

# Impact of the COVID-19 Pandemic on the Diagnosis of Congenital Cytomegalovirus Infection in Spain

Serena Villaverde, MD, \*† Estrella Esquivel, BSc, MSc, † Fernando Baquero-Artigao, MD, ‡§  
 Antoni Noguera-Julian, PhD, MD, §¶||\*\* Marie Antoinette Frick, MD, †† Pablo Rojo, PhD, MD, \*†§  
 and Daniel Blázquez-Gamero, MD, PhD\*†§; on behalf of the Spanish Registry of Children with Congenital CMV ‡‡‡

**Abstract:** We conducted an observational study performed within the Spanish Registry of Children with congenital cytomegalovirus (cCMV) to evaluate the impact of the COVID-19 pandemic on the diagnosis of new cases of cCMV. Our study suggest a significant decrease in the monthly rate of new cCMV diagnoses during the COVID-19 pandemic.

**Key Words:** COVID-19, congenital cytomegalovirus infection

(*Pediatr Infect Dis J* 2022;XX:00–00)

Since the beginning of the COVID-19 pandemic in March 2020, there have been important behavioral changes in society. Hygienic measures (hand washing, extensive face masking), school closures, and social distancing were adopted in many countries during the last year, and profound changes in the epidemiology of viral infections like respiratory syncytial virus and influenza were observed in many countries.<sup>1,2</sup> Moreover, the number of new diagnosis of many prevalent diseases has been impacted by the overwork in health care settings.<sup>3,4</sup> We aimed to evaluate the impact

of the COVID-19 pandemic on the diagnosis of new cases of congenital cytomegalovirus (cCMV) infection in Spain.

## MATERIALS AND METHODS

This was an observational study performed within the Spanish Registry of Children with congenital CMV (REDICCMV), a prospective national cohort of children with cCMV that started in 2011, within 53 hospitals from Spain. Children with confirmed cCMV infection (positive polymerase chain reaction in urine/blood/cerebrospinal fluid within the first 14 days of life) followed in participating centers were included in the Registry. Indications for testing for cCMV and microbiological test performed are based on the recommendations of the most recent European guideline and were uniform for all centers.<sup>5</sup> There was no universal screening for cCMV in any center, and there were no changes in the screening practices and in the availability of CMV tests during the time of the study.

Clinical information was collected and stored using the REDCap data collection system. REDCap was hosted in a secure online server located at the Instituto de Investigación Hospital 12 de Octubre, and REDICCMV has been approved by the Ethics Committee of Hospital Universitario 12 de Octubre (CEIC code: 11/316). Parents or legal guardians sign an informed consent at inclusion in the registry.

Two periods were evaluated: from January 2011 to February 2020 (prepandemic) and from March 2020 to June 2021 (COVID-19 pandemic period). Total number of children diagnosed with cCMV per month were calculated. The analyses and plots were executed by using R software via the rate difference function in the `fmsb` and `ggplot` packages, respectively.<sup>6</sup>

## RESULTS

Overall, 677 patients with cCMV were included in REDICCMV during the study period. Numbers of new diagnoses have remained similar during the prepandemic period (Fig. 1), with a mean rate of 5.30 children infected per month. In the pandemic period, the rate of newly diagnosed children per month dropped to 2.73 children each month ( $P < 0.0001$ ). The birth rate since 2011 decreased from 10.07‰ to 7.19‰ in 2020. Analysis of the pandemic period by months shows that the frequency of children diagnosed remains stable from March to November 2020 (mean rate of 3.77 children infected per month). In December 2020 and January 2021, 0 new diagnoses were collected. From February to June 2021, there is a progressive increase in new diagnoses (1, 2, 6, and 2 infected children were collected, respectively). The decrease in cCMV diagnoses in each of the hospitals was uniform. The percentage of parents who positively signed the informed consent remains similar in both periods (nearly 100%).

## DISCUSSION

In our registry, the number of children diagnosed with cCMV significantly dropped during the COVID-19 pandemic period in Spain.

