

Servidio Alessia Giuseppina (Orcid ID: 0000-0001-7421-0703)
Conti Rosaura (Orcid ID: 0000-0002-5312-2090)
Barbi Egidio (Orcid ID: 0000-0002-6343-846X)

Title: COVID-19 was mild in hospitalised infants younger than 90 days

Authors: Alessia Giuseppina Servidio¹, Giacomo Visentin¹, Rosaura Conti¹, Giorgio Cozzi², Laura Travan², Jenny Bua², Egidio Barbi¹⁻², Alessandro Amaddeo²

Corresponding author: Alessia Giuseppina Servidio (servidioalessiag@gmail.com)

1. Department of Medicine, Surgery, and Health Sciences, University of Trieste, Italy
2. Institute for Maternal and Child Health, IRCCS Burlo Garofolo, Trieste, Italy

This article has been accepted for publication and undergone full peer review but has not been through the copyediting, typesetting, pagination and proofreading process which may lead to differences between this version and the [Version of Record](#). Please cite this article as doi: [10.1111/apa.16624](https://doi.org/10.1111/apa.16624)

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Clinical manifestations of COVID-19 are generally milder in children than adults. Severe acute respiratory distress syndrome is rarely reported, even though cardiovascular diseases, diabetes and chronic lung diseases have been associated with severe outcomes.¹ Children under one year of age are more likely to be hospitalised, but it is not clear whether this is precautionary or due to increased disease severity.² One case series found that 20 infants who tested positive for the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) had relatively mild infections. Two required supplementary oxygen and one needed a high-flow nasal cannula.¹

This retrospective study was carried out at the Institute for Maternal and Child Health, IRCCS Burlo Garofolo, Trieste, Italy. We reviewed the clinical charts of all infants under 90 days of age who presented to our paediatric emergency department (PED) from 1 February 2020 to 28 February 2022. We tested symptomatic patients who presented to the PED using nasopharyngeal polymerase chain reaction tests from 1 February 2020. From March 2021, only symptomatic patients who were hospitalised were tested. We compared the clinical outcomes of infants who tested positive and negative by collecting various data from their medical records (Table 1).

Fisher's exact test was used to compare categorical variables. A two-sided p value of less than 0.05 was considered statistically significant.

The Institutional Review Board approved the study and the parents or legal guardians provided informed consent. During the study period 1260 infants under 90 days of life presented to the PED with acute illnesses. We excluded 1101 who were not hospitalised and 20 without parental consent. This means that 139 infants were hospitalized and included in the study and 29 (21%) tested positive for SARS-CoV-2. Six infants who tested negative had associated diseases or comorbidities: four had congenital heart disease, one had Down syndrome, two had congenital anomalies of the kidney and

urinary tract and two had congenital cytomegalovirus infections. None of the positive infants had associated conditions. Table 1 summarises the main characteristics of the population.

Virus positive infants presented more frequently with fever than those who tested negative (66% versus 27%, $p=0.0001$). None of the 11 subjects who appeared to be ill tested positive and three were diagnosed with bronchiolitis. We found that 31/110 who tested negative were admitted to the intensive care unit, including seven who had bronchiolitis. Nasal swabs were positive for the respiratory syncytial virus in 18/30 cases of bronchiolitis. One virus positive patient was not included in the study. He presented with fever and a urinary tract infection, was hospitalized for 36 hours, took oral antibiotics and was discharged home. We also noted that 10 of the 110 infants who tested negative were hospitalised and needed respiratory support. None of those who tested positive required this support. One who tested negative required continuous positive airway pressure and one required oxygen. Another patient who tested negative had an unscheduled visit to the PED with new symptoms, namely cough and rhinitis seven days after discharge, but was not hospitalised.

