Original

Epidemiology of SARS-CoV-2 infection in Navarre (Spain)

María Urretavizcaya Martínez[a], Laura Moreno Galarraga[b], Jesús Castillac, Marcos García Howard[a], Amaia Belza Mendikute[a], Mercedes Herranz Aguirre[d]

[a]Servicio de Pediatría. Complejo Hospitalario de Navarra. Servicio Navarro de Salud. Pamplona. España • [b]Servicio de Pediatría. Complejo Hospitalario de Navarra. Servicio Navarro de Salud. Pamplona. IdiSNA. Instituto de Investigación Sanitaria de Navarra (IdiSNA). Pamplona. España • [c]Instituto de Investigación Sanitaria de Navarra (IdiSNA). Pamplona. Instituto de Salud Pública y Laboral de Navarra. Pamplona. CIBER Epidemiología y Salud Pública (CIBERESP). España • [d]Sección de Enfermedades Infecciosas Pediátricas. Servicio de Pediatría. Complejo Hospitalario de Navarra. Servicio Navarro de Salud. Pamplona. IdiSNA. Instituto de Investigación Sanitaria de Navarra. Pamplona. España.

Date of online publication:
29-march-2021

María Urretavizcaya-Martínez:
mariaurretavizcayamartinez@gmail.com

Introduction: since the beginning of the COVID-19 pandemic, numerous studies have been published on the subject, but the data on the impact of infection by SARS-CoV-2 in the paediatric population is still scarce. The incidence and clinical presentation in the paediatric population remain unclear, so further research is required to understand paediatric COVID-19.

Methods: we conducted a multicentre retrospective study, analysing the incidence and clinical characteristics of children with laboratory-confirmed COVID-19 in Navarre, Spain, during the first wave of the pandemic (February 28-May 31, 2020).

Results: the cumulative incidence of COVID-19 in the paediatric population of Navarre in a 3-month period was of 3 cases per 1000 children. Of the 309 confirmed cases, 85.7% were in children with a household contact with confirmed infection; 32.1% were asymptomatic; the clinical manifestations were heterogeneous and only 15.8% had a "typical" presentation with fever and respiratory symptoms; 49% was managed by telephone and only 11.6% required additional diagnostic tests. Thirteen patients were admitted to hospital (4.2%), 2 with moderate disease (1 with respiratory symptoms requiring oxygen therapy and 1 with epileptic seizures treated with anticonvulsant drugs) and 1 with severe paediatric inflammatory multisystem syndrome temporarily associated with SARS-CoV-2 that required admission to the paediatric intensive care unit. All patients had favourable outcomes free of sequelae. Of the total patients, 45.2% did not require any treatment and the rest were treated with analgesics, inhaled bronchodilators or antibiotics in case of coinfection; 2.3% received hydroxychloroquine.

Conclusions: epidemiological reports are relevant for the purpose of improving our knowledge of COVID-19 in children and helping paediatricians identify this disease and treat it more effectively.

Key words:
• COVID-19
• Paediatric coronavirus
• SARS-CoV-2

Epidemiología de la infección SARS-CoV-2 en Navarra (España)

Resumen

Introducción: desde el inicio de la epidemia de COVID-19, se han publicado numerosos estudios, pero la información sobre el impacto de la infección por SARS-CoV-2 en población pediátrica es todavía limitada. La incidencia y características en población pediátrica siguen siendo inciertas, por lo que se necesitan más estudios para entender el COVID-19 pediátrico.

Material y métodos: estudio multicéntrico retrospectivo en el que se describen la incidencia y características clínicas de los niños con COVID-19 confirmada en Navarra (España) durante la primera ola epidémica (28 de febrero-31 de mayo de 2020).

How to cite this article: Urretavizcaya Martínez M, Moreno Galarraga L, Castilla J, García Howard M, Belza Mendikute A, *et al*. Epidemiología de la infección SARS-CoV-2 en Navarra (España). Rev Pediatr Aten Primaria. 2021;23:53-61.

