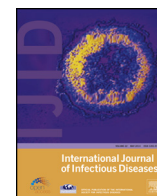


Contents lists available at ScienceDirect

International Journal of Infectious Diseases

journal homepage: www.elsevier.com/locate/ijid

Characteristics of anti-hepatitis C virus antibody-positive patients in a hospital setting in Douala, Cameroon



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ARTICLE INFO

Article history:

Received 11 December 2015

Received in revised form 1 February 2016

Accepted 17 February 2016

Corresponding Editor: Eskild Petersen, Aarhus, Denmark.

Keywords:

Hepatitis C virus

Clinical

Virological

Histological

Genotype

SUMMARY

Introduction: Hepatitis C virus (HCV) infection is a major public health problem, especially in resource-limited settings where many patients are diagnosed at the stage of complications. In Cameroon, where HCV is endemic, little is known about the clinical, biological, and virological profile of HCV-infected patients.

Methods: A clinical case note review of all patients positive for antibodies against HCV diagnosed at the gastroenterology outpatient clinic of the Douala General Hospital, Cameroon, from January 2008 to December 2014, was performed.

Results: A total of 524 patients were included in the study, 53% of whom were female. The mean age was 56 ± 13 years. A history of blood transfusion and a history of scarification were the most common potential risk factors for HCV exposure, as found in 16% and 13% of the study population, respectively. Current alcohol use was found in 24% of patients. Co-infection with hepatitis B virus and HIV was 3.6% and 3.4%, respectively. Among the patients, 39% had no complaint at diagnosis; only 16% were diagnosed through a routine medical checkup. Clinically, the most common finding was hepatomegaly (26.1% of patients). Transaminases above the upper limit of normal were found in 55.2% of patients, particularly those aged >57 years ($p = 0.001$). Genotypes 1 (43.95%), 2 (25.11%), and 4 (28.25%) were the most common. Liver cirrhosis was present in 11% of patients and hepatocellular carcinoma in 4%, the latter being more common in males ($p < 0.001$) and in those aged >57 years ($p = 0.03$).

Conclusions: In the gastroenterology clinic of Douala General Hospital, while almost 40% of patients who were anti-HCV antibody-positive were asymptomatic and diagnosed fortuitously, some already presented complications, including cirrhosis and hepatocellular carcinoma. There is an urgent need to put in place programs to increase awareness and diagnosis of HCV infection and to develop extensive and targeted anti-HCV treatment guidelines to improve the management of these patients in Cameroon.

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1. Introduction

Hepatitis C virus (HCV) infection is a major public health problem.¹ Globally about 185 million people are chronically infected, 90% of whom are in low and middle income countries,^{2–5} resulting in substantial morbidity and mortality.⁶ HCV infection

often remains asymptomatic and unrecognized until complications arise, and for many who have been diagnosed, treatment remains unavailable.⁷ HCV can induce hepatic inflammation, which may result in progressive fibrosis leading to cirrhosis and hepatocellular carcinoma (HCC).^{8,9} Standardized mortality ratios for liver-related death are 16- to 46-fold higher in infected individuals than in the general population.^{6,10,11} In Cameroon, the prevalence of anti-HCV antibody positivity is estimated to be about 13%.¹²

The societal, clinical, and economic burdens imposed by untreated HCV are expected to continue to soar in coming years

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as more patients progress to advanced liver disease.¹³ This high burden and low access to HCV services emphasizes the urgent need for resource-limited settings to be included in the global HCV agenda. As such, programs aimed at improving awareness and reducing disease progression and transmission need urgent scale-up without further delay. Consequently, epidemiological studies to improve the understanding of disease burden and HCV service provision and uptake are indispensable if the global control of HCV infection is to be achieved.¹⁴ However, data on access to HCV diagnostic and treatment services in resource-limited settings are very scarce.¹⁴ Population-based studies on HCV prevalence, molecular epidemiology, and clinical and laboratory characteristics have been performed only in a few African countries, and most of these have been based on small groups of individuals.¹⁵

