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Liver Cancer Survival and Prognostic Factors in a High Endemic Area of Hepatitis B

Kounpièlimè Sosthène Somda[1,2*], Abdoul Fataho Kabore[1], Aboubacar Coulibaly[1,2], Sandrine Marie Odile Soudre[2], Toussaint Vebamba[1], Christiane Bere[1], Arsène Roger Sombie[1,2]

[1]Department of Hepato-Gastroenterology, Yalgado Ouedraogo University Hospital, Ouagadougou, Burkina Faso
[2]Department of Medicine, Joseph KI Zerbo University, Ouagadougou, Burkina Faso
Email: *sosthenesomda@gmail.com

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Abstract

Background: Hepatitis B infection is a global public health problem especially in developing countries with high prevalence, and liver cancer is its most feared complication. In these countries the majority of infections occur in early childhood with the corollary of a frequent transition to chronicity and increased risk of liver cancer. For various reasons, these cancers are diagnosed at a late stage, resulting a high mortality rate. The aim of this work was to study survival and prognostic factors in patients with liver cancer in the gastroenterology department at the Yalgado Ouédraogo University Hospital in Burkina Faso. **Patients and Methods**: it was a cross-sectional, descriptive and analytical study with retrospective collection in the Gastroenterology department at the Yalgado Ouédraogo University Hospital. The collection period was 12 months, from January 1st to December 31st 2023. The study population consisted of all the patients who had been hospitalized in the Gastroenterology department during the period. Any patient in whom the diagnosis of liver cancer was established was included. The diagnosis was established on clinical and paraclinical criteria. Patients hospitalized with another diagnosis were excluded. The data were analyzed by Epi-Info software. Texts, graphs and table have been produced by Word and Excel Software 2016. Quantitative variables were expressed as mean and standard deviation, and qualitative variables as number and percentage. A difference was considered significant when the p-value was less than 5%. **Results**: During the study period, 339 patients were hospitalized,107 of whom had liver cancer, representing a prevalence of 31.56%. The mean age was 40.56 years. Men were the most affected, with a sex ratio of 4.6. The mean antecedents were alcohol 33.96%, and hepatitis B. The majority (59.43%) of our patients consulted between 1 and 3 months. Seventy percent of patients were under 60 years old. Hepatitis virus B and/or C were

found in 89.7% of cases; 60.74% of our patients were in stage D of BCLC classification; 66.33% had died. The median survival was 2 months, with overall survival at 6 months estimated at 30% and zero at 14 months. In the multivariate cox model, after adjusting for the other covariables, Child-Pugh stage C, BCLC stage D and sex male were statistically associated as prognostic factors of death with Hazar ratios of 2.66; 3.75 and 2.21 respectively. **Conclusion:** Liver cancer is often diagnosed late in our context with a median survival less than 2 months. Viral hepatitis is the main cause so, preventive measures should be taken as well to decrease liver cancer prevalence.

Keywords

Liver Cancer, Survival, Prognostic Factors, Burkina Faso

1. Introduction

Hepatitis B infection is a global public health problem especially in developing countries with high prevalence, and liver cancer is the most feared complication. In these countries, the majority of infections occur in early childhood with the corollary of a frequent transition to chronicity and increased risk of liver cancer. For various reasons, these cancers are diagnosed at a late stage, resulting a high mortality rate. These cancers can be primary, *i.e.* developed directly at the expense of the liver, or they can be secondary, in which case the liver is only a site of extension of a malignant tumor developed at the expense of another organ. Primary liver cancers are epithelial malignancies, intrahepatic bile ducts, blood vessels, or connective tissues of the liver [1].

The leading causes of primary liver cancer include hepatitis B virus (HBV), hepatitis C virus (HCV), alcohol consumption, non-alcoholic fatty liver disease (NAFLD), and other causes of liver disease that lead to cirrhosis [2]. In Sub-Saharan Africa region, the hepatitis B virus is the leading cause of liver cancer, also the role of Aflatoxin B in cancer cannot be neglected. Survival for liver cancer depends largely on the stage at the time of diagnosis. Liver cancer is one of the most aggressive digestive cancers. In recent years, treatments have made great progress due to the therapeutic revolution [3]. Ward *et al.* found that the baseline estimated survival was 4.1% in low income countries [4].