Resultados: la incidencia acumulada de COVID-19 pediátrico en Navarra en tres meses fue de tres casos por 1000 niños. De los 309 casos confirmados, el 85,7% tenían contacto domiciliario positivo; el 32,1% fueron asintomáticos; los síntomas fueron variados y solo el 15,8% tenían presentación "típica" de fiebre y síntomas respiratorios; 49% recibió atención telefónica y solo 11,6% requirió estudio complementario. Trece pacientes ingresaron en hospital (4,2%), dos fueron casos moderados (un cuadro respiratorio que requirió oxigenoterapia y un cuadro convulsivo tratado con antiepilépticos) y uno grave con el síndrome inflamatorio multisistémico pediátrico vinculado a SARS-CoV-2 que ingresó en la unidad de cuidados intensivos (UCIP). Evolución favorable en todos los casos sin secuelas. Un 45,2% no necesitó tratamiento, el resto tratados con analgésicos, inhaladores o antibióticos en caso de sobreinfección; 2,3% recibió Hidroxicloroquina.

Conclusiones. Los reportes epidemiológicos son importantes para mejorar el conocimiento sobre COVID-19 en niños, ayudando a los pediatras a reconocer y tratar mejor la enfermedad.

Palabras clave:
- Coronavirus pediátrico
- COVID-19
- SARS-CoV-2

INTRODUCTION

In December 2019, a cluster of cases of pneumonia of unknown aetiology was reported in Wuhan, China. In January 2020, the causative agent was identified as a novel coronavirus, which was eventually named severe acute respiratory syndrome-coronavirus-2 (SARS-CoV-2). The disease caused by this novel virus mainly affected the respiratory system and is referred to as coronavirus disease 2019 (COVID-19).[1,2] After the initial outbreak in China, the disease spread quickly around the world; in January 30, 2020, the World Health Organization declared it a "global health emergency" and in March 11 it was officially declared a pandemic.[3]

In Spain, the first confirmed case of COVID-19 was reported on January 31, and community transmission was established in a few weeks, leading to an exponential increase in cases.[4] On March 14, 2020, the Spanish government declared the state of alert and implemented drastic measures, including lockdown of the population, travel restrictions and closure of schools and non-essential establishments. Due to the restriction of travel between autonomous communities in Spain, the evolution of the pandemic was different in each of them.

The clinical features of COVID-19 have been identified over time, as this is a new disease. At first, it was believed that it mainly affected adults and the lungs, presenting with pneumonia and acute respiratory distress syndrome (ARDS).[1,2] In children, transmission seemed less frequent and the forms of disease less severe.[5,6] In time, it became clear that the transmission rate in children is similar to the rate in adults, as are the patterns of transmission, although children do not usually develop the pulmonary forms of disease typical in adults, tend to have milder symptoms and have a lower mortality.[7-11]

Nevertheless, severe presentations of SARS-CoV-2 infection have been described in children, especially in infants with respiratory complications. In addition, from early May, paediatricians all over Europe started to report paediatric cases of COVID-19 that manifested with an inflammatory syndrome with clinical and laboratory features found in Kawasaki disease, toxic shock syndrome or macrophage activation syndrome, a form of disease that was labelled paediatric inflammatory multisystem syndrome temporarily associated with SARS-CoV-2 (PIMS-TS) or multisystem inflammatory syndrome in children (MIS-C). These patients tended to be adolescents with severe forms of disease that could rapidly progress to myocarditis and haemodynamic instability and required intensive care.[12,13]

Since there are still many unknowns in SARS-CoV-2 infection, we believe it relevant to describe its patterns in the paediatric populations of different socioeconomic and demographic characteristics. To this end, we designed a study to establish the detected incidence of COVID-19 in Navarre in the first wave of the pandemic (March-May 2020). We also described the clinical and epidemiological characteristics of the infection in children, their clinical management and the patient outcomes.

MATERIAL AND METHODS

We conducted a multicentre retrospective descriptive study describing the clinical and epidemiological characteristics, management and outcomes of confirmed paediatric cases of SARS-CoV-2 infection in Navarre during the first wave of the pandemic.

Navarre is an autonomous community Spain with 660 887 inhabitants, including 101 056 children under 15 years (15.3%).[14] The study covered a 3-month period from 28 February, 2020, when the first case of COVID-19 was confirmed in Navarre (adult patient), to May 31, when the virus circulation dropped below the epidemic threshold (< 40 cases per 100 000 inhabitants).

