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A CROSS-SECTIONAL STUDY ON CLINICAL AND IMMUNOLOGICAL RESPONSE IN CHILDREN AGAINST COVID

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ABSTRACT

Background: COVID-19 is an infectious disease caused by severe acute respiratory syndrome Coronavirus 2 (SARS-CoV-2) created a devastating impact on global health and economy. This study aids in understanding the clinical and immunological response of children during third wave of COVID.

Methods: A Cross sectional study conducted among school going children of age 4-17 during Jan 22 to April 22.Demographic and clinical parameters were assessed based on structured questionnaire. Serum samples were collected from volunteered children who were not vaccinated against COVID-19. COVID-19 Ig G antibodies were estimated using CLIA and the data analyzed using SPSS.

Results: 87 children were enrolled from a school.32.2% were girls; 67.8% were boys.78% of the children had fever, 86% had cold, 64% had cough and 64% had headache. Majority were having symptoms for 3-5 days. Serum samples were collected for COVID-19 IgG levels from 23 COVID-19 unvaccinated children, out of which 19(82.6%) were positive for COVID. The mean COVID-19 IgG level around 2 months after recovery was 24.6 IU.

Conclusion: This study suggests that children who had fever, cold and cough during third wave had COVID-19 disease and had an overall better prognosis. Future longitudinal studies are necessary to confirm our findings and to better understand the protective IgG levels which prevent further infections in COVID-19 vaccinated and unvaccinated children.

Keywords: COVID-19, SARS CoV -2 IgG, Children

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Introduction:

Corona virus disease 2019 (COVID-19) is an infectious disease caused by severe acute respiratory syndrome Corona virus 2 (SARS-CoV-2), which first appeared in China, in December 2019 and spread worldwide and poses a great threat to public health. Recent epidemics reflect that coronaviruses impose a continuous threat to human beings and the economy as they emerge unexpectedly, spread easily, and lead to catastrophic consequences.

The most drivers of emerging and reemerging infections were ecological and anthropological influences being the majority [1]. Early detection and understanding the disease epidemiology were essential in the control of new emerging risk. As the UN Framework for the Immediate Socio-economic Response to COVID-19, published in April 2020, says: “The success of post-pandemic recovery will also be determined by a better understanding of the context and nature of risk”[2].

Children who are infected may be asymptomatic or may have mild symptoms, and they may not undergo testing. There might be a greater number of infected children than those diagnosed. Eventhough the disease burden is high in the community, there is limited data on exact burden of covid in children.[3,4]The WHO study in selected states, estimates 55.7% seropositivity among the 2-to-17 year age group which includes combined SARS CoV2 (IgG and IgM) antibodies.[5]

In India in the fourth round survey conducted by ICMR among above 10 years age participants during May to June 2021 stated 67.6% seroprevalence. In Kerala, the fourth round survey showed a seroprevalence of 42.7%. [6]

As the number of recovered patients with COVID-19 continues to be increasing, the strength and duration of immunity after infection is an important point to be studied. Moreover, understanding this issue is a critical point for controlling this epidemic. Neutralizing antibodies are crucial for the establishment of a protective immunity, but the dynamics of humoral immune responses in children still remain unknown. At the time of initiation of the study, there was limited data on seroprevalence in children. Therefore, this study aids in understanding the clinical and immunological response in children during and after third wave of covid.

Material and Methods:

A school based cross-sectional study was conducted in the rural area of Krishna, India. The data was collected from January to April 2022. For this study, children in the age group of 4 to 17 years, who were attending schools, were included. Those children whose parents and children were willing to participate were only included in the study. During the study period schools were open and covid vaccination program was initiated for children above 12 years in our state. The third wave was peaked in January in Andhra Pradesh. We enrolled children who were symptomatic during the study period and data was collected using a semi structured questionnaire. Our study enrolled 87 children in the 4-to-17 years age group from the school. The study variables collected were socio demographic details, history of previous Covid 19 positivity, COVID 19 related symptoms, treatment details, history of contact with positive patients. Data was collected by direct or phone interview by a trained surveyor.

No laboratory investigations were done during symptomatic period. Blood samples were collected from willing children who were not covid vaccinated during the study period. Blood samples were collected in the last week of March. The sample collection was done in accordance with normal laboratory practice. The sample was then packed and transported to the laboratory. COVID IgG antibodies to SARS CoV2 S1 RBD antigen in the serum sample was estimated by fully automated CLIA [Chemiluminescence immunoassay].The reference range of positivity for Covid IgG is ≥ 1 IU.Prevalence is estimated by assessing symptoms (Probable covid cases as per the revised case definition for covid. [NCDC, MOHFW, GOI]) and serological parameters.

