Ethnic epidemiological profiles and antiviral therapy among patients infected with hepatitis C virus genotype 4 : a multicenter study from Belgium

Marcel Nkuize[1], Jean-Pierre Mulkay[1], Christophe Moreno[2], Luc Lasser[3], Peter Michielsen[4], Chantal de Galocsy[5], Robert Scheen[1], Collins Assene[6], Jean Delwaide[7]

(1) CHU Saint-Pierre, Brussels, Belgium ; (2) Hôpital Erasme, Brussels, Belgium ; (3) CHU Brugmann, Brussels, Belgium ; (4) UZ Antwerpen, Belgium ; (5) HIS Bracops ; (6) HIS Molière Brussels, Belgium ; (7) CHU Sart-Tilman, Liège, Belgium.

Abstract

Background : **Hepatitis C virus genotype 4 (HCV-4) is the most prevalent genotype in Central Africa.**

Aim : **To compare epidemiology, clinical characteristics and any differences in access to HCV therapy in two populations of HCV-4 patients residing in Belgium.**

Methods : **This multicenter study selected 473 HCV-4 patients from seven hospital databases and compared them according to ethnic origin, i.e., Black African (n = 331) or not (n = 142), for epidemiological, clinical, biological and histological characteristics. Interleukin 28B polymorphism (CC-genotype) was evaluated in a second cohort of 69 Black African and 30 non-Black African patients.**

Results : **Compared to other patients, the Black African patients were more likely to be female and were older, commonly overweight, frequently had abnormal glucose metabolism and arterial hypertension ; they were less likely to have dyslipidemia, a history of alcohol consumption or ALT elevation. The route of infection was more frequently unknown in Black African than in other patients. Black African patients had more HCV-4 subtypes, were less frequently of IL28B CC-genotype and had less severe liver fibrosis. The proportion of patients who received antiviral treatment was similar in the two groups.**

Conclusion : **In this Belgian cohort, patients with HCV-4 infection were more frequently of Black African origin than of other origin. Infected Black African patients were more commonly female, older at diagnosis, and had more co-morbidities than other patients ; they also had less advanced liver fibrosis than infected non-Black African patients and fewer had a CC genotype.** (Acta gastroenterol. belg., **2015**, 78, **365-372**).

Key words : chronic hepatitis C, HCV, genotype 4, ethnicity, epidemiology, antiviral treatment, DAA, metabolic factors.

Introduction

Hepatitis C virus (HCV) is widely recognized as a global public health burden, causing severe complications, such as cirrhosis and hepatocellular carcinoma (1). Six HCV genotypes and numerous subtypes have been distinguished (1,2). Genotyping is of great importance in the management of HCV-infected patients as the genotype may affect the response to antiviral therapy and is crucial in understanding the epidemiological aspects of HCV infection, notably infection risk factors and geographic distribution (2-10). For example, HCV genotype 4 (HCV-4) is highly prevalent in Egypt and the Middle East (80% of HCV infections in Egypt and over 30% in Syria) and Central Africa (100% in the Democratic Republic of Congo and Rwanda, 16 to 36% in Cameroon and 6.5% in Gabon) (3,9,11-15). As a result of population migration and differing lifestyles, HCV-4 was present in 1-3% of HCV-infected patients from Western countries during the 1990s. This prevalence is increasing in Europe (10,16-19). In Belgium, it increased from 4% for the period 1992-1994 to 12% in 2000-2002 (19).

Most studies on HCV-4 epidemiology have been carried out in Egypt and the Middle East. Because of the cost of diagnosing and genotyping HCV infection and the limited budget allocated to public health, large-scale trials to evaluate patient characteristics in sub-Saharan Africa are lacking, and infected patients in these countries are often untreated (in part due to under-diagnosis). However, it is possible to study the epidemiology of HCV-4-infected Black African (BA) patients who have immigrated to Europe. Therefore, the aim of this study was to compare the demographic characteristics of HCV-4 infected BA and non-Black African (non-BA) patients living in Belgium and evaluate any differences in therapy access.

