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Outbreaks of Human Metapneumovirus in Western Sydney Aged-Care Facilities in 2018

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Abstract

Background

Human metapneumovirus (hMPV), first described in 2001, is a cause of acute respiratory tract infection in the elderly, with symptoms ranging from mild to severe, including pneumonia, but outbreaks are rarely described.

Methods

Between 1 July and 31 December 2018, there were three outbreaks of Influenza-like Illness (ILI) where hMPV was the primary pathogen observed, among 64 aged-care facilities (ACFs) in Western Sydney. These outbreaks were investigated by the Western Sydney Local Health District (WSLHD) Public Health Unit (PHU); multiplex polymerase chain reaction (PCR) testing was performed on nasopharyngeal swabs collected by the ACF.

Results

hMPV was the main causative pathogen in three outbreaks (27, 28, and 15 symptomatic cases, respectively) in late winter and early spring. Fifty-five residents and 15 staff cases (70 total cases) were identified; hMPV was detected in 12 of 63 specimens submitted. Of the cases in residents, eight were hospitalised (8/63; 15%), including five with confirmed hMPV and a further one epidemiologically linked to a positive case. Six residents died (6/63; 11%) during the hMPV outbreaks; four of these had laboratory-confirmed hMPV, with a further case epidemiologically linked to a hMPV case, with a primary diagnosis of pneumonia/viral pneumonia. The sixth death was not epidemiologically linked, nor did this case exhibit any respiratory symptoms during the outbreak; however, it was reported in line with public health guidelines.

Conclusion

A major challenge in 2018 was the incompleteness of testing for, and awareness of, hMPV as a viral cause of ILI by facilities, laboratories, and emergency departments, which generally opted for rapid testing for influenza and RSV only. There is no licensed vaccine or approved treatment for hMPV, so efficient infection control measures are most important.

Keywords: Viral respiratory illness; aged care; human metapneumovirus

Introduction

Human metapneumovirus (hMPV) is an enveloped negative-sense RNA virus in the *Pneumoviridae* subfamily of the *Paramyxoviridae* family and is one of two viruses in this subfamily; the other virus in this subfamily, avian metapneumovirus, is not known to infect humans.

HMPV was first described in 2001 in children from The Netherlands;¹ however, there is serological evidence that it has been circulating for far longer in human populations. A historical sero-epidemiological study on samples from people of various ages, collected in 1958, demonstrated that there was 100% seroprevalence of neutralising antibodies in people aged 10 years and older,¹ with high seropositivity also reported from similarly-aged samples collected in Germany (86.6%);² Japan in 2002 (100%);³ Canada (100%);⁴ and Connecticut, United States of America (95.5% in individuals aged 11–20).⁵

As with other respiratory viruses, hMPV circulates seasonally, usually during late winter through spring in Australia.⁶ Whilst most infections occur in young children, a four-year prospective cohort study of hospitalised patients aged 65 years and older found that hMPV was implicated in 8.5% (range 4.3–13.2% annually) of acute respiratory tract infections which resulted in acute hospitalisation in Rochester, New York.⁷ A small number of hMPV outbreaks have been reported in residential aged care facilities (ACFs) in Australia and overseas, with some infections leading to pneumonia and death.^{8,9}

In 2017, there were 47 outbreaks of influenza in ACFs in Western Sydney (c.f. 35 in 2016) and 588 in all of New South Wales (c.f. 279 in 2016), emphasising the need for enhanced respiratory viral surveillance and infection control. From 1 July 2018, WSLHD undertook to enhance routine surveillance through the increasing use of on-site Point of Care (PoC) testing for influenza A/B and respiratory syncytial virus (RSV),

improved data collection, and expanding the scope of surveillance to all viral respiratory illness outbreaks, including hMPV, in ACFs.

There was laboratory-confirmed evidence of hMPV in 2018 as the main causative pathogen in ACF outbreaks in Western Sydney. This paper documents the descriptive epidemiology of three respiratory outbreaks, notified to the PHU between 1 July and 31 September 2018, in which hMPV was identified as the major causative organism.

Methodology

Based on the Communicable Diseases Network Australia (CDNA) influenza guidelines for residential aged care facilities,¹⁰ an outbreak of ILI is declared when three or more epidemiologically linked cases of ILI occur within a 72-hour period. Data were collected prospectively throughout the duration of the outbreaks, including details of public hospitalisations, using an electronic medical record, PowerChart (Cerner Corporation, North Kansas City, Missouri, United States of America).

PHU staff requested that ACFs follow influenza infection control guidelines for all ILI outbreaks to limit spread. The measures included: isolation of cases, cohorting of symptomatic residents and staff, droplet precautions, use of personal protective equipment (PPE), additional environmental cleansing, exclusion of symptomatic staff, the restriction of visitors and new admissions, and the postponement of group activities. The PHU contacted the facilities daily to ascertain whether there were additional cases; these were notified via an illness register.

