

CORRESPONDENCE

Research Letter

High Seroprevalence of SARS-CoV-2 in Preschool Children in July 2022

A Cross-Sectional Data Collection in Day-Care Centers

Till November 2021 the rate of SARS-CoV-2 infection among preschool children in Germany was very low (1). The SARS-CoV-2 seroprevalence rate in children attending day-care centers (DCC) in Würzburg, Germany was 2.3% in March 2021 and 2.2% in July 2021 (2, 3). Since May 2022, vaccination against COVID-19 has been recommended for all children aged 5 years upwards.

With the spread of the Omicron variant at the beginning of 2022, the infection rate increased rapidly in children. Currently, however, it is unknown how many children have been infected with SARS-CoV-2 and developed antibodies to the virus. This information is relevant for assessing the current immunity and planning future preventive measures.

Results

The parents of 366 (45%) of the 810 children attending the DCC (median age 4.5 years, IQR 3.2–5.7; 48.4% female) agreed to take part in the study. Of these children, 13.9% (51/366; median age 6.1 years, IQR 5.6–6.4) had received at least one dose of the SARS-CoV-2 vaccine Comirnaty (BioNTech/Pfizer). From 277 children a blood sample was obtained (75.7% of 366). The seroprevalence of S-AB, which occur following vaccination and/or illness, was 69.6%. The prevalence of N-AB, which appear exclusively after infection, was 60.3% (Table). The proportion of children in whom S-AB were detected increased with age (Figure) from 55.3% in 2-year-olds to 90.7% in 6-year-olds ($p = 0.001$); for N-AB it was 53.2% in

TABLE

Antibodies against the spike protein and the nucleocapsid protein in the group of children as a whole and in vaccinated and unvaccinated children

		Antibodies to spike protein	Antibodies to nucleocapsid protein
Participating children; n (%) [95% CI]	277	193 (69.6%) [64.3; 75.1]	167 (60.3%) [54.5; 66.1]
Vaccinated children; n (%) Titer, median (IQR)	43	40 (93.0%) 2836 BAU/mL (1351.5–7838.8)	22 (51.2%) 10.6 (4.5–70.2)
Unvaccinated children; n (%) Titer, median (IQR)	234	153 (65.4%) 49 BAU/mL (19.4–170.5)	145 (62.0%) 16.5 (5.4–55.0)

Antibodies against the spike protein were determined quantitatively, antibodies against the nucleocapsid protein qualitatively. BAU, Binding antibody units; IQR, interquartile range; 95% CI, 95% confidence interval

Method

In a cross-sectional survey performed in July 2022, antibodies against SARS-CoV-2 were determined from finger-tip capillary blood samples from preschool children (age 2–6 years) at nine DCC in Würzburg.

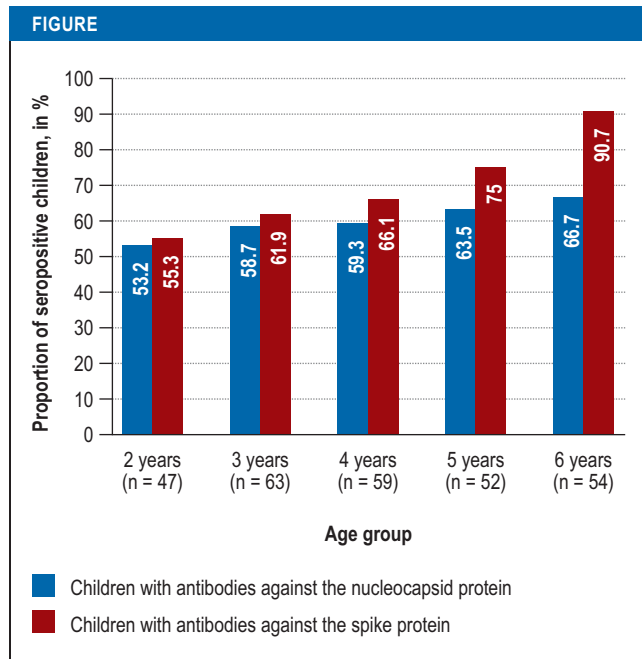
An electrochemoluminescence assay (CLIA; Roche Diagnostics GmbH, Mannheim) was used for antibody determination. Antibodies against the spike (S) protein (S-AB), which appear after vaccination and/or illness, were measured quantitatively (positive cut-off level of 0.8 binding antibody units [BAU]/mL). Antibodies against the nucleocapsid (N) protein (N-AB), which are specific for earlier infection, were assessed qualitatively (positive if the assay-specific cut-off index was ≥ 1.0).

Demographic data, SARS-CoV-2 infection history, and vaccination status were documented using a standardized questionnaire developed in the context of the pediatric projects of the University Medicine Network (*Netzwerk Universitätsmedizin*). SPSS Statistics (IBM, version 28, 2021) was used for statistical analysis.

