

Evaluation of immigration status, race and language barriers on chronic hepatitis C virus infection management and treatment outcomes

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Objective Hepatitis C virus (HCV) prevalence in certain Canadian immigrant populations is higher than that of the overall population. Disparities in care related to immigration status as well as to race and language are well recognized. Identifying and understanding these disparities is vital to the provision of optimal and inclusive HCV care.

Methods and materials HCV RNA-positive patients assessed at The Ottawa Hospital Viral Hepatitis Clinic between June 2000 and June 2007 were identified using a clinical database. As measures of access to care, liver biopsy rates, treatment initiation rates, supportive care provision (i.e. erythropoietin for treatment-related anemia) and sustained virological response (SVR) rates were assessed as a function of immigration status, race and spoken language.

Results Nine hundred and ten patients were evaluated, of which 20% were immigrants. Biopsy rates (54 vs. 51%), HCV treatment initiation (37 vs. 38%), erythropoietin prescription (13 vs. 18%) and SVR rates (52 vs. 51%) did not differ between immigrants and Canadian-born individuals. Spoken language and race did not

influence access to treatment. SVR was predicted by genotype, HIV status and race.

Conclusion In the context of a multidisciplinary, multilingual universal health care system, by studying the influence of barriers to HCV investigation and successful therapy can be abrogated. *Eur J Gastroenterol Hepatol* 21:963–968 © 2009 Wolters Kluwer Health | Lippincott Williams & Wilkins.

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Introduction

First-generation immigrants make up a significant proportion of populations in Canada, the USA, Europe and Australia [1–4]. Many of these individuals originate from Hepatitis C Virus (HCV)-endemic regions of the world, and are diagnosed with HCV infection after immigration and subsequently referred to viral hepatitis clinics for disease management. Immigrants may face multiple barriers to receiving optimal health care. Communication issues resulting from physician–patient language discordance are known to influence health care satisfaction [5–8]. Racial and ethnic disparities concerning access to health care are well recognized [9–11]. Socioeconomic status is another potential obstacle to health care delivery, even in countries with publicly funded universal health care systems [12–14].

To provide optimal care to all patients, identifying and understanding barriers to care related to immigrant status, race and language in HCV management is essential. To this end, we compared differences in HCV management between Canadian-born and immi-

grant patients in the context of a universal medical system within the setting of a diversely populated, urban-located, tertiary care hospital-based multidisciplinary viral hepatitis programme.

Methods

Data for this study are drawn from the Viral Hepatitis Program Clinical Database housed at The Ottawa Hospital Division of Infectious Disease Viral Hepatitis Clinic in Ottawa, Canada. Patients evaluated in the clinic between June 2000 and June 2007, 18 years of age or older at the time of enrollment, and chronically infected with HCV (defined as HCV RNA positive more than 6 months after initial exposure) were included in this analysis. Patient data extracted included age, sex, race, language, immigration status (defined as a foreign-born resident of Canada), the number of months in Canada since immigration, history of mental health illness, history of injection drug use, HCV genotype, HCV RNA level, alanine aminotransferase, aspartate aminotransferase, HIV status and HBV status. Hepatitis B surface antigen positive patients were excluded from

this analysis. If a patient received more than one course of HCV antiviral therapy, only the most recent one was considered. HCV antiviral therapy was defined as any formulation of interferon and ribavirin.

To obtain information on the socioeconomic status of patients, we extracted data from the 2006 Canadian Census database. All patients were assigned to a census dissemination area by using their residential postal code. On the basis of this, average measures of socioeconomic variables, as represented in the census tract denominations, were attributed to each patient. The census dissemination-level socioeconomic variables included in the analyses were percentage of residents with post-secondary education, percentage of residents who were unemployed, percentage of residents living below the Canadian poverty line, and median neighbourhood household income (before tax).

Our analyses focused on the following outcomes measures: (i) pre-HCV antiviral therapy management, (ii) HCV drug treatment (iii) supportive care while on HCV treatment and (iv) treatment success. Access to pre-HCV treatment was evaluated by the proportion receiving a liver biopsy. This was selected as it is considered a standard care procedure for many being evaluated for HCV treatment. This was evaluated as a function of genotype to account for the potential influence of this parameter on biopsy frequency. Access to treatment was determined by antiviral treatment initiation rates. Access to supportive care was estimated by erythropoietin use while on HCV antivirals. Erythropoietin is expensive, restricted by the provincial drug reimbursement plans and requires considerable effort by HCV clinic staff to obtain. Therefore, it is an appropriate indicator of access to supportive care. This was controlled for by genotypes receiving high doses of ribavirin (i.e. genotype 1, 4, 5, 6). Treatment success was evaluated by sustained virological response (SVR) rates (defined as HCV RNA negative 6 months after the completion of HCV antiviral therapy). Genotype was considered for this outcome as well.

