Mode of transmission, rather than the hepatitis C virus, as a major determinant of poor interpersonal relationships in patients with chronic hepatitis C

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BACKGROUND: Recent studies have demonstrated that patients with the hepatitis C virus (HCV) have significant neurocognitive impairment.

OBJECTIVE: To assess whether chronic HCV infection impacts on patient marital status, living arrangement and employment.

METHODS: The charts of patients with chronic hepatitis C and hepatitis B were reviewed.

RESULTS: The mean ($\pm$ SD) age of the 129 patients with the hepatitis B virus (HBV) was 46 ± 15 years and that of the 428 patients with HCV was 48 ± 15 years. Sixty-seven per cent of HBV patients were men, compared with 68% of HCV patients. Eighty per cent of HCV patients were Caucasian, compared with 44% of patients with HBV. The main modes of transmission were intravenous drug use (37%) and transfusion of blood products (37%) for HCV, compared with country of origin (76%) for HBV. There were no differences in marital status rates between HBV- and HCV-infected patients (HBV – married (73%), single (21%) and divorced (6%); and HCV – married (66%), single (23%) and divorced (10%); $P=0.20$). HCV patients lived alone more often than HBV patients (HBV – 13%, HCV – 22%; $P=0.03$). There was no difference in overall employment rate between HCV and HBV patients (81% versus 87%; $P=0.15$). Though there may not have been overall differences between HCV and HBV marital status and employment status, there were differences in the HCV subgroups. These subgroup differences were discovered in the multivariate analysis; mode of transmission was identified as the only predictor of the patients' marital status and employment status.

CONCLUSIONS: The most important determinant of interpersonal relationships was the mode of transmission of the viral hepatitis rather than the type of viral infection: past intravenous drug users had lower level relationships.

Key Words: *Neurocognitive impairment; Social function; Substance abuse*

Hepatitis C infection affects over 170 million people worldwide, an overall prevalence of approximately 3% of the world's population (1). While it is well established that the hepatitis C virus (HCV) causes inflammation in the liver, leading to fibrosis, not all signs and symptoms expressed by infected patients can be related to the degree of fibrosis. A number of reports have indicated that symptoms such as fatigue, malaise and depression are common in patients with chronic HCV

Plutôt que le virus de l'hépatite C lui-même, son mode de transmission serait un facteur majeur de la piètre qualité des rapports interpersonnels chez les patients atteints d'hépatite C chronique

HISTORIQUE : Selon de récentes études, les patients qui ont contracté le virus de l'hépatite C (VHC) présentent d'importantes atteintes neurocognitives.

OBJECTIF : Vérifier si l'infection chronique au VHC agit sur la situation de famille des patients, sur leurs conditions de logement et leur situation d'emploi.

MÉTHODE : Les dossiers de patients atteints d'hépatite C ou B chronique ont été passés en revue.

RÉSULTATS : L'âge moyen ($\pm$ É.-T.) des 129 patients souffrant d'hépatite B était de 46 ± 15 ans et celui des 428 patients atteints d'hépatite C était de 48 ± 15 ans. Soixante-sept pour cent des patients atteints d'hépatite B étaient des hommes, contre 68 % des patients atteints d'hépatite C. Quatre-vingts pour cent des patients atteints d'hépatite C étaient de race blanche, contre 44 % des patients atteints d'hépatite B. Les principaux modes de transmission étaient l'utilisation de drogues intraveineuses (37 %) et la transfusion de produits sanguins (37 %) dans le cas du VHC, contre le pays d'origine (76 %) dans le cas du VHB. On n'a noté aucune différence quant à la situation de famille entre les patients infectés par le VHB ou le VHC (VHB : mariés [73 %], célibataires [21 %] et divorcés [6 %]; et VHC : mariés [66 %], célibataires [23 %] et divorcés [10 %], $p = 0,20$). Les patients atteints d'hépatite C vivaient seuls plus souvent que les patients atteints d'hépatite B (VHB – 13 %, VHC – 22 %, $p = 0,03$). On n'a noté aucune différence quant au taux d'emploi global entre les patients infectés par le VHC et le VHB (81 %, contre 87 %, $p = 0,15$). Bien qu'il n'ait pas semblé y avoir de différence globale entre la situation de famille et le statut professionnel des patients atteints de VHC et de VHB, on a noté des différences dans les sous-groupes du VHC. Ces différences de sous-groupe ont été découvertes lors de l'analyse multivariée. Le mode de transmission a été le seul prédicteur de la situation de famille et d'emploi des patients.

