Community Respiratory Virus Infection in Hematopoietic Stem Cell Transplantation Recipients and Household Member Characteristics

Kay A. Sams, RN, MPH, CIC, Richard R. Reich, PhD, Alice R. Boyington, RN, PhD, and Elsa M. Barilec, RN, BSN, CCRN

Community respiratory virus (CRV) infections are a health threat and are responsible for substantial global disease. CRVs include respiratory syncytial virus (RSV), influenza, adenovirus, and parainfluenza virus (PIV). Patients with impaired immune systems (e.g., hematopoietic stem cell transplantation [HSCT] recipients) particularly are vulnerable in developing CRV infection. The risk of CRV infection occurs throughout all phases of HSCT—pre-engraftment, postengraftment, and in the latent phase (Tomblyn et al., 2009). High mortality rates have been associated with the progression of CRV infection to the lower respiratory tract, particularly with RSV infection (Avetisyan, Mattsson, Sparrelid, & Ljungman, 2009; Chemaly et al., 2012; Nichols, Gooley, & Boeckh, 2001). Patients who acquire CRV infection may have unscheduled hospital readmissions, lengthy treatment of the infection, and increased medical costs. Outpatient HSCT recipients are particularly at risk for acquiring CRV infection because of varied community exposure to viruses, and challenges associated with seeking timely interventions (Tomblyn et al., 2009).

Understanding potential reservoirs and how transmission occurs in the household setting is vital to minimizing the risk of CRV infection in patients undergoing transplantation. A reservoir for infection is an infected host who is capable of shedding a virus that can infect others. Children, particularly those of preschool age and in day care, are reservoirs for transmission of respiratory viruses because of increased exposure to CRV infection and inadequate personal hygiene practices (Goldmann, 2000; Heikkinen & Järvinen, 2003; Monto, 2002). Compared to adults, children can shed respiratory viruses longer (Centers for Disease Control and Prevention [CDC], 2012). CRV infection primarily is spread through droplet transmission, usually contained in a large droplet expelled from a cough or sneeze, or via direct contact with contaminated hands or objects (CDC, 2012; Goldmann, 2000).

Purpose/Objectives: To determine if children or the number of contacts living in an immediate household increases the risk of community respiratory virus (CRV) acquisition in hematopoietic stem cell transplantation (HSCT) recipients.

Design: Retrospective, exploratory study.

Setting: National Cancer Institute–designated comprehensive cancer center located in the Southeast.

Sample: 720 adult outpatients post-autologous or allogeneic HSCT.

Methods: Data were gathered using a retrospective medical record review from July 1, 2006, to December 31, 2009. Summary statistics were used to describe sample characteristics. Binary logistic regression was used to determine whether the number of household member contacts or number of children in each age group was a significant predictor of CRV infection. Multivariate linear regression was used to investigate predictors of the number of CRV infections.

Main Research Variables: The dependent variable was acquisition of CRV infection. Independent variables included the number of children in the household and the number of household members.

Findings: Across all HSCT recipients, children aged 0–4 years ($p = 0.01$) and 5–12 years ($p = 0.001$) predicted CRV infection. The allogeneic group had the greatest incidence of CRV infection and was most sensitive to the presence of young children. The total number of household members was not a predictor of CRV infection.

Conclusions: Households with children aged 12 years and younger more than doubled the risk of an HSCT recipient acquiring CRV infection. Additional studies are needed to test interventions designed to interrupt household transmission of CRV infection from children to vulnerable HSCT recipients.

Implications for Nursing: Household contacts, particularly children, should be included in HSCT teaching. As indicated by the potentially high number of days from transplantation to acquisition of CRV infection, re-education and continuing focus on prevention of CRV infection should be reinforced throughout the lengthy transplantation period.

Key Words: community respiratory virus; hematopoietic stem cell transplantation

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HSCT recipients' initial recovery after transplantation usually occurs in a hospitalized setting during the acute phase of engraftment; however, complete recovery of the immune system occurs during outpatient treatment one to two years following transplantation (Tomblyn et al., 2009). For prevention of CRV infection in the outpatient setting, patients undergoing transplantation are instructed to avoid close contact with people with respiratory virus symptoms. If close contact with a symptomatic person is unavoidable, then the patient and the symptomatic contact should perform hand hygiene frequently (Tomblyn et al., 2009). The symptomatic contact also should consider wearing a surgical mask or, at minimum, covering his or her mouth and nose with disposable tissue when sneezing and coughing (Tomblyn et al., 2009).