The aim of this study was to determine the survival and the prognostic factors associated with the survival of patients with liver cancer at Yalgado Ouédraogo University Hospital in gastroenterology department.

2. Patients and Methods

It was a cross-sectional study with descriptive and analytical aims with retrospective collection in Gastroenterology department at Yalgado Ouédraogo University Hospital; conducted from January 1st to December 31st 2023. All patients of both

sexes hospitalized in gastroenterology department were the study population. Were included whom with a diagnosis of primary liver cancer. The diagnosis of primary liver cancer was established on the basis of clinical and paraclinical arguments. The clinical arguments were hepatomegaly with an irregular surface associated or not with an alteration in general condition, jaundice, ascites, hepatic encephalopathy. The paraclinical arguments were ultrasound or computed tomography (CT) showing intrahepatic characteristic nodules of liver cancer (wash in and wash out in CT) associated or not with an increase in the feto protein alpha level greater than or equal to 400 IU/ml. The staging procedures were based on the Barcelona Clinic Liver Classification (BCLC), and the prognostic factors on the Child-Pug Classification. The therapeutic procedures were BCLC criteria adapted to local conditions.

The data were collected on a collection sheet, then entered on a laptop computer and analyzed using EPI-INFO software. The texts, graphs and tables were created with Word and Excel 2016 software. Quantitative variables are expressed as mean and standard deviation; qualitative variables in terms of number and percentage.

3. Results

- **Frequency**

During the study period, 339 patients were hospitalized in the hepato-gastroenterology department. Among them, 107 cases of primary liver cancer representing a hospital frequency of 31.56%.

- **Socio-demographic characteristics**

✓ Distribution by sex, occupation and area of residence

The mean age was 40.56 years. Men were the most affected, with a sex ratio of 4.6.

✓ Distribution of patients according to the time taken before the consultation

- **Prognostic factors**

Liver Cancer and Child Pugh Classification: Class B represented 40 patients, *i.e.* 37.38% of cases; followed by class C with 34.57% and finally class A with 28.03% of cases.

Liver cancer and BCLC classification: sixty-five patients were classified as BCLC C stage (60.74%). Forty-two patients classified as BCLC D stage (39.25%). No patients were classified as stage A or stage B.

✓ Distribution of patients according to etiologies

- **Survival: the overall survival was 2 months and male survival was lower than female**

✓ Survival according to BCLC classification: the survival decreases according the stage of BCLC classification. The survival is lower in stage D than the stage C.

✓ Factors associated with survival

The stage D of BCLC ($p = 0.001$), the Child Pugh C ($p = 0.006$) and the sex male ($p = 0.049$) are identified as factors negatively associated to the survival.

4. Discussion

- **Socio-demographic characteristics of patients**

Our study consisted of 82.24% men and 17.78% women, *i.e.* a sex ratio of 4.6 in favour of men (Table 1). The predominant male involvement is classic according to THOT'O *et al.* [5] in Côte d'Ivoire in 2007, the sex ratio was 2.54. BOUGLOUGA *et al.* [6] in Togo in 2012 found a sex ratio of 2.9 in favour of men. The male predominance was also found by SOME *et al.* [7] in Burkina Faso and DIARRA *et al.* [8] in MALI with a sex ratio of 3 and 3.5 respectively. The high prevalence of male patients in this study confirms previous findings that the diagnosis of hepatocellular carcinoma (HCC) is up to four times more common in men than in women. Hepatitis virus B and/or C were the etiologies of liver cancer in 89.7% of cases (Table 2). This male predominance is explained by the high exposure of men to risk factors such as tobacco, alcohol consumption, chronic HBV or HCV infection. Estrogen, through its inhibitory effect on the secretion of interleukin-6, would also help to better protect women [9].

Table 1. Distribution by sex, occupation and area of residence (N = 107).

