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Cirrhosis: Therapeutic Aspects and Outcome for Hospitalized Patients in Burkina Faso

Eric Nagaonlé Somé[1*], Félicité W. Nana[1], Isabelle Télarpoa Lompo[2], Drabo Maxime[1], Roger Sombié[2]

[1]Institut de Recherche en Sciences de la Santé (IRSS), Biomedical and Public Health Department, Ouagadougou, Burkina Faso
[2]Université Joseph Ki-Zerbo, UFR des Sciences de la Santé, Gastro-Enterology Department, Ouagadougou, Bukina Faso
Email: *eric.some@gmail.com, felynanaw@gmail.com, telarpoa@yahoo.fr, mdrabok@gmail.com, docsomb@gmail.com

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Abstract

Introduction: Cirrhosis represents 27.63% of the hepatobiliary diseases in Burkina Faso. We aimed at studying the therapeutic and evolutionary features of the cirrhosis. **Patients and methods:** We implemented a cross-sectional and descriptive study, collecting retrospectively the data from 1st January 2012 to 31st March 2014. The diagnosis of cirrhosis was based on 1) clinical criteria (an edema-ascitic syndrome with a heterogeneous hepatomegaly with a sharp inferior border or atrophic liver and a portal hypertension); 2) biological criteria (a hepatocellular insufficiency syndrome); and 3) ultrasound imaging suggesting cirrhosis. Qualitative variables were presented as frequencies and percentages while quantitative ones were presented as means. **Results:** The data of 273 patients representing 33.9% of all hospitalizations were analyzed. The hepato-biliary diseases represented 74.7% of all diagnosis. The participants' mean age was 46.9 years and the sex ratio, 2.7. The HBs antigen and anti-HCV antibodies were positive in 76.5% and 14.6% of the cases, respectively. Ascites was treated with puncture in 40.2% of patients, a salt-free diet (38.8%) and diuretics (54.2%). Hepatic encephalopathy was treated with lactulose in 73.6% of patients and two patients (1.3%) underwent esophageal varices ligation to treat their gastrointestinal bleeding. Lamivudine, tenofovir, and lamivudine-tenofovir combination were administered to 57.4%, 32.8%, and 10% of HBs Antigen positive patients, respectively. **Conclusion:** Cirrhosis still mostly affects the young and active male population at the gastro-enterology department of the university teaching hospital Yalgado Ouédraogo. Patients show up at a very advanced stage of the disease in poorly prepared health centres. In this context, prevention by the anti-hepatitis B immunization and early systematic screening with treatment when indicated are very efficient weapons at our disposal.

Keywords

Cirrhosis, Hepatitis B Virus, Treatment, Prognosis, Sub-Saharan Africa

1. Introduction

All chronic liver diseases can lead to cirrhosis, an irreversible lesion that combines fibrosis, a process of nodular regeneration and profound modification of the vascularization of the parenchyma. Among the many possible causes of cirrhosis, one of the most important is alcohol consumption, which is the main cause in developed countries [1] [2]. In contrast, in developing countries, chronic viral hepatitis is the leading cause [3] [4] [5] [6]. According to the WHO, 350 million people suffer from chronic liver disease in the world, and Africa has 60 million with a quarter of all deaths per year [7]. Indeed, Africa is considered with the Southeast Asia as a highly endemic area where the prevalence of chronic hepatitis B is estimated at least at 8%. In Burkina Faso, the prevalence of chronic carriage of the hepatitis B surface antigen (HbsAg) is estimated at 9.1% [8], despite the existence of an effective vaccine which should have contributed to reducing the incidence of the hepatitis B. In 2002, in Burkina Faso, cirrhosis dominated hepatobiliary pathologies with 27.63% of cases. In addition, these conditions affect young and active subjects, which hinders the emergence of already fragile economies [9]. There are several curative treatments that allow stabilization or even a regression of the lesions. The cases management is limited to the prevention of the occurrence of complications. But the effective curative treatment remains the liver transplant. We aimed to study the therapeutic and evolutionary aspects of cirrhosis at the university teaching hospital Yalgado Ouedraogo (UTH-YO) in Ouagadougou, the capital city of Burkina Faso.