The data was entered in Microsoft Excel and analyzed using SPSS software version 25. 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. The significance level was set as *P* value of < 0.05.

Ethical considerations:

The study was approved by Institutional Ethics Committee. Informed consent was obtained from parents, and assent from children 7 to 17 years was taken before data collection and sample collection. The purpose of the investigation was explained to children, parents and teachers. The results were communicated to the study subjects through the school teacher and those with symptoms were referred to the medical officer in charge of the area.

Results:

In our study a total of 87 children were surveyed from a school that were of age 4 to 17. The median age of the study population was 11 [95%CI: 10-12]. The study participants were categorized into two age groups 4 to 11 and 12 to 17 respectively. Table one show the baseline characteristics of the participants. 49 (56.3%), 38 (43.7%) were in the age group of 4 to 11 and 12 to 17 respectively. In the study 59 (67.8%) were male and 28 (32.2%) were female.

Table1: Baseline characteristics of study participants (n=87)

Category	Frequency (%)
Age group	
4-11	49 (56.3%)
12-17	38 (43.7%)
Gender	
Male	59 (67.8%)
Female	28 (32.2%)
Socioeconomic status	
White Card Holder	86 (98.8%)

85 children (97.7%) reported one or the other symptom related to COVID-19 during the study period. The main symptoms were cold 75 (86.2%), fever 68 (78.2%), cough 56 (64.4%), headache 56 (64.4%). The prevalence of various symptoms related to COVID-19 was shown in table 2. The other symptoms reported were sore throat, cough with sputum, body pains, sleeplessness, loss of smell, breathlessness, chest pain, conjunctivitis, diarrhea, vomiting and giddiness.

The days of suffering from cold, cough, and fever were in the range of 0-15 and the majority were suffered for 3-5 days. Fever was absent in 19 (21.8%) children. Among the children who reported fever; 21(24.1%) , 37(42.5%), 10 (11.5%) suffered for less than 3 days,3-5 days and more than five days respectively. Children who reported cold for less than 3 days,3-5 days and more than five days were 18 (20.7%), 39 (44.8%), and 18 (20.7%) respectively. 18 (20.7%) participants reported cough for less than 3 days where as 30 (34.5%) and 8 (9.2%) reported for 3-5 days and more than five days respectively.fig 1-4 showed the pattern of symptoms in the two age groups.

Majority of the children in the age group 4-11 had fever and cold. The suffering from cold was statistically significant among both age groups [$P<0.05$]. The presence of cough and headache were statistically significant between the age groups 4-11 and 12-17; $P<0.0001$ and 0.003 respectively. There was no significant association between gender and symptoms. Table 3 showed the determinants of symptoms and their significance statistically.

Table 2: Prevalence of COVID related symptoms in study participants (n=87)

symptom	Frequency (%)
Fever	68 (78.2%)
Cough	56 (64.4%)
Cold	75 (86.2%)
Cough with Sputum	13 (14.9%)
Sore Throat	3 (3.4%)
Headache	56 (64.4%)
Sleeplessness	5 (5.7%)
Loss of Smell	1 (1.1%)
Abdominal Pain	8(9.2%)
Asthma	10(11.5%)
Body Pains	24(27.6%)
Breathlessness	4 (4.6%)
Chest Pain	2 (2.3%)
Conjunctivitis	4 (4.6%)
Diarrhea	4 (4.6%)
Giddiness	2 (2.3%)
Vomiting	13 (14.9%)

Table 3: Determinants of Symptoms among participants. (n=87)

Symptom/ Variable		Age				Gender			
	Total	4-11	12-17	*P*-Value	Chi-Square	Female	Male	*P*-Value	Chi-Square
Fever									
Yes	68	36 (52.9%)	32 (47.1%)	0.23	1.4	22 (32.4%)	46 (67.6%)	0.94	0.004
No	19	13 (68.4%)	6 (31.6%)			6 (31.6%)	13 (68.4%)		
Cold									
Yes	75	39 (52%)	36 (48%)	0.04*	4.1	23 (30.7%)	52 (69.3%)	0.45	0.5
No	12	10 (83.3%)	2 (16.7%)			5 (41.7%)	7 (58.3%)		
Cough									
Yes	56	22 (39.3%)	34 (60.7%)	0.0001*	18.3	22 (39.3%)	34 (60.7%)	0.06	3.6
No	31	27 (87.1%)	4 (12.9%)			6 (19.4%)	25 (80.6%)		
Headache									
Yes	56	25 (44.6%)	31 (55.4%)	0.003*	8.6	18 (32.1%)	38 (67.9%)	0.99	<0.01
No	31	24 (77.4%)	7 (22.6%)			10 (32.3%)	21 (67.7%)		

**P* value less than 0.05 is statistically significant

None of the participants were hospitalized during the symptomatic period. None were isolated during the symptomatic period. None were tested for COVID-19 during the symptomatic period. All the participants had contact with the symptomatic persons. No deaths were reported.

