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SARS-CoV-2 IgG antibodies in adolescent students and their teachers in Saxony, Germany (SchoolCoviDD19): persistent low seroprevalence and transmission rates between May and October 2020

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Abstract:

Objective: To quantify the number of SARS-CoV-2 infections in secondary schools after their reopening in May 2020.

Design: Repeated SARS-CoV-2 seroprevalence study after the reopening of schools and 4 months later.

Setting: Secondary school in Dresden/Germany

Participants: 1538 Students grade 8-12 and 507 teachers from 13 schools.

Interventions: Serial blood sampling and SARS-CoV-2 IgG antibody assessment.

Primary and secondary outcome measure: Seroprevalence of SARS-CoV-2 antibodies in study population. Number of undetected cases.

Results: 1538 students and 507 teachers were initially enrolled, and 1334 students and 445 teachers completed both study visits. The seroprevalence for SARS-CoV-2 antibodies was 0.6% in May/June and the same in September/October. Even in schools with reported Covid-19 cases before the lockdown of March 13th no clusters could be identified. Of 12 persons with positive serology 5 had a known history of confirmed COVID-19; 23 out of 24 participants with a household history of COVID-91 were seronegative.

Conclusions: Schools do not play a crucial role in driving the SARS-CoV-2 pandemic in a low prevalence setting. Transmission in families occurs very infrequently, and the number of unreported cases is low in this age group. These observations do not support school closures as a strategy fighting the pandemic in a low prevalence setting.

Trial registration: DRKS00022455

Strengths and limitations of this study:

Strengths:

Seroprevalence can detect mildly- or asymptomatic SARS-CoV-2 infections

Longitudinal study designs tracks individuals over time

Older students with multiple social contacts are a relevant target for pandemic control meassures

Limitations:

Loss to follow up

Funding Statement:

This study was supported by a grant from the state of Saxony

Grant name: CoviDD19

The funder of the study had no role in the study design, data collection, data analysis, data interpretation, or writing of the report. The corresponding authors had full access to all the data in the study and had final responsibility for the decision to submit for publication.

Competing Interest statement:

All Authors declare no competing interests.

Word Count: 1752

Introduction:

Since the identification of the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) as the cause of COVID-19 in December 2019 [1], the virus spread rapidly around the world, leading to the declaration of a pandemic by the World Health Organization on March 12th 2020. By March 18th 2020, 126 countries—including Germany—had implemented school closures as part of their pandemic control measures, with the number of countries peaking at 194 on April 10th 2020 and more than 90% of the world's student population being affected at this point[2, 3].

These actions were mainly based on the assumption that children play a similar role in transmitting SARS-CoV-2 as they do in transmitting influenza during outbreaks, for which evidence exists that school closures reduce the peak of the outbreak[4]. However, there is reason to believe that children play a less significant role in SARS-CoV-2 transmission compared to influenza, making control measures focused on this age group less effective: Most countries—including Germany—report a much lower proportion of cases in children compared to their population size[5–7]. In addition, several tracing studies in schools in different countries could only identify minimal spread of SARS-CoV-2 in educational settings. [8–10]

However, currently available data is insufficient to rule out that children are as likely as adults to be infected by and to transmit SARS-CoV-2, but simply show little to no symptoms of the disease.

We therefore aimed to quantify the proportion of adolescent schoolchildren and teachers in Saxony, one of the eastern Federal States of Germany, that already have developed antibodies against SARS-CoV-2. Until autumn 2020, in Saxony, the infection rates were comparatively low with 245-laboratory-confirmed SARS-CoV-2 infections per 100,000 inhabitants as of October 13th 2020.

Methods:

Study Design

After the reopening of the schools in Saxony on May 18th, 2020 students grade 8–11 and their teachers in 13 secondary schools in eastern Saxony were invited to participate in the SchoolCoviDD19 study. After teachers, students, and their legal guardians provided informed consent, 5 mL of peripheral venous blood were collected from each individual during visits at each participating school between May 25th and June 30th, 2020. In addition, participants were asked to complete a questionnaire on age, household size, previously diagnosed SARS-CoV-2 infections in themselves or their household contacts, comorbidities and regular medication. Students were also asked about regular social contacts outside their household or classroom.

A second visit and repeat blood sampling took place between September 15th and October 13th 2020.