To our knowledge this was the largest case series of COVID-19 in infants under 90 days of age and it provides additional evidence that COVID-19 is mild disease in this age group, with better clinical outcomes than infants with other acute illnesses. Few severe COVID-19 cases have been reported under 90 days of age, with some cases of respiratory distress. All the virus positive infants in our study appeared well and did not have severe disease or require intensive care or respiratory support. The most frequent symptom was fever, followed by respiratory symptoms, such as a cough and mild breathing difficulties, as previously reported.³ None of the virus positive infants developed bronchiolitis, in line with other data.⁴ In fact, infants in the virus negative group were more likely to need intensive care for bronchiolitis and the respiratory syncytial virus, despite the dramatic decreases in these during the first year of the pandemic.⁵

Our study had some limitations. It was retrospective and monocentric and our findings may not be generalisable to other settings, such as low-income countries. Also, until February 2021 all infants with symptoms that suggested SARS-CoV-2 infections were tested, but from March 2021 only patients who were hospitalised were tested. Finally, none of the infants who tested positive had associated diseases or comorbidities and we were not able to analyse whether underlying conditions had an impact on clinical outcomes.

In conclusion, this study showed that COVID-19 was milder in infants than viral bronchiolitis and other acute illnesses, suggesting that precautionary hospitalisation of infants who do not appear ill is not necessary. According to this preliminary evidence, such infants under 90 days of age could be treated the same as those with any other viral infections and be discharged to a reliable family, with adequate follow up. More data are needed to confirm these results.

Abbreviations

SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; PED, paediatric emergency department.

Conflict of interests

None

Funding

None

Reference

1. Leibowitz J, Krief W, Barone S, et al. Comparison of Clinical and Epidemiologic Characteristics of Young Febrile Infants with and without Severe Acute Respiratory Syndrome Coronavirus-2 Infection. *J Pediatr* 2021; 229:41-47.e1.
2. Hause AM, Baggs J, Marquez P et al. COVID-19 Vaccine Safety in Children Aged 5–11 Years — United States, November 3–December 19, 2021. 2021; 70:32.
3. Bellini T, Rotulo GA, Caruggi S et al. Characteristics of COVID-19 patients up to 6 months of age admitted to a paediatric emergency department. *Acta Paediatr* 2022; 111:272–4.
4. Cozzi G, Cortellazzo Wiel L, Amaddeo A et al. Prevalence of SARS-CoV-2 positivity in infants with bronchiolitis: a multicentre international study. *Arch Dis Child* 2022:archdischild-2021-323559.
5. Amaddeo A, Cason C, Cozzi G et al. Social distancing measures for COVID-19 are changing winter season. *Arch Dis Child* 2021.

Table 1. Characteristics and outcomes of the 139 study subjects

	Positive for SARS-CoV-2 (n=29)	Negative for SARS-CoV-2 (n=110)	p values
Sex			
F	16 (55%)	53 (48%)	0.64
M	13 (45%)	57 (52%)	
On admission			
Triage code			0.36
1	0	3 (2%)	
2	20 (69%)	59 (54%)	
3	9 (31%)	46 (42%)	
4	0	3 (2%)	
Appeared ill	0	11 (10%)	0.16
Symptoms			
Fever	19 (66%)	30 (27%)	0.0001
Cough and rhinitis	9 (31%)	30 (27%)	0.16
Respiratory distress	4 (14%)	18 (16%)	0.21
Vomiting	1 (3%)	10 (9%)	0.22
Irritability	0 (0%)	6 (5%)	NA
Others	6 (21%)	12 (11%)	0.09
Clinical outcomes			
Median length of hospitalization (days)	1	1	
Respiratory support*	0	10 (9%)	0.12
Antibiotic therapy	5 (17%)	17 (15%)	0.78
Ward admitted to			
PICU/NICU	0	31 (28%)	0.0003
PED (OBI)	27 (93%)	71 (65%)	0.0024
General ward	2 (7%)	8 (7%)	1
Final diagnosis, n (%)			
COVID-19	29 (21%)		
Bronchiolitis	30 (22%)		
Upper respiratory tract infection	18 (13%)		
Urinary tract infection	11 (8%)		
Fever of unknown origin	8 (6%)		
Gastroenteritis	4 (3%)		
Acute otitis media	3 (2%)		
Other	36 (26%)		

* Respiratory support: oxygen, high-flow nasal cannula, continuous positive airway pressure
 PICU, paediatric intensive care unit, NICU, neonatal intensive care unit, PED, paediatric emergency department, OBI, brief intensive observation.