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ORIGINAL ARTICLE

COVID-19 in Australia: our national response to the first cases of SARS-CoV-2 infection during the early biocontainment phase

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Key words

COVID-19, SARS-CoV-2, clinical characteristics, models of care, pandemic.

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Abstract

Background: On 31 December 2019, the World Health Organization recognised clusters of pneumonia-like cases due to a novel coronavirus disease (COVID-19). COVID-19 became a pandemic 71 days later.

Aim: To report the clinical and epidemiological features, laboratory data and outcomes of the first group of 11 returned travellers with COVID-19 in Australia.

Methods: This is a retrospective, multi-centre case series. All patients with confirmed COVID-19 infection were admitted to tertiary referral hospitals in New South Wales, Queensland, Victoria and South Australia.

Results: The median age of the patient cohort was 42 years (interquartile range (IQR), 24–53 years) with six men and five women. Eight (72.7%) patients had returned from Wuhan, one from Shenzhen, one from Japan and one from Europe. Possible human-to-human transmission from close family contacts in gatherings overseas occurred in two cases. Symptoms on admission were fever, cough and sore throat (n = 9, 81.8%). Co-morbidities included hypertension (n = 3, 27.3%) and hypercholesterolaemia (n = 2, 18.2%). No patients developed severe acute respiratory distress nor required intensive care unit admission or mechanical ventilation. After a median hospital stay of 14.5 days (IQR, 6.75–21), all patients were discharged.

Conclusions: This is a historical record of the first COVID-19 cases in Australia during the early biocontainment phase of the national response. These findings were invaluable for

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establishing early inpatient and outpatient COVID-19 models of care and informing the management of COVID-19 over time as the outbreak evolved. Future research should extend this Australian case series to examine global epidemiological variation of this novel infection.

Introduction

A novel coronavirus disease (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) spread rapidly worldwide since it was first reported to the World Health Organization (WHO) on 31 December 2019.[1] A COVID-19 pandemic was declared 71 days later.[2,3] Symptoms of COVID-19 infection include fever, cough, sore throat, myalgia and dyspnoea, with risk factors for moderate to severe disease including age, hypertension, diabetes mellitus and other acute or chronic respiratory infections.[4,5] Transmission from asymptomatic carriers has been reported[6–8] and has likely contributed to sustained community transmission. Global efforts to reduce the spread of COVID-19 have included international and national travel restrictions, mandatory quarantine of travellers, close contacts and affected patients, extensive contact tracing, and widespread physical distancing measures. As of 11 August 2020, there have been 20 092 855 confirmed cases and 736 254 deaths globally.[9]

The first confirmed case of COVID-19 in Australia was reported on 25 January 2020.[10,11] As of 11 August 2020, there have been 21 397 confirmed COVID-19 cases and 313 deaths in Australia.[12] Following the peak of COVID-19 cases in Australia in late March 2020, it was reported that approximately 63% of all confirmed cases were acquired overseas.[13] However, recent developments in Victoria (VIC) and New South Wales (NSW) have seen increasing numbers of locally acquired infections, with 50.2% of cases across Australia now linked to a confirmed case.[12] In this paper, we report the clinical features, epidemiological characteristics, laboratory data and outcomes of the first group of 11 patients with laboratory-confirmed COVID-19 associated with recent international travel that presented in NSW, VIC, Queensland (QLD) and South Australia (SA). Patients were treated and managed during the early biocontainment phase of the national response, where patients were mostly managed in hospital and under quarantine following advice from state public health units. These findings form part of an important historical record of the COVID-19 pandemic in Australia.

Methods

Study population and settings

This clinical case series includes 11 patients with laboratory-confirmed COVID-19 who were admitted to four tertiary referral hospitals in four Australian states: NSW, QLD, VIC and SA.

Study design

Retrospective, multi-centre case series

Human research ethics approvals. Human Ethics Research Committee (HREC) ethics approval was obtained from Western Sydney Local Health District HREC (2001-08) and Central Adelaide Local Health Network HREC (12891). The Monash Health HREC (RES-20-0000-150Q) and Gold Coast Hospital and Health Service HREC (LNR/2020/QGC/61587) did not require HREC review. Informed consent was obtained from all 11 patients.

