

Updated Review on the Panorama of Liver Diseases in Benin

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Abstract

Introduction: The aim of this work was to take stock of the epidemiological aspects of liver diseases in Benin. **Methods:** Two methods were used: documentary research and collection of the position of gastroenterologists on the subject. For the literature search, the sources interviewed were Medline, African Journal On Line (AJOL), Google and Google scholar. Additional searches were made on the websites of European gastroenterology societies (AFEF, EASL). A collection of the opinions of gastroenterologists, most of them members of the Beninese Society of Hepato-gastroenterology was made. **Results:** From a nosological point of view, the most frequent and serious liver diseases in Benin are mainly infectious: viral hepatitis B and C (9.9% and 4.12% of the general population in 2013). Bacterial liver diseases (ascites fluid infections and tuberculosis of the liver) come in 3rd position after cirrhosis and hepatocellular carcinoma. Amoebic abscesses of the liver tend to regress. The toxic causes are dominated, in addition to alcoholic liver diseases (steatosis, cirrhosis), by drug lesions: two fatal cases of hepatotoxicity by artesunate-amodiaquine combination and asymptomatic and transient cytolysis in 23.8% of 63 children less than 5 years old treated with arthemether-lumefantrine combination have been described. Phytotherapy, alone or in combination with modern drugs, can in some cases be hepatotoxic. Plants with recognized medicinal virtues (may be harmful to the liver (Senna, Moringa oleifera, tamarind). Chronic aflatoxicoses secondary to the consumption of contaminated food (maize, cassava or peanuts) are relatively under-documented. Overload diseases (in particular alcoholic or non-alcoholic fatty liver) are on the increase (3.19% of 662 ultrasounds in 1995 against 14.5% of 411 in 2011

in Cotonou) partly due to the demographic and nutritional transition underway in Benin. These diseases, often blamed on spells cast, lead to hospital deaths from cirrhosis or hepatocellular carcinoma in young economically active subjects. **Conclusion:** Despite anti-infectious therapeutic advances, the prevention of toxic and metabolic hepatopathies is essential. Clinical research is crucial.

Keywords

Viral Hepatitis, Drug-Induced Hepatitis, Benin, Viral Hepatitis, Toxic Hepatitis

1. Introduction

Liver diseases are common in Benin. Their extent is not clearly defined. Piece-meal data exist, which relate to the most frequent diseases such as viral hepatitis. The frequency of the latter is estimated at 9.9% of the blood donor population for hepatitis B and 4.12% for hepatitis C [1].

They are responsible for significant morbidity: 20.82% (437/2098) of patients received between 1 January 2010 and 31 December 2016 in the Department of Hepato-Gastroenterology had a viral hepatitis B or C as the reason for consultation or hospitalisation [2].

Their clinical translation consists of jaundice (most often in the acute forms) and asthenia (in the chronic forms). On physical examination, a hepatomegaly is found (102/1930; 5.28% of cases of hospitalisation in the CNHU Department of Internal Medicine and Medical Oncology between 2012 and 2016) [3].

In the acute forms, the evolution is often towards recovery without sequelae, rarely towards hepatocellular insufficiency and death. Chronic forms evolve towards cirrhosis (46.6%) and liver cancer. This cancer is primary in 30.1% of cases and secondary in 13.6% of cases [4]. Mortality is also high (21/52 of patients hospitalised for cirrhosis had died) [5].

The present work takes stock of the different nosological entities of liver diseases in Benin and the costs inherent to their management.

2. Methods

Two methods were used: documentary research and the collection of the position of gastroenterologists on the subject. For the literature search, the sources interviewed were Medline, the African Journal on Line (AJOL), Google and Google scholar. Additional searches were made on the websites of European gastroenterology societies such as the Association Française pour l'Etude du Foie (AFEF) and the European Association for the Study of the Liver (EASL). In addition, a reading of the theses and dissertations produced at the Faculty of Health Sciences was also carried out. The key words were "hépatite ou hépato-

pathies—Republique du Bénin” for searches in French or “hepatitis, liver diseases—Republic of Benin”. The opinions of the hepato-gastroenterologists of Benin, most of whom are members of the Beninese Society of Hepato-gastroenterology, were collected.

