Original article

Epidemiology of Hepatitis B-Associated Hepatocellular Carcinoma in Cameroon.

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Abstract

Background

Chronic hepatitis B virus (HBV) infection and cirrhosis are major risk factors for the development of hepatocellular carcinoma (HCC). In Cameroon, which is a highly endemic zone for HBV, its epidemiologic characteristics are not known. The aim of our study was to determine the epidemiologic characteristics of hepatitis B-associated HCC in our milieu for a better management of the disease.

Methods

Patients suffering from HCC in two hospitals in Yaounde were sampled and screened for HBV, HCV and HDV. Only HBV related HCC were enrolled. Demographic characteristics, presence or not of cirrhosis, excessive alcohol consumption (>80g/day) and smoking were analyzed.

Results

A total of 34 cases of HCC were identified. The mean age was 38.5±12.3 years (extremes 18 – 74 years); 79.4% (27/34) were males (sex ratio 3.9:1); 55.9% (19/34) had cirrhosis while 44.1% (15/34) were non cirrhotic. Also, 44.1% (15/34) were smokers and 2.9% (1/34) were alcoholics. The prevalence of HCC was 14.7%, 47.7%, 20.6%, 11.8% and 5.9% amongst those below 30 years, 30–39 years, 40–49 years, 50–59 years and 60 years and above respectively. There was no statistically significant difference between the mean ages of cirrhotic and non cirrhotic patients (38.9±11.3 vs. 38.0±14 years, p=0.08). The majority of patients below 30 years had no cirrhosis at the moment the diagnosis of HCC was made (80% vs. 39.9%, p=0.08). Cirrhosis was more frequent amongst those aged 30–39 years (68.8% vs. 44.4%, p=0.16). There was no other difference between cirrhotic and non cirrhotic patients. Neither alcohol nor smoking had no a synergic effect in the development of HCC.

Conclusion

Most patients with hepatitis B-associated HCC in Cameroon are aged below 40 years. Cirrhosis is not always present at diagnosis. The epidemiologic profiles of cirrhotic and non cirrhotic patients are similar. The influence of alcohol and tobacco is negligible. The introduction of HBV vaccine in the extended immunization program in 2005 was thus necessary in our country.

Key words:

Hepatocellular carcinoma, hepatitis B, developing countries, epidemiology, Cameroon.

Résumé :

Objectifs

L'infection chronique au virus de l'hépatite B (VHB) et la cirrhose sont les risques majeurs du développement du carcinome hépatocellulaire (CHC) à l'échelon mondial. Au Cameroun, zone hyper endémique au VHB, les caractéristiques épidémiologiques du CHC ne sont pas déterminées. Le but de notre étude était de déterminer les caractéristiques du CHC lié au VHB dans notre milieu pour une meilleure prise en charge de l'affection.

Méthodes

Etude prospective dans deux hôpitaux de Yaoundé, chez les malades atteints de CHC confirmé et dépistés pour le VHB, le virus C et le virus Delta, de mars 2012 à janvier 2013. Les cas de CHC associés au VHB ont été enrôlés. Les caractéristiques démographiques, la présence de cirrhose, l'abus d'alcool (>80g/jour) et le tabagisme ont été enregistrés.

Résultats

Au total 34 cas de CHC avérés ont été identifiés. L'âge moyen était de 38,5±12,3 ans (extrêmes 18-74ans) ; 79,4% (27/34) étaient de sexe masculin (sex ratio H/F : 3,9) ; 55,9% (19/34) avaient une cirrhose, 44,1% (15/34) sans. Aussi, 44,1% (15/34) étaient fumeurs et 2,9% (1/34) étaient alcooliques. La prévalence du CHC était significative dans la tranche d'âge de 30-39 ans avec 47,7% (16/34). La moyenne d'âge des cirrhotiques et non-cirrhotiques n'était pas différente (38,9±11,3 versus 38,0±14 ans, p=0,8). La majorité des sujets de < 30 ans n'avaient pas de cirrhose au moment du diagnostic du CHC (80% versus 39,9%, p=0,08). La cirrhose était fréquente chez les sujets de 30-39 ans (68,8% versus 44,4%, p=0,16). Il n'y avait pas d'autres différences entre patients cirrhotiques et non-cirrhotiques. Le rôle synergique de l'alcool ainsi que l'influence du tabagisme au développement du CHC n'étaient pas établis.

Conclusion

La majorité des patients atteints d'un CHC associé au VHB au Cameroun ont moins de 40 ans. La cirrhose n'est pas toujours présente au moment du diagnostic et les caractéristiques du CHC chez le patient cirrhotique et non cirrhotique sont similaires. L'influence de l'alcool et du tabac est négligeable. D'où l'importance des mesures préventives de contamination et du Programme Elargi de Vaccination (PEV), incluant l'hépatite B, initié dans notre pays depuis 2005 pour prévenir l'infection initiale.