Approval

The SchoolCoviDD19 study was approved by the Ethics Committee of the Technische Universität (TU) Dresden (BO-EK-156042020) and was registered on July 23rd 2020 and assigned the clinical trial number DRKS00022455.

Laboratory Analysis

We assessed SARS-CoV-2 IgG antibodies in all samples using a commercially available chemiluminescence immunoassay (CLIA) 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 re-tested with two additional serological tests: These were a chemiluminescent microparticle immunoassay (CMIA) 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 having antibodies against SARS-CoV-2.

Statistical Analysis

Analyses were performed using IBM SPSS 25.0 and Microsoft Excel 2010. Results for continuous variables are presented as medians with interquartile ranges (IQR) 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 are able to receive their personal serological test result upon request.

Results:

A total of 1538 students and 507 teachers from 13 different schools participated in the first visit of the study, 1334 students and 445 teachers completed the second visit. Demographic data is shown in Table 1.

Seroprevalence of SARS-CoV-2 antibodies was 0.6% (12/2045) at the initial visit (May/June) with twelve participants—eleven students and one teacher—having detectable antibodies against SARS-CoV-2 in at least two different assays and thus being considered seropositive. At the follow-up visit

(September/October) seroprevalence was 0.7% (12/1779) with still eleven seropositive students and one teacher. Remarkably, one participants who tested positive in 2 assays in the initial sample tested positive in only one assay at the second timepoint and one participant who had equivocal results initially did test positive 3 months later. In 7 out of 13 schools, seropositive participants could be identified, with four seropositive participants in one school as the maximum. The seroprevalence ranged from 0 to 2.2 per individual school.

Of the few participants with a personal history of a SARS-CoV-2 infection, 4/5 were seropositive, with the fifth showing only an equivocal test result in one of the assays. Of all participants with a household history of a SARS-CoV-2 infection, 23/24 were seronegative, with 22/24 showing negative results in all three assays and one showing an equivocal result in only one assay.

During the study period laboratory-confirmed SARS-CoV-2 infections per 100,000 inhabitants in Saxony increased from 139 to 245.

Discussion:

The findings from this unique study in older students and their teachers indicate that the prevalence of IgG antibodies against SARS-CoV-2 was very low after the first wave of the corona pandemic in Germany and during the reopening of the schools in May 2020 and remained low after summer holidays 2020. While this finding is consistent with local surveillance data[11] that shows a prevalence of PCR-confirmed cases of 0.8%, it clearly indicates that schools did not develop into silent hotspots of SARS-CoV-2 transmission during the first wave of the pandemic and even more importantly after reopening of the schools in May 2020. Even more important is the fact, that there was no increase in seropositivity and infections, respectively, in the four months between May after reopening and October after the summer holidays and the first weeks of back to school in the fall period. It has to be pointed out, however, that the infection rate in Saxony was constantly low during this time period. Nevertheless, the most relevant observation is that infection rates do not increase silently in schools when infection rates in the population are low. Of course, this does not preclude that with increasing infection rates in the population, infection rates in schools may also increase which is an important reminder that the general population has to act prudently in order to keep schools open.

In fact, 5 of the 12 participants with antibodies against SARS-CoV-2 had a personal or household history of COVID-19, yielding a ratio of unidentified to identified cases of 1.4, which is much smaller than that previously assumed by some authors[12]. We could not detect a single cluster of infections in the participating schools, even though at least three schools did have confirmed SARS-CoV-2 cases before the March 13th lockdown in Saxony. This is consistent with findings from the 2003 SARS outbreak [13, 14], and calls the effectiveness of transmission control measures focused mainly on the student population into question. This is especially relevant since there are clearly described adverse effects of school closures, 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 in vulnerable populations, as well as economic harm caused by loss to productivity due to parents being forced from work to childcare[15, 16]. Additionally, even with school closures in place, social contacts continue as informal child care and non-school gatherings[17], thereby reducing the potential benefit of school closures further. Our data support this finding this finding since an overwhelming majority

of not less than 80% of the participating students in our study reported to have regular social contacts outside their household or classroom.

Close contact with COVID-19 patients—especially in the same household—has been shown to increase viral transmission[18]. However, in our study, only one out of 24 participants with a confirmed SARS-CoV-2 infection in the same household became indeed infected as measured by antibody production. This suggests that either the transmissibility of the virus is lower than previously assumed or that there are certain quarantine and separation measures than can effectively reduce the probability of viral transmission even in close contact situations.