Patients and Methods

Patient selection

Patients were identified from databases in seven Belgian hospitals (CHU Saint-Pierre, CHU Brugmann, Hôpital Universitaire Erasme, Hôpital Bracops and CH Molière, Brussels ; CHU Sart Tilman, Liège ; University Hospital, Antwerp), which are located in the three largest Belgian cities. Most patients were from Brussels. Patients were eligible for the study if they were aged > 11 years and had HCV-4 infection diagnosed between 1999 and 2007.

Since the effect of interleukin 28B (IL28B) polymorphism was unknown at the time of the original study, this characteristic was subsequently evaluated in two of the study centers (CHU Saint-Pierre, Hôpital Universitaire Erasme) in a second cohort of 99 consecutive, treatment-naïve HCV-4 infected patients.

Correspondence to : Marcel Nkuize, M.D., Department of Hepatology and Gastroenterology, CHU Saint-Pierre of Brussels, Rue Haute 322, 1000 Brussels, Belgium. E-mail : marcelnkuize@hotmail.com

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The study was conducted in conformity with the principles of the Declaration of Helsinki and local laws and regulations. The institutional review boards of the participating centers and the ethical committee of the main investigating center (CHU Saint-Pierre, Brussels, OM 007) approved the study protocol.

Baseline parameters

Recorded baseline parameters included the following : demographics, including ethnic origin (BA, defined as an individual whose parents were both from central Africa, Caucasian whites and North Africans), sex, age at diagnosis, body weight (kg), body mass index (BMI ; kg/m^2) and risk factors for infection.

Co-morbidities, including being overweight or obese (BMI > 25 or > 30 kg/m^2, respectively), having dyslipidemia (on treatment, or above the upper limit of normal (ULN) for serum cholesterol and/or triglycerides), glucose metabolism impairment (including intolerance if fasting glycemia > 100 but < 125 mg/dL and overt diabetes, treated or not), arterial hypertension (on treatment, or blood pressure > 130/85 mmHg), renal insufficiency (if serum creatinine was over the ULN), alcohol consumption (classified as never, occasional (less than 3 drinks per month), active (equal to or above 3 drinks per month)or past intake (no drink in the year preceding inclusion)), co-infection with hepatitis B virus (HBV) (presence of HBs antigen) and/or human immunodeficiency virus (HIV ; positive for antibodies and viremia) were recorded. Previous HBV infection was defined as the presence of antibodies against the hepatitis B core antigen.

HCV-4 viral load was categorized as < 400,000 IU/mL or > 400,000 IU/mL, and viral subtypes were also studied.

The alanine aminotransferase (ALT) to ULN ratio was classified as < 2 or > 2, or persistently normal ALT (NALT) over a 6- to-12-month period.

Liver biopsy specimens obtained before treatment were evaluated (locally and without blinding) using the METAVIR classification for activity grade (A), liver fibrosis stage (F) and degree of steatosis (20) . The following groups were distinguished : METAVIR grade (A) < 2 and ≥ 2 ; METAVIR stage (F) < 2 and ≥ 2. Degree of steatosis was based on the pathology report and graded as 0 to < 10%, 10 to 30% and > 30% (21).

With respect to IL28B genes, the frequency of the SNP rs12979860 CC-genotype was evaluated in a subgroup of 99 patients as mentioned above.

Virology tests

Quantitative tests measuring HCV RNA levels (expressed in IU/ml) were performed using a Cobas Amplicor HCV monitor, version 2.0 (Roche Systems), a Versant HCV RNA 3.0 assay (Bayer HealthCare) or the Cobas Taqman HCV test (Roche Systems) and Abbott Real Time (Abbott Diagnostic). Qualitative tests were performed using a Cobas Amplicor HCV monitor, version 2.0 (Roche Systems) or an Amplicor HCV monitor, version 2.0. The HCV limit of detection in qualitative assays was 50 IU/mL. Genotyping was performed using assays from INNO-LIPA HCV II, Innogenetics, Ghent, Belgium or the Versant HCV genotyping assay, Bayer HealthCare.

Treatment regimens

The criteria for starting antiviral therapy in Belgium followed international guidelines. To obtain antiviral treatment reimbursement in Belgium, social security approval must be obtained.

Statistical analysis

Epidemiological profiles, whether or not therapy was received, and reasons for not receiving treatment were recorded and compared in the two groups of patients

Baseline characteristics are presented as numbers of cases and percentages for categorical data, and as means with standard deviation (SD) or median and range for continuous data.