Features	effective	percentages
Sex (n = 107)		
Man	88	82.22
Wife	19	17.78
Profession (n = 107)		
Farmer	43	40.18
merchant	14	13.08
Housewife	11	10.28
Public servant	9	8.41
Retirement	10	9.34
Informal private sector	11	10.28
Student and pupil	9	8.41
Residence area (n = 107)		
Urban	36	33.64
Rural	71	66.36

Table 2. Distribution of patients according to etiologies (n = 107).

Etiology	workforce	Percentages
Hepatitis B	68	63.55
Hepatitis C	7	6.54
Hepatitis B and C	6	5.60
Mixed*	15	14.01
Unknown	11	10.28

*Mixed: viral + alcohol; Hepatitis virus B and/or C were found in 89.7% of cases.

In our study, the mean age of the patients was 40.56 years as shown in Figure 1. This result is similar to the mean ages found by SOME *et al.* [7] in Burkina Faso in 2017 and NOAH *et al.* [10] in Cameroon in 2014 which were 43.9 years and 41.2 years respectively. In Benin, GNANGNON *et al.* [11] in 2023 reported an average age of 51.7 years. Our data are different from those found by FOUCARD *et al.* [12] in France in 2014 and PIRSON in Belgium [13] which found an average age of 69 and 65 years respectively. This age difference could be explained on the one hand by the rate of HBsAg carriage in young African people whose contamination would have occurred in the perinatal period or during childhood due to residence in an area of high HBV prevalence and on the other hand by the alcoholic origin of cirrhosis degenerated into carcinoma in Europe where alcohol consumption increases with age. The mean antecedents were alcohol 33.96%, and hepatitis B as shown in Figure 2. The majority (59.43%) of our patients consulted between 1 and 3 months as shown in Figure 3. Our study shows that farmers were the most affected, *i.e.* 40.18% of cases which is shown in Table 1. In New Zealand, Bevin *et al.* [14] also reported a high frequency among male, *i.e.* 65% of cases. Unlike Bouglouga *et al.* [6] in Togo, who found a higher frequency among civil servants. Our results are in agreement with the data in the literature according to

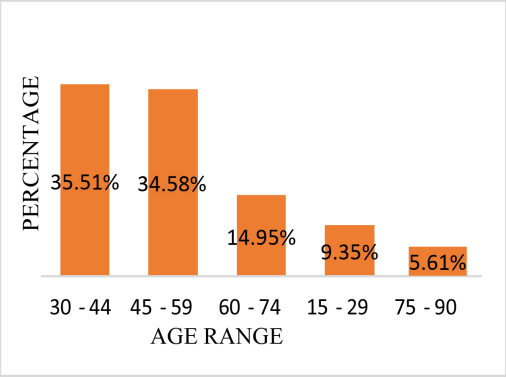

Figure 1. Age distribution of patients (n = 107).

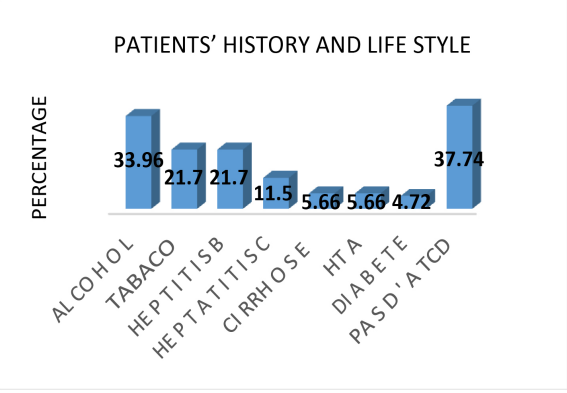

Figure 2. Distribution of patients according to their history (n = 107).