2. Patients and Methods

A cross-sectional descriptive study with a retrospective data collection, from January 1st, 2012 to March 31st, 2014 was implemented in the hepato-gastroenterology department of the UTH-YO in Ouagadougou. All records of patients diagnosed with cirrhosis during the study period were included. The cirrhosis was diagnosed on the basis of 1) clinical criteria (edemato-ascitic syndrome, heterogeneous hepatomegaly with a sharp lower edge or atrophic liver, portal hypertension); 2) biological criteria (hepatocellular insufficiency syndrome); and 3) medical imaging (ultrasound and CT scan) suggesting cirrhosis. Patients whose records were incomplete or could not be used were excluded. A data collection form was used as the data collection tool. The form included an identification section, a clinical, and biological, variables section as well as the imaging results parts and other investigations' results such as the endoscopy and the CT scan data. Finally the form included also data on the treatments and the pro-

gression of the disease under treatment. A descriptive analysis was implemented and qualitative variables were pooled as frequencies and percentages while the quantitative ones were calculated as means with standard deviations. Data were entered and analyzed using EPI-INFO software, version 3.5.3 and EXCEL 2010.

3. Results

3.1. Sociodemographic Characteristics

Overall, 803 patients were hospitalized in the hepato-gastroenterology department during the study period. Hepatobiliary pathology represented 74.7% of the cases. The data of 273 patients (33.9% of hospitalizations) were included in the analysis.

The mean age (±standard deviation) was 46.9 (±13.8) with a range of 16 - 82 years. The most represented age group was 41 - 60 years. The sex ratio was 2.7. Farmers and housewives accounted for 34.2% (93/272) of the patients (Table 1). The mean duration from the first clinical manifestations to medical visit was 99 days.

3.2. Etiologies and Seriousness of Cirrhosis

Overall, 239 (87.5%) patients, were screened for HBsAg and 183 (76.5%) tested positive while 191 (69.9%) were screened for anti-hepatitis C virus antibodies (anti-HCVAb) and 28 (14.6%) were tested positive. Viral load was performed for 48 (17.5%) HBsAg+ patients and the mean viral load was 23,295,569.7 IU/ml, with a range of 23 to 110,000,000 IU/mL and was undetectable in two patients. C-RNA (HCV) was performed in 04 (14.2%) of the 28 anti-HCV Ab+ patients with a mean viral load of 2749 IU/ml.

Table 1. Socio-demographic characteristics.

variable	Frequency	Percent (%)
Sex = female	73	26.74
Age group		
0 - 20	4	1.46
21 - 40	101	37.00
41 - 60	116	42.5
>60	52	19.04
Occupation		
Pupil/Student	13	4.76
Famers	49	17.95
Civil servants	44	16.12
Housewives	44	16.12
Retired	5	1.83
Informal sector	33	12.09
Not specified	85	31.13

The results of various non-specific laboratory tests, the dosage of prothrombin, concentration and serum albumin (protidogramme) and previous clinical examination were used to classify 28 patients according to Child Pugh categories [10] (https://en.wikipedia.org/wiki/Child%E2%80%93Pugh_score). Fourteen, 11 and three patients were in Child Pugh's classes C, B or A, respectively.

3.3. The Therapeutic Features

Symptomatic treatments

To treat ascites, punctures were realized in 110 (40.2%) patients with a mean fluid quantity of 3.5 L ± 1.3 per patient. A salt-free diet and diuretic medications were administered to 38.8% and 54.2% of the cases, respectively.

Lactulose was used in 73.6% of cases as a treatment for both inaugural hepatic encephalopathy and encephalopathy occuring during hospitalization. Twenty-four (16.2%) patients received emergency transfusion during acute episodes of anaemia at admission or during hospitalization. The gastrointestinal bleeding by rupture of esophageal varices was treated by ligation in 02 (1.3%) patients.

Etiological treatment and efficacy of the treatment

The main cause of cirrhosis was HBV (HBsAg + in 76.5% of cases). In our study, the main used antivirals were lamivudine which was administered to 35 patients (57.4%) and tenofovir to 20 (32.8%) patients. Tenofovir has been combined with lamivudine in six (9.8%) patients.

Using lamivudine, the virological response was complete (DNA-HBV undetectable) in 08 patients (72.7%) among those whose viral load was performed regularly. Four patients (6.5%) developed resistance. With tenofovir, the virological response was complete in 07 patients (87.5%). With the lamivudine-tenofovir combination, the virological response was complete in all patients.

With regard to the biochemical response, the ALAT returned to normal range in 63.6%, 75% and 100% of lamivudine, tenofovir, and tenofovir-lamivudine treated patients, respectively. The duration of the hospitalization ranged from 0 to 35 days with a mean duration of 8.5 ± 6.3 days. The different treatments administered and their outcomes, the duration of spontaneous survival of those who died are shown in **Table 2**.