Nasopharyngeal swabs were collected from 49 residents and 14 staff members in the data collection period of the three outbreaks. All swabs collected from ill residents were obtained by the ACF staff, while symptomatic staff were requested by their facility to visit their general practitioner (GP) to have a swab collected for testing; a negative result was required prior to resumption of work by the staff member.

Case definition

For the purpose of this study, confirmed cases were defined as: a resident or staff member having a nasopharyngeal swab which returned a positive result by RT-PCR for hMPV. Probable cases were those who presented with:

1. sudden onset of symptoms;
2. one or more respiratory (cough [new or worsening], coryza, sore throat) or systemic (fever, headache, fatigue, rigors, joint/muscle aches) symptoms;
3. no positive test for another respiratory virus; and
4. an epidemiological link to a positive hMPV case.

Possible cases were symptomatic ACF residents or staff for whom no discernible epidemiological link could be identified and who had not tested positive for another respiratory virus.

Laboratory testing

PHU staff requested that symptomatic ACF staff and residents undertake a full respiratory panel, to be tested at a private pathology laboratory.

Statistical analysis

An illness register was developed using Excel 2013 (Microsoft Corporation, Redmond, Washington, United States of America) by the WSLHD PHU in collaboration with the National Centre for Immunisation Research and Surveillance (NCIRS). Data collected included key demographic data, symptoms and laboratory results, as well as comorbidities, particularly immunocompromising conditions. The register was completed by staff at their respective ACF, and univariate analysis of the outbreak data was collated using Excel 2013 and analysed using R Studio (version 1.3.1056).

Ethics

The study was approved for low and negligible risk by the WSLHD Human Research Ethics Committee (HREC 2020/ETH00822).

Results

In three separate outbreaks, hMPV was identified as the predominant circulating respiratory virus. Seventy people were affected during these three outbreaks, comprising 15 staff members and 55 residents. The mean ages at the time of the respective outbreaks were 43 ± 12.4 years (range: 20–56 years) for affected staff and 88 ± 9.9 years (range: 59–101) for affected residents. Table 1 provides a summary of the outbreaks, including number of cases, laboratory confirmed cases, hospitalisations, and deaths.

Examination of both hospital inpatient and ACF records showed that 6/8 hospitalised residents in these outbreaks received a final diagnosis of pneumonia/viral pneumonia, of which five had a confirmed hMPV diagnosis (5/12). Of the six deaths reported across 3 outbreaks, four had confirmed hMPV (4/12), with a further case that was symptomatic and epidemiologically linked to a positive case. The sixth death was not attributed to the hMPV outbreak.

During outbreak 1, there were 14 of 75 residents reported to the PHU with respiratory symptoms, three with confirmed hMPV and one symptomatic, confirmed hMPV case in a staff member. Additionally, one case of enterovirus was detected in a resident in the same section of the facility. All but two resident cases were localised to one of the three levels of the facility, with the confirmed staff member also having worked in this section of the facility whilst infectious. In total, there were three confirmed cases of hMPV, eight probable cases and two possible cases during this outbreak. All affected residents reported becoming symptomatic within three days of each other. There were four deaths reported to the PHU; two of the four who died were hospitalised and subsequently tested positive for hMPV. A third hMPV positive

Table 1: Summary of reported outbreaks of hMPV at Western Sydney ACFs in 2018

Facility		1	2	3
Total staff		100	95	159
Total bed capacity ^a		76	108	129
Length of outbreak (in days) ^b		14	34	29
Date of onset of outbreak		21/07/2018	23/07/2018	03/09/2018
Number of symptomatic cases	Residents	14	27	14
	Staff	1	0	14
Laboratory confirmed	Residents	3 – hMPV 1 – Enterovirus	4 – hMPV 3 – Rhinovirus 2 – RSV-B	3 – hMPV 1 – Rhinovirus
	Staff	1 – hMPV	0	1 – Influenza A 1 – hMPV 2 – Rhinovirus
Hospitalisations		3	3	2
Deaths		4	1	1

a ACFs generally reserve beds for temporary and respite accommodation and the total number of residents in the facility may fluctuate over time.

b 'Outbreak' is defined as date of first onset to eight days after the onset of the final resident case.