Accepted for publication March 14, 2022

From the \*Pediatric Infectious Diseases Unit, Department of Pediatrics, Hospital Universitario 12 de Octubre, Universidad Complutense de Madrid, Madrid, Spain; †Pediatric Research and Clinical Trials Unit (UPIC), Instituto de Investigación Hospital 12 de Octubre (imas12), Madrid, Spain; ‡Pediatrics, Infectious and Tropical Diseases Department, Hospital Universitario La Paz, Instituto Investigación Hospital La Paz (IDIPaz), Madrid, Spain; §Red de Investigación Translacional en Infectología Pediátrica, Madrid, Spain; ¶Malalties Infeccioses i Resposta Inflamatòria Sistèmica en Pediatria, Unitat d'Infeccions, Servei de Pediatria, Institut de Recerca Pediàtrica Hospital Sant Joan de Déu, Barcelona, Spain; ||Departament de Pediatria, Universitat de Barcelona, Barcelona, Spain; \*\*Centro de Investigación Biomédica en Red de Epidemiología y Salud Pública, Madrid, Spain; and ††Pediatric Infectious Diseases and Immunodeficiencies Unit, Department of Pediatrics, Hospital Universitari Vall d'Hebron, Barcelona, Spain.

S.V. is funded by the Spanish Ministry of Science and Innovation—Instituto de Salud Carlos III and Fondos FEDER (Contrato Río Hortega CM20/00173). This work was funded by projects PI 16/00807, PI19/0009, and PI 19/01333, from the Instituto de Salud Carlos III (Ministry of Economy, Industry, and Competitiveness) and cofunded by the European Regional Development Fund. D.B.-G. was supported by the Spanish Ministry of Science and Innovation—Instituto de Salud Carlos III and Fondos FEDER by “Contratos para la intensificación de la actividad investigadora en el Sistema Nacional de Salud, 2020 (INT20/00086).” A.N.-J. was supported by “Subvencions per a la Intensificació de Facultatius Especialistes” (Departament de Salut de la Generalitat de Catalunya, Programa PERIS 2016–2020) [SLT008/18/00193]. D.B.-G. has received fees from MSD as speaker in educational activities. The remaining authors have no conflicts of interest to disclose.

‡‡‡Members of Spanish Registry of Infants with Congenital Cytomegalovirus Infection (REDICCMV) are listed in the Acknowledgments.

Address for correspondence: Serena Villaverde, MD, Pediatric Infectious Disease Unit, Pediatric Research and Clinical Trials Unit (UPIC), Department of Pediatrics, Hospital Universitario 12 de Octubre, Universidad Complutense de Madrid, Av. de Córdoba, s/n, 28041 Madrid, Spain. E-mail: serenavillaverde@outlook.es.

Copyright © 2022 Wolters Kluwer Health, Inc. All rights reserved.