In Navarre, during the period under study, SARS-CoV-2 tests were performed in patients admitted to hospital or those that presented to emergency departments or primary care centres with symptoms compatible with COVID-19 and in asymptomatic patients with comorbidities, disabilities or social risk factors. Testing was also performed in the context of contact tracing. We defined confirmed COVID-19 case as a case with a positive reverse transcription polymerase chain reaction (RT-PCR) test or antibody test. None of the cases were diagnosed by serologic testing, as this method was not used for diagnosis of acute infection during the period under study.

We obtained data on the positive cases and their epidemiological characteristics from the epidemiologic surveillance system of our region, which integrates data from laboratory test results, health records and epidemiological surveys. The management of confirmed paediatric cases of COVID-19 was centralised in the tertiary care referral hospital, the Complejo Hospitalario de Navarra, the paediatric intensive care unit (PICU) was located at the Clínica Universidad de Navarra, and ambulatory cases were followed up at the corresponding primary care centre.

The inclusion criteria were age < 15 years at the beginning of the study period, confirmed infection by SARS-CoV-2, ability of researchers to contact the patient and consent to participation in the study. The ethics committee of the hospital approved the study, and we obtained oral consent to participation prior to inclusion in the study. We collected data through telephone surveys and by reviewing health care records and laboratory and diagnostic test results.

The variables under study were age and sex of the patient, reason for performance of the diagnostic test, detection of positive household contacts, the signs and symptoms of disease, diagnostic tests performed, treatments and medical care. We performed a descriptive analysis, expressing continuous variables as median and interquartile range (IQR) and qualitative variables as percentages. We analysed the data with the software STATA version 12.0 and Microsoft Excel version 2010.

Ethical considerations

The clinical research ethics committee of the Complejo Hospitalario de Navarra approved the study in May 2020 (PI_2020/38: *Estudio epidemiológico de las infecciones respiratorias causadas por el nuevo coronavirus SARS-CoV-2 en la población pediátrica*).

RESULTS

In the period under study, from the time the first COVID-19 case was detected in Navarre (28 February) to May 31, a total of 309 patients aged less than 15 years had a confirmed infection by SARS-CoV-2 in Navarre (**Figure 1**), with no paediatric cases detected in February. This corresponds to a cumulative incidence for the 3-month period of 3 cases per 1000 children. Of the total of 309 cases, 259 patients participated in the study (83.8%), and we were unable to reach the rest. None of the patients or families we contacted refused to participate. The age of the patients ranged from 1 month to 15 years, with a median of 8.74 years (IQR, 5.26-12.02). The sex ratio was 1 male: 1.14 female.

When it came to the reason for performing SARS-CoV-2 tests in children, we found that in most pae-

diatric COVID-19 cases, testing was performed in the context of routine contact tracing (52.1%), while in 36.7% of patients it was performed due to symptoms compatible with COVID-19. The remaining tests were performed as part of the screening strategy in children with risk factors (1.2%), in patients that participated in clinical trials related to infection by SARS-CoV-2 (3.1%), as part of the protocol preceding certain medical visits or before hospital admission for other reasons (6.6%). Regardless of the reason that prompted testing, most infected children reported a household contact that had tested positive for SARS-CoV-2 (85.7%).

The clinical features of COVID-19 in our sample were heterogeneous, and 32.1% of the children were completely asymptomatic. In symptomatic patients, the most frequent manifestations were fever (43.2%) and respiratory symptoms (27.4%); Figure 2 details other manifestations of COVID-19. Only 15.8% of patients reported the typical presentation in adults with fever and respiratory symptoms.

Most children in our case series did not require additional diagnostic tests (88.4%). In the group of cases that required them, the most frequent tests were chest X-rays (8.5%), blood tests and other laboratory tests (8.5%), electrocardiography (2.7%) and the rapid strep test (1.5%), among others.

Sixty-one percent of the patients required medical care and the rest did not, since they either were asymptomatic or had mild symptoms. Even so, most medical consultations were held on the telephone (49%); and only 21.1% of the patients required in-person care. Thirteen patients (4.2%) were admitted to hospital and the rest were managed at the outpatient level. All patients had favourable outcomes free of sequelae.

