ORIGINAL ARTICLE ASIAN JOURNAL OF MEDICAL SCIENCES

Seroprevalence of antiSARS-CoV-2 IgG antibodies in children with household exposure to confirm cases of COVID-19 during the second wave of COVID-19 pandemic in Kota, Rajasthan

Vijay Sardana[1], Deepika MIttal[2], Saurabh Sharma[3], Ashutosh Sharma[4]

[1]Principal and Controller, Senior Professor in Neurology, [2]Professor, [4]Associate Professor, Department of Community Medicine, [3]Assistant Professor, Department of Microbiology, Government Medical College, Kota, Rajasthan, India

Submission: 06-02-2022 Revision: 30-04-2022 Publication: 01-06-2022

ABSTRACT

Background: Weather and the susceptibility of children to SARS-CoV-2 infection is still a debated question particularly in view of important decisions regarding opening schools. Therefore, we planned this cross-sectional analysis of antiSARS-CoV-2 Immunoglobulin-G (IgG) antibodies in children with known household exposure to SARS-CoV-2. This serosurveillance, to find the presence of IgG antibodies among children of probable household exposure of confirmed COVID-19 cases will help in the better understanding of the immune response after COVID-19 infection/exposure. **Aims and Objectives:** The aim of the study was to investigate the prevalence of anti-SARS-CoV-2 antibodies in children among the families who had confirm case/cases of COVID 19 during the second wave of the COVID-19 pandemic. This study is designed as a cross-sectional serosurveillance study in Kota, Rajasthan India. **Materials and Methods:** Population-based serosurveillance among children with probable household exposure to confirmed COVID-19 cases who was admitted in Govt. Medical College attached COVID 19 dedicated hospital was carried out during October 2021 to December 2021 using the COVID IgG Antibody Detection Enzyme-Linked Immunosorbent Assay kits. Seropositivity among children was measured and with various other factors to understand the immunity status among COVID-19 cases. Descriptive statistical analysis done. **Results:** 156/1285 eligible candidates (19.53%) having a total of 251 household contacts of <17 years age group agreed to participate in study while rest of them refused. Anti-SARS-CoV-2 IgG antibodies were present in 127/251 household contacts (50.59%). Among them maximum 28.68% of seropositive were from age group 11–17 years age, symptoms were observed in 29.13% IgG positive contacts, maximum seropositivity was seen when only one family member was hospitalized, 63% seropositivity was seen when primary relative of child was hospitalized as compared to secondary. Maximum seroreactivity (55.9%) was seen when the Chest CT score of index case was high, that is, 14–25. max reactivity was observed 76/127 (59.84%) when hospital duration of index case is <1 week. 118/127 (92.91%) of seroreactive children were found when the index case was unvaccinated or partially vaccinated. **Conclusion:** Seropositivity of 50.59% suggests that all the cases may not have IgG antibodies. Among the seronegative cases, the antibodies either not developed, or are undetectable, or have disappeared during the post COVID period. Seropositivity based on gender difference is statistically not significant. Proportion of positivity shows an increasing trend with increasing age among pediatric household contacts. Complete COVID-19 vaccination is an effective tool to minimize the disease frequency/severity. Severe disease patients with high CT score transmits the infection to household contacts more efficiently.

Key words: Anti-SARS-CoV-2 antibodies; Children; COVID-19; SARS-CoV-2; Seroprevalence

Access this article online

Website: http://nepjol.info/index.php/AJMS

DOI: 10.3126/ajms.v13i6.42970

E-ISSN: 2091-0576

P-ISSN: 2467-9100

Address for Correspondence:
Dr. Ashutosh Sharma, Associate Professor, Department of Community Medicine, Government Medical College, Kota, Rajasthan, India.
Mobile: +91-9462565548. **E-mail:** drashutosh.sharma@hotmail.com

