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

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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

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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.[1,2] Moreover, the number of new diagnosis of many prevalent diseases has been impacted by the overwork in health care settings.[3,4] We aimed to evaluate the impact of the COVID-19 pandemic on the diagnosis of new cases of congenital cytomegalovirus (cCMV) infection in Spain.

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MATERIALS AND METHODS

This was an observational study performed within the Spanish Registry of Children with congenital CMV (REDICCMV, cmv-congenito.com), 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.[5] 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.[6]

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.

There are different reasons that could explain this finding. On one hand, important changes in social behaviors and hygiene

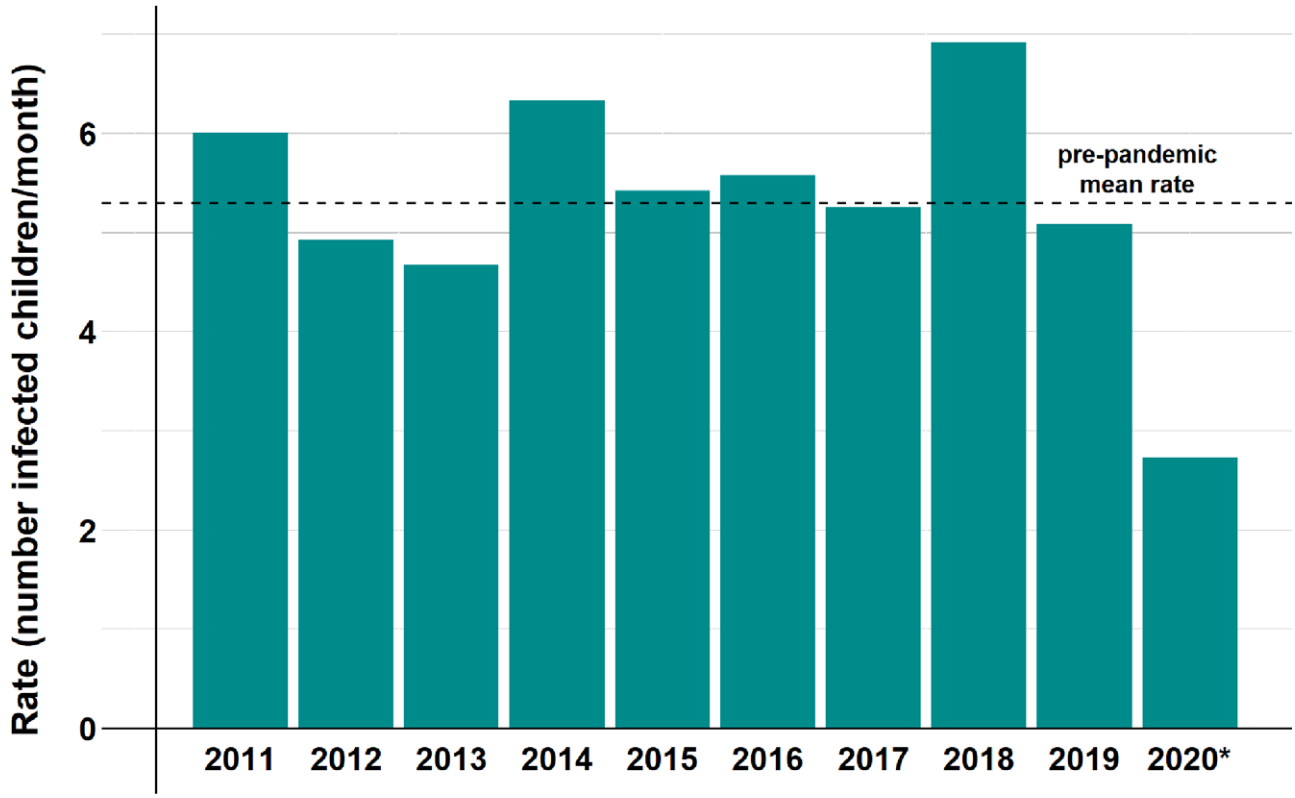

FIG. 1. Rate of infection along the study period (January 2011–June 2021) standardized like the number of children infected per month. *Period between March 2020–June 2021. full color online

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.[8] 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.[1,2,7]

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.[1,2] During this period, overloaded health professionals faced a tsunami of COVID-19 cases and, sometimes, non-COVID-19 conditions remained underdiagnosed.[3,4] 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.[9] 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.[9] 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.

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