

COVID-19 in Children: Experience from a Tertiary Care Hospital in Bangladesh

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Abstract

Background: Children are generally at low risk of infection and data on COVID-19 in children are scarce. This study was undertaken to document data from a tertiary care hospital in Bangladesh on the incidence, presentation and immediate outcome of COVID-19 in children. Methodology: It was a crosssectional study conducted in the fever clinic and the department of Pediatrics, Bangabandhu Sheikh Mujib Medical University (BSMMU) over a period of one year from July 2020 to June 2021. All the RT-PCR positive pediatric cases (1 month to 18 years) were enrolled. Data were collected by a structured, predesigned and pre-tested questionnaire. Data were analyzed using Microsoft Excel spreadsheet software 2010. Frequency, percentage and chi-square tests were done for statistical analysis. Result: Among 8203 suspected pediatric COVID-19 cases, 850 (10.36%) was RT PCR positive. The highest number of RT-PCR positive COVID-19 cases was found in April 2021. More than 63% of cases were in the age group of 10 to 18 years. Male: female ratio was 0.97:1. Fever was the most common (75.9%) presenting feature followed by breathing difficulty and chest pain in 9.6% and 7% of patients respectively. Mild infection group was predominant (56.7%). Among the symptomatic cases, 16.7% were hospitalized. Oxygen inhalation and bronchodilators were needed in 75% of hospitalized patients. All the severe and critical cases were managed in the inpatient department and in pediatric PICU when indicated. Most of the patients (99.4%) improved with or without any complication. Four critically ill patients (0.75%) developed multi-organ dysfunction and expired in PICU. Conclusion: The majority of COVID-19 cases belonged to the older age group. More than 75% cases were symptomatic. History of contact was present in 78% cases. More than 99% children recovered with or without sequelae and 0.8% children with pre-existing co-morbidities expired.

Keywords

COVID-19 Infection, Severity, Age Group, Co-Morbid Conditions

1. Introduction

Coronavirus disease 2019 (COVID-19) is a highly contagious viral illness caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). It has created a catastrophic effect on the world's demographics resulting in more than 6 million deaths worldwide. Though substantial progress in clinical research has led to a better understanding of diagnosis, management and prevention of COVID-19, limiting viral transmission still remains as an issue of concern. Many countries have been experiencing a second, third or even fourth wave of outbreaks of COVID-19 probably due to emergence of mutant variants of the virus [1].

Despite vaccine development and global mass vaccination efforts including vaccine boosters, people are still being affected worldwide. A recent epidemiological update by WHO reported that more than 200 countries of the world reported SARS-Co-V-2 variants of concern of which Omicron has been reported by 76 countries. The U.S. has experienced the highest number of SARS-CoV-2 infections and COVID-19 related deaths followed by Brazil and India [2].

The American Academy of Pediatrics and the Children's Hospital Association are collaborating to collect and share all publicly available data from different States of the U.S. on child COVID-19 cases. A total of 14,282,482 COVID-19 cases have been reported, of whom, 18.4% were children. The overall rate was 18,976 cases per 100,000 children in the population [3]. In 2021, a prospective observational study was conducted in the fever clinic and the Department of Pediatrics, Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka, Bangladesh. Among 2091 suspected COVID-19 cases, 462 (22.09%) were real-time polymerized chain reaction (RT-PCR) COVID-19 positive [4].

Children and adolescents are generally at low risk of infection, if infected it is likely to be mild. However, some children and young people have severe experiences. In April 2020, reports from different countries documented a Kawasaki Disease (KD) like hyper-inflammatory syndrome in children in the presence of SARS-CoV-2 infection [5]. After several changes, CDC and WHO renamed this illness as Multi System Inflammatory Illness in Children (MIS-C) [6] [7] [8].

Till now MIS-C cases remain as one of the most challenging and mysterious issues for pediatricians [9].

Children have been suffering more from the consequences of the pandemic including disruption of the education system, essential health services, routine immunization, mental health issues, etc. Gadget, online and television dependency increased significantly during the pandemic, and 21.5% children developed some psychological abnormalities like agitation, excessive anger and anxiety who were mentally healthy before [10].

As data on the rate and severity of SARS-CoV-2 infections in children are scarce, the current study was undertaken to document data from a tertiary care hospital in Bangladesh on the incidence, presentation and immediate outcome of COVID-19 in children over a period of one year.