INTRODUCTION

About 20 months after the first reported case in Jaipur, Rajasthan,[1] the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) pandemic is still putting pressure on the health systems. There are concerns raised regarding the probable third wave of COVID-19 where children and young age group is thought to get mostly affected. A much-debated aspect of the disease concerns its impact on small children. Weather and the susceptibility of children to SARS-CoV-2 infection are still a debated question and currently a hot topic, particularly in view of important decisions regarding opening schools. Serosurveillance involving cross-sectional analysis of antiSARS-CoV-2 immunoglobulin G (IgG) antibodies in children with known household exposure to SARS-CoV-2 uncovers the asymptomatic and subclinical infection and thus helps in understanding the disease dynamics in a better way for planning an appropriate public health response.

Many countries with higher number of reported COVID 19 cases, the incidence data of COVID-19 in the pediatric population from epidemiological reports show only a small proportion of children (0–19 years) in the total number of patients. In China, children under 18 amounted to 2–5%, Italy 1.2%, United States 7.3%, and in Australia 4% of all COVID- 19 positive cases.[2-7] Very less proportion of COVID-19 positive children developed a severe illness which required intensive care support and prolonged mechanical ventilation.[8] Thus, overall, there are proportionally fewer cases of and deaths from COVID-19 disease for children and adolescents than for adults. Thus, this data suggest that children show clinical symptoms less often than adults. Due to mild or asymptomatic infections, children are not included in the routine molecular testing (reverse transcriptase polymerase chain reaction) for COVID-19 and according to existing data, it is impossible to accurately determine the number of infected children.[9] In this way the number of infections is probably underestimated. In this context, seroprevalence studies are important in the assessment of the extent of infection in the population.

Children particularly aged 3–18 years attend schools. Classrooms could be a possible outbreak cluster. It is further assumed that those children could transfer the infection to their elderly grandparents and other family elders with comorbidities who have a higher mortality risk due to COVID-19. This happens to be a major reasoning given for closure of schools and thereby disadvantaging children in receiving education.[10,11]

We, therefore, undertook a community-based serosurvey for COVID-19 antibody among household exposure children of previously confirmed COVID positive cases. The objective of the study was to determine the COVID-19 seropositivity rate among children. It will help in monitoring changes in the seroprevalence over time which will ultimately help in planning adequate public health measures.

Aims and objectives

The aim of the study was to investigate the prevalence of anti-SARS-CoV-2 antibodies in children among the families who had confirmed case/cases of COVID 19 during the second wave of the COVID-19 pandemic. Epidemiological significance will be determined that how use of restrictive and preventive measures towards probable exposure of children to COVID-19 infection affect this prevalence.

MATERIALS AND METHODS

Design and study setting

This is a population-based, age-stratified cross-sectional COVID-19 seroprevalence study conducted by Govt. Medical College Kota. Population-based serosurveillance among children of <17 years of age with probable household exposure to confirmed COVID-19 cases (index case) who was previously hospitalized in Govt. Medical College attached COVID-19 dedicated hospital, was carried out during October 2021 to December 2021. Index case was defined as the first identified laboratory confirmed case in the household. Household contacts (children <17 years of age) of COVID 19 patients underwent serology test. We defined household contact a person who lived in the household of the COVID 19 patient (index case) at the time of diagnosis, for example, the other partner and/or children living in the same house. Non household contacts were not included in the study. Similarly, index patients not living with children younger than 17 years of age were excluded.

Eligibility criteria

Participants were eligible for enrolment if they were between the ages of <17 years, and if their parent or legal guardian gave informed consent to participate. Multiple children per household were eligible as long as they all are household contact of index case.

Ethical considerations

Written informed consent was obtained from the study participant's parents/guardians. To maintain the covertness, dignity and confidentiality of the participants, the details were not disclosed. The study is approved by the Ethical Committee of our Institution.

