Original Article

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Seropositivity among Children of COVID-19 RT-PCR Confirmed Health Care Workers

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Abstract

Background: Coronavirus Disease 2019 (COVID-19) affects children mildly most of the cases. The study was done among the children of COVID-19 confirmed healthcare workers to see antibody response against COVID-19.

Materials and methods: This cross-sectional study was conducted by the Children of COVID-19 confirmed Health Care Workers (HCWs) of Chittagong Medical College (CMC). After enrolling the HCWs, who were RT-PCR positive within the last 14 days to 6 months, blood samples of their children were collected and tested for COVID-19 antibody. To determine the association of different characteristics, Fisher's exact and Mann Whitney by U test were done.

Results: Total 100 Children were tested for two variants of SARS-CoV-2 Antibody, UK and African variant. SARS-CoV-2 antibodies were detected in 41% of children for both variants. The Mean Antibody titer against UK and African variants was found 83.00±11.39% and 72.30±20.68% respectively. Symptomatic children showed significantly (p-0.00) higher SARS-CoV-2 seropositivity and asymptomatic children were also capable of developing response against SARS-CoV-2.

Conclusion: Antibody titers were significantly higher in symptomatic children, approximately half of children with positive antibody tests for SARS-CoV-2 reported no symptoms.

Key words: COVID-19; Children; Seropositivity.

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Introduction

The COVID-19 (SARS CoV-2) virus affected children with varying degree of severity.[1-2] From March 2020, the virus started spreading in Bangladesh. While the global mutation rate of coronavirus was 7.23 % in average, the rate was 12.6 % in Bangladesh.[3]

Health Care Workers (HCWs) are the essential workers designated as the people serving in health care settings who have potential for exposure to patients or infected materials.[4] According to WHO, the HCWs including doctors, nurses and health stuffs comprised 11% of the total COVID-19 cases in Bangladesh.[5] Our frontline fighters were at increased risk for COVID-19 infection along with their family.[6,7,8]

During the first wave of the SARS-CoV-2 pandemic in England, children accounted for just 1% of confirmed infections,[9] had a milder clinical course, a pattern similar to other international settings.[9-12] Children were relatively unaffected by COVID-19 infection with an unknown proportion remain asymptomatic.[13] The majority of children infected by SARS-CoV-2 had documented household contact.[14] A study done in Dhaka Shishu hospital found that 54.93% of children had documented home exposure.[14] In contrast, adults had nosocomial exposure.[15]

Facing this unknown pathogen, it was unclear what proportion of children were asymptomatic and which symptoms were associated with pediatric COVID-19 infection as there was no published data from Bangladesh. By antibody testing, it is easier to detect previous infections. This study was aimed at determining the impacts on children contact with COVID-19 RT-PCR confirmed cases. Thus, this study reported the presence and titers of COVID-19 antibodies in children of HCWs and to report the symptomatology as well as the asymptomatic rate in Children of our country. Updated evidence reported from this study will help clinicians and

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researchers to monitor the spread of infection among families and to plan strategies for protecting the HCWs, their children and families, as well.

Rationale

Our health care workers are our front liners. They have to visit crowded hospitals regularly even during lock-down periods and leads to repeated exposure to SARS- CoV-2 virus, thus affected more than others. So, the Chance of getting COVID-19 infection is higher in their children and family members. It is observed that most children are either asymptomatic or mildly symptomatic, like other countries. But there is a lack of data in this regard in our country. So, this study will add to report that these asymptomatic and mildly symptomatic children can develop an antibody response to COVID-19. This study reported the presence of COVID-19 antibodies in healthy children of HCWs and to describe the symptomatology of infection. This study will help future researchers to monitor the spread of infection among families and to plan strategies for protecting the children and families of HCWs. The purpose of the study to find out the seropositivity rate among asymptomatic or mildly symptomatic children of COVID-19 RT-PCR Confirmed HCWs.

Materials and methods

It was an observational cross-sectional study done in Department of Pediatrics, Chittagong Medical college Hospital from January to June 2022. One hundred Children of 1 month to 15 years of age were taken as a sample as inclusion criteria.

Inclusion criteria

- Children of COVID-19 RT-PCR confirmed HCWs aged 1 month -15 years of age after 14 days of symptoms.

Exclusion criteria

- Children of COVID-19 RT-PCR confirmed HCWs, 14 days before.
- Children who had severe COVID-19 infection with requiring hospitalization.

The prevalence of home exposed children with COVID-19 confirmed cases was found 53.93% in our country.[14] The calculated sample size was 384. For time constraint, 100 samples were taken by convenient sampling.