Researchers have investigated the acquisition of CRV infection in the HSCT recipient population. Avetisyan et al. (2009) conducted a retrospective, case-control cohort study that examined the incidence, clinical features, and outcome of HSCT recipients who acquired RSV. Patient characteristics included age, gender, underlying disease, stem cell source, donor type, conditioning therapy, graft-versus-host disease incidence, absolute neutrophil count, lymphocyte count, and acquisition of RSV. No significant correlation of any patient characteristics in the development of lower respiratory tract infection in the RSV-positive patient population was found. In a retrospective, two-year review investigating the impact of CRV infection on immunocompromised patients, the risk of acquiring CRV infection was associated with the status of the patient (87% outpatient compared to 13% inpatient), and age (younger than 65 years) was significant in acquiring CRV infection. No statistical significance was found between acquisition of CRV infection and age, gender, type of infection, neutrophil and lymphocyte counts, therapy, or outcome (Chemaly et al., 2006). Nichols et al. (2001) studied the acquisition of PIV or RSV infection with many of the same patient characteristics, with the exception of outpatient status. For RSV infection, only male gender was identified as an increased risk factor, and for PIV infection, the only risk factor identified was the use of an unrelated stem cell donor.

In non-HSCT populations, studies have correlated CRV infection and spread in households with secondary family members. A large prospective study conducted during the winter season in France by Viboud et al. (2004) sought to quantify the risk factors of influenza transmission in households in the community. Transmission of influenza infection was associated with age (preschool- and school-aged children) of the primary infected person and his or her household contacts. MacIntyre et al. (2012) conducted a study to examine the rate of transmission of influenza and other respiratory viruses from children to household family members. Findings revealed that in 61% of the children, CRV infection was detected. Clinical signs and symptoms of influenza-like illness occurred in 12% of exposed healthy family members and indicated a 3% transmission rate of acquisition of CRV infection in the household.

The number of household members also has been associated with transmission of CRV infection, particularly to vulnerable household members. Law et al. (2004) determined that having more than five members in a household with an infant who was premature at birth was closely associated with the infant developing RSV infection. In a large case-control study, infants diagnosed with RSV infection were assessed for household member risk factors. Having more than four adults in the household was a significant predictor of RSV infection (Figueras-Aloy et al., 2008). In addition, this study also found that having a school-aged child in the household was a significant predictor of RSV infection in infants in the same household.

Understanding the risk factors that may be associated with HSCT recipients acquiring CRV infection is important. Outpatient status seems to significantly increase the risk of the transplantation recipient acquiring CRV infection transmission. Children are known sources of CRV infection, particularly to other household members. The number of household members also has been shown to increase the risk of CRV infection to vulnerable household members. A gap exists in the literature in assessing whether a child living in the immediate household or the number of household members of an HSCT recipient increases the risk of acquiring CRV infection for the transplantation recipient. Therefore, the association of these factors to acquisition of CRV infection by transplantation recipients warrants additional studies.

The purpose of this study was to explore the relationships between the number and age of immediate household contacts in HSCT recipients and acquisition of CRV infection.

Methods

Medical records of adult outpatients who received HSCT from July 1, 2006, to December 31, 2009 were used in this retrospective, exploratory analysis. Control variables were abstracted from the cancer center's HSCT database and included patient age, date of transplantation, type of transplantation, underlying disease, donor type, and gender. The number of members and age of each child younger than 18 years of age in the household were obtained from the HSCT psychosocial assessment performed prior to transplantation.

