ABSTRACT

The purpose of this analysis was to assess the validity of self-reported transfusion histories in dialysis patients. Using data from a cross-sectional study of a dialysis population being investigated for hepatitis C virus (HCV) infection, the correspondence between self-reported transfusion history and transfusion records was explored. Demographic data and dialysis histories were examined in relation to the accuracy of self-reports. Overall, the questionnaire data and the blood bank records agreed for 89% of participants. The Kappa statistic was 0.72 (95% CI: 0.61, 0.83) indicating an acceptable level of agreement. The effect of non-differential exposure misclassification on the risk estimates for transfusion history as a determinant of HCV infection is demonstrated. Exploring the discrepancies between self-reports and documented transfusion histories underlines the need to communicate clearly medical interventions in chronically ill patients. Additionally, it suggests that studies into transfusion-acquired blood-borne pathogens should use all available information sources to establish exposure.

ABRÉGÉ

Cette analyse avait pour but d'évaluer la validité des antécédents auto-déclarés de transfusion chez les patients dialysés. À partir des données provenant d'une analyse transversale sur des patients dialysés pour détecter les cas d'infection au virus de l'hépatite C (VHC), on a étudié la correspondance entre les antécédents auto-déclarés de transfusion et les dossiers en attente. Les données démographiques et les antécédents de dialyse ont été étudiés par rapport à l'exactitude des auto-déclarations. De façon générale, les données du questionnaire et les dossiers des banques de sang concordait pour 89 % des participants. Le résultat de l'analyse statistique Kappa était 0,72 (95 % IC : 0,61 - 0,83) indiquant un niveau de concordance acceptable. On a démontré l'effet des erreurs de classification de l'exposition non différentielle sur les estimations du risque pour les antécédents de transfusion comme déterminant de l'infection au VHC. L'examen des disparités entre les auto-déclarations et les antécédents de transfusion documentés souligne la nécessité de communiquer les interventions médicales subies par des malades chroniques. En outre, cela suggère que les études faites sur les pathogènes à diffusion hémotogène transmis par des transfusions devraient utiliser toutes les sources d'information disponibles pour établir l'exposition.

Validation of Self-reported Transfusion Histories in Renal Dialysis Patients

Jat S. Sandhu, MSc,¹ Patricia M. Campbell, MD,² Jutta K. Preiksaitis, MD,³
Keumhee C. Carriere, PhD,⁴ Patrick A. Hessel, PhD¹

Blood transfusions were commonly given to patients with end-stage renal disease prior to the introduction of recombinant erythropoietin.¹ Despite the introduction of a variety of pharmacological agents and greater awareness of existing and emerging blood-borne diseases, blood transfusions persist as an important therapy to combat anemia and other complications arising in dialysis patients.²

Most investigations of the relationship between transfusion history and hepatitis C status in dialysis populations have relied on self-reported information.³⁻⁶ Self-reported exposure data are vulnerable to recall bias, which threatens the internal validity of a study. Retrospective interviews rely heavily on respondents' recall, and often there are no existing records available for validation of the self-reported exposures.⁷ Factors that may influence accuracy of self-report include: 1) the importance of the exposure(s) to the individual, 2) the way the exposure is defined and its interpretation by the participant, 3) the time frame in which the exposure(s) occurs, 4) the participant's knowledge about the exposure and how precisely it is disclosed to the interviewer and 5) the health of the participant.^{8,9}

The purpose of this analysis was to assess the validity of self-reported transfusion histories in dialysis patients. Using data from a cross-sectional study of a dialysis population being investigated for hepatitis C

infection, the correspondence between self-reported transfusion history and transfusion records was explored. Demographic data and dialysis histories were examined in relation to the accuracy of self-reports. The data may have implications for other studies involving patients with chronic conditions.