Although it is irrefutable that extensive assessments are mostly limited to patients who are subsequently treated, thus reflecting an attempt to conserve limited health resources, hope is not lost that antiviral treatment will increasingly be offered in resource-limited settings through government and donor agency interventions, particularly to those with severe liver disease.¹⁶ Paradoxically, in a region with a high disease burden, published data on disease characteristics still remain very scarce,¹⁷ although such data are of great importance in improving our understanding of the disease and in targeting patient treatment, especially in resource-limited settings aspiring to improve HCV treatment. Thus the present study was performed to describe the epidemiological, clinical, biochemical, virological, and histological characteristics of anti-HCV antibody-positive patients attending the gastroenterology outpatient clinic of Douala General Hospital (DGH), with the aim of improving our understanding of HCV infection in Cameroon, in order to have a template on which to create an HCV treatment clinic in this hospital.

2. Methods

2.1. Study design and setting

This descriptive cross-sectional study was carried out in DGH, a tertiary health facility in Douala, the largest city and economic capital of Cameroon, with an estimated population of over three million inhabitants. This hospital has a capacity of 320 beds and hosts many services and units, among which is a gastroenterology unit to which most patients with liver diseases are referred. It also has a fully functional laboratory (subject to periodic quality control and validation) where most baseline tests relevant to HCV diagnosis and management are done.

2.2. Data collection and laboratory analysis

The study was approved by the DGH Ethics Committee for Research. A thorough clinical case note review was performed. All patients tested and declared positive for anti-HCV antibody at the gastroenterology outpatient clinic between January 2008 and December 2014 were included. Information obtained from the files included socio-demographic characteristics (age, sex, marital status, profession, place of residence), circumstances of HCV diagnosis, potential risk factors (blood transfusion, scarification, piercing, tattoo, surgery, family history of liver disease or cancer), comorbidities (diabetes mellitus, hypertension, current alcohol use and smoking), insurance, symptoms and signs associated with HCV infection (pedal edema, ascites, splenomegaly, hepatomegaly, jaundice), and laboratory test results (alanine aminotransferase (ALT), aspartate aminotransferase (AST), serum albumin, full blood count, hepatitis B surface antigen (HBsAg), and anti-HIV serology).

At DGH, anti-HCV testing is done first using a rapid test on plasma, the DiaSpot HCV Test Strip (DiaSpot Diagnostics, USA). For those who are positive, confirmation is carried out using a third-generation solid-phase ELISA (Recombi LISA HCV Antibody Test, Ref. E0511; CTK Biotech, San Diego, CA, USA) following the manufacturer's instructions. This test, which qualitatively detects IgG and IgM for HCV, is highly sensitive and specific (100%), as indicated in the manufacturer's manual. Following anti-HCV positive testing, further evaluation is proposed to those who can afford it, including HCV RNA quantification, HCV genotyping, and the assessment of liver fibrosis with the FibroTest (BioPredictive, Paris, France) and HCV activity using ActiTest (BioPredictive). HCV RNA quantification and genotyping are done by real-time PCR (RT-PCR). These tests are not performed routinely in Cameroon. Thus, blood samples from HCV-positive patients are collected in ethylenediaminetetraacetic acid (EDTA) tubes, as specified by the respective test procedures, separated, frozen, and packaged in temperature-controlled thermochip containers and transported to an accredited laboratory in Paris, France where they are analyzed; the results are reported within 10 days either by fax or by e-mail.

Hepatitis B virus (HBV) was detected using a one-step HBsAg test strip (DiaSpot HBsAg; DiaSpot Diagnostics), which if positive was confirmed with an HBsAg ELISA test (BIOREX; Biorex Diagnostics Limited, Antrim, UK).

HIV diagnosis was done using a positive rapid test (Determine HIV 1/2; Alere Medical Co., Chiba, Japan) and confirmed according to the Cameroon National AIDS Control Program guidelines by antibody detection in two successive samples using a third-generation ELISA test (BIOREX; Biorex Diagnostics Limited).

The diagnosis of liver cirrhosis and HCC were done mainly through clinical, laboratory, and radiological assessments by the resident gastroenterologists; these were recorded in the files.

