A pilot observational survey of hepatitis C in Belgium

S. De Maeght[1], J. Henrion[1], N. Bourgeois[2], C. de Galocsy[3], P. Langlet[4], P. Michielsen[5], H. Reynaert[6], G. Robaeys[7], D. Sprengers[8], H. Orlent[9], M. Adler[2]

(1) CH Jolimont, (2) CHU Erasme, (3) CH Bracops, (4) CHU Brugmann, (5) UZ Antwerpen, (6) AZ VUB, (7) Zol Genk, (8) St Augustinus Antwerpen, (9) St Jan Brugge.

Abstract

Aim of the study : **There is a lack of epidemiological data on hepatitis C (HCV) infected patients in Belgium. Therefore our purpose was to address this important question and to evaluate the feasibility of a national HCV observatory.**

Patients and methods : **From November 2003 to November 2004, every new patient prospectively seen for HCV antibody positivity in 9 Belgian hospital centres was recorded and a standardised 10-items questionnaire was completed during the consultation, including a Quality of Live (QOL) visual analogue scale.**

Results : **Three hundred and eighteen consecutive patients were recruited. Fifty five percent were male with a median age of 45 y (11-87 y). The main risk factors for infection were IV drug use (27%), blood transfusion (23%), and invasive medical procedure (11%). On the QOL scale, ranging from 0 and 100, mean value was 61 ± 31. Transaminases were abnormal in 66% with a median elevation 2 times above normal value. HCV RNA was positive in 87% with a viral load above 800 000 IU/ml in 42%. Genotype 1 was predominant (59%), followed by genotypes 3 (19%) and 4 (14%). A liver biopsy was performed in 190 patients, with minimal fibrosis (METAVIR F0-F1) in 43%, moderate fibrosis (F2) in 35% and advanced stages (F3-F4) in 22%. Antiviral treatment was not considered in 53% because of normal ALT (30%), old age (7%), minimal histological stage (6%) or patient refusal (4%).**

Conclusions : **This study highlights the feasibility of a national HCV survey using a simple questionnaire. This pilot study could be generalised throughout Belgium, and, if repeated, could allow a regular assessment of the changes in epidemiology and management of HCV infection in our country.** (Acta gastroenterol. belg., **2008**, 71, **4-8**).

Key words : hepatitis C virus, epidemiology, treatment, quality of life, survey, questionnaire.

Abbreviations

ALT	Alanine aminotransferase
BMI	body mass index
HCV	hepatitis C virus
IQR	interquartile interval
IVDU	intravenous drug use
N	normal
QOL	quality of live
ULN	upper limit of normal values

Introduction

Hepatitis C virus (HCV) infection has become a worldwide health preoccupation. A significant part of the undiagnosed chronically infected population will become progressively symptomatic and the incidence of advanced diseases, including cirrhosis and hepatocarcinoma, is on the rise (1-3). Therefore a careful monitoring of the disease epidemiology is mandatory. Nevertheless very few epidemiological data on this disease have been published in our country (4-10). The aim of this study was to highlight the epidemiological characteristics of HCV infected patients in Belgium, and to evaluate the feasibility of a national observatory.

Patients and methods

From November 2003 to November 2004 a prospective registration was conducted including all consecutive HCV patients seen for the first time by a hepatologist, during either consultation or hospitalisation. Only HCV patients referred for the first time or newly diagnosed were enrolled in the study. Nine hepatology units from 5 different Belgian provinces agreed to participate. During consultation, a standardised questionnaire was filled by the patient and the specialist in charge. This questionnaire included 10 relevant demographic, clinic, biochemical, virological, histological and therapeutic items. The participants were asked to rate their health state with a Quality of Live (QOL) visual analogue scale that ranged from 0 to 100 (best imaginable heath state), by drawing a stroke on a linear scale (11-14). The use of alcohol and HBV or HIV co-infections were not systematically recorded in our questionnaire.

