

Epidemiology and Prognosis of Hepatocellular Carcinoma (HCC) in the Internal Medicine Department of the Bouake University Hospital (Côte d'Ivoire)

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Abstract

Background and Objective: Hepatocellular carcinoma (HCC) is a public health problem due to its high incidence and high mortality rate. The epidemiology and prognosis of this disease is poorly documented in Bouake. The aim of the study was to describe the epidemiological aspects and identify the predictors of death in patients hospitalized for HCC in the Internal Medicine Department of the Bouake University Hospital in order to improve patient management. **Material and Methods:** We conducted a cross-sectional study from 1 January 2020 to 31 December 2022 in the Internal Medicine Department of Bouake University Hospital, involving 160 patients. **Results:** The prevalence of HCC was 3.6%, the mean age was 48.86 ± 14.5 years with extremes of 14 and 90 years and the sex ratio was 2.90. Viral hepatitis B was observed in 81% of patients, with HBs Ag positivity in 71.2%. The performance status of WHO was ≥ 2 in 93.2% of cases. HCC was discovered at advanced stage respectively in 51% for BCLC C and 47.8% for BCLC D stage. The nodules were multiple (89.3%), and superior to 3 cm. The hospital mortality was 20% and BCLC D stage of HCC was significantly associated with death ($p = 0.04$) in the univariate analysis. The BCLC D stage of HCC was significantly associated with death. Length of stay inferior to 5 days (OR = 0.77; CI 95: 0.61 - 0.96) and hepatic encephalopathy (OR = 1.39; CI 95: 1.10 - 1.77), were the two independent predictors of mortality. **Conclusion:** HCC mainly affected young men infected with chronic viral hepatitis B. Short

length of stay and hepatic encephalopathy were independent predictors of mortality.

Keywords

Liver Cancer, Viral Hepatitis, Death, West Africa

1. Introduction

HCC is the most common form of primary liver cancer and a major public health problem [1]. It is the sixth most common cancer in the world, responsible for more than 700,000 deaths per year [2], and generally occurs in the most active age group of the population between 30 and 60 years of age, particularly in sub-Saharan Africa with high mortality [3] [4].

The geographic distribution of the incidence of HCC tends to mirror that of its major risk factors, chronic hepatitis B and hepatitis C virus infection, which account for approximately 56% and 20% of all HCC cases, respectively [5]-[7]. Historically, sub-Saharan Africa has been classified as hyper-endemic for chronic hepatitis B based on the detection of HBsAg among $\geq 8\%$ of the general population [8]. A general population survey led by Boa in Côte d'Ivoire, found that prevalence of chronic hepatitis B was 13 [9]. Diagnostic methods of HCC have evolved considerably over time, allowing easy diagnosis using minimally invasive methods and early detection using increasingly specific biomarkers, particularly in medically advanced countries [10]. Treatment of HCC is well codified and depends upon the stage of the disease, defined by classifications. The Barcelona clinic liver cancer (BCLC) classification is one of the most widely used [11] [12]. When HCC is discovered at an early stage, curative treatment such as transplantation, liver resection or radiofrequency may be proposed. Unfortunately, in countries with limited resources, HCC mortality remains very high due to late diagnosis and absence of any real program to raise awareness and screen for the main HCC risk factors [8]. Several west African studies have already focused on HCC, but few of them have clearly identified the predictors of poor prognosis of this disease [13]-[16]. A recent study carried out at University Hospital of Bouake, in the Internal Medicine Department showed that HCC accounts for 58.8% of all cancers, but did not deal specifically with epidemiology and prognosis of HCC [17]. The aim of the study was firstly to describe epidemiological aspects and then identify the predictors of mortality to improve management of patients.