2. Materials and Methods

It was a cross-sectional study conducted in the fever clinic and the department of Pediatrics, Bangabandhu Sheikh Mujib Medical University (BSMMU) over a period of one year (July 2020-June 2021). BSMMU, the pioneer institute in the health care sector in Bangladesh, launched a specialized fever clinic on 29th April 2020, especially for the treatment of patients with fever and cough and later in July 2020, BSMMU launched a COVID-19 dedicated in-patient center [11].

A semi structured questionnaire was developed for the study by the researchers themselves and feedback was taken from 4 senior pediatricians in the country and psychometricians and the questionnaire was finalized. Pre-testing was done on 25 cases to test the reliability of the questionnaire by test-retest method. The questionnaire was developed in Bengali and later on it was translated in English by one medical and one non-medical persons. These two questionnaires were edited and compiled into one by an expert in English (**Appendix 1**).

More than eight thousand pediatric patients (8203) having COVID like symptoms attended BSMMU for diagnosing COVID-19 infection during this one year period. All the RT–PCR positive confirmed pediatric cases (1 month to 18 years) were enrolled in the present study by purposive sampling. After taking ethical clearance from the institutional review board of BSMMU (BSMMU/2020/6667, date: 23/06/2020), data of initial visit of each child was collected by using the predesigned questionnaire. Collected data included necessary socio-demographic and clinical information.

If there had been admission criteria according to the BSMMU management synopsis, patients were shifted to red zone (RT-PCR positive and having symptoms), yellow zone (symptoms suggestive but RT-PCR negative) and ICU (critical patients). Patients were grouped into mild, moderate, severe and critical categories and treatment was given according to BSMMU protocol which is given below [12].

Grouping of COVID-19 patients according to BSMMU COVID-19 Management Synopsis [12]

Mild Case:

1) Mild clinical symptoms (Fever, cough, sore throat, malaise, headache, muscle pain, loss of taste & smell sensation, diarrhea, redness of eye, skin rash etc.)

2) No shortness of breath

3) No radiological findings of pneumonia in CXR or HRCT chest

Moderate Case:

Symptoms of mild case plus radiological findings of pneumonia in CXR or HRCT chest AND

1) Respiratory distress < 30 breaths/min

2) O_2 saturation (SpO₂) > 93% on pulse oximeter

Severe Case:

Criteria of moderate case plus any one of the following criteria:

1) Respiratory distress (>30 breaths/min)

2) O_2 saturation (SpO₂) \leq 93% at rest on pulse oximeter

3) Arterial partial pressure of oxygen (PaO₂)/fraction of inspired oxygen

 $(FiO_2) < 300 \text{ mmHg} (1 \text{ mmHg} = 0.133 \text{ kPa}) \text{ in ABG or } SpO_2/FiO_2 < 315 \text{ mmHg}$

Critical Case:

Cases of any stage presented with any of the following features:

Respiratory failure & requiring mechanical ventilation, Shock, ARDS, with other organ failure that requires ICU care.

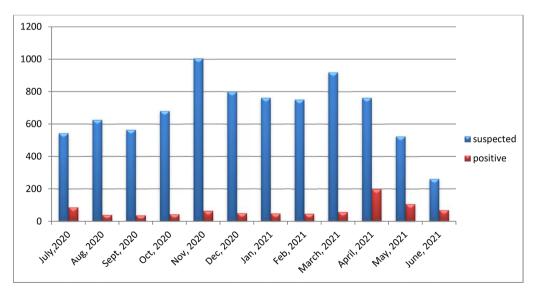
Few (5) Multisystem Inflammatory Syndrome in Children (MIS-C) cases, which is a post COVID-19 complication were also included. All the MIS-C cases were RT-PCR negative, but COVID antibody (IgG) positive. COVID-19 IgG antibody was detected by Enzyme Linked Immunosorbent Assay (ELISA) from serum. Antibody index value of more than 1.1 was considered as positive.

Clinical course of each of the admitted patients were monitored during their hospital stay.

Collected data were recorded in the questionnaires and analyzed using Microsoft Excel spreadsheet software 2010. One researcher read the values, while another researcher entered the data in the spread sheet. Frequency, percentage and chi-square tests were done for statistical analysis.

