Health and Socioeconomic Status Differences Among Antibody Hepatitis C Positive and Negative Transfusion Recipients, 1986-1990

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ABSTRACT

Objective: To characterize the socioeconomic and health status, disease symptoms of anti-HCV-positive and negative transfusion recipients.

Methods: A cross-sectional interviewer-administered survey of subjects identified through the British Columbia Blood Recipient Program. Study subjects were 18 years and over and had to have had a transfusion between August 1, 1986 and June 30, 1990 and completed an interview of satisfactory quality. Anti-HCV-positive subjects were those seeking monetary compensation from the provincial and Canadian governments and the comparison group was randomly selected from a pool of anti-HCV-negative subjects. The study was designed to detect an assumed difference of 20% in signs and symptoms between the two groups. Statistical comparisons were conducted using bivariate and multivariate logistic regression analyses.

Results: A total of 241 and 222 anti-HCV-positive and negative subjects were respectively interviewed and met the study's eligibility criteria. Results from the multivariate analysis indicated that anti-HCV-positive recipients were more likely to have two or more clinical symptoms (OR = 3.53; 95% CI: 1.44, 8.70), to be in worse health status as compared to ten years previous (OR = 1.60; 95% CI: 1.30, 1.96), to have a higher illness intrusiveness rating (OR = 1.35; 95% CI: 1.25, 1.46), and to be younger (OR = 0.97; 95% CI: 0.95, 0.98).

Conclusion: Our results show that persons exposed to HCV were more likely to have had two or more clinical symptoms, be male, have worse health status as compared to ten years previous, have a higher illness intrusiveness rating, and be younger in age.

La traduction du résumé se trouve à la fin de l'article.

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In Canada, as in other parts of the world, there has been considerable concern about blood safety, especially in relation to the transmission of hepatitis C and HIV.¹ Of the 250,000 persons currently infected with hepatitis C in Canada, approximately one fifth of these individuals likely contracted this infection through a blood transfusion.^{2,3} In June 1997, following the interim recommendations of the Commission of Inquiry on the Blood System in Canada,⁴ a generalized look-back campaign of blood transfusion recipients between 1990 and 1986 was carried out in the province of British Columbia.⁵ Of the 38,989 men and women who underwent testing for hepatitis C, 1,948 (5.0%) were antibody positive. Most of the persons who tested positive in this look-back were eligible to seek monetary compensation through a class action lawsuit launched in British Columbia and the provinces of Ontario and Quebec against the federal and provincial governments as well as the Red Cross Society.

This study was based on persons who had a blood transfusion in British Columbia between the period of August 1, 1986 to June 30, 1990 and were either hepatitis C antibody positive (anti-HCV-positive) and part of the class action lawsuit, or hepatitis C antibody negative (anti-HCV-negative) and part of the provincial look-back study. The purpose of this study was to characterize the socioeconomic and health status, and disease symptoms of anti-HCV-positive and negative transfusion recipients in this province.

METHODS

The study was conducted by the British Columbia Centre for Excellence in HIV/AIDS in consultation with the Provincial Blood Coordination Office. The study was conducted over the period of October 1998 to February 1999 and received ethics approval from St. Paul's Hospital Ethics Committee for Human Experimentation which is affiliated with the University of British Columbia.

Study subjects

We estimated *a priori* that we would need a minimum sample size of 212 anti-HCV-positive and 212 anti-HCV-negative participants to provide an accurate estimate of the proportion of individuals with symp-

toms and signs. Anti-HCV-positive subjects were defined as persons who were anti-HCV-positive and part of the class action lawsuit; while the comparison group were a random sample of the anti-HCV-negative transfusion recipients identified from the British Columbia Blood Recipient Notification Program. Study participants also had to be aged 18 years and over, to have self-reported that they had a transfusion between August 1, 1986 and June 30, 1990, and completed an interview that the interviewer felt was of satisfactory quality.

Data collection instrument

The development of the questionnaire was overseen by the study investigators, an external advisory panel of physicians with expertise in hepatology and quality of life issues, and a community advisory board. The questionnaire was pre-tested on persons with hepatitis C who were not part of the class action suit. Interview and data entry techniques were also standardized to ensure the quality of the data.

