

Comparative study of Hepatitis B and C related Hepatocellular Carcinoma in Cotonou from 2014 to 2020

AR Kpoussou,^{1,2} FHR Gnangnon,^{1,3,4} K N'Tcha,¹ C Toumé,³ SA Amidou,^{3,5} CNM Sokpon,^{1,2} RK Vignon,^{1,2} DG Gbessi,^{1,4} N Kodjoh,⁶ J Séhonou^{1,2}

¹Faculty of Health Sciences, University of Abomey-Calavi, Benin

²Clinique Universitaire d'Hépatogastroentérologie, Centre National Hospitalier Universitaire Hubert Koutoukou Maga, Benin

³Cotonou Cancer Registry, National Programme Against Noncommunicable Diseases, Ministry of Health, Benin

⁴University Visceral Surgery Clinic, Centre National Hospitalier Universitaire Hubert Koutoukou Maga, Benin

⁵Laboratory of Chronic and Neurological Diseases Epidemiology, Faculty of Health Sciences, University of Abomey-Calavi, Benin

⁶Clinique de la Marina, Cotonou, Benin

Corresponding author, email: kpoussou.raimi@yahoo.fr

Introduction: The burden of hepatocellular carcinoma (HCC) remains high in developing countries. This study compared HCC associated with hepatitis B virus (HBV) and hepatitis C virus (HCV) in Cotonou.

Methods: This was a retrospective, cross-sectional analysis from January 2014 to December 2020. All cases of HCC due to HBV or HCV identified by the Cotonou Cancer Registry were included.

Results: A total of 91 cases of HCC were included, 79.1% associated with HBV and 20.9% with HCV. The mean age was 52.3 years. Mortality was 100%, with a mean survival time of 63.9 days. Male gender predominated with a M:F ratio of 2.5:1. HBV-associated HCC patients were younger than the HCV-associated group (mean age 51.4 vs. 55.7 years; $p = 0.01$). There was no difference regarding education ($p = 0.05$), religion ($p = 0.44$), alcohol or tobacco consumption ($p = 0.59$), or physical activity ($p = 0.99$).

Conclusion: HBV-associated HCC predominated with patients in this group younger when compared to the HCV group. The outcome was universally fatal, with no patients surviving.

Keywords: hepatocellular carcinoma, hepatitis B, hepatitis C, comparative study, Cotonou

Introduction

Globally, hepatocellular carcinoma (HCC) ranked sixth in incidence and second in mortality among all cancers in 2020.¹ Worldwide, HCC is most frequent in Asia (72.5%), Europe (9.7%), and Africa (7.8%).¹ In Africa, it is the second most common cancer in men and the fourth in women; it was the third leading cause of death for all sexes combined, with 66 944 deaths in 2020.¹ Benin, a sub-Saharan African country, has a burden of HCC. According to GLOBOCAN (Global Cancer Observatory) data, there were 6 747 cases of cancer in Benin, and HCC ranked fifth with 7.4% of cases in 2020.² It was the second most common cancer in men ($n = 336$) and the fifth most common in women ($n = 163$), with a sex ratio of 2.1.³ These figures may be underestimated due to the lack of nationwide epidemiological data collection in Benin. Benin currently has two cancer registries, one in Cotonou (in the south) and the other in Parakou (in the north), both experiencing difficulties with ongoing data collection.

With a prevalence that continues to rise throughout the world, it is estimated that more than 50% of HCC cases worldwide are diagnosed at a locally advanced stage, with vascular invasion leading to a dreadful prognosis and an extremely low survival time of between two and five months.⁴ Moreover, HCC affects young people who die of the disease, resulting in lost years of life and impoverished households, with major economic resource loss in opportunities for patients, families, employers, and society.⁵ It is a real development problem in sub-Saharan Africa.