It was reported recently, that SARS-CoV2 spike-reactive CD4+ T cells could be detected in 35% of SARS-CoV2 unexposed healthy blood donors arguing for a certain level of T-cell crossreactivity. Such reactions could arise from exposure to commonly encountered Corona viruses. With children being frequently exposed to common Corona viruses it might be hypothesized that they are less susceptible to SARS-CoV2 infection due to a background of T-cell crossreactivity[19].

Currently no gold standard serological testing strategy for SARS-CoV-2 exists. Even though immunoassays yield better performance than rapid point-of-care tests[18] and the targeted SARS-CoV-2 S protein and nucleoprotein show a similarity of less than 30% to endemic betacoronaviruses[20], false positive results are still a concern, especially in low-prevalence populations and when interpreting results on a personal rather than a population-based level. By using a combination of three different immunoassays and only regarding participants with at least two positive results as seropositive for SARS-CoV-2, we could exclude ten participants with a positive and six with an equivocal initial test by negative confirmatory testing. In our population, a positive predictive value of 42.9% could be observed which was nearby an expected PPV of 45.3% for a prevalence of 0.59% population and the given test characteristics (sensitivity 97.6%, specificity 99.3%). By using this approach, we could reliably identify patients with confirmed seropositivity against SARS-CoV-2 in a low-prevalence population.

Conclusion:

As for now, students and teacher do not seem to play a substantial role in driving the SARS-CoV-2 pandemic in Germany when observing the period after reopening of schools in May as well as after summer holidays until early autumn 2020 before facing the second pandemic wave. Transmission in families appears to occur very infrequently, and the number of unreported cases obviously is low in this age group. For serological testing, a combination of different immunoassays seems to be effective to increase the number of true positive test results.

Author contribution statements:

J.A, R.B. and A.D designed the study and wrote the protocol. J.A., M.U. and C.K. collected samples. A.D. and C.L. performed serological testing. J.A., M.U., C.K. and R.B. analyzed the data. J.A. and C.K. wrote the manuscript. M.U. A.D., C.L. and R.B. reviewed the manuscript.

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Table 1: Demographic data

	first study visit (May/June)		second study visit (September/October)	
	students	teachers	students	teachers
participants	1538 (75.2%)	507 (24.8%)	1334 (75.0%)	445 (25.0%)
age (median)	15 (14–16)	51 (37–57)	15 (14-16)	50 (36-57)
female	802 (52%)	357 (70%)	680 (51%)	313 (70%)
household size	4 (3–5)	2 (2–4)	4 (3-5)	2 (2-4)
Seropositive	11	1	11	1
Regular social contacts outside the student's household/classroom during the March 2020 Lockdown	1230 (80%)			
respiratory symptoms between study visits			587 (44%)	71 (16%)
febrile illness between study visits			67 (5%)	4 (0.9%)

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SARS-CoV-2 SEROPREVALENCE in students and teachers – a longitudinal study from May to October 2020 in German secondary schools

Carolin Kirsten1, Manja Unrath[1], Christian Lück[2], Alexander H. Dalpke[2], Reinhard Berner[1], Jakob P. Armann[1],

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Design: Repeated SARS-CoV-2 seroprevalence study after the reopening of schools and 4 months later.

Setting: Secondary school in Dresden/Germany

Participants: 1538 Students grade 8-12 and 507 teachers from 13 schools.

Interventions: Serial blood sampling and SARS-CoV-2 IgG antibody assessment.

Primary and secondary outcome measure: Seroprevalence of SARS-CoV-2 antibodies in study population. Number of undetected cases.

Results: 1538 students and 507 teachers were initially enrolled, and 1334 students and 445 teachers completed both study visits. The seroprevalence for SARS-CoV-2 antibodies was 0.6% in May/June and the same in September/October. Even in schools with reported Covid-19 cases before the lockdown of March 13th no clusters could be identified. Of 12 persons with positive serology 5 had a known history of confirmed COVID-19; 23 out of 24 participants with a household history of COVID-91 were seronegative.

Conclusions: Schools do not play a crucial role in driving the SARS-CoV-2 pandemic in a low prevalence setting. Transmission in families occurs very infrequently, and the number of unreported cases is low in this age group. These observations do not support school closures as a strategy fighting the pandemic in a low prevalence setting.