Figure 1. Newly diagnosed cases of SARS-CoV-2 per week in paediatric patients in Navarre, Spain, March-May 2020

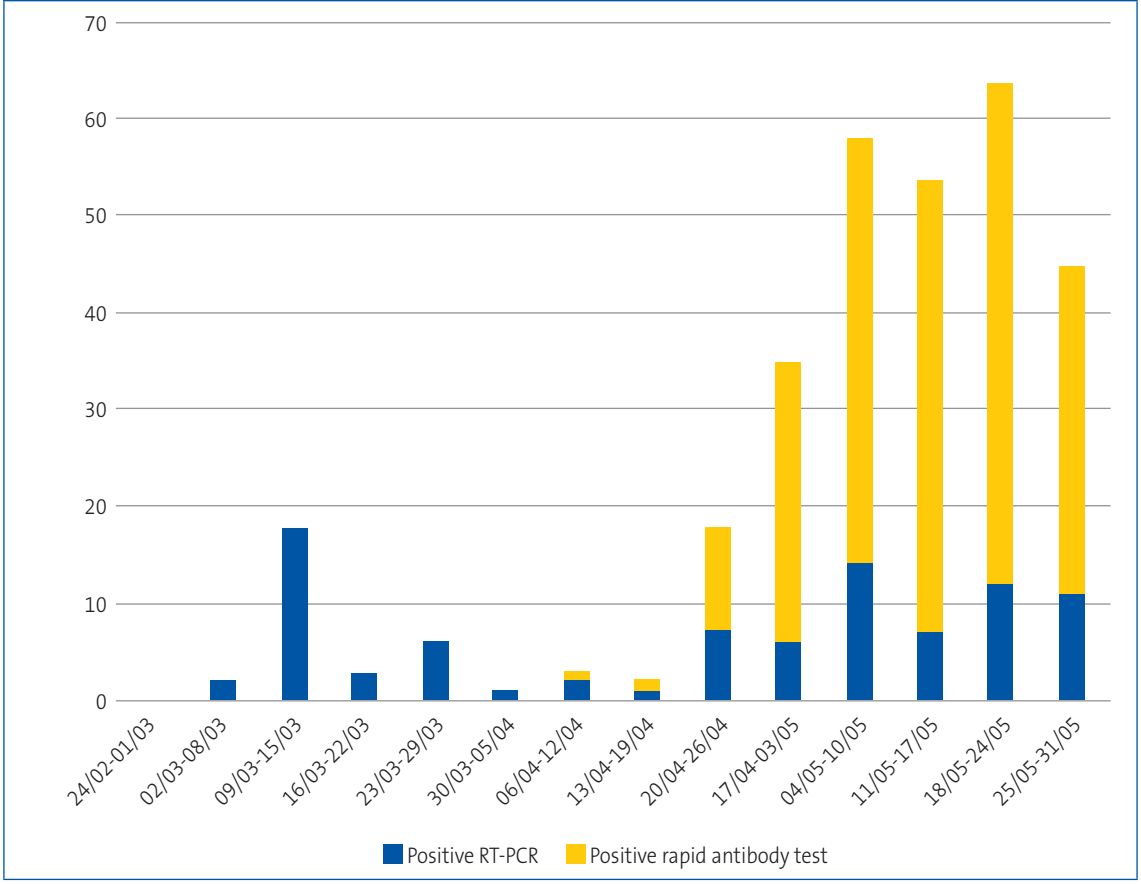
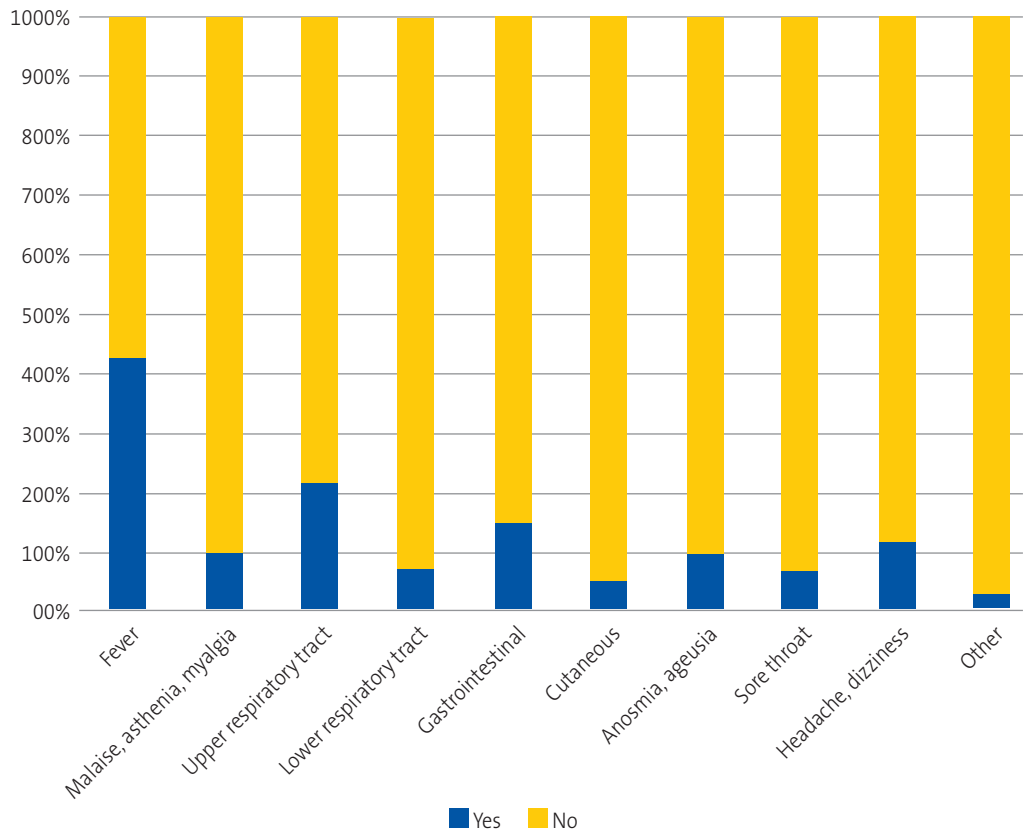