The most common form of primary liver cancer is HCC, which develops at the expense of hepatocytes. The other HCCs are intrahepatic cholangiocarcinoma and haemangiosarcoma, which develop respectively at the expense of the intrahepatic bile ducts and liver vessels. HCC occurs in over 80% of cases in cirrhotic livers. The leading causes are hepatitis B virus (HBV), and hepatitis C virus (HCV), and alcohol.⁴

In Benin, HCC due to HBV is the most common and occurs at a much younger age than HCC due to HCV.⁶ HCC seemingly dominates in men, but data are lacking to clarify whether this predominance is independent of the cause of HCC. A comparative study of HCC according to B or C viral cause will provide a better understanding of this condition so appropriate preventive measures can be developed.

Materials and methods

The study was based in Cotonou, the economic capital of Benin. This retrospective observational cohort study was based on data from patients diagnosed with HCC and registered in the Cotonou Cancer Registry. The study population consisted of all patients residing in Cotonou diagnosed with HCC between 1 January 2014 and 31 December 2020. All patients with another cancer at the same time were excluded. During the study period, 150 cases of HCC were diagnosed and documented in the Cotonou Cancer Registry database.

HCC diagnosis was based on cross-sectional contrast-based imaging, including computed tomography and magnetic resonance imaging. In patients with liver cirrhosis or other high-risk factors, hepatic lesions with typical imaging characteristics can be diagnosed as HCC without needing other exams. Hepatic lesions with atypical imaging characteristics required additional imaging exams, follow-up over time, or histopathological analysis with a biopsy of the lesion. In non-cirrhotic patients, HCC diagnosis was made based on pathology. Hepatitis B was diagnosed with a positive HBsAg (Hepatitis B surface antigen), and HCV was diagnosed based on HCV ribonucleic acid (RNA) positivity.

We used exhaustive sampling. The registry used the CanReg software developed by the International Agency for Research on Cancer for data entry and verification checks. Registrations were traced from the registry back to the source of the registration. Information was verified or updated, and duplicates were excluded. Two data collection techniques were used. These were tabulation using a survey form and structured interviews using a standardised questionnaire. From 1 June to 31 July 2020, patient records were searched in the sources (hospitals and clinics). For patients who were lost to follow-up in these centres, relatives were contacted by telephone when the contact was provided. A home visit was organised if necessary. All data was verified by a cancer specialist who supervised the telephone calls and home visits.

This study used anonymised data from the Cotonou Cancer Registry database. Authorisations were obtained from the National Programme Against Noncommunicable Diseases (PNLMNT), which hosts the Cotonou Cancer Registry. Access to the database was restricted to authorised persons only. The files were anonymised and coded before electronic or email transfer. Patient names were replaced with codes. Similarly, the terms of the variables were coded.

The dependent variable was post-viral HCC “post-HBV or post-HCV”. The various independent variables were grouped by category: sociodemographic factors (age, sex, place of residence, level of education, profession, religion, marital status, ethnicity), aetiological, clinical, and paraclinical factors, and outcome data (follow-up time, survival time).

Data were entered into EpiData software version 3.1 French, and statistical analysis was performed in SAS Studio. Categorical variables were expressed as percentages, and continuous variables as a mean with standard deviation. Comparisons between means were made using t-test and between proportions using Pearson’s chi-square or Fischer’s exact test as appropriate. Univariate and multivariate analyses to determine the factors associated with death could not be carried out, as the patients had all died at the time of the survey. The survival curve was constructed using the Kaplan–Meier estimator.

Results

Frequency

Over seven years, 91 cases of viral hepatitis HCC were recorded in the Cotonou Cancer Registry (from a total of 150 HCC cases).

There were 72 cases of HCC due to HBV (79.1%) and 19 cases of HCC due to HCV (20.9%). Eight cases of HCC with HBV and HCV coinfection were excluded.