Analyses focused on the following stratification of explanatory variables: (i) immigrant status: Canada-born or immigrant, (ii) self-reported race: White, Black, Asian and Aboriginal, (iii) spoken language: English, French, other, (iv) median before tax household income. For language analysis, we classified our population into the following two groups: (i) English and/or French speaking, (ii) Non-English and non-French speaking. Of note, clinical services are provided in French and English.

For each step of HCV management mentioned above, χ^2 analyses were conducted to evaluate whether these measures of access differed by immigrant status, race,

language or socioeconomic status. Predictors of SVR were assessed by logistic regression analysis. Variables included genotype, age, fibrosis stage, HCV RNA level and HIV status as well as sex, race, immigration status, length of time in Canada following immigration, language category, history of mental health illness and history of injection drug use. A multivariate logistic regression model was constructed consisting of well established predictors of SVR and variables with *P* values of less than 0.10 in univariate analysis.

All data were analysed using SPSS version 16.0 (SPSS Inc., Chicago, Illinois, USA). All significance tests were two-sided and *P* values of less than 0.05 were considered statistically significant. Ottawa Hospital Research Ethics Board approval and patient consent were obtained for the use of these data for research purposes.

Results

Between June 2000 and June 2007, 910 patients with chronic HCV infection were evaluated, of which 185 (20%) were immigrants (Table 1). Immigrants had

Table 1 Baseline characteristics of HCV patients as a function of immigration status

| | Immigrant | Canadian-born | <i>P</i> value |
|--------------------------------------|---|---|----------------|
| Continuous variables mean (SD) | | | |
| <i>N</i> (% of total) | 185 (20) | 725 (80) | – |
| Age (years) | 49 (13) | 44 (9) | <0.001 |
| Weight (kg) | 75 (18) | 79 (17) | <0.01 |
| HCV RNA (IU/ml) | 2.0×10^6 (9.6×10^6) | 1.6×10^6 (5.6×10^6) | 0.55 |
| ALT (IU/l) | 76 (58) | 83 (70) | 0.23 |
| AST (IU/l) | 61 (43) | 66 (62) | 0.30 |
| Categorical variables | | | |
| <i>n</i> | 185 | 725 | |
| Male sex (%) | 61 | 74 | <0.001 |
| HIV seropositive (%) | 5 | 14 | <0.01 |
| History of mental health illness (%) | 26 | 54 | <0.001 |
| History of injection drug use (%) | 20 | 67 | <0.001 |
| Genotype (%) | | | <0.001 |
| 1 | 54 | 71 | |
| 2 | 7 | 9 | |
| 3 | 9 | 19 | |
| 4 | 23 | <1 | |
| 5 | 2 | <1 | |
| 6 | 5 | 0 (0) | |
| Race (%) | | | <0.001 |
| White | 43 | 97 | |
| Black | 35 | <1 | |
| Asian | 21 | <1 | |
| Aboriginal | 1 | 3 | |
| Language barrier ^a (%) | 18 | 0 | <0.001 |
| Spoken language (%) | | | <0.001 |
| English | 64 | 81 | |
| French | 18 | 19 | |
| Vietnamese | 7 | 0 | |
| Arabic | 6 | 0 | |
| Chinese | 4 | 0 | |
| Other | 1 | 0 | |

ALT, alanine aminotransferase; AST, aspartate aminotransferase; HCV, hepatitis C virus.

^aDefined as non-English and non-French speaking.

lived in Canada a mean 209 months (quartiles: 64, 172, 296) at the time of initial assessment. Immigrants were more likely to be female, non-White, older and infected with genotypes 4, 5 and 6 when compared with Canadian-born patients. The burden of HIV coinfection, history of injection drug use and mental health illness were less in immigrants. A language barrier was identified in 18% of immigrants and not in Canadian-born patients.