Serum samples were collected from 23 volunteered covid unvaccinated children, around two months after the onset of symptoms. Among them, 19 (82.6%) children had seropositivity for SARS CoV2 IgG. Fig 5 and 6 showed the effects of age group and the days of fever, cold, cough on seropositivity. IgG levels ranged from 0.3 to 55.9 and median value was 20.41 IU [95%CI 5.22 to 38.96]. There was no statistical significance between covid sero positivity and the age group. Fig 7-9 showed box plots depicting effect of IgG levels with age and symptoms such as fever, cold and cough. The determinants and their association were depicted in table 4.

Fig:1-4 showed the symptom pattern in study participants of two age groups 4-11 and 12-17.

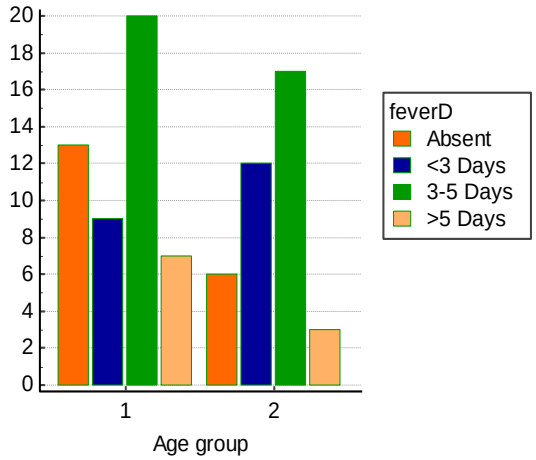

Fig:1

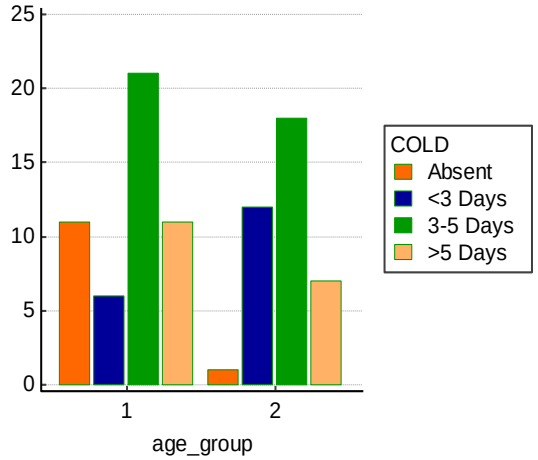

Fig:2

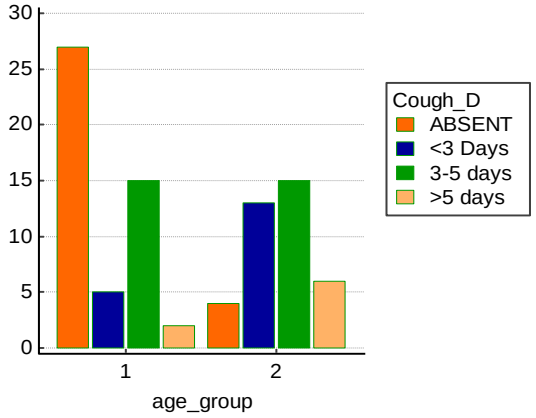

Fig:3

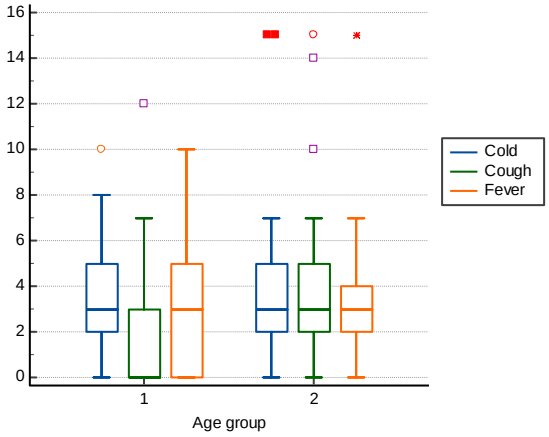

Fig:4

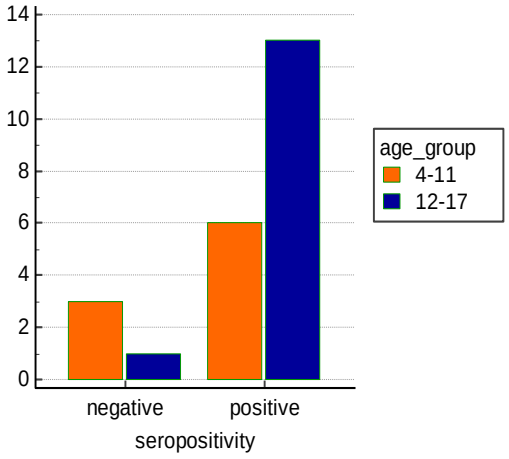

Fig :5 Effect of age group on seropositivity

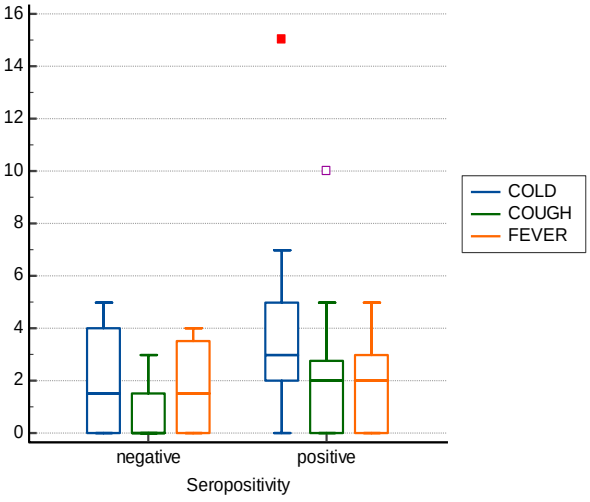

Fig:6 Effect of symptoms on seropositivity

Fig:7-10 showed the effect of SARS CoV IgG levels in response to symptoms such as cold, cough and fever and distribution in different ages.