Figure 2. Distribution of signs and symptoms in paediatric patients with infection by SARS-CoV-2 in Navarre, Spain, March-May 2020



In the group of patients admitted to hospital with SARS-CoV-2 infection, the median age was 6.67 years, and 46.2% of patients were male. Five patients (38.5%) had comorbidities, such as obesity, pulmonary malformation, congenital heart defect or cerebral palsy. The median length of stay was 4 days (minimum, 2; maximum, 11) and most patients (76.9%) had mild disease. Two patients developed moderate compromise; one developed hypoxaemia that resolved with supplemental oxygen and the other had convulsive seizures that required anticonvulsant treatment. In addition, one patient presented with severe COVID-19 and developed PIMS-TS with myocarditis that required intensive care. **Table 1** summarizes other clinical features found in hospitalised patients, and a previously published article provides a detailed description of the clinical characteristics and laboratory findings in hospitalised patients with COVID-19 in Navarre along with their management and outcomes.[7]

In our sample, 45.2% of the patients did not require treatment of any kind. In the patients that did, the most frequent treatments were antipyretic and analgesic agents (paracetamol 42.9%, ibuprofen 10.4%), followed by inhaled bronchodilators (4.6%) and oral corticosteroids (3.5%). In the total sample, 10.8% of patients received some form of antibiotherapy (oral penicillin 5.8%, intravenous ceftriaxone 3.1%, oral azithromycin 5%, other antibiotics 1.2%) and 2.3% received hydroxychloroquine. The patient that developed PIMS-TS required intravenous vasoactive drug therapy, high-dose steroid therapy, tocilizumab and intravenous immunoglobulin (IVIG).

Table 1. Main characteristics and clinical manifestations of paediatric patients admitted to hospital with COVID-19 in Navarre, Spain, March-May 2020

