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Hepatitis C: Epidemiological, Clinical and Therapeutic Aspects in Dakar (Senegal)

Salamata Diallo[1], Mariéme Polele Fall[1], Marie Louise Bassène[1], Mamadou Ngoné Gueye[2], Mame Aissé Thioubou[3], Cheikh Ahmadou Bamba Cissé[2], Alioune Badara Fall[1], Abdoul Aziz Atteib Fall[1], Alsine Yauck[1]

[1]Cheikh Anta Diop University of Dakar, Hospital Aristide Le Dantec, Dakar, Senegal
[2]Cheikh Anta Diop University of Dakar, Hospital Idrissa Pouye, Dakar, Senegal
[3]Assane Seck University of Ziguinchor, Hospital de la Paix, Ziguinchor, Senegal
Email: oldou@hotmail.fr

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Abstract

Viral hepatitis C is a major public health problem. The aim of our work was to determine the epidemiological, diagnostic and treatment profiles of patients with HCV in Dakar (Senegal). We conducted a retrospective, descriptive, multicentre study between January 1, 2010, and December 31, 2019. We included 26 patients. The mean age of the patients was 53.5 years [28 - 70 years] and 46.2% were males. Of the 26 patients included, 7 (26.9%) were Senegalese, and the majority were from other African countries. Risk factors for contamination found were surgery in 11 patients (42.3%) and blood transfusion in 1 patient (3.8%). The mean viral load was 6.47 log IU/ml [4.26 - 7.26 log IU/ml]. Ten patients were infected by genotype 4. No patients were co-infected with HIV or HBV. Six patients (23.1% of patients) had significant fibrosis, of which five (19.2% of patients) were in the stage of cirrhosis. Twelve patients (46.2%) started treatment. Eleven were treatment-naïve and 1 did not respond to ribavirin-pegylated interferon-based therapy after 48 weeks. Ten cases of antiviral therapy were based on DAA and ribavirin-pegylated interferon in 2 patients. For the patients treated with peginterferon and ribavirin, a rapid virologic response was observed at 12 weeks in one patient, and the other patient was lost to follow-up. Among DAA-treated patients, 7 had sustained virologic responses at 12 weeks, 2 persisted, and 1 was lost to follow-up. Moderate thrombocytopenia and weight loss were observed in one patient receiving peginterferon and ribavirin. In our study, no patient died on treatment and no patients developed de novo HCC during or after DAA therapy. **Conclusion:** Viral hepatitis C is rare in Senegal. Despite the progress made in the therapeutic management of viral hepatitis C, it remains a challenge in Senegal. Indeed, DAAs are expensive and are not marketed, which

makes them inaccessible to most patients.

Keywords

Hepatitis C, Epidemiology, Diagnosis, Treatment, Senegal

1. Introduction

Hepatitis C (HVC) is a leading cause of chronic hepatitis. Globally, HCV seroprevalence ranges from 2% to 3%, with an estimated 71.1 million patients with active viremia [1]. In 2016, approximately 399,000 people died from viral hepatitis C and its complications [2]. HCV infection is a major public health problem in developing countries. In Africa, there are regional and national differences in reported seroprevalence for HCV infection. There are few HCV seroepidemiological data in this region. A recent meta-analysis found that the overall HCV seroprevalence in sub-Saharan Africa was 2.98% [1].

About 10 - 15 million people in sub-Saharan Africa have viremia.

Countries with the highest population prevalence of viremia include Gabon (7%), Egypt (6.3%), Nigeria (1.4%) and Ghana (1.4%) [1]. In Senegal, the prevalence of HCV infection is unknown due to the lack of epidemiological studies in the general population. The seroprevalence is estimated at 1% [3].

HCV causes acute hepatitis, which in most cases becomes chronic. This chronic hepatitis can progress to cirrhosis and hepatocellular carcinoma (HCC).

The goal of antiviral therapy is to eradicate the virus, defined as undetectable viral ARNs. Eradication of the virus reduces the risk of progression to cirrhosis, HCC, liver transplantation, and liver-related mortality, as well as extrahepatic manifestations of HCV infection (e.g., cryoglobulinemic vasculitis) [1] [4].