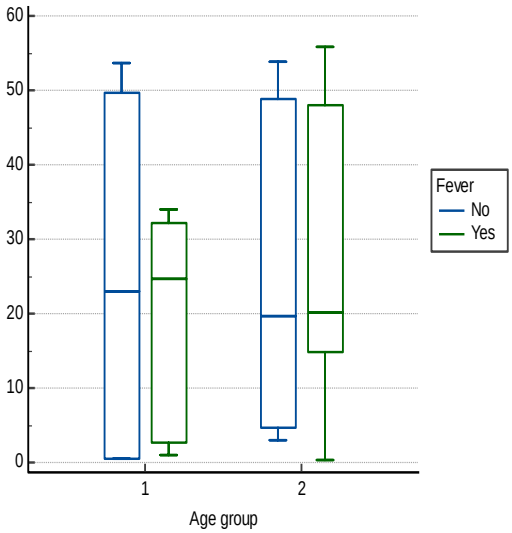

Fig: 7

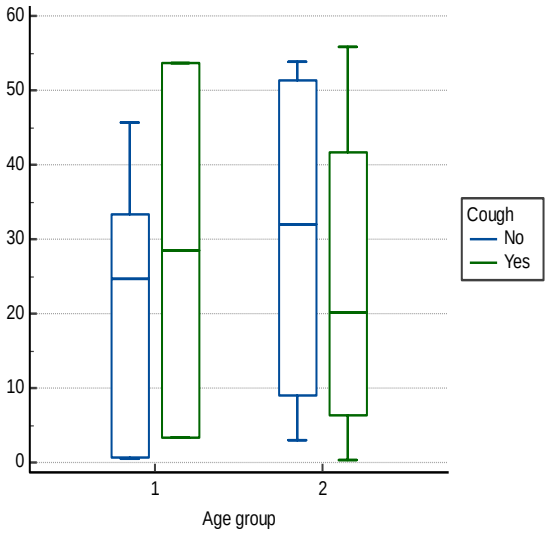

Fig:8

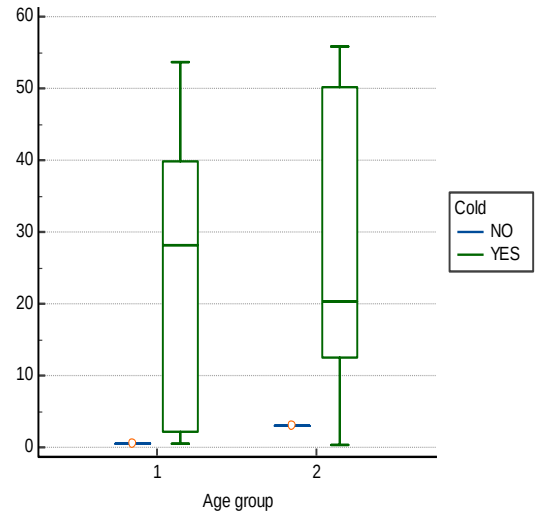

Fig 9

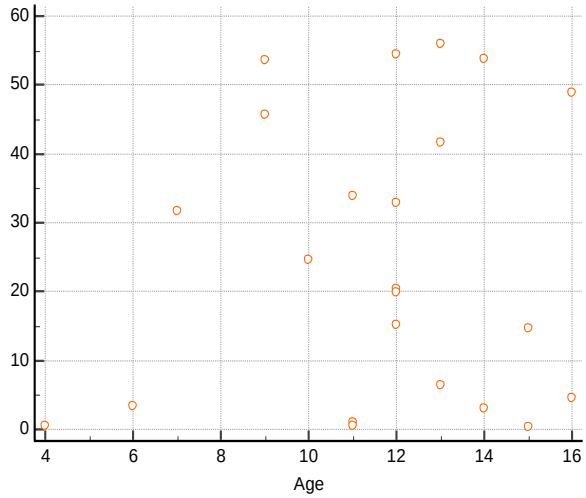

Fig: 10

Table 4: Determinants of Seropositivity (n=23)

Variable	Total Participants	Seroprevalence	*P*-Value	Chi-Square
Age Group				
4-11	9	6 (66.7%)	0.11	2.5
12-17	14	13 (92.9%)		
Total	23	19 (82.6%)		
Fever				
Yes	13	11 (84.6%)	0.78	0.08
No	10	8 (80%)		
Cold				
Yes	21	18 (85.7%)	0.21	1.6
No	2	1 (50%)		
Cough				
Yes	12	11 (91.7%)	0.24	1.4
No	11	8 (72.7%)		

Discussion:

We conducted this study among school going children in the semi urban region. At the time of the study covid restrictions were relaxed and schools were open. Active infections were peak in the field area of the study. The clinical picture can be compared with the earlier studies in children and adults. Majority had symptoms such as fever, cold, cough, and headache. Cough and headache were more in the 12- 17 year age group children and the association was statistically significant [*p* value < 0.05]. The median duration of symptoms was 3 to 4 days.

The prevalence of SARS CoV-2 IgG antibodies against spike protein was 82.6% after around two months of onset of symptoms, which was comparable with the meta analysis report of prevalence in Southeast Asia region, which ranges between 17.9 to 81.8%.[7]. Robert Markowitz etal study reported (81.3%) seropositivity for IgA and/or IgG antibodies against the Spike-protein of SARS-CoV-2[8] .Gudbjartsson et el. also reported that three months after recovery from a lab confirmed infection with SARS-CoV-2, 3.9% of the examined patients remained seronegative for antibodies of all classes against both the S- and the N-protein of SARS-CoV-2 [9].

There is a lack of evidence regarding the long-term duration of antibody response against SARS-CoV-2, especially in children. In adult patients, recent reports suggest that antibody response to SARS-CoV-2 declined significantly in the 3 months following SARS-CoV-2 infection [10–14].