Data collection. Site leads obtained and gathered clinical and laboratory data from all patients using their respective laboratory and hospital-based patient information systems.

Statistical analysis. Descriptive statistical analyses, including median and interquartile range (IQR), were undertaken on continuous variables. Categorical variables were described as percentages and frequency rates. All analyses were performed using SPSS Statistics (IBM SPSS Statistics for Windows, version 26.0, 2019; IBM Corp., Armonk, NY, USA).

Results

Patient demographics

Four patients were admitted in NSW, three were treated in VIC, two were admitted in QLD, and two were managed in SA. The nine patients in NSW, VIC and QLD were admitted to hospital between 23 January and 1 February, and were amongst the first COVID-19 cases in each respective state. The authors were unable to obtain consent from the first two patients with confirmed COVID-19 in SA. The patients included in this study were the third and fourth COVID-19 cases in SA and were admitted in late February to early March. The median age of the patients was 42 years (IQR, 24–53;

range, 21–66), with male and female patients making up 54.5 and 45.5% of the cohort respectively (Table 1).

Epidemiological characteristics

Eight (72.7%) patients had travelled to Wuhan, Hubei Province but had no direct contact with hospitals, the Huanan Seafood Wholesale Market, or cases of COVID-19. SA-11 had travelled to Europe and developed infection upon return but had no known contact with a confirmed case. Human-to-human transmission via close contact was presumed to have occurred for two of the patients while overseas. NSW-2 patient had dined with relatives in Shenzhen, Guangdong province, and later tested positive for SARS-CoV-2. His relatives had recently travelled to Wuhan prior to the family gathering. SA-10 was repatriated to Adelaide from Yokohama, Japan after being diagnosed with COVID-19. Her partner had confirmed COVID-19 infection 1 week prior and was hospitalised in Japan for 3 weeks. Both were passengers from the Diamond Princess, an international cruise ship that was linked to one of the first COVID-19 outbreaks reported outside of China.[14]

Infection prevention and control measures

All patients were admitted and managed using standard, contact and droplet precautions. Airborne precautions were utilised for aerosol-generating procedures. Although not required by jurisdictional public health guidelines, negative pressure rooms were used. In NSW, patients with confirmed COVID-19 were cared for in an intensive care quarantine class (Class Q) negative pressure single room with a dedicated ensuite and separate anteroom. While undergoing investigation, suspected cases or patients with COVID-19 infection of mild severity were housed in a specially requisitioned ward with 11 standard class (Class S) rooms. In QLD, patients were admitted to a 24-bed isolation unit in a negative pressure (Class N) isolation room. In SA, patients were admitted to a 16-bed isolation unit and cared for in Class Q and Class N negative pressure rooms. In VIC, patients were admitted to a single N-class room. VIC-7 was clinically stable and hospital admission was not required. Home isolation was arranged in conjunction with the Victorian Department of Health and Human Services.

Laboratory diagnostics

Nasopharyngeal swabs, combined nose and throat swabs and/or sputum samples were collected under appropriate precautions according to the COVID-19 Communicable Diseases Network Australia (CDNA) National Guidelines for Public Health Units.[15] Blood samples (ethylenediaminetetraacetic acid and serum), urine and faeces were collected in selected patients. Laboratory methods for SARS-CoV-2 testing in each state are summarised in Table 2. In the early stages of the Australian epidemic, most laboratory assays were in-house developed gel-based PCR methods which were yet to be validated to National Pathology Accreditation Advisory Council (NPAAC) standards and were not included on the Australian Register of Therapeutic Goods (ARTG).

