Original Research Article

Clinical Profile Of COVID 19 Infection And SARS-Cov-2 IgG Antibody Response In Children Under 18 Years Of Age In A Tertiary Care Centre In North Kerala

Abstract

Background

The Global Pandemic Coronavirus disease, was first reported in December 2019 in Wuhan and in March 11, 2020, got declared as global pandemic by World Health Organisation (WHO) . The morbidity and mortality of the disease have been rising with second wave of pandemic hitting worldwide.

Objectives:

To study the clinical profile of children under 18 years of age with COVID 19 infection and to study the IgG antibody response in covid infected children .

Materials and Methods

Children under 18 years of age except neonates who had COVID 19 infection and recovered from MMC Covid hospital were included for the study. After discharge, blood samples were collected for COVID 19 IgG Antibody research. Data was entered into Microsoft excel sheet and statistical analysis done with SPSS VERSION 21.

Results

21 children who fulfilled the inclusion criteria were taken up for the study. Median age in this study was 10 years, extreme (-). All affected children got infection from their family members. 62% of them had fever as the presenting symptom. 19 children showed positive IgG antibody and 2 out of 21 children showed negative IgG antibody level . There is significant association between IgG titre and timing of of antibody testing after covid infection

Conclusion

Measures to prevent transmission of covid infection from family members to children will decrease covid infection in children. Antibody following Covid infection will last only for few months , making children susceptible to covid infection again. Vaccination among children is necessary to prevent rapid spread of covid infection.

Keywords - Clinical profile, COVID-19 Infection, IgG Antibody.

Introduction

The Global Pandemic Coronavirus disease (COVID-19) was first reported in December 2019 in Wuhan, China (1). On March 11, 2020, the World Health Organization declared COVID-19 as a global pandemic (2). By now COVID 19 infection is having an impact in all our lives. This viral infection has a wide variety of symptoms including cough, breathlessness, fever, chills, muscle pain, headache, sore throat, loss of smell or taste, and gastrointestinal symptoms. Clinical manifestations in patients were classified as mild, moderate, severe, and critically severe according to clinical diagnosis protocol (3,4).

SARS-CoV-2 is an enveloped, single-stranded RNA virus of the family Coronaviridae. This virus contains four structural glycoproteins: envelope (E), membrane (M), nucleocapsid (N), and spike (S) (5, 6). Detection of SARS-CoV-2 viral RNA by reverse transcriptase polymerase chain reaction (RT-PCR) followed by a real-time PCR (QPCR) in samples collected from nasopharyngeal swabs or saliva is the gold standard diagnostic test to confirm early COVID-19 infection (7,8). Detection of antibodies may further contribute to the identification of the immune status of infected individuals (9, 10) and improve the sensitivity of identifying children with asymptomatic infection. These antibodies have been reported to appear in serum or plasma of infected individuals after a few days to 2 weeks after the onset of symptoms (Reference). The sensitivity of combining viral RNA with antibody results has been reported as > 99% (Reference). The persistence of IgG antibodies allows identification of people who have been infected in the past, recovered from the illness, and possibly become immune (11). IgG detection and other serological assays will play an important role in research and surveillance (12). Currently, the antibody responses against SARS-CoV-2 remain poorly understood and the clinical utility of this serological testing is unclear especially in children (13). Very few studies are available in children with covid 19 infection and antibody response. Hence to address this gap, we conducted this cross sectional observational study to assess the clinical profile of covid 19 infection and SARS-Cov2 IgG antibody response in children under 18 years of age in a tertiary care centre in north Kerala.

Objectives:

(1) To study the clinical profile of children under 18 years of age with covid 19 infection.
(2) To study the IgG antibody response in covid 19 infected children .

Materials and Methods

Study design: Observational Study.

Study setting: Malabar Medical College Covid Hospital, Modakkallur.

Study period: November 2020 to March 2021.

Study subjects:

- Inclusion criteria: Children under 18 years of age who had COVID 19 infection and recovered from Malabar Medical College Covid Hospital, Modakkallur.

- Exclusion criteria: Neonates were not included in our study.

Data collection Methods and Data Analysis:

All children with Covid 19 infection fulfilling the inclusion criteria were taken for the study . A detailed history and physical examination findings were assessed either from patient directly or from case sheets and was entered in a structured profoma. Detailed clinical history includes onset of symptom, duration of hospital stay, comorbid conditions, presenting symptoms, and outcome and detailed physical examination includes general and systemic examination and nutritional assessment. All the patients were treated as per COVID 19 guidelines (5). After discharge, all children were followed up for a period of 6 months. During follow-up they were re-examined in detail and blood samples were collected for COVID 19 IgG Antibody.

The SARS-CoV-2 IgG assay was done by an automated, two-step immunoassay, for the qualitative detection of IgG antibodies to SARS-CoV-2 in human serum and plasma using chemi luminescent microparticle immunoassay (CMIA) technology. Reagent used for the test was SARS-CoV-2 IgG Reagent Kit 6R86. The cut off value to call IgG titre as positive was 1.4 or more and titres less than 1.4 were reported as negative. The manufacturer's reported sensitivity is 84% if tested within 7 to 14 days and thereafter 100% and specificity is 99% .