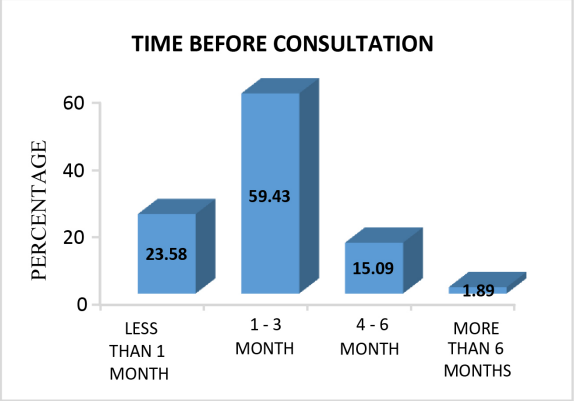

Figure 3. Distribution of patients according to their history (n = 107).

which primary liver cancer is highly common in low-income social strata [8]. This can be explained on the one hand by the unhealthy lifestyle and exposure to the hepatitis B virus by transfusion or sexual route and the consumption of alcohol, especially adulterated in Burkina Faso [10]. And on the other hand, by the exposure of the rural population to aflatoxin B due to the poor storage of cereals.

- **Prognostic factors associated with survival**

In multivariate cox model, after adjusting for the other covariables, Child-Pugh stage C, BCLC stage D and sex male were statistically associated as prognostic factors of death with Hazar ratios of 2.66; 3.75 and 2.21 respectively which is summarized in **Table 3**.

Table 3. Represents the final model of our multivariate analysis.

FEATURES	HR	95% IC	P
Sex			
Women	—	—	
Man	2.21	1.00 – 4.86	**0.049**
Child Pugh Classification			
Child Pugh A	-	-	
Child Pugh B	1.76	0.89 - 3.46	0.10
Child Pugh C	2.66	1.32 - 5.39	**0.006**
BCLC classification			
BCLC C	-	-	
BCLC D	3.75	1.25 - 3.68	**0.001**

Child-Pugh Classification: In our study, stage B was the most represented with 37.38% of cases; stage C was the most represented with 34.57%, and stage A was

the most represented with 28.03% of cases. The higher percentage of patients in classes B and C can be explained by a delay in the diagnosis of our patients. In Burkina Faso, Ouili *et al.* [15] reported frequencies of 30.9%, 25.7% and 43.4% for the three (3) stages A, B and C in the same order. In Egypt, YANG *et al.* [16] reported frequencies of 36% for stage A, 62% for stage B, and 2% for stage C. In Senegal, DIALLO *et al.* [17] found 15.8% of cases at stage A, 59.6% of cases at stage B and 24.6% of cases at stage C. In France CONDAT *et al.* [18] noted 36.1% for stage A, 45.8% for stage B and 15.3% for stage C.

BCLC Classification: In our study, 60.74% of our patients were classified as BCLC stage C and 39.25% as stage D. None of our patients were classified as stage A, which testifies to the delay in consultation in our context. These proportions are similar to those found by OUILI *et al.* [15] in Burkina Faso, which reported 57.7% for stage C and 42.3% for stage D. In Côte D'Ivoire, DIOMANDE *et al.* [19] also found similar figures, *i.e.* 65% for stage C and 33% for stage D. NGATALI *et al.* [20] in Congo reported 5.41% of cases at stage B, 62.16% of cases at stage C and 32.4% at stage D (no patients were at stage A). In France, CONDAT *et al.* [18] reported in 2022; 6.1% of patients in stage 0, 29.8% in stage A, 28.8% in stage B, 32.1% in stage C and 3.2% in stage D. From these studies, it appears that the majority of patients in Africa (71% to 97.62%) as in our study, are at the advanced or terminal stage (C and D) [21]. This is explained by the late diagnosis of patients.