Trial registration: DRKS00022455

Strengths and limitations of this study:

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Seroprevalence can detect mildly- or asymptomatic SARS-CoV-2 infections

Longitudinal study designs tracks individuals over time

Older students with multiple social contacts are a relevant target for pandemic control meassures

Limitations:

Loss to follow up

Funding Statement:

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These actions were mainly based on the assumption that children play a similar role in transmitting SARS-CoV-2 as they do in transmitting influenza during outbreaks, for which evidence exists that school closures reduce the peak of the outbreak[4]. However, there is reason to believe that children play a less significant role in SARS-CoV-2 transmission compared to influenza, making control measures focused on this age group less effective: Most countries—including Germany—report a much lower proportion of cases in children compared to their population size[5–7] and a recent review on population-based seroprevalence studies found no evidence of overrepresentation of schoolchildren [8] In addition, several tracing studies in schools in different countries could only identify minimal spread of SARS-CoV-2 in educational settings. [9–11]

However, currently available data is insufficient to rule out that children are as likely as adults to be infected by and to transmit SARS-CoV-2, but simply show little to no symptoms of the disease.

We therefore aimed to quantify the proportion of adolescent schoolchildren and teachers in Saxony, one of the eastern Federal States of Germany, that already have developed antibodies against SARS-CoV-2. Until autumn 2020, in Saxony, the infection rates were comparatively low with 245-laboratory-confirmed SARS-CoV-2 infections per 100,000 inhabitants as of October 13th 2020.

Methods:

Study Design

After the reopening of the schools in Saxony on May 18th, 2020 students grade 8–11 and their teachers in 13 secondary schools in eastern Saxony were invited to participate in the SchoolCoviDD19 study. Schools were chosen by the state office for schools and education without involvement of the study team and all eligible students and teachers were invited to participate at each school. Participation rates varied from 12%-50% per school.

After teachers, students, and their legal guardians provided informed consent, 5 mL of peripheral venous blood were collected from each individual during visits at each participating school between May 25th and June 30th, 2020. In addition, participants were asked to complete a questionnaire on

age, household size, previously diagnosed SARS-CoV-2 infections in themselves or their household contacts, comorbidities and regular medication. Students were also asked about regular social contacts outside their household or classroom.

A second visit and repeat blood sampling of the same participants took place between September 15th and October 13th 2020. Between the two study visits schools in Saxony remained open with the regular summer break from July 20th until August 28th 2020.

Approval

The SchoolCoviDD19 study was approved by the Ethics Committee of the Technische Universität (TU) Dresden (BO-EK-156042020) and was registered on July 23rd 2020 and assigned the clinical trial number DRKS00022455.

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A total of 1538 students and 507 teachers from 13 different schools participated in the first visit of the study, 1334 students and 445 teachers completed the second visit. Demographic data is shown in Table 1.

Seroprevalence of SARS-CoV-2 antibodies was 0.6% (12/2045) at the initial visit (May/June) with twelve participants—eleven students and one teacher—having detectable antibodies against SARS-CoV-2 in at least two different assays and thus being considered seropositive. At the follow-up visit (September/October) seroprevalence was 0.7% (12/1779) with still eleven seropositive students and one teacher. Remarkably, one participants who tested positive in 2 assays in the initial sample tested positive in only one assay at the second timepoint and one participant who had equivocal results initially did test positive 3 months later. Using more liberal (>/= 1 test positive) or more conservative (3 tests positive) definitions for seropositivity does not change the persistent low seroprevalence in the study population. In 7 out of 13 schools, seropositive participants could be identified, with four seropositive participants in one school as the maximum. The seroprevalence ranged from 0 to 2.2 per individual school.

Of the few participants with a personal history of a SARS-CoV-2 infection, 4/5 were seropositive, with the fifth showing only an equivocal test result in one of the assays. Of all participants with a household history of a SARS-CoV-2 infection, 23/24 were seronegative, with 22/24 showing negative results in all three assays and one showing an equivocal result in only one assay.

During the study period laboratory-confirmed SARS-CoV-2 infections per 100,000 inhabitants in Saxony increased from 139 to 245 and 7-day incidence rates ranged from 1/100.000 to 30/100.000.