INTRODUCTION

Chronic hepatitis B virus (HBV) infection and cirrhosis are the major risk factors of hepatocellular carcinoma (HCC) [1-4], with a 60% – 90% risk in adults and almost 100% risk in children living in highly endemic zones [5]. HCC is a public health problem, with 80% of cases occurring in developing countries where rates of HBV infection are high [3, 4, 6]. About 500000 to 626000 new cases annually, with an annual incidence amongst cirrhotics varying between 2.5% to 7% [6, 7]. Mortality due to HCC ranks among the highest in the world with close to 650000 deaths yearly, 70% of which occurs in developing countries [4, 8, 9]. Managing HCC is challenging as most patients present late in the course of the disease whence effective treatment is no more possible. This underscores the importance prevention to reduce its morbidity and mortality [4]. Improved knowledge of the epidemiologic profile of patients with HCC coupled with vaccination against HBV, with proven efficacy in the reduction of HCC in Taiwan stand as cornerstones in the prevention of HCC [5, 10]. Cameroon is a highly endemic zone for HBV infection. However, the epidemiologic profile of hepatitis B-associated HCC is not known.

The aim of our study was to determine the epidemiologic profile of hepatitis B-associated HCC in Cameroon and to analyze the role of the presence or absence of cirrhosis amongst our patients in order to better organize management.

PATIENTS AND METHODS

A total of 40 patients with HCC were enrolled from March 2012 to January 2013 at the Yaounde University Teaching Hospital and Yaounde General Hospital. Demographic data (age, gender, race), alcohol consumption (>80g/day), smoking, presence or absence of cirrhosis were all recorded in a data entry form, filled by a resident in internal medicine.

Hepatitis B surface antigen (HBsAg) was tested using a 3rd generation ELISA test, with the commercial kit (DIA-HBV®, DiaProph.Med, Ukraine, Russia). The test was considered positive when the optical density of the test sample was above the threshold. It was considered negative when the optical density of the test sample was below the threshold.

The diagnosis of HCC was made on the basis of ultrasound or computed tomography. That of cirrhosis was made on the basis of radiologic criteria, which were all performed by a single radiologist. Patients co-infected with HCV or HDV, including cases in which the diagnosis of HCC and cirrhosis were doubtful were excluded.

Data was analyzed using Epi info 6.04 and Excel 2007. For quantitative variables, means, standard deviations and medians were calculated. For qualitative variables, proportions were calculated with their confidence intervals (CI).

To examine the relationship between two discrete variables, we used Pearson's χ^2 test with Yates correction and Fischer's exact test for small sample sizes, with a p value set at 0.05. Kruskall Wallis test was used to compare the mean ages of cirrhotic and non cirrhotic patients.

RESULTS

Forty patients with HCC were identified, of which 6 were excluded owing their HBV/HCV co-infection. A total of 34 patients hepatitis B-associated HCC met our inclusion criteria. The mean age was 38.5±12.3 years (extremes 18 – 74years), with 79.4% (95% CI 62.1-91.3) (27/34) being males (sex ratio 3.9:1). Of the 34 patients, 55.9% (95% CI 37.9-72.8) (19/34) had cirrhosis against 44.1% (95% CI 27.2-62.1) (15/34) without cirrhosis. Amongst them, 44.1 % (15/34) (95% CI 27.2-62.1) were smokers and 2.9 % (1/34) (95% CI 0.1-15.3) were alcoholics. The prevalence of HCC was significantly high amongst patients aged 30-39 years old, being 47.7% (95% CI 29.8-64.9) (16/34). From this age group, the prevalence decreased progressively with increasing age to reach 5.9% (95 % CI 0.7-19.7) (2/34) amongst those aged 60years old and above. Table I.

Table I: Prevalence of Hepatitis B-Associated Hepatocellular Carcinoma with Respect to Age, Gender and Cirrhosis (n=34).

Variables	Nb	(%)	95%CI
Age (years)			
<30	5	14.7	5-31.1
30-39	16	47.1	29.8-64.9
40-49	7	20.6	8.7-37.9
50-59	4	11.8	3.3-27.5
≥60	2	5.9	0.7-19.7
Gender			
Men	27	79.4	62.1-91.3
Women	7	20.6	8.7-37.9
Cirrhosis			
Yes	19	55.9	37.9-72.8
No	15	44.1	27.2-62.1

No. number, % percentage, CI Confidence Interval

Table II shows the epidemiologic characteristics of hepatitis B-associated HCC in cirrhotic and non cirrhotic patients namely age, gender, alcohol and tobacco consumption.