Participants described as 'insured' were those who had full or partial compensation for medical expenses. 'Alcohol use' was reserved for those who admitted to drinking alcohol by a simple 'yes' to the question "Do you drink alcohol?" A 'routine checkup' was a scheduled health checkup appointment with a doctor that involved a physical examination and appropriate screening tests for specific diseases with the aim of monitoring health as well as assisting in the prevention and early detection of disease. 'Systematic screening', on the other hand, was reserved for mass screening of specific population groups, symptomatic or not, for the presence of anti-HCV antibodies. The METAVIR score, which is a conversion from the FibroTest/ActiTest results, was used to categorize fibrosis in chronic hepatitis C according to a 5-stage classification: F0 (no fibrosis), F1 (portal and periportal fibrosis without septa), F2 (portal and periportal fibrosis with rare septa), F3 (numerous septa without cirrhosis), and F4 (cirrhosis). The METAVIR score also categorized activity according to a 4-grade classification: A0 (no activity), A1 (minimal activity), A2 (moderate activity), and A3 (severe activity).

2.3. Statistical analysis

Data were entered into Epidata version 3.1 software and exported for analysis into Stata version 12.0 statistical software (Stata Corp., College Station, TX, USA). Categorical variables were presented as counts and their percentages. Continuous variables were presented as the mean (with the standard deviation (SD)) or median (with the interquartile range (IQR)) where appropriate, or as counts and percentages after categorizing using predefined cut-offs or the median. Comparisons of different variables were done by sex and age (categorized by median age) using Pearson's Chi-square test or Fisher's exact test and the Student *t*-test or the Wilcoxon rank sum test, where appropriate; the reported *p*-value was considered significant if it was less than 0.05.

3. Results

A total of 524 clinical case files of anti-HCV antibody-positive patients were examined.

3.1. Socio-demographic characteristics of the study participants

The mean age of the study population was 56 (SD 13) years; 90% were above the age of 40 years. Female sex was predominant (53%), although this was not statistically significant. Most of the patients were of urban origin (76%) and more than 90% of the study population had no health insurance coverage. Only 16% of the study population had been diagnosed at a routine checkup (Table 1).

3.2. Potential risk factors, comorbidity, and co-infection

A potential risk factor for acquiring HCV infection was identified in 37.9% (199/524) of participants. The most frequent were a history of surgery, history of blood transfusion, and history of scarification (18%, 16%, and 13% of the study population, respectively). A history of blood transfusion and scarification were significantly more common in females than males ($p < 0.05$) (Table 2). Blood transfusion was also a factor strongly associated with HCV acquisition in those who were aged ≤ 57 years ($p = 0.008$). Among the patients studied, 3.6% ($n = 19$) were co-infected with HBV and 3.4% ($n = 18$) were co-infected with HIV. Diabetes and hypertension were common, present in 18% ($n = 95$) and 39% ($n = 204$) of patients, respectively (Table 2).

3.3. Clinical and laboratory characteristics

In 39% of patients confirmed to be anti-HCV positive, there was no suggestive presenting complaint. The most common physical sign was a hepatomegaly, present in 26.1% of patients, predominantly found in men ($p = 0.017$). Presumed symptoms of extra hepatic HCV manifestation (joint pains) was found in 9% of patients (Table 1). Transaminases above the upper limit of normal were found in 55% of patients (Table 3). HCV genotype and viral load results were available for 43.5% (228) and 42.2% (221) patients respectively, of which 19 subtypes were identified. The most common genotype was type 1 in 43.4% of patients. Men were more likely to have a higher median viral load for HCV non-genotype 2 than women (Table 3). The male sex and advanced age were factors significantly associated with advanced fibrosis-Metavir F3 F4 ($p < 0.05$). Liver cirrhosis and hepatocellular carcinoma (HCC) were more significantly common in those aged above 57 year ($p < 0.05$) and men were more likely to develop HCC than women ($p < 0.001$) (Table 4).

