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ORIGINAL ARTICLE

Characteristics and outcomes of SARS-CoV-2 infection in Victorian children at a tertiary paediatric hospital

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Aim: Victoria experienced two 'waves' of COVID-19 between March and September 2020 and more cases than any other jurisdiction in Australia. Although world-wide reports of COVID-19 reflect that children are less likely to experience severe disease compared with adults, hospitalisations and deaths have been reported. We report testing and outcomes of children with SARS-CoV-2 infection presenting to a tertiary paediatric hospital in Melbourne.

Methods: We conducted a prospective cohort study at The Royal Children's Hospital (RCH), including all children and adolescents (aged 0–18 years) who presented and were tested for SARS-CoV-2 over a 6-month period, between 21 March 2020, up to the 21 September 2020. Detailed epidemiological and clinical data were recorded.

Results: A total of 19 708 tests for SARS-CoV-2 were performed in 14 419 patients. One hundred and eighty patients tested positive for SARS-CoV-2 (1.2%). 110 (61%) were symptomatic, 60 (33%) were asymptomatic and 10 (6%) were pre-symptomatic. Close contacts of a positive case were associated with a higher risk of a testing positive for SARS-CoV-2 (120/2027 (6%) vs. 60/14589 (0.4%), RD 5.5 (95% CI 4.5 to 6.5), $P < 0.001$). Eighteen (10%) SARS-CoV-2-positive patients were admitted to hospital with one patient requiring intensive care. All patients recovered fully with no deaths.

Conclusion: In Victorian children presenting to a tertiary hospital, SARS-CoV-2 infection caused predominantly mild or asymptomatic infection, with most children not requiring hospitalisation.

Key words: COVID-19; general paediatrics; infectious disease.

What is already known on this topic

1 SARS-CoV-2 causes less severe disease in children than adults, however some children require hospitalization

What this paper adds

1 Most children with SARS-CoV-2 had mild disease, and 30% were asymptomatic.
2 Hospitalisation of children who had COVID-19 was rare, and of those, very few required medical intervention, with no deaths.

The global pandemic from coronavirus disease 2019 (COVID-19) has caused almost 200 million confirmed cases world-wide.[1] In most countries or cohorts where COVID-19 cases were reported, children made up less than 5% of overall cases[2–4] apart from in the USA where the proportion was 8.6%.[5] Victoria (population 6.3 million), Australia, has experienced two 'waves' of COVID-19 and has taken a public health approach of aggressive suppression[6] with freely available testing encouraged for any person and mandatory testing of confirmed contacts of COVID-19. The first wave between March and April was characterised by infections in predominantly overseas arrivals. The second wave from June to September was represented by local, community-based transmission. In Australia until September 2020, Victoria had 73% (20 345/27 789) of all confirmed cases of SARS-CoV-2 and 86% (3261/3789) of all cases amongst children and adolescents.[7] Sixteen percent (3261/20345) of those who tested positive for SARS-CoV-2 in Victoria were under the age of 19.[7]

Reports of COVID-19 reflect that children are less likely to experience severe disease compared with adults.[8,9] Most children experience mild or asymptomatic infection with symptoms typical of acute respiratory infections.[3,10] Children are less likely than adults to become hospitalised or require intensive care.[10–13] However, children appear at higher risk of severe disease if aged less

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than 1 month, male or with pre-existing medical conditions.[14,15] Children with severe disease may present with a relatively brief illness duration and atypical symptoms.[15] Up until April 20, 2021, there had been 297 cumulative child deaths in the USA representing 0.06% of total deaths.[16] Deaths have been reported in Brazil[17] and Italy,[18] mostly in children with comorbidities.

More information is needed to describe the presentation, clinical course and outcomes of COVID-19 in children, in particular amongst Australian children. Here we report testing and outcomes of children SARS-CoV-2 in children presenting to a tertiary paediatric hospital in Victoria.

Methods

Study design and participants

We conducted a prospective cohort study at The Royal Children's Hospital (RCH), a large tertiary paediatric hospital in Melbourne, Australia. We used similar methodology to a previously published paper from the first month of the pandemic.[14] We included all paediatric patients (aged 0–18 years) who were tested for SARS-CoV-2 from the first positive confirmed case at RCH (21 March 2020), for 6 months until 21 September 2020, corresponding with the epidemiologic peaks in Melbourne.[19] Testing sites included patients presenting to a dedicated walk-in testing clinic (Respiratory Infection Clinic (RIC)), Emergency Department (ED), Hospital in the Home and inpatient wards. We also included patients who were admitted to RCH (> 4 h in hospital), those treated for COVID-19 who tested positive at an external location or by an RCH outbreak investigation outreach team. Admitted patients were followed up and outcomes were collected at discharge and from follow-up at a dedicated COVID-19 clinic. Ethics approval was obtained from the institutional human research and ethics committee (RCH HREC 62062).