Serological samples and laboratory analysis

Samples were collected by dedicated sample collection teams (SCT) who collected door to door samples after contacting

the index case telephonically whose details were obtained from hospital database. Samples were collected from household contacts of eligible candidates (having children of age group <17 years as household contact). After pretest counseling and informed consent, 5 ml of blood was collected in a test tube using all aseptic precautions and is properly labeled. A proper requisition form with date, age, and relevant history was completed before collection of samples in EDTA vials. The collected blood was allowed to clot than centrifuged at 3000 rpm for 5 min to separate out serum. Precaution was taken to avoid hemolysis. The samples were forwarded for analysis and immediately after analysis; the remaining serum was separated into labeled plastic tubes and stored at - 20°C (maximum 3 weeks) as per manufacturer's instructions. The CE certified version of the ErbaLisa COVID-19 Immunoglobulin-G (IgG) Antibody Detection Enzyme Linked Immunosorbent Assay (ELISA) kits (Erba Mannheim, calbiotech, Inc. EL Cajon, USA), which was validated by ICMR (https://www.icmr.gov.in/ckitevaluation.html, dated 30.11.2020), was used to detect IgG antibodies against SARS-CoV-2 according to manufacturer's recommendation (https://erbalisacovid19.erbamannheim.com/products/covid-19-elisa/). The kit used in study has a sensitivity of 98.3% and specificity of 98.1% for IgG antibody detection and based on the principle of indirect ELISA using recombinant spike subunit antigen. Optical density was determined by colorimetric reaction which allowed the detection of IgG in the samples and the evaluation of the signal generated by SARS-CoV-2 specific antibodies against the antigen confirmed whether subjects were seropositive. Parents were informed about their child's serostatus telephonically.

RESULTS

A total of 2291 adults were admitted in Govt. Medical Collage dedicated COVID hospital during the second wave of COVID 19 during the period April 2021 to June 2021. Among them, 1285 were living in a household with children of <17 years of age. Table 1 shows of those 1285 eligible, 156 (19.53%) agreed to participate in study while rest of them refused. These 156 cases were considered as the index cases. At the time of COVID19 diagnosis/hospitalization of these 156 index cases, a total of 251 household contacts of <17 years age group were living in the same household and were enrolled in the study, (mean age 11.12, range: 0.9–17 in years). Anti SARS-CoV-2 IgG antibodies were present in 127 out of 251 household contacts (50.59%). Among them, 17 were <5 years age, 38 were of age group 6–10, 72 were of age group 11–17 years age. Among 127 COVID-19 IgG seropositive household contacts, 61 were male and 66 were female. Of these 37/127 (29.13%) IgG positive pediatric contacts developed COVID19 related symptoms

Table 1 : Analysis of COVID-19 serosurvey positivity among household pediatric contacts of index cases during second wave of COVID-19

Demographic characteristics	Pediatric household contacts, n (%)	
	Reactive	Non-reactive
Total (251)	127 (50.60%)	124 (49.40%)
Gender		
Male	61 (48.03%)	61 (49.19%)
Female	66 (51.97%)	63 (50.81%)
Age (in years)		
<5	17 (13.38%)	9 (7.25%)
6–10	38 (29.92%)	37 (29.83%)
11–17	72 (56.70%)	78 (62.92%)
Number of index case in family		
1	65 (51.18%)	71 (57.25%)
2	37 (29.13%)	28 (22.58%)
3	11 (8.66%)	10 (8.06%)
>4	14 (11.03%)	15 (12.09%)
Relation to parents		
Primary	80 (63%)	83 (66.93%)
Secondary	47 (37%)	41 (33.07%)
CT score of patients		
<5	4 (3.14%)	7 (5.64%)
6–13	52 (40.94%)	22 (17.74%)
14–25	71 (55.92%)	95 (76.62%)
Duration of stay in hospital		
1 week	76 (59.85%)	93 (75.01%)
1–2 weeks	27 (21.26%)	13 (10.48%)
>2 weeks	24 (18.89%)	18 (14.51%)
Vaccination status of family members		
Unvaccinated/Partial	118 (92.91%)	111 (89.51%)
Fully Vaccinated	09 (7.09%)	13 (10.49%)
Clinical status of child		
Asymptomatic	90 (70.86%)	91 (73.38%)
Symptomatic	37 (29.13%)	33 (26.62%)

