Original Article

Seroprevalence of SARS-CoV 2 antibodies & its determinants in children of 5-to-18-year age group in an urban setting, Kerala

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Abstract

Background: There were limited data on the true burden of COVID 19 infection in children since the majority of the infections are asymptomatic or paucisymptomatic. This study aimed to measure the prevalence of SARS CoV2 antibodies in children of the 5-to-18 years age group. **Methods:** A community-based cross-sectional study was conducted in the field practice area attached to a tertiary care hospital in Kerala. Two hundred four children of the 5-to-18 year age group were enrolled in our study. The data regarding sociodemographic details, symptoms suggestive of COVID 19, exposure to confirmed COVID 19 cases and history of COVID 19 positivity were collected from the study participants. 2 ml venous blood was collected from each participant, and the seroprevalence of SARS CoV2 combined antibodies was assessed using WANTAI antibody test kit. **Results:** The seroprevalence of SARS Cov2 antibodies in children of 5-to-18 years age group was 41.7% (95% CI,34.9% to 48.43%). The seroprevalence was high in the 13-to-15 year age group, almost similar in both gender and socio-economic groups. The seropositivity was significantly associated with history of confirmed COVID 19 positivity, children with a history of symptoms suggestive of COVID 19 and the presence of positive contact in the household ($P < 0.05$). Seroprevalence was also significantly high in children whose mothers were health care workers. **Conclusion:** Approximately 41.7% of children showed seropositivity to COVID 19 infection. More than 50% of the children remain susceptible. Among seropositive, 56.5% were asymptomatic. Thus there is a need to test even asymptomatic children in COVID 19 positive households.

Keywords: Children, determinants of seropositivity, Kerala, seropositivity to COVID 19

Introduction

Severe acute respiratory syndrome coronavirus 2 (SARS CoV2) emerged from Wuhan, China, in December 2019 and has become a rapidly spreading pandemic. Around the world, 220 countries and territories have reported the coronavirus COVID 19 and a death toll of 5,077,907.[1] The available data from various countries in the early stages of the pandemic showed that children had a lower incidence rate compared to adults. Children below 18 years accounted for 1 to 2% of detected COVID 19 cases across countries.[2]

Most of the infection among children is asymptomatic or with mild symptoms, and many of them may not undergo testing. Hence there were a greater number of infected children than those diagnosed. The data showing the accurate burden of the pandemic in children are limited even with a high disease burden in the community.[3,4] The majority of currently available data are restricted to laboratory-confirmed cases for symptomatic patients. The true extent of the burden of COVID 19 in the population may be underestimated. The population-based studies

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measure the infection either through viral RNA detection or by detecting antibodies to the SARS CoV2 virus, indicating the previous infection with COVID 19 virus.[5]

Serological detection of specific antibodies against SARS-CoV-2 could help estimate the truedisease burden. The advantages of antibody tests include a comparatively longer detection window, ease of operation and safety of blood collection to respiratory samples. It has got an important role in population-based surveillance and epidemiological assessment.[6]

Various studies reported a seroprevalence rate of 0.7 to 5.8% in children below 19 years in the early stages of the pandemic.[7]

In India, the first national population-based serosurvey by the Indian Council for Medical Research (ICMR) among those aged above 18 years was done in May–June 2020, indicating that 0.73% of adults in India were exposed to SARS-CoV-2 infection.[8] The seroprevalence in the Second (August to September 2020) and the Third round national serosurvey (December to January 2021), showed an increasing trend of 6.6% and 24.0% in the above 10 year age group. 27.2% seroprevalence was reported in the 10-to-17 year age group.[9,10] Under the WHO study, the seroprevalence estimates among the 2-to-17 year age group from selected states showed 55.7% seropositivity among children to SARS CoV2 combined (IgG and IgM) antibodies.[11]

The technical document ICMR stated a seroprevalence of 67.6% in the above 10 years in India in the fourth round survey during May to June 2021. Similarly, seroprevalence in Kerala from the first, second and third round in three selected districts is 0.33%, 0.88% and 11.6%. The fourth round survey showed a seroprevalence of 42.7% in Kerala. It implied that a major proportion of the population was not exposed to COVID 19 infection.[12]

Children, though more susceptible, had a lower probability of exposure due to lockdown restrictions and closure of schools. There were no published studies that estimated seroprevalence in those below 18 years. So, our study aims to estimate seroprevalence to SARS CoV2 combined antibodies in children of age 5 to 18 years and to measure the determinants to seropositivity among study subjects. The findings of this study are relevant in the context of school re-opening and relaxation of lockdown restrictions. Our study will help to stress the need for continuous surveillance in the community and additional precautions to be taken for preventing transmission from children to high-risk persons in the family by primary care providers since the majority of infections in children remained asymptomatic.