All patients met the clinical and epidemiological criteria for suspect cases of COVID-19 as per the CDNA National Guidelines for Public Health Units.[24,25] As such, respiratory samples were collected from all patients on admission. The median duration from onset of symptoms to the first SARS-CoV-2 RNA positive sample was 2 days (IQR, 1–5; range, 0–11). Faecal and urine samples were also sent for SARS-CoV-2 testing in QLD, VIC and SA. Urine samples were negative for SARS-CoV-2 RNA for all seven patients. SARS-CoV-2 viraemia was not detected in blood samples from the two SA patients. However, SARS-CoV-2 was detected in faecal samples from four patients (VIC-7, QLD-8, SA-10 and SA-11). Faecal samples from VIC-7 demonstrated persistent positivity for SARS-CoV-2 from Days 12–17 of her illness, despite the absence of diarrhoea or loose stools. She was asymptomatic by Day 10 of illness, and nose and throat swabs were negative from Day 11. For QLD-8, faecal samples were positive for SARS-CoV-2 on Days 2 and 8 of his illness. This was associated with the presence of loose stools. Faecal samples from SA-10 and SA-11 tested positive for SARS-CoV-2 on Days 6 and 7 of their illness and both reported diarrhoea and loose stools. However, the relative viral load measured by SARS-CoV-2 real-time reverse transcriptase–polymerase chain reaction (RT-PCR) cycle threshold (Ct), showed that Ct values in faecal samples were higher than that of respiratory samples in these patients, suggesting that faeces was likely to have lower SARS-CoV-2 viral load compared to respiratory samples. The median duration from onset of symptoms to the first SARS-CoV-2 negative sample (nose and throat swabs) was 12 days (IQR, 3.50–15.75; range, 1–35).

Clinical characteristics

VIC-7 presented to Monash Medical Centre on Day 3 of illness and self-quarantine at home. Apart from a temperature of 37.8°C, other investigations were unremarkable. The patient was discharged to home isolation, with community monitoring by the Department of Health and Human Services Victoria. The other

Table 1 Clinical characteristics of patients on admission

Characteristic	No. patients (*n* = 11)
No. patients at each site	
NSW	4
VIC	3
QLD	2
SA	2
Median age (IQR) (years)	42 (24–53)
Sex, *n* (%)	
Male	6 (55)
Female	5 (45)
Travel history (*n*)	
None	0
Travel to China	
Wuhan, Hubei Province, *n* (%)	8 (73)
Other cities/provinces in China	1
Travel to Europe	1
Travel to other regions	1
Direct contact with a confirmed COVID-19 case, *n* (%)	
Yes	2 (18)
No	9 (82)
Co-morbidities	
None, *n* (%)	6 (55)
Hypertension, *n* (%)	3 (27)
Hypercholesterolaemia, *n* (%)	2 (18)
Fatty liver	1
Type 2 diabetes mellitus	1
Gout	1
Former smoker	1
Hypothyroidism	1
Anxiety	1
Signs and symptoms, *n* (%)	
Fever	9 (82)
Cough	9 (82)
Sore throat	9 (82)
Fatigue	8 (73)
Diarrhoea or loose stools	7 (64)
Myalgia	6 (55)
Chills	4 (36)
Headache	3 (27)
Nasal congestion	2 (18)
Dyspnoea	2 (18)
Nausea	2 (18)
Backache	2 (18)
Vital signs on admission	
Temperature, median (range) (°C)	37.8 (37.3–38.4)
Pulse rate, median (range) (b.p.m.)	99 (90–109)
Respiratory rate, median (range) (b.p.m.)	18 (16–20)
Oxygen saturation on room air, *n* (%) (SaO_2)	
≥95%	9 (82)
90–94%	2 (18)
Chest radiograph (CXR) and chest computed tomography (CT) scan, *n* (%)	
CXR performed	8 (73)
CT scan performed	4 (36)
Radiological abnormality	7 (64)
Bilateral involvement	5 (45)
Peripheral ground-glass opacities	4 (36)
Onset of symptoms (days) to:	

Table 1 *Continued*

Characteristic	No. patients (n = 11)
Hospital admission, median (IQR)	4.5 (1.0–6.5)
Home isolation, median	3†
Onset of symptoms to first SARS-CoV-2 positive sample, median (IQR) (days)	2 (1–5)
Onset of symptoms to SARS-CoV-2 clearance‡, median (IQR) (days)	12 (3.50–15.75)
Onset of symptoms to discharge, median (IQR) (days)	
Hospital admission	14.5 (6.75–21)
Home isolation	22†

†One case only (VIC-7). ‡Date when respiratory sampling was first found to be negative. IQR, interquartile range.