Patient groups were compared using either Fisher's exact test for binary categorical variables or chi-squared techniques for categorical variables with more than two levels. A crude odds ratio (OR) with its 95% confidence interval (CI) is presented for each comparison made.

Continuous variables were compared using a Student's t test. The between-group differences are presented as the difference between the means of each group, with a 95% CI for each comparison made**.** To assess whether there was a difference in the degree of steatosis by BMI between ethnic groups, the Cochran-Mantel-Haenszel statistic was used. To identify risk factors for bridging fibrosis/cirrhosis, ORs adjusted for factors with a p value < 0.1 in crude (unadjusted) analysis were calculated ; baseline parameters used for this analysis included the following : age, sex, Black African versus other ethnicity, mode of HCV infection, alcohol intake, BMI, HCV viremia and necroinflammatory activity. Computational procedures were performed using SPSS for Windows version 17.0 (SPSS Inc., Chicago, IL, USA).

A p-value less than 0.05 was considered significant.

Results

Epidemiological data for all patients

In total, 473 patients (331 BA and 142 non-BA) with HCV-4 were identified (Table 1).

B A patients were from the Democratic Republic of Congo (n = 200), and Angola, Burundi, Cameroon, Gabon or Rwanda (n = 131). Non-BA patients were Caucasian Europeans from Belgium, France, Greece, Italy, Portugal, Spain and Russia (n = 110) and North Africans, mainly from Morocco but also from Algeria, Egypt and Tunisia (n = 32).

Table 1. — **Baseline epidemiological data of the study cohort stratified according to ethnicity : Black African vs. other**

Patient characteristics n	Black African* 331	other * 142	Odds ratio (95%CI) **	P-value ***
Male (%)	128/331 (38.7%)	83/142 (58.5%)	2.23 (1.50 to 3.33)	< 0.001
Age at diagnosis (years) Mean (SD) Range	(n = 320) 48.0 (12.6) 11 to 77	(n = 141) 41.4 (12.8) 17 to 81	6.7 (4.2 to 9.2)	< 0.001
Patients older than 40 years (%)	233/320 (72.8%)	70/141 (49.6%)	2.72 (1.80 to 4.10)	< 0.001
Infection risk factors				
Transfusion	70/330 (21.2%)	18/142 (12.6%)		
IVD user	9/330 (2.7%)	58/142 (40.8%)		0.012
Unknown	215/330 (65.5%)	56/142 (39.4%)		
Other (sex, tattoo, intra-familial)	10/330 (3.0%)	8/142 (5.6%)		
Weight (kg) at inclusion Mean (SD) Range	(n = 264) 76.1 (13.3) 45 to 133	(n = 100) 70.6 (15.9) 40 to 136	5.5 (2.2 to 8.7)	0.001
Co-morbidities – Body mass index at inclusion (kg/m²) Mean (SD) Range	(n = 239) 27.2 (4.5) 14.8 to 42.8	(n = 89) 24.2 (4.3) 17.0 to 40.1	3.0 (1.9 to 4.1)	< 0.001
– Alcohol Intake				
No intake	181/252 (71.8%)	56/103 (54.4%)		
Active intake	40/252 (15.9%)	30/103 (29.1%)		0.01
Past intake	15/252 (6.0%)	10/103 (9.7%)		
Occasional intake	16/252 (6.3%)	7/103 (6.8%)		

* In each group, data are presented as number of cases (percentages).
** CI : confidence interval.
*** P value comparing Black African (case) group versus other group.
IVD : intravenous drug.

Among the BA patients, 203 (61.3%) were female compared to 59 (41.5%) in the non-BA group ($p < 0.001$). BA patients were significantly older than other patients at the time of diagnosis ($p < 0.001$) and there were significant differences in risk factors for infection between the groups ($p < 0.012$). In the majority of BA patients the mode of transmission of HCV was unknown ; in other patients, intravenous drug use was the most commonly reported mode of transmission.