Methods

Study design, study setting

A community-based cross-sectional study was conducted in the urban field practice area attached to a tertiary care centre, Thiruvananthapuram, Kerala, India. The centre caters to a population of 120,000. The data was collected from August to October 2021.

Study subjects and selection criteria

For this study, children in the age group of 5 to 18 years were included. Those children whose parents were willing to participate were only included in the study. The children who were positive for COVID 19 and undergoing quarantine at the time of the survey were excluded. The sample size was estimated to be 210 based on 27.2% seroprevalence in the third round of the ICMR survey with a significance level of 95% and absolute precision of 6%.[10] Our study enrolled 204 children in the 5-to-18 years age group from the survey area. We randomly selected 21 ASHA workers from the field practice area to recruit children. Children who were willing to participate were identified with the help of ASHA workers. Each worker enrolled ten eligible children from their area. Data was collected using a semi-structured questionnaire. The primary outcome variable was the prevalence of SARS CoV2 combined with IgG and IgM antibodies. The study variables collected were sociodemographic details, history of previous Covid 19 positivity, COVID 19 related symptoms, treatment details, history of contact with positive patients, history of travel outside home and exposure to crowded places. Data was collected by direct interview by a trained surveyor. 2 ml blood sample was collected from each participant after completing the interview. The sample collection was done in accordance with normal laboratory practice. The sample was then packed and transported to the virology laboratory attached to the Department of Microbiology, Government Medical College, Thiruvananthapuram. WANTAI SARS-COV 2 Ab ELISA diagnostic test kit was used for the qualitative detection of total antibodies. It is an enzyme-linked immunosorbent assay (ELISA) for the detection of total antibodies (combined IgG and IgM) to S-RBD SARS CoV2 virus in human serum or plasma specimens as per the manufacturer's protocol. It has a sensitivity of 94.4% and a specificity of 100%.[13]

Data analysis

The data was entered in Microsoft Excel and analysed using SPSS software version 27.

The seroprevalence of SARS CoV-2 antibodies was expressed in proportions with 95% confidence intervals. Basic demographic and clinical details were described in mean (SD) and proportions as appropriate. Univariate analysis using the Chi square test was done to measure the association between seropositivity and independent variables. Multivariate analysis was done using binary logistic regression for variables with P value < 0.05 to predict the determinants of seropositivity.

Ethical considerations

The study was done in accordance with the ethical standards of the institutional committee on human experimentation and with the Helsinki Declaration of 1975, as revised in 2000. Ethical

clearance for the study was obtained from Institutional Ethics Committee (HEC NO: 06/42/2021/MCT -Dated 19/7/2021). Informed consent was obtained from parents, and assent from children 7 to 18 years was taken before data collection. The purpose of the investigation was explained to all individuals. The results were communicated to the study subjects over the phone, and those with symptoms were referred to the medical officer in charge of the centre.

Results

The mean age of the study participants was 11.46 (SD3.43) years. Of the 204 children surveyed, 23% belonged to 5–8 years, 37.3% in 9–12 years age, 26.5% in 13–15 years and 13.2% in the age group 16–18 years. Table 1 shows the baseline characteristics of the study subjects. One hundred twenty-one (59.3%) study participants were females. In the study, 59.3% belonged to the priority group as per the states socioeconomic status measuring criteria, as shown in Table 1.

45.7% of mothers and 49% of fathers completed high school education. 72.1% of the mothers were unemployed. Health care workers constituted 8.3% of the mothers, as shown in Figure 1.