3. Results

3.1. Epidemiological Aspects

3.1.1. Infectious Liver Diseases

- *The parasitic liver: amoebic abscess of the liver*

Between 1991 and 1995, Boco and Hountondji [6] reported 33 cases of liver abscess out of 577 abdominal ultrasounds performed in the CNHU’s medical imaging department.

This pathology has become rare and anecdotal: no case was found in the series of 411 abdominal ultrasounds performed by a gastroenterologist between 2009 and 2011 [7]; this is due to the availability of a modern treatment, metronidazole. This effective treatment is often prescribed at all levels of the health chain in Benin. It is often the first drug used in self-medication for most colonic diseases.

- *Liver damage due to malaria*

Is under-documented. In a study of children under 60 months recruited at the Hôpital Mère Enfant Lagune (HOMEL), Sehonou *et al.* [8] found hepato-cytolysis corresponding to this entity in 5 out of 68 cases (7.35%).

- *Viral liver diseases*

On the other hand, viral hepatitis is common. Viral hepatitis B is often acquired in childhood by essentially horizontal transmission; it is a disease of the young male subject. Viral hepatitis C, on the other hand, is a disease of older women, transmitted mainly by parenteral transmission [2]. Both of these diseases predispose to cirrhosis and hepatocellular carcinoma (HCC).

Table 1 with references [9]-[19] and **Table 2** with references [2] [10] [12] [16] [20] [21] [22] summarise the main Beninese studies of viral hepatitis B and C respectively.

- *Bacterial liver diseases*

Very few publications exist on bacterial infections in Benin.

3.1.2. Toxic Liver Diseases

- *Alcohol-related causes*

They are favoured by a high prevalence of alcohol consumption in the general population. According to the STEPS-Benin 2015 survey [23], the percentage of adults aged 18 - 69 years who engage in episodic heavy drinking (six or more units/glasses of alcohol on a single occasion in the past 30 days) was 7.6% (11.3% among men, 3.9% among women). However, harmful alcohol consumption was relatively low (0.5% - 1% in men and 0.1% in women). They contribute to the occurrence of cirrhosis, which is the second most common cause of cirrhosis (13.3%) in Benin after viral hepatitis [5].

Table 1. Prevalence of viral hepatitis B (and/or delta) in various populations in Benin (2002-2019) [9]-[19].

Authors [Reference]	Period	Hepatitis	Population	Sample size	Prevalence (%)
Kei [9]	2002	B	Blood donors	500	4.8
Ade [10]	2005	B	Blood donors	7654	7.5
Sehonou [11]	2007	B	HIV* at the CNHU-HKM**	205	11.2
Sehonou [12]	2007	B	HIV in Comè	150	11.3
Affolabi [13]	2012	B	HIV and tuberculosis in Cotonou	171	11.1
Amidou [14]	2012	B	Consultants at the CHD*** Parakou	1516	13.9
Sehonou [15]	2013	B	Hemodialysis patients in Cotonou	140	6.0
De Paschale [16]	2014	B	Pregnant women in Tanguiéta	283	15.5
Affolabi [17]	2015	B	Persons deprived of liberty in Cotonou Abomey, Parakou, Porto-Novo (Benin)	503	11.7
Kpossou [2]	2016	B	Consultants or hospitalized at the CNHU-HKM	2060	15.2
Saké [18]	2019	B	Pregnant women in Parakou	214	14.0
Kpossou [19]	2019	B + D	Patients with HBsAg in Cotonou (CNHU-HKM and Atinkanmey)	156	3.8

*: Human immunodeficiency virus; **: National and University Hospital Hubert Kou-toukou Maga; ***: departmental hospital centre.