Clinical and biological characteristics

BA patients were significantly heavier ($p = 0.001$) than other patients and dyslipidemia was less common ($p = 0.039$). Glucose intolerance, overt diabetes and arterial hypertension were more frequent in BA patients (all $p = < 0.01$) (Table 2). The frequencies of HBV and/or HIV co-infection were similar in the two groups of patients, as was renal insufficiency. Alcohol consumption was less common in BA than in other patients ($p = 0.01$). There was a significant difference in baseline ALT levels between groups ($p < 0.001$), with normal levels more common among BA patients. The median viral load was similar in the two groups. BA patients showed greater diversity with respect to viral subtypes than other patients ($p < 0.001$). Analysis of the predominant recognized viral subtypes revealed that subtype 4e, 4a and 4h were 9 folds, 5 folds, and 3 folds respectively more prevalent in BA patients than non-BA.

The SNP rs12979860 CC-genotype was present in 14/99 (14.1%) patients overall and in 6/69 (8.6%) BA compared with 8/30 (26.6%) non-BA patients ($p = 0.01$).

Histological findings

There was no significant difference in necroinflammatory activity between the two groups (Table 3). Progression of liver fibrosis was less common in BA than in other patients ($p = 0.04$) as was bridging fibrosis/cirrhosis ($p = 0.03$).

Steatosis did not reach a significant difference between the two groups but the degree of steatosis stratified by BMI was found significantly less common in BA patients ($p = 0.02$) (Table 4).

Age, ethnicity and necroinflammatory activity were identified as statistically significant risk factors for bridging fibrosis/cirrhosis in univariate and multivariate analysis (Table 5).

Treatment and reason for non-treatment

In this cohort, 273 patients received anti-viral therapy (Table 6). There was no difference in the proportion of treated patients in the BA and non-BA patients : 195/331

Table 2. — **Clinical and biological data of the study cohort stratified according to ethnicity : Black African vs. Other**

Patient characteristics	Black African *	Other *	Odds ratio (95%CI) **	P-value ***
Comorbidities – Dyslipidemia	55/250 (22.0%)	32/98 (32.7%)	0.59 (0.35 to 0.98)	0.03
– Glucose intolerance or diabetes (%)	77/274 (28.1%)	15/105 (14.3%)	2.35 (1.28 to 4.31)	0.007
– Arterial hypertension	103/266 (38.7%)	10/127 (7.8%)		< 0.001
– Hepatitis B				
Active hepatitis B	**24/289 (8.3%)**	**7/127 (5.5%)**		0.10
Past hepatitis B§	**82/289 (28.3%)**	**26/127 (20.5%)**		
No hepatitis B	**183/289 (63.3%)**	**94/127 (74.0%)**		
– HIV-positive (%)	38/319 (11.9%)	24/134 (17.9%)	0.62 (0.36 to 1.09)	0.12
– Abnormal renal function	45/271 (16.6%)	16/104 (15.4%)	1.10 (0.59 to 2.04)	0.77
HCV viral load (x10^3 IU/ml) Median 1st-3rd	(n = 257) 798.9 343 to 1492	(n = 115) 850.0 304 to 1838		0.35
Patients with viral load > 400× 10^3 IU/ml (%)	187/257 (72.8%)	82/115 (71.3%)	1.08 (0.66 to 1.75)	0.77
Subtype				
unrecognized subtype 4	**198/326 (60.7%)**	**57/136 (41.9%)**		
subtype 4a	**17/326 (5.2%)**	**1/136 (0.7%)**		
subtype 4b	**1/326 (0.3%)**	**1/136 (0.7%)**		
subtype 4c	**3/326 (0.9%)**	**0/136 (0%)**		
subtype 4c/4d	**44/326 (13.4%)**	**67/136 (49.2%)**		
subtype 4d	**0/326 (0%)**	**1/136 (0.7%)**		
subtype 4e	**39/326 (11.9%)**	**4/136 (2.9%)**		< 0.001
subtype 4h	**19/326 (5.8%)**	**4/136 (2.9%)**		
subtype 4a Δ	**1/326 (0.3%)**	**0/136 (0%)**		
subtype 4a ΔΔ	**1/326 (0.3%)**	**0/136 (0%)**		
subtype 4k	**2/326 (0.6%)**	**0/136 (0%)**		
subtype 4e Δ	**1/326 (0.3%)**	**1/136 (0.7%)**		
Transaminase ALT				
Normal	84/303 (27.7%)	20/133 (15.0%)		
< 2 ULN	159/303 (52.4%)	63/133 (47.4%)		< 0.001
≥ 2 ULN	60/303 (19.8%)	50/133 (37.6%)		
IL28B polymorphism CC-genotype	6/69 (8.7%)	8/30 (26.6%)	3.82 (1.19-12.39)	0.01

* In each group, data are presented as number of cases (percentages).
** 95% CI, 95% confidence interval.
*** P value comparing Black African (case) group versus other group.
§P-value= 0.09.
1st -3rd, first - third quintiles.
Δ and ΔΔ mixture with HCV genotype 1a and 1b respectively.
ULN upper limit of normal.