METHODS

Data were taken from a study into risk factors for hepatitis C infection among the Northern Alberta dialysis population. This was a cross-sectional survey of patients actively dialyzing on the Northern Alberta Renal Program (NARP) on July 1, 1997. The NARP serves all renal dialysis patients in northern Alberta. Three hundred and thirty-six patients, representing 92% of eligible patients aged 18 years and older provided informed consent. The study protocol was approved by the Medical Ethics Review Board of the Faculty of Medicine at the University of Alberta. Participants and non-participants were comparable for age and gender. Participants were interviewed by the same interviewer using a questionnaire comprising demographic, dialysis-specific, medical history and lifestyle variables. A combination of in-person and telephone interviews with identical questionnaire content was employed. No systematic differences were seen between the two interview methods and interviewees were comparable for age and gender irrespective of interview method.

Participants were asked whether they had ever had a blood transfusion. Separate questions enquired about transfusions while on dialysis and transfusions prior to dialysis. The number of transfusions and their locations were also requested.

University of Alberta, Edmonton, AB

1. Department of Public Health Sciences

2. Department of Medicine - Nephrology

3. Department of Medicine - Infectious Diseases

4. Department of Mathematical Sciences

Correspondence and reprint requests: Dr. Patrick A. Hessel, Department of Public Health Sciences, 13-103 Clinical Sciences Building, University of Alberta, Edmonton, AB, T6G 2G3, Tel: 780-407-7135, Fax: 780-407-3608, E-mail: pat.hessel@ualberta.ca

The transfusion records of the University of Alberta Hospital (UAH) Blood Bank have been computerized back to 1988. The UAH Blood Bank records all transfusions of dialysis patients in the NARP. Although complete transfusion histories were sought from the UAH Blood Bank records for all dialysis patients, there was less confidence in the completeness of these records prior to the use of a computer database in 1988. Therefore, the present analysis was limited to dialysis patients who enrolled in the NARP since 1988 (n=294). The accuracy of the self-reports was assessed by comparison with the UAH Blood Bank records (i.e., "gold standard"). Ten of the participants (6 females, 4 males) who were enrolled in the NARP since 1988 reported a history of blood transfusion prior to their enrollment that could not be documented in the blood bank records. In all cases the transfusion occurred outside of the northern Alberta region. Because these respondents were able to recall both the year and place of transfusion prior to dialysis, the validity of the report was accepted (i.e., a "true positive"). In the study of HCV risk factors, a sensitivity analysis was conducted that excluded these 10 participants. The odds ratios and confidence limits for the main risk factors changed little and statistical significance was unchanged.¹⁰ Included among these 10 participants were 5 who received transfusions during surgery, 1 who received a transfusion following a motor vehicle collision, 3 who were transfused after a Caesarian section, and 1 who received a transfusion as a result of cancer chemotherapy.

With the exception noted directly above, participants were classified as true positives if the blood bank records and the questionnaires both indicated that a transfusion had been received. True negatives had no record of a transfusion on either the questionnaire or the blood bank records. False positives reported a transfusion that was not documented by the blood bank, and false negatives had documentation of a transfusion in the blood bank records but denied having had a transfusion in the questionnaire.

Agreement between the two transfusion history measures was summarized by the

TABLE I
Description of the Study Population

Characteristic	n = 294
Age in Years (mean $\pm$ SD)	58.9, $\pm$ 15.2
Gender (n, %)	
Males	181 (61.6)
Females	113 (38.4)
Years of Dialysis* (mean $\pm$ SD)	2.4, $\pm$ 2.0
Current Dialysis Mode (n, %)	
Peritoneal Dialysis	124 (42.2)
Haemodialysis	170 (57.8)

* Excluding time on transplant

TABLE II
Comparison of Questionnaire Response and Blood Bank Records for a History of a Blood Transfusion

		Blood Bank Records			
		Yes		No	
		n	(%)	n	(%)
Questionnaire Response	Yes	194	(93.3)	19	(22.1)
	No	14	(6.7)	67	(77.9)
		208	(100)	86	(100)