Procedures

At the RCH since early March, any patient presenting to the ED or RIC underwent COVID-19 screening questions according to Victorian Department of Health and Human Services guidelines.[19] Patients who attended the RIC were asked to complete a questionnaire to report epidemiological risk factors, symptoms and comorbidities. The decision to admit or discharge a patient was made on clinical grounds.

Combined nasopharyngeal and oropharyngeal or deep nasal and oropharyngeal flocked swabs with or without viral transport medium (as available) were processed at the RCH molecular microbiology laboratory. SARS-CoV-2 nucleic acid detection was performed using LightMix Modular SARS and Wuhan CoV *E*-gene assay (TIB Molbiol, Berlin, Germany) and the AusDiagnostics Respiratory Pathogens 16-well assay (Ausdiagnostics, Mascot, Australia).

Demographic data, presenting symptoms and history, risk factors, underlying comorbidities, examination findings, laboratory testing and imaging, were obtained from the electronic medical records. Outcomes from hospital admission, or dedicated COVID-19 follow-up clinic, if required, were included. Each record was reviewed for all SARS-CoV-2-positive patients, whilst a summary extraction was performed for SARS-CoV-2-negative patients. These data were entered into a Research Electronic Data Capture (REDCap) database.[20]

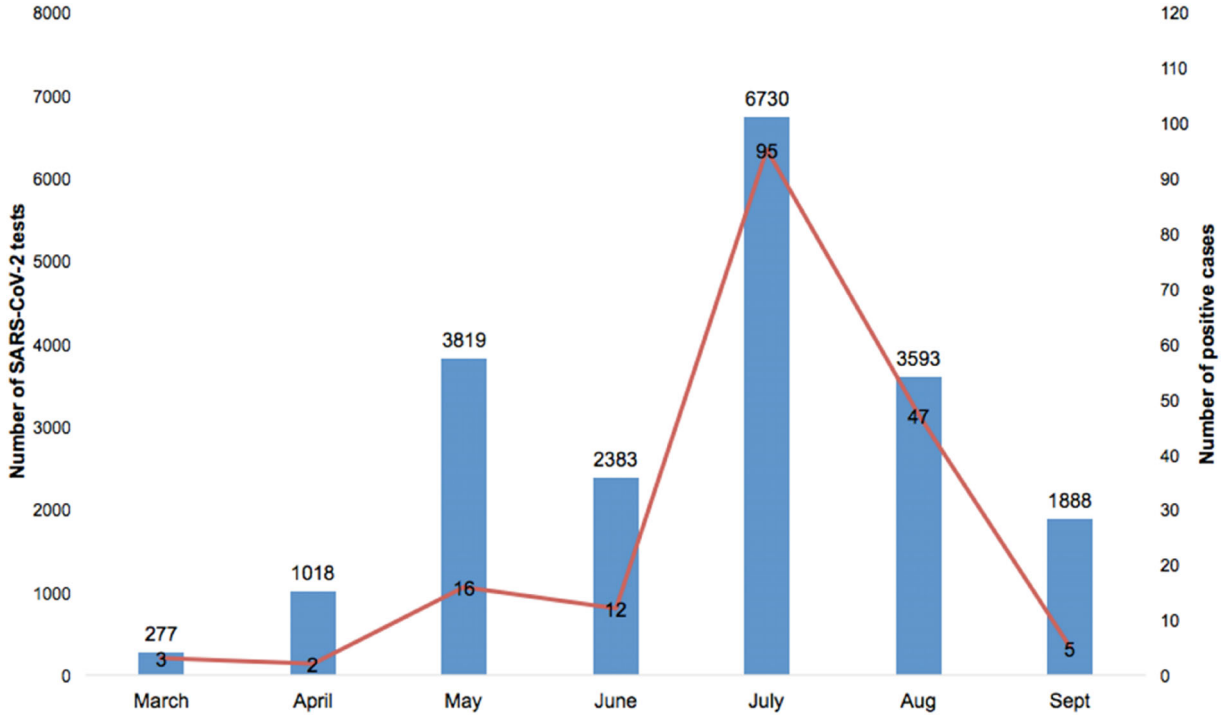

Fig 1 Number of SARS-CoV-2 tests and SARS-CoV-2-positive cases by month. (■) SARS-CoV-2 tested and (——) SARS-CoV-2 positive.