Patients were described with normal or abnormal ALT value with regard of blood tests in file at the time of their registration. Due to the prospective registration process, more than one ALT determination anteriority were sometimes not available at enrolment. Therefore the term of *persistently* normal ALT value was not used for patients with normal ALT value. Indication for liver biopsy was submitted to the decision of the physicians in charge. Histological analysis was performed locally and fibrosis was assessed according to the METAVIR scoring system (15). Median and interquartile range (IQR) were used for quantitative values except for QOL expressed as mean ± standard deviation. Chi-square, Student t and Mann Whitney tests were used for qualita-

Correspondence to : Stéphane De Maeght, CH Jolimont, Rue Ferrer, 159, 7100 Haine Saint Paul. E-mail : s.dm@scarlet.be

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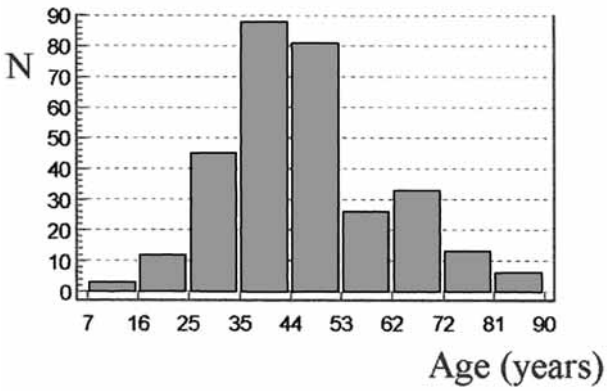

Fig. 1. — Age distribution of the whole cohort

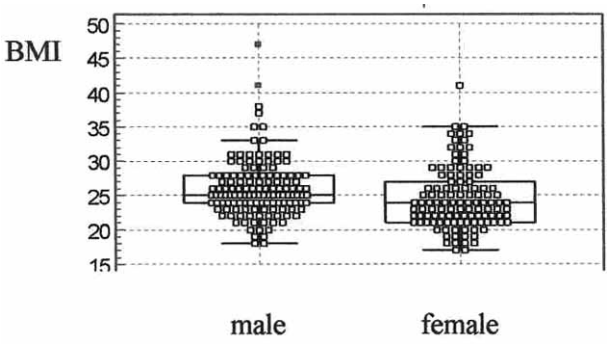

Fig. 2. — BMI distribution by sex (Box and Whisker plot)

tive and semi quantitative comparisons when appropriate.

Results

Three hundred and eighteen consecutive patients with HCV antibody positivity were registered during the 12 months inclusion period. Caucasian origin was largely predominant (85%) followed by African origin (9%) and the M/F sex ratio was 1.3. Median weight and BMI were 72 kg (IQR : 46-137) and 25 kg/m^2 (IQR : 18-47), respectively. Median age was 45 y (11-87 y) with a normal distribution similar between genders (Fig. 1). In contrast weight and BMI distributions were different between genders, with a significantly higher BMI in male patients ($p < 0.001$) (Fig. 2).

The main risk factors for HCV infection were intravenous drug use (IVDU) in 27% of the patients, blood transfusion before 1990 in 23%, invasive medical procedure in 11% and from unknown origin in 23%. The delay between first HCV antibody detection and recruitment was less than one year in 50% of the patients and between 1 and 5 years in 33%. The circumstances of HCV detection were fortuitous in 65%, due to general symptoms in 30%, or to extra-hepatic manifestations in 5%. The QOL visual scale procedure demonstrated an unhealthy feeling in these patients (mean QOL 61 ± 31)

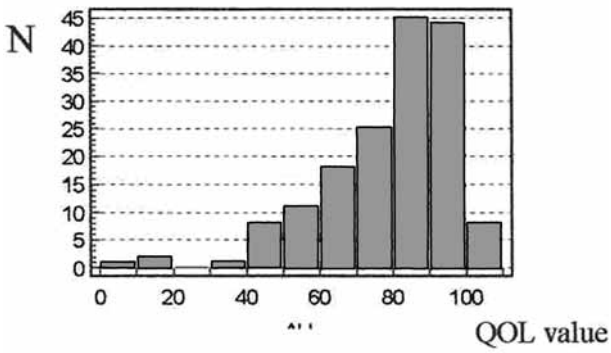

Fig. 3. — Quality of Live (QOL) visual analogue scale results for the whole cohort. The scale ranges from 0 to 100 (best imaginable heath state).

