



Rhinovirus Infections in Pediatric Solid Organ Transplant Patients

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Background

Since the introduction of clinically approved polymerase chain reaction (PCR) based respiratory viral testing, human rhinovirus (HRV) has been found to be one of the most frequently detected viruses in pediatric patients. Much remains unknown about HRV infections in pediatric solid organ transplant (SOT) recipients. Adult studies have shown it to be the most common viral respiratory pathogen in organ and hematopoietic stem cell transplant patients (1, 2). Studies of adults and pediatric patients have demonstrated that while HRV primarily results in asymptomatic or upper airway disease, it can also lead to severe lower respiratory tract disease and episodes of rejection have been reported in immunocompromised patients (3). Co-infections are also known to occur with some frequency but there remains limited data regarding the contribution of HRV to overall illness in pediatric SOT patients.

Objective

We set out to describe HRV infections in the pediatric SOT recipients at Stanford Children's Hospital (SCH) to better understand seasonal trends, symptomatology, co-infections, hospitalizations and disease burden.

Design/Methods

This was a retrospective observational study of all rhinovirus infections detected in the pediatric SOT population at SCH since introduction of our laboratory's rhinovirus PCR (GenMark Dx assay) in December of 2012. Information was collected by means of querying our electronic medical record database for all pediatric SOT patients (liver, kidney, heart, lung, and intestinal transplants) by means of billing and procedure codes and cross referencing unique MRNs with positive rhinovirus PCR tests (4). Information from the EMR data pull and subsequent chart review was then entered into REDCap for quantitation and analysis.

Results

1073 pediatric solid organ transplant patients with unique MRNs were treated between October 2004 to May 2014 (Figure 1). All were cross referenced with the respiratory PCR query between December 2012 to November 2014 with relative percentages of positive tests per organ shown (Figure 1). There were 39 pediatric SOT patients who tested positive for HRV a total of 61 times. HRV was present in 30% of all positive respiratory PCRs performed in the study period (Figure 2). Mean age of patients at time of positive test was 6.8 years and median age was 3.6 years. Co-infections were detected in 18% of these positive rhinovirus PCR tests (Figure 3). Of all the positive HRV episodes, 74.1% of patients were hospitalized at time of testing. Four patients demonstrated continuous HRV positive PCRs greater than a month apart; these patients included 2 renal transplant patients, 1 liver transplant patient, and one lung transplant patient. Cough was the most prominently reported symptom (Figure 4). Trends in seasonality are reported (Figure 5). No deaths that occurred in the study period were directly attributed to HRV infection.

Fig. 1: Pediatric SOT Patient Numbers and Relative Rhinovirus Positive Tests by Organ