The Children were enrolled whose parents were HCWs and COVID-19 RT-PCR confirmed within last 14 days to 6 months (Who were suffered from July to December 2021) working in Chittagong Medical College Hospital (CMCH). The different wards of CMCH were regularly searched for HCWs who previously suffered RT-PCR confirmed COVID-19 infection. They were included in the study with informed consent. The history and demographic features were recorded in a predetermined questionnaire. A total of 118 children were eligible, 4 children had severe COVID-19 infection required hospitalization, 8 children were discarded for incomplete data, 6 parents denied giving consent.

Laboratory technician was sent to collect blood samples of children to their address for doing COVID-19 antibody by STANDARD F SARS-CoV-2 nAb FIA. It is the immunoassay for qualitative measurement of neutralizing antibodies against SARS Cov-2 virus by SD BIOSENSOR kit. Blood (5 ml) was collected and transported to the laboratory for testing by two color devices of the kit (Pink for UK, blue for African variant).

Statistical Package for Social Science (SPSS, version 23) was used for analysis of data. Absolute numbers and percentages were used to describe the categorical data. To describe numerical data and central tendency measures, the mean value and standard deviation was used. Seroprevalence rates between symptomatic and asymptomatic children were compared using Fisher's exact test. All variables were analyzed using univariate analysis with Fisher's exact and Mann-Whitney U test. The associations between the variables were considered significant if the value was <0.05.

Prior approval was obtained from the Ethical Review Committee of CMC. The anonymity of patients and confidentiality of the secondary data was ensured.

Results

SARS-CoV-2 antibodies were detected in forty one percent (41%) of children for both variant (UK And African Variant) and 63% UK Variant, 44% African variant separately.

Among Parents (HCWs) 18% were Doctors, 20% were Nurse, 23% were medical stuff in case of

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UK variant and 14% Doctor, 16% Nurse, 15% Medical stuff in case of African variant. Most of the parents were mothers who were confirmed COVID-19 positive. (44% in UK variant and 32% in African Variant). Among father 10% were Antibody positive for Uk Variant and 6% were African variant.

The Cut-off value for positive Antibody titer was 25% in this testing method. The Mean Antibody titer against UK and African variant was 83.00±11.39% and 72.30±20.68% respectively.

The children were divided into four groups. The two group (2-5 years and 5-10 years) were titer positive for UK variant one fifth cases (22%) and 21% cases of 2-5 years age group were also titer positive for African variant. In all age group, totals 63% and 44% were titer positive for UK variant and African variant respectively. Among the titer positive cases majority (54%) of the children were male for both the variants.

All parents were diagnosed with RTPCR, 7% of parents were confirmed by both RTPCR and antigen test. Sixty-one percent of affected parents were in isolation, 96% of them were in home quarantine. Most (98%) of the parents were symptomatic, 55% of which had respiratory aerosol generating conditions.

Mean age of antibody positive children were 6.3±3.89 years and 53.5% children were symptomatic.

Sixty-three percent (63%) children were seropositive for UK Variant and the mean Antibody level was significantly higher (76.19% P value 0.05) among age groups of 10-15 years, lowest in age 1 to 12 months.

African Variant was found seropositive in 44% children and the mean Antibody level of this Variant was significantly higher (60%, p value 0.00) in 2-5 years age group, lowest in age 1 to 12 months.

Antibody level of children in relation to symptom status:

There were 39/100 children who were found symptomatic and seropositive in UK Variants. Mean antibody level (83%) was higher in symptomatic cases than in asymptomatic cases (45%) (p value 0.000). Here, 24 children were found asymptomatic but seropositive (Mean antibody level 45%).

There were 34/100 children found symptomatic and seropositive in African variants. Mean antibody level (72%) was found higher in symptomatic cases than asymptomatic cases (18%) (p value 0.000). Ten asymptomatic children were found seropositive (Mean antibody level 18%).

Table I Nonparametric test (Kruskal-Wallis tests) to evaluate the mean Differences in antibody (UK variant and African variant respectively) level according to age group

Age group	Case-Ab-1 Cat-Uk variant (+ve)	(-ve)	Total	Case-Ab-2 Cat-African variant (+ve)	(-ve)	Total
Cat1: 1-12m	3(27.27	8(72.72)	11	1((.09)	10	11
Cat2: 12.1-60m	22(62.86)	13(37.14)	35	21(60)	14	35
Cat3: 60.1-120m	22(66.67)	11(33.33)	33	10(30.30)	23	33
Cat4: 120.1-180m	16(76.19)	5(23.81)	21	12(57.14)	9	21
Total	63	37	100	44	56	100
p value	χ^2=7.89, p-0.05			χ^2= 13.06, p=0.00		

The Table shows the frequency of positive UK and African variant antibody among the different age groups.