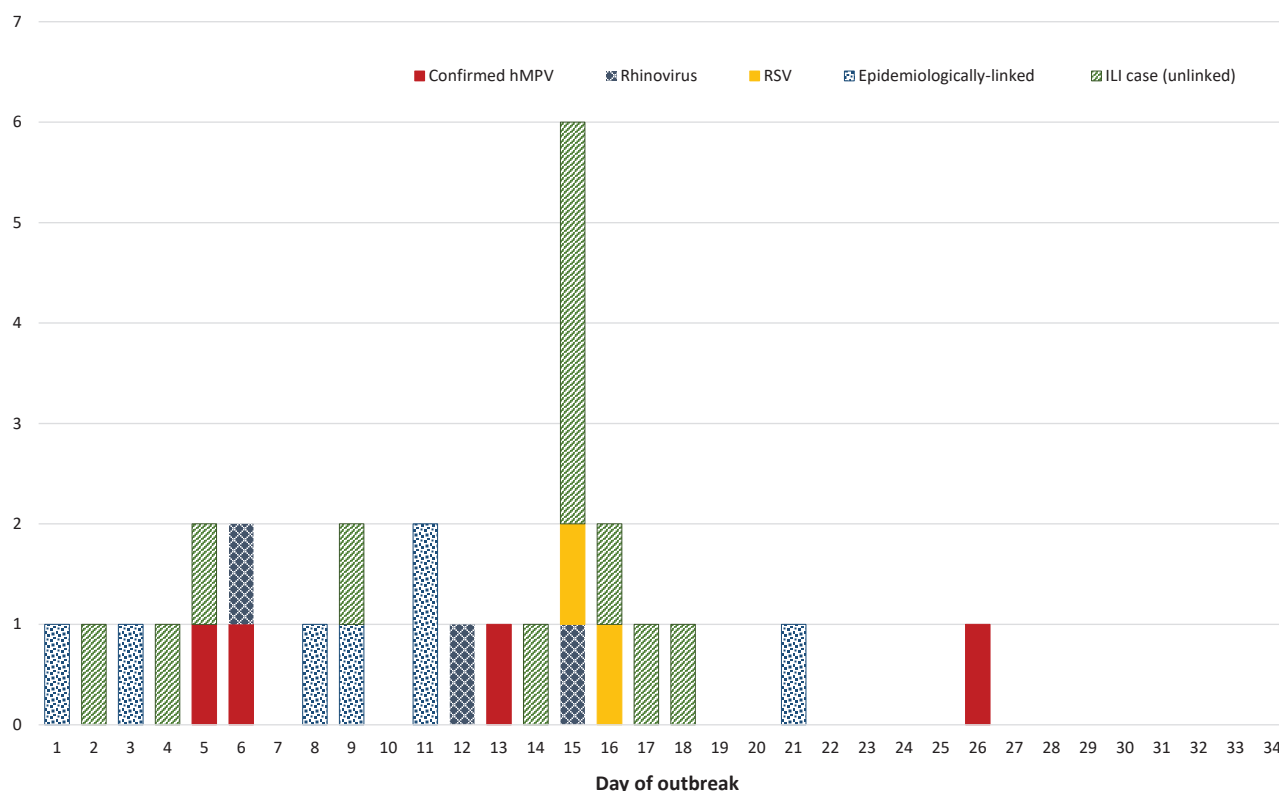
resident passed away in the facility and the fourth received a final diagnosis of pneumonia and was epidemiologically linked, however they were not tested.

During outbreak 2, there were 27 of 98 residents reported to the PHU with respiratory symptoms: four with confirmed hMPV; seven were probable cases, meeting the case definition; eight were only possible cases, with no ascertainable epidemiological link found (Figure 1). The 11 confirmed or probable cases were contained within one unit (11/36) with shared double rooms; 31% of residents were within that unit. Five cases were ruled out with another viral infection, either rhinovirus or RSV-B, and another three were ruled out because they had an epidemiological link to the three rhinovirus cases, indicating a concurrent outbreak at this facility. Notably, no staff were reported to the PHU as having respiratory symptoms or work absence throughout the 34-day outbreak. Further, oral antibiotics were prescribed for 15/27 residents, including three with confirmed hMPV, one with RSV-B, and

two with rhinovirus. The death reported during this outbreak was not attributable to the hMPV outbreak.

During outbreak 3, there were 14 of 129 residents reported to the PHU with respiratory symptoms, three with confirmed hMPV, with a simultaneous rhinovirus outbreak in a separate unit. As well as the three confirmed hMPV cases, an additional ten met the case definition of a possible case. One resident passed away in hospital during this outbreak following a positive hMPV result. The facility has five units; however, half of all resident cases and 5/14 symptomatic staff, including one confirmed resident and one confirmed staff member who worked while infectious, were localised to a single section of the facility. One resident and two staff members were excluded with a rhinovirus infection and another staff member with an influenza A infection.

Figure 1: Epidemiological curve of residents in outbreak 2 from day of first ILI onset to closure of outbreak^a



^a Confirmed hMPV, RSV, epidemiologically linked, and unlinked ILI cases are colour coded as per legend.