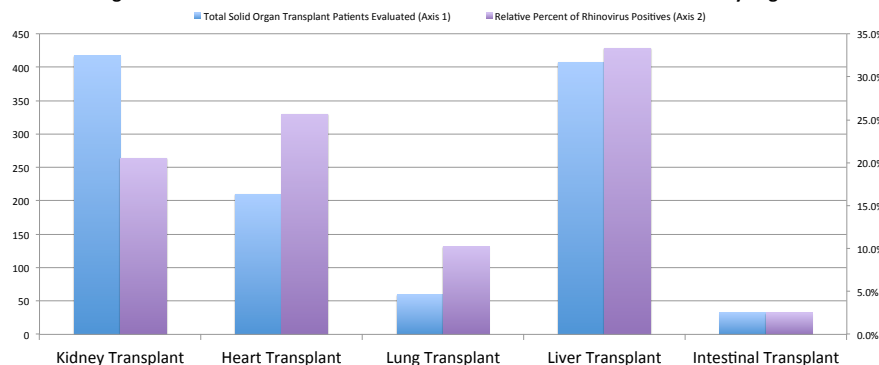


Fig. 2: Viral Respiratory PCR Positives in SOT Patients since December 2012

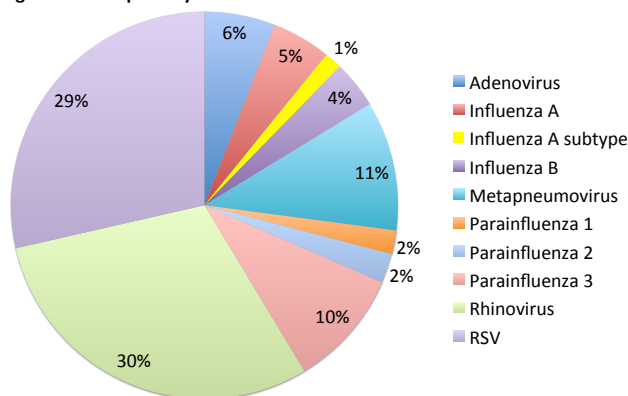


Fig. 4: Symptoms Reported Per Positive Rhinovirus Episode

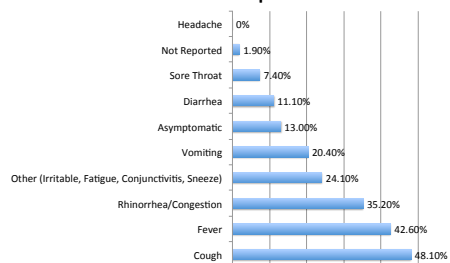
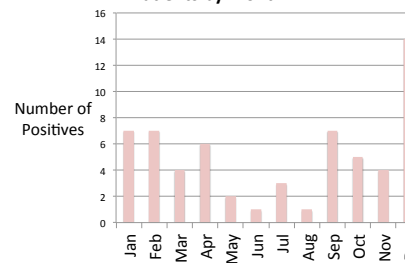


Fig. 3: Co-infections

Co-Infection	Number
RSV	5
Parainfluenza 3	2
Adenovirus	2
Metapneumovirus	1
Influenza B	1

Fig. 5: Positive Rhinovirus PCRs in SOT Patients by Month



Conclusion

- These results suggest that HRV is the most common detectable viral respiratory infection in pediatric SOT patients at our institution, though RSV remains quite prevalent as well.
 - HRV does show relatively frequent co-infections with other viral respiratory pathogens in the pediatric SOT population, which suggests its presence may predispose individuals to additional infections.
 - We saw no deaths directly related to HRV in our cohort though co-infections in this population require greater study.
 - Seasonal patterns were similar to that seen in other pediatric populations, but isolates were present year round.
 - Repeat testing suggests possible prolonged shedding in some SOT patients lasting up to 3 months, though new HRV infections could also explain these findings.
 - In comparison to our total pediatric SOT population of which 38% are kidney transplant patients, a relatively smaller proportion of rhinovirus infections were seen in kidney transplant patients (20%), especially when compared to liver and heart transplant groups suggesting potential risk factors which need to be further studied.
 - Symptomatology was similar to that seen in healthy children with cough, fever and rhinorrhea predominating (3).
- Future directions of study will include the addition of other respiratory viral pathogens to our database along with ongoing evaluation of risk factors such as medications (particularly immunosuppressive medications), timing of infection related to transplant or rejection, co-infections, and exposures/prophylactic measures. Such information will shed light on potential high-risk host factors. We also look forward to evaluating additional data in this cohort about newly added respiratory viruses such as coronavirus and parainfluenza virus 4 from our hospital's PCR panel.

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•Study data were collected and managed using REDCap electronic data capture tools hosted at the Stanford Center for Clinical Informatics. REDCap (Research Electronic Data Capture) is a secure, web-based application designed to support data capture for research studies, providing: 1) an intuitive interface for validated data entry; 2) audit trails for tracking data manipulation and export procedures; 3) automated export procedures for seamless data downloads to common statistical packages; and 4) procedures for importing data from external sources.
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