TABLE III
Validity Measures of Self-reported Transfusion History

Measure	Transfusion Since Dialysis	
Sensitivity [95% CI]	0.93	[0.89, 0.96]
Specificity [95% CI]	0.78	[0.67, 0.85]
Positive Predictive Value [95% CI]	0.91	[0.86, 0.94]
Negative Predictive Value [95% CI]	0.83	[0.72, 0.90]

TABLE IV
Effect of Transfusion History Misclassification on HCV Risk Estimates

Transfusion History	Total No. of Patients	Anti-HCV Positive n (%)	Odds Ratio	95 % C.I.
Questionnaire				
Yes	213	8 (3.8)	1.01	0.24, 6.09
No	81	3 (3.7)	1.0	(referent)
Blood Bank Records				
Yes	208	9 (4.3)	1.90	0.40, 18.04
No	86	2 (2.3)	1.0	(referent)

kappa statistic. Chi-square tests were used to compare the demographic and dialysis history characteristics of participants who were categorized according to the accuracy of measurement. For continuous variables (e.g., age and years on dialysis), the groups were compared using an F-test.

RESULTS

The mean age of the dialysis population (Table I) was 58.9 years. Nearly two thirds were males and the mean length of dialysis was less than two and one-half years.

Almost 60% of participants were undergoing haemodialysis.

Comparison of the two sources of transfusion histories (Table II) showed that 66.0% of the participants were true positives (194/294), 6.5% were false positives (19/294), 4.8% were false negatives (14/294) and 22.8% were true negatives (67/294). Overall, the questionnaire data and the blood bank records agreed for 89 percent of participants. The Kappa statistic was 0.72 (95% CI: 0.61, 0.83), indicating an acceptable level of agreement that was significantly greater than that expected by chance.¹¹

TABLE V
Comparison of Age and Years on Dialysis for Dialysis Patients Classified by Agreement Between Blood Bank Records (Reference) and Self-report

	True Positives Mean $\pm$ SD	False Positives Mean $\pm$ SD	False Negatives Mean $\pm$ SD	True Negatives Mean $\pm$ SD	F-test, p value
Age (yrs)	59.9 $\pm$ 15.7	60.2 $\pm$ 9.8	64.9 $\pm$ 8.8	54.6 $\pm$ 15.1	F=2.91, p=0.006
Years on Dialysis	2.8 $\pm$ 2.2	2.3 $\pm$ 2.0	2.6 $\pm$ 2.1	1.4 $\pm$ 1.1	F=8.59, p=0.001

TABLE VI
Comparison of Dialysis Patients Classified by Agreement Between Blood Bank Records (Reference) and Self-report

	True Positives n (%) [*]	False Positives n (%)	False Negatives n (%)	True Negatives n (%)	χ^2 statistic, p value
Education					
≤ Grade 9	74 (71.8)	7 (6.8)	8 (7.8)	14 (13.6)	12.9, 0.04
Grade 10 - 12	75 (63.0)	6 (5.0)	6 (5.0)	32 (26.9)	
Post-Secondary	45 (62.5)	6 (8.3)	0 (0)	21 (29.2)	
Proxy Interview					
Yes	23 (88.5)	0 (0)	1 (3.8)	2 (7.7)	6.9, 0.07
No	171 (63.8)	19 (7.1)	13 (4.9)	65 (24.3)	
Dialysis Centre					
Haemodialysis	124 (72.9)	7 (4.1)	12 (7.1)	27 (15.9)	19.3, 0.001
Peritoneal	70 (56.5)	12 (9.7)	2 (1.6)	40 (32.3)	
Transplant					
Yes	31 (88.6)	1 (2.9)	1 (2.9)	2 (5.7)	9.3, 0.03
No	163 (62.9)	18 (6.9)	13 (5.0)	65 (25.1)	

* Numbers in parentheses are row percents, representing the distribution of classifications within each category.