We also noted that in outbreaks one and three, the first laboratory confirmed cases were in ‘lifestyle’ or ‘activity’ staff members, who had worked while symptomatic.

Discussion

The six-month study period primarily included winter and spring months. While hMPV cases are identified all year round in New South Wales, the majority of notifications collected by Health Protection NSW, via sentinel laboratories, are identified in late winter and early spring.¹¹ Similarly, outbreaks of hMPV in Western Sydney ACFs have, thus far, only occurred in the late winter and early spring months, in keeping with the seasonality reported in previous studies.⁶

The PHU endeavoured to send a team to visit a facility after the report of an outbreak, but it was not feasible to visit each time there was an additional case. While a full respiratory screen

was requested by PHU staff, one problem arising was the necessity to utilise multiple private pathology laboratories with a resultant variety of available multiplex PCR tests, some of which did not target hMPV RNA in their routine respiratory screen. As hMPV is not nationally notifiable, it is not routinely tested for by private pathology laboratories, unless specifically requested by the treating doctor e.g. when respiratory viruses are prevalent in the community.

During visits to a number of facilities, and further informed by conversations with facility management, the study team concluded that staff in activity/lifestyle roles commonly have unrestricted movement throughout the facility and engage closely with multiple residents daily. As these staff are generally not trained in infection control but may eventually have close contact with most residents on a day-to-day basis, additional care should be taken with training, and screening, of such staff for respiratory infections.

Generally, the WSLHD PHU conducts a site visit during an influenza outbreak, especially when a death has occurred because of the outbreak, or when the total number of cases is approaching 50% of residents at the facility. As an enhancement to routine surveillance, the study team expanded this approach to all ILI outbreaks; the team also conducted a further visit when an outbreak was prolonged (> 21 days). We noted that facilities with prolonged outbreaks, requiring a second visit, had not appropriately isolated cases and may also not have ceased group activities. There are currently no approved antiviral treatments for hMPV (or RSV or rhinovirus), and isolation is less feasible for some residents, particularly in those with dementia; but prevention through isolation of cases and through restriction of movement for healthy residents is an important intervention for elderly residents.

With outbreak 2, thirteen days elapsed between the epidemiologically-linked third and fourth laboratory confirmed hMPV cases, possibly indicating that transmission between these residents was indirect (Figure 1). As no further genetic typing could be completed on the samples, we were unable to ascertain whether these were independent infections of separate lineages. There are a number of potential examples already described in the literature that may provide an explanation, including an under-reporting of symptomatic cases in residents and staff, as well as infectious asymptomatic/presymptomatic cases going unnoticed.¹² In 2018, it was not routine to collect a nasopharyngeal swab from asymptomatic residents and these were not requested, but evidence suggests that these may account for up to 39% of infections in this age group and up to 71% in healthy young adults.⁷ The severity of hMPV varies by age, with the elderly particularly susceptible to more severe infections.

While the signs and symptoms for various respiratory viruses can be similar, those which are used to survey for influenza do not exactly match those for hMPV or RSV. Wheezing and shortness of breath, while not typical of an

influenza infection, are very common in hMPV infections, particularly in adults, especially the elderly.⁷ Other common respiratory findings include hypoxia and pneumonia. While outbreak facilities were proactive in reporting additional signs and symptoms, streamlining of such reporting and inclusion in future ILI illness registers may provide further insight into the prevalence of these additional signs and symptoms during outbreaks.

Since its discovery, there has been little progress on a vaccine for hMPV. There have been a number of vaccine candidates to date utilising a variety of technologies. Most recently, a combined hMPV and parainfluenzavirus type 3 mRNA vaccine candidate has completed Phase I clinical trials in healthy adults; it was well tolerated and produced a functional immune response to both viruses.¹³ Due to the 2020 SARS-CoV-2 pandemic, vaccine research, including clinical trials, for other viral pathogens such as hMPV, has been relatively stagnant.

Strengths of the study were that the investigation was embedded within a PHU that had already developed good viral surveillance systems in place, with ethics approval to report on respiratory virus outbreak data. Weaknesses included only having access to routinely collected data prior to the study period with no comprehensive clinical assessment about the cases in each outbreak.

hMPV is an important cause of morbidity and mortality in the elderly. Our experience has illustrated that a major challenge is the lack of testing for, and awareness of, hMPV as a viral cause of ILI by ACFs, laboratories, and emergency departments, which generally opt for rapid testing only to detect influenza and RSV. There is no licensed vaccine or approved treatment. Our findings highlight the need for additional prevention measures, typically reserved for influenza or SARS-CoV-2 outbreaks, to be extended to the control of other viral respiratory illness in ACFs.

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