3. Result

In this cross-sectional study, 8203 children were considered as suspected COVID-19 cases from July 2020 to June 2021. Among them, 850 (10.36%) were RT-PCR positive for COVID-19 and they were considered as the study population. Highest number of suspected COVID-19 cases was found in November 2020, followed by March 2021, but highest number of RT-PCR positive COVID-19 cases was found in April 2021 followed by May 2021 (**Figure 1**).



Among the 850 RT PCR positive cases, 698 responded to the questionnaire.

(X axis: Month and year, Y axis: Absolute number of suspected and positive cases).

Figure 1. Month-wise distribution of suspected and RT PCR positive pediatric cases (n = 8203).

More than 63% of positive cases were in the age group of 10 to 18 years and 21% were in the age group of 5 to 10 years. No neonatal case was found in the study. Male: female ratio was 0.97:1.

A good number of patients (24.5%) had associated co-morbid conditions including acute leukemia, bronchial asthma, thalassemia, chronic liver disease, chronic kidney disease, malignancy, congenital heart disease, rheumatologic conditions etc. History of contact with known COVID-19 cases was present in 78% cases and among them 98% children had household contact. Two children had history of travel abroad. Only 34% children used mask as a personal protective measure (**Table 1**).

Among 698 RT-PCR positive children, 75.9% were symptomatic. Fever was the most common (75.9%) clinical feature followed by runny nose, cough, dys-geusia, and anosmia.

Breathing difficulty and chest pain was found in 9.6% and 7% patients respectively (**Table 2**). Cases of mild infection were predominant (56.7%). There were 3.7% severe cases and 3.4% critical cases including MIS-C (**Table 2**). Incidences of severe and critical illness were more in older children, though not statistically significant (**Table 3**).

Among the 530 symptomatic cases, 89 (16.7%) were hospitalized. All the admitted patients needed anti-pyretic and intravenous antibiotics. Oxygen inhalation and bronchodilators were needed in 75% of hospitalized patients. More than 50% of hospitalized patients needed I/V steroid. IVIG was given 5 (5.6%) patients who had MIS-C. A number of moderate cases (47%) and all the severe and critical cases were managed in the inpatient department and in pediatric ICU when indicated (**Table 4**).

Profile	Frequency	Percentage
Age Group		
1 month - 5 year	103	14.7
>5 year - 10 year	150	21.5
>10 year - 18 year	445	63.8
Gender		
Male	344	49.2
Female	354	50.7
M:F	0.9	7:1
Co-morbid Conditions (eg. nephrotic syndrome, bronchial asthma, acute leukaemia, connective tissue disease etc.)	171	24.5
History of contact with known COVID -19 positive patients	545	78.0
History of travel	2	0.3
Use of mask	238	34.0

 Table 1. Socio-demographic profile of RT-PCR positive cases (n = 698)

All children having mild illness and most of the moderate illness cases were managed in the outdoor (63.2%) with anti-pyretic (100%), anti-histamine (100%) and nasal decongestant. Thirteen of these patients (2.9%) needed oral steroids.

Clinical Features	Frequency Percent	
Symptomatic	530	75.9
Constitutional		
Fever	530	75.9
Headache	212	30.3
Body ache	189	27.0
Conjunctivitis	74	10.6
Chills and rigor	40	5.7
Respiratory		
Runny nose	259	37.1
Cough	249	35.7
Anosmia	232	33.2
Nasal Congestion	183	26.2
Sore throat	100	14.3
Breathing difficulty	67	9.6
Chest Pain	49	7.0
GIT		
Disgeusia	241	34.5
Loose motion	86	12.3
Nausea, Vomiting	57	8.1
Abdominal Pain	38	5.4
Musculoskeletal		
Joint pain	48	6.9
Joint swelling	2	0.3
Rash	25	3.6
Asymptomatic	168	24.0
Classification		
Asymptomatic infection	168	24.0
Mild case	396	56.7
Moderate case	85	12.2
Severe case	25	3.7
Critical case including MISC	24	3.4

Table 2. Clinical presentation and classification of RT PCR positive Cases (n = 698).

	Table 3. Severity	of presentation in	n children of different	age groups ($n = 530$).
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Age group	Mild 396 (74.7%)	Moderate 85 (16.0%)	Severe and Critical 49 (9.2%)	<i>P</i> value
1 month - 5 year	64 (16.2%)	22 (25.9%)	7 (14.2%)	
>5 year - 10 year	91 (23.0%)	21 (24.7%)	17 (34.6%)	0.071772
>10 year - 18 year	241 (60.9%)	42 (49.4%)	25 (51.0%)	

*Chi-square Test. The result is significant at p < 0.05.