CONCLUSIONS : Le plus important déterminant des relations interpersonnelles a été le mode de transmission du virus de l'hépatite plutôt que l'infection virale elle-même. Les utilisateurs de drogues intraveineuses semblaient avoir de moins bons rapports interpersonnels.

infection (2-10), but these symptoms cannot be correlated with hepatic histopathological findings or viral load (5,11,12). It has been postulated that this may be a further extrahepatic manifestation of HCV (13-17). However, little is known whether HCV infection, with this postulated extrahepatic manifestation, has an impact on patients' interpersonal relationships.

The aim of the present study was to assess whether chronic HCV infection, with its known neurocognitive impairment, is

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TABLE 1

Comparison of the marital status, living arrangement and employment status among the subgroups of patients with hepatitis C virus (HCV) and hepatitis B virus (HBV)

Variable	Marital status			Living arrangement			Employment status		
	Married	Single	Divorced	Alone	With family	With friends	Employed	Unemployed	Retired
Sex, n (%)									
HCV									
Male	143 (63)	66 (29)	18 (8)	57 (24)	173 (74)	5 (2)	148 (66)	48 (21)	28 (13)
Female	74 (71)	13 (13)	17 (16)	19 (17)	93 (82)	1 (1)	54 (54)	13 (13)	33 (33)
HBV									
Male	52 (78)	14 (21)	1 (1)	13 (19)	52 (76)	3 (5)	46 (69)	6 (9)	15 (22)
Female	25 (66)	8 (21)	5 (13)	1 (3)	38 (95)	1 (1)	21 (68)	5 (10)	5 (16)
Ethnic background, n (%)									
HCV									
Caucasian	164 (62)	69 (26)	32 (12)	69 (25)	202 (73)	5 (2)	164 (63)	53 (20)	45 (17)
African Canadian	20 (87)	2 (9)	1 (4)	4 (15)	23 (85)	0 (0)	14 (61)	2 (9)	7 (30)
East Asian	16 (76)	3 (14)	2 (9)	0 (0)	20 (100)	0 (0)	11 (65)	2 (12)	4 (24)
Other*	15 (71)	5 (23)	1 (5)	3 (15)	16 (80)	1 (5)	15 (65)	4 (17)	4 (17)
HBV									
Caucasian	30 (71)	10 (24)	2 (5)	9 (20)	33 (75)	2 (5)	25 (57)	7 (16)	12 (27)
African Canadian	5 (100)	0 (0)	0 (0)	1 (20)	3 (60)	1 (20)	3 (100)	0 (0)	0 (0)
East Asian	28 (72)	8 (21)	3 (8)	2 (5)	37 (95)	0 (0)	31 (82)	2 (5)	5 (13)
Other*	11 (73)	3 (20)	1 (7)	2 (13)	13 (81)	1 (6)	7 (64)	1 (9)	3 (27)
Mode of transmission, n (%)									
HCV									
Intravenous drug use	42 (46)	31 (34)	19 (21)	38 (40)	56 (58)	2 (2)	55 (63)	31 (36)	1 (1)
Blood products before 1992	74 (63)	34 (29)	9 (8)	22 (18)	97 (80)	2 (2)	82 (70)	20 (17)	15 (12)
Immigration from a high-risk country	40 (85)	3 (6)	4 (9)	5 (9)	48 (91)	0 (0)	25 (50)	3 (6)	22 (44)
Other	15 (71)	5 (24)	1 (5)	5 (25)	15 (75)	0 (0)	9 (47)	2 (11)	8 (42)
HBV									
Intravenous drug use	1 (33)	2 (67)	0 (0)	0 (0)	3 (100)	0 (0)	0 (0)	1 (100)	0 (0)
Blood products before 1992	4 (100)	0 (0)	0 (0)	3 (27)	7 (64)	1 (9)	2 (33)	3 (50)	1 (17)
Immigration from a high-risk country	51 (76)	12 (18)	4 (6)	1 (13)	7 (87)	0 (0)	50 (78)	4 (6)	10 (16)
Other	13 (59)	8 (36)	1 (5)	9 (12)	65 (84)	3 (4)	10 (53)	2 (11)	7 (37)

Categories may have missing data because some patients had incomplete data sets. *Included Latin American, Native Canadian, Middle Eastern and South Asian

associated with impairment in the social functioning of patients.

PATIENTS AND METHODS

The charts of 428 anti-HCV-positive patients and 129 hepatitis B surface antigen-positive patients of one hepatologist at the McGill University Health Centre (Montreal, Quebec) were reviewed. Subjects with other chronic liver diseases were excluded from the study. For each patient, the data were collected from the original consultation document with the hepatologist. The possible predictor variables recorded were age, sex, ethnic background, mode of transmission, presence of decompensated liver disease (defined by Child-Pugh score class B or C) and etiology of liver disease (hepatitis B or hepatitis C). The outcome variables recorded were marital status, living arrangement and employment. Marital status was classified as married (or living in a common-law relationship), single or divorced. Living arrangement was classified as alone, with family or with friends. Employment was classified as employed, unemployed or retired.