Patients	1	2	3	4	5	6	7	8	9	10	11	12	13
Clinical characteristics													
Age (years-months)	1 m	2 years and 9 months	1 year	15 years	12 years and 11 months	9 years and 8 months	3 months	4 years and 5 months	13 years and 8 months	9 years and 5 months	7 months	9 years and 2 months	6 years and 8 months
Sex	Female	Male	Male	Male	Female	Female	Female	Female	Male	Female	Female	Male	Male
Comorbidities	No	Yes	No	Yes	Yes	No	No	Yes	No	No	No	No	Yes
Household contact	Not known	Not known	Not known	Not known	Not known	Confirmed	Suspected	Confirmed	Confirmed	Suspected	Confirmed	Suspected	Confirmed
Signs and symptoms at admission													
Fever	Yes	Yes	No	Yes	Yes	Yes	No	No	Yes	No	Yes	Yes	Yes
Cough	Yes	Yes	No	Yes	Yes	No	No	No	No	No	Yes	No	No
Breathing difficulty	No	Yes	No	No	Yes	No	No	No	No	No	Yes	No	No
Vomiting	No	No	Yes	No	No	Yes	No	No	Yes	No	No	No	Yes
Abdominal pain	No	No	No	No	No	Yes	No	No	Yes	Yes	No	No	Yes
Diarrhoea	No	Yes	No	Yes	No	No	Yes	No	No	No	No	Yes	Yes
Other	Nasal congestion, nausea, irritability	No	Head trauma	No	No	Haematuria	Seizures	No	No	No	Nasal congestion	No	Exanthema
Hospitalization													
Length of stay (days)	11	6	2	4	7	8	7	2	9	3	3	3	3
Severity	Mild	Mild	Mild	Moderate[a]	Mild	Mild	Moderate[b]	Mild	Severe[c]	Mild	Mild	Mild	Mild

[a]Supplemental oxygen.
[b]Epileptic seizures.
[c]Haemodynamic instability, PIMS-TS, admission to PICU.

DISCUSSION

EThe findings of our study of paediatric COVID-19 cases were similar to those of previously published case series, with generally mild to moderate symptoms and heterogeneous and nonspecific manifestations compared to the presentations observed in adults.[5-11] To our knowledge, this is one of the first studies analysing the incidence of COVID-19 in children at the population level, which seemed to be low. However, this outcome could be due in part to underdiagnosis of the infection, as the criteria used to order tests for detection of SARS-CoV-2 at the beginning of the pandemic were restrictive and variable. In the region of Navarre, tests were initially performed only in symptomatic patients with a history of travel to countries with a high incidence of COVID-19, such as China or Italy, and in contact tracing. Later on, travel history was no longer required, but tests were only performed in patients with moderate or severe symptoms requiring medical care or hospital admission. In April, rapid antigen tests in blood or serum samples started to be used, and the criteria for performance of RT-PCR became less stringent.

In terms of the clinical picture, paediatric patients do not usually present with the "typical" respiratory symptoms that are common in adult patients with COVID-19.[11] In addition, one third of our patients were completely asymptomatic. We believe that the proportion of asymptomatic patients in this case series may have been smaller compared to other series due to the initial restrictions on testing (when it came to asymptomatic patients, the only children that were tested were those with a positive close contact); as time passed and the number of tests performed increased, we were able to identify more cases in children with no or few symptoms.

None of our patients developed ARDS and the maximum level of ventilatory support required was supplemental oxygen (in only 1 patient who received low-flow oxygen therapy through nasal prongs). However, other authors have described

cases of infants under 12 months with severe respiratory manifestations, and therefore infants should be considered a risk group in regards to this disease.[8,9,11] It is likely that our series did not include any such case due to the small sample size. At any rate, we consider important that paediatricians remain particularly vigilant for cases of COVID-19 in infants under 12 months and prioritise in-person care delivery in this age group.

In children, severe COVID-19 is frequently associated with PIMS-TS. These patients are usually adolescents presenting with symptoms similar to those of Kawasaki disease that eventually progress to haemodynamic compromise requiring intensive care.[12,13] In our series, 1 male patient aged 13 years that was previously healthy developed myocarditis and ventricular arrhythmia secondary to a COVID-19 and required inotropic support and IVIG.[15] We also identified one patient with neurologic impairment, and infant aged 3 months that developed afebrile epileptic seizures and required treatment with anticonvulsant drugs.

It is believed that most children acquire the infection at home, as in most patients the index case of SARS-CoV-2 was one of the parents, a relative or another member of the household.[7] However, this situation may have been influenced by the extraordinary lockdown measures, and under different conditions children may get infected in the course of their daily activities. Adequate contact tracing following diagnosis of a case is of vital importance, as is followup.

