Impact of infection prevention precautions on adenoviral infections during the COVID-19 pandemic: experience of a tertiary hospital in Singapore

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To the Editor,

We read with interest the article by Wong et al. describing the impact of infection-control measures introduced during the COVID-19 pandemic on nosocomial transmission of influenza and respiratory-syncytial-virus (RSV).1 However, while the authors experienced zero nosocomial transmission of enveloped respiratory viral infections (RVIs), non-enveloped RVIs, such as adenoviruses, may pose greater challenges in infection-prevention. Indeed, given the relative hardiness of the non-enveloped adenoviruses, evidence of contamination with adenoviruses has been reported in healthcare environments,2 as well as on the outer surface of medical masks used by healthcare workers (HCWs).3 Given the potential of adenoviruses to persist on inanimate surfaces and retain infectivity, and the limited effectiveness of alcohol-based hand disinfection in eliminating this viral pathogen,4 adenovirus outbreaks can occur even in the setting of good hand hygiene compliance.5 While adenoviruses generally cause self-limiting disease in immunocompetent hosts, infections in vulnerable populations, such as transplant recipients and neonates, can be potentially devastating.6 We therefore sought to determine if infection-prevention measures introduced during the COVID-19 pandemic could potentially impact transmission of adenoviral infections.

In Singapore, a Southeast Asian city-state, various infection-prevention measures were implemented across all public hospitals soon after the first reported case of COVID-19 in end-January 2020. At our institution, the largest acute tertiary hospital in Singapore, an integrated strategy was introduced from February 2020 to mitigate healthcare-associated transmission of SARS-CoV-2; focusing on universal masking for all HCWs, adherence to basic infection-prevention measures including hand hygiene, and improved segregation of patients with respiratory symptoms.7 Pre-pandemic, patients were predominantly nursed in multi-bedded open-plan wards. During the pandemic, patients with respiratory symptoms were segregated in dedicated wards with reduced bed density and HCWs used disposable gloves, gowns, eye protection, and N95 respirators until COVID-19 was excluded.7 While the combined infection-prevention bundle successfully prevented patient-HCW transmission of SARS-CoV-2 and reduced healthcare-associated influenza transmission,7,8 the impact on transmission of adenoviral infections was not specifically assessed. Our institution has neonatal services, as well as an active bone-marrow and solid-organ transplant program. During the pandemic, our institution continued to function and accept patients as-usual. Over a nine-month study period during the COVID-19 pandemic from February-October 2020, all symptomatic inpatients were tested for SARS-CoV-2; adenovirus was also tested as one of the 16 common circulating RVIs on our institution’s multiplex PCR panel. Adenoviral infections were categorized as healthcare-associated if the RVI was identified beyond the maximum incubation period (14 days) from admission. Comparisons of adenoviral
infection rates (both community-acquired/healthcare-associated) during the pandemic period were made with the corresponding period pre-pandemic (January 2015-January 2020) using the incidence-rate-ratio method. Our institution’s institutional-review-board approved waiver of informed consent.

Pre-pandemic, the incidence of healthcare-associated adenoviral infections was 0.40 cases per-10,000 patient-days (94 cases; 2,368,810 patient-days). After implementation of the integrated infection-prevention bundle in February 2020, the incidence of healthcare-associated adenoviral infections fell to 0.03 cases per-10,000 patient-days (1 case; 349,130 patient-days), a statistically-significant decrease (incidence-rate-ratio, IRR=0.07, 95%CI=0.01-0.41, p<0.05). The sole case of potential healthcare-associated infection during the pandemic occurred in a returning COVID-19-positive traveler, who was isolated in a negative-pressure airborne-infection-isolation-room (AIIR) in our institution’s isolation ward (IW) for 21-days (Supplementary Figure 1a). He was re-tested for RVIs due to new-onset respiratory symptoms. While respiratory specimens at admission were negative for adenovirus, repeat specimens at D21 were positive. All HCWs used disposable gloves, gowns, eye protection, and N95 respirators, changed at each patient encounter. Hand hygiene compliance remained at ≥90% and compliance with personal-protective-equipment usage was maintained at ≥90%. The patient was confined to the same AIIR throughout and our IW had a strict no-visitor policy, although one-way transfer of personal items into the AIIR was allowed to mitigate the psychological effects of prolonged isolation. Though a fomite source is possible, it could not be conclusively proven. The mortality rate amongst all patients with adenoviral infections was 5.53% (42 deaths, 759 cases) (Supplementary Figure 1b). From March-October 2020, there were zero cases of healthcare-associated adenoviral infections over a sustained 8-month period, an observation unprecedented in the preceding 5 years of surveillance (Supplementary Figure 2).