(58.9%) and 78/142 (54.9%) respectively ; OR 1.16, 95% CI (0.78 to 1.73), p = 0.46. The treatment prescribed for BA (n = 195) and non-BA (n = 78) patients included : interferon (IFN) alone (8 vs. 4), IFN plus ribavirin (RBV) (23 vs. 16), IFN plus RBV plus amantadine (AM) (4 vs. 0), pegylated-IFN (peg-IFN) alone (1 vs. 1), peg-IFN plus RBV (128 vs. 48), peg-IFN plus RBV plus AM (31 vs. 8) and peg-IFN plus AM (0 vs. 1).x

Two hundred patients (136 BA and 64 non-BA patients) did not receive treatment. There were no statistically significant differences between groups in the reasons for lack of therapeutic intervention (Table 6).

Discussion

In this large population of HCV-4 infected patients, epidemiological, clinical, biological, histological and treatment characteristics were analysed.

Although less than 1% of the Belgian population (22) is of BA origin, 70% of patients in this observational study were BA, originating from central Africa. Therefore we decided to compare patients of BA origin and those of other ethnic origin.

These patients were more likely to be female than were the other patients, possibly due to more frequent

Table 3. — **Liver histology of patients stratified according to the ethnicity : Black African vs. Other**

Stage of Activity (A)	Black African (n = 228)	Other (n = 89)	p-value
A-0	29 (12.7%)	10 (11.2%)	
A-1	118 (51.8%)	57 (64.0%)	
A-2	73 (32.0%)	17 (19.1%)	0.98
A-3	8 (3.5%)	5 (5.6%)	
Stage of fibrosis (F)	Black African (n = 247)	Other (n = 111)	p-value
F-0	46 (18.6%)	18 (16.2%)	
F-1	85 (34.4%)	41 (36.9%)	
F-2	71 (28.7%)	21 (18.9%)	0.04
F-3	20 (8.1%)	20 (18.0%)	
F-4	25 (10.1%)	11 (9.9%)	
Degree of steatosis (S)	Black African (n = 174)	Other (n = 79)	p-value
S-0 or < 10%	141 (81.0%)	56 (70.8%)	
S-10-30%	26 (14.9%)	15 (18.9%)	0.09
S- > 30%	7 (4.0%)	8 (10.1%)	

Table 4. — **Relationship between steatosis and body mass index stratified according to the ethnicity : Black African vs. Other**

Steatosis*	Black African		Other	
	BMI < 25 (n = 45)	BMI ≥ 25 (n = 114)	BMI < 25 (n = 39)	BMI ≥ 25 (n = 32)
Steatosis < 10%	42 (93%)	84 (73.6%)	27 (69.2%)	21 (65.6%)
Steatosis ³ 10%	3 (6.6%)	25 (21.9%)	12 (30.7%)	11 (34.3%)

*P = 0.02.

BMI Body Mass Index (kg/m²) ; Among 174 Black African and 79 other patients who had the steatosis evaluation, BMI data were unavailable in 15 (8.6%) Black African and in 6 (7.5%) non-Black African patients.

HCV screening in women (i.e. antenatal testing), although this could also reflect the demography of the sub-Saharan African population in Belgium at the time when the study was carried out (22,23).

Overall, the BA patients in our study were older than the non-BA patients and HCV-4 infection was diagnosed later in life (Table 1). Age and duration of infection are factors predictive of fibrosis and response to therapy, including pegIFN and ribavirin (4,24,25).