2-year-olds and 66.7% in 6-year-olds ($p = 0.206$). Of the 43 vaccinated children, 93.0% showed S-AB and 51.2% N-AB.

The parents of 50.2% of the children (139/277) reported a prior SARS-CoV-2 infection, confirmed by a PCR test and/or rapid flow test (RFT) (116 PCR positive, 118 RFT positive). One hundred ten (79.1%) of these 139 infections were detected in the period from February to April 2022. According to the parents, 75.5% of the children (105/139) who tested positive for infection had typical SARS-CoV-2 symptoms and/or fever, 5.0% (7/139) had unspecific signs of illness, and 15.8% (22/139) had no symptoms.

Of the children with previous SARS-CoV-2 infection, 85.6% (119/139) showed S-AB, while 79.1% (110/139) displayed N-AB. Of the 123 children for whom no confirmed SARS-CoV-2 infection was reported, 51.2% (63/123) showed S-AB, which appear after vaccination and/or infection. Fifty (40.7%) of the 123 also exhibited N-AB, which occur exclusively after infection. This included 33/123 children (26.8%) in whom the parents had suspected infection in the absence of a positive test.



Antibodies (%) against the SARS-CoV-2 spike protein (detectable after vaccination and/or infection) and nucleocapsid protein (only after infection) in 275 children aged 2–6 years attending day-care centers (data on two children missing). Age-dependent statistically significant increase in seroprevalence for the spike protein (Kendall Tau-b 0.16; $p = 0.001$), non-significant increase for the nucleocapsid protein (Kendall Tau-b 0.07; $p = 0.206$)

Discussion

Our Würzburg DCC cohort, followed since September 2020, showed a sharp increase in SARS-CoV-2 seroprevalence rate, from initially 2% to 70%, between February and April 2022. This can most likely be explained by the high number of often oligosymptomatic or asymptomatic infections during the Omicron wave in early 2022. In around 15% of the children, no antibodies could be detected despite a prior positive SARS-CoV-2 test result, which suggests that the infection rate may be even higher. The older children in this cohort showed higher seropositivity rates than the younger children, regardless of SARS-CoV-2 vaccination status. Moreover, vaccinated children demonstrated much higher S-AB titers than non-vaccinated infected children—similar to the findings of a study in Italy (4). Furthermore, 50% of the vaccinated children had N-AB, showing that they had been infected with SARS-CoV-2.

In addition to its regional nature and the relatively low sample size, our study may be limited by a selection bias in favor of more careful parents tending to adhere to advice on the subject of preventive measures.

Conclusion

The steep increase in seroprevalence among the DCC children points to a high rate of SARS-CoV-2 infections in this age group, often oligosymptomatic or asymptomatic. The use of preventive measures, e.g., further mass screening of asymptomatic DCC children and DCC closures, should therefore be weighed up carefully against the negative effects of restricted DCC services.

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Conflict of interest statement

Nicole Toepfner is a board member of the German Society for Pediatric Infectiology (Deutsche Gesellschaft für Pädiatrische Infektiologie, DGPI).

Reinhard Berner states that he is a member of the following bodies: the Expert Commission of the German Federal Government, the Expert Commission on Pandemic Respiratory Infections of the Robert Koch Institute (RKI), the Pandemic Working Group of the Standing Committee on Vaccination (STIKO), the Medical Pandemic Commission of the German Medical Association (BÄK), the Long COVID Syndrome Working Party of the BÄK Scientific Council, and the Coronavirus Task Force of the German Society for Pediatrics and Adolescent Medicine (Deutsche Gesellschaft für Kinder- und Jugendmedizin, DGKJ).

Oliver Kurzai is a member of the SARS-CoV-2 expert panel of the city and rural district of Würzburg.

Astrid Petersmann has received payments for training events from Roche Diagnostik GmbH.

The remaining authors declare that no conflict of interest exists.

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References

1. Wöchentlicher Lagebericht des RKI zur Coronavirus-Krankheit-2019 (COVID-19), 30.12.2021 – aktualisierter Stand für Deutschland, verkürzter Bericht. www.rki.de/DE/Content/InfAZ/N/Neuartiges_Coronavirus/Situationsberichte/Wochenbericht/Wochenbericht_2021-12-30.pdf?__blob=publicationFile (last accessed on 9 August 2022).
2. Forster J, Streng A, Rudolph P, et al.: Feasibility of SARS-CoV-2 surveillance testing among children and child care workers at German day care centers. *JAMA Netw Open* 2022; 5: e2142057.
3. Engels G, Forster F, Streng A, et al.: Acceptance of different self-sampling methods for semiweekly SARS-CoV-2 testing in asymptomatic children and childcare workers at German day care centers. *JAMA Netw Open* 2022; 5: e2231798.
4. Mari A, Garancini N, Barcellini L, et al.: SARS-CoV-2 seroprevalence among school-age children in Milan: How has it changed with the fourth pandemic wave? *Pediatr Infect Dis J* 2022; 41: e344–e5.

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