

## BRIEF REPORT

# SARS-CoV-2 in asymptomatic Danish infants and their mothers from April 2020 to January 2022

SARS-CoV-2 causes a clinical syndrome (COVID-19) with a spectrum of mild-to-severe manifestations. Knowledge about asymptomatic infections and immunity against SARS-CoV-2 is essential for the planning of COVID-19 policies. The incidence and risk of severe symptoms in children have been low<sup>1</sup> compared with adults, even in children with comorbidities.<sup>2</sup> Moreover, up to one-fourth of SARS-CoV-2 infections in children <5 years of age remain asymptomatic.<sup>2</sup> Consequently, only little is known about transmission patterns of SARS-CoV-2 in infancy including mother-child transmission. Although knowledge about COVID-19 in children is increasing rapidly, a better understanding of SARS-CoV-2 in the youngest, nonhospitalised children is still warranted. Therefore, we aimed to document SARS-CoV-2 RNA and/or serology in children below 2 years of age and their mothers.

We consecutively collected nasopharyngeal swabs for SARS-CoV-2 ribonucleic acid (SARS-CoV-2 RNA) and blood for SARS-CoV-2 serology (IgM and IgG) in a subpopulation of children and their mothers, participating in the MMR vaccine trial<sup>3</sup> (Supplementary S1) from 22 April 2020 to 7 January 2022 to monitor the risk of SARS-CoV-2 spread in this research setting. A Real-time Polymerase Chain Reaction (RT-PCR) assay was used for detecting SARS-CoV-2-RNA. Samples with a cycle threshold (Ct) of <36 for at least one of the virus-specific N-gene targets were considered positive.

For the detection of SARS-CoV-2-IgM and -IgG, we used the YHLO iFlash IgG assay (specificity ≥99%, sensitivity 94%) and YHLO iFlash IgM assay (specificity ≥99%, sensitivity 42%). We defined values ≥8.0 AU/mL as *positive* and <8 AU/mL as *negative* for both IgM and IgG. The assays detected nucleotide antibodies, which are specific for natural SARS-CoV-2 infection. Written informed consent was collected from all participating caregivers.

In total, 680 mother-child pairs were included. Demographic information is presented in Supplementary S1. The prevalence of positive swabs and serology is presented in Figure 1. Altogether, we detected 49 families with positive findings in child or mother in at least one visit. In 11 mother-child pairs, both were IgG-seropositive. However, in 2/11 mother-infant pairs, we could not exclude the possibility that positive infantile IgG was transferred maternal antibodies rather than infantile antibodies in response to infection

because of age <8 months and no prior negative result. Further, 16 IgG-seropositive mothers had a seronegative child and 13 IgG-seropositive children had a seronegative mother. Only one child and five mothers were IgG-seropositive in more than two visits. Nine children and three mothers were IgM-seropositive but none within the same family. In six children and one mother, IgM seropositivity in visit one or two was not followed by an IgG-seropositive result in the following visit (Supplementary S2).

In a population-based longitudinal design, we tested 680 mother-child pairs for the detection of SARS-CoV-2 RNA and IgM and IgG antibodies through the first, second and the early part of the third wave of the COVID-19 epidemic in Denmark. We found only four asymptomatic individuals with positive SARS-CoV-2 RNA and very limited positive SARS-CoV-2 IgM and IgG serology. Our results add to the increasing evidence<sup>1,2</sup> that SARS-CoV-2 prevalence until now has been low in the youngest children. However, the number of positive samples increased over time (Supplementary S3). Denmark has one of the highest test frequencies in the world leading to high-quality epidemiological surveillance; by 21 January 2022, the percentage positive of SARS-CoV-2 RNA was 1.7% among children aged 0-2 years.<sup>4</sup> It is notable that the appearance of the Omicron variant in December 2021 has changed the picture, as incidence in children, including the youngest, has increased.<sup>4</sup>

The incongruence between mother and child in terms of positive findings in swabs or serology adds to the previous findings from other studies that children contributed less to transmission than adults.<sup>5</sup> Interestingly, we found a higher number of positive IgM serology in children that were not followed by corresponding increase in IgG compared with mothers. This suggests that children were less likely to develop an immunological IgG response after being exposed to SARS-CoV-2, maybe because they were less immunologically stimulated.