Respiratory viral cultures were followed for 24 months after the date of transplantation and included parainfluenza 1, parainfluenza 2, parainfluenza 3, RSV, influenza A, influenza B, and adenovirus. Respiratory viral cultures were performed by the microbiology department at the cancer center. Patients with positive respiratory virus infections acquired during an inpatient hospital admission of longer than 48 hours were excluded from the study to rule out the possibility of nosocomial transmission. Repeat respiratory viral cultures in patients were counted only if the culture was collected more than six months from the date of the initial culture. A medical record audit form was created to assist with data collection. Data captured for clinical care and recorded in medical records were used in this study. To ensure the precision of the data abstracted from the medical records, inter-rater reliability was performed with 10% of the abstracted data checked and validated by the principal or coinvestigator. Approval to conduct this study was obtained from the cancer center's scientific review committee and the University of South Florida Institutional Review Board.

Table 1. Sample Characteristics

	Total (N = 628)		Autologous (n = 270)		Allogeneic (n = 344)		Other (n = 14)	
Characteristic	$\bar{X}$	SD	$\bar{X}$	SD	$\bar{X}$	SD	$\bar{X}$	SD
Age (years)	52.3	12.8	55.5	11.6	49	12.1	53.5	10.6
Characteristic	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**
Female	254	40	97	36	151	44	6	43
Have a child in the household	172	27	54	20	114	33**	4	29
Child aged 0–4 years	46	7	12	4	32	9	2	14
Child aged 5–12 years	88	14	30	11	55	16	3	21
Child aged 13–18 years	74	12	23	9	51	15	–	–
Participants With CRV	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**
Overall	66	11	9	3	55	16	2	14
Have a child in the household	26	15	2	4	23	20	1	25
Child aged 0–4 years	10	22	2	17	7	22	1	50
Child aged 5–12 years	18	21*	2	7	15	27*	1	33
Child aged 13–18 years	5	7	–	–	5	1	–	–

* $p < 0.05$; ** $p < 0.01$
CRV—community respiratory virus

Statistical Analysis

Summary statistics included sample size, mean, median, standard deviation, and range for continuous variables, and counts and percentages for categorical or ordinal variables. Because this was an exploratory study, multiple approaches were used to address the research questions. To determine the relationship between the number of immediate household contacts of HSCT recipients and acquisition of CRV infection, the outcome variable (CRV infection) was treated as a binary variable. The number of household contacts was treated as a continuous variable. Binary logistic regression was used to determine if the number of household contacts predicted CRV infection.

The next set of analyses examined the importance of household members younger than age 18 years in predicting CRV infection acquisition in HSCT recipients. Again, multiple statistical approaches were used. Using binary logistic regression, separate age categories (0–4 years, 5–12 years, and 13–18 years) were used as predictors of CRV infection (again used as a binary outcome). Also, the total number of household contacts younger than 18 years was used as a predictor of CRV infection.

Results

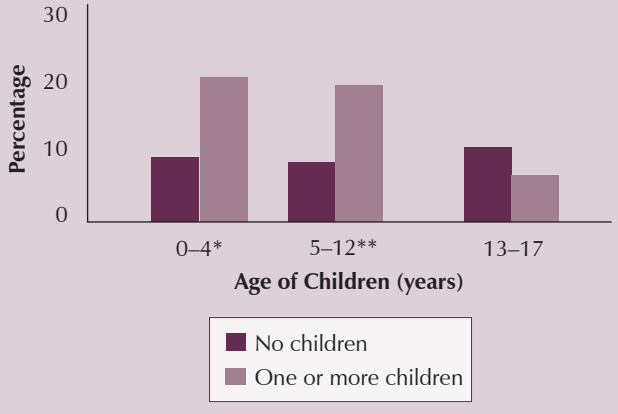
The sample (N = 628) had a mean age of 52 years (SD = 12.8); 54% were in the allogeneic group, 43% were in the autologous group, and 2% were in other HSCT groups (see Table 1). Other groups consisted of synergistic and tandem HSCT. The mean and median number of days to CRV infection for all groups was 283 and 220 days post-transplantation, respectively. The allogeneic group had the greatest incidence of CRV infection (16% versus 4% in the autologous group; $\chi^2 = 26.68$, df = 3, $p < 0.001$).