In recent decades, the treatment of CHC has been based on the combination of interferon (IFN) and ribavirin (RBV). Dual "PEG-IFN" and RBV therapy achieved SVR rates of 40% to 50% in patients with genotype 1 and approximately 80% SVR rate in genotype 2, 3, 5 and 6; genotype 4 results are interim results [4]. IFN-based therapy has significant side effects, contraindications, and limited tolerability, leading to poor adherence or early discontinuation. The discovery of direct-acting antiviral drugs (DAAs) has revolutionized the treatment of viral hepatitis C. The introduction of first-generation DAAs resulted in SVR rates of approximately 65% - 75% for all genotype combinations. The real revolution came with the discovery of the second generation of pan genotypic DAAs. Sustained virological response (SVR) rates for these drugs were greater than 95% [4]. The rapid virological response observed with the effective DAA combination resulted in a progressively shorter duration of treatment. A major limitation of DAA therapy is the inaccessibility of the drug due to the high cost.

Viral hepatitis C studies in Senegal are few and small-scale studies involving special populations. The treatment of hepatitis C in Senegal remains a challenge,

especially the accessibility of treatment. DAA is not sold in Senegal, and the cost of the drug is high. It is in this context that we conducted a retrospective, descriptive, multicentric study. The objective of the study is to describe the epidemiological, clinical, paraclinical, therapeutic and evolutionary profile of patients with hepatitis C.

2. Patients and Method

We conduct a descriptive study based on the retrospective collection of data in the hepatogastroenterology unit of the Hospital Aristide Le Dantec of Dakar (Senegal), in the hepatogastroenterology unit of the Hospital Principal of Dakar (Senegal) and in two private practice from January 1, 2010 to December 31, 2019. The study population consisted of all patients who had positive hepatitis C virus antibody. We included all patients who had positive hepatitis C virus antibody with viral replication. A data processing sheet was established and included the following data: clinical, epidemiological data, liver function test, ultrasound, fibroscan, fibrotest and biopsy were collected including gender, age at diagnosis, prior history of HCC, presence of cirrhosis, the Child-Pugh (CP) score, hemogram, alanine aminotransferase (ALT), aspartate aminotransferase (AST), total bilirubin, albumin, prothrombin, viral genotype C, viremia in UI/ml and Log UI. The treatments carried out, drugs used and evolution after treatment. The primary endpoint of treatment was defined by the absence of HCV in polymerase chain reaction conducted at 12 weeks after the completion of the treatment (SVR12). Patients with unusable records were not included.

Statistical Analysis

The data were entered and analysed with Microsoft Sphinx Plus Version 5 software.

3. Results

In total, 26 patients were included in this study from January 1, 2010, to December 31, 2019. The baseline characteristics of the patients are summarized in Table 1. The mean age was 53.5 years [28 - 70 years] and 46.2% of the patients were males. There was no family history of HCC.

Of the 26 patients included, 7 (26.9%) were Senegalese, and the majority were from other African countries in 73.1% (Table 2). Eleven cases had a history of surgery, and 01 had a history of blood transfusion. One patient had a history of blood transfusion and surgery. The circumstances of discovery were specified in 16 patients. The discovery was made during a systematic check-up in 8 cases, clinical signs in 7 cases and donation of blood in 1 case. No extrahepatic manifestations were found. The mean viral load was 6.47 log IU/ml [4.26 - 7.26 log IU/ml]. The mean rate of ALT was 88 IU/L [12 - 192]. The baseline biological characteristics of the patients before treatment are summarized in Table 3.

Genotypes were searched in 21 patients (80.8%). The different genotypes ob-

served were genotype 4, genotype 2 and genotype 1 in 47.6%, 38.1% and 14.3% of cases respectively. HBsAg was detected in 19 patients and all patients were negative. HIV serology was performed on 16 patients, and they were negative. Liver fibrosis was assessed in 20 patients (76.9%). Liver fibrosis was assessed by fibrotest in 7 patients, fibroscan in 10 patients and biopsy in 3 patients. Significant fibrosis was present in 6 patients, 5 of which were in the stage of cirrhosis.

Table 1. Baseline patient characteristics.

Characteristics	Frequency (percentage)
Age, years, mean	53.5
Male, n (%)	12 (46.2%)
Patients with cirrhosis, n (%)	5 (19.3%)
Liver biopsy performed, n (%)	3 (11.5%)
Non-invasive markers of fibrosis, n (%)	17 (65.4)
Fibrosis stage (METAVIR), n (%)	
F0 - F1	11 (42.3%)
F2	3 (11.5%)
F3	1 (3.8%)
F4	5 (19.3%)

Table 2. Country of origin of patients.