while 90/127 (70.86%) were found asymptomatic. Among household pediatric symptomatic contacts with SARS-CoV-2 IgG antibodies, 10/37 (27.02%) got confirmed microbiologically through PCR on nasopharyngeal swab. These diagnoses among household contacts happened after the initial diagnosis of the index case, and they were diagnosed as part of the contact tracing and epidemiologic assessment done by the Local Health Authorities once the index case had been reported by the hospital. In reference to the total number of positive COVID-19 patients in the family, maximum seropositivity (65/127) was seen when only one of the family members was hospitalized while seropositivity was found 37/127, 11/127 and 14/127 when number of hospitalized patients were 2, 3, 4, or more, respectively. Comparing reactivity with social relationship, 80/127 (63.00%) were found seropositive when one or both of the primary relative got hospitalized (father, mother, brother, and sister) while 47/127 (37.00%) were found reactive when secondary social group was involved (Like uncle, aunt, landlord, tenant, etc.) living in the same household. Maximum seroreactivity 71/127 (55.9%) was seen among household pediatric contacts when the chest CT score of index case was high, that is, 14–25.

Comparing seroreactivity with duration of hospital stay of index case, max reactivity was observed 76/127 (59.84%) when hospital duration is <1 week. 118/127 (92.91%) of seroreactive children were found when the index case was unvaccinated or partially vaccinated. (Table 1).

DISCUSSION

Based on our findings the average seropositivity among pediatric household contacts of index case was of 50.59%. However, it also implies that the remaining 49.41% have either not developed the antibodies, have antibodies but in undetectable proportion, or the antibodies might have disappeared, after their development, during the post-COVID period as the study was done approximately 6 months after possible exposure. IgG antibodies levels reach its peak at during the 3rd month and then declines gradually over the next few weeks/months.[12,13] This indicates that these antibodies may not be long-lasting. The prevalence in pediatric household contact was found slightly more among females participants compared to males. However, there was no statistically significant difference (P=0.853) in seropositivity between two genders. This finding suggests equal risk between both the gender groups and similar findings were recorded in other studies as well[14,15] The higher seropositivity rate in children aged 11–17 years may be hypothesized due to their more mobility, more interactive nature and more sense of independence as compared to the younger children. Similar results were found in other studies where higher rate was found for household contacts of school-aged children and the lowest for household contacts of children 0–9 years.[14] In the present study, a large proportion of children (70.86%) remained asymptomatic. Children appear more likely to be asymptomatic than adults and several case series have identified asymptomatically infected children, usually during contact tracing.[16] However, such asymptomatic household contact could behave like carriers that had the potential to transmit the coronavirus to other family members. Our study showed increasing seropositivity trend among household pediatric contacts as the chest CT score of index case was increasing. This could be explained on the basis of increasing severity of disease among index case having high viral load, thus heavy viral shedding which could possibly infected clinically/sub clinically, household contacts including children. In our study, most of the seropositive contacts 80/127 (63.00%) were found to be primary relative of index case (father, mother, brother, and sister). This could be explained by fact that most of the pediatric contacts remain in close proximity of parents/primary relative in the same household, preferably in the same room with more frequent exposures. Hence, if any of the primary relative got infected, there are very good chances to transfer the clinical/subclinical infection to the pediatric contact. More seropositivity is seen in those household pediatric contacts when index case is hospitalized for 1 week or less while seropositivity declines with increase in duration of hospital stay. This could be explained by fact that during the first wave of COVID-19, positive hospitalized patients were discharged only after 3 consecutive negative RTPCR reports. However, this was not the scenario in second COVID-19 wave. Due to an unprecedented surge in demand of medical oxygen/oxygen beds across the country during the second wave of COVID-19 there was immense pressure on hospitals and health infrastructure. Thus, to cope up the situation, patients were discharged as soon as they became asymptomatic with advice for home isolation. But most of them might not have followed the quarantine guidelines resulting in infecting the household contacts. In the present study, most of the seropositive pediatric contact were found in those families where members were non or partially vaccinated (taken single dose of vaccine) while seropositivity was less among children of fully vaccinated family members. This explains that complete COVID vaccination is very effective in combating the disease which, in turn, deceases the chances of viral shedding and infecting other household contacts including children.

