1920 cases (13% of all cancers). It is also the leading cause of mortality. It is the second most common cancer in men after prostate cancer and third among women after breast and cervical cancer in Sub-Saharan Africa, where diagnostic resources are limited, the diagnosis of HCC is made difficult by the population's limited access to diagnostic resources. While abdominal CT is the radiological examination for the diagnosis of HCC and histology is the reference examination, the diagnosis of HCC in many African countries is still made by abdominal ultrasound associated with alpha fetoprotein. At the Regional Teaching Hospital of Ouahigouya, the acquisition of the CT dates back to 2019, the majority of our patients only benefited from ultrasound. The diagnosis of HCC remains late nowadays at a time when curative treatment possibilities are exceeded. This study aimed to examine the epidemiological, diagnostic and therapeutic aspects of hepatocellular carcinoma (HCC) at Regional Teaching Hospital of Ouahigouya in Burkina Faso.

2. Patients and Methods

This was a descriptive retrospective study carried out using data collected in the hospitalization register of the Hepato-Gastroenterology Department at Regional Teaching Hospital of Ouahigouya.

The study included patients hospitalized during the period from February 22, 2014 to December 13, 2022 for CHC.

The diagnosis of HCC was made based mainly on the following arguments:

- Clinical Features: Right hypochondrium pain, a large, hard, painful liver suggesting a tumorous liver, and a liver with a sharp lower edge suggesting a cirrhotic liver. Ascites, collateral venous circulation, jaundice, hepatic encephalopathy;

- Biological: The dosage of alpha fetoprotein. The normal value in adults was less than 20 ng/mL. An alpha fetoprotein level ≥ 200 ng/mL was considered significant, but a level < 200 ng/mL did not formally eliminate the diagnosis of HCC;
- Radiological: Nodules > 2 cm on helical CT performed with triple arterial, parenchymal and portal acquisition: the most suggestive sign of HCC was the existence of a hypervascularized nodule in the early arterial phase ("wash in"), with wash-out in the portal phase or late phase ("wash-out"), hepatic dysmorphism and signs of portal hypertension on ultrasound or CT;
- Endoscopic: Esophageal varices, cardiogastric varices or portal hypertension gastropathy.

The unavailability of the pathology department did not allow for microbiopsies on hepatic nodules or fine needle aspiration cytology for the histological diagnosis of HCC. Indeed, this department was only opened at the Regional Teaching Hospital of Ouahigouya in 2021.

This study did not include patients with a benign liver tumor or a secondary malignant tumor. It was the same for the incomplete files. They should have included an abdominal ultrasound and/or a CT scan and the dosage of alpha-fetoprotein.

The data were collected using a survey form specifying the patient's civil status, socio-demographic characteristics (age, sex, profession), clinical data (general condition according to the WHO classification, the presence of abdominal collateral venous circulation, jaundice, hepatomegaly, ascites, splenomegaly, digestive hemorrhage, hepatic encephalopathy), biological data (transaminases, prothrombin rate, albumin, bilirubin, blood count, alpha-fetoprotein, viral markers for hepatitis B and C), radiological examinations (abdominal ultrasound, abdominal CT scan) specified the characteristics of the tumor (the number, size and location of the nodules).

The data was entered into Microsoft Access 2013, exported to Excel, and then imported into SPSS software 28 for data analysis. The description of the sample consisted of calculations of proportions for qualitative variables and means with their standard deviation for quantitative variables.

Ethically, the anonymity was respected in the collection of data on the forms developed for this purpose. Consent could not be obtained from patients due to the death of the majority of them, and the unavailability of phone numbers in most of the files. The results of this study will be transmitted to the senior management of the Regional Teaching Hospital and to the Ministry of Health of Burkina Faso.

3. Results

During the study period from February 22, 2014 to December 13, 2022, three hundred and twenty-two (322) cases of HCC were included. The average length of hospitalization was 6.46 ± 4.2 days, with extremes of 1 and 30 days.

Our patients had a mean age of 48.07 ± 15.1 years with extremes of 15 to 86 years.

Sex ratio was 2.42. The occupations were dominated by farmers/breeders (56.02%). The main occupations are shown in Table 1. They were dominated by farmers/breeders in 55.7% of cases.

Table 1. Distribution of patients according to profession (n = 322).

Occupation	Effective	Percentage (%)
Farmer/breeder	186	57.7
Housewife	96	29.9
Civil servant	12	3.8
Trader	8	2.5
Not specified	6	1.9
Student	5	1.5
Worker	4	1.2
Informal sector	3	0.9
Others*	2	0.6
Total	322	100

Others*: 1 day laborer, 1 religious worker.