In our study median SARS CoV-2 IgG antibody levels against spike protein after two months of onset of symptoms was 20.4 IU. There was no significant difference in IgG levels with age and symptoms. Our study observed no gender variation in the reported symptoms. Bloise etal study reflected median IgG level as 90.61 AU/ml after 30 days of onset of symptoms and the gradual decline of antibodies to 16.53 at 6 months[15].Our study results were correlating with these values. We observe a slight increase in sero positivity in the 12 to 17 years age group but the association was not statistically significant. It could be because of the less sample size. The study in Kerala by Mini etal stated that the seroprevalence was high in the 13-15 year age group [16].In another study, 12–16 years adolescents mounted higher median antibody titers in the Omicron compared to Delta period. This could be attributed to the higher secondary attack and reinfection rate of Omicron in households compared to previously circulating variants, which was noted by other large-scale studies [17, 18].

Conclusions:

This study suggests that children who had fever, cough during third wave had COVID-19 disease and had an overall better prognosis. Worldwide data was supportive of higher seroprevalence rates during January and April 2022 suggesting higher transmissibility rates and reinfection rates. Future longitudinal studies are necessary to confirm our findings and to better understand the protective IgG levels which prevent further infections in covid vaccinated and unvaccinated children.

Financial support: None

Conflicts of interest: None

Data: The data that support the findings of this study are available from the corresponding author upon reasonable request.

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