In the study, 66 (32.45%) reported any one of the COVID 19 related symptoms within the last six months, as shown in Table 2. The main symptoms were fever: 45 (22.1%), cough: 40 (19.6%), sore throat: 24 (11.8%), runny nose: 23 (11.3%) and headache: 13 (6.4). Very few reported anosmia: 6 (2.9%) and loss of taste: 5 (2.5%). Among children with symptoms, 38 (57.5%) needed treatment for their symptoms. Most of them required only outpatient care: 30 (73.7%). There was no history of severe hospitalization among symptomatic. Only one child required inpatient care. Twenty-eight (13.7%) children had a history of confirmed COVID 19 positivity previously. History of contact with COVID 19 cases was recorded in 39 (19.1%) of the children. Among these, 30 (77%) had to contact with a positive household member.

Of the 204 children, 85 tested positive for combined IgG and IgM antibodies against the SARS CoV2 virus, resulting from a seroprevalence of 41.7% (95% CI, 34.9% to 48.43%). Table 3 shows seropositivity across various determinants. The highest seropositivity was recorded in the 13-to-15 years age group. Seropositivity was almost similar across the gender ($P < 0.05$), as shown in Figure 2. There was no statistically significant relationship between socioeconomic status and seropositivity. Seropositivity was found significantly high in children whose mothers were health care workers (64.7%).

Children who were positive for COVID 19 infection previously, had higher seroprevalence: 25 (89.3%) compared to those who were negative: 60 (34.7%). Seroprevalence was significantly higher in those with symptoms (56.1%) compared to those without symptoms (34.8%). Among seropositive children, 37 (43.5%) reported a history of symptoms suggestive of COVID 19. Significantly higher seropositivity was obtained in children who reported fever ($P = 0.004$) and cough ($P = 0.03$). Seropositivity was also found higher in children who reported anosmia (5 out of 6, 83.3%) and loss of taste (4 out of 5, 80.0%) but was not statistically significant. There was no history of severe hospitalization among symptomatic children. Only one child among the symptomatic children required inpatient care.

Seropositivity among children with a known history of contact with an infected person was 61.5%, as shown in Table 3. Among the type of contact, children with household contacts reported higher seroconversion: 21 (70%) compared to those who had contact within community: 3 (33.3%). Children with a history of travel outside the home had higher seropositivity (43.7%) compared to children without travel history (40.6%), but it

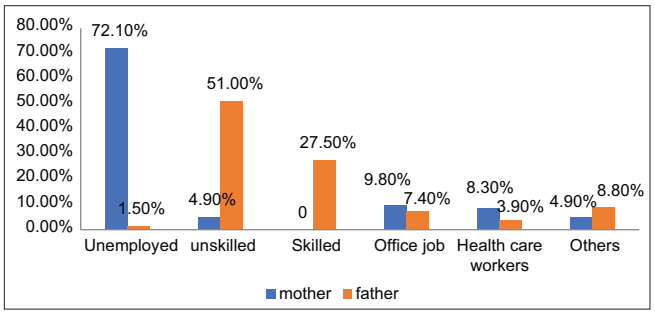

Figure 1: Occupation of parents

Table 1: The baseline characteristics of study subjects

Category	Frequency (%)
Age group	
5-8 years	47 (23)
9-12 years	76 (37.3)
13-15 years	54 (26.5)
16-18 years	27 (13.2)
Gender	
Male	83 (40.7)
Female	121 (59.3)
*Socioeconomic status classification	
White card (Non priority group)	23 (11.4)
Blue card (Non priority with subsidy)	60 (29.3)
Pink card (Priority group)	105 (51.5)
Yellow card (AAY group)	16 (7.8)
Educational status of mother	
Illiterate	2 (1.0)
Primary education	3 (1.5)
High school	92 (45.7)
Pre degree and Degree	84 (41.3)
Professional	23 (11.3)
Educational status of father	
Illiterate	3 (1.5)
Primary education	22 (10.8)
High school	100 (49.0)
Pre-degree and Degree	68 (33.3)
Professional	11 (5.4)
Others	18 (8.8)

*Socioeconomic status classification was based on the criteria fixed by State planning, Kerala board, Kerala

was not statistically significant. Children who were exposed to social gatherings had higher seropositivity (44.4%) than those who were not exposed (41.1%) but it was not statistically significant.

