TRENDS IN ADENOVIRUS INFECTIONS IN SINGAPORE CHILDREN AND OUTCOMES OF CIDOFOVIR TREATMENT IN THE SEVERELY ILL

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BACKGROUND

An increase in human adenovirus (HAdV) infections among hospitalized children in Singapore was observed since 2013 [1,2]. Severe HAdV infections can result in significant mortality particularly among pediatric transplant recipients [3].

Cidofovir, a monophosphate nucleotide analogue of cytosine, inhibits viral DNA polymerases and exhibits activity against multiple DNA viruses including HAdV [3]. Cidofovir is often used to treat severe HAdV infections despite limited data, particularly in non-transplant patients and children [4,5].

Our hospital, KKH, is the largest pediatric hospital in Singapore. Here, we describe the epidemiology and outcomes of children with severe HAdV disease requiring high dependency (HD) or intensive care unit (ICU) admission in KKH.

METHODOLOGY

This is a retrospective cohort study of HAdV-infected children admitted to HD and ICU in KKH from January 2013 to September 2017. Children with a positive HAdV result on nasopharyngeal aspirate, bronchoalveolar lavage, conjunctival swab, blood, urine or stool on immunofluorescence or polymerase chain reaction as identified from laboratory records were included.

Positive samples were genotyped at the Singapore National Public Health Laboratory. Severe infections were defined as those who required HD or ICU admission. Characteristics and outcomes of those who received IV cidofovir were compared.

This study was approved by the SingHealth Centralised Institutional Review Board.

RESULTS

Figure 1: Children admitted for HAdV infection in KKH from Jan 2013 to Sep 2017

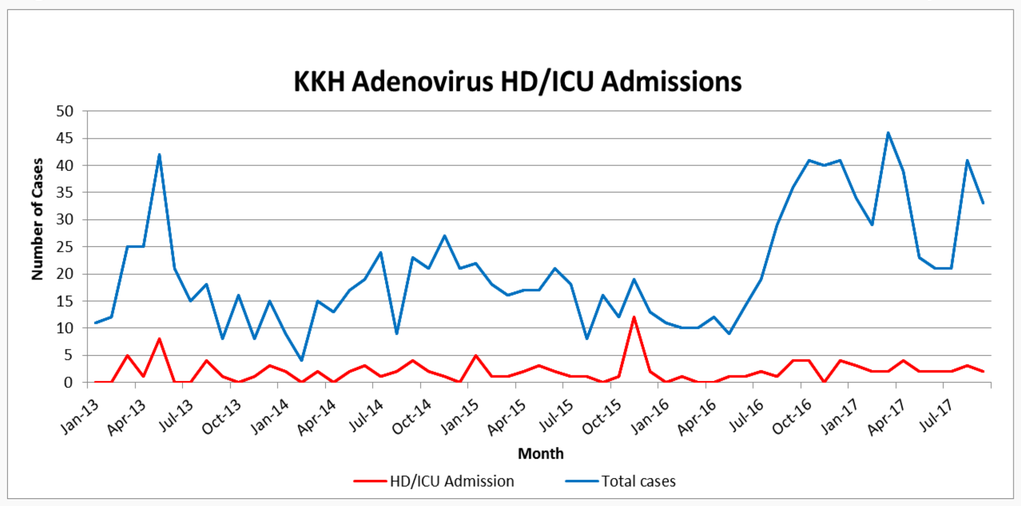
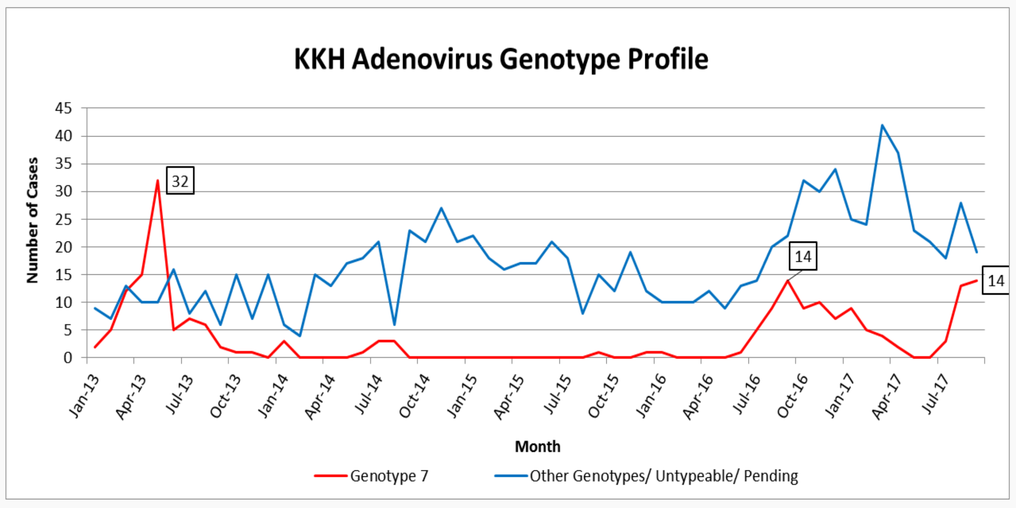