Table 2 SARS-CoV-2 laboratory testing and methods

	NSW	QLD	VIC	SA
Testing laboratory	Centre for Infectious Diseases and Microbiology Laboratory Services (CIDMLS), NSW Health Pathology, Institute for Clinical Pathology and Medical Research (ICPMR)	Public Health Virology, Forensic and Scientific Services (FSS), Health Support Queensland	Victorian Infectious Diseases Reference Laboratory (VIDRL)	South Australia Pathology (SA Pathology)
Clinical specimens collected	Nasopharyngeal, combined nose and throat, sputum	Nasopharyngeal, pharynx swab, aspirate, sputum, faeces	Nasopharyngeal, sputum, urine, faeces, serum	Nasopharyngeal, combined nose and throat, sputum, blood, urine, faeces
SARS-CoV-2-specific assay	E gene[16]	ORF1ab region[17] and E gene[16]	In-house RdRP and pancoronavirus PCR[11,18]	E and RdRp genes[16]
Confirmatory testing	Sanger sequencing of amplicon to confirm 100% homology with published genome[19] (performed at VIDRL) and whole genome sequencing (performed at CIDMLS, ICPMR)	Sanger sequencing of RdRp gene[20,21] and whole genome sequencing[22]	Sanger sequencing and whole genome sequencing	N/A
Multiplex PCR testing for other respiratory pathogens	Yes; comprising influenza A, influenza B, parainfluenzaviruses 1–3, respiratory syncytial virus, human metapneumovirus, adenovirus, rhinovirus and enterovirus[23]	N/A	N/A	Yes; comprising influenza A, influenza B, parainfluenzaviruses 1–3, respiratory syncytial virus, human metapneumovirus, adenovirus, rhinovirus, *Mycoplasma pneumoniae* and *Bordetella pertussis*

N/A, not applicable; PCR, polymerase chain reaction.

10 patients were all admitted to hospital. On admission, the three most common symptoms were fever (n = 9; 81.8%), cough (n = 9; 81.8%) and sore throat (n = 9; 81.8%), followed by fatigue (n = 8; 72.7%), diarrhoea or loose stools (n = 7; 63.6%), and myalgia (n = 6; 54.5%). Headache, nasal congestion, dyspnoea and coryza were uncommon (Table 1). The median duration from symptom onset to hospital admission was 4.5 days (IQR, 1.0–6.5; range, 0–10).

Five patients had underlying comorbidities. Three (27.3%) patients had hypertension and two (18.2%) had hypercholesterolaemia. Other chronic medical conditions included type two diabetes mellitus, gout, fatty liver, hypothyroidism and anxiety. One patient was a former smoker. Admission laboratory testing results are shown in Table 3. Almost all test results are within laboratory reference ranges. The median C-reactive protein reading at 13.3 mg/L (IQR, 4.0–47.0 mg/L) was mildly elevated. Mild lymphopenia was also observed (median, 1.14×10^9/L; IQR, $0.80–1.63 \times 10^9$/L).

Clinical illness was mild for most patients in this Australian clinical case series, as per the WHO guidelines,[26] with none developing severe acute respiratory distress syndrome and/or requiring mechanical ventilation (see

Table 3 Laboratory findings of patients on admission

Laboratory test	Laboratory reference range	Median (IQR)
Alanine aminotransferase (U/L)	5–40	27 (15–39)
Aspartate aminotransferase (U/L)	5–35	25.5 (16.5–50.5)
Gamma-glutamyl transpeptidase (U/L)	5–50	27 (13–72)
Alkaline phosphatase (U/L)	30–110	71 (49–81)
Albumin (g/L)	32–45	39 (37–41)
Creatinine (μmol/L)	45–110	66 (60–76)
White blood cell count ($\times 10^9$/L)	4–11	4.83 (3.76–5.30)
Neutrophil count ($\times 10^9$/L)	2.0–7.5	2.79 (2.20–3.64)
Lymphocytes count ($\times 10^9$/L)	1.5–4.0	1.14 (0.80–1.63)
C-Reactive protein (mg/L)	0–5	13.3 (4.0–47.0)

IQR, interquartile range.