The highest frequency being in category4 age group. The Pearson chi-quire test shows an association between the categories (Age and Uk Variant ab) which is statistically significant (χ^2=7.89, df=3, p=.05) at the 5% level.

The highest frequency being in category 2 age group. The Pearson chi-quire test shows an association between the categories (Age and African variant ab) which is statistically significant (χ^2=13,06, df=3, p=.00) at the 5% level.

Table II Bivariate analysis (Pearson Chi-square Tests) to evaluate the mean differences in antibody V1 (UK variant) level according to Symptomatic vs Asymptomatic case

		case_ab V1cat Positive	Negative	Total
Case status	Asymptomatic	24 (45%)	29 (54%)	53
	Symptomatic	39 (83%)	8 (17%)	47
Total		63	37	100

χ^2=15.19, p=0.000 (p<.05)

The Table shows the association between antibody-1 (UK variant) category and the case symptom status. It depicts that both categories are significantly associated (p<.05).

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Table III Bivariate analysis (Pearson-Chi-square Tests) to evaluate the mean differences in antibody V2 (African variant) level according to Symptomatic vs Asymptomatic case

		Case_ab V2cat		
		Positive	Negative	Total
Case status-15	Asymptomatic	10 (18%)	43 (81%)	53
	Symptomatic	34 (72%)	13 (27%)	47
Total		44	56	100

χ^2=28.91; p=.000 (p<.05)

The Table shows the association between antibody-2 (African Variant) category and the case symptom status. It depicts that both categories are significantly associated (p<.05).

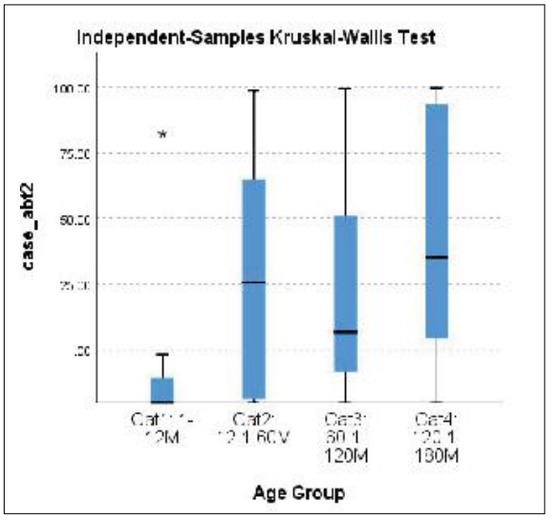

Figure 1 Case-ab1 across Age Group Independent-Samples Kruskal-Wallis Test

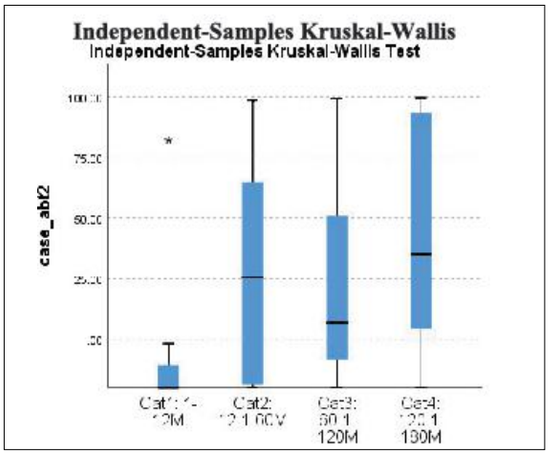

Figure 2 Case-ab2 across Age Group Independent-Samples Kruskal-Wallis

Discussion

Corona virus variants were categorized into two different groups by World Health Organization (WHO): Variant of Concern (VOC) and Variant of Interest (VOI). VOCs were responsible for new waves in many countries. The B.1.1.7 variant, emerged in United Kingdom in 2020. The other VOCs B.1.351, first identified in South Africa. VOCs were associated with higher virulence than the coronavirus of Wuhan, China, attributes to higher hospitalizations of younger people.[16]

All participant children were not vaccinated, as the Government of Bangladesh did not started vaccination against SARS CoV-2 in participant's age group during data collection period. Mean Antibody level against UK and African variant was 83±17.9% and 72.30±20.68%. The antibody level found by Jahan Ara et al. against SARS CoV-2 was 66.99% where study participants were adult resided in Chittagong.[17] In this study, antibody level was found higher for both the variants in the same area, but study participant were children. Another two study, One in Sitakunda, Chittagong from March to June 2021, other study by ICDDRB in Chittagong from October 2020 to February 2021 found a bit lower antibody level (64.1% and 55%).[18] This study was done in later period, from July to December 2021 and got higher seropositivity, assuming that seropositivity in Chittagong has been progressively increasing over time, maybe due to high infection levels. During the same period, the seroprevalence in Dhaka was found to be 71%.[19] which matched with our result.