4. Discussion

4.1. The Study Limitations

Our study has some limitations which are specific to retrospective studies in general including the missing data. An important missing data was the direct cause of death. This gap did not allow us to identify the most frequent causes of cirrhosis mortality in our context. However, the robustness of the variables collected as well as the descriptive nature of our study minimized the impact of this gap.

Table 2. The different treatments received by patients.

Treatment's option	Frequency	Percent (%)
Salt-free diet	106	38.8
Ascites puncture	110	40.2
Diuretics (furosemide, spironolactone)	148	54.2
Pain-killers	160	58.6
Lactulose (duphalac)	201	73.6
Blood transfusion	24	08.7
Treatment's outcome		
Improved status (patients discharged)	128	46.88
Discharge against medical advice	60	22.00
Death	85	31.13
Spontaneous survival (n = 68)		
<1 month	31	45.58
1 - 3 months	22	32.35
3 - 6 months	09	13.35
6 - 9 months	01	1.47
9 - 12 months	02	2.94
>12 months	03	4.40

4.2. Sociodemographic, Epidemiological and Etiological Aspects

The mean age of our patients was 46.9 ± 13.8 years. It was similar to the mean age reported by other published studies [11] or not published ones [12] [13] in Burkina Faso. These results showed that African patients are younger, as compared to patients in developed countries where the mean age ranges between 51 - 58 years [13] [14]. The difference in risk factors for cirrhosis in developed countries (predominance of alcohol consumption and delayed onset of the disease) compared to limited resources settings (predominance of viral hepatitis infection which is acquired early in the first years of life) may explain this difference in the mean ages [2] [4] [6].

As to the gender, it is established that the liver diseases (infections or cancers) are predominantly male's pathologies [15] [16] [17] [18]. The sex ratio of 2.7 found in our work once again corroborated this observation. The male gender would be associated with a greater mortality from bleeding caused by ruptured esophageal varices [19]. Regarding the causes of cirrhosis, the in-hospital proportions of patients testing positive for HBsAg and anti-VHCAb was 76.5% and 14.6%, respectively, as in many other studies [11] [13].

The mean duration between the onset of the first symptoms and the first medical visit was 99 days. This long delay could in itself explain the advanced stage of the disease when the patients show up: 50% of them were already in the Child Pugh's class C whereas the mean viral load was 23,295,569, 7 IU/ml [20] [21].

4.3. Therapeutics Aspects

Symptomatic treatment

Ascites is one of the most common complications that often reveals cirrhosis [22] [23]. In our study, 40.2% of patients with ascites received a puncture, 38.8% observed a salt-free diet and 54.2% took diuretics. In the literature, it has been shown that a low-sodium diet combined with diuretics intake was very effective in 90% of cases in the treatment of ascites [23]. When ascites is refractory (ascites not responding to treatment with diuretics associated with the salt-free diet or relapsing after high doses of diuretic [23] [24], other therapies can be initiated including repeated ascites punctures, peritoneo-venous shunts or abdominal drainage. Shunts and drainage have the advantage to better control ascites, reducing frequent hospitalizations and the financial burden on patients and the healthcare system, and improving patients' lives without anyway significantly affecting their survival as compared to traditional punctures [22] [24]. These interventions should be assessed in a broader context of palliative care for end-of-life patients with chronic liver disease [22].

Hepatic encephalopathy with an unfavorable outcome as per the West Haven criteria [25] is associated with higher short-term mortality (within 90 days) [26]. The treatment of encephalopathy is primarily based on the treatment (if possible) of the triggering cause. In addition to nutrition, the use of disaccharides and non-absorbable antibiotics (rifaximin) are part of the therapeutic means [25]. Treatments aiming to modify the colonic bacterial flora and accelerate intestinal transit may prove efficacious. The most commonly used treatment is the lactulose or lactilol (non-absorbable disaccharide) [25] [26] [27]. In our study, this treatment was administered in 73.6% of the cases. However, treatment combining lactulose and rifaximin would be more efficacious (incidence rate ratio (IRR) = 0.28 confidence interval (CI) 95% (0.27 - 0.30)) than lactulose alone (IRR = 0.31 95% CI (0.30 - 0.32)), itself more effective than rifaximin alone (IRR + 0.49 95% CI (0.45 - 0.53)) [28].