Across all patients, the first set of analyses indicated that the total number of household members was not a predictor of CRV infection ($p > 0.1$). Age, however, did emerge as an important factor. Households with children aged 0–4 years increased the risk of CRV infection (OR = 2.26; 95% CI [1.23, 5.57]; p = 0.01). Households with children aged 5–12 years also increased the risk of CRV infection (OR = 2.65; 95% CI [1.46, 4.83]; p = 0.001). Households with children aged 13–18 years were not at increased risk for CRV infection (OR = 0.45; 95% CI [0.67, 4.41]; p = 0.23) (see Figure 1). Because several

households had children in multiple age groups, all age groups were included in a multivariate binary logistic regression model. This model indicated that households with children aged 0–4 years did not provide a unique prediction of CRV infection (p = 0.14) when included with households of children aged 5–12 years (p = 0.002) (see Table 2).

Discussion and Limitations

This study observed that young children, particularly children aged 5–12 years in an HSCT recipient household, increase the risk of the recipient acquiring CRV infection. These findings are consistent with previous studies in other populations that demonstrated household transmission of CRV infections by children to household members. The number of members living in a household did not increase the risk of HSCT recipients acquiring CRV infection. This could be explained by socioeconomic status or educational background of study participants, which was not addressed in this study. An important finding was that the mean and median number of days from transplantation to acquisition of CRV infection was greater than six months. Patients may not be aware of the risk over extended periods of recovery. Such results should be considered when providing re-education and post-transplantation follow-up for an HSCT recipient. Limitations of this study included patients being lost to follow-up, the use of virology testing methods, and the use of a retrospective design. Patients who were treated at other facilities for acquisition of CRV infection were not included because of lack of CRV culture results performed by the cancer center. These exclusions may have decreased the CRV sample size, but whether this would have altered the study findings is unknown.



*p = 0.01 for 0–4 age group; **p = 0.001 for 5–12 age group

Figure 1. Comparison of Participant Variables

Table 2. Binary Logistic Regression Results With Children Age Categories Predicting Community Respiratory Virus Infection

	B	SE	df	p	OR
Gender	–0.436	0.287	1	0.129	0.647
0–4 years	0.608	0.416	1	0.144	1.837
5–12 years	1.045	0.335	1	0.002	2.844
13–18 years	–0.748	0.508	1	0.141	0.474
Constant	–2.166	0.182	1	0.00	0.115

Note. Gender used as a covariate.
B—unstandardized regression coefficient; OR—odds ratio; SE—standard error

Implications for Practice and Further Research

Because preventative and medical treatment for CRV infection (with the exception of influenza) is limited, interventions and research should focus on prevention efforts in the HSCT recipient household setting. Age-appropriate hand hygiene evidence-based interventions should be included for HSCT recipients and their household members, particularly for children. Researchers in school settings have found a decrease in absenteeism related to illness when a hand-washing educational program was initiated (Morton & Schultz, 2004).

In several studies in daycare settings, respiratory infections decreased when hygiene education (e.g., hand washing, disinfection of common surfaces) was implemented (Jefferson et al., 2009; Rabie & Curtis, 2006). Physical hand hygiene reminders (e.g., signs, posters) have been effective tools in healthcare and community settings in increasing compliance; this also may be effective in HSCT recipient household settings (Johnson, Sholcosky, Gabello, Ragni, & Ogonosky, 2003; Nevo et al., 2010).

Intervention studies to establish effective barriers to prevent transmission of CRV infection in HSCT recipient household environments also are warranted. Hand hygiene technique and frequency interventions have been studied in community school settings and were shown to decrease the incidence of CRV infection for study participants (Lau et al., 2012; Roberts et al., 2000). Disinfection of artificial surfaces (particularly high-touch surfaces) is known to decrease nosocomial infections in healthcare settings, but it has not been studied in household environments (Weber, Rutala, Miller, Huslage, & Sickbert-Bennett, 2010). The use of facemasks to prevent household transmission of CRV

Knowledge Translation

Acquisition of community respiratory virus infection by hematopoietic stem cell transplantation (HSCT) outpatients is associated with children in households.

Known infection prevention strategies (e.g., hand hygiene) may be effective and warrant additional studies in HSCT populations.

