Screening and Severity of Coronavirus Disease 2019 (COVID-19) in Children in Madrid, Spain

As the pandemic of coronavirus disease 2019 (COVID-19) spreads, new data emerge and understanding of the disease improves. Reports associated with children are growing but still scarce.1-3 The epicenter of the epidemic has displaced to Europe. The first case in Spain was declared on January 31, 2020, and the first case in the Madrid region was declared on February 27, 2020.

Methods | With the aim of obtaining an overview of the proportion of confirmed cases among those tested and the severity of the disease in children, a registry of tested cases was performed from March 2, 2020, to March 16, 2020, by pediatricians in 30 secondary and tertiary hospitals in Madrid, Spain, during the first 2 weeks of the epidemic. Children were screened according to Spanish Public Health recommendations, which included those patients with a significant disease who were admitted, or likely to be admitted, at the time of evaluation according to the attending pediatrician or patients with signs or symptoms compatible with COVID-19 and the risk of complications due to baseline disease. This study was approved by the ethics committee of Hospital 12 de Octubre. Data collection was allowed by verbal consent with subsequent written consent provided by patients with positive results. Data were deidentified. The test used for diagnosis was real-time polymerase chain reaction.4 The reported sensitivities for the E gene and RdRp gene assays are 5.2 and 3.8 copies per reaction at 95% detection probability, respectively.4 Both genes needed to be amplified to report a positive result.

Results | During the first 2 weeks of the epidemic in Madrid, Spain, 365 children were screened within the 30 hospitals. During the first week, 6 of 103 patients (5.8%) had positive test results. At the end of the second week, 41 of 365 patients (11.2%) had positive test results (Table). By March 16, 2020, 41 of the 4695 confirmed cases (0.8%) in Madrid region were children younger than 18 years.

The median age of the tested patients was 3 years (interquartile range, 0.9-6 years; range, 0-15 years) and the median age of the patients with positive results was 1 year (interquartile range, 0.35-8.5 years; range 0-15 years). Twenty five of 41 children with confirmed COVID-19 (60%) were hospitalized, 4 of 41 (9.7%) were admitted to a pediatric intensive care unit (PICU), and 4 of 41 (9.7%) needed respiratory support beyond nasal prongs (Table). Of these, 1 of 4 (25%) had only 1 previous condition (recurrent wheezing). No patients died. Initial syndromic diagnoses were

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<th>Table. Clinical Features of Participants Tested for Severe Acute Respiratory Syndrome Coronavirus 2</th>
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<td>Features</td>
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<td>Sex</td>
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<tr>
<td>Male</td>
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<tr>
<td>NA</td>
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<tr>
<td>Contact with person with confirmed case</td>
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<td>Yes</td>
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<td>No/community transmission</td>
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<tr>
<td>Hospitalization</td>
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<td>Yes</td>
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<td>PICU admission</td>
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<td>Respiratory support beyond oxygen in nasal prongs</td>
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<tr>
<td>High-flow ventilation</td>
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<td>Underlying disease</td>
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<td>Yes</td>
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Abbreviations: NA, data not available; PICU, pediatric intensive care unit.

* The P value was calculated as χ² with Fisher correction as needed.
upper respiratory tract infection (14 [34%]), fever without a source (11 [27%]), viral-like pneumonia (6 [15%]), bronchiolitis (5 [12%]), gastroenteritis or vomiting (2 [5%]), bacterial-like pneumonia (2 [5%]), and asthma flare (1 [2%]). Two patients (5%) had a coinfection with influenza B.

Discussion | Our series agrees with those previously published, suggesting that only 2% of affected individuals are younger than 19 years. In Madrid, 60% of confirmed infections in children required admission. The usual criteria for admission in our region because of respiratory problems coincide with the definition of severe disease in China. Only 21 of 731 children with confirmed COVID-19 (2.8%) in China had severe disease (hypoxia and oxygen saturation less than 92%) or critical disease. The key issue regarding the high percentage of admissions is the number of children tested. Initially, only children with contact with a person with COVID-19 were tested, but the situation changed rapidly. From March 9, 2020, onwards, Madrid was declared an area of community transmission. Afterwards, the recommendation was to test only hospitalized children with symptoms and signs of COVID-19 or patients with comorbidities and a high risk of complications. Some children at risk of hospitalization were also tested, although they were ultimately discharged. In other settings, several children with mild disease were tested and the proportion of admissions was lower. Therefore, testing may have been biased to moderate to severe patients, and results must be interpreted with caution. Other reasons for the different proportion of hospitalizations, PICU admissions, and respiratory support may be associated with an increased awareness of COVID-19, different criteria for hospitalization and initiation of high-flow oxygen therapy, or different host responses to the infection.

