


SARS-CoV-2 transmissions in students and teachers: seroprevalence follow-up study in a German secondary school in November and December 2020

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ABSTRACT

Objective To quantify the number of undetected SARS-CoV-2 infections in educational settings.

Design Serial SARS-CoV-2 seroprevalence study before and during the second wave of the COVID-19 pandemic.

Setting Secondary school in Dresden, Germany.

Participants Grade 8–12 students and their teachers were invited to participate in serial blood sampling and SARS-CoV-2 IgG antibody assessment.

Main outcome measure Seroprevalence of SARS-CoV-2 antibodies in study population.

Results 247 students and 55 teachers participated in the initial study visit and 197 students and 40 teachers completed follow-up. Seroprevalence increased from 1.7% (0.3–3.3) to 6.8% (3.8–10.1) during the study period mirroring the increase of officially reported SARS-CoV-2 infections during this time. The ratio of undetected to detected SARS-CoV-2 infections ranged from 0.25 to 0.33.

Conclusions We could not find evidence of relevant silent, asymptomatic spread of SARS-CoV-2 in schools neither in a low prevalence setting nor during the second wave of the pandemic, making it unlikely that educational settings play a crucial role in driving the SARS-CoV-2 pandemic.

Trial registration number DRKS00022455.

INTRODUCTION

Since the worldwide spread of coronavirus 2 (SARS-CoV-2) starting in December 2019¹ and the declaration of a pandemic by WHO in March 2020, various measures intended to slow down transmission rates were put in place in countries across the globe including school closures in most countries.²

Meanwhile, the role of children and adolescents, specifically in educational settings, is still unclear.

Several tracing studies in schools^{3–5} found only minimal spread of SARS-CoV-2. In fact, most countries, including Germany, report a much lower proportion of cases in children in comparison to their population size^{6–8} and some studies showing lower SARS-CoV-2

What is known about the subject?

- ▶ Children and adolescents are under-represented in official COVID-19 cases compared with their population size.
- ▶ Tracing studies could only detect minimal SARS-CoV-2 spread in educational settings.

What this study adds?

- ▶ There is no evidence of large-scale asymptomatic hidden transmissions in educational settings even in a high prevalence setting.
- ▶ The ratio of undetected to detected SARS-CoV-2 infections in this age group is very low.

seroprevalence in young children compared with adults.^{9 10}

Nonetheless, the concern of a high rate of undetected cases especially in adolescents, due to mild or even asymptomatic infections in this age group, remains, as therefore hidden transmissions could lead to higher rates of infection in the general population.

In spite of the risks of hidden transmissions in school settings, the adverse effects of long-term school closures on children and adolescents, as well as their parents, such as loss of education, loss of social contacts and social control, nutritional problems in children who rely on school meals, increases in harm to child welfare, as well as economic harm caused by lowered productivity of parents being forced from work to childcare^{11 12} are clearly described. In this context, scientific studies on possible undetected spreads of SARS-CoV-2 in schools are essential, as they may inform policymakers and public health authorities in regard to future policy measures in an ongoing pandemic.

In order to gain further insight into a possible silent advance of coronavirus infections in schools, we conducted a serial seroprevalence study in a secondary school in Dresden, Germany. Students and teachers' serum samples were analysed at the beginning of November and a second time 6 weeks after the first sampling in mid-December. The first testing dated 8 weeks after one of the students had tested positive for SARS-CoV-2 and had remained in school for 2 days post-testing due to delays in reporting. The second round of samples was taken at the height of a second wave of infections in Saxony after the summer, with a 7-day average of SARS-CoV-2-infections over 300 cases per 100.000.

METHODS

Study design

Eight weeks after the identification of a SARS-CoV-2-positive student in their school, grade 8–12 students (mean class size 23.8 students) and their teachers in a secondary school in a metropolitan area in Dresden (capital of the Federal State of Saxony, Germany, with approximately 557.000 inhabitants) were invited to participate in a seroprevalence study. After teachers, students and their legal guardians provided informed consent, 5 mL of peripheral venous blood was collected from each individual during visits to the school on 3 and 6 November 2020. In addition, participants were asked to complete a questionnaire asking about age, household size, previously diagnosed SARS-CoV-2 infections in themselves or their household contacts, mandated quarantine measures, comorbidities and regular medication. All eligible students and teachers were invited to participate in a repeat blood sampling 6 weeks later that took place on 10 and 11 December 2020.

