



Submitted on: 06/30/2020

Approved on: 07/06/2020

ORIGINAL ARTICLE

COVID-19 in pediatrics: a view between incidence and mortality

João Ricardo Azevedo Silva¹, Ana Cláudia de Araujo Argentino², Luana Deon Dulaba², Rafaela Rodrigues Bernardelli², Edmara Laura Campiolo²

Keywords:

Child,
Coronavirus,
Severe Acute
Respiratory Syndrome,
Coronavirus Infections.

Abstract

Objectives: Compare the data obtained in the Brazilian literature with those in the world literature, focusing on the severity and mortality rate of the pediatric population infected by COVID-19. **Methods:** Cross-sectional study conducted with data from the world and Brazilian literature obtained in articles selected through the UpToDate platform, which met with the inclusion criteria of the study, on the involvement of children by the new coronavirus (COVID-19) in the period of January 31 to May 31, 2020. The data obtained was organized using absolute frequency to indicate the results obtained through graphs formulated in Microsoft Word Excel. **Results:** The countries analyzed were Brazil, England, Spain and Portugal, countries that published data according to age. In relation to England, until May 20, 2020, there were 2,365 cases of COVID-19 in patients between 0 and 19 years old, accounting for 30 deaths in this age group. In Spain, 1,399 cases were confirmed in children younger than 14 years and only 3 deaths in the period. In Portugal, until May 23, 1,552 cases were recorded in the pediatric population, with no reported deaths. In Brazil, until 5/23/2020, 916 cases were registered between 0 and 18 years old, with only 548 having registered evolution and 99 evolving to death. **Conclusion:** This study is in accordance with the information obtained by the other analyzed articles, when it shows that the pediatric population is less affected and has a better evolution in relation to COVID-19.

¹ Regional University Hospital of Maringá, Pediatrics Residency - Maringá - Paraná - Brazil.

² Pontifical Catholic University of Paraná, School of Medicine - Londrina - Paraná - Brazil.

Correspondence to:

João Ricardo Azevedo Silva.

Hospital Universitário Regional de Maringá. Av. Mandacaru, 1590 - Parque das Laranjeiras, Maringá - PR, Brazil. CEP: 87083-24.

E-mail: jr.azevedo93@gmail.com



INTRODUCTION

The Coronavirus Disease 2019 (COVID-19) pandemic originated in Wuhan, China, in November 2019, and spread globally in a matter of a few months.¹ The first cases of the disease were observed in a local seafood market and reportedly stemmed from direct contact with animals. However, COVID-19 is not deemed a direct zoonosis, since transmission occurs chiefly between humans² though respiratory droplets.³ The disease may cause severe acute respiratory syndrome (SARS).⁴

Until 2019, six coronavirus species were known to cause disease in humans, four of which — 229E, NL63, OC43, and HKU1 — were highly prevalent and typically associated with colds and mild upper respiratory tract infection in immunocompetent patients of all ages. The two remaining strains — severe acute respiratory syndrome coronavirus (SARS-CoV) and Middle East respiratory syndrome Coronavirus (MERS-CoV) — have zoonotic origins and have been associated with severe symptoms and death by respiratory failure.⁵

COVID-19 is caused by SARS-CoV-2 (Severe Acute Respiratory Syndrome Coronavirus 2), an enveloped single-stranded RNA virus. The mean incubation time of the disease is 4-6 days, but 2.5% of the patients may develop symptoms earlier.⁶

The consequences of the pandemic have been devastating, placing it among the largest economic and public health crises of recent times.⁷ Described as a disease that affects predominantly adults, data from the World Organization (WHO) indicate that 8,497,293 cases of COVID-19 and 451,958 deaths by the disease had been recorded by June 18, 2020.⁸

Recent descriptions of COVID-19 involving pediatric patients have indicated that affected individuals generally have preexisting comorbidities and develop mild symptoms, with few requiring hospitalization or presenting complications, and even fewer dying of the disease. The scenario for adults is rather different, particularly as individuals aged 60+ years and subjects with comorbidities account for nearly all recorded deaths by the disease.⁹

The pathophysiology of the disease appears to explain the low rate of infection among individuals in the pediatric age range. Studies enrolling adults with severe disease have described poorer adaptive immunity response, with significantly lower total lymphocyte, T CD4+ and CD8+ cell, T helper cell, and memory cell counts. On the other hand, innate immune response is dysfunctional and exacerbated, with elevated levels of cytokines and neutrophil counts, which cause lung injury. Although additional studies are required on the profile of cytokines and lymphocyte subsets in pediatric patients, the immune response of children appears to be more appropriate, since most pediatric patients with COVID-19 have normal lymphocyte counts.¹⁰

OBJECTIVES

This study aims to describe and compare data from Brazilian and international literature about cases of COVID-19 involving pediatric patients, particularly information on

severity of disease and death rates based on presented comorbidities.