Another serious complication of cirrhosis is the gastrointestinal bleeding from ruptured oesophageal varices. Its incidence is estimated at between 12% and 15% per year with a mortality rate at up to 20% [19] [29]. Different therapeutic procedures are used including drug treatments (non-cardio selective beta-blockers, or isosorbide mononitrate or both), endoscopic interventions (ligation of oesophageal varices, or sclerotherapy), blood shunts (total shunt, transjugular portosystemic or distal splenorenal shunt). The superiority of an intervention over another has not been demonstrated [30]. However, the best treatment remains the prevention by treating the cause of the cirrhosis (alcohol withdrawal or effective antiviral treatment) [31]. In our study the ligation of esophageal varices was performed in 2 patients (8.3%). This low frequency of ligation could be explained by the high cost of the needed material to implement the intervention.

Etiological treatment

Antiviral therapy with nucleoside analogue has been systematically prescribed

every time it was indicated as suggested in the literature [7]. However, only 23.3% of all eligible patients were treated mainly because of financial constraints. A previous study in the same setting a few years ago found similar results with 20.3% of the patients in need of antiviral treatment, able to afford the cost of the medicines [7]. Actually in Burkina Faso, the hepatitis B infection does not benefit from health policy easing the access to the antivirals as it is provided for HIV patients.

Antiviral molecules used to treat hepatitis B include tenofovir, entecavir, and lamivudine [32] [33] [34]. A total of 57.4% of our patients were treated with lamivudine. Sombié [7] found a higher proportion (96.7%) of patients on lamivudine as antiviral to treat the HBV. At the time of his study, tenofovir was not yet introduced in Burkina Faso.

The efficacy of lamivudine to slow down the HBV-born cirrhosis has been demonstrated. However, it is no more currently recommended by the WHO because of its weak virological barrier and the quick emergence of resistant strains [33]. Indeed, the main drawback of lamivudine is its high risk of resistance (20% per year) [7]. In our study, we noted resistance to lamivudine in 6.5% of the cases. This low rate of resistance was also noted by Sombié [7] (6.7% of his cases). This would be explained by the small number of treated patients and the shorter duration of the follow-up.

Overall, 32.8% of patients received tenofovir. With tenofovir, HBV-DNA was undetectable in 87.5% of the cases. This proportion was within the range of the complete virological response reported and which is greater than 76% and was higher than the result found by Yao [35] who reported 72.7%. No cases of resistance to tenofovir were observed in our study. This result confirms the data in the literature which have not reported any case of resistance to tenofovir to date [36].

Tenofovir was administered in combination with lamivudine to 9.8% of the patients. This proportion was higher than the 6.4% observed by Sombié [7]. The viral load was undetectable in all six patients treated with a lamivudine-tenofovir combination (including four patients who faced resistance to lamivudine).

With respect to the biochemical response, the ALAT returned to normal range in 63.6% of the lamivudine-treated patients. This proportion was comparable to SIA's result from a study implemented in the same hospital [37] in Burkina, and comparable to Yao's [35] in China, which reported biochemical response rates of 71.8% and 79.1%, respectively. Under tenofovir this rate was 75%, similar to the rates of 77% within one year of treatment in the literature [35].

4.4. The Disease Progression

In our study, the duration of follow-up was relatively short, with a mean duration of 8.5 ± 6.3 days. Actually, once the diagnosis is known, and after they experience some relief of their symptoms, most patients were discharged because they could no longer afford to pay for the care and the hospitalization. Most of them requested to be discharged. Before our study, Tinto and Sawadogo respec-

tively, found the same result with 90.4% and 100% of the hospitalized patients staying less than one month [12] [13]. The in-hospital case fatality rate was high at 32.3% comparable to the results of previous studies in the same setting which were between 28.5% and 33.3% [12] [13]. The causes of this high mortality would mainly be the gastrointestinal bleeding and hepatic encephalopathy [19] [26] [28].

5. Conclusion

In the gastroenterology department of the UTH-YO, cirrhosis was a very frequent reason for medical visit and hospitalization. It affects the male, young and active population. Patients show up very late at an advanced stage of the disease. The hepatitis B and C viruses are the most frequent etiologies. The available therapeutic means are quite limited, due to an under-equipped health system, but also to very poor patients. This context leads to an excess lethality by cirrhosis and a shorter survival time. A survival analysis on a cohort of cirrhotic patients during a longer period of follow up in our LMIC context may better highlight the details of the disease progression as well as the risk factors for death. The prevention by vaccination (anti-hepatitis B) and early systematic screening with treatment when indicated are very efficient and effective weapons at our disposal.

Conflicts of Interest

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

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