Sociodemographic characteristics

Sociodemographic characteristics are summarised in Table I. The mean age of patients with post-viral hepatitis HCC was 52.3 ± 14.6 years (extremes of 25–89). The modal age range was 44–64 years ($n = 46$, 50.5%). Men predominated ($n = 65$, 71.4%) with a sex ratio of 2:5. Regarding levels of education, more subjects ($n = 35$, 38.5%) had not attended school. Farmers were the most represented occupation ($n = 33$, 36.3%).

Aetiological, clinical, and paraclinical characteristics

The clinical and paraclinical characteristics are summarised in Tables II and III below. In addition to viral hepatitis, alcohol consumption was the main risk factor for HCC in these patients ($n = 75$, 82.4%) (Table II). HCC was diagnosed mainly on radiological grounds ($n = 47$, 51.6%). Histopathology was available in only 26.4% of cases ($n = 24$) (Table III).

Table I: Sociodemographic characteristics of patients with HBV or HCV associated HCC according to the Cotonou Cancer Registry, 2014–2020

	Frequency	Percentage
Mean age (standard deviation)	52.3 (14.6) years	
Age (years)		
24–44	29	31.9
44–64	46	50.5
≥ 64	16	17.6
Sex		
Female	26	28.6
Male	65	71.4
Education level		
None	35	38.5
Primary	23	25.3
Secondary	7	7.7
University	26	28.6
Profession		
Farmer	33	36.3
Hairdresser	8	8.8
Trader	7	7.7
Dressmaker	1	1.1
Student	2	2.2
State civil servant	5	5.5
Private sector civil servant	18	19.9
Mechanic	4	4.4
Retired	6	6.6
Welder	3	3.3
Tailor	4	4.4
Religion		
Christian	82	90.1
Muslim	9	9.9

HCC – hepatocellular carcinoma

Table II: Other risk factors for patients with post-viral hepatitis HCC according to the Cotonou Cancer Registry, 2014–2020

	Frequency	Percentage
Alcohol		
No	16	17.6
Yes	75	82.4
Tobacco		
No	78	85.7
Yes	13	14.3
Comorbidity		
No	43	47.2
Yes	48	52.7

HCC – hepatocellular carcinoma

Table III: Modalities of diagnosis in patients with post-viral hepatitis associated HCC according to the Cotonou Cancer Registry, 2014–2020

	Effective	Percentage
Clinical	1	1.1
Histology/tumour	24	26.4
Paraclinical investigations (imaging and others)	47	51.6
Specific marker	19	20.9

HCC – hepatocellular carcinoma

Table IV: Comparative analysis of the characteristics of HCC according to sociodemographic and aetiological characteristics (Cotonou, 2014–2020)

	HBV	HCV	p-value
Mean age (standard deviation)	51.4 (15.4) years	55.7 (10.9) years	0.26
Age (years)			0.01
24–44	27 (37.5)	2 (10.5)	
44–64	31 (43.1)	15 (78.9)	
≥ 64	14 (19.4)	2 (10.5)	
Sex			0.14
Female	18 (25)	8 (42.1)	
Male	54 (75)	11 (57.9)	
Education level			0.05
None	30 (41.7)	5 (26.3)	
Primary	14 (19.4)	9 (47.4)	
Secondary	7 (9.7)	0	
University	21 (29.2)	5 (26.3)	
Religion			0.4
Christian	64 (88.9)	18 (94.7)	
Muslim	8 (11.1)	1 (5.3)	
Alcohol			0.8
No	13 (18.1)	3 (15.8)	
Yes	59 (81.9)	16 (84.2)	
Tobacco			0.6
No	61 (84.7)	17 (89.)	
Yes	11 (15.3)	2 (10.5)	

HBV – hepatitis B virus, HCC – hepatocellular carcinoma, HCV – hepatitis C virus

Evolutionary characteristics

The mean duration of follow-up was 86.9 ± 100.3 days. All 91 patients had demised at the time of inclusion, resulting in a 100% case fatality rate. The mean overall survival time was 63.9 ± 39 days (extremes of 2–160). The median survival was 54 days (interquartile range 23–80).