During the first wave of the pandemic, the care delivery model changed due to the risk of transmission of SARS-CoV-2. With the aim of avoiding crowding in primary care centres, some of the non-urgent visits started to be held by telephone. When it came to cases of COVID-19, patients that were asymptomatic or had mild symptoms were managed at the outpatient level through the telephone to isolate them from the rest of the population and thus prevent transmission. This newly introduced telephonic care model has been maintained to date and seems to have been effective in our region, as none of the paediatric patients with COVID-19 followed up by telephone developed complications.

The majority of paediatric patients with COVID-19 did not require any form of treatment, as they had asymptomatic or mild forms of disease. The rest received symptomatic treatment with antipyretics or conventional treatment for bronchitis, if needed, with inhaled bronchodilators and oral corticosteroids. Paracetamol was preferred over ibuprofen for antipyresis because at the beginning of the pandemic there was concern that the latter could have adverse effects on patients with COVID-19 due to its role in increasing the levels of angiotensin-converting enzyme 2 (ACE2).[17]. As for other treatments, some of the first patients admitted to hospital received hydroxychloroquine for the disease, which was eventually removed from the SARS-CoV-2 treatment protocols.[18] In patients with bacterial coinfection (suspected or with microbiological confirmation), the antibiotic selected most frequently for intravenous therapy was ceftriaxone on account of the 24-hour interval between doses, which made it more convenient in that it reduced the exposure of health care staff. Tocilizumab was only used in the patient with severe disease, and high-dose steroid therapy was only used to treat the inflammatory syndrome (PIMS-TS).

We believe that our study is particularly relevant because we made an extensive search of all cases of SARS-CoV-2 in Navarre, one of the regions most affected by SARS-CoV-2 in Spain. We collected data corresponding to the first wave of the pandemic, and because of the lockdown measures, the sample was akin to a closed population. We found very few paediatric cases of moderate to severe COVID-19, consistent with the data of other case series regarding the low incidence of complications in children. On the other hand, the data collection was retrospective and we collected most of the evidence from telephone interviews, so there is a risk of recall bias, especially when it comes to the manifestations of the disease.

In conclusion, we ought to highlight that we are confronting a new disease of which we had no in-

formation at the beginning, and whose characteristics we have been learning over time. We believe that epidemiological reports such as this one are essential to deepen our knowledge of specific aspects of infection by SARS-CoV-2 in paediatric patients and to help us improve the detection, management and treatment of the infection.

CONFLICTS OF INTEREST

The authors have no conflicts of interest to declare in relation to this study.

ABBREVIATIONS

ARDS: acute respiratory distress syndrome • **COVID-19:** coronavirus disease 2019 • **IQR:** interquartile range • **PICU:** paediatric intensive care unit • **PIMS-TS:** paediatric inflammatory multisystem syndrome • **RT-PCR:** reverse transcription polymerase chain reaction • **SARS-CoV-2:** severe acute respiratory syndrome coronavirus 2 temporarily associated with SARS-CoV-2 • **WHO:** World Health Organization.

ACKNOWLEDGMENTS

We thank the Department of Microbiology and the Instituto de Salud Pública y Laboral for their outstanding effort in diagnosis and epidemiologic surveillance. We also thank all health care workers in the Spanish public health system for their extraordinary work in managing the COVID-19 pandemic.

FUNDING

We received funding for the SARS-CoV-2 tests performed during the study in the framework of the Horizon 2020 program of the European Commission (I-MOVE-COVID-19, grant no. 101003673), and from the Instituto de Salud Carlos III and the European Regional Development Fund (COV20/00542 and INT19/00028). Other than these, the authors have no financial relationships to disclose in the context of this study.

