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Asymptomatic COVID-19 or are we missing something?

Jazmin K Daniells, Helen L MacCallum, David N Durrheim

Abstract

A closer review of the asymptomatic COVID-19 cases recorded during the first pandemic wave in the Hunter New England area found that seven of the 26 'asymptomatic' patients actually had experienced COVID-19-like symptoms, with five reporting symptoms prior to testing on review of all available clinical records. There is a need to delve deeper into the symptom history of 'asymptomatic' cases than initially recommended in national guidelines.

Introduction

Coronavirus disease 2019 (COVID-19) is a disease caused by the novel coronavirus SARS-CoV-2, which first emerged in late 2019. Australia recorded its first case on 25 January 2020.¹ The Hunter New England Local Health District (HNELHD) provides health care to 920,370 people in regional New South Wales (NSW), Australia.² As of 30 May 2020, HNELHD recorded 279 confirmed cases of COVID-19. Of the 279 cases recorded in the Hunter New England area, 26 were initially recorded as 'asymptomatic'. The focus of Australian testing for all cases during the study period was to find symptomatic cases, with strict clinical and epidemiological criteria needing to be met for a swab to be performed.

Internationally the reported percentage of asymptomatic cases of COVID-19 ranges from 6 to 41%.³ Many of the published reports have not used widespread community testing and have calculated the asymptomatic ratio based on small numbers of tests. For example, one report of 565 Japanese citizens evacuated from Wuhan estimated an asymptomatic rate of 30.8%.⁴ However, in this study only 13 people were swabbed using reverse transcription–polymerase chain reaction (RT-PCR) testing and the asymptomatic ratio was calculated based on four of these people being asymptomatic. Another

study considering the cohort of patients on the Diamond Princess cruise ship estimated that the total number of asymptomatic cases was 17.9%.⁵

There is currently no strong evidence to suggest that asymptomatic transmission is a major contributor to the spread of COVID-19. A meta-analysis and systematic review of asymptomatic transmission found only two studies that described possible forward transmission from asymptomatic cases.³ There are case reports of presumed asymptomatic transmission, including one family cluster in Wuhan, China where the presumed index case had no symptoms or computed tomography (CT) chest changes.⁶ The evidence is more compelling that patients are infectious in the pre-symptomatic period from 2.3 days (95% CI 0.8–3.0 days) before symptom onset, and that this pre-symptomatic transmission plays a more important transmission role than asymptomatic transmission.⁷

Methods

Ethics approval for this project was not required as COVID-19 is a notifiable disease and this is covered by the NSW *Public Health Act 2010*. A case line-list from the Notifiable Conditions Information Management System (NCIMS) that was filtered to include asymptomatic cases was created from the original epidemiological line-list of COVID-19 cases. This captured all

cases from 5 March to 30 May 2020 who, at their initial case interview, reported to be asymptomatic. Each case identified on the line-list was then audited independently by two public health medical officers. NCIMS and the local hospital Clinical Application Portal (CAP) were both reviewed for each case: these sources contain initial case interviews, any hospital presentations or hospital-based care (including HNELHD's COVID-19 community outreach service), close contacts and any follow-up documentation for cases. Cases were not re-interviewed. Each case was closely investigated for symptoms or changes to baseline symptom severity pre- or post-COVID-19 testing, as well as for any evidence of transmission to identified close contacts. Evidence of transmission was any close contact returning a positive COVID-19 RT-PCR swab; close contacts who were co-exposed were excluded.

Results

Of 279 cases of COVID-19 in HNELHD during the first pandemic wave, there were 26 cases initially classified as asymptomatic. Of these 26 cases, five were found to have mild symptoms in the two weeks prior to being swabbed, and another two subsequently developed symptoms in the following 2–5 days (Figure 1). Nineteen cases (19/279; 7%) were truly asymptomatic; thus, over a quarter of the initially identified 'asymptomatic' cases had been misclassified as asymptomatic. Of the truly asymptomatic cases, 9 were female (47%) (Table 1). The asymptomatic patients ranged from 9 to 83 years of age, with the most prevalent group aged 9–18 years ($n = 5$; 26%). Patients who were truly asymptomatic had a range of comorbidities, including those that are recognised as risk factors for more severe COVID-19 disease.