ISSN: 0891-3668/22/XXXX-0000

DOI: 10.1097/INF.0000000000003532

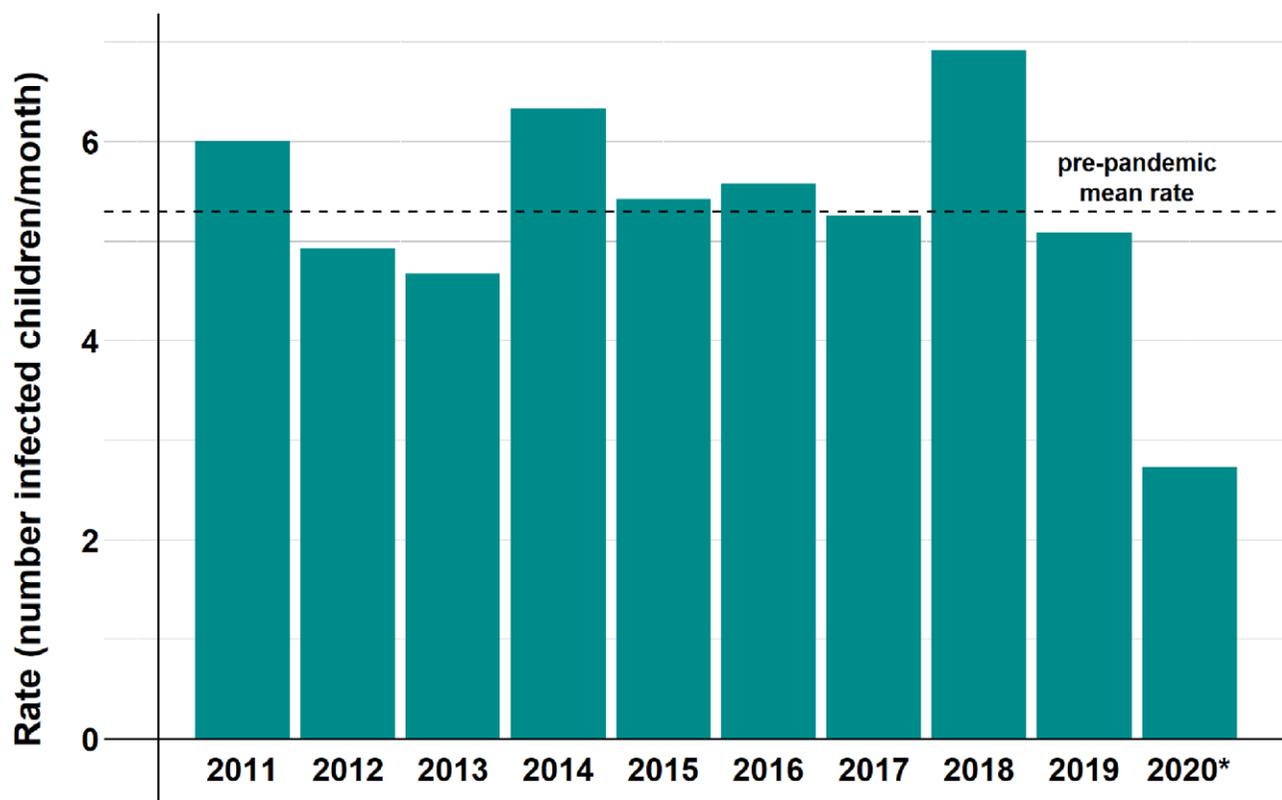


FIG. 1. Rate of infection along the study period (January 2011–June 2021) standardized like the number of children infected per month. \*Period between March 2020–June 2021.

There are different reasons that could explain this finding. On one hand, important changes in social behaviors and hygiene habits at a population level have been implemented to prevent the spread of COVID-19. It should be noted that one of the most important routes of CMV transmission is through direct contact with body fluids (saliva or urine). On March 15, 2020, a lockdown began for 99 days in Spain and all nonessential workers stayed at home without other social contacts. Moreover, schools and nurseries were closed from March 10, 2020, to September 2020 (approximately 170 days). However, schools and workplaces did not regain full activity until months after the designated dates, so both children and adults stayed home even longer. Since a major source of CMV transmission to parents is from young children in daycare, this could be a powerful declining factor, especially considering that these temporary measures were maintained for at least 6 months.<sup>8</sup> Universal masking and boosted hand washing may have also contributed to decreased CMV transmission rates, as demonstrated for other viruses such as respiratory syncytial virus and influenza when compared with the prepandemic era.<sup>1,2,7</sup>

On the other hand, the ability of health care systems to concomitantly diagnose and treat non-COVID-19 diseases during the COVID-19 pandemic has been strained.<sup>1,2</sup> During this period, overloaded health professionals faced a tsunami of COVID-19 cases and, sometimes, non-COVID-19 conditions remained underdiagnosed.<sup>3,4</sup> Pregnant women and newborns experienced some limitations in accessibility to health care resources during the pandemic period as well, potentially contributing to a decrease in the diagnosis of congenital infections.<sup>9</sup> Regarding the lack of availability of CMV detection tests, the laboratories of REDICCMV centers did not report a decrease in material resources, so we do not believe that this could be a contributor. Nonetheless, the possibility of a

subnotification of new patients to the registry, related to the difficulties in the normal work routines, is low because of the care burden of REDICCMV pediatricians during the pandemic has not increased significantly, so underreporting is not expected. On the other hand, it should be noted that REDICCMV centers did not alter their usual screening routines during the pandemic period.