Limitations of the study

Participation in this study was voluntary. So not all eligible candidates gave their consent to participate in this study. This study did not take consideration of children to adult transmission of COVID-19 diseases which should be study separately.

CONCLUSION

Seropositivity of 50.59% among COVID-19 cases household pediatric contacts suggest that all the cases may not have IgG antibodies. Among the seronegative cases, the antibodies are not developed, or are undetectable, or have disappeared during the post-COVID period. The reason for the seronegative results in COVID-19 cases needs further in-depth scientific research. The difference in seropositivity based on gender is statistically not significant. Proportion of positivity shows an increasing trend with increasing age among pediatric household contacts. Complete COVID-19 vaccination is an effective tool to minimize the disease frequency/severity and thus limit the transmission. Severe disease patients with high CT score transmits the infection to household contacts more efficiently, so they should be treated and isolated properly. Given the transmission among household contacts within families, personal protective measures should be used at home to reduce the risk for transmission. If feasible, measures like cohort isolation outside of hospitals, such as in a Community Centre/quarantine home, might be a viable option for reducing household transmission. To understand better about

SARS-CoV-2 transmission patterns in children, more studies with sufficiently larger data including the household designs are required like (1) the stringent selection of cases where a true index patient bringing the infection into the household is known, (2) monitoring of all household members by serial PCR or rapid antigen tests during the quarantine period, (3) investigating the hygiene measures, duration, and adherence to them during the quarantine period, and (4) analyzing serologically all the household contacts after the infectious period. Thus a arduous prospective study design should help to improve in better understanding of transmission patterns of SARS-CoV-2 between children and adults.

ACKNOWLEDGMENT

We thank the members of SCTs, department of transfusion medicine, blood bank, MBS hospital, GMC Kota for their continuous support. Special thanks to the participating subjects who allowed us to investigate the extent of infection, as determined by seropositivity in the paediatric household contact, in which COVID-19 virus infection has been reported.