Most individuals with IgG seropositivity were identified in the third and last visit, and no conclusion about the lasting effect of the antibodies can be made.

A strength of the study is the longitudinal data collected in a population that is often difficult to access. The study is limited by the lack of information on maternal vaccination status to assess the impact on maternal prevalence after introduction in the late Spring

<sup>†</sup>Trial sponsor. Contact information: [lone.graff.stensballe@regionh.dk](mailto:lone.graff.stensballe@regionh.dk), The Juliane Marie Center, The Danish National University Hospital 'Rigshospitalet', Blegdamsvej 9, 2100 Copenhagen East, Denmark

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	Child (n=680)			Mother (n=680)		
	Visit 1 (n=402*)	Visit 2 (n=414*)	Visit 3 (n=675*)	Visit 1 (n=402*)	Visit 2 (n=414*)	Visit 3 (n=675*)
SARS-CoV-2 RNA positive	n=0/399 (0.0%)	n=1/392 (0.3%)	n=1/516 (0.2%)	n=0/398 (0.0%)	n=0/408 (0.0%)	n=2/599 (0.3%)
IgM ≥ 8.0 AU/ml Min max	n=4/342 (1.2%) 0.11-10.72	n=2/359 (0.6%) 0.11-8.9	n=3/571 (0.8%) 0.14-13.09	n=2/398 (0.5%) 0.12-9.75	n=0/405 (0.0%) 0.12-6.89	n=2/600 (0.3%) 0.09 - 33.53
IgG ≥ 8.0 AU/ml Min max	n=1/341 (0.4%) 0.03-35.54	n=5/359 (1.4%) 0.02- 99.52	n=19/571 (3.3%) 0.02-123.3	n=6/397 (1.5%) 0.03 - 94.5	n=6/405 (1.5%) 0.05-88.91	n=21/600 (3.5%) 0.03 - 133.59
IgM + IgG ≥ 8.0 AU/ml	n=0/341 (0.0%)	n=0/357 (0.0%)	n=0/571 (0.0%)	n=1/397 (0.3%)	n=0/404 (0.0%)	n=1/600 (0.2%)

**FIGURE 1** Prevalence of positive swabs and serology. \*Total mother-child pairs eligible for analyses. Missing results (e.g. for children, 3/402 SARS-CoV-2 RNA in visit 1) were mainly due to difficulties in parental refusal for sample collection or nonattendance (mothers). However, in eight children and ten mothers, the assay for SARS-CoV-2 RNA was inconclusive. In nine children and fourteen mothers, serology results were missing due to technical problems

2021. However, participating mothers were not expected to be vaccinated against COVID-19 for most of the study period.

The results confirm that the youngest children and their mothers had a low prevalence of SARS-CoV-2 and were not significant drivers of the COVID-19 epidemic at the beginning of the COVID-19 epidemic.

#### CONFLICT OF INTEREST

The authors have declared that no competing interests exist.

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Michelle Malon<sup>1</sup> 

Andreas Jensen<sup>1</sup>

Jakob Hjort<sup>2</sup>

Nikolai Søren Kirkby<sup>3</sup>

Anne Cathrine Lund Laursen<sup>1</sup>

Jesper Kiehn Soerensen<sup>1</sup>

Dorthe Maria Vittrup<sup>4</sup>

Lone Graff Stensballe<sup>1,†</sup> 

<sup>1</sup>The Child and Adolescent Clinic, The Juliane Marie Center, The Danish National University Hospital "Rigshospitalet", Copenhagen, Denmark

<sup>2</sup>Department of Clinical Medicine, Health, Aarhus University, Aarhus, Denmark

<sup>3</sup>Department of Clinical Microbiology, The Danish National University Hospital "Rigshospitalet", Copenhagen, Denmark

<sup>4</sup>The Child and Adolescent Department, The University Hospital Herlev, Herlev, Denmark

#### Correspondence

Michelle Malon, The Child and Adolescent Clinic, The Juliane Marie Center, The Danish National University Hospital 'Rigshospitalet', Copenhagen, Denmark.  
Email: [michelle.malon@regionh.dk](mailto:michelle.malon@regionh.dk)

#### ORCID

Michelle Malon  <https://orcid.org/0000-0002-2436-4293>

Lone Graff Stensballe  <https://orcid.org/0000-0003-1569-153X>

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#### SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.