The results of patients infected with the HCV were compared with those infected with the hepatitis B virus (HBV). Statistical analysis was performed using Sigma Stat 2.0 (Jandel

Scientific, USA). Continuous variables were compared using Student's *t* test, and categorical variables were compared by χ^2 analysis. $P < 0.5$ was used to define statistical significance. Using the variables of the present study's univariate analysis (Table 1) with a stepwise backward logistic regression ($P < 0.10$), multiple logistic regression was used to identify the best predictive model.

RESULTS

Patient characteristics

Table 2 shows the demographic characteristics of the patients evaluated. Both groups had similar age and sex distributions. Ethnic background was classified as Caucasian, African Canadian, East Asian and others. The subclass 'others' included Latin American (HCV, 2.1%; HBV, 4.0%), Native Canadian (HCV, 0.7%; HBV, 0%), Middle Eastern (HCV, 3.1%; HBV, 5.7%) and South Asian (HCV, 1.2%; HBV, 4.0%) patients. In the HCV group, Caucasian was the dominant ethnic background (79.8%), whereas in the HBV group the Caucasian background was noted for 44.4% of patients, followed by the East Asian background (36.3%).

Mode of transmission was categorized as intravenous (IV) drug use, blood products and/or solid organs before 1992, and

immigration from high-risk countries. High-risk countries of origin for HBV were countries from Southeast Asia. High-risk countries of origin for HCV were countries from the Middle East and Southern Europe (mostly Southern Italy). Exposure to blood products and past IV drug use were the most common modes of HCV transmission, and most subjects with HBV were from endemic areas. Among 129 IV drug users in the HCV group, 93.1% were Caucasian, 1.5% were African Canadian, 0% were East Asian and 5.3% were labelled as 'others'. All three IV drug use patients in the HBV group were Caucasian.

Also, of the 402 HCV and 121 HBV patients with known alcohol status, 159 HCV patients were abstinent from alcohol (40%), compared with 75 of those with HBV (62%). Forty-five patients with HCV (10%) and 17 with HBV (13%) were known to have decompensated liver disease.

Marital status

Overall, there was no difference observed in the marital status of patients infected with HBV (married [73%], single [21%] and divorced [6%]) versus HCV (married [66%], single [23%] and divorced [10%]) ($P=0.20$) as well as their frequency of having children (HCV, 63%; HBV, 65%; $P=0.76$). However, there were major differences among the subgroups, as shown in Table 1. Fewer men with HCV were involved in a meaningful relationship than men with HBV (63% versus 78%; $P=0.03$), whereas no significant difference was observed between the two groups of women. As well, fewer Caucasians with HCV were married or living in common-law relationships than patients with HCV of other ethnic backgrounds (62% versus 78%; $P=0.02$). Moreover, significantly fewer past IV drug users with HCV were involved in a meaningful relationship than patients who acquired HCV through other modes (46% versus 70%; $P<0.001$).

By multivariate analysis, mode of transmission was identified as the only predictor of the patients' marital status (OR 1.91; 95% CI 1.51 to 2.42). In other words, IV drug use was associated with a higher prevalence of not being married or living in a common-law relationship.

Living arrangement

Overall, more patients with HCV lived alone than those with HBV (13% versus 22%; $P=0.02$). As shown in Table 1, there was no significant difference among the subgroups based on sex. However, more HCV-infected Caucasians lived alone than HCV-infected patients of other ethnic groups (25% versus 10%; $P=0.01$). Also, many more past IV drug users with HCV lived alone than those who acquired the disease through other modes (40% versus 16%; $P<0.001$).

By multivariate analysis, mode of transmission and ethnic background were identified as predictors of the patients' living arrangements (mode of transmission – OR 1.58, 95% CI 1.20 to 2.09; ethnic background – OR 1.28, 95% CI 1.06 to 1.54). This means that being Caucasian and/or a past IV drug user with HCV was associated with a higher tendency to live alone.