2. Material and Methods

We conducted a cross-sectional study using the medical records of patients hospitalized for HCC on a healthy liver or on a cirrhosis liver from 01 January 2020 to 31 December 2022. This was an exhaustive sample of 160 patients with HCC who met the following inclusion criteria:

- All patients with a hepatic nodule on a cirrhotic liver with wash-in wash-out vascular kinetics on abdominal CT;
- All patients with a hepatic nodule or mass on a cirrhotic liver with evidence of portal thrombosis on ultrasound or abdominal CT;
- All patients with histologically confirmed HCC in non-cirrhotic liver with or without significant elevation of AFP. The normal adult value was less than 20 ng/ml. An AFP level ≥ 400 ng/ml was considered significant but a level < 400 ng/ml did not rule out the diagnosis.

Non-inclusion criteria:

- Inpatients without abdominal ultrasound or CT scan;
- Patients with another form of primitive liver cancer;
- Patient with secondary liver cancer;
- Insufficient information in the medical record for the studied parameters.

Data were collected on an anonymous, standardized survey form designed for this purpose. The parameters studied were:

- Socio-demographic (age, sex, level of education, profession, marital status);
- Clinical (performance status (WHO), signs of hepatocellular insufficiency, signs of portal hypertension, Glasgow score, oedema-ascitic decompensation).
- Prognosis: Child's score, BCLC score, patient outcome;
- Complications of cirrhosis: infection of ascites fluid, digestive hemorrhage, etc.
- Ultrasound parameters (size of liver, number of nodules, presence of portal thrombosis, liver metastases).

Data were processed and analyzed using epi info7 software. Word and Excel were used for graphical representations. Quantitative variables were expressed as median or mean with extremes, and qualitative variables were expressed as proportion. The Chi-square test was applied to find a relationship between qualitative variables. When the expected number of participants was less than 5, the Fisher test was applied. The significance level was less than 5% for univariate analyses. Then we performed multivariate analysis when a link was found.

The study respected the principles of the Declaration of Helsinki.

3. Results

During the study period, 4341 patients were hospitalized in the Internal Medicine Department, including 160 for HCC, representing a prevalence of 3.6%. The mean age was 48.86 ± 14.5 years, with extremes of 14 and 90 years, and the sex ratio was 2.90. Patients were mainly farmers (41%) and housewife (21%). The sociodemographic characteristics of patients are presented in **Table 1**. The performance status was ≥ 2 in 93.2%. Hepatic encephalopathy was found in 28.1% and HCC was discovered at an advanced stage in 98.8%. The nodules size was > 3 cm (89.3%), multiple (72.1%) with vascular invasion (34.4%) and extra-hepatic metastasis (43.4%) as detailed in **Table 2**, showing clinical and radiological characteristics of patients with HCC. In-hospital mortality was 20% and BCLC D score was significantly associated with death in univariate analysis. Length of stay < 5 days, RR =

0.77 (0.61; 0.96) and hepatic encephalopathy, RR = 1.39 (1.10; 1.77), were the two independent predictors of mortality (**Table 3**).

Table 1. Socio-demographic characteristics of patients with HCC.

Characteristics	Number of Patients (n = 160)	Percentage
Age		
<35	24	15.0
35 - 64	113	70.6
≥65	23	14.4
Gender		
Male	119	74.4
Female	41	25.6
Education Level		
No	53	33.1
Primary	73	45.6
Secondary	27	16.9
University	07	04.4
Profession		
Farmer	67	41.9
Housewife	35	21.9
Trader	18	11.2
Civil Servant	14	08.8
Craftsman	14	08.8
Other	12	07.4
Marital Status		
Single	127	79.4
Married	26	16.3
Widowed	07	04.3
Religion		
Christian	49	30.6
Muslim	99	61.9
Animist	12	07.5

Table 2. Clinical and radiological and prognostic characteristics of patients with HCC.

