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Brief communication

Trends in SARS-CoV-2 seroprevalence amongst urban paediatric patients compared with a nationwide cohort in the Netherlands

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ABSTRACT

Objectives: The extent of SARS-CoV-2 infection amongst children and their role in transmission remains unclear. Therefore, we aimed to estimate the SARS-CoV-2 antibody seroprevalence amongst children who presented to our hospital for non-COVID-19-related morbidity during the first and second epidemic wave in 2020 and compared these to the general Dutch paediatric population.

Methods: We collected residual plasma samples from all paediatric patients (1 month-17 years of age) visiting our clinic or emergency room, who had blood drawing for various medical reasons. Samples were analysed for the presence of total antibodies against SARS-CoV-2 by Wantai ELISA. The seroprevalence in two separate periods (July-Sep 2020, and Oct-Dec 2020) was compared to regional and national data (PIENTER-Corona study, September 2020), and associations with co-morbidities were assessed.

Results: A total of 209 samples in period 1 and 240 samples in period 2 were collected (median age 7.1 years, IQR 1.5–13.5). SARS-CoV-2 antibodies were detected in 4.1% and 13.8%, respectively ($p< 0.001$). Seroprevalence was higher compared to national paediatric data, but did not differ with regional estimates. Most children with SARS-CoV-2 antibodies were seen in the outpatient clinic for general paediatric problems with no differences in medical reasons for presentation between the two periods.

Conclusions: These data confirm a rapid three-fold increase in SARS-CoV-2 seroprevalence in paediatric patients in the second half of 2020 with a trend towards a higher seroprevalence compared to randomly-selected children in a nationwide study. Underlying morbidity in children might not play an important role in acquiring SARS-CoV-2 infection.

1. Introduction

During the early phase of the coronavirus disease 2019 (COVID-19) pandemic, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infections were assumed to be less prevalent amongst children [1–4]. However, children were also less likely to be tested, because they often exhibit mild symptoms and due to restrictive testing policies. In the Netherlands for instance, children younger than 13 years of age with non-severe symptoms of COVID-19 were not tested during the first national epidemic wave (March-May 2020). Alternatively, serological testing, as a sound indicator of cumulative infection, might provide more insight into the prevalence of COVID-19 in children [5,6]. Less frequent use of reverse transcriptase polymerase chain reaction (RT-PCR) diagnostics for recognizing acute COVID-19 cases in children may have led to an underestimation of the true COVID-19 burden in children. The Rotterdam area, in the province of South-Holland, had a high incidence of COVID-19 amongst adults, especially during the second wave of COVID-19 [4].

We determined SARS-CoV-2 antibody seroprevalence amongst children who presented themselves to our urban hospital located in Rotterdam for non-COVID-19-related reasons on two consecutive points in time and compared these to national estimates. Additionally, we investigated the association between serostatus and chronic co-morbidities in these paediatric patients.

2. Methods

We collected all available residual plasma samples from consecutive paediatric patients (1 month-17 years of age) who visited our (outpatient) clinic or emergency room and underwent blood drawing for any

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Table 1
Characteristics of hospital patient cohorts in Rotterdam, the Netherlands.

	All children period 1; July-September 2020 (n = 209)	All children period 2; October-December 2021 (n = 240)	p-value
Age (years)	7.8 (1.8–12.8)	6.7 (1.4–14.3)	0.72
Sex (boys)	116 (55.5)	125 (52.1)	0.47
Admission type Outpatient Emergency Inpatient Paediatrics Neonatology	141 (67.5) 46 (22.0) 22 (10.5) 9 13	163 (67.9) 53 (22.1) 24 (10.0) 9 15	0.98
Chronic medication use	64 (30.6)	77 (32.1)	0.82

Data are presented in median (interquartile range) or number (percentage). P-values were calculated by Chi-square test or Mann-Whitney-U test.