Table 2

History of potential risk factors and associated comorbidities in 524 anti-HCV-positive patients, compared by sex and median age

Risk factors and comorbidities	Female	Male	<i>p</i> -Value ^a	≤ 57 years	> 57 years	<i>p</i> -Value ^a	Total (%)
Risk factors							
History of blood transfusion	58 (21)	27 (11)	0.002	55 (20)	30 (12)	0.008	85 (16)
History of scarification	43 (16)	23 (9)	0.035	38 (14)	28 (11)	0.31	66 (13)
History of piercings	1 (0.36)	0 (0)	-	1 (0.37)	0 (0)	-	1 (0.2)
History of tattoo	0 (0)	2 (0.82)	-	1 (0.37)	1 (0.40)	-	2 (0.4)
History of jaundice	26 (9)	9 (4)	0.01	16 (6)	19 (8)	0.47	35 (7)
History of surgery	55 (20)	37 (15)	0.17	43 (16)	49 (19)	0.31	92 (18)
History of ascites	10 (4)	3 (1)	0.083	0 (0)	13 (5)	-	13 (2)
History of liver cancer in the family	8 (3)	5 (2)	0.55	7 (3)	6 (2)	0.86	13 (2)
Family history of viral hepatitis	10 (4)	8 (3)	0.86	9 (3)	9 (4)	0.89	18 (3)
Comorbidities							
Diabetes	48 (17)	47 (19)	0.55	36 (13)	59 (24)	0.003	95 (18)
Hypertension	106 (38)	98 (40)	0.66	70 (26)	134 (53)	< 0.0001	204 (39)
Current alcohol use	39 (14)	85 (35)	< 0.0001	75 (28)	49 (20)	0.027	124 (24)
Current cigarette smoking	6 (2)	26 (11)	< 0.0001	25 (9)	7 (3)	0.002	32 (6)

^a Chi-square test or Fisher's exact test.

Table 1

General characteristics of the study population

Variables	Number	Count (percentage)
Age in years	524	
< 20		3 (0.57)
20–39		51 (9.9)
40–59		262 (59.8)
≥ 60		208 (39.6)
Male gender	524	245 (47)
Marital status	524	
In couple (married/cohabitating)		369 (70)
Alone (single/divorced/widowed)		155 (30)
Profession	524	
Employed		281 (54)
Unemployed		243 (46)
Residence	524	
Urban		398 (76)
Rural		126 (24)
Insured	524	53 (10)
Diagnosis circumstances	524	
Asthenia		19 (4)
Jaundice		6 (1)
Routine check up		79 (16)
Fever		19 (4)
Blood donation		9 (2)
Systematic screening		17 (3)
Unknown		150 (29)
Others		225 (44)
Clinical Findings	524	
Joint Pains		45 (9)
Ankle Oedema		45 (9)
Hepatomegaly		137 (26)
Splenomegaly		44 (8)

Results are presented as count (percentage) or otherwise stated

4. Discussion

The natural history, epidemiology, diagnosis, and therapy of HCV are the object of continuing research.^{18,19} The present study highlights the epidemiological, clinical, and laboratory characteristics of patients with a positive HCV antibody serology in a region known to have a high prevalence of HCV disease but with little published clinical and laboratory data. The full magnitude of the burden of HCV-related chronic liver disease may not be realized, as most patients are asymptomatic or are evaluated only when complications occur.^{20,21}

A main finding of this study was that 90% of the patients were over the age of 40 years. A past history of surgery, blood transfusion, and scarification were the most prominent potential risk factors. Hypertension and diabetes mellitus were the most common comorbid factors, present in 39% and 18.2%, respectively. Alcohol use was 23.8%. Co-infection with HIV and HBV were low in

Table 3
General laboratory characteristics of the study population

Parameter	Number	n (%)
AST	447	
Normal (<40 IU/l)		201 (44.9)
Above the upper limit of normal		246 (55.1)
ALT	444	
Normal (<40 IU/l)		199 (44.8)
Above the upper limit of normal		246 (55.2)
Hemoglobin	426	
<12 g/dl		146 (34.3)
≥12 g/dl		280 (65.7)
Platelets	415	
<100 × 10 ⁹ /l		62 (14.9)
≥100 × 10 ⁹ /l		353 (85.1)
Albuminemia (normal >35g/l)	170	
<35 g/l		71 (41.8)
≥35 g/l		99 (58.2)
Bilirubin (normal <11 U/l)	109	
<11 U/l		75 (68.8)
≥11 U/l		34 (31.2)
HCV genotype	228	
G1		99 (43.4)
G2		56 (24.6)
G4		67 (29.4)
Mixed (1+4; 2+4; 4+5; 1,4+5)		6 (2.6)
Viral load by genotype	221	
<6 × 10 ⁵ copies/ml G2		118 (53.4)
<8 × 10 ⁵ copies/ml non-G2		
≥6 × 10 ⁵ copies/ml G2		103 (46.6)
≥8 × 10 ⁵ copies/ml non-G2		