Table 2: Symptom profile of study participants

Total participants=204	Frequency (%)
History of COVID related symptoms	
Any of the symptoms related to COVID 19	66 (32.4)
Fever	45 (22.1)
Cough	40 (19.6)
Sore throat	24 (11.8)
Runny nose	23 (11.3)
Headache	13 (6.4)
Anosmia	6 (2.9)
Loss of taste	5 (2.5)
Symptomatic children who needed treatment, *n*=66	
Yes	38 (57.5)
Type of treatment for symptoms, *n*=38	
Outpatient care	28 (73.7)
Inpatient care	1 (2.6)
Home care	9 (23.6)
Previous history of confirmed Covid 19 positivity	
Yes	28 (13.7)
History of contact with a confirmed Covid-19 case	
Yes	39 (19.1)
Type of contact=39	
Household	30 (77.0)
Community	9 (23.0)

On bivariate analysis [Table 3], children with a previous history of confirmed COVID 19 positivity, known history of contact with a COVID 19 case, with history of COVID 19 related symptoms and occupation of mothers were found as significant determinants of seropositivity.

After multivariable analysis, the independent determinants of COVID seropositivity in children were being positive with COVID 19 infection and the mother being a health care worker [Table 4].

Discussion

Our seroprevalence study among children in the field practice area of a tertiary care centre was done during the declining phase of the second wave in Kerala. The study was done at a time when active infections in other states in India had already declined. The findings of the study are highly relevant for evidence-based decision making in the context of school reopening. The seroprevalence to SARS CoV2 combined antibodies among children in the age group of 5 to 18 years old in our study was 41.7% (95% CI, 34.9% to 48.43%). The Government of Kerala serosurveillance report showed a similar prevalence in children 5 to 17 years old.[14] The survey reported a prevalence of 40.2% to SARS CoV2 IgG-specific antibodies. The same report showed a higher seroprevalence of 82.6% in the adult population compared to children. The seroprevalence obtained in our study was lower than that reported in other states of India.[11] This may be because the children were less

Table 3: Bivariate analysis of determinants of Sero positivity

Variables	Total Participants	Seroprevalence (%)	*P**	Odds ratio
Gender				
Male	83	35 (42.2)	0.9	0.97 (0.55-1.7)
Female	121	50 (41.3)		
Socioeconomic status				
Non priority group	23	10 (43.5)	0.28	
Non priority group with subsidy	60	26 (43.3)		
Priority group	105	46 (43.8)		
AAY	16	3 (18.8)		
Occupation of mothers				
Health care workers	17	11 (64.7)	0.04	2.8 (1.00-7.89)
Others	187	74 (39.6)		
Previous history of confirmed Covid 19 Positivity				
Yes	28	25 (89.3)	<0.001	16.11 (4.67-55.53)
No	176	60 (34.7)		
History of COVID related symptoms				
Yes	66	37 (56.1)	0.01	2.39 (1.32-4.35)
No	138	48 (34.8)		
History of contact with known Covid 19				
Yes	39	24 (61.5)	0.005	2.73 (1.33-5.59)
No	165	61 (37.0)		
Children with history of travel outside home			0.63	
Yes	71	31 (43.7)		1.13 (0.63-2.03)
No	133	54 (40.6)		
Children with history of exposure to social gatherings				
Yes	45	20 (44.4)	0.69	1.15 (0.58-2.23)
No	158	65 (41.1)		

*Chi square test

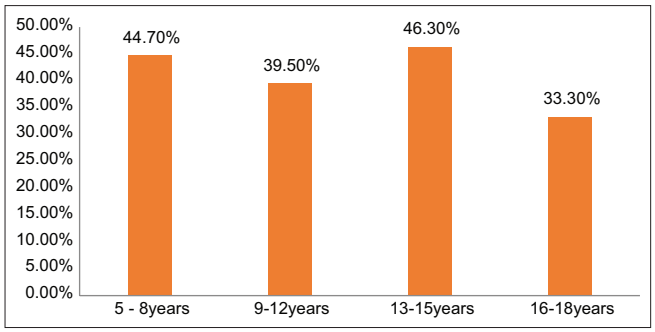

Figure 2: Seroprevalence across age group, *P* value = 0.66

Table 4: Results of Multivariable logistic (binary) regression

Variable	Adjusted odds ratio (95% CI)	*P*
Previously history of confirmed COVID 19 Positivity	14.58 (3.74-56.90)	<0.001
Mother being a health care worker	3.10 (1.04-9.35)	0.04
History of COVID 19 related symptoms	1.47 (0.71-3.0 5)	0.29
History of contact with confirmed COVID 19	0.87 (0.32-02.38)	0.79