Table 2
SARS-CoV-2 seroprevalence in the Rotterdam hospital cohorts in the first (July-September 2020) and second (October-December 2020) period, and comparison with Dutch provincial and national estimates from September 2020.

	Rotterdam - July-September 2020 (N = 209)	Rotterdam - October-December 2020 (N = 240)	South-Holland province end of September 2020 (N = 133)	p-value Rotterdam period 1 vs. province	National end of September 2020 (N = 1020)	p-value Rotterdam period 1 vs. national
Overall (1–17 years) *	4.1 (1.1–7.1)	13.8 (9.0–18.7)	2.4 (0.0–4.9)	0.38	1.3 (0.5–2.1)	0.03
1 month-1 year	5.4 (0.0–13.0)	13.3 (3.0–37.7)	–	NA	–	NA
1–3 years	2.7 (0.0–8.2)	5.9 (0.0–12.6)	0.0 (NA)	NA	0.0 (NA)	NA
4–12 years	3.5 (0.0–7.5)	15.3 (6.8–23.8)	3.6 (0.0–7.5)	0.98	1.3 (0.2–2.4)	0.21
13–17 years	6.0 (0.0–12.8)	18.1 (9.0–27.2)	1.1 (0.0–3.6)	0.10	2.1 (0.4–3.8)	0.20

Data are presented as (weighted and corrected for provincial and national) SARS-CoV-2 seroprevalence with 95% confidence intervals. NA=not applicable. Dissimilarities in seroprevalence rates between the hospital cohort in July-September 2020, and the national or regional cohort were identified by, firstly, estimating the parameters of the beta distribution for these seroprevalence rates using the methods of moments. Thereafter, Monte Carlo simulations of these estimates were used to calculate risk ratios and p-values.
*hospital cohorts included 1 month-1 years of age; Dutch provincial and national cohort 1–17 years, therefore overall data described for 1–17 years.

medical reason after the first wave (period 1: July 19-September 19, 2020) and during the second wave (period 2: October 19-December 19, 2020) of the COVID-19 epidemic in the Netherlands (Supplementary Figure 1). The local ethics committee approved the study and waived the need for informed consent (protocol number 2020–072).

Samples were analysed for the presence of total antibodies directed against the receptor binding domain of the SARS-CoV-2 spike protein by enzyme-linked immunosorbent assay (Beijing Wantai Biological Pharmacy Enterprise Co., Ltd., China) [7]. Children with known current COVID-19 related conditions (e.g., respiratory tract infection or multisystem inflammatory syndrome in children (MIS-C) with proven positive SARS-CoV-2 PCR and/or antibodies) were excluded from the analysis. If a child had multiple blood samples drawn during the inclusion period, the first blood sample was selected for analysis.

Subsequently, we compared our data with seroprevalence rates from a Dutch nationwide population-based serosurvey [4]. This study estimated the seroprevalence amongst 6093 randomly-selected persons (from the population registry, 1–91 years) in the end of September 2020, using a validated immunoassay quantifying IgG antibodies against the spike S1 antigen of SARS-CoV-2 [8].

3. Results

The samples of a total of 209 and 240 children were collected in period 1 and 2, respectively. Median age was 7.1 years (IQR 1.5–13.5) and 241 (53.7%) were male (Table 1). SARS-CoV-2 antibodies were detected in 4.1% (95% CI 1.1–7.1) in period 1, and 13.8% (95% CI 9.0–18.8) in period 2 (p<0.001) (Table 2). There were no differences between seropositive versus seronegative children with respect to age, gender, type of morbidity and medication use; likewise, no significant differences were observed between seropositive children from the first and second period concerning these variables (data not shown). Most children with SARS-CoV-2 antibodies were seen in the outpatient clinic for general paediatric problems with no clear differences in visiting reasons between the two periods. For both periods, seroprevalence in children with respiratory and allergic disorders was not statistically significantly different in comparison to those with other disorders (Supplementary Figure 1). A trend towards a higher positivity rate was observed in children <1 and ≥13 years, albeit not statistically significant (Table 2).