Liver biopsy rates were similar between immigrant and Canadian-born patients [54% ($n=100$) vs. 51% ($n=369$), $P=NS$]. Amongst immigrants, the length of time in Canada did not influence the likelihood of liver biopsy (205 months in those who underwent biopsy vs. 214 months; $P=0.75$). The median biopsy grade (2/4) and stage (2/4) (Butt-Ludwig System) did not differ by group suggesting that biopsies were offered at a similar stage of disease. The proportion with advanced fibrosis (stage 3 or 4) was similar between immigrants (18%) and Canadian-born (25%) ($P=NS$). Canadian-born patients infected with genotypes 2 or 3 were less likely to receive a liver biopsy (39%) than if infected with genotypes 1, 4, 5 and 6 (55%) ($P<0.001$). In contrast, the biopsy rate was similar by these genotype groupings in immigrant patients (53 vs. 54%, $P=NS$). This may reveal a physician bias in work-up.

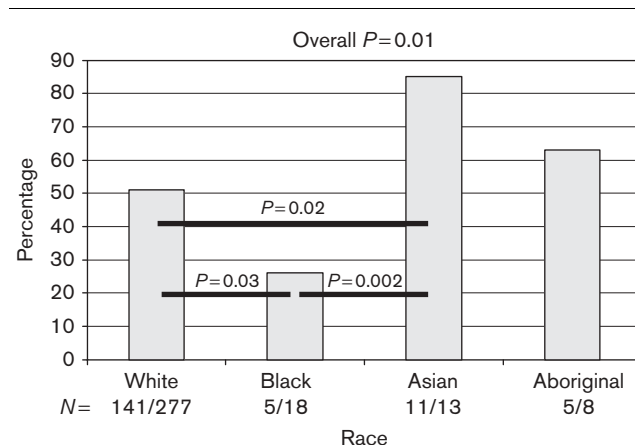
HCV treatment initiation was similar for immigrant [37% ($n=69$)] and Canadian-born patients [38% ($n=277$)] ($P=NS$). The mean time in Canada since immigration did not influence the likelihood of treatment initiation (209 months in both those initiating therapy and those who did not; $P=0.99$). Genotype 2-infected and genotype 3-infected patients were more likely to initiate therapy than those who were infected with genotypes 1, 4, 5 or 6 irrespective of whether an immigrant (57 vs. 33%, $P=0.02$) or Canadian-born (43 vs. 36%, $P=0.09$). Erythropoietin was prescribed and administered to nine immigrants (13%) and 50 (18%) Canadian-born patients ($P=NS$). The use of erythropoietin in genotypes 1, 4, 5, and 6-infected patients receiving the highest doses of ribavirin did not differ [eight of 52 (15%) in immigrants vs. 42 of 188 (22%) in Canadian-born, $P=NS$]. In total, 51% of patients (162 of 318) who initiated HCV therapy and where final treatment outcome data were available achieved an SVR. SVR rates did not differ by immigrant status [52% (32 of 61) vs. 51% (130 of 255)] ($P=NS$). This was true for specific genotypes (Table 2). The length of time in Canada did not predict the likelihood of SVR (194 in those with SVR vs. 228 with non-SVR; $P=0.45$).

The influence of race on HCV work-up, treatment initiation and access to supportive care was evaluated. A greater proportion of Blacks was above 60 years of age at presentation (25 vs. 4%, $P<0.001$). No statistically

Table 2 Sustained virological response by immigrant status

| Genotype | Immigrant | Canadian-born | <i>P</i> value |
|----------|------------|---------------|----------------|
| All (%) | 52 (32/61) | 51 (130/255) | 0.84 |
| 1 (%) | 53 (17/32) | 40 (67/168) | 0.16 |
| 2 (%) | 67 (4/6) | 85 (23/27) | 0.29 |
| 3 (%) | 63 (5/8) | 68 (40/59) | 0.77 |
| 4 (%) | 33 (4/12) | 0 (0/1) | – |
| 5 (%) | – | – | – |
| 6 (%) | 67 (2/3) | – | – |

Fig. 1



Sustained virological response as a function of race. Sustained virological response is influenced by race. Sustained virological response is highest in Asian treatment recipients and lowest in Blacks.

significant difference in treatment initiation was identified. However, there was a trend towards more frequent HCV treatment initiation in Whites compared with Blacks (38 vs. 29%, $P=NS$). SVR rates differed by race, whereby Blacks had the lowest SVR [28% (five of 18)] and Asian patients had the highest SVR [85% (11 of 13)] ($P=0.02$) (Fig. 1). Eight of nine genotype 1-infected and two of three genotype 6-infected Asians achieved SVR. The low number of Asian and Black patients on HCV antiviral therapy precluded the evaluation of immigration status and language barrier on our outcome measures in this population.

Language barriers within the immigrant population did not influence access to work-up, HCV treatment initiation, erythropoietin prescription or treatment outcome (data not shown). No difference in access to HCV care or outcome between French and English-speaking Canadian-born patients was identified.