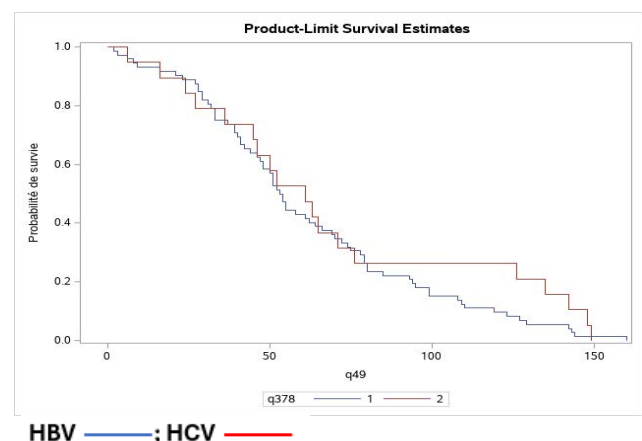
Comparative analysis of the characteristics of HBV versus HCV-associated HCC according to sociodemographic and aetiological factors

Table IV summarises the comparison of the characteristics of the two risk factors associated with HCC. The mean age of patients with HCV-associated HCC was older than HBV-associated HCC (55.7 vs. 51.4 years), but the difference was not statistically significant ($p = 0.26$). HBV HCC affected both the 24–44 and 44–64 age groups, whereas HCV HCC mainly affected the 44–64 age group, with a statistically significant difference ($p = 0.01$). Regarding sex, a male predominance was noted for both viruses, with no significant difference ($p = 0.14$). No difference was observed based on alcohol or tobacco consumption ($p = 0.59$).

Comparative analysis of the characteristics of HBV HCC versus HCV HCC according to patient survival

Figure 1 illustrates the respective survival curves for HBV and HCV HCC. When analysing these survival curves, the probability of survival for HCV HCC patients appears higher over time than for HBV patients. However, no statistically significant difference was observed between the two curves in this cohort.

For HBV HCC, the median overall survival was 53.5 days (95% confidence interval [CI] 48 to 64, extremes of 2–160), whereas for HCV HCC, the median survival was 75 days (95% CI 40 to 123, extremes of 6–149). However, the difference was not statistically significant ($p = 0.6$). Given that 100% of patients had died at



Equality test on discretisation levels

Test	khi-2	DDL	Pr > khi-2
Log-rank	0.8751	1	0.3495
Wilcoxon	0.1985	1	0.6559
-2Log(LR)	0.2402	1	0.6241

HBV – hepatitis B virus, HCC – hepatocellular carcinoma, HCV – hepatitis C virus

Figure 1: Survival curves for cases of HCC as a function of HBV and HCV

the time of the study, it was not possible to study the factors associated with survival.

Discussion

HBV predominated as the major factor driving HCC in Cotonou, reconfirming the dominant role of hepatitis B in the occurrence of HCC in sub-Saharan African countries, such as Benin. Globally, 54% of HCC is associated with HBV and 31% with HCV.^{7,8} At the same time, hepatitis B is responsible for 90% of HCC cases in East Asia and sub-Saharan Africa.⁹ These are highly endemic regions for HBV.¹⁰ For example, the prevalence of hepatitis B found during mass screening in 2019 was 6%, while it was 1% for HCV in Benin.^{11,12} In Tunisia, Dorra et al.¹² reported 53 HCV cases (63.1%) and 31 HBV cases (36.9%) out of 84 HCC cases. According to Ng et al.,¹³ 16% of HCC cases are due to HBV and 48% due to HCV in the United States. Shiratori et al.¹⁴ reported 71% of HCC as HCV and 11% as HBV associated in Japan. Thus, the predominant virus that causes HCC varies depending on the geographical location.