Discussion:

The findings from this unique study in older students and their teachers indicate that the prevalence of IgG antibodies against SARS-CoV-2 was very low after the first wave of the corona pandemic in Germany and during the reopening of the schools in May 2020 and remained low after summer holidays 2020. While this finding is consistent with local surveillance data[12] that shows a prevalence of PCR-confirmed cases of 0.8%, it clearly indicates that schools did not develop into silent hotspots of SARS-CoV-2 transmission during the first wave of the pandemic and even more importantly after reopening of the schools in May 2020. Even more important is the fact, that there was no increase in seropositivity and infections, respectively, in the four months between May after reopening and October after the summer holidays and the first weeks of back to school in the fall period. Therefore, herd immunity in the population of students and teachers appears not to contribute substantially to protection in a low prevalence setting.

It has to be pointed out, however, that the infection rate in Saxony was constantly low during this time period. Nevertheless, the most relevant observation is that infection rates do not increase silently in schools when infection rates in the population are low. Of course, this does not preclude that with increasing infection rates in the population, infection rates in schools may also increase which is an important reminder that the general population has to act prudently in order to keep schools open.

In fact, 5 of the 12 participants with antibodies against SARS-CoV-2 had a personal or household history of COVID-19, yielding a ratio of unidentified to identified cases of 1.4, which is much smaller

than that previously assumed by some authors[13]. We could not detect a single cluster of infections in the participating schools, even though at least three schools did have confirmed SARS-CoV-2 cases before the March 13th lockdown in Saxony. This is consistent with findings from the 2003 SARS outbreak [14, 15], and calls the effectiveness of transmission control measures focused mainly on the student population into question. This is especially relevant since there are clearly described adverse effects of school closures, 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 in vulnerable populations, as well as economic harm caused by loss to productivity due to parents being forced from work to childcare[16, 17]. Additionally, even with school closures in place, social contacts continue as informal child care and non-school gatherings[18], thereby reducing the potential benefit of school closures further. Our data support this finding this finding since an overwhelming majority of not less than 80% of the participating students in our study reported to have regular social contacts outside their household or classroom.

While close contact with COVID-19 patients—especially in the same household—has been shown to increase viral transmission[19] a review of household transmission studies found secondary attack rates of only 0.17 [20] with underage household members being less likely affected compared to adults. Our finding that only one out of 24 participants with a confirmed SARS-CoV-2 infection in the same household became indeed infected as measured by antibody production supports these findings as well as findings that children in general appear to be less susceptible to SARS-CoV-2 compared to adults [21, 22]. In addition, these results support studies showing that certain quarantine and separation measures than can effectively reduce the probability of viral transmission even in close contact situations [23].

The fact that we could not detect one additional seropositive participant in over 4 months is surprising even in a low prevalence setting, given that the reported cases doubled in the same period of time in Saxony. One explanation might be the recently reported detection of SARS-CoV2 spike-reactive CD4+ T cells in 35% of SARS-CoV2 unexposed healthy blood donors arguing for a certain level of T-cell crossreactivity. Such reactions could arise from exposure to commonly encountered Corona viruses. With children being frequently exposed to common Corona viruses it might be hypothesized that they are less susceptible to SARS-CoV2 infection due to a background of T-cell crossreactivity [24].

Currently no gold standard serological testing strategy for SARS-CoV-2 exists. Even though immunoassays yield better performance than rapid point-of-care tests[19] and the targeted SARS-CoV-2 S protein and nucleoprotein show a similarity of less than 30% to endemic betacoronaviruses[25], false positive results are still a concern, especially in low-prevalence populations and when interpreting results on a personal rather than a population-based level. By using a combination of three different immunoassays and only regarding participants with at least two positive results as seropositive for SARS-CoV-2, we could exclude ten participants with a positive and six with an equivocal initial test by negative confirmatory testing. In our population, a positive predictive value of 42.9% could be observed which was nearby an expected PPV of 45.3% for a prevalence of 0.59% population and the given test characteristics (sensitivity 97.6%, specificity 99.3%). By using this approach, we could reliably identify patients with confirmed seropositivity against SARS-CoV-2 in a low-prevalence population.