Mitigation strategies

The following mitigation strategies were implemented by the Federal State of Saxony and did not change during the study period:

- ▶ Students were seated 1.5 m apart in classrooms, mask wearing in common areas was strongly recommended for students and teachers but not mandated. Student mixing was decreased by a reduction in extracurricular activities.
- ▶ Students were not allowed to attend school when they were tested positive for SARS-CoV-2, had close contact to an infected individual within 14 days or showed symptoms of a respiratory infection—with the exception of an isolated runny or stuffed nose—until symptoms resolved for more than 48 hours or tested negative for SARS-CoV-2.

These measures were not part of the study protocol nor assessed or controlled by the study team.

Laboratory analysis

We assessed SARS-CoV-2 IgG antibodies in all samples using a commercially available chemiluminescence

immunoassay technology for the quantitative determination of anti-S1 and anti-S2-specific IgG antibodies to SARS-CoV-2 (DiaSorin LIAISON SARS-CoV-2 S1/S2 IgG Assay). Antibody levels >15.0 AU/mL were considered positive and levels between 12.0 and 15.0 AU/mL were considered equivocal.

All samples with a positive or equivocal LIAISON test result, as well as all samples from participants with a reported personal or household history of a SARS-CoV-2 infection, were retested with two additional serological tests. These were a chemiluminescent microparticle immunoassay intended for the qualitative detection of IgG antibodies to the nucleocapsid protein of SARS-CoV-2 (Abbott Diagnostics ARCHITECT SARS-CoV-2 IgG) (an index (S/C) of <1.4 was considered negative whereas one ≥ 1.4 was considered positive) and an ELISA detecting IgG against the S1 domain of the SARS-CoV-2 spike protein (Euroimmun Anti-SARS-CoV-2 ELISA) (a ratio <0.8 was considered negative, 0.8–1.1 equivocal, >1.1 positive).

Participants whose positive or equivocal LIAISON test result could be confirmed by a positive test result in at least one additional serological test were considered to be seropositive for SARS-CoV-2. Seropositive participants were considered undetected if neither themselves nor a household contact was tested positive for SARS-CoV-2 by PCR prior to the serological testing.

Statistical analysis

Analyses were performed using IBM SPSS V.25.0 and Microsoft Excel V.2010. Results for continuous variables are presented as medians with IQRs and categorical variables as numbers with percentages, unless stated otherwise.

Patient and public involvement

The public was not involved in the design, recruitment and conduct of the study. Participants were able to receive their personal serological test result on request.

RESULTS

In the first study visit in November, a total of 247 students (median age 15) and 55 teachers were sampled. These numbers represent 53% of all students in grades 8–12 and 79% of teachers in this particular school. (Demographic data are shown in [table 1](#).) Five study participants—all students—had detectable antibodies against SARS-CoV-2 in at least two different assays and were therefore considered seropositive, indicating a seroprevalence of 1.7% (0.3%–3.3%). While one of the seropositive participants reported to have no knowledge of a previous SARS-CoV-2 infection, the other four seropositive students reported to have been tested positive for SARS-CoV-2 previously by PCR. (Two of the positive students reported to have been tested positive in March, during the first wave of the pandemic, the remaining two did not report the date of testing.) The ratio of undetected to detected cases was therefore 0.25.

Table 1 Demographic data

	First study visit (November 2020)		Second study visit (December 2020)	
	Students	Teachers	Students	Teachers
Participants	247 (82%)	55 (18%)	197 (85%)	40 (15%)
Proportion of all eligible students/teachers	246/464 (53%)	55/70 (79%)	197/464 (42%)	40/70 (51%)
New participants at second visit	–	–	17	1
Age (median)	15 (14–17)	51 (44–56)	16 (14–17)	52 (42–57)
Female	131 (53%)	33 (66%)	109 (57%)	23 (64%)
Household size	4 (4–5)	3 (2–4)	3 (3–5)	3 (2–3)

At follow-up 6 weeks after the initial visit, 180 students and 39 teachers gave repeat blood samples and an additional 17 students and one teacher were sampled for the first time. These sample numbers represent 42% of all students grade 8–12 and 57% of all teachers (table 1).