Table 4. Treatment modalities an	id outcome of cases ($n = 530$).
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Variables	Frequency	Percentage 16.7	
Hospitalization	89		
Antipyretic	89/89	100	
IV Antibiotic	89/89	100	
Oxygen Inhalation	67/89	75.2	
Bronchodilator	67/89	75.2	
IV steroid	49/89	55.0	
IVIG	5/89	5.6	
Outdoor patients	441	83.2	
Antihistamine	441/441	100	
Anti-pyretic	441/441	100	
Nasal decongestant	441/441	100	
Oral Antibiotics	127/441	28.8	
Bronchodilator	51/441	11.6	
Oral steroid	13/441	2.9	
Outcome			
Improved (with or without complication)	526	99.2	
Expired	04	0.8	

No patient received antiviral drugs or thromboembolic prophylaxis (**Table 4**). After management, most of the patients (99.2%) improved with or without any complication or residual illness. Four critically ill patients (0.8%) developed multi-organ dysfunction and expired in ICU (**Table 4**).

4. Discussion

The clinical spectrum of COVID-19 in children ranges from asymptomatic infection to mild respiratory tract symptoms to severe pneumonia with acute respiratory distress syndrome and multi-organ dysfunction. Understanding of COVID-19 disease and its management is still evolving. The World Health Organization, The Center for Disease Control and Prevention, American Academy of Pediatrics, and other expert groups are providing guidance for evaluation, management, and prevention which are also frequently changing [13]. The rising rate of pediatric infection has been a challenge for the clinicians, as there are possible changes in clinical manifestation and post-infectious manifestations including MIS-C. Findings of the present study may help in managing COVID-19 affected children effectively and in raising awareness among pediatricians for early diagnosis of suspicious cases.

In this cross-sectional study, among the suspected 8203 children, 850 (10.36%) RT-PCR positive cases were considered as the study population. During the initial pandemic phase with the ancestral strain from December 2019 to October 2021, children under five years of age represented 2% of reported global cases and 0.1% of reported global deaths [14]. Reported COVID-19 cases among children spiked dramatically in 2022 during the Omicron variant surge at a time when most countries relaxed public health and social measures. In the United States, by July 2022, children represented 18.6% of all reported cases [3]. In Bangladesh, a prospective observational study in a tertiary care center showed 22.09% confirmed COVID-19 pediatric patients among suspected children [4].

The present study reflects a picture of infection rate and testing of COVID-19 over a period of 1 year from July 2020 to June 2021. The first wave of COVID-19 in Bangladesh started from March 2020 [15]. Case detection rate was increasing day by day till the end of June 2020 and March 2020 to June 2020 was considered as the first wave in Bangladesh [16].

As per the national database Institute of Epidemiology Disease Control and Research (IEDCR), the total number of confirmed cases was decreasing gradually from July 2020 to December 2020 with a little rise in the month of November and December [16]. The period from December 2020 to the end of February 2021 had the lowest rate of infections. In Bangladesh, the positivity rates remained below 5% from mid-January 2021 to early March 2021. From April 2021, positivity rate again started rising as second wave [17]. Though the national data included cases from all age groups, similar picture is found in our study on pediatric population (**Figure 1**), where the case detection rate was low from August 2020 to March 2021 with a rise in April and May 2021 [16].

According to IEDCR, Bangladesh, there was an alarming rise in cases with a steep rise in June 2021 and May 2021 to August 2021 was considered as the third wave in Bangladesh [18]. The present study has reflected first 2 waves, as study period did not cover third wave period.

Most of the children (63.8%) in the present study were older (>10 year with a mean of 10.7 year (**Table 1**). A situation analysis study in Bangladesh in 2020 showed that among the total confirmed COVID-19 cases in all age groups, 3% were <10 years and 7% were between 11 - 20 years [19]. Age disparities in observed cases could be explained by the facts of younger children having lower susceptibility to infection, lower propensity to show clinical symptoms or both. Decreased susceptibility could result from immune cross-protection from other

coronaviruses or from non-specific protection resulting from recent infection by other respiratory viruses which younger children experience more frequently [20] [21].