- Survival

Overall survival: 66.33% of our patients had died, and the median survival was estimated at 2 months as shown respectively in **Figure 4** and **Figure 5**. In Burkina Faso, Mande *et al.* [4] reported a median survival of 3.6 months while Ouili *et al.* [15] reported a median survival of 1 month. In Benin, GNANGNON *et al.* [11] corroborated our results with a median survival of 2 months. In Central Africa, in Cameroon, NOAH *et al.* [10] found a median survival of 3.45 months. BOUALI *et al.* [22] in Tunisia reported a median of 5 months. The low median survival in Africa compared to Western countries could be explained: on the one hand, by a delay in diagnosis due to late consultation; on the other hand, the lack of financial resources for patients as well as the limited technical platform. Indeed, in France, FOUCARD *et al.* [12] reported a median survival of 15.6 months after diagnosis. These data are much higher than ours and observations in Africa. In an international study PARK *et al.* [23] in 2015 reported a median survival of 60, 33, 31, 24 and 23 months for patients from Japan, North America, South Korea, Europe and China respectively ($P < 0.0001$). Primary liver cancer is therefore associated with a very poor prognosis in the world in general and specifically in sub-Saharan Africa. Our study showed an overall survival rate after 6 months of 10% and zero at 13.5 months. Bouglouga *et al.* [6] in Togo reported an estimated 6-month survival rate of 40%. Our results in Africa are significantly lower than those of BELTRAN *et al.* [24] in France, which found an overall survival at 6 months estimated at 79%. In the same country, GRADOS *et al.* [25] found 83.9% overall survival at 6 months. These French data are significantly lower than those from Japan, where

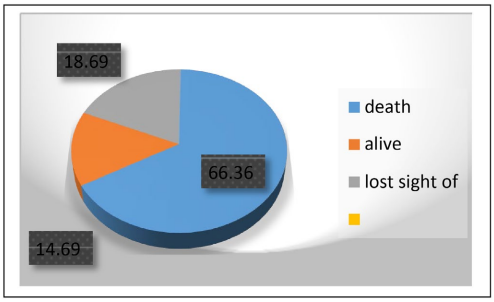

Figure 4. Distribution of patients according to mortality (n = 107).

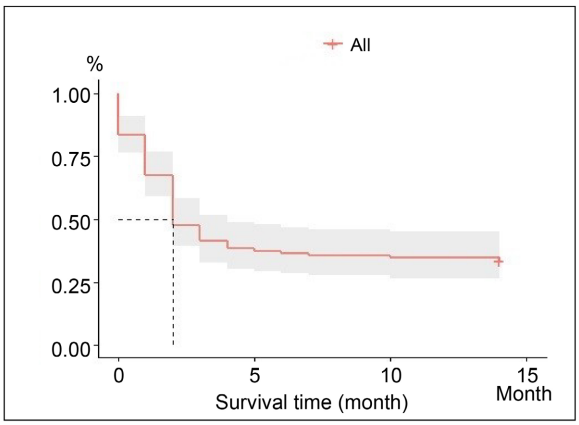

Figure 5. Overall survival curve of all patients (p = 0.001).

several authors such as GOUTTE *et al.* [26] and ROSA *et al.* [27] have noted a 6-month survival rate estimated at 90% and 91%, respectively. These high proportions compared to ours may testify to a treatment advance such as liver transplantation in these developed countries. Indeed, liver transplantation treats HCC and the underlying liver disease at the same time, thus improving survival. Moreover, the CPF remains associated with a poor prognosis at the global level, the mortality/incidence ratio was estimated at 0.95 according to GLOBOCAN 2012. *Survival and BCLC Classificatio*n: in our study the survival was significaly different between the stages as shown in **Figure 6** (P = 0.049). The median survival was 1.8 months for BCLC C and 1.4 months for BCLC D. In Canada, a study conducted by the Canadian Cancer Society in 2019 reported a median survival of 11 to 13 months with treatment, and 6 to 8 months without treatment for BCLC C stage [28]. According to GRADOS *et al.* [25], in France, median survival was eight times higher than ours for BCLC C stages and 6 months for BCLC D. The percentages of survival at 6 months were 8% and 6% respectively for patients classified as BCLC stages C and D. The mean survival was better in female than in male as shown in **Figure 7** (P = 0.05). KEDAR *et al.* [28] found a survival rate of 30% for Egypt and 15% for sub-Saharan Africa at 6 months in patients classified as BCLC C stage. In the same study, KEDAR *et al.* [28] reported a survival rate of 17% for Egypt and 10% in sub-Saharan Africa for BCLC D stage, 6 months after diagnosis.

