Community Respiratory Viruses Are Generally Well-Tolerated in Hematopoietic Stem Cell Transplant Recipients: A Brief report from the TRANSPIRE study.

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BACKGROUND

- Hematopoietic stem cell transplantation (HSCT) is an effective treatment for malignant and non-malignant diseases in pediatric patients but comes with increased risk of infections.
- The introduction of rapid respiratory viral panel testing via polymerase chain reaction (PCR) has led to a significant increase in the identification of common respiratory viral pathogens.
- Two different adult studies in HSCT patients have shown a high morbidity and mortality in HSCT patients with viral pneumonias with 15-30% causing respiratory failure requiring mechanical ventilation or death.
- It has not yet been reported how pediatric HSCT patients are tolerating these seasonal respiratory viral infections and whether viral identification should change clinical management.

METHODS

- **TRANSPIRE** is a multi-institutional prospective cohort of pediatric patients receiving allogeneic-HSCT
- All allogeneic HSCT patients between 0-24 years old are eligible to participate
- TRANSPIRE is currently open and actively enrolling at all 7 institutions including Boston Children's Hospital, Cincinnati Children's Hospital Medical Center, Children's Hospital of Philadelphia, Seattle Children's Hospital, Texas Childrens' Hospital, University of Minnesota and University of California San Francisco
- Data for this study was taken from patients seen at Cincinnati Children's Hospital Medical Center that were enrolled in the TRANSPIRE study.
- All patients received standard pulmonary evaluations, biological sample collection, and clinical data collection at set timepoints throughout their transplant course and in response to any significant clinical events.
- Evaluations were done pre-transplant and post-transplant at day 60, day 100, 6 months, and annually starting at 12 months post-transplant.
- All reported infections for this study were identified on nasopharyngeal swabs or broncho-alveolar lavage (BAL) samples that were obtained for clinical purposes.

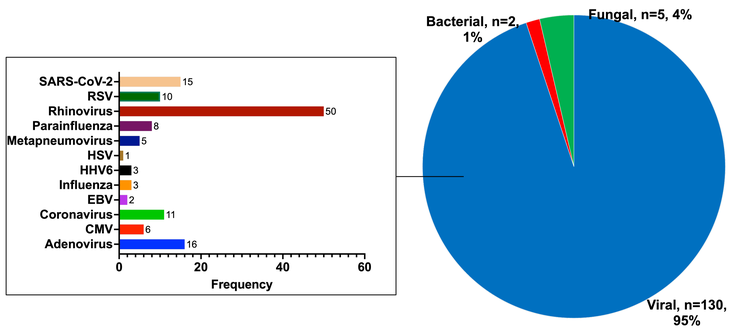
RESULTS

Table 1. Cohort demographics and transplant characteristics

	Total Cohort n=146	Infectious Event n=78	No Infectious Event n=68	*p-value*
Sex, n (%)				
Male	78 (53.3)	46 (59)	32 (47.1)	0.47
Female	68 (46.6)	32 (41)	36 (52.9)	
Race, n (%)				
White	101 (69.2)	56 (71.8)	46 (67.6)	0.18
African American	9 (6.1)	7 (9)	3 (4.4)	
Asian	4 (2.7)	1 (1.3)	3 (4.4)	
Mixed	3 (2)	2 (2.6)	1 (1.5)	
Unknown/Not reported	25 (17)	12 (15.3)	15 (22.1)	
Primary diagnosis, n (%)				
Malignancy	47 (32.2)	25 (32)	22 (32.4)	0.89
Marrow failure	34 (23.3)	18 (23.1)	16 (23.5)	
Benign Hematology	21 (14.4)	14 (18)	7 (10.3)	
Immune Deficiency	37 (25.3)	16 (20.5)	21 (30.9)	
Genetic/Metabolic	7 (4.8)	5 (6.4)	2 (2.9)	
Age in years at HSCT, median (range)	9.1 (8.6-24.1)	6.8 (0.3-23)	11.4 (0.2-24.1)	**0.02**
Stem cell source, n (%)				
Bone marrow	89 (60.9)	47 (60.3)	42 (61.8)	0.77
Peripheral blood stem cell	39 (26.7)	20 (25.6)	19 (27.9)	
Cord	18 (12.4)	11 (14.1)	7 (10.3)	
Conditioning regimen, n (%)				
Myeloablative	74 (50.6)	47 (60.3)	27 (39.7)	0.09
Reduced-intensity	72 (49.4)	31 (39.7)	41 (60.3)	
TBI*	17 (11.6)	9 (11.5)	7 (10.3)	
Degree of match, n (%)				
Fully matched	92 (63)	47 (60.3)	45 (66.2)	0.11
Mismatched	54 (37)	31 (39.7)	23 (33.8)	
Donor source, n (%)				
Related	51 (34.9)	30 (38.5)	21 (30.9)	0.72
Unrelated	95 (65.1)	48 (61.5)	47 (69.1)	
GVHD# prophylaxis, n (%)				
Calcineurin-based	122 (83.6)	67 (85.9)	55 (80.9)	0.6
T-cell depletion	24 (16.4)	11 (14.1)	13 (19.1)	
GVHD Day 100 Grade, n (%)	*n=121*	*n=69*	*n=52*	
None	94 (77.7)	46 (66.7)	48 (92.3)	**0.002**
Grade I	12 (9.9)	12 (17.4)	0	
Grade II	10 (8.3)	8 (11.6)	2 (3.8)	
Grade III	5 (4.1)	3 (4.4)	2 (3.8)	