Male:female ratio in the present study is 0.97:1 indicating almost equal risk of infection in both the genders (**Table 1**). Previous clinical studies on adult population have shown that females are less susceptible to acquire viral infections and reduced cytokine production. Female patients have a higher macrophage and neutrophil activity as well as antibody production and response. Furthermore, *in-vivo* studies of the angiotensin-converting enzyme 2 (ACE2) showed higher expression of ACE 2 in the kidneys of males than females, which may explain the differences in susceptibility and progression of COVID-19 between male and female patients [22].

During Covid-19 pandemic, initially much emphasis was given on the elderly and those having pre-existing health conditions like obesity, hypertension, diabetes etc. as because they are at high risk of serious illness. But it is now clear that male sex is also a risk factor. The epidemiological findings reported across different parts of the world indicated higher incidence, morbidity and mortality in males than females [23] [24] [25] [26] [27]. Male predominance was not found in the present study. It could be due to small sample size, genetic or ethnic variation.

Almost 25% children had different co-morbid conditions including bronchial asthma, chronic liver disease, chronic kidney disease, malignancies, congenital heart disease and rheumatologic conditions (Table 1). In 2021, a systematic review investigated the effects of pediatric comorbidities on COVID-19 severity in children, where, severe COVID-19 was present in 5.1% of children with comorbidities in contrast to only 0.2% without comorbidities [28]. Children with chronic diseases are immune-compromised and probably more vulnerable to infection. This may explain the high incidence of co-morbidities with COVID-19 in different studies including the present study.

Children with COVID-19 usually become affected from household contacts. In this study, 78% patients had history of contact with known COVID-19 positive patients and among them more than 90% had household contacts (**Table 1**). In 2021, a systematic review and meta-analysis of 29 studies suggested that, COVID-19 transmission to children is more likely to occur within household settings from other family members. Many children had a history of close contact with at least one parent having SARS-CoV-2 [29].

The clinical spectrum of SARS-CoV-2 infections in children ranges from asymptomatic to life-threatening. Although severe and fatal cases have been reported, most children are asymptomatic or mild to moderately symptomatic [30] [31] [32].

A review of electronic health records of 82,798 United States children < 18 years of age with laboratory-confirmed SARS-CoV-2 infection found that 66 percent were asymptomatic and 27%, 5% and 2% had mild, moderate and severe

infection respectively. A small number presented in critical condition and were admitted in ICU with MIS-C [32]. In the present cohort, 75.9% children were symptomatic and 24% of patients were asymptomatic and were diagnosed incidentally (Table 2). Among the symptomatic, most of the children (56.7%) had mild infection; followed by moderate, severe and critically ill including MIS-C (Table 2). Children having fever and other constitutional symptoms without fast breathing or radiological findings were categorized as mild illness group. Those having radiological findings of pneumonia, but no fast breathing and stable oxygen saturation were the moderate cases. Children with moderate case criteria plus either fast breathing, or low oxygen saturation or reduced arterial partial pressure of oxygen were in severe case group. Cases of any stage presented with respiratory failure, shock, ARDS or other organ failure requiring ICU were in critical case group [12]. Incidences of severity of illness were more in older children in this study, though not statistically significant (Table 3). Why COVID-19 appears to be less severe in children than in adults is unclear. One possibility is that children have a less-intense immune response to the virus than adults; cytokine release syndrome is thought to be important in the pathogenesis of severe COVID-19 infections [33] [34] [35].

Most of the (63.2%) patients were managed in the outpatient department with anti-pyretic, anti-histamine, nasal decongestants, bronchodilators etc. Oral steroid was also advised to children with acute exacerbation of asthma and children who were on steroid therapy prior to this illness ("e.g." nephrotic syndrome, ALL, SLE etc.). Hospitalized cases were managed by oxygen therapy, mechanical ventilation, intravenous steroid and intravenous immunoglobulin depending on indication and clinical response. More than 99% children improved with or without complications. Only 4 critically ill children developed multi-organ dysfunction and expired in ICU, all of whom had associated co-morbid conditions. To prevent post discharge dissemination of infection, home isolation for 1 week was advised to all (Table 4). A retrospective study at a tertiary care pediatric teaching hospital in Northern India from April 2020-October 2020 found that among 255 COVID-19 positive cases, 56.47% were managed in outpatient and 43.6% required admission. Perhaps their study population included more severe and critical cases that were different than our cohort. The mortality rate was also higher (11.4%) in comparison to the present study (0.6%) [36].