Table 2. Prevalence of HCV antibodies in various studies in Benin (2002-2019) [2] [10] [12] [16] [20] [21] [22].

Authors [reference]	Period	Population	Sample size	Prevalence (%)
Sehonou [20]	2002	Recruits of the Beninese Armed Forces	506	7.5
Sehonou [21]	2003	HIV in Cotonou	103	3.0
Ade [10]	2005	Blood donors	7654	4.1
Sehonou [22]	2005	Hemodialysis patients in Cotonou	65	29.2
Sehonou [12]	2008	HIV in Comè	150	14.0
De Pascale [16]	2015	Pregnant women in Tanguiéta	283	7.4
Kpossou [2]	2016	Consultants or hospitalized at the CNHU-HKM	2060	5.7

- *Drug-related causes*

Drug-induced liver damage is most often acute. The most frequently studied are liver diseases due to artemisinin derivatives. Two cases of fulminant hepatitis and one case of hepatonephritis have been reported respectively by Guévert *et al.* [24], and Sabi *et al.* [25].

However, the combination of arthemether and lumefantrine (AL), the basic treatment for malaria, is responsible for moderate, transient and often asymptomatic hepato-cytolysis. Out of 63 children aged between 6 and 59 months who had been given AL at therapeutic doses, this hepato-cytolysis was found in nine patients (14.28%) on the third day (D3), two patients (3.17%) on D7, four patients (6.34%) on D14 and zero patients (0%) on D21. It was always moderate (less than twice the upper limit of normal aminotransferases), transient (one to two weeks) and asymptomatic. Hepatitis B and C serologies were negative in all the children who presented with hepato-cytolysis. AL attribution was possible in 23.8% [8].

- *Hepatopathies by phytoxicity. Case of aflatoxin*

Chronic aflatoxicosis is common in Benin; it is linked to the consumption of cereals contaminated by mycotoxins produced by *Aspergillus flavus*. According to a study published in 2017 on the quality of maize sold in markets in Benin and Niger, the number of maize samples with a contamination rate of more than 20 parts per billion (ppb) of aflatoxin was 29.5% among wholesalers, 9.1% among retailers, and 4.2% among producers [26].

Links are currently being established between poverty, food consumption of maize and hepatocellular carcinoma. However, aflatoxin appears to be involved in the genesis of HCC through its association with viral hepatitis B [27].

Liver diseases related to phytotoxicity have been little reported in Benin. However, phytotherapy is common: 80% of the Beninese population uses it at some point in their lives [28]. The medicinal properties of plants should not obscure their possible hepatic side effects. Moreover, there is currently a craze among the Beninese population for medicinal plants: among these, *Moringa olifera* has been the subject of much research showing its beneficial properties in the treatment of certain metabolic (diabetes) and cardiovascular diseases. However, recent study describes that feeding obese mice with *Moringa olifera* leaf extract had a beneficial effect on liver steatosis [29].

3.1.3. Liver Overload Disease

- *Liver steatosis*

Overload diseases are dominated in Benin by hepatic steatosis, which has increased sonographically from 3.19% (21/662) in 1995 [30] to 14.5% (60/411) between 2009 and 2011 [7]. The reasons for this increase in prevalence are unclear. The causes could be metabolic: between 2008 and 2015 there was an increase in the prevalence of diabetes (2.6% to 12.4%), hypercholesterolemia (1.8% to 18.2%), low consumption of fruit and vegetables 78% to 93.1% and physical inactivity from 9% to 15.9%. However, over the same period, the prevalence of

obesity decreased from 9.4% to 7.4% [23].

Liver steatosis in people living with HIV [31] are described (102/259; 39.4%) as are liver steatoses in malnourished people (57/94; 60.6%) [32]. Steatoses linked to viral hepatitis B or C were frequent (36/339; 10.6%) [33]. They were associated with the presence of diabetes (20%), high blood pressure (18.7%) and alcohol consumption (12%), not necessarily linked to obesity, and have a particular pathophysiology. They are noted in subjects with excessive consumption of sugary drinks [34] [35].