AST, aspartate aminotransferase; ALT, alanine aminotransferase.

this population at 3.4% and 3.6%, respectively. Among the patients, 39% did not have a presenting complaint, and a medical checkup was the most common diagnostic circumstance. On clinical examination, hepatomegaly and splenomegaly were present in 26.1% and 8.4% of the population, respectively, and presumed extra-hepatic manifestations of HCV were present in 9% of

patients. Genotypes 1 (43.95%), 2 (25.11%), and 4 (28.25%) were the most common.

As concerns the description of clinical and laboratory aspects of patients found to be anti-HCV-positive, not much has been done in Sub-Saharan Africa. In most countries like Cameroon, Nigeria, and Burkina Faso, previous studies have described the prevalence of anti-HCV antibodies as well as their genotype distribution in specific populations,^{22,23} most with a small number of patients.²⁴ In the present study population, over 90% of patients were aged over 40 years. This finding is consistent with those of previous studies in Cameroon suggesting a cohort effect with an old, possibly iatrogenic group exposure, rather than continuous exposure.^{23,25} A similar hypothesis of a cohort effect was postulated in Turkey, Spain, Italy, Japan, and China, where the risk of HCV infection was higher in the distant past 40–60 years previously.²⁶ However, although the present study found a low prevalence in those aged below 40 years, there is no room for complacency, especially as many of the study patients admitted to potential risk factors for HCV transmission, notably a history of surgery, blood transfusion, and scarification. The latter is still common practice in this region and should be addressed. This calls for thorough reinforcement of the World Health Organization 2014 guidelines on the health care-associated transmission of infections and blood safety.⁷ Although potential risk factors for HCV transmission in the present study were consistent with those of previous studies in Cameroon, they contrast greatly with those of middle and high income countries where most HCV infections occur among injection drug users.^{7,27}

Comorbidity was prominent in the study population, including diabetes and hypertension. This could be simply because the study population was made up mostly of people above the age of 40 years. The presence of numerous comorbidities in this population is a call for concern when treatment becomes more available, because these may be factors associated with a poor response to antiviral drugs or adherence issues related to a high pill burden. Another problem is that of alcohol use: one in four used

Table 4
Clinical biochemical, virological, and histological characteristics, stratified by sex and median age^a

Parameters	Female	Male	p-Value	≤57 years	>57 years	p-Value	Total (%)
Clinical							
Hepatomegaly	61 (45)	76 (55)	0.017	64 (24)	73 (29)	0.19	137 (26)
Joint pains	24 (53)	21 (47)	0.9	21 (47)	24 (53)	0.50	45 (9)
Jaundice	3 (43)	4 (57)	0.71	2 (29)	5 (71)	0.27	7 (1)
Lower limb edema	21 (47)	24 (53)	0.4	8 (18)	37 (82)	<0.0001	45 (9)
Splenomegaly	23 (52)	21 (48)	0.89	15 (34)	29 (66)	0.016	44 (8)
Cirrhosis	32 (56)	25 (44)	0.64	11 (19)	46 (81)	<0.0001	57 (11)
Hepatocellular carcinoma	3 (14)	18 (86)	<0.0001	6 (29)	15 (71)	0.032	21 (4)
Laboratory							
Hemoglobin, median (IQR), g/dl	12.4 (11.1–13.3)	13.4 (11.5–14.6)	<0.0001	12.9 (11.5–14.1)	12.6 (10.9–13.6)	0.03	12.7 (11.3–13.9)
Platelets, median (IQR), ×10 ⁹ /l	198 (140–243)	170 (128–222)	0.0043	199 (150–250)	165 (114–223)	0.0001	180 (130–230)
AST, median (IQR), IU/l	42 (27–74)	46 (31–78)	0.12	38 (26–63)	55 (32–88)	<0.0001	45 (29–77)
ALT, median (IQR), IU/l	40 (27–66)	46 (32–78)	0.01	40 (27–65)	50 (30–77)	0.01	43 (28–71)
Bilirubin, median (IQR), U/l	7 (4.1–12.3)	9.9 (5.8–15.1)	0.17	8 (4.4–12.3)	7.9 (4.2–13.5)	0.89	8 (4.4–13)
Albuminemia, median (IQR), g/l	36 (29.5–42)	36.1 (31.6–43)	0.46	38 (32–43)	35.7 (28.4–41)	0.035	36 (30.7–42.3)
Viral load, ×10⁵							
Genotype 1	3.4 (1.2–16.9)	7.2 (2.0–19.7)	0.21	4.1 (1.4–15.5)	5.6 (2.8–23.3)	0.13	5.4 (1.7–17.4)
Genotype 2	18.1 (3.9–28.1)	8.3 (2.9–48.9)	0.71	3.5 (1.6–28.2)	19.8 (6.1–36.7)	0.057	13.1 (2.9–31.2)
Genotype 4	5.5 (3.6–13.0)	10.7 (4.8–28.2)	0.12	7.0 (3.6–19.0)	10.3 (4.7–15.7)	0.49	7.3 (4.1–18.3)
Fibrosis score							
F0/F1/F2	51 (71)	25 (35)		58 (62)	18 (35)		76 (53)
F3/F4	21 (29)	47 (65)	<0.0001	35 (38)	33 (65)	0.002	68 (47)
Score activity							
0/1	53 (62)	33 (38)		61 (71)	25 (29)		86 (55)
2/3	16 (31)	37 (69)		30 (59)	23 (41)		51 (45)