Employment

In general, there was no difference in the unemployment rate between patients with HCV and those with HBV (19% versus 11%; $P=0.09$). As shown in Table 1, there was no difference between the subgroups based on ethnic background. However, in terms of sex distribution, more men with HCV were unemployed than men with HBV (21% versus 9%; $P=0.04$), whereas

TABLE 2
Demographic distribution of patients with hepatitis C virus (HCV) versus hepatitis B virus (HBV)

Predictor variable	Patients with HCV (n=428)	Patients with HBV (n=129)
Age in years (mean $\pm$ SD)	48 $\pm$ 15	46 $\pm$ 13
Sex, n (%)		
Male	291 (68)	87 (67.4)
Female	137 (32)	42 (32.6)
Ethnic background, n (%)*		
Caucasian	335 (79.8)	55 (44.4)
African Canadian	31 (7.4)	7 (5.7)
East Asian	24 (5.7)	45 (36.3)
Other†	30 (7.1)	17 (13.7)
Mode of transmission, n (%)*		
Intravenous drug use	129 (37.4)	3 (2.6)
Blood products and/or solid organ before 1992	130 (37.7)	6 (5.2)
Immigration from a high-risk country	62 (18.0)	80 (69.6)
Other	24 (7.0)	26 (22.6)

*Information was not available for every patient, therefore some patients are not included in the presented data; †Included Latin American, Native Canadian, Middle Eastern and South Asian

no significant difference was observed between the female groups. Moreover, regarding mode of transmission, more IV drug users with HCV were unemployed than patients with HCV who acquired it through other modes (36% versus 13%; $P<0.001$).

By multivariate analysis, mode of transmission was identified as the only predictor of the patients' employment status (OR 3.90; 95% CI 2.24 to 6.80). In other words, being a past IV drug user was associated with a higher probability of being unemployed.

DISCUSSION

As part of our expanding knowledge on HCV since its discovery in 1989, extrahepatic manifestations, such as glomerulonephritis and essential mixed cryoglobulinemia, have been uncovered (18). Compared with patients with other chronic liver diseases, patients living with chronic HCV frequently report a multiple of symptoms that they attribute to their infection. Besides complaints about physical unwellness such as fatigue, malaise, musculoskeletal and right upper abdominal discomfort, they have also reported memory impairment, depression, anxiety and mental clouding (2-10).

Clinicians have traditionally referred to the degree of inflammation to prioritize who should be treated. Given that quality of life is what drives consultation and that hepatic inflammation is a poor marker for detecting the patients whose quality of life has been significantly affected by HCV, the use of objective markers of inflammation alone is not sufficient.

The extrahepatic symptoms reported from patients have led many researchers to question whether patients with HCV infection have poorer quality of life and social functioning than those with HBV. Not surprisingly, most of the studies have reported a consistent and significant reduction in health-related quality of life in patients with chronic HCV compared with population norms (5,6,9,19-22).

For instance, Gallegos-Orozco et al (9) compared the quality of life of 157 HCV patients, without previous interferon therapy, to historical normal controls using the 36-item Short

Form Symptomatology Questionnaire (SF-36). They demonstrated that the chronic HCV patients in their study scored significantly lower in all eight domains of the SF-36. Similarly, Foster et al (5) used the SF-36 to compare the quality of life of patients with chronic HCV to those with chronic HBV. They showed that patients with HCV had significant reductions in their SF-36 scores for all modalities tested. For the social functioning domain in particular, Foster et al (5) reported that the subjects with chronic HCV perceived themselves to be more unwell than those with HBV.

In the present study, the patients' social functioning was assessed not through any standard questionnaire, but through direct questioning of their marital status, living arrangement and employment status at the time of their first encounter with the hepatologist. To assess patient social functioning, psychiatrists obtained a social history, which included marital status, living arrangement and employment status (23). In *Bates' Guide to Physical Examination and History Taking* (24), a classic reading for undergraduate medical training, 'significant others', 'home situation' and 'employment' were the first elements in the section on social history. So, for the practical purposes of the medical interview, marital status, living arrangement and employment were judged to be appropriate markers of the patient's social functioning. Language spoken was not assessed per se, but the questioning was simple and completed through an interpreter if needed. The assessed social functioning of the HCV patients was, overall, not significantly impaired. There were no statistical differences in marital status, frequency of having children and unemployment rate between the two groups, but more patients with HCV lived alone than those with HBV. The difference between our findings and previous studies on significantly reduced social functioning of HCV patients suggests that these patients perceive their ability to function more poorly than it is.

In the study by Zickmund et al (25), patients reported having experienced stigmatization, which they attributed to the infection; this was associated with higher anxiety, depression and worse quality of life. Zickmund et al showed concern that the emotionally burdensome experience of stigmatization can erode social support in patients infected with HCV. Our analysis did not support their concern. Indeed, no previous systematic evaluation has been done to study whether HCV infection, per se, has a significant impact on patients' social interactions. Overall, in our study, HCV did not appear to affect social functioning, but the IV drug use subgroup did not function as well, and social stigmatization could not be excluded.

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