Study participants who completed a consent form were asked to complete an interview in person or over the phone. The survey instrument elicited information about the participant's demographic characteristics, employment and educational history, personal and household income in 1997, health status, social support, transfusion history, restriction of activities and disabilities, fatigue and sleeping disorders, and disease symptomatology in the previous 12 months. A number of self-reported health and illness intrusiveness scales were incorporated into the survey instrument, including the RAND 36-item Health Survey,⁶ the Epworth Sleepiness Scale,⁷⁻¹⁰ the Fatigue Severity Scale,¹¹ and the Illness Intrusiveness Rating Scale.^{12,13} In addition to the participant survey instrument, the study used 1996 Canadian census data for British Columbia to compare the community level sociodemographic characteristics of respondents and non-respondents.

Statistical analyses

Comparisons of anti-HCV-positive and negative transfusion recipients were conducted using both parametric and distribution-free methods. Stepwise multivariate logistic regression was used to identify independent predictors of anti-HCV-positivity and to adjust for potential confounding vari-

TABLE I

Comparison of Transfusion History Between Anti-HCV-positive and Negative Subjects

Variables	Anti-HCV-positive n (%)	Anti-HCV-negative n (%)	p-value
Ever had a blood transfusion			
Yes	241 (100)	222 (100)	1.000
No	0 (0)	0 (0)	
Hospital transfusion episodes			
Prior to the 1960s	1 (0.4)	6 (2.7)	0.059
1960 to 1969	14 (5.8)	4 (1.8)	0.026
1970 to 1979	16 (6.6)	20 (9.0)	0.341
1980 to 1985	30 (12.5)	20 (9.0)	0.240
1986 to 1990	241 (100)	222 (100)	1.000
1991 to 1995	24 (10.0)	11 (5.0)	0.042
1996 onward	11 (4.6)	12 (5.4)	0.685
Underlying medical reason*			
Respiratory and digestive system	57 (23.6)	38 (17.1)	0.082
Accidental cause	56 (23.2)	26 (11.7)	0.001
Other causes	38 (15.8)	34 (15.3)	0.893
Heart disease	36 (14.9)	55 (24.8)	0.008
Pregnancy	20 (8.4)	27 (12.2)	0.169
Musculoskeletal system	20 (8.3)	28 (12.6)	0.128
Cancer	15 (6.2)	10 (4.5)	0.413
Nervous system	4 (1.7)	5 (2.2)	0.743

* Restricted to transfusion episodes between 1986 to 1990. Subjects can be represented once in each of the 8 listed categories

TABLE II

Comparison of Sociodemographic Characteristics Between Anti-HCV-positive and Negative Subjects

Variables	Anti-HCV-positive n (%)	Anti-HCV-negative n (%)	p-value
Gender			
Male	126 (52.3)	91 (41.0)	0.015
Female	115 (47.7)	131 (59.0)	
Age in years			
Median	50	65	<0.001
Interquartile range	41-64	49-76	
Duration of residence			
Less than 10 years	3 (1.2)	1 (0.5)	0.050*
10 to 19 years	29 (12.0)	16 (7.2)	
20 or more years	209 (86.7)	205 (92.3)	
Marital status			
Legally married	120 (49.8)	145 (65.3)	0.001
Separated or divorced	52 (21.6)	33 (14.9)	
Widowed	13 (5.4)	26 (11.7)	
Common-law arrangement	23 (9.5)	6 (2.7)	
Never married	33 (13.7)	12 (5.4)	
Country of birth			
Canada	195 (80.9)	165 (74.3)	0.008†
Europe	30 (12.5)	40 (18.0)	
U.S.A.	3 (1.2)	10 (4.5)	
Asia (East and South East)	4 (1.7)	5 (2.2)	
Asia (South)	4 (1.7)	2 (0.9)	
Other regions	5 (2.0)	0 (0.0)	
Current employment status			
Full-time employment	43 (23.6)	51 (47.7)	0.001
Part-time employment	15 (8.2)	10 (9.4)	
Self-employed	9 (8.4)	11 (6.0)	
Not employed	113 (62.1)	37 (34.6)	

* Based on comparison of 20 or more years of residence in British Columbia versus less than 20 years.

† Comparison of respondents who were born in Canada with those born outside of Canada

ables. All variables included in the multivariate models were observed to be statistically significant ($p \leq 0.05$) in the bivariate analyses.