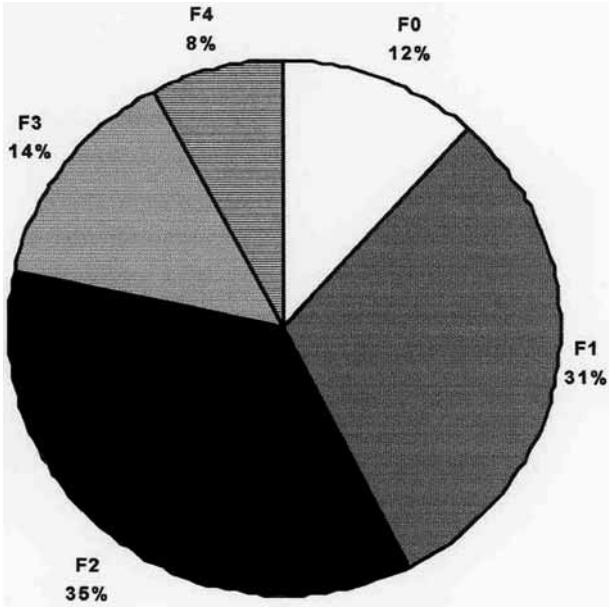

Fig. 4. — METAVIR fibrosis stages distribution

(Fig. 3). ALT value determinations were available in 309 patients and normal values were found in 102 (33% of these patients). In the other cases, abnormal ALT values were predominantly distributed between 1 and 5 times the upper limit of normal (ULN), with 2 times ULN as a median. Eighty seven percent of the patients were viremic, with a low viral load (< 800.000 IU/ml) in 61% of them (n = 130/214). Genotype determination was performed in 212 patients. Genotype 1 was predominant, found in 59 % (n = 125), followed by genotypes 3 (19%) and 4 (14%).

One hundred ninety patients (60 %) underwent a liver biopsy, including 35 patients with normal ALT. Minimal fibrosis stage (METAVIR F0-F1) was observed in 82 patients (43% of the biopsied population), while 22% had advanced fibrosis (F3-F4), including 8% with cirrhosis (Fig. 4). Distribution of fibrosis stage according to ALT values is represented in Figure 5, with

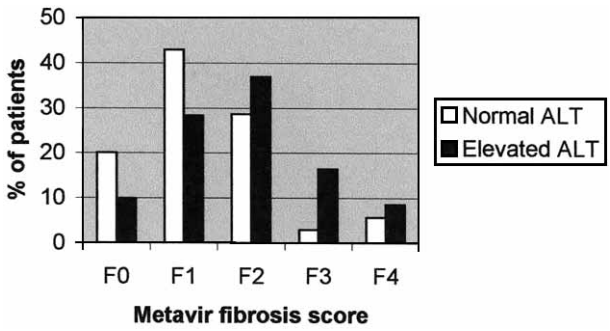

Fig. 5. — METAVIR fibrosis stages distribution in patients with Normal (n = 35, black line) and Abnormal (n = 152, white line) ALT value.

significantly less severe fibrosis stages in patients with normal ALT ($p < 0.02$). For example METAVIR scores F3-F4 were observed in 3 patients (8.6%) with normal ALT, when observed in 38 patients (25%) with elevated ALT. An antiviral treatment was planned in 141 patients (47% of our population). The reasons for unplanned treatment were normal ALT values (30%), old age (7%), minimal disease stage at liver biopsy (6%), or patient refusal (4%).

Discussion

To our knowledge this is the first observational study analyzing epidemiological, clinical, virological and histological characteristics of HCV infected patients in Belgium. Although incomplete, this survey provides a valid and accurate assessment of the way of presentation of new HCV patients attending secondary and tertiary health care facilities in Belgium during the year 2003-2004. In France similar efforts have been performed by more systematic regional cross-sectional surveys collecting clinical information originating from newly diagnosed patients. These data were provided anonymously by regional laboratories performing HCV serology, and thereafter by the medical practitioner who prescribed the serology (16-19). Few similar attempts were published elsewhere in Europe (20-22).

In comparison with previous studies (16-19,36), risk factors in our population showed a similar distribution with 11% of nosocomial transmission and 23% of unknown origin while the IVDU risk factor was underrepresented in our study. Elapsed time between HCV antibody first detection and recruitment of the patient in specialised centres was superior to twelve months for half of the patients, and more than 5 years for 17%. These observations are explained by the fact that HCV infection was asymptomatic in 65 % in our series, confirming that HCV epidemic is silent and that screening in the presence of risk factors is mandatory. Along the same line, the delay between contamination and first serological diagnosis needs to be shortened, in order to propose treatment earlier, ensuring a greater chance of virus eradication (23-25).