Our proportions are lower than those found in Europe, in fact GRADOS [25] in France recorded a 6-month survival rate estimated at 69.8% for the BCLC C stage and 50.9% for the BCLC D stage. In Japan, ROSA *et al.* [27] reported 6-month survival percentages estimated at 75% for the BCLC C stage and 60% for the BCLC D stage. This difference in the proportion of data in our study and those of Europe and other parts of the world can be explained by a less adequate technical platform in our context where the most advanced treatments are not yet a reality.

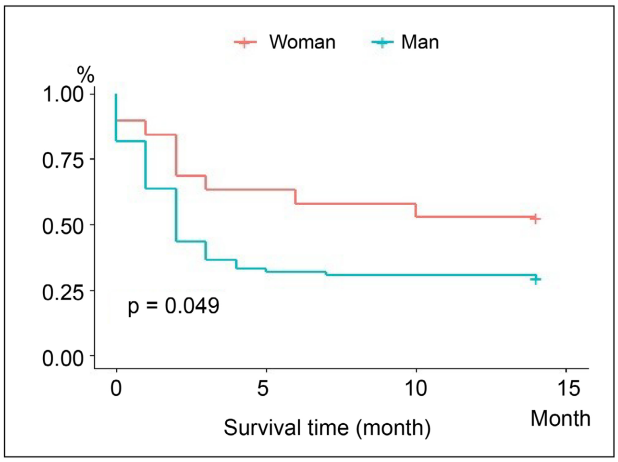

Figure 6. Sex-specific survival curve of patients (p = 0.049).

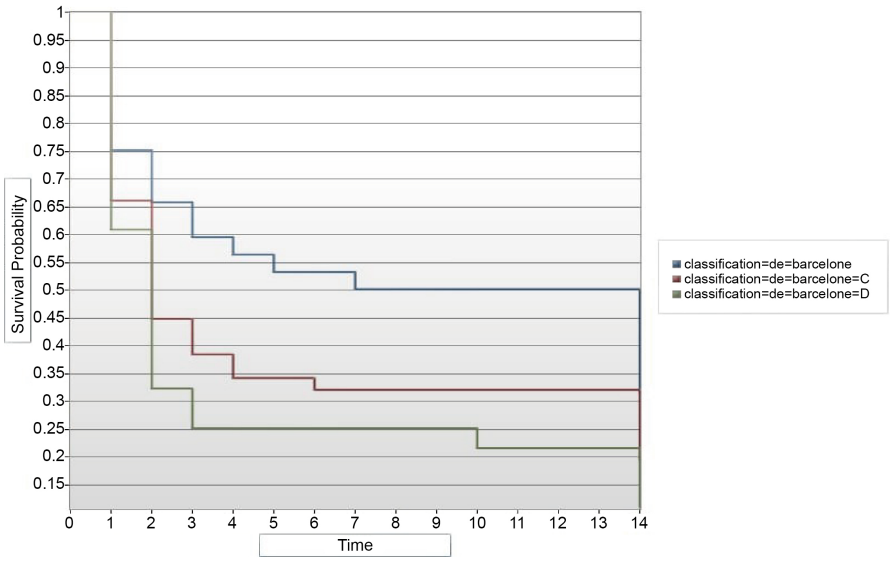

Figure 7. Survival according to BCLC classification (p = 0.055).

5. Conclusion

Primary liver cancer remains a major challenge in terms of survival. Progress in understanding prognostic factors such as: tumor characteristics, liver function, the patient's general condition and the treatments performed, which in turn depend on other prognostic factors, is essential to improve clinical outcomes. The

adoption of a multidisciplinary approach from the early stages of the pathology, combined with the integration of targeted therapeutic advances, raises certain hope for improved long-term outcomes. In sum, this descriptive and analytical study allowed us to highlight factors associated with survival such as male sex, the Child-Pugh classification and the BCLC D classification. It was therefore necessary to relentlessly promote further research to better understand the mechanisms of the disease and to develop treatment strategies more effective in improving survival and quality of life in patients with liver cancer.

Conflicts of Interest

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

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