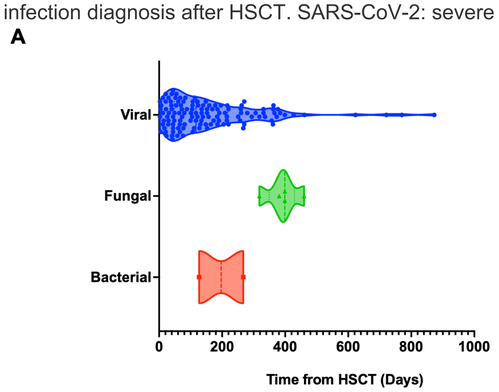
*TBI: Total body irradiation; #GVHD: graft-vs-host-disease

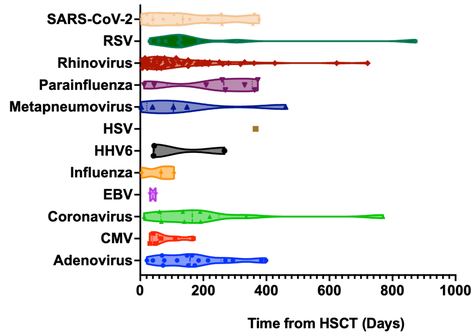
Figure 2. Frequency of infections after hematopoietic stem cell transplant. The pie chart shows the distribution of viral (blue), fungal (green) and bacterial (red) infections that were identified after HSCT. Viral infections were the most frequent infections identified (n=130, 95%) followed by fungal (n=5, 4%) and bacterial (n=2, 1%). The specific organisms identified for each subtype of infection are summarized in the boxes. Rhinovirus (n=50, 38.5%) was the most common viral infection identified after HSCT.



RESULTS

Figure 3. Timing of infections after hematopoietic stem cell transplant. (A) Violin plot showing the time from HSCT infections were diagnosed. (B) A violin plot summarizing the timing of viral infection diagnosis after HSCT. SARS-CoV-2: severe acute respiratory syndrome coronavirus 2.





Organism	Time from HSCT (days)
Viral infections, median days from HSCT (IQR)	
Adenovirus	158 (73-256.3)
CMV	57 (38.3-125.5)
Coronavirus	165 (65.5-249)
EBV	40 (31-49)
Influenza	40
HHV6	44 (42-267)
HSV	366
Metapneumovirus	105 (21-304.5)
Parainfluenza	265 (85.3-355)
Rhinovirus	100.5 (46-193)
RSV	126 (74.5-215.3)
SARS-CoV-19	135 (40-259)

Only 4.1% (n=6) of patients included in this study required mechanical ventilation in the PICU after diagnosis of a respiratory infection. Four of these patients requiring mechanical ventilation were infected with CMV, one with adenovirus and one with aspergillus. Importantly, none of those requiring escalation of care including mechanical ventilation were due to common community respiratory viral infections.

CONCLUSIONS

- Viral infections are frequent after HSCT, but serious morbidity is largely limited to well-know pathogens like CMV and adenovirus.
- This is important to consider when counseling patients and families on the risks of viral infections post-HSCT and planning in-patient or out-patient care for patients.
- This data should be taken into consideration when weighing the cost-benefit analysis of ordering expensive PCR-based respiratory viral panel testing.