IQR, interquartile range; AST, aspartate aminotransferase; ALT, alanine aminotransferase.

^a Results are expressed as the count (percentage) unless stated otherwise. Statistical significance was assessed by Chi-square test, Fisher's exact test, Wilcoxon rank sum test, or Student *t*-test (with a Welch correction of variance when necessary).

alcohol, which needs to be addressed by the introduction of programs for alcohol-related harm reduction, even before antiviral treatment becomes easily accessible in this setting.^{7,14}

Clinically, HCV often remains asymptomatic and unrecognized until complications of the virus arise. When symptoms are present, they are non-specific and can be extra-hepatic in about three-quarters of patients with mild hepatic disease in some series.²⁸ In the present study, about a tenth of patients presented with chronic joint pain presumed to be an extra-hepatic manifestation. On clinical examination, about a third of the study population had hepatomegaly, unlike a study performed in London in 1993 in which it was found that about one in two patients presented with hepatomegaly.²⁹ This suggests that care-givers should thoroughly investigate any patient who presents with hepatomegaly, especially in the setting of the present study where routine checkup is not common practice, and an association with splenomegaly and ankle edema could be indicative of decompensated liver cirrhosis, as over 10% of the study population presented with cirrhosis.

Having in mind the implementation and scale-up of targeted anti-HCV treatment, systematic genotyping following quantitative HCV RNA results is important if the epidemiology of the virus is to be fully understood. Although the present findings are in conformity with the large heterogeneity in HCV genotype distribution in Cameroon, predominantly 1, 2, and 4,^{22,23} a particularity of this study population is the presence of genotype 5, dual genotypes, and multiple subtypes. Unlike other studies which have described genotype 4 to be predominant in 50–75% of patients with HCV in Cameroon^{22,23} and in all patients in a small study in neighboring Gabon,¹⁵ genotype 1 was found to be most common. The presence of numerous subtypes in the study population could be explained by the study being hospital-based, where the patients have diverse regions of origin, but does not fully explain why genotype 1 was predominantly found. However, the finding of diverse genotypes and subtypes iterates the fact that scaling up treatment should be patient-specific, as the cost of each treatment might be affected by the viral response, which depends on the particular genotype.

In the assessment of the degree of liver fibrosis in HCV infection, liver biopsy is the gold standard.⁷ Not only is it an invasive procedure with associated risks, but it also requires highly trained and skilled histological interpretation,⁷ which is not readily available in the present study setting. Although the FibroTest has been validated as a proxy for liver biopsy, it is still not locally available, thus limiting the ability to thoroughly evaluate those patients who are positive for HCV. However, in resource-limited settings, based on a systematic review of performance and taking cost into consideration, the AST-to-platelet ratio index (APRI) and FIB4 test are considered more suitable,⁷ a recommendation that must be included in our local guidelines. This therefore means that setting up an anti-HCV treatment program in the present study setting should not only address drug availability and accessibility, but should also consider paraclinical workup.