In this study we got 63% and 44% of children were positive for UK and African Variant respectively and 41% children were positive for both types. As only non-vaccinated children were tested, this result gives idea about the variants of virus in Chittagong. Here we got higher number of UK variant than African Variant and fair number of mixed infections. All the seropositivity was achieved from natural infections. The study by Thomas waterfield et al. got positive antibody in 6.9% (UK) cases in UK during early period of COVID pandemic.[13] This difference may be due to high rate of infection in later periods of pandemics.

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Among parents of UK variant positive children 18% were Doctors, 20% were Nurse and 23% were medical staff. Whereas Parents of African variant positive children 14% doctors, 16% Nurses and 15% were medical stuff. Study by Thomas waterfield tested only for UK variant found 36.2% parents were hospital medical staff, 19.3% were Nursing staff.[13]

Mean age of the children in this study were 6.3±3.89 years and 54% children were male in both variants. Study by Thomas waterfield found the median age 10.1 years.[13] This difference may be due to our study is a hospital-based with a small sample, but the percentages of gender (54%) were almost near to that of the study (51%).[13] Among Participant children, 53 % were symptomatic which also matched with Thomas Waterfield study (50%).[13]

Sixty-three percent (63%) of children in this study were seropositive for UK variant SARS CoV-2. The mean Antibody level was found highest (76.19%) among 10-15 years and lowest in 1 to 12 months. Forty four percent (44%) of children were seropositive for African Variant SARS CoV-2. The mean Antibody level was higher (60%, 57%) between 2-5 years and 10-15 years, lowest among 1 to 12 months. This shows, higher Antibody level in older children. There was significant association between the age categories and antibody level in both variants (p value 0.05 and 0.00 respectively).

The bivariate analysis identified that symptomatic children were significantly (p 0.00) associated with higher (UK-82% and African-72%) SARS-CoV-2 seropositivity than asymptomatic cases (45%and 18%) in both variants. This finding has similarities of the studies by Alkurt et al. and Long Q X et Al. which showed that asymptomatic people had lower mean IgG levels.[20,21] Thomas Waterfield (50%) study also supports this statement using the Abbott Architect SARS-CoV-2 IgG assay.[13] Adult serological tests revealed that people suffering from severe sickness have a much higher antibody response than mild or asymptomatic disease.[22-24] This has raised worries that youngsters with milder disease may not develop a substantial antibody response. But new adult data indicate, even asymptomatic adults can develop a potentially long-lasting and effective immune response.[25,26] In our study, antibody titers were significantly higher in symptomatic compared with asymptomatic children (p=0.00). But it remains unknown how much the severity of symptoms in children affects the antibody response, as well as the threshold amount to prevent the infection.

Our scenario of infection burden of children was difficult to assess due to asymptomatic infection, limited testing with under reporting of COVID-19 cases. Moreover, molecular testing of Oro-nasal swabs with RTPCR underestimate infection of children due to less sensitivity. In this study 53% of children were asymptomatic, among which 24% and 10% were seropositive for UK and African variant respectively. It could be concluded that asymptomatic children can develop an antibody response. These asymptomatic children were epidemiologically important because they can be superspreader. So, in families with history of SARS Cov-2 infection, all children either symptomatic or asymptomatic must maintain Quarantine to prevent spread of infection.

Limitations

The limitations are, the absolute sample size was relatively small, there was selection bias as it was a single hospital-based study, the children were only diagnosed with symptoms, No RTPCR or antigen testing planned for them. Due to the retrospective nature of data collection for symptomatology, there was a possibility of recall bias.

Conclusion

This research reveals that antibody titers were significantly higher in symptomatic children compared to asymptomatic children, that almost half of children with positive SARS-CoV- 2 antibody reported no symptoms.

Recommendation

Children who are asymptomatic must keep the quarantine to prevent the spread of the transmission of SARS-Cov-2 infection.

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Contribution of authors

KN-Acquisition of data, data analysis, interpretation of data, drafting & final approval.

SI-Design, interpretation of data, drafting & final approval.

ZC-Conception, acquisition of data, interpretation of data, critical revision & final approval.

AF-Acquisition of data, data analysis, drafting, critical revision & final approval.

MAHC-Design, interpretation of data, critical revision & final approval.

SHH-Conception, acquisition of data, data analysis, critical revision & final approval.

Disclosure

All the authors declared no conflict of interest.

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