In our study, HBV HCC patients were younger than those with HCV HCC, but the difference was not significant. The study by Dorra et al.¹² in Tunisia showed the same trend (60.1 years for HBV versus 68.9 years for HCV, with a statistically significant difference [$p = 0.03$]). Ng et al.¹³ confirmed these data in the United States. In another United States study, Hiotis et al.¹⁵ found that 26% of HBV HCCs were less than 40 years old compared with 0% for HCC due to HCV ($p < 0.001$). In Japan, Shiratori et al.¹⁴ reported a mean age of 62 years for HCV HCC versus 52 years for HCV HCC ($p < 0.05$).

The young age of HBV HCC cases is mainly explained by the dominant mode of perinatal transmission of this virus, especially in highly endemic areas, such as sub-Saharan Africa and Asia. As a result, infection occurs earlier, and HCC develops in younger subjects than HCV, whose transmission is essentially parenteral.¹⁶ There were 37 patients aged < 44 years, mainly those with HBV, underpinning the occurrence of this cancer in a younger population, given the dominant childhood acquisition of HBV.¹⁷

HCC remains a predominantly male disease, more so in HBV than HCV. This result is similar to Shiratori et al.¹⁴ in Japan, who found a sex ratio of 7 for HBV versus 3.3 for HCV, with no significant difference. In the Dorra et al.¹² study, the sex ratio for HCV was 9.3 and 1.4 for HBV ($p < 0.001$). This confirms the trend found in our work and that of Shiratori et al.¹⁴ Oestrogen, which plays a possibly protective role in women, has been associated with lower HBV infection rates. This correlation is supported by the observation that HBV-related HCC occurs more frequently in men, while a significant increase in HCC incidence is noted in postmenopausal women.¹⁸

Our study confirms the universally poor outcome of HCC in sub-Saharan Africa, with a 100% fatality rate. According to Lee et al.,¹⁹ HCC is one of the most fatal cancers, with more than half a million deaths each year worldwide. There was no significant difference in survival according to virus type (62.2 days for

HBV versus 70 days for HCV; $p = 0.6$). Shiratori et al.¹⁴ found no significant difference in survival in Japan. Conversely, Dorra et al.¹² observed that the survival of HBV HCC was poorer than HCV HCC survival (8.6 vs. 23.9 months; $p = 0.03$) in Tunisia.

The poorer prognosis of HBV HCC could be explained by the fact that these cases involve perinatal HBV transmission, with the disease progressing quietly over many years before the diagnosis is made at an advanced stage. However, the lack of programmatic HCC screening contributes to late presentation. In this study, we were unable to obtain data on tumour size. However, in one of our hospital-based studies of HCC, we noted that more than half of the patients (68/123, 55.3%) were in Barcelona Clinic Liver Cancer (BCLC) stage C (i.e. an advanced stage of the disease). Over a third (46/123, 37.4%) were already at a terminal stage (stage D).²⁰ The mean survival time observed in this series was 3.1 months (extremes of 0.4–19.) The study by Hiotis et al.¹⁵ showed that HCC due to HBV were larger (78% > 5 cm vs. 28% > 5 cm for HCV; $p < 0.001$) and had higher alpha-fetoprotein levels (median 1 000 ng/ml for HBV vs. 37 ng/ml for HCV; $p = 0.002$).

The factors influencing the earlier onset and prognosis of HCC are varied: they include genetic and epigenetic factors, environmental factors (alcohol abuse, obesity and metabolic syndrome, exposure to aflatoxin) or ethnic and geographic socioeconomic factors (poverty, level of education, lack of insurance).²¹ HBV is the main aetiological factor in Benin.

HBV is childhood-acquired in Benin, and the HBV vaccine was introduced to the vaccine schedule in 2005. The September 2020 introduction of a hepatitis B birth dose vaccine within 24 hours of delivery may influence the benefits in the future and drive down chronic HBV infection and, thus, HCC.²²

Our study highlighted the relative importance of hepatitis B and C driving HCC in Benin. However, the study has limitations. Being retrospective, we were confronted with numerous missing data. For example, it was not possible to obtain data for staging HCC. Furthermore, the number of HCCs recorded does not seem to reflect the reality in the city of Cotonou. The difficulties of having a permanent registrar at the Cotonou Cancer Registry could explain why the collection of cases was not exhaustive.