Data collected was entered into Microsoft excel sheet and graphical and statistical analysis was performed with the help of statistical package for the social sciences (SPSS VERSION 21, year and manufacturer). Categorical variables were expressed as proportions and quantitative variables were expressed as median and interquartile range. Statistical test of significance –chi square test for categorical variables and non parametric test using Mann-Whitney Test and Kruskal-Wallis Test were used for quantitative variables.

Ethical Considerations : This study was reviewed and approved by Ethics Committee of our hospital.

Results:

During the study period total 36 covid positive children were admitted and treated in our hospital. Twenty-one children who fulfilled the inclusion criteria were taken up for the study. Age distribution in this study was from (1year 6 months to 17 years) and median age was 10 years and inter quartile range (IQR) was 6.5 to 13, Figure 1.

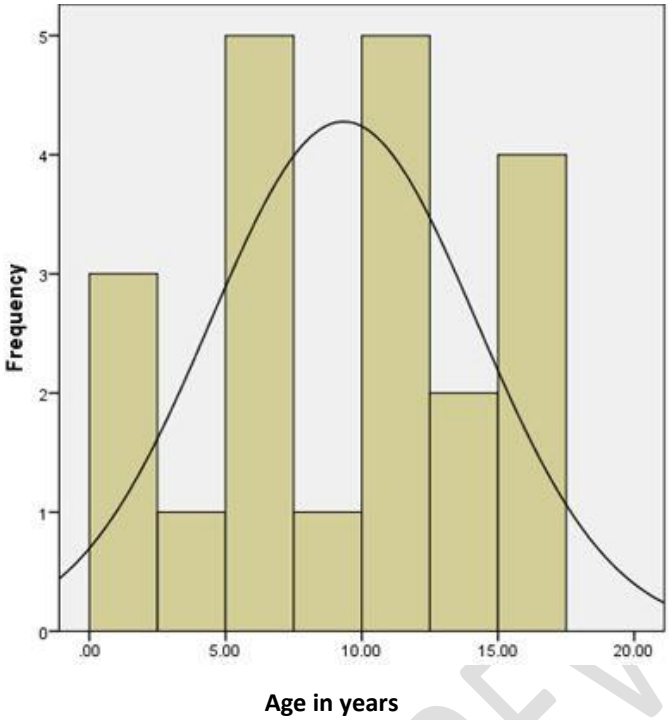

Figure 1- Age distribution in Histogram

In the study group 76% were boys and 24% were girls. Nutritional status of 71% children fell in between 3rd and the 50th percentile according to the IAP growth chart while 29% fell in between 75 and 97 percentile . Family members were the source of contact in all children. 76.2 % children did not have any comorbidities, 9.5% of children had bronchial asthma, and the others had allergic rhinitis (4.8%), migraine (4.8%), and seizures (4.8%) as comorbidities. No significant association was found between the severity of disease and comorbidities. 62% of patients had fever as the presenting or the first symptom while 14% had headache, 10% had upper respiratory infection symptoms as their presenting symptom (**Table 1**).

First symptom or presenting symptom	Number of patients (n=21)	Percentage
Fever	13	61.9
Headache	3	14.3
URI	2	9.5
Asymptomatic	3	14.3
Total	21	100.0

Table 1- Presenting symptoms

14.3% children in this study were asymptomatic. 47.6% of children were relieved of COVID symptoms within 2 days, 9.6% within 4 to 5 days and 19% within 14 days. However, 9.6% children took 1 to 2 months ~~time~~ for the relief of symptoms. None of the patients in this study

had severe morbidity or mortality. Average hospital stay in all children was around 10 days .This is because repeat COVID antigen test was done on the 10th day as per hospital policy. Even after becoming covid negative, 14% of patients had symptoms like myalgia , tiredness and anosmia. We did not have any patient with multisystem inflammatory syndrome in children. Serum samples were collected over the course of six months to provide an information about SARS-CoV-2 serology responses.

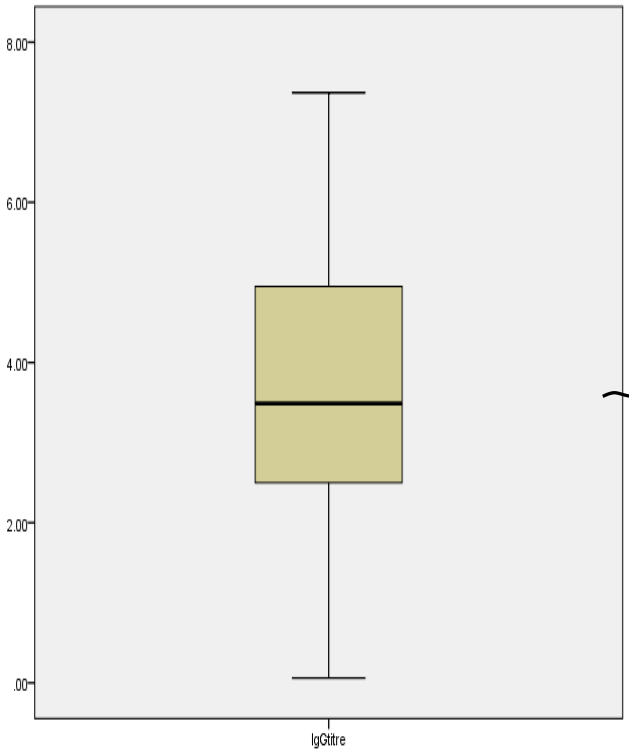

Figure 2-Box and whisker plot of Ig G titre.