Based on the data from our sample, we believe it plausible that the need to keep adults and children at home during the COVID-19 pandemic may have contributed to the decrease CMV infection in pregnant women. Given that there is little progress in preventing cCMV, our results could provide additional data to support efforts to educate parents, and especially pregnant women, on steps to reduce the risk of CMV infection during pregnancy. The results observed may not be generalizable to other countries; however, Fernández et al have already reported a decrease in the prevalence of cCMV comparing 2019 and 2020 in the context of universal screening program carried out in 4 Portuguese hospitals.<sup>9</sup> It would be interesting to maintain continuous surveillance of the prevalence of cCMV to see if this trend continues.

To conclude, our data suggest a significant decrease in the monthly rate of new cCMV diagnoses in Spain during the COVID-19 pandemic, which could be both because of the prevention and hygiene measures adopted by the population to prevent SARS-CoV-2 infection and least likely, to the underdiagnoses caused by the strained health care systems.

## ACKNOWLEDGMENTS

Spanish Registry of Infants with Congenital Cytomegalovirus Infection (REDICCMV): Reigosa Agúndez- (Hospital Infanta Leonor), Ojembarrena Alonso- (Hospital Puerta del Mar),

Breciano Álvarez- (Hospital San Agustín de Avilés), Hernández Aracil- (Hospital Universitario Nuestra Señora de Candelaria), Tur Barja- (Hospital Moncloa), Mosquera Beceiro- (Hospital Universitario Príncipe de Asturias), Espuny Bringué- (Hospital Universitario Arnau de Vilanova), Garsaball Calavia- (Hospital Joan XXIII), Gallego Carazo- (Hospital Regional Universitario de Málaga), Colom Carrasco- (Hospital Universitario 12 de Octubre), Vilella Castells- (Hospital General de Catalunya), Ortega Cilleruelo- (Hospital Universitario Puerta de Hierro), Gil Colino- (Hospital Universitario Insular de Gran Canaria), Sánchez Corredera- (Hospital Clínico San Carlos), Pérez Cuadrado- (Hospital Universitario de Getafe), Navio Del Castillo- (Hospital de Badajoz), Rabes Del Rosal- (Hospital Universitario La Paz), Pérez del Valle- (Hospital Universitario Infanta Sofía), Martín Díez- (Hospital de Mataró), García Escosa- (Hospital Universitario La Paz), Alejandro Fenoy- (Hospital de Tarrasa), Fernández-Gutiérrez del Álamo (Hospital Puerta del Mar), Antolín Ferreras- (Hospital Carlos Haya), Posse Filgueira- (Hospital Son Llatzer), Guasch Fortuny- (Hospital Sant Joan de Déu), del Río Galán- (Hospital Fuenlabrada), Reymundo García- (Hospital de Mérida), García García- (Hospital San Pedro de Alcántara), Llanos Garrote- (Hospital de Basurto), Bravo González- (Hospital Universitario de Las Palmas de Gran Canaria), de Liria Gonzalo- (Hospital Universitario Germans Trias i Pujol), Tejada Grande- (Hospital Universitario Infanta Cristina), Ibáñez Guarch- (Hospital Josep Trueta), Pérez Herrero- (Hospital Son Llatzer), Ramos Illan- (Hospital Clínico San Carlos), Jiménez Jiménez- (Fundación Jiménez Díaz), López Joaquín- (Hospital General de Catalunya), - Lahoz (Hospital Joan XXIII), Martín Llana- (Hospital HM Torrelodones), Romano Llorente- (Hospital Sureste Arganda), Chacón Malumbres- (Complejo Hospitalario de Navarra), Claros Medina- (Hospital de la Axarquía), Ruiz Menasalvas- (Hospital Clínico Universitario Virgen de la Arrixaca), Calderón Moliner- (Hospital de la Santa Creu i Sant Pau), Martín Montero- (Hospital Comarcal de Melilla), Zuriarrain Muga- (Hospital de Donostia), López Nicolás- (Hospital Universitario Germans Trias i Pujol), Arnal Olabarrieta- (Hospital Severo Ochoa Leganés), Cid Pérez- (Hospital Universitario Infanta Sofía), Pisón Pinillos- (Hospital Universitario Miguel Servet Zaragoza), Ribera Porta- (Hospital Dexeus), Cuello Pronzato- (Hospital General de Castellón), Amador Ramos- (Hospital Clínico San Carlos), Millán Reyes- (Hospital Universitario Nuestra Señora de Candelaria),