Adult pre- and post-transplantation discharge teaching should include all members of a household, particularly children.

infection in other populations has been shown to be ineffective in several studies (Cowling et al., 2009; Jefferson et al., 2009). This practice might create a false sense of security for HSCT recipients, and additional studies should be conducted to determine if facemask use is beneficial in reducing CRV infection for HSCT recipient populations. Additional research and education also would have implications for other immunocompromised populations that may be vulnerable to CRV infection.

Conclusions

This study is the first to find that households with children doubled the risk of an HSCT recipient acquiring CRV infection. Additional studies are needed to test interventions designed to interrupt transmission of CRV infection from children to vulnerable HSCT recipients. Household contacts should be included in transplantation teaching. Because of the potentially high number of days from transplantation to acquisition of CRV infection, re-education and continuing focus on CRV prevention should be reinforced throughout the post-transplantation period.

Kay A. Sams, RN, MPH, CIC, is an infection preventionist at the Moffitt Cancer Center and Research Institute (MCCRI) in Tampa, FL; Richard R. Reich, PhD, is an assistant professor in the Department of Psychology at the University of South Florida, Sarasota-Manatee; and Alice R. Boyington, RN, PhD, at the time of this writing, was the director of nursing research and Elsa M. Barilec, RN, BSN, CCRN, is an intensive care unit staff nurse and educator, both at MCCRI. No financial relationships to disclose. Sams can be reached at kay.sams@moffitt.org, with copy to editor at ONFEditor@ons.org. (Submitted May 2014. Accepted for publication July 22, 2014.)

References

Avetisyan, G., Mattsson, J., Sparrelid, E., & Ljungman, P. (2009). Respiratory syncytial virus infection in recipients of allogeneic stem-cell transplantation: A retrospective study of the incidence, clinical features, and outcome. *Transplantation, 88*, 1222–1226. doi:10.1097/TP.0b013e3181bb477e

Centers for Disease Control and Prevention. (2012). Clinical signs and symptoms of influenza. Retrieved from http://cdc.gov/flu/professionals/acip/clinical.htm

Chemaly, R.F., Ghosh, S., Bodey, G.P., Rohatgi, N., Safdar, A., Keating, M.J., . . . Raad, I.I. (2006). Respiratory viral infections in adults with hematologic malignancies and human stem cell transplantation recipients: A retrospective study at a major cancer center. *Medicine, 85*, 278–287. doi:10.1097/01.md .0000232560.22098.4e

Chemaly, R.F., Hanmod, S.S., Rathod, D.B., Ghantoji, S.S., Jiang, Y., Doshi, A., . . . Champlin, R. (2012). The characteristics and outcomes of parainfluenza virus infections in 200 patients with leukemia or recipients of hematopoietic stem cell transplantation. *Blood, 119*, 2738–2745. doi:10.1182/blood-2011-08-371112

Cowling, B.J., Chan, K.H., Fang, V.J., Cheng, C.K., Fung, R.O., Wai, W., . . . Leung, G.M. (2009). Facemasks and hand hygiene to prevent influenza transmission in households: A cluster randomized trial. *Annals of Internal Medicine, 151*, 437–446. doi:10.7326/0003-4819-151-7-200910060-00142

Figueras-Aloy, J., Carbonell-Estrany, X., Quero-Jimenez, J., Fernández-Colomer, B., Guzmán-Cabañas, J., Echaniz-Urcelay, I., & Doménech-Martinez, E. (2008). FLIP-2 study: Risk factors linked to respiratory syncytial virus infection requiring hospitalization in premature infants born in Spain at a gestational age of 32 to 35 weeks. *Pediatric Infectious Disease Journal, 27*, 788–793. doi:10.1097/INF.0b013e3181710990

Goldmann, D.A. (2000). Transmission of viral respiratory infections in the home. *Pediatric Infectious Disease Journal, 19*(10 Suppl.), S97–S102. doi:10.1097/00006454-200010001-00002

Heikkinen, T., & Järvinen, A. (2003). The common cold. *Lancet, 361*(9351), 51–59. doi:10.1016/S0140-6736(03)12162-9

Jefferson, T., Del Mar, C., Dooley, L., Ferroni, E., Al-Ansary, L.A., Bawazeer, G.A., . . . Rivetti, A. (2009). Physical interventions to interrupt or reduce the spread of respiratory viruses: Systematic review. *BMJ, 339*, b3675. doi:10.1136/bmj.b3675