Supporting Information Appendix S1 for individual clinical case narratives). Nine of the cases had radiologic studies performed. Seven of these had abnormal chest radiography with bilateral lung involvement in five, and classic peripheral ground glass opacities was demonstrated in four patients (Fig. 1). VIC-5 required nasal prong oxygen therapy at flow rate of 3 L after he became increasingly hypoxic on day three of admission. Antimicrobial therapy was prescribed to four patients (36.4%), with ceftriaxone and azithromycin given to two, oral amoxicillin and clavulanic acid to one, and piperacillin-tazobactam to another. QLD-8 was commenced on oral lopinavir-ritonavir on Day 7 of illness following a persistent fever (on admission: 38.8°C; peak at Day 7: 39.4°C) which resolved after 4 days. His initial symptom was diarrhoea but also developed rhinorrhea, mild hypoxia, cough and chest discomfort during hospitalisation.

Outcomes and discharge disposition

The discharge criteria for the patients in this series were developed *de novo* and evolved over time to reflect those later set out in the COVID-19 Series of National Guidelines.[27] Initially this comprised of resolution of all acute symptoms for the previous 24 h and two consecutive negative SARS-CoV-2 PCR of results from combined nasopharyngeal and throat swabs taken at least 24 h apart. The median duration from onset of symptoms to discharge was 14.5 days (IQR, 6.25–21; range, 5–25). At the time of writing, all 11 patients were discharged and/or released from isolation and were well at post-discharge reviews.

Discussion

This multi-state clinical case series describes the clinical and epidemiological features, laboratory data, and outcomes of 11 patients with COVID-19 disease in Australia during the early biocontainment phase of the national response. This clinical case series follows the reporting of the first diagnoses of COVID-19 in Australia.[11]

The impact of widespread international travel has been reflected in the rapid international spread of COVID-19. The first recorded case outside of China was reported on 13 January 2020 in Thailand from an individual who had travelled from Wuhan.[28] The nine patients who were admitted between 23 January and 1 February 2020 to NSW, VIC and QLD were the first cases of COVID-19 in each respective state. These patients were among the first 10 cases of COVID-19 in Australia. Eight of these patients had recently travelled to Australia from Wuhan, the initial epicentre of infection. The other patient had travelled from Shenzhen, China. None had attended or had direct epidemiological links to The Huanan Seafood Wholesale Market, which was directly linked to the majority of the earliest described cases of COVID-19.[15,29] The two SA patients in this study were admitted in late February to early March. SA-10 was diagnosed in Japan and was repatriated to Adelaide. There was presumed human-to-human transmission as her partner was diagnosed in Japan 1 week earlier. Both were passengers on the Diamond Princess cruise ship in Yokohama that was linked to an outbreak of 700 cases of COVID-19.[30–32] Thus, it is possible that SA-10 was exposed to other COVID-19 contacts onboard. The recent overseas travel history for SA-11 included London, Rome, Paris and Amsterdam. France reported three cases of COVID-19 from returned travelled from Wuhan on 24 January, marking the first confirmed cases in Europe.[33]

The median age of our patient cohort was 42 years. Data published by the Australian COVID-19 National Incident Room Surveillance Team indicate that prior to April 2020, the median age of confirmed cases in Australia was 47 years (IQR, 29–62).[34] Similar to our cohort, cases of COVID-19 across male and female groups are relatively equal. The clinical characteristics and laboratory findings in this report correlate with other published international COVID-19 case series.[29,35–39] The most reported symptoms were fever, cough and sore throat. None of the patients in this study required intensive care unit (ICU) admission and/or mechanical ventilation. Critically ill patients requiring ICU admission and mechanical ventilation had a higher median age of 60–65 years[36,38,40] and had several co-morbidities, which may account for more of the severe clinical outcomes seen with advanced age. Hypertension and type two diabetes mellitus are the top two most reported co-morbidities in COVID-19 patients.[41]