REFERENCES

1. Huang C, Wang Y, Li X, Ren L, Zhao J, Hu Y, *et al.* Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. Lancet. 2020;395:497-506.
2. Guan W, Ni Z, Hu Y, Liang W, Ou C, He J, *et al.* Clinical characteristics of coronavirus disease 2019 in China. N Engl J Med. 2020;382:1708-20.
3. Statement on the second meeting of the International Health Regulations (2005). Emergency Committee regarding the outbreak of novel coronavirus (2019-nCoV). In: World Health Organization [online] [accessed 23/03/2021]. Available at www.who.int/news/item/30-01-2020-statement-on-the-second-meeting-of-the-international-health-regulations-(2005)-emergency-committee-regarding-the-outbreak-of-novel-coronavirus-(2019-ncov)
4. Enfermedad por nuevo coronavirus, COVID-19. In: Ministerio de Sanidad, Consumo y Bienestar Social [online] [accessed 23/03/2021]. Available at www.mscbs.gob.es/profesionales/saludPublica/ccayes/alertasActual/nCov/home.htm
5. Zheng F, Liao C, Fan Q, Chen H, Zhao X, Xie Z, *et al.* Clinical characteristics of children with coronavirus disease 2019 in Hubei, China. Curr Med Sci. 2020;40:275-80.
6. Jiehao C, Jing X, Daojiong L, Zhi Y, Lei X, Zhenghai Q, *et al.* A case series of children with 2019 novel coronavirus infection: clinical and epidemiological features. Clin Infect Dis. 2020;71:1547-51.
7. Moreno-Galarraga L, Urretavizcaya-Martínez M, Alegría-Echauri J, García-Howard M, Ruperez-García E, *et al.* SARS-CoV-2 infection in children requiring hospitalization: the experience of Navarra, Spain. World J Pediatr. 2020;16:614-22.
8. Swann OV, Holden KA, Turtle L, Pollock L, Fairfield CJ, Drake TM, *et al.* Clinical characteristics of children and young people admitted to hospital with COVID-19 in United Kingdom: prospective multicentre observational cohort study. BMJ. 2020;370:m3249.
9. Götzinger F, Santiago-García B, Noguera-Julián A, Lanaspa M, Lancella L, Calò Carducci FI, *et al.* COVID-19 in children and adolescents in Europe: a multinational, multicentre cohort study. Lancet Child Adolesc Health. 2020;4: 653-61.
10. Zachariah P, Johnson CL, Halabi KC, Ahn D, Sen AI, Fischer A, *et al.* Epidemiology, Clinical Features, and Disease Severity in Patients With Coronavirus

Disease 2019 (COVID-19) in a Children's Hospital in New York City, New York. JAMA Pediatr. 2020;174: e202430.

11. Han Y, Feng Z, Sun L, Ren X, Wang H, Xue Y. A comparative- descriptive analysis of clinical characteristics in 2019- coronavirus- infected children and adults. J Med Virol. 2020;92:1596-602.

12. Moraleda C, Serna-Pascual M, Soriano-Arandes A, Simó S, Epalza C, Santos M, *et al.* MultiInflammatory Syndrome in Children related to SARS-CoV-2 in Spain. Clin Infect Dis. 2020;ciaa1042.

13. Jiang L, Tang K, Levin M, Ifran O, Morris SK, Wilson K, *et al.* COVID-19 and multisystem inflammatory syndrome in children and adolescents. Lancet Infect Dis. 2020;20:276-88.

14. Padrón de Habitantes a 1 de enero de 2020. Datos provisionales. In: Instituto de Estadística de Navarra, Government of Navarre [online] [accessed 23/03/2021]. Available at www.navarra.es/home_es/Gobierno+de+Navarra/Organigrama/Los+departamentos/Economia+y+Hacienda/Organigrama/Estructura+Organica/Instituto+Estadistica/NotasPrensa/Padron+Continuo+de+Habitantes.htm

15. Gutiérrez-Jimeno M, Ibanez Sada A, Gavira JJ, Cebrián-Nebot C, Martín López L, Macias Mojon M, *et al.* Severe cardiac and abdominal manifestations without lung involvement in a child with COVID-19. Int J Clin Pediatr. 2020;9:92-7.

16. García-Howard M, Herranz-Aguirre M, Moreno-Galarraga L, Urretavizcaya-Martínez M, Alegría-Echauri J, Gorría-Redondo N, *et al.* Case Report: Benign Infantile Seizures Temporally Associated With COVID-19. Front Pediatr. 2020;8:507.

17. Kutti Sridharan G, Kotagiri R, Chandiramani VH, Mohan BP, Vegunta R, Vegunta R, *et al.* COVID-19 and avoiding Ibuprofen. How good is the evidence? Am J Ther. 2020;27:e400-e402.

18. Das S, Bhowmick S, Tiwari S, Sen S. An updated systematic review of the therapeutic role of Hydroxychloroquine in Coronavirus Disease-19 (COVID-19). Clin Drug Investig. 2020;40:591-601.