Table II: Epidemiologic Characteristics of Hepatitis B-Associated Hepatocellular Carcinoma in Cirrhotic and Non Cirrhotic Patients

Variables	No. of cases	Cirrhotic patients		non-cirrhotic patients		p-value
		No. of cases	(%)	No. of cases	(%)	
Mean ages (year)			38.9±11.3		38.0±14	0.8
Age (years)						
<30	5	1	20.0	4	80.0	
30-39	16	11	68.8	5	31.3	
40-49	7	4	57.1	3	42.9	
50-59	4	2	50.0	2	50.0	
≥60	2	1	50.0	1	50.0	0.437
Gender						
Men	27	15	55.6	12	44.4	
Women	7	4	57.1	3	42.9	1.000
Alcohol						
Yes	1	1	100	0	-	
No	33	18	54.5	15	45.5	1.000
Tobacco						
Yes	15	11	73.3	4	26.7	
No	19	8	42.1	11	57.9	0.140

No. number, % percentage

There was no statistically significant difference between cirrhotic and non cirrhotic patients (mean age 38.9±11.3 vs. 38.0±14, p=0.8). Patients aged 30 years and below had a greater propensity to develop HCC on non cirrhotic liver than others (80% vs. 39.9%, p=0.08). Cirrhosis on the contrary was most frequent amongst those aged between 30–39 years old (68.8% vs. 44.4%) though this difference was not statistically significant (p=0.16).

The relative risk (RR) of developing cirrhosis for those aged between 30–39 years was 1.55 (95% CI 0.84-2.86). There was no other identified statistically significant difference between cirrhotic and non cirrhotic patients with respect to the epidemiological characteristics. The RR of cirrhosis was 1.03 (95% CI 0.5-2.12, p=1.00) for women, 1.74 (95% CI 0.95-3.20, p=0.14) for smokers and 1.83 (95% CI 1.34-2.50, p=1.00) for alcoholics. There was no established synergistic role of HBV infection and alcoholism in the development of hepatitis B-associated HCC.

DISCUSSION

HCC is one of the most frequent causes of cancer-related deaths worldwide [8, 11, 12]. Its epidemiology is characterized by its geographic variation (Africa and Asia different from that of Europe) and demographic variations (age, gender and race) [4, 12 – 15]. The aim of this study was to determine the epidemiologic characteristics of hepatitis B-associated HCC in Cameroon. In our study, as in many others [13, 14, 16], hepatitis B-associated HCC occurs more frequently amongst men and on cirrhotic liver. However, the proportion of HCC occurring on non cirrhotic liver was particularly high in our study (44.1%), especially amongst those aged below 30 where 80% of hepatitis B-associated HCC were without cirrhosis at diagnosis. Wan et al. in a study amongst HBV infected Asian immigrants to the United States of America who had HCC had similar results [16]. It can be accounted for by the mode of contamination in our environment. As a matter of facts, in hyper endemic zones particularly in Africa and pacific Asia, early vertical and horizontal transmission is the major route of contamination [10]. Infected individuals develop chronic liver diseases early than their counterparts in other parts of the world [15, 16]. Other factors such as family history, environmental factors (aflatoxine), smoking, pesticides and schistozomiasis have been postulated [4, 7, 16, 17] to be responsible for the development of HCC in non cirrhotic livers in Africa and Pacific Asia. It is well known that HCC is a disease of the elderly (mean age: 65 years) and that its prevalence increases progressively after 40 years [13]. In our study, its prevalence decreased progressively after 40years. This result could be accounted for by the low life expectancy in our milieu, the patient's age at infection and the duration of infection [4, 15, 18]. No significant difference was noted when comparing the epidemiologic profiles of cirrhotic and non cirrhotic patients in our study, as has been described in other studies [1, 16, 19]. Age, gender, excessive alcohol consumption (>80g/day) or smoking were similar in both groups. Contrary to findings in other parts of the world, especially Europe, alcohol and HBV had no synergistic role [14, 20]. Zidan et al. in Iran had a similar finding [2].

CONCLUSION

Hepatitis B-associated HCC indistinctly occurs in cirrhotic and non cirrhotic livers in Cameroon. The epidemiologic characteristics of hepatitis B-associated HCC in cirrhotic patients are similar to those of non cirrhotic patients. Hepatitis B-associated HCC is more frequent among those aged below 40 years, due to early vertical and horizontal transmission, justifying the

introduction of vaccination against HBV into the expanded immunization program in 2005.

CONFLICTS OF INTEREST:
None

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