Statistical analysis

We presented continuous variables as mean (SD) and categorical variables as numbers (%). We compared means of continuous variables between groups using independent group t tests when values were normally distributed; otherwise, we used the Mann–Whitney U test. We compared proportions for categorical variables between groups using χ^2. We judged a two-sided α less than 0.05 statistically significant. All data analyses were done with Stata IC version 15.1 (StataCorp, College Station, TX, USA).

Results

Over a 6-month period from 21 March 2020 to 21 September 2020, 19 708 tests for SARS-CoV-2 were performed in 14 419 patients. A total of 14 419 (73%) patients were tested once, 3098 (16%) patients were tested twice, and 2212 (11%) were tested three or more times. The number of tests performed and positive cases both peaked in July (Fig. 1). Stratified by age groups, 2051 (14%) were less than 1 year, 7903 (55%) were 1–5 years, 2608 (18%) were 5–10 years, 1857 (13%) were more than 10 years (Table 1). Totally 2574 (18%) of 14419 tests were in hospitalised patients.

SARS-CoV-2-positive patients

One hundred and eighty patients tested positive for SARS-CoV-2 (see Table 1). The location of testing for positive results was: RIC (n = 121, 67%), ED (n = 39, 22%), home through the Hospital-in-the-Home service (n = 10, 6%), hospital inpatient wards (n = 4, 2%), community sites through outreach testing (n = 3, 2%) and other hospitals and other sites within RCH (n = 3, 2%). With regards to epidemiological risk factors, there were 120 (67%) of180 positive patients with a history of close contact, 86 (72%) of whom were through household contact and 5 (3%) had a history of recent overseas travel.

At the time of testing positive, 60 (33%) of 180 patients were asymptomatic. Ten (6%) were pre-symptomatic and subsequently developed symptoms. The median time to developing symptoms for these pre-symptomatic patients was 2 days (range 2–11 days). In the 14 days prior to testing positive, there were 16 (9%) of 180 patients who tested negative.

Most of the 180 patients with COVID-19 had either fever (n = 47, 26%) or respiratory tract symptoms (n = 102, 56%). Headache was reported by 21 (12%) patients. Comorbidities were present in 25 (14%) of positive patients: asthma (n = 9), heart disease (n = 6), prematurity (n = 2), diabetes mellitus (n = 2), immunosuppressed (n = 5) and developmental delay (n = 1).

Hospitalised SARS-CoV-2-positive patients

Eighteen (10%) SARS-CoV-2-positive patients were admitted to hospital and median age was 1.8 years (IQR 4.8 months to 10 years). Of these, four were observed in ED short stay (between 5 and 10 h), one was admitted for observations at home under HITH, nine were admitted to the hospital wards and one patient was transferred directly to the paediatric intensive care unit (PICU) from a different hospital. The remaining three were inpatients who were admitted for non-COVID-19 reasons and subsequently tested positive whilst

Table 1 Epidemiological and clinical features of children stratified by COVID-19 status

	Total	SARS-CoV-2 positive	SARS-CoV-2 negative		
	No. (%)	No. (%)	No. (%)	Risk or mean difference (95% CI)	*P* values
Demographics					
Total patients (*n*)	14 419	180 (1)	14 239 (99)		
Female	6651 (46)	82 (46)	6569 (46)	−0.00 (−0.1 to 0.1)	0.88
Age less than 1 year	2051 (14)	31 (17)	2020 (14)	0.02 (−0.0 to 0.1)	0.24
Age 1 to 5 years	7903 (55)	89 (49)	7814 (55)	−0.04 (−0.1 to 0.0)	0.22
Age 6 to 10 years	2608 (18)	29 (16)	2579 (18)	−0.01 (−0.1 to 0.0)	0.51
Age more than 10 years	1857 (13)	31 (17)	1826 (13)	0.03 (−0.0 to 0.1)	0.12
Admitted to hospital	2574 (18)	18 (10)	2559 (17)	−0.08 (−0.04 to −0.12)	<0.001
Admitted to Intensive Care	498 (6)	2 (1)	498 (3)	−0.02 (−0.04 to −0.01)	0.10
Deaths	5 (<1)	0	5 (<1)	−0.00 (−0.00 to −0.00)	0.80
Risk factors present at time of test					
Contact with positive case	2027/16616 (12)	120 (67)	1907/16436 (12)	0.55 (0.48 to 0.62)	<0.001
Shared closed space for ≥2 h		10 (6)	N/A	N/A	N/A
Household member		86 (48)			
Close contact in school/childcare		24 (13)			
Exposure to known outbreak		1 (1)			
Overseas travel in last 14 days	43/19657 (<1)	5 (1)	38/19477 (<1)	0.02 (0.00 to 0.05)	<0.001
Symptoms present at time of test					
Fever (37.5° Celsius or more)/ chills	4855 (30)	47 (39)	4810/16097 (30)	0.09 (0.00 to 0.18)	0.03
Respiratory symptoms	10 623 (65)	101 (56)	10 522/16089 (65)	−0.09 (−0.17 to −0.02)	0.009
Asymptomatic	2450 (15)	60 (33)	2390/16097 (15)	0.18 (0.12 to 0.25)	<0.001