Of all patients initially thought to be asymptomatic: 15 (58%) were swabbed because they were cruise ship passengers; three (11%) were investigated as a part of a family cluster; three (11%) were tested because they were close contacts of cases; for three (11%) the reason for testing

was unclear; one (4%) was tested for international travel clearance; and one (4%) fabricated current symptoms to be tested.

There was no evidence of COVID-19 transmission from an asymptomatic case, though cases were effectively isolated which reduced the potential for transmission.

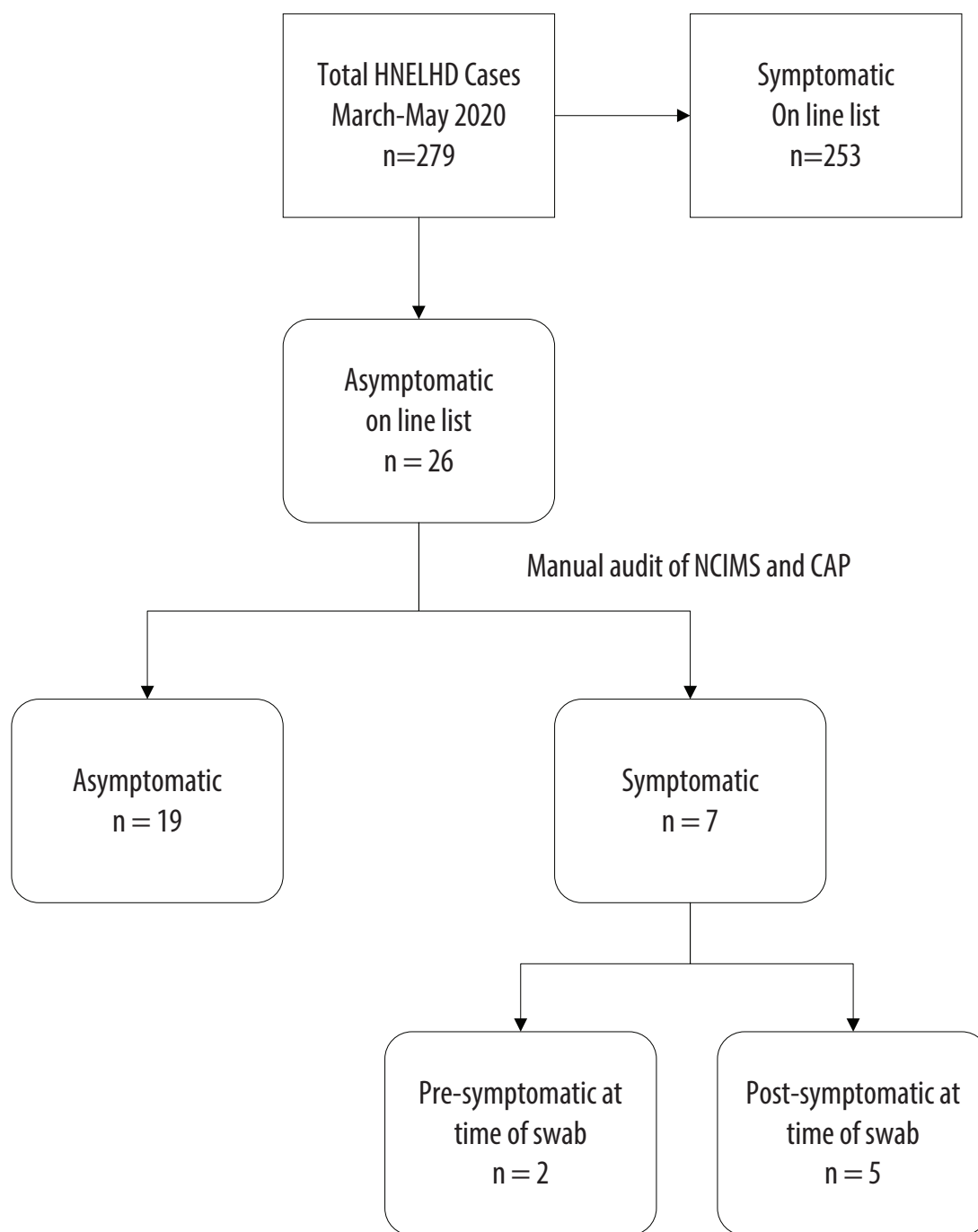
Discussion

The detection of asymptomatic patients within the first wave of COVID-19 in HNELHD was likely underestimated in the context of strict testing criteria focused on fever and/or respiratory symptoms. Despite this, our findings highlight the need to thoroughly investigate the past history of asymptomatic cases, and to also follow these cases forward, to avoid misclassification as asymptomatic. As of 17 June, the SoNG revision (version 3.2) would capture missed symptomology as it directs thorough investigation of asymptomatic cases.¹⁰

During the initial case interviews emphasis was placed on contact tracing to ensure isolation of cases and close contacts. It is possible that mild symptoms that occurred in the days prior (up to 20 days) may have been missed as our case interview questionnaire only prompted for current symptoms (based on the CDNA National Guidelines at the time). The availability of laboratory testing capacity during this period was limited and the public health focus was appropriately on mitigating the risk of ongoing community spread.

We now know that COVID-19 can cause a prolonged period of viral RNA shedding, with a median time of 20 days reported by a cohort study in Wuhan.^{8,9} Due to this, cases who had mild symptoms in the past (which had subsequently resolved) may be inaccurately labelled as asymptomatic. This distinction is important if there is a suspected difference in infectivity of patients with mild symptoms compared to those with no symptoms at all. It would be interesting to review other studies, such as that conducted by Mizumoto et al,⁵ to determine if asympto-