In the second sampling, 16 participants were seropositive, including the five seropositive students from the initial visit. Six seropositive participants reported a previous SARS-CoV-2 infection diagnosed by PCR and nine reported a SARS-CoV-2-positive household contact, leading to a ratio of undetected to detected cases of 0.33 (table 2). This results in a seroprevalence of 6.8% (3.8%–10.1%) and a fourfold rise in seroprevalence within 6 weeks. Since 4 out of the 16 seropositive students were only sampled at the second visit, we also analysed the group of participants with two blood samples (n=219) separately, resulting in a 2.4-fold seroprevalence increase, from 2.3% (0.5%–4.6%) to 5.5% (2.3%–8.7%) (table 2).

Overall, 92 participants reported an episode of cold-like symptoms between study visits. Seroprevalence did not differ significantly between those with and without reported symptoms (7.6% vs 6.2%).

Fifty participants reported to have been in an officially mandated quarantine at least once between the two visits. Five (10%) out of those quarantined newly developed SARS-CoV-2 antibodies, three of these newly seropositive participants reported to have been tested SARS-CoV-2 positive by PCR and one reported a SARS-CoV-2-positive household contact leading to a ratio of undetected to detected cases of 0.25 in this subsample.

DISCUSSION

While school-age children remain under-represented among the officially reported confirmed cases, the concern remains that open schools lead to silent transmissions into the general population due to large numbers of asymptomatic children. In order to establish a better understanding of the numbers (and possible risks) of silent transmissions in school settings, we conducted a repeated seroprevalence study of a representative sample of students and teachers. The first study sampling took place 8 weeks after a SARS-CoV-2 PCR-positive student spent 2 full days in school before quarantine measures were taken, and again 6 weeks later in midst a second wave of the pandemic. The results do not show evidence for widespread undetected transmission of SARS-CoV-2 in the examined school's student and teacher population. The measured seroprevalence of 1.7% in November is higher than the general population's prevalence of PCR-confirmed cases at this time (cumulative prevalence in Dresden on 27 October 2020: 0.35%¹³). However, four of the five participants with antibodies against SARS-CoV-2 had a PCR-confirmed SARS-CoV-2 infection, yielding a ratio of undetected to detected cases of only 0.25, which is much smaller than previously assumed by some authors.¹⁴ This finding calls into question the assumption of a high number of asymptomatic, undetected cases in children and adolescents. Furthermore, at least two of the five seropositive participants had already been infected during the first wave of the pandemic in March

Table 2 SARS-CoV-2 seroprevalence

	First study visit (November 2020)	Second study visit (December 2020)
Seroprevalence % (CI)	1.7 (0.3 to 3.3)	6.8 (3.8 to 10.1)
Seroprevalence % (CI)—for participants with two samples available		5.5 (2.3 to 8.7)
Number of participants who reported cold-like symptoms between study visits		92
Seroprevalence % (CI)—for participants with cold-like symptoms		7.6 (3.3 to 13.0)
Seroprevalence % (CI)—for participants without cold-like symptoms		6.2 (2.8 to 10.3)
Ratio of undetected to detected cases	1/4 (0.25)	4/12 (0.33)
Ratio of undetected to detected cases in participants with mandated quarantine measures between visits		1/4 (0.25)



and not after the reopening of the schools on 18 May or in the fall semester. Our findings support the hypothesis that schools did not develop into silent hot spots of SARS-CoV-2 transmissions after the reopening in May until the start of the second wave of the pandemic. This is further substantiated by the fact that we could neither detect a single case of a seropositive student in the grade of the mentioned index case nor in the class of the one undetected seropositive student.