Country of origin	Frequency (percentage)
Senegal	7 (26.9%)
Rwanda	3 (11.5%)
Guinea Conakry	2 (7.7%)
Guinea Bissau	2 (7.7%)
Mali	1 (3.8%)
Mauritania	1 (3.8%)
Togo	1 (3.8%)
Nigeria	1 (3.8%)
Equatorial Guinea	1 (3.8%)
Cameroon	1 (3.8%)
Burundi	1 (3.8%)
Chad	1 (3.8%)
Kenya	1 (3.8%)
Madagascar	1 (3.8%)
Lebanon	1 (3.8%)
France	1 (3.8%)

Table 3. Baseline biological characteristics before treatment.

Characteristics	Mean
ALT, IU/L	88 (12 - 192)
Bilirubin mg/L	9 (3 - 12)
Albumin g/L	36 (27 - 44)
Prothrombin %	79 (59 - 100)
Platelets/mm^3	288,234 (187,934 - 345,235)
RNA log IU/mL	6.47 (4.26 - 7.26)
Alfafoetoprotein ng/mL	6.9 (2 - 11)

ALT: Alanin Aminotransferase.

Twelve patients (46.2%) started treatment. 11 were treatment-naïve and 1 failed 48 weeks of ribavirin and peginterferon. Of the 14 patients (53.8%) who did not receive treatment, 11 were lost to follow-up, 2 had limited financial resources, and 1 wished to become pregnant. Antiviral treatment was based on the combination of DAAs in 10 cases and on the combination of ribavirin and pegylated interferon in 2 patients. The available DAA regimens were sofosbuvir/daclatasvir (4 patients), sofosbuvir/velpatasvir (2 patients), sofosbuvir/velpatasvir/ribavirine (1 patient), Sofosbuvir/ribavirine (2 patients), sofosbuvir/ledipasvir (1 patient). In the patients treated with peginterferon and ribavirin, we observed a rapid virologic response with undetectable viral load at 12 weeks in one patient, and a loss to follow-up in the other patient. Among DAA-treated patients, 7 had sustained virologic response at 12 weeks, 2 persisted, and 1 was lost to follow-up. Thrombocytopenia ranging from 108,000 to 138,000 was noted in 1 patient on pegylated interferon and ribavirin, weight loss was reported by one patient on pegylated interferon and ribavirin. No one died on treatment. No patients developed de novo HCC during or after DAA therapy.

4. Discussion

The mean age in our series was 53.5 years. These results are comparable to those of Luma *et al.* in Cameroon, whose mean age was 56 years [5]. The study conducted by Sombié *et al.* in Burkina Faso, found a mean age of 47 years [6]. In our study the risk factors found were surgery and blood transfusion. Surgery was reported in 42.3% of cases. In the study by Kowo *et al.* in Cameroon, it occurs in 54.2% of cases [7]. This route of transmission was common in the 1950s and 1970s, when medical equipment was reused, and HCV disinfection measures were inadequate. One patient was diagnosed with blood transfusion before 1990. Study in France in 2010 [8] found blood transfusion to be a risk factor in 49.9%. In Cameroon it was present in 21.5% of cases [7]. Before 1991, blood transfusion was an important factor in the transmission of HCV. Today, that risk has almost completely disappeared. In fact, blood donations are systematically screened, and at-risk donors are excluded [9]. Of the 26 patients included,