Characteristics	Number of Patient	Percentage
Performance Status		
0	02	01.2
1	09	05.6

Continued

2	71	44.4
3	59	36.9
4	19	11.9
	160	
Hepatic Encephalopathy		
No	115	71.9
Yes	45	28.1
Grade I	24	15.0
Stade II	14	08.8
Stade IIIa	06	03.7
Stade IIIb	01	0.6
	160	
Abundance of Ascites		
Low	54	33.8
Moderate	40	25.0
High	66	41.2
	160	
Child-Pugh Score		
A	29	18.1
B	110	68.8
C	21	13.1
	160	
BCLC		
A	-	-
B	2	01.2
C	82	51.3
D	76	47.5
Nodules Size		
2 - 3 cm	8	10.7
>3 cm	67	89.3
	75	
Number of Nodules		
1 - 3	45	27.9
Multiple	115	72.1
	160	
Vascular Invasion		
Yes	55	34.4

Continued

No	105	65.6
	160	
Extrahepatic Metastasis		
Ganglion	23	43.4
Peritoneum	15	29.4
Pleura	13	25.5
Lung	12	23.5
Heart	02	03.9
Spine	01	01.9
	53	

Table 3. Factors associated with death through univariate and multivariate analysis.

Characteristics, n (Patients)	Death+	Death-	P-Value	Risk-Ratio CI 95%	Adjusted Odd-Ratio	P-Value
Gender, (160)						
Male	27	92	0.14	1.13		
Female	05	36		(0.97; 1.31)		
Age, (160)						
≥65 years	05	16	0.63	0.94		
<65 years	27	112		(0.73; 1.21)		
HBS Antigen, (132)						
Yes	20	74	0.97	0.99		
No	08	30		(0.82; 1.21)		
Length of stay, (160)						
≥5 days	15	29	0.006	0.77	0.28	0.001
<5 days	17	99		(0.61; 0.96)	(0.12; 0.68)	
Child-Pugh score C, (160)						
Yes	06	15	0.29	1.13		
No	26	113		(0.85; 1.50)		
Encephalopathy, (160)						
Yes	17	22	0.0004	1.39	3.63	0.004
No	15	100		(1.10; 1.77)	(1.49; 8.85)	
Performance Status (WHO) ≥ 3						
Yes	20	58	0.08	1.13		
No	12	70		(0.95; 1.35)		
Extra-Hepatic Metastasis, (160)						
Yes	16	45	0.10	1.14		
No	16	83		(0.98; 1.35)		

Continued

		Portal Vein Invasion, (149)					
Yes	10	45	0.76	1.02			
No	19	75			(0.87; 1.20)		
		BCLC D, (158)					
Yes	20	57	0.04	1.15	1.63	0.28	
No	12	71			(0.98; 1.35) (0.65; 4.05)		
		Gastro-Intestinal Hemorrhage, (158)					
Yes	03	26	0.14	1.15			
No	29	100			(0.70; 8.90)		
		Ascitic Fluid Infection, (155)					
Yes	09	33	0.83	0.98			
No	23	90			(0.82; 1.18)		

4. Discussion

The aim of the study was to describe the epidemiology and determine prognostic factors of HCC in the Internal Medicine Department of Bouake University Hospital in order to improve patients management.

Epidemiology of HCC

The hospital prevalence of HCC (3.6%) was relatively low in our study. Two West African studies found similar prevalences, notably those of Kpossou in Benin (3.4%) and Touré in Senegal (3.15%) [18] [19].

In Abidjan (Côte d'Ivoire), Kissi found a prevalence of 12% in the hepato-gastroenterology department [20]. Thus, the prevalence of HCC varied considerably depending on the study site. This difference in prevalence could be explained by the multiplicity and diversity of pathologies encountered in internal medicine. Within this multitude of pathologies, HCC affected, in accordance with the literature, young adults with an average age of 48 years and a clear male predominance. The mean age at diagnosis of HCC, although very heterogeneous, is lower overall in sub-Saharan Africa (46.3 years) than in Europe (63.2 years), the United States (58.2 years) or East Asia (58.8 years) [21]. The relative youth of HCC patients in African studies could be explained by the earlier vertical or horizontal transmission of viral hepatitis B, the main risk factor for HCC in Africa [3]. The predominance of males in the disease was observed in the studies, with different ratios of up to 4 to 8 in areas of high incidence [15] [19], partly explained by the protective role of estrogens in women [22].