A large population of 524 anti-HCV-positive patients is described herein. Nonetheless, this study had some limitations. It was hospital-based, from clinical files, which most of the time are not subject to uniform recording (systematic differences in the way information is collected by each practitioner), thus there is the possibility of missing or limited information. Moreover there were no denominators from which to calculate any measure of the burden of the disease in this study. The high cost of HCV RNA quantification and FibroTest and the lack of local availability of such tests limited the complete evaluation of patients. Being a single-center study, this may represent only a partial insight into the reality of HCV infection in the hospital setting in Cameroon. However, the results permit us to have a baseline clinical and

biological profile of the patients, which is an important template required to set up extensive and targeted anti-HCV treatment.

In conclusion, a good number of anti-HCV-positive patients attending DGH have no presenting complaints; as such, many patients are diagnosed fortuitously, some of whom already have complications including cirrhosis and HCC. Genotype 1 was the most commonly found in this hospital setting. There is an urgent need to put in place programs to increase awareness and diagnosis of HCV infection and to develop extensive and targeted anti-HCV treatment guidelines to improve the management of these patients in Cameroon.

Acknowledgement

The authors wish to sincerely thank Aliane Kenfack for her contribution to the data collection.

Ethical approval: The study was approved by the Douala General Hospital Ethics Committee for Research.

Conflict of interest: The authors declare no conflict of interest. This work did not benefit from any funding.

Author contributions: HNL, ICD, AM, and SAFBE conceived the study. ET, SAFBE, AM, ODS, and DNN collected the data. ET, HNL, ICD, and ODS analyzed the data and drafted the manuscript. HNL, ICD, DNN, ET, SAFBE, AM, and OSD proofread and corrected the manuscript. All authors agreed with the final manuscript to be submitted for publication.

References

- Williams R. Hepatitis C in 2006. *Eur J Gastroenterol Hepatol* 2006;**18**:309–11.
- Hadigan C, Kottitil S. Hepatitis C virus infection and coinfection with human immunodeficiency virus: challenges and advancements in management. *JAMA* 2011;**306**:294–301.
- Shepard CW, Finelli L, Alter MJ. Global epidemiology of hepatitis C virus infection. *Lancet Infect Dis* 2005;**5**:558–67.
- Mohd Hanafiah K, Groeger J, Flaxman AD, Wiersma ST. Global epidemiology of hepatitis C virus infection: new estimates of age-specific antibody to HCV seroprevalence. *Hepatology* 2013;**57**:1333–42.
- Lavanchy D. The global burden of hepatitis C. *Liver Int* 2009;**29**(Suppl 1):74–81.
- Amin J, Law MG, Bartlett M, Kaldor JM, Dore GJ. Causes of death after diagnosis of hepatitis B or hepatitis C infection: a large community-based linkage study. *Lancet* 2006;**368**:938–45.
- World Health Organization. Guidelines for the screening, care and treatment of persons with hepatitis C infection. WHO Geneva; 2014. Accessed January 29, 2015.
- Poynard T, Bedossa P, Opolon P. Natural history of liver fibrosis progression in patients with chronic hepatitis C. The OBSVIRC, METAVIR, CLINIVIR, and DOSVIRC groups. *Lancet* 1997;**349**:825–32.
- Perz JF, Alter MJ. The coming wave of HCV-related liver disease: dilemmas and challenges. *J Hepatol* 2006;**44**:441–3.
- Duberg AS, Torner A, Davidsdottir L, Aleman S, Blaxhult A, Svensson A, et al. Cause of death in individuals with chronic HBV and/or HCV infection, a nationwide community-based register study. *J Viral Hepat* 2008;**15**:538–50.
- Ford N, Kirby K, Singh K, Mills EJ, Cooke G, Kamarulzaman A, et al. Chronic hepatitis C treatment outcomes in low- and middle-income countries: a systematic review and meta-analysis. *Bull World Health Organ* 2012;**90**:540–50.
- Madhava V, Burgess C, Drucker E. Epidemiology of chronic hepatitis C virus infection in sub-Saharan Africa. *Lancet Infect Dis* 2002;**2**:293–302.
- Cramp ME, Rosenberg WM, Ryder SD, Blach S, Parkes J. Modelling the impact of improving screening and treatment of chronic hepatitis C virus infection on future hepatocellular carcinoma rates and liver-related mortality. *BMC Gastroenterol* 2014;**14**:137.
- Solomon SS, Mehta SH, Srikrishnan AK, Solomon S, McFall AM, Laeyendecker O, et al. Burden of hepatitis C virus disease and access to hepatitis C virus services in people who inject drugs in India: a cross-sectional study. *Lancet Infect Dis* 2015;**15**:36–45.
- Ndong-Atome GR, Makuwa M, Njoum R, Branger M, Brun-Vezinet F, Mahe A, et al. Hepatitis C virus prevalence and genetic diversity among pregnant women in Gabon, central Africa. *BMC Infect Dis* 2008;**8**:82.
- Cacoub P, Goderel I, Morlat P, Sene D, Myers RP, Alric L, et al. Management of chronic hepatitis C in French departments of internal medicine and infectious diseases. *Epidemiol Infect* 2005;**133**:305–14.
- Bellentani S, Pozzato G, Saccoccio G, Crovatto M, Croce LS, Mazzoran L, et al. Clinical course and risk factors of hepatitis C virus related liver disease in the general population: report from the Dionysos study. *Gut* 1999;**44**:874–80.