With dramatically increasing numbers during the second wave of the pandemic in Saxony, the seroprevalence of the study population increased as well. Officially reported SARS-CoV-2 infections in the state's capital city of Dresden increased fourfold from 1939 cases (348 per 100 000 inhabitants) on 27 October 2020—1 week before the first visit—to 7737 cases (1390 per 100 000 inhabitants) on 3 December 2020—1 week before the second visit. The different increase rates between the analysis of all study participants and that of only participants who were also tested on the first visit (fourfold respectively 2.4-fold) might be due to the fact that students with a history of a SARS-CoV-2 infection during the second wave of the pandemic, after our first visit, might have had a higher interest in participating in our study in comparison to other students.

Even with a tripling of the seroprevalence, the ratio of undetected to detected cases remained extremely low (0.33). Therefore, we did not find evidence for a significant underestimation of SARS-CoV-2 infections in schools by PCR testing. It must also be noted that our study was performed among an age group, which is considered to be at higher risk for infection and transmission than primary school children. Yet, the fact that the measured seroprevalence increased to a lesser or the same degree compared with the officially reported cases does not indicate that schoolchildren can be considered the main drivers of the SARS-CoV-2 pandemic.

There is some concern that the SARS-CoV-2 antibody response is not stable over time especially in asymptomatic individuals¹⁵ leading to an underestimation of SARS-CoV-2 infection in seroprevalence studies. However, there are longitudinal studies of the SARS-CoV-2 antibody response kinetic in children¹⁶ and adults¹⁷ that show antibody titres remain detectable for at least 62 days. Given the short intervals between exposure and first and second study visits of 6–8 weeks and the fact that all seropositive participants in the first visit remained seropositive in the second visit, we feel confident that the risk of missing a relevant number of infections due to vanishing antibody titres is low.

Coming from moderate levels of SARS-CoV-2 infections in Dresden in early November, there was a fast increase in case numbers in early December, with schools remaining open during this period. The time frame of our investigation is thus a particular strength of the study, as one can assume that the impact of schools on the dynamics of the pandemic can best be studied under these given circumstances. Another strength is the method of antibody testing itself,

since asymptomatic or undetected cases of SARS-CoV-2 are not missed, and the method is not as dependent on a certain timepoint as is PCR—or antigen testing. By testing the majority of students and teachers in one school with isolated reported cases of SARS-CoV-2, we are convinced that our results very closely represent the actual seroprevalence among students and teachers. Given the possibility of virus transmissions among students, as well as between students and teachers, due to one undetected case and one case where the student still visited classes for 2 days after his PCR test being positive, these findings should also be applicable to other educational settings. The findings cannot confirm concerns about widespread undetected virus transmissions in schools.

There are several limitations to our study. Mainly, that this is a single-centre study with a limited number of participants and a relevant loss of participants in the follow-up sampling. In addition, there is a certain percentage of SARS-CoV-2-infected individuals who do not form detectable antibodies and are therefore not detected by a seroprevalence study. Additional immunological studies including T cell-based assays would provide an even more comprehensive picture.

CONCLUSION

The study could not provide evidence for a relevant silent, asymptomatic spread of SARS-CoV-2 in schools, neither in a low prevalence setting nor during a second higher incidence wave of the pandemic, adding to the evidence that educational settings do not play a crucial role in driving the SARS-CoV-2 pandemic—even if there are single imported cases. These results warrant further studies to evaluate if social distancing strategies such as the reduction of students of different classes mixing at school, paired with symptom-based screening strategies, contact tracing and quarantine measures for identified cases are as effective as full school closures, with less adverse effects on the student population.

Contributors JPA, RB and AD designed the study and wrote the protocol. JPA, LG, LH and EK collected the samples. AD and CL performed serological testing. JPA, LH, EK and RB analysed the data. JPA, LG and EK wrote the manuscript. LH, AD, CL and RB reviewed the manuscript.

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Competing interests None declared.

Patient and public involvement Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

Patient consent for publication Not required.

Ethics approval The investigation is part of the SchoolCoviDD19 study which was approved by the Ethics Committee of the Technische Universität (TU) Dresden (BO-EK-156042020).

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement Data are available upon reasonable request. All data relevant to the study are included in the article or uploaded as supplemental information. jakob.armann@uniklinikum-dresden.de.

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