Limitations. | One limitation of this study is the sensitivity of the test. Some authors state that pharyngeal and nasal swab sensitivity is as low as 32% to 63%. Although the sensitivity and specificity of the polymerase chain reaction may have improved, the actual number of children with infection may be higher.

Conclusions | Infections in children occur early in COVID-19 epidemics. The proportion of confirmed patients among those with compatible symptoms was 11%. Severe infections may occur, needing PICU admission or high-flow ventilation. Further information is warranted to shape the features of this disease in children.

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Correction: This article was corrected on May 11, 2020, to fix errors in the Table.

Author Contributions: Dr Tagarro had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Concept and design: Tagarro, Moraleda, Calvo.
Acquisition, analysis, or interpretation of data: All authors.
Drafting of the manuscript: Tagarro, Moraleda, Calvo.
Critical revision of the manuscript for important intellectual content: All authors.
Statistical analysis: Tagarro.
Administrative, technical, or material support: Epalza, Moraleda.
Supervision: Tagarro, Epalza, Sanz-Santaeufemia, Moraleda, Calvo.

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COMMENT & RESPONSE

Scientific Ambiguity in the Time of Coronavirus Disease 2019

To the Editor We read with interest the work by Tagarro et al and we are concerned about several issues that we would like to discuss. The first case of severe acute respiratory illness coronavirus 2 (SARS-CoV2) infection in Madrid, Spain, was reported at La Paz University Hospital on February 25, 2020, two days earlier than what the authors state. Although a minor issue, this should be clarified.

The Spanish Ministry of Health recommended that patients who were going to be admitted into a hospital be tested for SARS-CoV2 infection. It is surprising that the need for admission was misjudged in 40% of the children. This may indicate that testing policies were not compliant with official recommendations, generating an excessive consumption of resources in a time of severe constraints and representing an unnecessary delay of care.

The World Health Organization defined coronavirus disease 2019 (COVID-19) as the disease produced by the virus severe acute respiratory illness coronavirus 2 (SARS-CoV2). It is extremely important that the distinction between having COVID-19 and being an asymptomatic carrier is made to avoid confusion. The authors do not provide data on how many patients showed symptoms suggestive of COVID-19 on presentation, a fact that makes their conclusions hard to interpret. Thus, we find that concluding that 60% of confirmed infections in children required admission could be an overestimation.

The authors report a 10% pediatric intensive care unit admission rate. This is the highest rate reported to date and more than doubles the official rate published by the Spanish Ministry of Health, making the lack of discussion on this topic remarkable. It is particularly relevant that there are no details on the criteria used for pediatric intensive care unit admission or the degree of severity of COVID-19 in these patients. It could be that these patients were admitted for other reasons and then tested positive for SARS-CoV2. Providing clinical data such as standardized severity scores, the presence of respiratory distress, chest radiograph findings, or the oxygen saturation by pulse oximetry to fraction of pulse oximetry ratio could help the reader understand this excessive admission rate. Lastly, the authors fail to report any financial support for this project, especially regarding the acquisition of personal protective equipment and polymerase chain reaction tests, as it is required by JAMA Pediatrics’ instructions for authors.

In summary, we consider that with the data presented, Tagarro et al make unsound generalizations that could be a cause of concern for the general population. In a serious situation, such as this pandemic, rigor and accuracy should not pay the cost of immediacy.

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In Reply We welcome the opportunity that our colleagues from La Paz University Hospital provide to explain our findings further. First, we appreciate the clarification about the first case of severe acute respiratory illness coronavirus 2 (SARS-CoV2) infection in Madrid, Spain. At this point, few people still argue against testing. World Health Organization Director General Tedros Ghebreyesus stated in a press conference on March 16, 2020: “We have a simple message for all countries: test, test, test. Test every suspected case.”