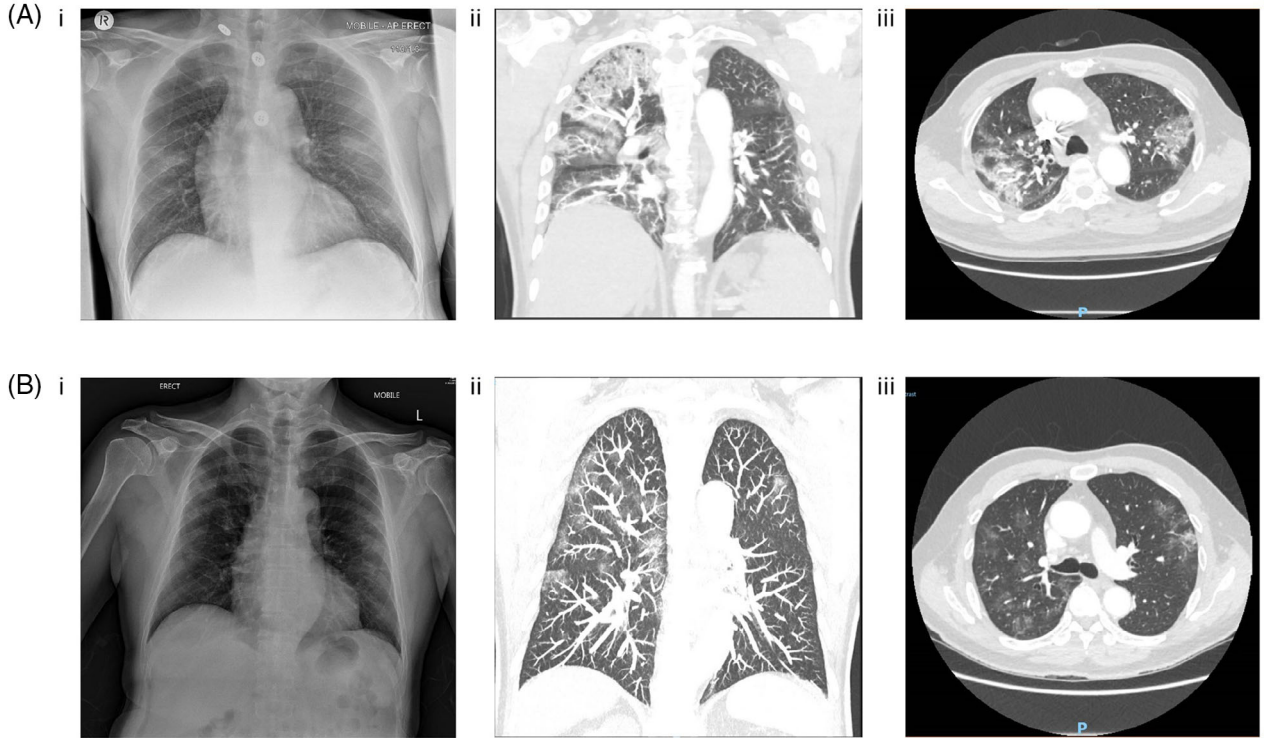

Figure 1 Chest radiographs and computed tomography (CT) images of the two patients from Victoria (VIC-5 and VIC-6) with COVID-19. (A): (i) Chest radiograph on admission demonstrating subtle ill-defined opacities within the mid zones bilaterally and left lower zone; (ii) Day 4 chest CT (coronal maximum intensity projection, MIP); and (iii) Day 4 chest CT axial demonstrating extensive ground-glass opacities in a peribronchovascular and peripheral distribution favouring mid to upper zones of the lungs. (B): (i) Chest radiograph on Day 6 demonstrating patchy opacity within the lateral aspect of the right upper lobe; (ii) Day 11 chest CT (coronal MIP); and (iii) Day 11 chest CT axial images demonstrating bilateral peripheral upper zone predominant ground-glass opacities (more on the right).