Of those 208 patients who had a record of a blood transfusion, 93% reported this on their questionnaires (i.e., sensitivity = 0.93) (Table III). Of those remaining patients who did not have a record of a blood transfusion, 78% were correctly classified by the questionnaire. In this population with 71% having a documented history of a blood transfusion, 91% of those who reported a blood transfusion had a documented history (i.e., positive predictive value = 0.91). Eighty-three percent of those who claimed no history of a transfusion had no documented evidence of a transfusion.

To explore the effect of exposure misclassification on the risk estimates, hepatitis C status was compared to transfusion history classified according to the blood bank records and the questionnaire responses (Table IV). The odds ratio for HCV infection based upon self-reported transfusion history was 1.01 (95% CI: 0.24, 4.96). This is in contrast to the odds ratio for hepatitis C infection being 1.90 (95% CI: 0.40, 13.02) using blood bank records.

The groups were found to differ significantly by age and by years on dialysis (Table V). The average age of the false negatives was the highest and the true negatives the lowest of the four groups. The true negatives had the lowest mean number of years of dialysis.

There was a significant association between the validity of the self-report and education (Table VI). The overall level of agreement was greatest for those with at least some post-secondary education. None of the participants with post-secondary education were false negatives (i.e., had a documented history of a transfusion but stated they did not).

Some of the participants (n=26) were unable to complete the questionnaires themselves. Twenty-four of these had been transfused and the proxies were aware of 23 of them.

As expected transfusion was more common among haemodialysis patients compared to those on peritoneal dialysis. Of the haemodialysis patients, 80% had a history of transfusion (true positives plus false

negatives) compared to 58% of the peritoneal dialysis patients. Nearly equal proportions of both groups were misclassified by the questionnaire. Only 2 of the 124 peritoneal dialysis patients (1.6%) were unaware of a past transfusion.

Those who had received a transplant in the past were more likely to have received a blood transfusion and were more likely to accurately recall their transfusion history. Of those who had not undergone a transplant, 25% had received a transfusion that was not acknowledged on the questionnaire.

DISCUSSION

Use of the blood bank records as the 'gold standard' implies certain assumptions that may not be true in all cases. It is possible, for example, that patients may have been transfused while on dialysis but outside of northern Alberta. This would have affected mainly the rate of false positives but may also have affected the true negatives. Those with transfusion during dialysis but outside of the NARP would have been wrongly included as false positives while those who were transfused outside of the NARP and did not recall their transfusion would have been incorrectly classified as true negatives. It should be noted that clinical charts were reviewed for all participants. It is likely that transfusions received outside of the catchment area would have been documented in the medical record on return to the area. Also this analysis included only patients who were continuously enrolled in the NARP since the time that the blood bank records were computerized. The comprehensive nature of the NARP and the blood bank records minimized the possibility of missing transfusion data.

The primary outcome of interest in the main study was the presence of hepatitis C infection. Despite an acceptable level of agreement between the two sources of transfusion history, there are profound implications of these discrepancies to the risk factor analysis. Using the blood bank records, the odds ratio for hepatitis C infection associated with blood transfusion was 1.90 (95% CI: 0.40, 13.02). Using the questionnaire response, the odds ratio was 1.01 (95% CI: 0.24, 4.96). This illustrates

the usual effect of nondifferential misclassification (i.e., bias towards the null).¹²

For the 26 proxy respondents in this study, there was 96% agreement between their recollection of the participant's transfusion history and that documented in the blood bank records. This is reassuring in this population that includes a significant number of older and/or very ill individuals. Misclassification of exposures by proxy respondents has been shown to bias estimates of exposure-disease associations.¹³

Under-reporting of transfusions caused by forgetting may account for the associations between both age and length of time on dialysis and the validity of the questionnaire responses. The possibility that this is a result of the impaired neuropsychological mechanisms in the abnormal chemical environment imposed by renal failure cannot be ruled out.¹⁴ However, although the blood bank database covered 10 years, more than 90% of the patients had been on dialysis for less than 5 years. Hence the high level of agreement between questionnaire data and blood bank records may reflect the shorter time on dialysis (i.e., 5-year as opposed to 10-year recall).