Conclusion

HCC is mostly driven by HBV in Cotonou affecting younger patients, while HCV HCC appears to affect slightly older patients. In both cases, males are more affected, and the prognosis is poor, with an average overall survival of two months. Preventive measures are needed to control these formidable diseases in Benin better.

Conflict of interest

The authors declare no conflict of interest.


Funding source

No funding source to be declared.

Ethical approval

Ethical approval before study commencement was obtained from the PNLMT review board, reference number: N°160/DNSP/PNLMT/SA.

ORCID

AR Kpossou  <https://orcid.org/0000-0002-6557-6540>
 FHR Gnanon  <https://orcid.org/0000-0003-0864-4751>
 K N'Tcha  <https://orcid.org/0009-0006-5382-9842>
 C Toumé  <https://orcid.org/0009-0009-2247-5377>
 SA Amidou  <https://orcid.org/0000-0002-5473-032X>
 CNM Sokpon  <https://orcid.org/0000-0001-5629-5758>
 RK Vignon  <https://orcid.org/0000-0003-0965-1144>
 DG Gbessi  <https://orcid.org/0000-0002-2740-6444>
 N Kodjoh  <https://orcid.org/0009-0004-8573-7630>
 J Séhonou  <https://orcid.org/0009-0009-8253-0198>