exposed to infections due to Covid 19 restrictions and the closure of academic institutions. This can also be attributed to effective contact tracing, isolation and quarantine measures implemented through the primary health care system in our state and its compliance by the community.[15] The seroprevalence in the below 18 years age group gives an extent of seropositivity following natural infection in the community as they constitute the only unvaccinated group in the community.

We didn't find any significant difference in seropositivity across the age groups. We obtained a slight increase in seropositivity in children above 13 years. It can be due to their increased mobility and social activities compared to the lower age group. A valid conclusion may not be possible because of a small amount of data in the higher age group. A similar finding was obtained in a study by Boey *et al.*[7] in Belgium, where children in secondary school had reported higher seropositivity compared to primary school children.

There was no significant difference in seropositivity across gender and socioeconomic status. This indicates similar susceptibility and exposure across both gender and different socioeconomic status. A meta analysis by Abate *et al.*[16] reported high seropositivity to Covid 19 in men.

Analysis of occupation of parents showed that the mother being a health care worker was associated with higher seropositivity. When most other occupational groups compared to health care workers were able to protect themselves by working from home during the lockdown, health care workers had no such option. So they were more at risk of exposure to COVID 19 compared to other occupational groups.[17] The children of health care workers in clinical care had shown a high seropositivity as reported by Waterfield *et al.*[18] in London.

In our study, children who reported Covid 19 related symptoms had significantly higher seropositivity than asymptomatic. There were data showing higher seropositivity in symptomatic children compared to asymptomatic children.[10,11,19] 43.5% of children reported any one of the symptoms related to Covid 19 infection in the seropositive group, while 56.5% of the children reported no Covid 19 related symptoms. This reflects asymptomatic transmission among children in the community. This finding signifies the expansion of the current testing strategy to include all children in a COVID 19 positive household irrespective of their symptoms.

The main symptoms reported in our study were fever (22.1%), cough (19.6%) and sore throat (11.8%). In our study, seropositivity was significantly high in children who reported fever and cough ($P < 0.05$). There were studies showing higher seropositivity in children who reported symptoms like fever and neurological symptoms (loss of taste and anosmia).[11,19]

The children with known history of COVID 19 positivity had higher seropositivity (89.3%), $P < 0.001$ as shown in Table 3. Twenty-five out of twenty-eight got seroconverted in our study. This is in accordance with other studies, where children and adults with confirmed COVID positivity showed greater seropositivity.[10,20] The report of a recent survey conducted in our state also showed a seroconversion of more than 90% in children who had a history of COVID 19 positivity.[14] The delta variant, which was the predominant strain circulating in the community at the time of the study, may be the reason for the higher proportion of seroconversion. Compared to the Wuhan strain, higher viral load has been observed with the delta strain, and that could lead to a greater seroconversion.[21]

Higher seropositivity was observed in children's history of contact with a known COVID 19 case (61.5%). Among them, those with a contact within their homes had higher seropositivity (70%) as compared to community contacts. There are reports of higher seropositivity in children who had an infected household contact. Hence it is important to test asymptomatic children as they may develop MIS-C at a later stage.[3] The multivariable analysis revealed a history of COVID 19 positivity {Adjusted OR, 14.58 (95% CI, 3.74- 56.90)} and mother being a health care worker {Adjusted OR, 3.10 (95% CI, 1.04- 9.35) as significant determinants of seropositivity.

Conclusion

Our study found a seroprevalence of 41.7% in the 5-to-18-year age group. This was lower than that reported in other parts of the country. More than 50% of the children remain susceptible. The state has relaxed its various Covid 19 restrictions and reopened schools and colleges. Children become more at risk of exposure to COVID 19. Hence there is a need to continue adherence to COVID 19 appropriate behaviour in educational institutions and in the community. Finally, we recommend a surveillance program to monitor the trend of infection in

children and to decide upon vaccination policy for children below the 18-year age group.

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Conflicts of interest

There are no conflicts of interest.

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