RESULTS

Letters of invitation were sent to the first 600 anti-HCV-positive men and women

who had tested positive for hepatitis C and came forward for compensation during the study period and 950 randomly selected anti-HCV-negative men and women who tested negative for hepatitis C. Of these, 241 (40.2%) anti-HCV-negative and 222 (24.7%) anti-HCV-positive men and women responded to our letter of invitation and were interviewed and included in

TABLE III**Comparison of Health Status Between Anti-HCV-positive and Negative Subjects**

Variables	Anti-HCV-positive n (%)	Anti-HCV-negative n (%)	p-value
Current health status			
Excellent	1 (0.4)	29 (13.1)	<0.001
Very good	16 (6.7)	55 (24.8)	
Good	59 (24.6)	87 (39.2)	
Fair	95 (39.6)	36 (16.2)	
Poor	69 (28.8)	15 (6.8)	
Current health status compared to status ten years previous			
Much better now	14 (5.8)	35 (15.8)	<0.001
Somewhat better now	20 (8.3)	35 (15.8)	
About the same	12 (5.0)	58 (26.2)	
Somewhat worse now	64 (26.6)	62 (28.1)	
Much worse now	131 (54.4)	31 (14.0)	
Long-term disability or handicap			
Yes	163 (68.2)	94 (42.7)	<0.001
No	76 (31.8)	126 (57.3)	
Primary cause of this condition*			
Disease or illness	115 (79.9)	53 (70.7)	0.028†
Injury from motor vehicle	12 (8.3)	2 (2.7)	
Work-related injury	7 (4.9)	5 (6.7)	
Natural aging process	5 (3.5)	10 (13.3)	
Existed at birth	3 (2.1)	4 (5.3)	
Psychological or physical abuse	2 (1.4)	1 (1.3)	

* Based on 458 respondents (238 anti-HCV-positive and 220 anti-HCV-negative subjects)

† Based on Fisher's exact test

TABLE IV**Independent Predictors of Anti-HCV Positivity**

Variable	Beta	Standard Error	Odds Ratio	95% CI
Two or more clinical symptoms	1.26	0.46	3.53	[1.44, 8.70]
Male	1.05	0.70	2.86	[1.65, 4.97]
Health compared to 10 years previous*	0.47	0.11	1.60	[1.30, 1.96]
Illness Intrusiveness Rating†	0.30	0.04	1.35	[1.25, 1.46]
Age in years§	-0.04	0.01	0.97	[0.95, 0.98]

* Expressed as an ordinal scale (1, 2, 3, 4, 5).

† Expressed as an ordinal scale (per 5 point increase).

§ Per 1 year increase in age

the final study sample. We observed no difference between responders and non-responders with respect to community sociodemographic characteristics taken from the 1996 Canadian Census.

As indicated in Table I, all participants in this study had at least one blood transfusion during the period 1986 through 1990. During this five-year period, anti-HCV-positive subjects were more likely to have had transfusions because of an underlying accidental cause (23.2% versus 11.7%; $p=0.001$) and less likely to have had a transfusion because of an underlying heart condition (24.8% versus 14.9%; $p=0.008$) than their anti-HCV-negative counterparts.

Socioeconomic status

As shown in Table II, anti-HCV-positive subjects were more likely to be males (52.3% versus 41.0%; $p=0.015$), younger (median 50 versus 65 years; $p<0.001$),

Canadian born (80.9% versus 74.3%; $p=0.008$), and to have resided longer in British Columbia ($p=0.050$), and were less likely to be married (49.8% versus 65.3%; $p=0.001$). There was no difference between the two groups with respect to ethnic or cultural origin, the number of persons residing in the household, or in educational attainment (all $p>0.05$).