References

1. International Agency for Research on Cancer 2020 [online]. Global Cancer Observatory; 2020. Available from: <https://gco.iarc.fr/en>. Accessed 18 April 2021.
2. Egue M, Gnanon FHR, Akele-Akpo M-T, Parkin DM. Cancer incidence in Cotonou (Benin), 2014-2016: first results from the cancer Registry of Cotonou. *Cancer Epidemiol*. 2019;59:46-50. <https://doi.org/10.1016/j.canep.2019.01.006>.
3. Aubry P, Gaüzère B-A. Les cancers dans les pays en développement [Internet]. Médecine Tropicale; 2020. French. Available from: <http://medecinetropicale.free.fr/cours/cancer.pdf>. Accessed 29 August 2021.
4. Yabroff KR, Lund J, Kepka D, Mariotto A. Economic burden of cancer in the United States: estimates, projections, and future research. *Cancer Epidemiol Biomarkers Prev*. 2011;20(10):2006-14. <https://doi.org/10.1158/1055-9965.EPI-11-0650>.
5. Kpossou AR, Gnanon FHR, Séidou F, et al. Epidemiological, clinical, paraclinical and therapeutic aspects of hepatocellular carcinoma in Cotonou. *Med Afr Noire*. 2020;67(10):537-45. French.
6. Parkin DM. International variation. *Oncogene*. 2004;23(38):6329-40. <https://doi.org/10.1038/sj.onc.1207726>.
7. Perz JF, Armstrong GL, Farrington LA, Hutin YJF, Bell BP. The contributions of hepatitis B virus and hepatitis C virus infections to cirrhosis and primary liver cancer worldwide. *J Hepatol*. 2006;45(4):529-38. <https://doi.org/10.1016/j.jhep.2006.05.013>.
8. Raza SA, Clifford GM, Franceschi S. Worldwide variation in the relative importance of hepatitis B and hepatitis C viruses in hepatocellular carcinoma: a systematic review. *Br J Cancer*. 2007;96(7):1127-34. <https://doi.org/10.1038/sj.bjc.6603649>.
9. World Health Organization. Global Hepatitis Report 2017. WHO, Geneva. 2017:1-83. Available from: <https://www.who.int/publications/i/item/9789241565455>.
10. Kpossou AR, Paraiso MN, Sokpon CN, et al. Seroprevalence of viral hepatitis B and its associated factors determined based on data from a screening campaign targeting the general population in Benin. *Pan Afr Med J*. 2020;37(247). French. <https://doi.org/10.11604/pamj.2020.37.247.26070>.
11. Paraiso MN, Kpossou AR, Sokpon CN, et al. Viral hepatitis C during a screening campaign in general population of Benin: seroprevalence and associated factors. *Open J Epidemiol*. 2021;11(2):178-88. <https://doi.org/10.4236/ojepi.2021.112016>.
12. Dorra T, Meriam S, Imen BA, et al. Characteristics and survival during hepatocellular carcinoma: comparison between hepatitis B and C viruses. *Ann Clin Hepatol*. 2019;3(2):1015. Available from: <https://www.remedypublications.com/annals-of-clinical-hepatology-abstract.php?aid=5313>.
13. Ng J, Wu J. Hepatitis B- and hepatitis C-related hepatocellular carcinomas in the United States: similarities and differences. *Hepat Mon*. 2012;12(10 HCC):e7635. <https://doi.org/10.5812/hepatmon.7635>.
14. Shiratori Y, Shiina S, Imamura M, et al. Characteristic difference of hepatocellular carcinoma between hepatitis B- and C- viral infection in Japan. *Hepatology*. 1995;22(4 Pt 1):1027-33. [https://doi.org/10.1016/0270-9139\(95\)90605-3](https://doi.org/10.1016/0270-9139(95)90605-3).
15. Hiotis SP, Rahbari NN, Villanueva GA, et al. Hepatitis B vs. hepatitis C infection on viral hepatitis-associated hepatocellular carcinoma. *BMC Gastroenterol*. 2012;12(64). <https://doi.org/10.1186/1471-230X-12-64>.
16. Alavian SM, Haghbin H. Relative importance of hepatitis B and C viruses in hepatocellular carcinoma in EMRO countries and the Middle East: a systematic review. *Hepat Mon*. 2016;16(3):e35106. <https://doi.org/10.5812/hepatmon.35106>.
17. Li Y, Zhang Z, Shi J, et al. Risk factors for naturally-occurring early-onset hepatocellular carcinoma in patients with HBV-associated liver cirrhosis in China. *Int J Clin Exp Med*. 2015;8(1):1205-12.
18. Huang C-Y, Tan K-T, Huang S-F, et al. Study of sex-biased differences in genomic profiles in East Asian hepatocellular carcinoma. *Discov Oncol*. 2024;15(276). <https://doi.org/10.1007/s12672-024-01131-9>.
19. Lee SY, Song KH, Koo I, et al. Comparison of pathways associated with hepatitis B- and C-infected hepatocellular carcinoma using pathway-based class discrimination method. *Genomics*. 2012;99(6):347-54. <https://doi.org/10.1016/j.ygeno.2012.04.004>.
20. Kpossou AR, Vignon RK, Sokpon CNM, et al. Therapeutic management of hepatocellular carcinomas at the Hubert Koutoukou Maga National University Hospital Centre in Cotonou. *Med Afr Noire*. 2021;68(5):269-78. French. Available from: https://www.santetropicale.com/resume_oa.asp?id_article=3464&revue=man.
21. Chavda V, Zajac KK, Gunn JL, et al. Ethnic differences in hepatocellular carcinoma prevalence and therapeutic outcomes. *Cancer Rep (Hoboken)*. 2023;6 (Suppl 1):e1821. <https://doi.org/10.1002/cnr.2.1821>.
22. iris.who.int [Internet]. Impact de la vaccination contre l'hépatite B: meilleures pratiques pour mener une enquête sérologique. Genève: Organisation Mondiale de la Santé; 2014. French. Available from: http://apps.who.int/iris/bitstream/10665/112854/1/WHO_IVB_11.08_fre.pdf. Accessed 28 December 2021.