Molino Rodríguez- (Hospital Universitario La Paz), Ramírez Romero- (Hospital Universitario Nuestra Señora de Candelaria), García Ruiz- (Hospital de Vic), Aguirre Rumbao- (Hospital Reina Sofía de Córdoba), Lozano Saavedra- (Hospital Universitario Gregorio Marañón), Mateos Sánchez- (Hospital Universitario Puerta de Hierro), Pintos Sánchez- (Hospital Barbanza), Sebastián Santos- (Hospital Universitario Gregorio Marañón), Palacin Soler- (Hospital Universitari Vall d'Hebron), Busselo Sota- (Hospital de Donostia), Sánchez Soto- (Hospital Universitario de Getafe), García Tagarro- (Hospital Universitario Infanta Sofía), Barrero Terol- (Hospital Universitario Virgen Macarena), Bedmar Vila- (Hospital Universitario 12 de Octubre), Restifo Vilagrassa- (Hospital Dexeus), González Vilas- (Hospital de Pontevedra) and Oños Vives- (Hospital Quirónsalud Barcelona).

## REFERENCES

1. Wong SC, Lam GK, AuYeung CH, et al. Absence of nosocomial influenza and respiratory syncytial virus infection in the coronavirus disease 2019 (COVID-19) era: implication of universal masking in hospitals. *Infect Control Hosp Epidemiol.* 2021;42:218–221.
2. Park KY, Seo S, Han J, Park JY. Respiratory virus surveillance in Canada during the COVID-19 pandemic: an epidemiological analysis of the effectiveness of pandemic-related public health measures in reducing seasonal respiratory viruses test positivity. *PLoS One.* 2021;16:1–11.
3. Einstein AJ, Shaw LJ, Hirschfeld C, et al; The INCAPS COVID Investigators Group. International impact of COVID-19 on the diagnosis of heart disease. *J Am Coll Cardiol.* 2021;77:173–185.
4. Richards M, Anderson M, Carter P, et al. The impact of the COVID-19 pandemic on cancer care. *Nat Cancer.* 2020;1:565–567.
5. Luck SE, Wieringa JW, Blázquez-Gamero D, et al; ESPID Congenital CMV Group Meeting, Leipzig 2015. Congenital cytomegalovirus: a European expert consensus statement on diagnosis and management. *Pediatr Infect Dis J.* 2017;36:1205–1213.
6. Subirana I, Sanz H, Vila J. Building bivariate tables: the compareGroups package for R. *J Stat Softw.* 2014;57:1–16.
7. Lee H, Lee H, Song K-H, et al. Impact of public health interventions on seasonal influenza activity during the COVID-19 outbreak in Korea. *Clin Infect Dis.* 2021;73:e132–e140.
8. Kotlar B, Gerson E, Petrillo S, et al. The impact of the COVID-19 pandemic on maternal and perinatal health: a scoping review. *Reprod Health.* 2021;18:10.
9. Fernandez C, Chasqueira MJ, Marques A, et al. Lower prevalence of congenital cytomegalovirus infection in Portugal: possible impact of COVID-19 lockdown? *Eur J Pediatr.* 2022;181:1259–1262.