The reasons for hospitalization of patients were dominated by deterioration of general condition (95%), followed by abdominal pain (86%) and abdominal distension (62.1%). The different reasons for hospitalization are summarized in Table 2.

Table 2. Distribution of patients according to reasons for hospitalization.

Reason for hospitalization	Effective	Percentage (%)
Impairment of general condition	306	95
Abdominal pain	277	86
Abdominal distension	200	62.1
Jaundice	175	54.3
Digestive hemorrhage	26	8

Clinical signs were dominated by hepatomegaly (76.1%), ascites (71.1%) and jaundice (54.3%). These signs were represented in Table 3.

Biologically, HBs antigen positivity was noted at 73.9% and anti-HCV antibody at 6.1% alpha-fetoprotein (AFP)was measured in 137 people. It was <20 ng/mL in 24.8% of patients, between 20 and 200 ng/mL in 18.2%, and >200 ng/mL in 56.9%. The biological parameters of the patients are represented in Table 4.

The prognostic assessment of underlying cirrhosis was performed using the Child-Pugh score, a clinical and biological score. A B score was noted in 35.5% of cases (105/295) and a C score in 64.4% of cases (190/295). No patient was assessed with an A score.

Table 3. Distribution of patients according to clinical signs.

Physical signs	Effective	Percentage (%)
WHO 0	0	0
WHO 1	2	0.6
WHO 2	97	30.1
WHO 3	178	55.2
WHO 4	45	13.9
Hepatomegaly	245	76.1
Ascite	229	71.1
Jaundice	175	54.3
Collateral venous circulation	83	25.7
Splenomegaly	68	21.1
Hepatic encephalopathy	51	15.8

Table 4. Distribution of patients according to biological signs.

Biological signs	Effective	Percentage (%)
HBS Ag positive	216/292	73.9
Anti-HBc positive	204/229	89.1
Ag HBe positive	3/16	18.7
Anti-HCV Ac positive	14/228	6.1
AFP < 20 ng/mL	34/137	24.8
AFP between 20 and 200 ng/mL	25/137	18.2
AFP > 200 ng/mL	78/137	56.9
Albumin < 35 g/l	94/189	49.73
TP < 65%	83/171	48.53
ASAT > 1.5 N	101/247	40.8
ALAT > 1.5 N	87/247	35.2

Table 5. Distribution of patients according to ultrasound data (n = 322).

Ultrasound aspects	Effective	Percentage (%)
Hepatomegaly	280/322	86.9
Number of nodules		
1 nodule	55/322	17.1
2 nodules	105/322	32.6
Multinodal (≥3)	162/322	50.4
Ascite	248/322	77
Portal thrombosis	47/322	14.5

Abdominal ultrasound was performed in all our patients (100%). Hepatomeg-

aly was present in 86.9% of patients, 17.1% had a single hepatic nodule, 32.6% had 2 nodules and 50.4% multiple nodules (≥3 nodules). Ascites was reported in 77% of cases, and portal thrombosis in 14.5% of cases. Ultrasound signs in HCC are presented in Table 5.

CT examination was performed in 25.7% of cases, or 83 patients. According to the BCLC classification, stage A (early) represented 9.7% of cases, stage B (intermediate) 13.2% of cases, stage C (advanced) 49.4% and stage D (terminal) 2 7.7% of cases. This distribution is given in Table 6.

Table 6. BCLC classification (n = 83).

BCLC classification	Effective	Percentage (%)
0 (very early stage)	0	0
A (early stage)	8	9.7
B (intermediate stage)	11	13.2
C (advanced stage)	41	49.4
D (terminal stage)	23	27.7

For the histological diagnosis of HCC, liver microbiopsy or cytopuncture of a liver nodule was not performed in any patient.

In terms of evolution, metastases were reported in 8.07% of patients (26/322), esophageal varices (OVs) in 90% of patients (54/60), and portal vein thrombosis in 14.5% (47/322).

Therapeutically, treatment consisted primarily of supportive care in 99.3% of patients (320/322). Tamoxifen-based hormonal therapy was administered to 15.5% of patients (50/322). Only 0.6% of patients (*i.e.*, 2 patients) received Sorafenib-based treatment.

None of our patients had undergone liver resection or percutaneous alcohol injection.

4. Discussion

This first study on hepatocellular carcinoma (HCC) aimed to clarify its epidemiological, diagnostic and therapeutic aspects at the Regional Teaching Hospital of Ouahigouya. The limitations of this study were those inherent to studies with retrospective data collection, but also to the absence of control cases. Thus, some information was missing in this case, risk factors such as exposure to aflatoxin B1, which is a co-carcinogen of HCC with the hepatitis B virus, but also the quantitative dosage of HBV DNA. During the period covered by the study (9 years), 342 patients had been hospitalized in the Medicine and Hepato-Gastroenterology Department for HCC. Among these, 10 files had not been retained, which ultimately gives 322 patients.