With regard to employment status, anti-HCV-positive subjects were less likely to be employed than their anti-HCV-negative counterparts ($p=0.001$). Among unemployed subjects, anti-HCV-positive participants were more likely to self-report that they were not currently working because they were disabled or recovering from illness (64.0% versus 37.8%; $p<0.001$). Examination of the respondent's employment history since 1990 revealed no differences between the two groups with respect to those employed full-time, part-time or self-employed, and social class. With

respect to income, anti-HCV-positive subjects reported a lower median household income (\$30,000 versus \$31,400; $p=0.046$) and were more likely to obtain income from social assistance and welfare (20.3% versus 4.5%; $p=0.001$) and long-term disability insurance (9.5% versus 4.1%; $p=0.020$). Anti-HCV-positive were less likely to have obtained income from Canada Pension Plan (32.4% versus 52.7%; $p=0.001$), savings (14.5% versus 25.7%; $p=0.003$) and other retirement pension plans (18.3% versus 44.6%; $p=0.001$). The primary source of income for both groups was wages and salaries.

Health status

As noted in Table III, anti-HCV-positive subjects were much less likely to report that their current health status was excellent or very good (7.1% versus 37.9%; $p<0.001$). A similar pattern held when the health status was compared to what it was ten years previous (14.1% versus 31.6%; $p<0.001$). Anti-HCV-positive subjects were also significantly more likely to report that they had a long-term disability or handicap (68.2% versus 42.7%; $p<0.001$) and to report that this condition was caused by a disease or illness (79.9% versus 70.7%; $p=0.028$).

Quality of life and fatigue

Anti-HCV-positive subjects were more likely to nap during the day (58.3% versus 37.8%; $p<0.001$), to have trouble going to sleep or staying asleep (61.9% versus 44.3%; $p<0.001$), and to have difficulty sometimes or most of the time staying awake when they want (52.7% versus 60.0%; $p<0.001$). Of the two groups, anti-HCV-positive men and women were also less likely to find sleep refreshing (36.3% versus 69.8%; $p<0.001$). However, there was no difference between the two groups with respect to the median number of hours of sleep per night ($p=0.808$). With respect to the four subjective rating scales, the Illness Intrusiveness Rating Scale, Epworth Sleepiness Scale, the Fatigue Severity Scale, and RAND 36-item Health Survey, anti-HCV-positive subjects were significantly worse off than anti-HCV-negative subjects with respect to scores for individual domains (except the religious expression domain of the Illness Intrusiveness Rating Scale) and total scores (all at $p<0.001$).

Clinical symptoms

With respect to major clinical symptoms, anti-HCV-positive subjects were more likely to report gastrointestinal (74.3% versus 42.3%; $p < 0.001$), general (95.4% versus 60.8%; $p < 0.001$), skin (53.9% versus 23.0%; $p < 0.001$), muscle and skeletal (75.5% versus 62.6%; $p = 0.003$), and metabolic (44.0% versus 31.1%; $p = 0.004$) problems. Both groups were similar with respect to cardiovascular conditions (34.4% versus 38.7%; $p = 0.337$).

Multivariate analysis

Results of the multivariate analyses are reported in Table IV. As indicated here, anti-HCV-positivity was independently associated with currently having two or more clinical symptoms (Odds Ratio [OR] = 3.53; 95% CI: 1.44, 8.70), being male (OR = 2.86; 95% CI: 1.65, 4.97), having worse health status as compared to ten years previous (OR = 1.60; 95% CI: 1.30, 1.96), having a worse illness intrusiveness rating (OR = 1.35; 95% CI: 1.25, 1.46), and being younger in age (OR = 0.97; 95% CI: 0.95, 0.98). In this model, clinical symptoms refer to the major clinical categories such as cardiovascular, gastrointestinal, or general problems. No significant interactions between these variables were detected.

DISCUSSION

This study demonstrated significant differences in health and quality of life between anti-HCV-positive and negative transfusion recipients. We have shown that anti-HCV-positivity was associated with having two or more clinical symptoms, worse health status as compared to ten years previous, a higher illness intrusiveness rating, and being male and younger in age.