Figure 2: Genotype profiles of HAdV infection in KKH from Jan 2013 to Sep 2017



RESULTS

HAdV admissions and genotype profiles in KKH are described in Figures 1 and 2 respectively. There were 85 children with severe HAdV infection, of which 17 (20%) received cidofovir for mainly viremia (8, 47.1%) and pneumonia (7, 41.2%). Of these 17 patients, 7 (41.2%) died.

More children treated with cidofovir had genotype 7 infection (8 of 17, 47.1%) versus 13 of 68 (19.1%) who did not (p = 0.027).

Characteristics of patients who received cidofovir are described in Table 1. None experienced adverse reactions from cidofovir.

Table 1: Comparison of characteristics of 17 children who received IV cidofovir

	Discharged (N=10)	Death (N=7)	P value
Age in years (median, IQR)	2.6 (1.7 – 3.7)	2.2 (1.2 – 5.9)	0.922
Male	5 (50.0)	6 (85.7)	0.304
Significant co-morbidities	5 (50.0)	6 (85.7)	0.304
Prematurity	0 (0.0)	1 (14.3)	0.412
Neurological	1 (10.0)	3 (42.9)	0.250
Cardiopulmonary	0 (0.0)	1 (14.3)	0.412
Immunodeficiency	3 (30.0)	1 (14.3)	0.603
Others	1 (10.0)	0 (0.0)	1.000
Disease presentation			
Pneumonia	1 (10.0)	6 (85.7)	0.004
Gastroenteritis	1 (10.0)	0 (0.0)	1.000
Neutropenic sepsis	0 (0.0)	1 (14.3)	0.412
Viremia	8 (80.0)	0 (0.0)	0.002
Days of symptoms prior admission (median, IQR)	6.5 (2.3 – 10.8)	4.0 (0.0 – 5.0)	0.350
Adenovirus genotype 7	4 (40.0)	4 (57.1)	0.637
Required ICU stay	5 (50.0)	7 (100.0)	0.044
Days to cidofovir (median, IQR)	7.0 (1.5 – 25.8)	12.0 (4.0 – 40.0)	0.434
Length of stay in days (median, IQR)	21.5 (15.0 – 63.5)	34.0 (16.0 – 43.0)	0.696

All are n (%) unless stated otherwise.

CONCLUSION

In our previous study, young age (<2 years) and significant co-morbidities were associated with more severe HAdV infections, including pneumonia.

In this study, more children with HAdV genotype 7 infection required cidofovir treatment. HAdV pneumonia and ICU admission are potential risk factors for mortality despite cidofovir treatment.

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