METHODS

This cross-sectional study included data from international and Brazilian literature about pediatric patients with COVID-19 seen between January 31 and May 31, 2020.

A search was made on platform UpToDate using the following keywords: “Children”; “Coronavirus”; “COVID-19”; and “SARS-CoV-2” in English and Portuguese. The search yielded 147 articles, of which 13 were included.

The following inclusion criteria were applied: cases reported within the time period of interest; authors without conflicts of interest; cases involving pediatric patients; presenting comparisons between healthy children and children with comorbidities; studies from countries with greater numbers of cases reported.

Epidemiological data were procured from weekly reports issued by the Brazilian Ministry of Health from January 31 to May 31, 2020; comparisons were made against data on severity of disease and death rates described in epidemiological reports issued by other nations, in which the number of cases of the disease and deaths by age group were mentioned (England, Spain, and Portugal).

Data sets were grouped, organized, and presented in absolute and comparative frequencies to indicate outcomes based on descriptive statistics through graphs produced on Microsoft Excel.

RESULTS

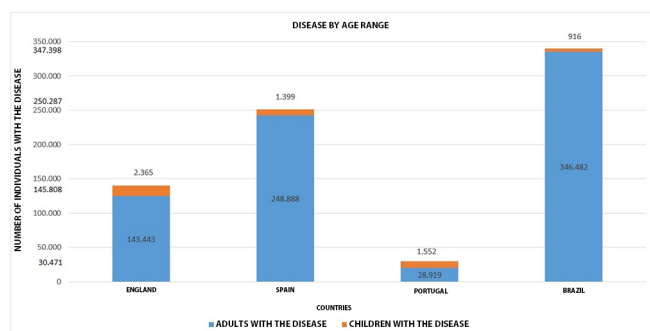
According to Special Epidemiological Report No. 17 of the Brazilian Ministry of Health, by the end of Epidemiological Week 21 (May 17-23, 2020) a total of 5,175,925 cases of COVID-19 and 338,089 deaths by the disease had occurred in the world. The United States ranked first in the list of confirmed cases of the disease with 1,601,434, followed by Brazil with 347,398 and Russia with 326,448.¹¹

In England, 145,808 cases had been reported by the week of May 14-20, 2020, of which 2,365 (1.6%) involved individuals aged 0-19 years, as seen in Graph 1. Deaths by COVID-19 amounted to 31,843, with fewer than thirty involving children,¹² as seen in Graph 2.

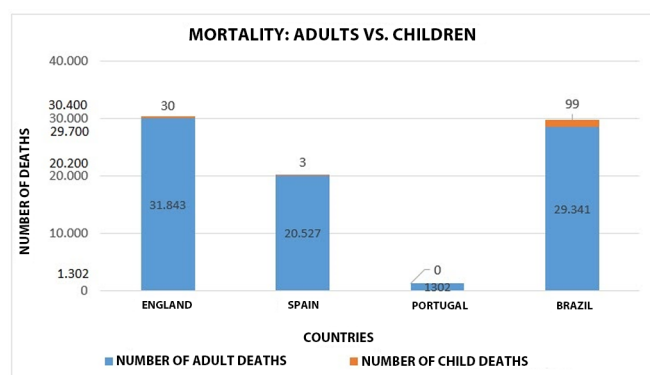
Graph 1 also shows the situation in Spain, ranked fifth in number of cases of the disease with 250,287, of which 1,399 (0.56%) involved children aged 14 years or younger. Deaths by COVID-19 amounted to 20,527, with only three deaths of children.¹³

Portugal reported 30,471 cases and 1,302 deaths by the disease by May 23, 2020. Cases involving children aged 0-19 years amounted to 1,552 (4.3%); no deaths were recorded for individuals in this age range,¹⁴ as seen in Graph 2.

Brazil had 916 cases of severe acute respiratory syndrome (SARS) by COVID-19 involving pediatric patients aged 0-18 years; 548 were followed, of which 449 were cured and 99 (10.8%) died by Epidemiological Week 21.¹¹



Graph 1. Adults and children with COVID-19.



Graph 2. Mortality: general population vs. pediatric population.

Health authorities in England, Portugal, and Brazil assign individuals aged 0-19 years to the pediatric patient group. In Spain, this group includes individuals aged 14 years or younger. Subjects aged 14+ years belong to the adult population.

DISCUSSION

This study comprised epidemiological data from four countries and compared them to the data of other previously published studies. An observational study based on data from the Chinese Center for Disease Control and Prevention showed that only 2% of 44,672 patients diagnosed with COVID-19 were aged less than 20 years,¹ indicating the low prevalence of the disease in children.