There are several limitations to our study. We cannot provide information on eligible but nonparticipating students and teachers in the selected schools requiring additional caution when generalizing these results. In addition, there is a relevant loss of participants in the follow-up

sampling. While we do not have information why certain individuals dropped out, the fact that the second study visit took place in a before the beginning of the second wave (7-day incidence rates around 30/100.000) makes it unlikely that personal illness or widespread quarantine measures were responsible for this drop in participation

Conclusion:

As for now, students and teacher do not seem to play a substantial role in driving the SARS-CoV-2 pandemic in Germany when observing the period after reopening of schools in May as well as after summer holidays until early autumn 2020 before facing the second pandemic wave. Transmission in families appears to occur very infrequently, and the number of unreported cases obviously is low in this age group. For serological testing, a combination of different immunoassays seems to be effective to increase the number of true positive test results.

Author contribution statements:

J.A, R.B. and A.D designed the study and wrote the protocol. J.A., M.U. and C.K. collected samples. A.D. and C.L. performed serological testing. J.A., M.U., C.K. and R.B. analyzed the data. J.A. and C.K. wrote the manuscript. M.U. A.D., C.L. and R.B. reviewed the manuscript.

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Table 1: Demographic data

	first study visit (May/June)		second study visit (September/October)	
	students	teachers	students	teachers
participants	1538 (75.2%)	507 (24.8%)	1334 (75.0%)	445 (25.0%)
age (median)	15 (14–16)	51 (37–57)	15 (14-16)	50 (36-57)
female	802 (52%)	357 (70%)	680 (51%)	313 (70%)
household size	4 (3–5)	2 (2–4)	4 (3-5)	2 (2-4)
Seropositive	11	1	11	1
Regular social contacts outside the student's household/classroom during the March 2020 Lockdown	1230 (80%)			
respiratory symptoms between study visits			587 (44%)	71 (16%)
febrile illness between study visits			67 (5%)	4 (0.9%)

Supplemental table 1: seroprevalence based on different seropositivity definitions

	first study visit (May/June)	second study visit (September/October)
>/= 1 serological test positive	22/2045 (1.1%)	25/1779 (1.4%)
>/= 2 serological tests positive	12/2045 (0.6%)	12/1779 (0.7%)
3 serological tests positive	9/2045 (0.4%)	5/1779 (0.3%)

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SARS-CoV-2 seroprevalence in students and teachers – a longitudinal study from May to October 2020 in German secondary schools

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Abstract:

Objective: To quantify the number of SARS-CoV-2 infections in secondary schools after their reopening in May 2020.

Design: Repeated SARS-CoV-2 seroprevalence study after the reopening of schools and 4 months later.

Setting: Secondary school in Dresden/Germany

Participants: 1538 Students grade 8-12 and 507 teachers from 13 schools.

Interventions: Serial blood sampling and SARS-CoV-2 IgG antibody assessment.

Primary and secondary outcome measure: Seroprevalence of SARS-CoV-2 antibodies in study population. Number of undetected cases.

Results: 1538 students and 507 teachers were initially enrolled, and 1334 students and 445 teachers completed both study visits. The seroprevalence for SARS-CoV-2 antibodies was 0.6% in May/June and the same in September/October. Even in schools with reported Covid-19 cases before the lockdown of March 13th no clusters could be identified. Of 12 persons with positive serology 5 had a known history of confirmed COVID-19; 23 out of 24 participants with a household history of COVID-91 were seronegative.

Conclusions: Schools do not play a crucial role in driving the SARS-CoV-2 pandemic in a low prevalence setting. Transmission in families occurs very infrequently, and the number of unreported cases is low in this age group. These observations do not support school closures as a strategy fighting the pandemic in a low prevalence setting.

Trial registration: DRKS00022455

Strengths and limitations of this study:

Strengths:

Seroprevalence can detect mildly- or asymptomatic SARS-CoV-2 infections

Longitudinal study designs tracks individuals over time

Older students with multiple social contacts are a relevant target for pandemic control meassures

Limitations:

Loss to follow up

Funding Statement:

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The funder of the study had no role in the study design, data collection, data analysis, data interpretation, or writing of the report. The corresponding authors had full access to all the data in the study and had final responsibility for the decision to submit for publication.

Competing Interest statement:

All Authors declare no competing interests.

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Introduction:

Since the identification of the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) as the cause of COVID-19 in December 2019 [1], the virus spread rapidly around the world, leading to the declaration of a pandemic by the World Health Organization on March 12th 2020. By March 18th 2020, 126 countries—including Germany—had implemented school closures as part of their pandemic control measures, with the number of countries peaking at 194 on April 10th 2020 and more than 90% of the world's student population being affected at this point[2, 3].