The mean age was 48.07 ± 15.1 years, and the sex ratio was 2.42. The young age and male predominance of our patients are found in most studies, notably that of Somé *et al.* and Zakari *et al.* in Burkina Faso [4] [5], which finds a sex ratio of 3;

and elsewhere in Africa [6]-[8]. However, in Algeria, Harir *et al.* [9] reported a mean age higher than ours, which was 62.35 years. The male predominance observed in our study (sex ratio: 2.42) was consistent with that reported by most African studies.

HCC is most often diagnosed late in our context. At this time, the symptoms are most often noisy. In our study, the most frequent reason for hospitalization was the alteration of the general condition (94.1%), followed by abdominal pain predominantly in the right hypochondrium (85.2%), as found in many African studies [6] [7] [10].

In our series, 99.37% of patients were at WHO stage ≥2, indicating an advanced stage of the disease.

Hepatomegaly was the predominant physical sign (76.1%), followed by ascites (71.1%), jaundice (54.3%), collateral venous circulation (25.7%), splenomegaly (21.1%), and hepatic encephalopathy (15.8%). This predominance of hepatomegaly and ascites is also reported by Kissi Anzouan-Kacou *et al.* [6] in Ivory Coast and Harir *et al.* [9] in Algeria. Somé *et al.* [4] in Burkina Faso reported a predominance of deterioration of the general condition (77.2%), followed by hepatomegaly (97.9%) and ascites (68.5%).

In 27 patients, the Child Pugh score could not be calculated due to the lack of certain biological tests such as prothrombin rate, total bilirubin and albumin levels. Lack of financial resources is the main explanation.

AFP was used as a useful marker for HCC diagnosis in our study, as recommended in Sub-Saharan Black Africans [11]. This is a protein that is present in the fetus and which increases in the event of cellular dedifferentiation, particularly in certain cancers such as HCC.

The diagnostic value of AFP varies among centers: greater than 500 ng/mL, greater than 400 ng/mL, or greater than 200 ng/mL. A progressively increasing serum AFP level, even if below the diagnostic threshold, strongly suggests the presence of HCC [11].

AFP was measured in 137 patients (42.54%). It was higher than 200 ng/mL in 56.9% of cases.

- Kissi Anzouan-Kacou *et al.* [6]: 61.6% of cases);

- Harir *et al.* [9] in Algeria: 53.2% (10 - 500 ng/mL) and 9.3% (AFP greater than 500 ng/mL);

- Bougouma *et al.* [12]: out of 9 patients, 4 had an AFP greater than 400 ng/mL.

HBs antigen was positive in 73.9% of cases, total anti-HBc antibodies in 89.1% of cases, and anti-HCV antibodies in 6.1% of cases. These markers confirm the etiologies of HCC in our context, dominated by viral hepatitis with a strong predominance of viral hepatitis B. This result is close to that of Somé *et al.* [4] in Burkina Faso, who reported a prevalence of HBs antigen in 76.1% of patients and total anti-HBc antibodies in 89.4% of cases. Bougouma *et al.* [12], also in Burkina Faso, reported a prevalence of HBs antigen in 75% of patients. Kissi Anzouan-Kacou *et al.* [6] in Ivory Coast reported a positive HBS antigen in 64% of cases, and total anti-HBc antibodies in 91.2% of patients.

As for the prevalence of HCV, it was lower than other prevalences reported in Burkina Faso by Somé *et al.* [4], which was 10.9% among cases and Bougouma *et al.* [12], 8.3%. Kissi Anzouan-Kacou *et al.* [6] in Ivory Coast reported a prevalence 9.1% higher than ours. Prevalences reported in hospital series may be higher than the averages of the countries concerned. The prevalence of anti-HCV antibodies in the general population in Burkina Faso is estimated at 3.6% (95% CI: 3.3% - 3.8%), placing the country in a low-intermediate prevalence zone. However, the prevalence is high (13.2%) in the Southwest region and particularly in the young age group of 15 to 20 years [13]. The prevalence of HCV infection in the northern region of Burkina Faso was 3.10% among blood donors [14].

In Sub-Saharan Africa, the predominance of HBV is a major risk factor for the occurrence of HCC. Indeed, HBV is responsible for 55 to 80% of HCC cases in countries with high endemicity, such as Burkina Faso [15]. Chronic HBV infection is often acquired vertically or perinatally in these areas, favoring a silent progression to cirrhosis and HCC [16]. Conversely, the low prevalence of hepatitis C virus (HCV), found in our series, reflects the low endemicity of HCV in West Africa. The prevalence of HCV among patients with HCC is generally less than 15%, unlike in North Africa, where it is a more frequent cause of HCC [17] [18].