Table 2 Characteristics of non-hospitalised patients who attended Respiratory Infection Clinic

	Total	SARS-CoV-2 positive	SARS-CoV-2 negative		
	No. (%)	No. (%)	No. (%)	Risk or mean difference (95% CI)	*P* values
Total patients	6736	165 (2)	6571 (98)		
Total tests	8708	189 (2)	8519 (98)		
Female	3199 (48)	76 (47)	3123 (48)	−0.01 (−0.1 to 0.1)	0.71
Age less than 1 year	467 (7)	26 (16)	441 (7)	0.10 (0.0 to 0.1)	<0.001
Age 1 to 5 years	7903 (55)	84 (51)	4079 (62)	−0.11 (−0.2 to −0.0)	0.004
Age 6 to 10 years	2608 (18)	27 (16)	1300 (20)	−0.03 (−0.1 to 0.0)	0.51
Age more than 10 years	779 (12)	28 (17)	751 (11)	0.06 (−0.0 to 0.1)	0.03
Risk factors					
Close contact	1738 (20)	113 (68)	1625 (19)	0.49 (0.4 to 0.56)	<0.001
Overseas travel		3 (2)	14 (0.1)	0.02 (−0.0 to 0.04)	<0.001
Symptoms					
Asymptomatic	2450 (28)	65 (42)	2385 (28)	0.14 (0.06 to 0.22)	<0.001
Cough	3667 (42)	68 (59)	3599 (42)	0.16 (0.07 to 0.25)	<0.001
Runny/stuffy nose	4415 (51)	68 (44)	4347 (51)	−0.07 (−0.15 to 0.01)	0.07
Sore throat	1439 (16)	22 (20)	1417 (17)	0.31 (−0.04 to 0.11)	0.32
Headache	437 (5)	17 (15)	420 (5)	0.06 (0.01 to 0.11)	<0.001
Muscle ache	131 (11)	4 (3)	127 (1)	0.01 (−0.01 to 0.03)	0.27
Fever or chills	1239 (14)	45 (39)	1194 (14)	0.25 (0.16 to 0.34)	<0.001
Diarrhoea	207 (2)	0	207 (2)	−0.02 (−0.03 to −0.02)	0.04
Anosmia	25 (1)	1 (<1)	31 (<1)	0.00 (−0.01 to 0.02)	0.25
Comorbidities					
Any comorbidity	617 (7)	18 (11)	599/8413 (7)	0.04 (−0.01 to 0.01	0.06
Asthma	398 (5)	9 (6)	389 (5)	0.01 (−0.02 to 0.05)	0.36
Immunosuppression/malignancy	277 (3)	3 (2)	274 (3)	−0.01 (−0.03 to 0.01	0.31
Prematurity	56 (1)	1 (1)	55 (1)	0.01 (−0.01 to 0.02)	0.43
Cardiac	44 (1)	4 (2)	40 (0.5)	0.25 (−0.00 to 0.51)	<0.001
Developmental delay/cerebral palsy	53 (1)	0	53 (1)	−0.00 (−0.01 to 0.01)	0.98

hospitalised. One patient was exposed by a confirmed positive parent. Despite comprehensive investigation for two other inpatients, a confirmed exposure source was not identified.

The median length of stay in hospital was 2 days (IQR 1–6 days). The majority of hospitalised patients only required observations ($n = 7$) and hydration support ($n = 2$) or treatment for a comorbid condition ($n = 8$). One patient with congenital cardiac disease required intensive care, for respiratory and inotropic support for 48 h, and received remdesivir, tocilizumab, dexamethasone and intravenous immunoglobulins with a 29-day total length of stay.[21]

Of the 25 children with comorbidities who tested positive to SARS-CoV-2, eight (32%) of 25 were hospitalised versus 10 (6%) of 155 without comorbidities who were hospitalised (RD 25.5 95% CI 6.9 to 44.4, $P < 0.001$). These comorbidities were: congenital cardiac defect ($n = 2$), immunosuppression/malignancy ($n = 2$), prematurity ($n = 2$), diabetes mellitus ($n = 1$), developmental delay ($n = 1$) and reactive airways ($n = 1$).