These actions were mainly based on the assumption that children play a similar role in transmitting SARS-CoV-2 as they do in transmitting influenza during outbreaks, for which evidence exists that school closures reduce the peak of the outbreak[4]. However, there is reason to believe that children play a less significant role in SARS-CoV-2 transmission compared to influenza, making control measures focused on this age group less effective: Most countries—including Germany—report a much lower proportion of cases in children compared to their population size[5–7] and a recent review on population-based seroprevalence studies found no evidence of overrepresentation of schoolchildren [8] In addition, several tracing studies in schools in different countries could only identify minimal spread of SARS-CoV-2 in educational settings. [9–11]

However, currently available data is insufficient to rule out that children are as likely as adults to be infected by and to transmit SARS-CoV-2, but simply show little to no symptoms of the disease.

We therefore aimed to quantify the proportion of adolescent schoolchildren and teachers in Saxony, one of the eastern Federal States of Germany, that already have developed antibodies against SARS-CoV-2. Until autumn 2020, in Saxony, the infection rates were comparatively low with 245-laboratory-confirmed SARS-CoV-2 infections per 100,000 inhabitants as of October 13th 2020.

Methods:

Study Design

After the reopening of the schools in Saxony on May 18th, 2020 students grade 8–11 and their teachers in 13 secondary schools in eastern Saxony were invited to participate in the SchoolCoviDD19 study. Schools were chosen by the state office for schools and education without involvement of the study team out of the 537 secondary schools in Saxony. Only the selected schools were contacted, none of them declined participation. All eligible students and teachers were invited to participate at each school. Participation rates varied from 12%-50% per school.

After teachers, students, and their legal guardians provided informed consent, 5 mL of peripheral venous blood were collected from each individual during visits at each participating school between

May 25th and June 30th, 2020. In addition, participants were asked to complete a questionnaire on age, household size, previously diagnosed SARS-CoV-2 infections in themselves or their household contacts, comorbidities and regular medication. Students were also asked about regular social contacts outside their household or classroom.

A second visit and repeat blood sampling of the same participants took place between September 15th and October 13th 2020. Between the two study visits schools in Saxony remained open with the regular summer break from July 20th until August 28th 2020.

Approval

The SchoolCoviDD19 study was approved by the Ethics Committee of the Technische Universität (TU) Dresden (BO-EK-156042020) and was registered on July 23rd 2020 and assigned the clinical trial number DRKS00022455.

Laboratory Analysis

We assessed SARS-CoV-2 IgG antibodies in all samples using a commercially available chemiluminescence immunoassay (CLIA) 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 – Sensitivity 97.6%, Specificity 99.3%). 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 re-tested with two additional serological tests: These were a chemiluminescent microparticle immunoassay (CMIA) intended for the qualitative detection of IgG antibodies to the nucleocapsid protein of SARS-CoV-2 (Abbott Diagnostics® ARCHITECT SARS-CoV-2 IgG – Specificity 99.6%, Sensitivity 97,9%) (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 - Specificity 98,3%, Sensitivity 96,9%) (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 having antibodies against SARS-CoV-2.

Statistical Analysis

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

A sample size calculation was performed based on a expected seroprevalence of 1% with 5% precision and a 95% confidence level which yielded a minimum sample size of 500 participants which we exceeded at both timepoints.

Patient and Public Involvement:

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

Results:

A total of 1538 students and 507 teachers from 13 different schools participated in the first visit of the study, 1334 students and 445 teachers completed the second visit. Demographic data is shown in Table 1.

Seroprevalence of SARS-CoV-2 antibodies was 0.6% (12/2045) at the initial visit (May/June) with twelve participants—eleven students and one teacher—having detectable antibodies against SARS-CoV-2 in at least two different assays and thus being considered seropositive. At the follow-up visit (September/October) seroprevalence was 0.7% (12/1779) with still eleven seropositive students and one teacher. Remarkably, one participant who tested positive in 2 assays May tested positive in only one assay in October and was therefore no longer considered seropositive per study definition, while one participant with equivocal results initially did test positive in two serological tests 3 months later. The remaining 11 seropositive participants had no changes in their test results. Using more liberal (>/= 1 test positive) or more conservative (3 tests positive) definitions for seropositivity does not change the persistent low seroprevalence in the study population. In 7 out of 13 schools, seropositive participants could be identified, with four seropositive participants in one school as the maximum. The seroprevalence ranged from 0 to 2.2 per individual school.