Johnson, H.D., Sholcosky, D., Gabello, K., Ragni, R., & Ogonosky, N. (2003). Sex differences in public restroom handwashing behavior associated with visual behavior prompts. *Perceptual and Motor Skills, 97*, 805–810. doi:10.2466/pms.2003.97.3.805

Lau, C.H., Springston, E.E., Sohn, M.W., Mason, I., Gadola, E., Damitz, M., & Gupta, R.S. (2012). Hand hygiene instruction decreases illness-related absenteeism in elementary schools: A prospective cohort study. *BMC Pediatrics, 12*, 52. doi:10.1186/1471-2431-12-52

Law, B.J., Langley, J.M., Allen, U., Paes, B., Lee, D.S., Mitchell, I., . . . Parison, D. (2004). The Pediatric Investigators Collaborative Network on Infections in Canada study of predictors of hospitalization for respiratory syncytial virus infection for infants born at 33 through 35 completed weeks of gestation. *Pediatric Infectious Disease Journal, 23*, 806–814. doi:10.1097/01.inf.0000137568.71589.bd

MacIntyre, C.R., Ridda, I., Seale, H., Gao, Z., Ratnamohan, V.M., Donovan, L., . . . Dwyer, D.E. (2012). Respiratory viruses transmission from children to adults within a household. *Vaccine, 30*, 3009–3014. doi:10.1016/j.vaccine.2011.11.047

Monto, A.S. (2002). Epidemiology of viral respiratory infections. *American Journal of Medicine, 112*(Suppl. 6A), 4S–12S. doi:10.1016/S0002-9343(01)01058-0

Morton, J.L., & Schultz, A.A. (2004). Healthy hands: Use of alcohol gel as an adjunct to handwashing in elementary school children. *Journal of School Nursing, 20*, 161–167. doi:10.1177/10598405040200030601

Nevo, I., Fitzpatrick, M., Thomas, R.E., Gluck, P.A., Lenchus, J.D., Arheart, K.L., & Birnbach, D.J. (2010). The efficacy of visual cues to improve hand hygiene compliance. *Simulation in Healthcare, 5*, 325–331. doi:10.1097/SIH.0b013e3181f69482

Nichols, W.G., Gooley, T., & Boeckh, M. (2001). Community-acquired respiratory syncytial virus and parainfluenza virus infections after

hematopoietic stem cell transplantation: The Fred Hutchinson Cancer Research Center experience. *Biology of Blood and Marrow Transplantation, 7*(Suppl.), 11S–15S. doi:10.1053/bbmt.2001.v7.pm11777098

Rabie, T., & Curtis, V. (2006). Handwashing and risk of respiratory infections: A quantitative systematic review. *Tropical Medicine and International Health, 11*, 258–267. doi:10.1111/j.1365-3156.2006.01568.x

Roberts, L., Smith, W., Jorm, L., Patel, M., Douglas, R.M., & McGilchrist, C. (2000). Effect of infection control measures on the frequency of upper respiratory infection in child care: A randomized, controlled trial. *Pediatrics, 105*, 738–742. doi:10.1542/peds.105.4.738

Tomblyn, M., Chiller, T., Einsele, H., Gress, R., Sepkowitz, K., Storek, J., . . . Boeckh, M.J. (2009). Guidelines for preventing infectious complications among hematopoietic cell transplantation recipients: A global perspective. *Biolology of Blood and Marrow Transplantation, 15*, 1143–1238. doi:10.1016/j.bbmt.2009.06.019

Viboud, C., Boélle, P.Y., Cauchemez, S., Lavenu, A., Valleron, A.J., Flahault, A., & Carrat, F. (2004). Risk factors of influenza transmission in households. *British Journal of General Practice, 54*, 684–689.

Weber, D.J., Rutala, W.A., Miller, M.B., Huslage, K., & Sickbert-Bennett, E. (2010). Role of hospital surfaces in the transmission of emerging health care-associated pathogens: Norovirus, Clostridium difficile, and Acinetobacter species. *American Journal of Infection Control, 38*(5, Suppl. 1), S25–S33. doi:10.1016/j.ajic.2010.04.196