This significant decrease in healthcare-associated transmission of adenoviral infections occurred despite increased driving pressure from admissions with community-acquired adenoviral infections in the initial pandemic phase (Figure 1a). During the first four months of the pandemic (February-May 2020), the incidence of community-acquired adenoviral infections was higher than baseline, at 2.23 cases per-1000-admissions (49 cases, 21,881 admissions), compared with a pre-pandemic rate of 1.19 cases per-1000-admissions (162 cases, 135,124 admissions) in the corresponding period (February-May, 2015-2019), a statistically-significant increase (IRR=1.87, 95%CI=1.33-2.59, p<0.001). Only after the imposition of a national “lockdown” period from 7th April 2020-1st June 2020 was there a significant decrease in the incidence of community-acquired adenoviral infections amongst admissions (pandemic period: 0.06 cases per-1000-admissions, 13 cases, 210,237 admissions; pre-pandemic period, June-October, 2015-2019: 1.32 cases per-1000-admissions, 226 cases, 171,408 admissions; IRR=0.05, 95%CI=0.02-0.08, p<0.001). This contrasted with observations made for enveloped RVIs, in which the introduction of community-wide public health
measures, such as social distancing and universal usage of face coverings, was associated with a significant decrease in influenza-incidence in the general population.  

The key finding of this study is that infection-prevention precautions were effective in reducing healthcare-associated transmission of adenoviral infections during the COVID-19 pandemic, despite the increased rate of community-acquired adenoviral infections in the corresponding period. However, the sole case of healthcare-associated transmission of adenoviral infection in a COVID-19-positive individual, despite full isolation precautions, demonstrates the significant infection-prevention challenges posed by this hardy non-enveloped viral pathogen.

**Author contributions:**

Concept and design: Wee, Venkatachalam

Analysis of data: Wee, Conceicao, Venkatachalam

Drafting of manuscript: Wee, Conceicao, Sim, Aung, Venkatachalam

Supervision: Venkatachalam

**Conflict of interest**

The authors report no conflicts of interest.
References


Figure 1: Trends in community-acquired (CA) adenoviral infections amongst all admissions to a tertiary hospital in Singapore.

Trend in community-acquired (CA) adenoviral infections, 2015-2020, by month, amongst all admissions

Public health measures introduced during 2020 COVID-19 pandemic:


b: Community transmission of COVID-19. Law enforced social distancing, gatherings limited to 10 people.

C: Nationwide lockdown started 7th April 2020. All schools and non-essential workplaces closed.

Supplementary Figure 1: Details of solitary case of healthcare-associated adenoviral infection during COVID-19 pandemic; and number of death cases with PCR-proven adenoviral infections at a tertiary hospital in Singapore

A

Purpose-built isolation ward

Negative-pressure air-tight isolation rooms, single occupancy, with en-suite toilet and ante-chamber; staff donned personal protective equipment prior to entry into ante-chamber

Healthcare-associated adenoviral infection during COVID-19 pandemic

Middle-aged returning traveller with concurrent COVID-19
- Duration of stay: 21 days
- Isolated in negative-pressure air-tight infection isolation room (NIR) throughout admission
- No visitors allowed

Respiratory specimen on admission: +ve for SARS-CoV-2, -ve for other viruses

Respiratory specimen on discharge: -ve for SARS-CoV-2, +ve for adenovirus

Personal protective equipment in isolation ward:
Disposable gloves, gowns, eye protection, N95 respirators (changed with every patient contact; no reuse)

B

Number of death cases with PCR-proven adenoviral infection, 2015-2020

NHC: National Heart Centre
SGH: Singapore General Hospital
Supplementary Figure 2: Trends in community-acquired (CA) and healthcare-associated (HA) adenoviral infections amongst all admissions to a tertiary hospital in Singapore