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Discussion:

The findings from this unique study in older students and their teachers indicate that the prevalence of IgG antibodies against SARS-CoV-2 was very low after the first wave of the corona pandemic in Germany and during the reopening of the schools in May 2020 and remained low after summer holidays 2020. While this finding is consistent with local surveillance data[12] that shows a prevalence of PCR-confirmed cases of 0.8%, it clearly indicates that schools did not develop into silent hotspots of SARS-CoV-2 transmission during the first wave of the pandemic and even more importantly after reopening of the schools in May 2020. Even more important is the fact, that there was no increase in seropositivity and infections, respectively, in the four months between May after reopening and October after the summer holidays and the first weeks of back to school in the fall period. Therefore, herd immunity in the population of students and teachers appears not to contribute substantially to protection in a low prevalence setting.

It has to be pointed out, however, that the infection rate in Saxony was constantly low during this time period. Nevertheless, the most relevant observation is that infection rates do not increase silently in schools when infection rates in the population are low. Of course, this does not preclude that with increasing infection rates in the population, infection rates in schools may also increase

which is an important reminder that the general population has to act prudently in order to keep schools open.

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There are several limitations to our study. We cannot provide information on eligible but nonparticipating students and teachers in the selected schools requiring additional caution when generalizing these results. In addition, there is a relevant loss of participants in the follow-up sampling. While we do not have information why certain individuals dropped out, the fact that the second study visit took place in a before the beginning of the second wave (7-day incidence rates around 30/100.000) makes it unlikely that personal illness or widespread quarantine measures were responsible for this drop in participation

Conclusion:

As for now, students and teacher do not seem to play a substantial role in driving the SARS-CoV-2 pandemic in Germany when observing the period after reopening of schools in May as well as after summer holidays until early autumn 2020 before facing the second pandemic wave. Transmission in families appears to occur very infrequently, and the number of unreported cases obviously is low in this age group. For serological testing, a combination of different immunoassays seems to be effective to increase the number of true positive test results.

Author contribution statements:

J.A, R.B. and A.D designed the study and wrote the protocol. J.A., M.U. and C.K. collected samples. A.D. and C.L. performed serological testing. J.A., M.U., C.K. and R.B. analyzed the data. J.A. and C.K. wrote the manuscript. M.U. A.D., C.L. and R.B. reviewed the manuscript.

Ethics approval statement

The SchoolCoviDD19 study was approved by the Ethics Committee of the Technische Universität (TU) Dresden (BO-EK-156042020) and was registered on July 23rd 2020 and assigned the clinical trial number DRKS00022455. All participants and their legal guardians – when applicable - provided informed consent.

Data availability statement

Data are available upon reasonable request. Proposals should be submitted to corresponding author (jakob.armann@uniklinikum-dresden.de).

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Table 1: Demographic data

	first study visit (May/June)		second study visit (September/October)	
	students	teachers	students	teachers
participants	1538 (75.2%)	507 (24.8%)	1334 (75.0%)	445 (25.0%)
age (median)	15 (14–16)	51 (37–57)	15 (14-16)	50 (36-57)
female	802 (52%)	357 (70%)	680 (51%)	313 (70%)
household size	4 (3–5)	2 (2–4)	4 (3-5)	2 (2-4)
Seropositive	11	1	11	1
Regular social contacts outside the student's household/classroom during the March 2020 Lockdown	1230 (80%)			
respiratory symptoms between study visits			587 (44%)	71 (16%)
febrile illness between study visits			67 (5%)	4 (0.9%)

Demographic and clinical Characteristics at baseline and follow-up. Data is presented as numbers with percentages except for age which is presented as median with interquartile range

Supplemental table 1: seroprevalence based on different seropositivity definitions

	first study visit (May/June)	second study visit (September/October)
>/= 1 serological test positive	22/2045 (1.1%)	25/1779 (1.4%)
>/= 2 serological tests positive	12/2045 (0.6%)	12/1779 (0.7%)
3 serological tests positive	9/2045 (0.4%)	5/1779 (0.3%)

Number of seropositive participants based on different definitions. Data is presented as numbers with percentages.