In addition to hepatitis B and C viruses, environmental factors [19] intervene as co-factors in the genesis of HCC. We can cite poor hygiene and aflatoxin B1. Aflatoxin B1 is a mycotoxin produced by Aspergillus flavus, which pollutes certain cereal stocks and constitutes one of the most potent carcinogens present in our environment. Indeed, the bad conservation of cereals and legumes in a hot country like Burkina Faso favors the development of Aflatoxin B1, co-carcinogen of hepatocellular carcinoma, with the high prevalence of the hepatitis B virus. Further studies should be carried out in Burkina Faso.

Advances in medical imaging associated with AFP dosage have made it possible to diagnose HCC. Computed tomography (CT) with injection of contrast agents or magnetic resonance imaging (MRI) should be performed in the event of any doubt regarding ultrasound or nodules larger than 2 cm. However, due to the low availability of CT, effective at Ouahigouya Teaching Hospital since 2019, and the absence of MRI, we have made that the diagnosis was mainly based on liver ultrasound for all our patients (100%). Indeed, according to El-Serag [20], marked elevation of AFP, associated with typical ultrasound images of hepatic masses on dysmorphic liver, is often used as a pragmatic diagnostic criterion in these settings. She was followed by abdominal CT scan (25.7%). The use of these two methods has made it possible to highlight multiple nodules in 50.4% of cases. The low use of CT scan is explained by the fact that it has been installed at Ouahigouya Regional Teaching Hospital only in 2019. Also, frequent breakdowns and the cost of the examination were also factors that limited its use.

Complications of HCC were reported on radiology and upper gastrointestinal endoscopy. These included liver metastases (26/322 or 8.07%) and portal thrombosis (47/322 or 14.5%) on abdominal ultrasound and computed tomography. Esophageal

varices were reported in 54 of 60 patients in whom upper gastrointestinal endoscopy was performed (90%).

For the histological diagnosis of HCC, liver microbiopsy or cytology of a liver nodule had not been performed in any patient. The pathological anatomy and cytology department was only opened at the Ouahigouya University Hospital in 2020. This examination was therefore not available on site. We recognize that diagnostic errors are so possible, especially in cases of atypical or mixed tumors. Other histological forms with different treatment and prognoses may be missed. Targeted therapies cannot be used for certain liver tumors due to lack of histological confirmation.

Our patients were diagnosed at an advanced stage of the disease, as is the case in most resource-limited countries [4] [6] [12] [17], making curative treatment options (liver resection, transplantation, radiofrequency, arterial chemoembolization) almost non-existent. Thus, the care consisted mainly of supportive care in 99.3% of patients. These were analgesics, painkillers, laxatives for constipation and prevention of hepatic encephalopathy, and ascites punctures. A Meta-analysis of 3989 patients in 15 Sub-Saharan African countries showed that only 6% of HCCs received curative treatment (resection, transplantation, ablation) [21]. This situation, which is common in countries with limited resources, requires, as suggested by Ducarroz *et al.* [22], the development of palliative care. Tamoxifen-based hormonal therapy was administered in 15.5% of patients (50/322). Only 0.6 of the patients (2) received Sorafenib-based therapy, systemic oral treatment indicated in advanced forms of CHC. Its access is limited by its cost, which puts it out of reach of the majority of patients [23]. The use of tamoxifen in 15.5% of patients in our cohort is an important point to note. Today, numerous studies, including clinical trials and meta-analyses, have clearly demonstrated that it is ineffective in the treatment of hepatocellular carcinoma. A meta-analysis by Farinati *et al.* [24] clearly demonstrates this. It was mainly used about ten years ago due to the unavailability of validated treatments such as sorafenib and locoregional treatments. Today, this molecule is rarely used in our practice. An update of our practices is therefore underway in light of available scientific studies.

5. Conclusion

During the period of our study, HCC was a frequent reason for hospitalization at the Regional Teaching Hospital of Ouahigouya, confirming its rank as the leading cancer for all sexes combined. Liver ultrasound coupled with alpha-fetoprotein dosage was the main diagnostic criterion used. CT scanning, which was supposed to be the main diagnostic criterion for nodules larger than 2 cm, was not available before 2019 and has since experienced frequent breakdowns. The late diagnosis of this cancer in our context did not allow for curative therapies; most of the treatment was palliative. A real public health strategy based on vaccination should be implemented to prevent contamination by the hepatitis B virus, the main cause of hepatocellular carcinoma in Africa.

Conflicts of Interest

The authors declare no conflict of interest regarding the publication of this paper.

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