In this analysis, age and gender are important predictors of hepatitis C positivity. Differences in age and gender between the two groups are likely related to two factors. First, anti-HCV-positive subjects were more likely to have had a transfusion that was related to an accidental event, like a motor vehicle accident. In the general population, these types of events are most likely to occur among young men. Second, anti-HCV-positive subjects may have had a higher rate of pre-study mortality, thus reducing the number of persons at older

ages who were originally infected between 1986 and 1990, but did not live to be part of the survey population.²

In this study, it is also reassuring that our findings regarding the relationship between anti-HCV-positivity and quality of life are consistent with the limited published literature in this area. In the most recent comprehensive study, Foster et al.¹⁴ clearly demonstrate that chronic infection with hepatitis C virus is associated with a significant reduction in quality of life, as measured by the SF-36 questionnaire, in persons without cirrhosis. The difference remained even after adjustment for the degree of liver inflammation or mode of acquisition of the infection. Davis et al.¹⁵ has also shown, using the sickness impact profile questionnaire, that persons with chronic hepatitis C infection perceived themselves as being unwell and having a reduced quality of life. Finally, Rodger and colleagues have demonstrated that both HCV-RNA and anti-HCV-positive individuals have significantly poorer subjective health 26 years after infection compared to population norms.¹⁶

Caution is advised in the interpretation of our results. Most notably, the non-random sampling of hepatitis C positive transfusion recipients from lawyers handling the compensation case was a potential source of referral bias, as men and women who progressed further along may have been more likely to have come forward. Thus, the true prevalence and full array of outcomes of anti-HCV-positivity may have been overestimated. However, the effect of this bias on the study may be small. First, nearly two thirds of the approximately 1,200 eligible hepatitis C transfusion recipients in this province have come forward for compensation. The 600 selected recipients obtained from the lawyers for this study were based on the first two thirds of these 900 recipients. Second, there are no significant differences between the two study groups with respect to select socio-demographic characteristics. Third, the proportion of individuals in our study who have developed progressive or symptomatic liver disease was in a range that is consistent with what is known about the natural history of hepatitis C.¹⁷ Fourth, our study sample does not include those with the most severe disease or near death as these individuals would have self-selected them-

selves out of the study due to the severity of their illness. Finally, although all anti-HCV-positive subjects had a blood transfusion, we are unable to determine whether these subjects may have acquired the virus through other means. Our survey did not elicit information on injection drug use or on other activities known to be associated with HCV transmission.

Overall, our study represents a valuable extension of previous literature that has looked primarily at quality of life in those acquiring HCV through injection drug use. Although we demonstrate an association between impaired socioeconomic and health status and transfusion-acquired HCV, we are unable to determine whether this association can be attributed solely to infection with HCV. Further research is needed to determine whether impaired socioeconomic and health status in this population are an artifact of our study sample or due to the direct consequence of an infection with a hepatotropic virus.

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RÉSUMÉ

Objectif : Caractériser la situation socio-économique, l'état de santé et les symptômes de maladie de transfusés séropositifs et séronégatifs pour le VHC.

Méthode : Enquête transversale menée par entrevues avec des sujets identifiés grâce au British Columbia Blood Recipient Program. Les sujets de l'étude avaient 18 ans et plus et devaient recevoir une transfusion de sang entre le 1er août 1986 et le 30 juin 1990, et leur entrevue devait être de qualité satisfaisante. Les sujets séropositifs pour le VHC étaient des personnes ayant demandé une compensation monétaire des gouvernements provincial et fédéral canadiens; le groupe témoin était composé de transfusés séronégatifs pour le VHC sélectionnés au hasard. L'étude visait à détecter une différence hypothétique de 20 % dans la sémiologie et les symptômes des deux groupes. Des comparaisons statistiques ont été effectuées à l'aide d'analyses de régression logistique à deux ou plusieurs variables.

Résultats : En tout, 241 sujets séropositifs et 222 sujets séronégatifs pour le VHC répondaient aux critères de l'étude. Selon les résultats de l'analyse multivariable, les transfusés séropositifs pour le VHC étaient plus susceptibles de présenter deux symptômes cliniques ou plus (RC = 3,53; IC de 95 % = 1,44-8,70), d'être en moins bonne santé que 10 ans auparavant (RC = 1,60; IC de 95 % = 1,30-1,96), de présenter un plus haut taux de perturbation de la maladie (RC = 1,35; IC de 95 % = 1,25-1,46) et d'être plus jeunes (RC = 0,97; IC de 95 % = 0,95-0,98).

Conclusion : Nos résultats montrent que les personnes exposées au VHC étaient plus susceptibles de présenter deux symptômes cliniques ou plus, ainsi qu'un plus haut taux de perturbation de la maladie, d'être des hommes, d'être en moins bonne santé que 10 ans auparavant et d'être relativement jeunes.

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