Differences in risk factors for transmission of HCV between patients of different ethnic origin may result from historical, cultural and financial differences (1,3,8-9). Older BA patients with no known risk factors for infection could have been infected during mass treatment campaigns against Trypanosomiasis (in the Democratic Republic of Congo, Gabon, and Cameroon), or during mass vaccination campaigns carried out in central Africa during the last century ; in both cases reuse of medical instruments without adequate sterilization has been described. Patients originating from North Africa could also have been exposed to this risk factor ; notably, in Egypt, HCV-4 was spread during mass treatment campaigns against Schistosomiasis, resulting in a high prevalence of HCV-4a in that country (3).

In Africa, blood transfusion has been an important risk factor for HCV infection for longer than in Europe, and was found to be a key risk factor in both younger and older BA patients. Other potential iatrogenic risk factors for HCV transmission in the BA population include intramuscular treatment for sexually transmitted infections or for malaria, dental procedures, and needle-stick accidents. Non-iatrogenic routes of HCV-infection in central Africa include traditional practices (scarification, piercing), circumcision/excision, razor sharing at barbers' shops, toothbrush sharing, and sexual contact (3,9).

HCV-4 subtypes are more diverse in BA patients than in patients of other ethnic origin, possibly because, historically, this genotype was well established in central Africa before spreading to other regions (2,3,5). For example, considering the recognized subtypes, subtypes 4e, 4a, and 4h were highly prevalent in the BA population in comparison to non-BA patients. In Europe, HCV-4 appeared only recently as a result of immigration and has been propagated by intravenous drug abuse and sexual behavior such as anal intercourse (3,7-8,11). Subtypes 4c/4d, the subtypes most frequently found in intravenous drug users, were significantly more common in the non-BA group (11).

Table 5. — **Risk factors for bridging fibrosis/cirrhosis**

	Unadjusted			Adjusted	
Parameters	**METAVIR fibrosis stage 3 or 4**		**P-value**	**OR, 95% confidence interval**	**P-value**
	No	**Yes**			
Age			0.01	0.30 (0.12-0.77)	0.01
≥ 40 (n = 195)	141 (72.3%)	54 (27.6%)			
< 40 (n = 75)	65 (86.6%)	10 (13.3%)			
Ethnicity			0.03	0.44 (0.21-0.96)	0.04
Black African (n = 247)	202 (81.7%)	45 (18.2%)			
non-Black African (n = 112)	80 (71.4%)	32 (28.5%)			
Sex			0.09	1.0 (0.53-2.03)	0.9
female (n = 195)	160 (82.0%)	35 (17.9%)			
male (n = 164)	122 (74.3%)	42 (25.6%)			
Alcohol			0.6	–	
abstainer (n = 196)	158 (80.6%)	38 (19.3%)			
others (n = 61)	46 (75.4%)	15 (24.5%)			
Risk factor			0.6	–	
unknown (n = 200)	159 (79.5%)	41 (20.5%)			
others (n = 159)	123 (773%)	36 (22.64%)			
Body mass index			**0.3**	–	
≥ 25 (n = 172)	**127 (73.8%)**	**45 (26.1%)**			
< 25 (n = 106)	**84 (79.25%)**	**22 (20.75%)**			
HCV viremia*			**0.6**	–	
≥ 800000 (n = 162)	**125 (77.1%)**	**37 (22.8%)**			
< 800000 (n = 197)	**157 (79.7%)**	**40 (20.3%)**			
necroinflammatory activity			< 0.0001	0.26 (0.13-0.5)	< 0.0001
No (n = 213)	186 (87.3%)	27(12.6%)			
Yes (n = 108)	70 (64.8%)	38(35.2%)			

OR odds ratio, *IU/ml.

Co-morbidities (excess weight, glucose metabolism impairment and arterial hypertension) were markedly more common among BA patients. However, despite being more frequently overweight, fewer BA patients had dyslipidemia, suggesting weight gain from a diet high in carbohydrates rather than in saturated fats. These co-morbidities (excess weight, glucose metabolism impairment, arterial hypertension, and dyslipidemia) are components of the metabolic syndrome, which has previously been shown to be prevalent in BA individuals (26). Moucari *et al*. found that metabolic syndrome and genotypes 1 and 4 were associated with insulin-resistance in non-diabetic patients with chronic hepatitis C (27). Despite this higher prevalence of metabolic syndrome, BA patients with HCV-4 infection in our study had a lower frequency of liver steatosis when stratified by BMI ; this observation has also been made among African-American patients (often infected with HCV genotype 1) (28,29). There is possibly a genetic explanation for this finding, which may also be relevant to those of BA origin.