Comparison of SARS-CoV-2-positive patients to SARS-CoV-2-negative patients

With regards to epidemiological risk factors, being a close contact of a positive case was associated with a higher risk of a positive SARS-CoV-2 test (120/2027 (6%) close contacts testing positive vs. 60/14589 (0.4%) non-close contacts testing positive, RD 5.5 (95%CI 4.5 to 6.5), $P < 0.001$). Fever was recorded in a higher proportion of SARS-CoV-2-positive patients but respiratory symptoms were higher in SARS-CoV-2-negative patients. For non-hospitalised patients who attended the RIC (Table 2), there were two distinguishing clinical features, which were headache and fever/chills. Headache was present in 17 (15%) of 116 SARS-CoV-2 patients and 420 (5%) of 8538 non-COVID-19 patients ($P = <0.001$). Presence of comorbidities was no different between the groups (18/165 (11%) vs. 599/8413 (7%), $P = 0.06$).

Discussion

Despite a sustained period of SARS-CoV-2 community transmission in Victoria, our description of paediatric cases at a tertiary hospital reveals most children had mild disease and 33% of those who tested positive for SARS-CoV-2 were asymptomatic. Only 1% of children required hospitalisation or intensive care. Children with comorbidities were over-represented amongst the hospitalised patients, although these numbers were small. Of those children hospitalised, most received only supportive therapy, and all made a full recovery.

Our finding of predominantly mild or asymptomatic infection in children with few hospitalisations is similar to international reports in children.[13] Children with comorbidities and younger children are usually considered at special risk of severe disease from viral lower respiratory tract infections.[22] However, COVID-19 appears to rarely impact younger children, and few infants required hospitalisation or intensive care in this cohort. Hypotheses for this difference in immune response for COVID-19 are evolving[23] and include partial protection from other coronaviruses, which are more common in children,[24] and a protective difference in innate response of children compared with adults.[25]

Symptom profiles did not distinguish COVID-19 from other infections. Identifying differences in disease profile, clinical severity and transmission will be important with emerging variants of concern emerge such as Delta. Asymptomatic infection was identified in 33% of patients. The true burden of asymptomatic infection in children and its significance with respect to onward transmission is not known. The lack of unique clinical features and high proportion of asymptomatic patients underscores the importance of testing to identify SARS-CoV-2 infection. In Victoria, contact tracing and mandatory testing of asymptomatic close contacts is likely to have identified more asymptomatic cases than in settings where testing is directed to more unwell or hospitalised patients. A study from South Korea where a large-scale, aggressive contact tracing and testing programme was used identified that 22% (20/91) of infected children were asymptomatic. Further information from contact tracing and household transmission studies are needed to determine the frequency and significance of asymptomatic childhood infection.

Victoria has had a higher proportion of positive SARS-CoV-2 cases in children and adolescence (16%), compared to other countries and cohorts, which range 0.8–2.2%.[11,26,27] This may reflect the aggressive suppression strategy with associated widespread testing, including school and childcare outbreaks, as well as a number of asymptomatic testing campaigns. Approximately 2.5 million tests were conducted between March and September 2020, with a test positive rate of 0.8% in Victoria, compared with states in the USA experiencing test positive rates of between 3.6% and 17.8% at the height of COVID19 pandemic.[28]

Whilst SARS-CoV-2 in children generally causes mild disease, the infection is associated with complications. There is increasing recognition of a Paediatric inflammatory multisystem syndrome temporally associated with SARS-CoV-2 (PIMS-TS also known as MIS-C) with potentially life threatening and serious effects.[29] To date, reports of PIMS-TS have occurred from higher SARS-CoV-2 incidence settings.[30,31]

This report has some limitations. Patients at RCH are seen up to age 18 years; there was likely a referral bias towards younger patients based on patients less than 5 years being directed to RCH for SARS-CoV-2 testing. Whilst the report was based on some manual data extraction, we optimised data collection by piloting a standardised electronic data form using trained abstractors and auditing the data extraction.

Conclusion

SARS-CoV-2 infection caused predominantly mild or asymptomatic infection, with most children not requiring hospitalisation. A higher proportion of children with comorbidities were admitted to hospital. Further information is needed regarding long-term impact from SARS-CoV-2 in children and differences in transmission and sequelae from emerging variants of concern.

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World Cat by Anna Warr (age 9) from Operation Art 2021