On the basis of the 2006 Canadian Census data, immigrant patients were more likely to live in urban settings characterized by higher rates of high school and post-secondary education (Table 3). The median income was higher in the neighbourhoods inhabited by immigrants.

However, unemployment rates and the proportion in the low-income strata were higher. This suggests a dichotomy of socioeconomic status within the Canadian immigrant population. The socioeconomic measures utilized in this study did not influence our selected outcome measures. Rates of biopsy referrals, treatment initiation and erythropoietin use were not related to financial or education status (data not shown). Furthermore, the overall SVR rate was not influenced by income status (Table 4).

Variables well established to influence SVR (i.e. genotype, age, fibrosis stage, HCV RNA level, HIV status) as well as sex, race, immigration status, language category, mental health illness and history of substance use were assessed by univariate logistic regression (Table 4). Immigration status and language were not found to be significant predictors of SVR. Genotype was the most important and consistent predictor of SVR when evaluated by multivariate logistic regression models [odds ratio: 2.73 (1.60, 4.06), $P < 0.001$ (model variables: genotype, HCV RNA level, race, HIV status, sex, age)].

Discussion

Immigration status, race and language barriers have been identified as factors that impede access to HCV-related health care in many developed countries [10,11]. Given

the heavy burden of HCV infection in immigrants living in Canada and other developed regions of the world, these factors need to be considered to ensure that immigrant populations receive adequate care [15]. Our analyses suggest that these issues do not necessarily need to detrimentally influence HCV care. Several factors may have facilitated the equity of care achieved in our setting. The universal system of health care provision in Canada likely influenced our findings. Within this system, the likelihood of visiting a physician is more related to healthcare needs and chronic conditions than socioeconomic or educational levels [12,16]. Theoretically, no disparities should exist with regard to access to care. However, lower socioeconomic and educational levels have been associated with reduced likelihood of referral to a specialist in the Canadian setting [12–14]. There is a long history of managing diverse populations within our urban, hospital-based clinics. As such, our staff may be more aware of these obstacles and as a consequence make a concerted effort to provide equal care to all patients. The institutional focus on equal access to health care services in both the official languages of Canada (French and English) may have increased health care providers' awareness of language barriers for other populations and minorities.

Communication between health care providers and patients may fail as a consequence of language barriers. It is a major determinant of the quality of patients' health care experience. Those with physicians speaking their native language report record higher functional scores and better well being [5,6]. Language discordance may result in reduced satisfaction with clinician communication, lower overall health care satisfaction, poor patient comprehension of received care, poor compliance with treatment recommendations, reduced medication adherence and missed follow-up visits [6–8,17,18]. Poor comprehension of medication dosing instruction alters therapeutic outcomes in the context of HCV care [19]. To overcome

Table 3 Socioeconomic characteristics by immigration status

| Measure | Immigrant | Canadian-born | <i>P</i> value |
|---|-----------|---------------|----------------|
| Yearly median neighbourhood household income (Canadian dollars) | \$28 609 | \$26 113 | <0.01 |
| Low income strata ^a (%) | 16 | 12 | 0.26 |
| Urban setting (%) | 96 | 83 | <0.001 |
| High-school education (%) | 83 | 79 | <0.001 |
| Bachelors degree or higher (%) | 29 | 19 | <0.001 |
| Unemployment (%) | 6.5 | 6.0 | 0.26 |

^aDefined as bottom quintile of neighbourhood household income.

Table 4 Predictors of diminished sustained virological response

| Variable | Univariate | | Multivariate model | |
|---|----------------------------------|----------------|----------------------------------|----------------|
| | Odds ratio (confidence interval) | <i>P</i> value | Odds ratio (confidence interval) | <i>P</i> value |
| Genotype 1 | 2.84 (1.76, 4.58) | <0.001 | 2.73 (1.60, 4.06) | <0.001 |
| HIV coinfection ($n=41$) | 2.90 (1.42, 5.92) | 0.003 | 2.70 (1.26, 5.81) | 0.01 |
| Black race | 2.90 (1.01, 8.32) | 0.03 | 2.66 (0.85, 8.29) | 0.09 |
| Viral load >400 000 copies/ml | 1.56 (0.94, 2.59) | 0.09 | 1.57 (0.91, 2.71) | 0.10 |
| Male sex | 1.67 (0.99, 2.81) | 0.05 | 1.48 (0.82, 2.68) | 0.19 |
| Increasing age (years) | 1.04 (1.01, 1.07) | 0.004 | 1.02 (0.99, 1.05) | 0.26 |
| Advanced fibrosis on biopsy ^a ($n=66$ of 204) | 1.52 (0.84, 2.73) | 0.17 | – | – |
| Immigrant | 0.94 (0.54, 1.65) | 0.84 | – | – |
| Non-English or Non-French speaking | 1.94 (0.48, 7.88) | 0.36 | – | – |
| History of mental health illness | 1.15 (0.74, 1.78) | 0.55 | – | – |
| Low-income status ^b | 1.70 (0.77, 3.72) | 0.19 | – | – |
| History of injection drug use | 1.10 (0.70, 1.72) | 0.67 | – | – |