19 children (90.5%) showed positive IgG antibody response and 2 children (9.5%) showed negative IgG antibody response. Median IgG titre was 3.49, and inter quartile range (IQR) was 2.42 to 5.31 **(**Figure 2). 9.5% children were tested for IgG antibody response at 1month ,33.5% at 2 months ,9.5% at 3 months, 19% tested at 4 months and 28.6% tested for antibody response at 5 months after COVID infection (table 2).

Timing of IgG antibody test after covid infection (in months)	Number of patients (n=21)	Percentage
1	2	9.5
2	7	33.3
3	2	9.5
4	4	19.0
5	6	28.6
Total	21	100.0

Table 2 - Timing of IgG antibody test after recovery from covid infection.

There is significant association between IgG titre and timing of of antibody testing after COVID infection according to Kruskal-Wallis test. After applying Post Hoc test in our study, we got significant difference in IgG titre done at 1 month after COVID infection and IgG titre done at 5 months .There is significant reduction in antibody response after COVID infection as time progresses. Maximum IgG titre was 7.37 at 1 month after infection and minimum IgG titre was 0.06 at 3 months after infection. No significant association was found between IgG response and gender, clinical symptoms, nutritional status, duration of hospital stay and post covid symptoms.

Discussion

Median age of patients in this study was 10 (IQR 6.5 -13), which is different from the study conducted by Christophers et al in which median age was 5 years (IQR =8) (16). Out of 21 children with COVID 19 infection, fever was the most common presenting symptom. "We couldn't find any association between fever and antibody response". Other presenting symptoms were headache, cold, cough and myalgia. "No significant association was seen between symptoms and antibody response".

Eventhough 71.4% had fever, only 61.9% of patients had fever as the initial presentation.14.3% patients were asymptomatic. In their study Christophers et al also shows similar results in which 62% of patient had fever at the time of presentation, 32% had cough and 21% were asymptomatic (16). We also noticed that initial clinical symptom were the same in children and in all family members (ie if ageusia) **?** was seen in a child it was present in majority of people in a family **?**. Children were not the first symptomatic patient in any of the family. Family members might have received the infection from other adults. In our study we also noticed that none of these children were admitted in PICU and none of them had severe disease course although some of their family members had very severe disease. The exact mechanisms underlying the different SARS-CoV-2 immune responses based on age remain unclear. "However, few possibilities have been suggested that children may have attenuated immune responses resulting in tolerance of the virus" (**unclear meaning of the sentence**) (18). Furthermore it has also been proposed that trained immunity may play a role and that immune memory generated by other vaccines such as measles, mumps, and rubella may confer a non specific protective immune response against SARS-CoV-2 (18).

The reduced respiratory symptoms and low incidence of Acute Respiratory Distress Syndrome (ARDS) in the pediatric age group suggest a distinct infection course, possibly due to lower expression of the viral receptor angiotensin-converting enzyme 2 (ACE2) in pediatric airway epithelial cells, or a more robust innate immune response in children (19) .

In this study most of the patients infected with SARS-CoV-2 have detectable SARS-CoV-2 IgG antibody. IgG antibody can be detected from serum after a period of 14 days after covid infection. Hence we had started to collect blood after a month up to six months. In this present study IgG were "~~detected to be~~" elevated in 90% of patients. A study conducted by DeSimone et al (15) also showed 81.2% positive antibody response.

In this study, we noticed that there is significant reduction in IgG titre as time progresses especially after 3 months. A study conducted by Isho et al (20) also showed that serum and saliva IgG antibodies to SARS-COV-2 are maintained in the majority of COVID-19 patients for at least 3 months. Another study conducted by Wang et al (21) showed that concentrations of IgG antibodies remained high for at least 3 months before subsequently declining. These studies and the present study have raised the suspicion that SARS-CoV-2

immune response following natural infection may be short lived causing concerns about the durability of infection induced protection.

Conclusion

In this first wave of covid 19, only few children were affected. All children got infection from their family members. So measures to prevent transmission of covid infection from family members to children has to be taken up seriously to decrease covid infection in children .

With this present study we would like to conclude that even though ~~post~~ SAR-Cov-2 infection induces IgG antibodies against SAR-Cov-2 in majority of patients, antibody titre starts decreasing after a period of 2 months . Antibody following Covid infection will last only for few months "and chances of natural immunity is less", making them susceptible to covid 19 infection again. Hence vaccination among children is necessary to prevent rapid spread of covid 19 infection.

Limitations

21 is a small sample size. This is because only few children were affected in the first wave. Serial IgG monitoring would have been better to provide persistence of IgG antibody level in blood.

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