18. Choo QL, Kuo G, Weiner AJ, Overby LR, Bradley DW, Houghton M. Isolation of a cDNA clone derived from a blood-borne non-A, non-B viral hepatitis genome. *Science* 1989;**244**:359–62.
19. Kuo G, Choo QL, Alter HJ, Gitnick GL, Redeker AG, Purcell RH, et al. An assay for circulating antibodies to a major etiologic virus of human non-A, non-B hepatitis. *Science* 1989;**244**:362–4.
20. Armstrong GL, Alter MJ, McQuillan GM, Margolis HS. The past incidence of hepatitis C virus infection: implications for the future burden of chronic liver disease in the United States. *Hepatology* 2000;**31**:777–82.
21. Deuffic S, Buffat L, Poynard T, Valleron AJ. Modeling the hepatitis C virus epidemic in France. *Hepatology* 1999;**29**:1596–601.
22. Njouom R, Pasquier C, Ayouba A, Sandres-Saune K, Mfoupouendoun J, Mony Lobe M, et al. Hepatitis C virus infection among pregnant women in Yaoundé, Cameroon: prevalence, viremia, and genotypes. *J Med Virol* 2003;**69**:384–90.
23. Pepin J, Lavoie M, Pybus OG, Pouillot R, Foupouapouognigni Y, Rousset D, et al. Risk factors for hepatitis C virus transmission in colonial Cameroon. *Clin Infect Dis* 2010;**51**:768–76.
24. Okwuraiwe AP, Salu OB, Anomneze E, Audu RA, Ujah IA. Hepatitis C virus genotypes and viral ribonucleic acid titers in Nigeria. *Nigerian Journal of Gastroenterology and Hepatology* 2012;**4**:67–72.
25. Nerrienet E, Pouillot R, Lachenal G, Njouom R, Mfoupouendoun J, Bilong C, et al. Hepatitis C virus infection in Cameroon: a cohort-effect. *J Med Virol* 2005;**76**:208–14.
26. Alter MJ. Epidemiology of hepatitis C virus infection. *World J Gastroenterol* 2007;**13**:2436–41.
27. Pearlman BL. Hepatitis C virus infection in African Americans. *Clin Infect Dis* 2006;**42**:82–91.
28. Samuel DG, Rees IW. Extrahepatic manifestations of hepatitis C virus (HCV). *Frontline Gastroenterol* 2013;**4**:249–54.
29. Merican I, Sherlock S, McIntyre N, Dusheiko GM. Clinical, biochemical and histological features in 102 patients with chronic hepatitis C virus infection. *Q J Med* 1993;**86**:119–25.