Current clinical management in Australia consists of supportive care and appropriate infection prevention and control measures.[27,42] QLD-8 presented with ongoing high-grade fever on Day 7 of his illness and was treated with lopinavir–ritonavir (antiviral therapy) and intravenous piperacillin/tazobactam. His fever finally resolved on day 11 of illness. Current Australian guidelines do not recommend the use of lopinavir-ritonavir outside of randomised trials with appropriate ethics approval.[42] International randomised trials have currently concluded that there is no clinical benefit in using lopinavir-ritonavir in hospitalised COVID-19 patients.[43-45]

Diagnostic testing for SARS-CoV-2 RNA by RT-PCR is primarily performed on nasopharyngeal swabs, combined nose and throat swabs, and sputum samples. Our findings reported the median duration from onset of symptoms to the first SARS-CoV-2 positive respiratory sample was 2 days. Median documented clearance of SARS-CoV-2 from respiratory samples was 12 days from symptom onset. Studies from Singapore and China have observed viral clearance by Days 10–12 post-onset, with mild cases having an early viral clearance.[37,46] Two patients in this case series had blood samples collected and none had SARS-CoV-2 RNA detected by RT-PCR. This correlates with the fact that neither patient developed severe acute respiratory distress, required ICU admission or mechanical ventilation. This is also consistent with published studies correlating blood viral load (RNAaemia) with disease severity.[47,48] Studies have also reported the presence of SARS-CoV-2 in faecal samples.[49] Faecal samples were collected from the seven patients in VIC, QLD and SA and samples from four patients were positive for SARS-CoV-2 RNA. These SARS-CoV-2 RNA positive samples correlated with days 12–17 of illness for VIC-7, Days 2 and 8 for QLD-8, and Days 6 and 7 of illness for SA-10 and SA-11 respectively. VIC-7 did not have any gastrointestinal symptoms yet the detection of virus in the faecal samples lasted up to 6 days after her last negative respiratory sample. One study found that faecal samples remained SARS-CoV-2 positive for an average of 11 days after respiratory tract

samples became negative.[49] The significance of ongoing PCR positivity in faecal samples of patients after resolution of symptoms is unclear in the absence of viral culture. As demonstrated in our patients, presence of SARS-CoV-2 in faeces did not correlate with more severe gastrointestinal symptoms or clinical severity.[50,51]

All 11 patients were discharged in accordance with jurisdiction public health requirements, with a median length of hospitalisation of 14.5 days. Clinical case series from China, South Korea and the United States have reported a similar median duration of hospitalisation of 12–17 days.[38,52,53] We note that in the early biocontainment phase of the COVID-19 outbreak in Australia, patients who would ordinarily have met clinical criteria for discharge, remained in hospital for quarantine purposes under direction from state-based public health units. Post-discharge, there were no reported secondary cases or any healthcare-worker acquisition from these 11 patients.

As of 11 August 2020, there have been 21 397 confirmed COVID-19 cases and 313 deaths in Australia.[12] Historical data from Australian states and territories reveal that the main epidemiological risk factors for confirmed COVID-19 cases in Australia were travel to Iran, Europe or the Americas or related to cruise ships.[13,54,55] Large-scale public health interventions such as travel restrictions, early and widespread testing and contact tracing, and strict quarantine and physical distancing measures[56,57] implemented by jurisdictional public health authorities and the Australian Government has successfully mitigated widespread community transmission of COVID-19. There has been recent resurgence of COVID-19 cases in Victoria and New South Wales, with increasing number and proportion of cases reported as being locally acquired.[58] Case clusters involving 30 to over 660 people have been reported in cruise ships, residential aged care facilities, hotels, workplaces and hospitals around Australia.[59–62]

Conclusion

In this paper, we report the first clinical case series of COVID-19 in Australia during the early biocontainment phase of the national response. The authors acknowledge that one of limitations of this study is our small case size of 11 patients. However, this clinical and laboratory data were collected from four independent states in Australia, providing a historical record of the first cases of COVID-19 prior to the Australian peak at the end of March 2020. As the COVID-19 pandemic evolves on a rapid scale, these findings from the Australian perspective are critical to the global reporting of this disease.

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Supporting Information

Additional supporting information may be found in the online version of this article at the publisher's web-site:

Table S1. Individual patient clinical characteristics and laboratory findings.
Appendix S1. Individual clinical case narratives.