^aStage 3 or 4 on scheuer classification system.

^bDefined as bottom quintile.

language barriers, health care providers often rely on language interpreters. Qualified language interpreters improve overall health care satisfaction in patients with low English proficiency [8,17,20,21]. When well trained language interpreters are utilized in care, patient satisfaction can approach that of English-speaking patients. In contrast, the use of untrained ad-hoc language interpreters may result in the communication of misinformation, poor patient satisfaction, reduced patient trust in their physician, increased misdiagnosis, inadequate or inaccurate treatment and overall lower quality of care [8]. In our clinic, the regular use of well trained language interpreters likely explains why language did not influence access to care and treatment outcomes among patients.

Although not statistically significant, a trend towards lower treatment initiation rates in Blacks (29%) compared with Whites (38%) was observed. When compared with Whites, Blacks presented at a similar stage of disease based on median liver biopsy fibrosis stage. A greater proportion of Blacks was above 60 years of age at presentation, which may have dissuaded a decision to pursue HCV treatment. We suspect that another key factor that contributes to lower treatment initiation in Blacks is physician knowledge of diminished SVR rates in this population, which may have resulted in a nontreatment initiation bias. Consistent with other reports, race did influence the likelihood of achieving SVR in our cohort. Lower SVR rates in Blacks have been consistently reported in other studies [22–25]. SVR rates in Blacks receiving pegylated interferon and ribavirin therapy were significantly lower than in Whites (19 vs. 52%) and (28 vs. 52%) [23,24]. It is also possible that Black patients with genotype 1 infection may have chosen not to undertake therapy when they are advised of the low expected SVR rates. Higher rates of SVR among individuals of Asian descent are also well documented in the literature [26–28], and were observed in our patient population. Little data is available in response to therapy among Aboriginal people. A recent analysis, however, reported similar SVR rates when compared with Whites [29]. The number of Aboriginal people on treatment in our cohort was insufficient to corroborate these results.

Lower socioeconomic status is known to decrease therapeutic outcomes among patients because of greater cost-related prescription nonadherence [30]. However, at our clinic, income did not influence access to work-up, treatment or SVR rates. This is likely a reflection of the publicly funded Canadian health care system, where access to health care services is theoretically universal. It is likely that such a finding would not be observed in privately funded health care systems. Neighbourhood household income, as opposed to individual income, was available for this analysis, which is a limitation.

Of the 1.1 million that reside in the Ottawa region, approximately 16% belong to a visible minority group [31] and many speak neither English nor French [32]. These characteristics are typical of large urban centres in North America, Europe and Australia [1–4]. As such, we believe that these results are broadly applicable; at least to countries with universal health care systems. Although our evaluation indicated that race and immigrant status did not influence the quality of care at our hospital-based clinic, we acknowledge that racial minorities may encounter difficulties in obtaining referral [9]. Within Canada's universal health care system, specialist referral is provided by family physicians. However, nearly four million Canadians do not currently have a regular family physician [33]. Furthermore, immigrants are less likely to have a regular family physician [34]. Even within Canada's universal health care system, lower socioeconomic and educational levels predict reduced likelihood of referral to specialists [12,14,15]. We were unable to consider these factors in our analysis. In our data collection process, only one language was recorded. The language entered may correspond to preferred language rather than the best understood. Given the low number of erythropoietin recipients, the potential for a type II statistical error should be considered. Although this was a retrospective database evaluation, there was minimal missing data and the dataset was meticulously reviewed for inaccuracies before conducting this analysis.

Equitable access to HCV care can be achieved despite the presence of well established barriers to health care provision and outcomes among those infected. The impact of these obstacles may be minimized by first acknowledging the potential for them to influence the quality of care and access to diagnostic investigations, therapeutic interventions and supportive care. Health care provision by a publicly funded, multidisciplinary team including trained language translators seems to facilitate the delivery of an equitable level of care to the majority of patients living with HCV.

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