Although the relationship between the validity of self-reported transfusion history and education level was not strong, the (generally) better recall among the more highly educated patients underlines the need to communicate clearly information on medical procedures in this population.

A recent inquiry into Canada's blood supply noted "few hospitals considered

asking patients to sign a consent form before they were given blood or blood products."¹⁵ Conceivably within a dialysis setting, where patients sign a one-time consent form to all medical treatments for their end-stage renal failure, patients may be unaware of being transfused while on haemodialysis. Given the findings presented here, it appears that epidemiological investigations (at least in Canada) into blood-borne pathogens acquired by transfusion in chronically ill patients will require strict scrutiny of all available information sources for patient transfusion histories. Communicating transfusion-related risk must be reasoned and based on the *best available* epidemiological evidence.

ACKNOWLEDGEMENTS

The study was supported by a grant from the University of Alberta Hospital Foundation and the Alberta Health Sciences Institute. The authors thank Maureen Strautman for abstracting patient transfusion histories from blood bank records.

REFERENCES

1. Pereira BJG, Levey AS. Hepatitis C virus infection in dialysis and renal transplantation. *Kidney Int* 1997;51:981-90.
2. Ifudu O, Macey LJ, Friedman EA. Resurgence of blood transfusion therapy in erythropoietin treated hemodialysis patients. *ASAIO J* 1995;41:426-30.
3. Dussol B, Berthezene P, Brunet P, et al. Hepatitis C Virus infection among chronic dialysis patients in the south of France: A collaborative study. *Am J Kidney Dis* 1995;25:399-404.
4. Knudsen F, Wantzin P, Rasmussen K, et al. Hepatitis C in dialysis patients: Relationship to blood transfusions, dialysis and liver disease. *Kidney Int* 1993;43:1353-56.
5. Neto MC, Rodrigues-Manzano SI, Canziani ME, et al. Environmental transmission of hepatitis B and hepatitis C viruses within the hemodialysis unit. *Artif Organs* 1995;19:251-55.
6. Niu MT, Coleman PJ, Alter MJ. Multicenter study of hepatitis C virus infection in chronic hemodialysis patients and hemodialysis center staff members. *Am J Kidney Dis* 1993;22:568-73.
7. Clark K, Fu C, Burnett C. Accuracy of birth certificate data regarding the amount, timing, and adequacy of prenatal care using prenatal clinic medical records as referents. *Am J Epidemiol* 1997;145:68-71.
8. Olson JE, Shu XO, Ross JA, et al. Medical records validation of maternally reported birth characteristics and pregnancy-related events: A report from the children's cancer group. *Am J Epidemiol* 1997;145:58-67.
9. Warnecke RB, Sudman S, Johnson TP, et al. Cognitive aspects of recalling and reporting health-related events: Papanicolaou smears, clinical breast examinations, and mammograms. *Am J Epidemiol* 1997;146:982-92.
10. Sandhu J, Preiksaitis JK, Campbell PM, et al. Hepatitis C: Prevalence and risk factors in the Northern Alberta dialysis population. *Am J Epidemiol* 1999 (in press).
11. Fleiss JL. *Statistical Methods for Rates and Proportions* 2nd Ed. New York: John Wiley & Sons, 1981.
12. Kelsey JL, Whittemore AS, Evans AS, Thompson WD. *Methods in Observational Epidemiology* 2nd Ed., New York: Oxford University Press, 1996.
13. Nelson LM, Longstreth WT, Koepsell TD, van Belle G. Proxy respondents in epidemiologic research. *Epidemiol Rev* 1990;12:71-86.
14. Brickman AL, Yount SE, Blaney NT, et al. Pathogenesis of cognitive complaints in patients on hemodialysis. *General Hosp Psychiatry* 1996;18:36-43.
15. Capen K. Informed consent and blood transfusions: What does Krever's interim report mean to doctors? *CMAJ* 1995;152:1663-65.

Received: June 9, 1998

Accepted: February 4, 1999