We found a low QOL in our seropositive population, this confirming other studies (24-29). This unhealthy feeling could be explained by HCV infection *per se,* but also by a "HCV *labelling effect*" (11,26,31). This effect means that patients, aware of their seropositivity, could score lower than patients unaware or successfully treated. Other explanations might be a higher percentage of general symptoms such as depression or asthenia, which can be associated with the underlying liver disease (26,32) or related to central nervous system involvement (33,34). The descriptive nature of our study is however not able to discriminate among all these causes.

The observation of normal ALT values in 33% of the patients confirms the poor value of ALT determination to diagnose or evaluate severity of HCV infection (21,35-37). Most of our HCV infected patients were viremic (87%), which is consistent with other data from France (81%), Italy (76%) or the US (74%) (38-40). The distribution of the genotypes was comparable to the French regions, except for genotype 4, which is known to be frequent in our country (17,41-43). A liver biopsy was performed in 60% of our patients, this percentage being comparable to a similar study in academic centres (42). Conversely in unselected cross sectional studies, this percentage ranges from 23 to 30% (16,18). Moreover in Belgium performance of liver biopsy is partly dictated by treatment reimbursement criteria.

METAVIR fibrosis stages showed a distribution comparable to similar studies (41,44). For patients with normal ALT, fibrosis stages were significantly less severe as previously reported (12,28,38,40). Six percent of this normal ALT population already suffered from cirrhosis. However this percentage could be overestimated for two reasons. A liver biopsy was not proposed for the whole group, and it seems logical that this procedure was proposed in priority to patients harbouring biological or radiological signs of a more severe liver disease. On the other hand, as previously explained, patients were described with normal ALT value with regard to blood tests in file at the time of their registration, sometimes without a six months ALT determination anteriority. Therefore we can't confirm that the whole group correspond to patients with *persistently* normal ALT values.

Treatment was planned in 47% of our whole population. This represents 70% of the patients with elevated ALT, and with such a large percentage of patients eligible for treatment, our results emphasize the importance of HCV screening programs in Belgium. This figure is nevertheless higher than in other recent studies (16,18). Our type of recruitment, coming from secondary and tertiary care providers, could explain this result. Prospective studies in France have described this bias, which accounted for a significant difference between academic and non-academic centres with 34 versus 7.5% patients treated respectively (44).

Our data however had some limitations. This was a prospective observatory, which included 318 consecutive patients. However the number of HCV patients

attending health care facilities in Belgium is larger, and not limited to secondary or tertiary care centres. Because it was described that patients followed in specialised units are younger and present characteristics favouring a treatment (44), we have to remain cautious when extrapolating the results from academic centres to a non-selected population.

Another limitation is the nature itself of our study, based on voluntary participation of the different practitioners, which carried the possibility of a selection bias. Indeed this study is an observatory and not a registry. The latter should be organised by the Ministries of Health and target the whole medical population including general practitioners and gastroenterologists. At this time, due to the lack of epidemiological data in our country, it is not possible to determine if our population is comparable to the general population of HCV infected patients.

Conclusions

These data emphasize the feasibility and the interest of a large national HCV survey in Belgium by using a very simple, no-time consuming questionnaire and with little expenses. This observatory allows defining the characteristic features of *newly consulting* patients infected with HCV. The majority were middle-aged patients (mean age 45 y), predominantly infected by IVDU or blood transfusion (50%) and recently diagnosed (< 1 y : 50%). Despite a diagnosis generally fortuitous (65%), this cohort scored an underrated QOL of 61. The majority had abnormal ALT values (65%) with a 2 ULN median elevation. On the other hand one third presented with normal ALT values. Eighty seven percent were viremic, a majority with a low viral load (58%), and were infected by genotype 1 (59%) or 3 (19%). Importantly half of these patients were planned for antiviral treatment, confirming the leading role of future screening programs and health care accessibility.

In Belgium we have no national surveillance program and very few epidemiological data are available about HCV patients, especially in the general population. We hope that such a survey will help to define a comprehensive national policy for HCV screening and patient management. Repeating this observatory after a few years should also help to follow our national HCV epidemiology. Indeed the poor recognition of HCV disease extent and severity contrasts in Belgium with the large number of patients susceptible to be treated.

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