However, we were very aware of laboratories’ overload, financial constraints, and need for a coordinated response. The criteria for testing patients followed the Ministry of Health recommendations, in coordination with each Hospital’s protocols, the Preventive Departments, and the Public Health Regional Department. At the contention phase of the epidemic, the recommendation of the Spanish Ministry of Health was to test “patients with symptoms of viral infection or respiratory symptoms and recent trips to risk areas or contact with cases of COVID-19.” From March 9, 2020, onwards, the epidemiologic criterion disappeared as Madrid was considered an area of community transmission. If the patient met the criteria of “case under investigation,” the case was communicated to the Hospital Management Team and to the Regional Public Health Department. This Department confirmed whether the case was to be investigated using molecular tests. Tests not compliant with official recommendations were simply not possible.

As stated, cases under investigation included patients at risk of admission with respiratory symptoms and patients with risk of complications owing to baseline disease and signs compatible with coronavirus disease 2019 (COVID-19) with epidemiologic contact or living in areas with community transmission. In cases under investigation, having the result was mandatory before discharge or admitting a patient to the ward. At that point, the turnaround time of the polymerase chain reaction was from 12 to 36 hours. Meanwhile, the patients remained in observation areas and received treatment. Eventually, 40% of patients with COVID-19 and 32% of patients
without COVID-19 were discharged without definitive admission. This rate falls within usual ones.4

All patients showed symptoms of viral infection or respiratory symptoms that the attending pediatricians considered consistent with COVID-19 on presentation.5 Diagnoses of the 41 patients admitted with COVID-19 are stated in the first paragraph of the second page. There were no asymptomatic carriers. Only 2 coinfections were found.1 There is no overestimation in describing that 25 of 41 children (60%) with confirmed infection were admitted.

Relating to the patients admitted in the pediatric intensive care units (PICUs), the syndromic diagnoses were asthma flare, bronchiolitis, and 2 pneumonia cases. Three of them required ventilatory support beyond nasal prongs, which is a common criterion for PICU admission. An additional child received high-flow therapy out of the PICU. All were admitted following pediatric intensivists’ criteria. Opposite to the authors’ remark, the PICU admission rate was lower than the 12.6% reported by the Spanish Authorities on April 23, 2020.6 Reasons for the high rate of hospital and PICU admissions were discussed in the last paragraph of the discussion, where we also stated that these results must be interpreted with caution.

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Factors Affecting Children’s Mental Health During the Coronavirus Disease 2019 Pandemic

To the Editor Coronavirus disease 2019 (COVID-19) has skyrocketed to be the “eye of storm” of a broad spectrum of issues, thus far affecting not only the safety of human life but also the public mental health in the long term. Xie et al1 have been conscious of such a problem and demonstrated that during the outbreak of COVID-19, the decrease of outdoor activities and social interaction may increase the occurrence of children’s depressive symptoms. The result provided straightforward evidence that COVID-19 to some extent has a negative impact on children’s mental health, which indicates that the corresponding approach is urgent to be explored. Yet, several concerns flooded into my mind.

First, with respect to the risk factors of children’s mental health, researchers enrolled some indicators including household income, parental mental or physical health, and parent emotional support. Thereinto, compared with children without MBDDs (mental, behavioral, and developmental disorders), those with MBDDs more often lived in the lowest income category (prevalence ratio [PR], 1.4) while fewer in the highest category (PR, 0.8), which indicated that household income plays an essential role in children’s mental health.2 Additionally, among children living at less than 100% of the federal poverty level, more than 1 in 5 (22%) had MBDD. Simultaneously, children of parents with mood or substance use disorders may be at increased risk of externalizing and internalizing disorders, and the same is true of those who are affected by violence, abuse, poverty, and maltreatment.3 The influence of these factors provokes our curiosity as well. Second, Ghandour et al4 proposed that diagnoses of depression and anxiety are more common with increased age, and behavior problems are more prevalent among children aged 6 to 11 years than children younger or older. Hence, the study of Xie et al4 with a large sample might lay a foundation for further studies among different age groups. Overall, the possibility of residual confounding and more hierarchical explorations are of great interest.

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Letters

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