Figure 1: Review of HNELHD asymptomatic cases



matic cases were in fact post-symptomatic, given the long time-frame in which viral RNA can be detected.

We acknowledge that this is a small sample in northern NSW and not representative of all asymptomatic cases, as these cases were tested and detected during a time that symptomatic testing was directed by national guidelines.

Nonetheless, this provides an important insight into disease dynamics within the local community.

There is clear evidence that a significant proportion of infections with SARS-CoV-2 are asymptomatic, including 7% of cases in the HNELHD.³ The implications of this in terms of infectivity and public health risk remain unclear and war-

Table 1: Demographics of truly asymptomatic and misclassified asymptomatic COVID-19 cases, Hunter New England Local Health District, NSW, March–May 2020

Characteristic	Truly asymptomatic cases	Percentage (%)	Misclassified asymptomatic cases	Percentage (%)
Age, years				
Median	37		66	
Range	9–83		19–86	
Age groups				
9–18	5	26	0	0
19–28	2	11	3	43
29–38	2	11	0	0
39–48	0	0	0	0
49–58	0	0	0	0
59–68	2	11	1	14
69–78	4	21	1	14
79–88	4	21	2	29
Sex				
Female	9	47	4	57
Male	10	53	3	43
Comorbidities				
Diabetes	4	21	1	14
Hypertension	4	21	2	29
Cardiovascular disease	2	11	1	14
≥3 Comorbidities	6	32	4	57
Aboriginal status				
Aboriginal or Torres Strait Islander	3	16	0	0
Non-Indigenous	16	84	7	100

rant further investigation. Misclassification of cases as asymptomatic, rather than pre- or post-symptomatic, may warp our understanding of transmission dynamics. To prevent this, the collection of sound surveillance data and thorough investigation of seemingly asymptomatic cases is required. Furthermore, symptom-based screening for COVID-19 — requiring present symptoms at time of testing — may exclude many positive patients; broader testing criteria will be required when the second pandemic wave occurs to accurately capture all cases.

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