We found a slightly higher frequency of HCV-4-HBV co-infection than reported in one French study (8). In regions of HBV endemicity, such as Africa, infection frequently occurs early in life ; hence superinfection with HCV may be more common than co-infection. The frequency of HCV-4/HIV co-infection we observed is consistent with reports from other studies (14,30).

Normal transaminase values were seen more commonly among BA patients in our study. In studies from the US, a trend towards normal or lower ALT profiles was seen among African-American patients, with normal ALT levels observed to be more common among females with a long history of HCV infection (31,32). It has been established that the distribution of ALT levels is influenced by factors such as duration of infection, ethnicity (lower levels in black African patients), sex (lower levels in women), obesity and geographic region (33-37).

Studies on chronic hepatitis C from the US have often shown a slower progression of fibrosis and an infrequent cirrhosis' state in African-American patients (31,32). In the present study, despite more frequent co-morbidities, BA patients were also less likely to have bridging fibrosis/cirrhosis than other patients. Moreover, in multivariate analysis, ethnicity appeared to be a strong predictor of bridging fibrosis/cirrhosis. One of the reasons for the slower progression of fibrosis among African-American patients relates to dysfunctional lymphocyte T CD4 responsiveness to HCV (38) ; this could also apply

Table 6. — **Number of patients receiving antiviral therapy and reasons for non-treatment stratified according to ethnicity : Black African vs. other**

Patient characteristics	Black African	other	OR (95%CI)	P-value
Treated patients (%)	195/331 (58.9%)	78/142 (54.9%)	1.16 (0.78 to 1.73)	0.46
Reason for non-treatment				
Normal ALT and/or fibrosis (stage 0 or 1)	74/136 (54.4%)	22/64 (34.3%)		
Co-morbidities [old age, hematologic diseases and low CD4 counts, renal or liver insufficiency, hematologic, liver, colonic and prostate cancers, psychiatric illness, severe alcohol addiction]	24/136 (17.6%)	18/64 (28.1%)		0.060
Unwilling	4/136 (2.9%)	2/64 (3.1%)		
Other (pregnancy, social issues, travel)	7/136 (5.1%)	5/64 (7.8%)		
Lost to follow-up	27/136 (19.8%)	17/64 (26.5%)		

OR, odds ratio.

to BA patients because of similarities in genetic background. Necroinflammatory activity was another factor associated with bridging fibrosis/cirrhosis in the multivariate analysis ; the role of necroinflammation in the mechanism of liver fibrosis has already been extensively reported (31). Being older than 40 also appears to be a strong predictor of cirrhosis. The reason for the more rapid progression from no fibrosis to cirrhosis in older patients is unclear (24,25).

In our study there were no significant differences between ethnic groups in terms of receipt of antiviral therapy. This observation contrasts with studies from the US showing that African American and Hispanic subjects may be less likely than Caucasians to receive therapy against HCV (32,41) ; this observation may be due to some care access differences between our public health systems. Consistent with current guidelines for management of HCV infection, normal ALT and/or mild fibrosis were the main reasons for lack of treatment in both groups (39,40).

The IL28B polymorphism (i.e., single nucleotide polymorphism (SNP) rs12979860, CC-genotype) has been shown to be variable across ethnicities and to be associated with the ability to clear the HCV infection with peg-IFN plus RBV therapy (42). The prevalence of IL28B SNP rs12979860 (CC-genotype) was studied in a second cohort of 99 consecutive naïve patients (69 BA) with HCV-4 infection at two centers in Brussels (Table 2). The CC-genotype was significantly less common among BA than other patients. Our results are similar to other published findings (42,43). In a previous study of Black African and non-BA patients infected with HCV-4 who were treated with peg-IFN and RBV, sustained virological responses of 28% and 52%, respectively was found (44) ; this difference in the sustained virological response rate could be explained by the lower frequency of the favorable CC-genotype among BA patients.

Conclusion

The majority of HCV-4 infected patients in Belgium were found to be of Black African origin. Although Black African patients showed less evidence of advanced liver disease, they were older, had more co-morbidities, and were less frequently of IL28B CC-genotype than non-Black African patients.

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