the majority were from Central African countries (Cameroon, Equatorial Guinea, Chad) and East Africa (Burundi, Rwanda, Kenya, Madagascar). Senegal is considered by the WHO as a low prevalence area (1%) for HCV [2]. Most of the countries in Central and East Africa are considered high prevalence areas [10]. In our study, the discovery occurred most frequently during routine examinations (50%). This finding has been reported in several studies. Kowo *et al.* [7] noted this in 86.8% of cases and Sombié *et al.* [6] in 37% of cases. The diagnosis of viral hepatitis C is often made at the stage of chronic hepatitis. This chronic hepatitis is most often asymptomatic. Thus, the diagnosis is usually made incidentally. In our series, the mean viral load was 6.47 log IU/ml [4.26 - 7.26 log IU/ml]. This is higher than that found by Sombié *et al.* [6] which was 5.98 log IU/ml. Viral load is important in pretreatment assessment and follow-up with antiviral therapy. It allows to define the response to treatment to be defined [11]. The different genotypes observed were genotype 4, genotype 2 and genotype 1 in 47.6%, 38.1% and 14.3% of cases respectively. These same genotypes were found by Kowo *et al.* [7] at different frequencies: genotype 1 in 42.7% of cases, genotype 2 in 20.5% of cases and genotype 4 in 35.9% of cases. Sombié *et al.* [6] found genotypes 1, 2 and 5 with a predominance of genotype 2 identified in 71.1% of cases. With the advent of pan-genotype therapy, genotype testing has become less common. However, it remains important in cirrhosis or recurrence [12]. The geographic distribution of genotype around the world is not uniform. The dominance of genotype 4 in our study can be explained by the fact that a large proportion of our study population is from Central Africa, where this genotype was found along with Egypt and the Middle East. Genotypes 1 and 2 are found all over the world. Liver fibrosis was assessed by fibrotest in 7 patients and fibroscan in 10 patients and biopsy in 3 patients. Although biopsy remains the gold standard for the evaluation of liver fibrosis, it remains invasive with low morbidity and mortality. Therefore, non-invasive fibrosis tests have been developed and validated for the assessment of liver fibrosis in HCV infection [13]. Six patients (23.1% of patients) had significant fibrosis, of which 5 (19.2% of patients) were in the cirrhosis stage. Cirrhosis is one of the major complications of HCV and 10 to 30% of patients with chronic viral hepatitis will develop cirrhosis, which will affect their prognosis. Antiviral therapy was initiated in 12 patients (46.2%). In 14 patients (53.8%) who did not start treatment. Eleven patients were lost to follow-up. Most of the patients in our series were temporarily living in Senegal for work or healthcare needs. Two patients had limited financial resources. The cost of antiviral C therapy is very high, making it unavailable to most patients treated in our country. A patient wishes to become pregnant. In the absence of preclinical data, it is recommended not to use direct-acting antivirals during pregnancy or breastfeeding, and to discontinue treatment if pregnant [14]. Antiviral treatment was based on the combination of DAAs in 10 cases and on the combination of ribavirin and pegylated interferon in 2 patients. The treatment of chronic hepatitis C has undergone major changes. Antiviral therapy was followed by standard inter-

feron (IFN) for 6 months and 12 months, followed by interferon + ribavirin, pegylated interferon + ribavirin dual therapy. The first specific viral protease C inhibitors, telaprevir and boceprevir, were introduced in 2011. These treatments have significant side effects. A new DAA was introduced in 2014. They have a higher genetic barrier to the emergence of drug-resistant viruses, are less toxic, come in tablet form, and allow for shorter treatment durations, with SVRs of 95% to 100% for all genotypes. However, they are still very expensive and therefore less readily available in our population. Only 9 of 26 patients treated with DAA [15]. Among patients on DAAs, 7 had sustained virologic response at 12 weeks, 2 persisted, and 1 was lost to follow-up. Of the two patients treated with pegylated interferon and ribavirin, one had a rapid virologic response with undetectable viral load at 12 weeks, and the other was lost to follow-up. Moderate thrombocytopenia and minimal weight loss were observed in one patient on pegylated interferon and ribavirin. Sombié *et al.* found haematological side effects including thrombocytopenia in 11.1% of patients on pegylated interferon and ribavirin [6]. In Benin, Kpossou *et al.* found thrombocytopenia in 20/26 patients followed [16]. The many serious side effects of these two molecules led to the search for treatments with better tolerance, leading to the discovery and commercialization of DAAs. In our study, no patient died on treatment and no patients developed de novo HCC during or after DAA therapy. The role of DAAs in the development of CHC is debated. A retrospective study by Conti *et al.* in Italy reported that in a cohort of 344 CHC patients treated with different DAA regimens, the incidence of HCC occurrence and recurrence were 3.16% (95% CI: 1.45 - 5.90) and 28.81% (95% CI: 17.76 - 42.07) [17]. In Portugal, Cardoso *et al.* found a 7.4% incidence of HCC during one-year follow-up of cirrhotic patients who achieved SVR after treatment with sofosbuvir and ledipasvir. These patients with de novo HCC were asymptomatic and detected on radiological screening [18]. In the United States, two large retrospective cohort studies have been conducted to investigate the role of DAAs in HCC. Ioannou *et al.* with a sample size of 62,354 and Kanwal *et al.* with 22,500 study participants. Both studies concluded that DAA was not associated with a significant risk of HCC compared with IFN-based therapy [19] [20]. The focusing on HCV patients and measuring the effect of DAAs on HCC progression or development will help to assess risk more accurately [21]. Our study has some limitations. The study was retrospective, and the number of patients was small. Our results need to be validated in future by long term multicentric, a prospective randomized clinical trial with larger numbers of patients.

5. Conclusion

Viral hepatitis C is rare in Senegal. Despite the progress made in the therapeutic management of viral hepatitis C, it remains a challenge in Senegal. Indeed, DAAs are expensive and are not marketed, which makes them inaccessible to most patients.

Conflicts of Interest

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

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