The data described in our study support this finding. In Brazil, the Latin American country with the largest number of cases of COVID-19, about 0.26% of the cases of the disease were described in individuals aged 0-18 years. In England, approximately 1.62% of the cases involved children, while in Spain the proportion of pediatric cases of the disease was 0.55%. In our study, the country with the highest pediatric prevalence of the disease was Portugal, with 5%.

However, despite the higher prevalence, no deaths of children by COVID-19 were recorded in Portugal. Spain ranked second in terms of child death rate by COVID-19 of individuals aged 14 years or younger, with 0.01%. England reported a

0.09% child death rate, while Brazil recorded the highest death rate by SARS, with 0.3% of all child deaths.

The findings reported in the included studies are in agreement with other previously published studies, in that children rarely develop severe forms of COVID-19.¹⁵

A cross-sectional study performed in the United States looked into the data from 46 intensive care units from March 14 to April 3, 2020. Forty-eight patients under the age of 21 years diagnosed with COVID-19 were admitted to an ICU.¹⁶ Forty had preexisting comorbidities (83%); 18 required invasive ventilation (38%); 11 had failure of two or more organ systems (23%); and one required extracorporeal membrane oxygenation (2%). At the end of the study, two patients had died (4%); 15 were still hospitalized; three were on ventilators; and one was on extracorporeal membrane oxygenation. As in adults, presence of preexisting comorbidities is an important factor in the severity of involvement by COVID-19; however, differently from individuals aged 21 years or older, severe cases requiring intensive care and invasive ventilation are less common in the pediatric population.

Comparatively, a study carried out in Madrid combining data collected in 30 pediatric secondary and tertiary hospitals in March 2-16, 2020¹⁷ found that 25 of 41 patients (60%) with positive tests for COVID-19 were hospitalized and four were referred to an intensive care unit and required respiratory support with a nasal cannula (9.7%). The fact that no deaths were recorded confirmed the finding that the rate of infection in patients aged less than 19 years is lower than the rates observed in adults, with individuals in the younger age range accounting for 2% of all patients with infection.

Shekerdemian L et al.¹⁶ analyzed data from China and found that pediatric patients presented lower complication rates, with only 21 of 731 children with COVID-19 developing severe symptoms.

The authors of a study performed at the Jinan Infectious Disease Hospital¹⁸ in China claimed that (i) pediatric patients had milder symptoms because they became infected at home by family members with second or third "generation" viruses with lower virulence after undergoing several mutations; (ii) innate immune response was more active in children; (iii) the number or function of ACE2 (angiotensin-converting enzyme 2) receptors in children was lower than in adults.

We believe that the death rate of children with COVID-19 is higher in Brazil than in other countries (Graph 2) because Brazil is a developing nation with precarious prevention and treatment policies.

Limitations

The main limitation concerning the collection of data in this study is that most countries do not include confirmed cases of COVID-19 and deaths by the disease by age range in their epidemiological reports, thus hampering the analysis of prevalence of the disease in pediatric patients.

CONCLUSION

The COVID-19 pandemic has been the subject of numerous studies and new information comes to light every day. Our study presented evidence to describe the epidemiology of the disease in pediatric populations and stressed that, despite the growth in the number of cases worldwide, children have been less involved by the disease and fared out better than adults, with small proportions eventually dying of the disease. Brazil was the country with the largest number of deaths in the study. We believe that this is due to the scarcity of prevention and treatment policies in effect in the country to combat COVID-19.