In our study, patients globally had a low level of education and more than 40% of them were farmers. This result is similar to that of Kondé in Mali [14], in which the majority (49.1%) of patients were farmers and highlights the negative impact of low socio-economic status on health. In fact, patients belonging to low socio-economic status are at a significant disadvantage due to low health literacy, limited

healthcare resources and access-including lack of insurance or ability to pay for care, especially for care of preventable diseases such as HBV [16].

5. Risk Factors

5.1. Viral Hepatitis B and C

In our study, chronic viral hepatitis B was the main risk factor for HCC, with HBsAg positivity in 70% of patients followed by chronic hepatitis C. Dicko, also found high proportion of patients with positive HBs Ag (60.2%) [23].

This can be explained by the high frequency of chronic hepatitis virus B in west Africa where 82.3 million people are infected [24]. For viral hepatitis C, the prevalence is much higher in North Africa [3] [13] [14] [25].

5.2. Other Risk Factors for HCC

In addition to hepatitis B and C, alcohol and diabetes were also observed in our study, but at a lower frequency. Alcohol consumption is the second leading risk factor for HCC after viral hepatitis [1].

The WHO estimates that 2.3 billion people are alcohol drinkers, consuming 32.8g of pure alcohol per day [26]. However, alcohol consumption varies widely from one continent to another, from 20 to 40% in sub-Saharan Africa and 40 to 80% in Europe and the United States of America [27]. Our study found a lower prevalence of alcohol consumption (10%); this prevalence was close to that of Kpossou (12%) and Kondé (12.7%), in West Africa [14] [18]. The low prevalence of alcohol consumption observed in our study could be explained by the hospital source of our data. Despite its low frequency in our HCC series, diabetes remains a risk factor for HCC in the literature, especially when the disease has progressed for more than 10 years [28].

6. Prognosis of HCC

The comparison of our prognostic results with those of other authors Africa (Côte d'Ivoire, Benin, Gambia) and Europe (France) consistently showed that patients presented late with advanced HCC at the time of diagnosis (BCLC C or D) in more than 80% of patients [18] [20] [29] [30]. However, the performance status (PS) was better in Lascols study (France), with a PS = 0 or 1 in 59.8% of cases [30], compared with a PS >1 in more than 90% in Côte d'Ivoire and Benin [18] [20], and over 60% in Gambia [29]. In our study, the nodules were larger than 3 cm in almost 90% of cases, multiple in two-thirds of cases and portal vein invasion was noted in one-third of cases. These results were comparable to those of Lascols and Nikiéma (Burkina Faso) in terms of size and number of nodules. However, the proportion of vascular invasion was much higher in the Nikiéma study (56.8%), whereas it was almost the same (34.5%) in the Lascols one [15] [30]. This difference in portal vein invasion is probably linked to the fact that the study of Nikiéma was carried out in a radiology department.

We found an in-hospital mortality rate of 20%. Other authors noted a considerably higher mortality close to 40% [18] [19]. This lower mortality observed in our work is probably related to the large number of patients who left against medical advice. Mortality was significantly associated with end-stage HCC in univariate analysis. Multivariate analysis found that length of stay < 5 days and hepatic encephalopathy were independent predictors of mortality. In the study of Natey in Ghana, hepatic encephalopathy was also identified as an independent predictor of mortality but the confidence interval was larger than in our study (OR = 5.66; CI 95: 1.10 – 29.2 vs OR = 3.63; CI 95: 1.49 – 8.85) [16]. However, this study was carried out on patients with HCC or cirrhosis without HCC, whereas our study concerned patients with HCC only.

One of the limitations of this study may be the fact that the patients were selected only in the Internal Medicine inpatient department could constitute a selection bias. However, very few cases are diagnosed as part of the follow-up of cirrhosis in our practice [20].

7. Conclusion

HCC mainly affected young men infected with chronic viral hepatitis B. The high mortality rate of HCC was linked to the advanced stage of the disease at the time of diagnosis. Short length of stay and hepatic encephalopathy were independent predictors of mortality. Vigorous management of patients during the first few days of hospitalization, including early treatment and prevention of hepatic encephalopathy, could reduce in-hospital mortality.

Conflicts of Interest

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

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