- **Iron overload**

Classically described as “African hemosiderosis” would be partly related to the consumption of local beer prepared and/or consumed in iron containers. It has been widely published in South Africa [36] [37] and Nigeria (8/98; 8.2% of apparently healthy women aged 26 - 71). In the latter case, self-prescription of iron for suspected anaemia could in some cases promote iron overload with liver and heart consequences [38].

It should be noted that autoimmune liver diseases (autoimmune hepatitis, primary biliary cholangitis) have been the subject of few publications. The weakness of the technical platform could partly explain this lack of information.

3.2. Therapeutic Aspects

Many therapeutic opportunities exist for hepatopathies: antiviral drugs, antivirals, improved traditional medicines. But prevention remains crucial: vaccination against hepatitis B, combating excessive alcohol consumption and obesity, improving the quality of food. In short, it is the fight for socio-economic development.

Research plays a key role in this fight.

3.3. Economic Aspects of Liver Diseases: A Challenge for Development

Liver diseases have a high cost. The direct costs, linked to diagnosis and treatment are often expensive: the diagnosis, involving the non-invasive evaluation of liver fibrosis and the viral load by polymerase chain reaction (PCR) amounts to approximately 350,000 F CFA (572 USD). The current treatment of viral hepatitis B by Interferon is of the order of 7,800,000 F (12,755 USD) for 48 weeks. That of hepatitis C is of the order of 900,000 to 1,500,000 F CFA (1472 to 2453 USD) for three months with direct action antiviral drugs in generic form.

The average cost per patient for the management of complicated cirrhosis was estimated at 300,080 F CFA (491 USD) for ascites, 344,406 F CFA (563 USD) for jaundice, 337,960 F CFA (553 USD) for digestive haemorrhage, and 331,690 F CFA (542 USD) for infections, 299,310 F CFA (489 USD) for hepatocellular carcinoma, 307,957 F CFA (504 USD) for hepatic encephalopathy, 267,480 F CFA (437 USD) for hematological disorders and 295,880 F CFA (484 USD) for hepato-renal syndrome [39].

To these direct costs must be added the indirect costs, for the individual (loss of vital energy, loss of productivity, years of life lost) and for society (loss of experience). To do this, cost-effectiveness analyses (CEA) are needed to put in place the different strategies for the prevention and management of viral hepatitis. As an example, the optimal management of viral hepatitis B would amount to 5% of Senegal's total health budget in 2012 [40]. In Benin there are national social security plans and private insurance schemes, undertaking part of patients' medical expenses. But the proportion of the population covered is currently quite low.

4. Discussion

On the evolutionary and therapeutic level, infectious liver diseases have a downward trend (decrease in viral hepatitis B and C). Thus, a study carried out in 2016 in a primary school in Gbahouté (Adjarra, Plateau department) showed a seroprevalence of hepatitis B of 1.6% (6/373) in children, compared with 8/44 (18%) in adults [41]; this is largely the result of hepatitis B vaccination introduced in Benin as part of the Expanded Programme on Immunisation since 2005. However, frequencies in the general population remain high, especially among adults. Conversely, toxic causes (alcoholism, drugs, phytotherapy) and metabolic causes (non-alcoholic hepatic steatosis) are on the increase.

Efforts should be made in the direction of health education to avoid replacing the infectious scourge by the metabolic or toxic one.

5. Conclusion

These liver diseases, which can lead to early death, can be prevented either by vaccination or by improving living conditions, or by providing therapeutic care for those already infected. Health education and the promotion of socio-economic development in Benin are major weapons in this fight. Research plays a fundamental role.

Conflicts of Interest

The authors declare no conflict of interest in this work.

Authors' Contribution

All the authors were involved in the active writing and editing of the article. All authors have read and approved the final version of the manuscript.

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