REFERENCES

1. Wu Z, McGoogan JM. Characteristics of and important lessons from the coronavirus disease 2019 (COVID-19) outbreak in China: summary of a report of 72314 cases from the Chinese Center for Disease Control and Prevention. *JAMA*. 2020 Feb;323(13):1239-42. DOI: <https://doi.org/10.1001/jama.2020.2648>
2. Hoffmann M, Kleine-Weber H, Schroeder S, Krüger N, Herrler T, Erichsen S, et al. SARS-CoV-2 cell entry depends on ACE2 and TMPRSS2 and is blocked by a clinically proven protease inhibitor. 2020 Abr; [acesso em 2020 Jun 20]; 181(2):271-280.e8. Disponível em: <https://pubmed.ncbi.nlm.nih.gov/32142651>
3. he J, Liu L, Liu W. COVID-19 epidemic: disease characteristics in children. *J Med Virol* [Internet]. 2020 Jul; [acesso em 2020 Jun 20]; 92(7):747-54. Disponível em: <https://pubmed.ncbi.nlm.nih.gov/32232980>
4. Ludwig S, Zarbock A. Coronaviruses and SARS-CoV-2: a brief overview. *Anesth Analg*. 2020 Jul;131(1):93-6.
5. Sociedade Brasileira de Pediatria (SBP). Departamento Científico de Infectologia. Documento Científico da Sociedade Brasileira de Pediatria. Novo coronavírus (COVID-19). Rio de Janeiro (RJ): SBP; 2020.
6. Lauer SA, Grantz KH, Bi Q, Jones FK, Zheng Q, Meredith HR, et al. The incubation period of coronavirus disease 2019 (COVID-19) from publicly reported confirmed cases: estimation and application. *Ann Intern Med* [Internet]. 2020 Mai; [acesso em 2020 Jun 20]; 172(9):577-82. Disponível em: <https://pubmed.ncbi.nlm.nih.gov/32150748>
7. Jin Y, Yang H, Ji W, Wu W, Chen S, Zhang W, et al. Virology, epidemiology, pathogenesis, and control of COVID-19. *Viruses* [Internet]. 2020 Mar; [acesso em 2020 Jun 20]; 12(4):372. Disponível em: <https://pubmed.ncbi.nlm.nih.gov/32230900>
8. World Health Organization (WHO). Coronavirus disease (COVID-19) – Dashboard [Internet]. Geneva: WHO; 2020; [acesso em 2020 Jun 18]. Disponível em: <https://covid19.who.int/>
9. Sociedade Brasileira de Pediatria (SBP). Departamento Científico de Infectologia. Documento Científico Sociedade Brasileira de Pediatria. Medidas para o pediatra relacionadas com a pandemia do COVID-19. Rio de Janeiro (RJ): SBP; 2020.
10. Dhochak N, Singhal T, Kabra SK, Lodha R. Pathophysiology of COVID-19: why children fare better than adults?. *Indian J Pediatr*. 2020 Mai 14; [Epub ahead of print]. DOI: <https://doi.org/10.1007/s12098-020-03322-y>
11. Ministério da Saúde (BR). Secretaria de Vigilância em Saúde. Boletim epidemiológico especial COE-COVID-19. Semana Epidemiológica 21 (17 a 23/05) [Internet]. Brasília (DF): Ministério da Saúde; 2020; [acesso em 2020 Jun 20]. Disponível em: <https://www.saude.gov.br/images/pdf/2020/May/29/2020-05-25---BEE17---Boletim-do-COE.pdf>
12. Public Health England (UK). The weekly surveillance report in England, Coronavirus (COVID-19) [Internet]. London, UK: Public Health England; 2020; [acesso em 2020 Jun 21]. Disponível em: https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/886696/COVID19_Weekly_Report_20_May.pdf
13. Red Nacional de Vigilancia Epidemiológica (RNVE). Informe sobre la situación de COVID-19 en España. Informe COVID-19 nº 32, 21 de mayo de 2020 [Internet]. Espanã: RNVE; 2020 Mai; [acesso em 2020 Jun 21]. Disponível em: <https://www.isciii.es/QueHacemos/Servicios/VigilanciaSaludPublicaRENAVE/EnfermedadesTransmisibles/Documents/INFORMES/Informes%20COVID-19/Informe%20n%C2%BA%2032.%20Situaci%C3%B3n%20de%20COVID-19>
14. República Portuguesa – Saúde (PT). Serviço Nacional de Saúde (SNS) de Portugal. Relatório de situação – Situação epidemiológica em Portugal [Internet]. Lisboa, PT: SNS; 2020 Mai; [acesso em 2020 Jun 21]. Disponível em: https://covid19.min-saude.pt/wp-content/uploads/2020/05/82_DGS_boletim_20200523.pdf
15. Safadi MAP. The intriguing features of COVID-19 in children and its impact on the pandemic. *J Pediatr* [Internet]. 2020 Mai/Jun; [acesso em 2020 Jun 20]; 96(3):265-8. Disponível em: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7158814/>
16. Shekerdemian LS, Mahmood NR, Wolfe KK, Riggs BJ, Ross CE, McKiernan CA, et al. Characteristics and outcomes of children with coronavirus disease 2019 (COVID-19) infection admitted to us and Canadian pediatric intensive care units. *JAMA Pediatr*. 2020 Mai 11; [Epub ahead of print]. DOI: <https://doi.org/10.1001/jamapediatrics.2020.1948>
17. Tagarro A, Epalza C, Santos M, Sanz-Santaeufemia FJ, Otheo E, Moraleda C, et al. Screening and severity of coronavirus disease 2019 (COVID-19) in children in Madrid, Spain. *JAMA Pediatr*. 2020 Abr 8; [Epub ahead of print]. DOI: <https://doi.org/10.1001/jamapediatrics.2020.1346>
18. Su L, Ma X, Yu H, Zhang Z, Bian P, Han Y, et al. The different clinical characteristics of corona virus disease cases between children and their families in China - the character of children with COVID-19. *Emerg Microbes Infect* [Internet]. 2020 Dez; [acesso em 2020 Jun 20]; 9(1):707-13. Disponível em: <https://pubmed.ncbi.nlm.nih.gov/32208917>