REFERENCES

1. Italian Tourist Tests Positive for Coronavirus in Rajasthan, Samples Sent to Pune for Confirmation. The New Indian Express; 2020.
2. Wu Z and McGoogan JM. Characteristics of and important lessons from the coronavirus disease 2019 (COVID-19) outbreak in China: Summary of a report of 72314 cases from the Chinese center for disease control and prevention. JAMA. 2020;323(13):1239-1242.
   https://doi.org/10.1001/jama.2020.2648
3. Qiu H, Wu J, Hong L, Luo Y, Song Q and Chen D. Clinical and epidemiological features of 36 children with coronavirus disease 2019 (COVID-19) in Zhejiang, China: An observational cohort study. Lancet Infect Dis. 2020;20:689-696.
   https://doi.org/10.1016/S1473-3099(20)30198-5
4. Livingston E and Bucher K. Coronavirus Disease 2019 (COVID- 19) in Italy. JAMA. 2020;323(14):1335.
   https://doi.org/10.1001/jama.2020.4344
5. Centers for Disease Control and Prevention. Information for Pediatric Healthcare Providers. Infections among Children. Available from: https://www.cdc.gov/coronavirus/2019-ncov/hcp/pediatric-hcp.html [Last accessed on 2020 Nov 20].
6. COVID-19 National Incident Room Surveillance Team. COVID-19, Australia: epidemiology report 11 (Reporting week to 23:59 AEST 12 April 2020). Commun Dis Intell (2018). 2020:44:34.
   https://doi.org/10.33321/cdi.2020.44.34
7. Buonsenso D, Valentini P, De Rose C, Pata D, Sinatti D, Speziale D, et al. Seroprevalence of anti-SARS-CoV-2 IgG antibodies in children with household exposure to adults with COVID-19: Preliminary findings. Pediatr Pulmonol. 2021;56(6):1374-1377.
   https://doi.org/10.1002/ppul.25280
8. Gotzinger F, Santiago-Garcia B, Noguera-Julian A, Lanaspa M, Lancella L, Calo Carducci FI, et al. COVID-19 in children and adolescents in Europe: A multinational, multicentre cohort study. Lancet Child Adolesc Health. 2020;4(9):653-661.
   https://doi.org/10.1016/S2352-4642(20)30177-2
9. Waterfield T, Watson C, Moore R, Ferris K, Tonry C, Watt A, et al. Seroprevalence of anti-SARS-CoV-2 antibodies in children: A prospective multicentre cohort study. Arch Dis Child. 2021;106(7):680-686.
   https://doi.org/10.1101/2020.08.31.20183095
10. Doyle T, Kendrick K, Troelstrup T, Gumke M, Edwards J, Chapman S, et al. COVID-19 in primary and secondary school settings during the first semester of school reopening Florida, August-December 2020. Morb Mortal Wkly Rep. 2021;70(12):437-441.
    https://doi.org/10.15585/mmwr.mm7012e2
11. Rajapakse N and Dixit D. Human and novel coronavirus infections in children: A review. Paediatr Int Child Health. 2021;41(1):36-55.
    https://doi.org/10.1080/20469047.2020.1781356
12. Sethuraman N, Jeremiah SS and Ryo A. Interpreting diagnostic tests for SARS-CoV-2. JAMA. 2020;323(22):2249-2251.
    https://doi.org/10.1001/jama.2020.8259
13. Rosado J, Pelleau S, Cockram C, Merkling SH, Nekkab N, Demeret C, et al. Serological signatures of SARS-CoV-2 infection: Implications for antibody-based diagnostics. medRxiv. 2020;2020:25691492.
14. Prakash O, Solanki B, Sheth JK, Joshi B, Kadam M, Vyas S, et al. Assessing sero-positivity for IgG antibodies against SARS-CoV-2 in Ahmedabad city of India: A cross-sectional study. BMJ Open. 2021;11(1):e044101.
    https://doi.org/10.1136/bmjopen-2020-044101
15. Abate BB, Kassie AM, Kassaw MW, Aragie TG and Masresha SA. Sex difference in coronavirus disease (COVID-19): A systematic review and meta-analysis. BMJ Open. 2020;10(10):e040129.
16. Dong Y, Mo X, Hu Y, Qi X, Jiang F, Jiang Z, et al. Epidemiological characteristics of 2143 pediatric patients with 2019 coronavirus disease in China. Pediatrics. 2020;145(6):e20200702.
    https://doi.org/10.1542/peds.2020-0702

Authors Contributions:
VS- Concept and design of the study; **DM-** Concept, coordination prepared first draft of manuscript; **SS-** Statistical analysis and interpretation, preparation of manuscript and revision of the manuscript, **AS-** Concept and design of the study, statistical analysis and interpretation, preparation of manuscript and revision of the manuscript.

Work attributed to:
Government Medical College, Kota - 324 005, Rajasthan, India.

ORCID ID:
Dr. Vijay Sardana- https://orcid.org/0000-0002-7604-1437
Dr. Deepika Mittal- https://orcid.org/0000-0002-1144-5983
Dr. Saurabh Sharma- https://orcid.org/0000-0001-6511-5368
Dr. Ashutosh Sharma- https://orcid.org/0000-0003-3131-1410

Source of Funding: Nil, **Conflicts of Interest:** None declared.