In the Dutch nationwide population-based serosurvey, the overall weighted seroprevalence was 4.9% (95% CI 4.1–5.6), and amongst children 1–17 years this was 1.3% (95% CI 0.5–2.1). For the province of South-Holland, the overall seroprevalence was 3.5% (95% CI 2.3–4.8), and in children 2.4% (95% CI 0.0–4.9) (Table 2). This regional paediatric seroprevalence was not statistically different from the seroprevalence amongst paediatric patients visiting our hospital during period 1 (p = 0.38), but the seroprevalence in this hospital cohort was higher compared to national data (p = 0.03).

4. Discussion

We observed a rapid increase in SARS-CoV-2 seroprevalence amongst the paediatric hospital cohort in the second half of 2020. Adult blood donor data also showed seroprevalences of 12–13% in December 2020, comparable to the studied paediatric cohort [9]. Nationally, schools were closed to help confine the pandemic from mid-March 2020 till mid-May 2020; and after December 22, 2020. School openings could partially account for the observed increase of SARS-CoV-2 seroprevalence amongst children but probably it largely reflects the changes in prevalence in the total population.

The seroprevalence amongst paediatric patients visiting a hospital for non-COVID-19-related diseases does not seem to be clearly different compared to healthy children. However, we could not rule out potential bias since the group of children presenting to the hospital might be a different group in terms of risks and underlying susceptibility compared to the nationwide study group.

We did not see differences of SARS-CoV-2 seroprevalence between the different morbidity groups or medication use, within and between study periods, including not for asthma or obesity. This is in line with other studies showing no elevated risk for SARS-CoV-2 infection in children with allergic diseases, such as asthma [10].

Interestingly, we found a relatively high number of very young infants (1 month-1 year) with SARS-CoV-2 antibodies in our hospital cohort. These included infants who were admitted at the neonatal ward (being over >1 month of age at sampling moment) because of premature birth or who were seen in the emergency department. Prenatal placental transfer of maternal SARS-CoV-2 antibodies might explain relatively high seroprevalence [11].

There are several study limitations. First, we could not track clinical data and family history regarding SARS-CoV-2 infection and we could also not rule out nosocomial transmission with subclinical infection. Second, our sample is possibly not representative of the general paediatric population of Rotterdam because only children seeking medical care who underwent blood draws were included. We excluded children with known active COVID-19. Due to discrepancies in study periods between our hospital data and the national cohort, we were not able to compare our estimates from the second period. However, our data provides insights into trends of SARS-CoV-2 infections in children in urban settings during the course of this epidemic. Furthermore, the study was not able to detect potential small differences amongst children with different co-morbidities with respect to the likelihood of acquiring SARS-CoV-2 infection, possibly because of the small numbers.

In conclusion, our study confirms a rapid three-fold increase in SARS-CoV-2 seroprevalence in general paediatric patients in the second half of 2020 with a trend towards a higher seroprevalence compared to randomly-selected children in a nationwide study. This might reflect increased exposure, and our urban setting with ensuing living conditions. Moreover, our data showed that underlying morbidity might not play an important role in acquiring SARS-CoV-2 infection.

Supplementary Figure 1. Reasons for visiting the hospital, in the first and second period with SARS-CoV-2 seroprevalence per morbidity type.

Abbreviations for morbidity classes: RESP/ALL= respiratory/allergy; GI-TRACT=gastro-intestinal; INF/IMM=infectiology/immunology; ENDO=endocrine; NEURO=neurological; PREM=prematurity (including follow-up); SYNDRO=syndromal

Declaration of Competing Interest

The authors declare no conflicts of interest.

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Contribution

DSYO, JGMK and GATS contributed to the conception and design of the study. ILMR and ERAV acquired the data. All authors contributed to the analysis and interpretation of the data. ILMR drafted the first manuscript and all other authors revised it critically for important intellectual content. All authors approved this manuscript version to be submitted.

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