5. Conclusion

The COVID-19 pandemic is a global public health concern. Research is progressing and knowledge regarding the disease in children is evolving from time to time. The present study reported data from a developing country showing demography, clinical profile, management and immediate outcome of Bangladeshi COVID-19 pediatric patients. The majority of COVID-19 cases in this study including most of the moderate, severe and critical cases belonged to the older age group. More than 75% cases were symptomatic. History of contact with known COVID-19 cases was found in 78% cases. More than 99% children recovered but four children (0.6%) with COVID-19 with pre-existing co-morbidity (0.6%) expired.

6. Recommendation

Based on the data in this study, the following recommendations can be made: Further research with a large size sample is needed including long-term followup to determine the clinical, psychological and social impact of COVID-19. Additional research is also required for further follow-up of this cohort to monitor their long-term outcome.

7. Limitations

Noble Coronavirus infection was a new disease. So no expert on this disease was found to help with the construction of questionnaire. Moreover, because of the urgency of the situation, all the steps of validity and reliability could not be fulfilled.

The study was done in a single center within a very short time frame on a limited number of patients. We could not formulate a conclusion on the long-term effects of COVID-19 on the pediatric population as study design did not include follow-ups.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

References

- Cascella, M., Rajnik, M., Aleem, A., Dulebohn, S.C. and Di Napoli, R. (2022) Features, Evaluation, and Treatment of Coronavirus (COVID-19). Statpearls. <u>https://www.ncbi.nlm.nih.gov/books/NBK554776/</u>
- [2] Ahmad, F.B., Cisewski, J.A., Miniño, A. and Anderson, R.N. (2021) Provisional Mortality Data—United States, 2020. *Morbidity and Mortality Weekly Report*, 70, 519-522. <u>https://doi.org/10.15585/mmwr.mm7014e1</u>
- [3] American Academy of Pediatrics (2022) Children and COVID-19: State Level Data Report. <u>https://www.aap.org/en/pages/2019-novel-coronavirus-covid-19-infections/childrenn-and-covid-19-state-level-data-report/</u>
- [4] Haque, M., Laila, K., Al-Mamun, M.H., Supti, S.H. and Rahman, S.A. (2021) Profile and Outcome of Children with COVID-19 Attending Bangabandhu Sheikh Mujib Medical University. *American Journal of Pediatrics*, 7, 72-78. https://doi.org/10.11648/j.ajp.20210702.17
- [5] Royal College of Paediatrics and Child Health (2020) Guidance: Paediatric Multisystem Inflammatory Syndrome Temporally Associated with COVID-19. RCPCH, London.
- [6] Hoang, A., Chorath, K., Moreira, A., Evans, M., Burmeister-Morton, F., Burmeister, F. and Moreira, A. (2020) COVID-19 in 7780 Pediatric Patients: A Systematic Re-

view. *EClinicalMedicine*, **24**, Article ID: 100433. https://doi.org/10.1016/j.eclinm.2020.100433

- [7] Whittaker, E., Bamford, A., Kenny, J., Kaforou, M., Jones, C.E., Shah, P. and Levin, M. (2020) Clinical Characteristics of 58 Children with a Pediatric Inflammatory Multisystem Syndrome Temporally Associated with SARS-CoV-2. *JAMA*, **324**, 259-269. https://doi.org/10.1001/jama.2020.10369
- [8] John, G., Sahajpal, N.S., Mondal, A.K., Ananth, S., Williams, C., Chaubey, A. and Kolhe, R. (2021) Next-Generation Sequencing (NGS) in COVID-19: A Tool for SARS-CoV-2 Diagnosis, Monitoring New Strains and Phylodynamic Modeling in Molecular Epidemiology. *Current Issues in Molecular Biology*, **43**, 845-867. <u>https://doi.org/10.3390/cimb43020061</u>
- [9] Rahman, S.A. (2021) COVID-19 Related Multi System Inflammatory Syndrome in Children: Spectrum of Kawasaki Disease or Different Entity? A Challenging Mystery for Paediatricians. *Bangladesh Journal of Child Health*, 45, 63-66. https://doi.org/10.3329/bjch.v45i2.60075
- [10] Laila, K., Islam, M.Z. and Rahman, S.A. (2021) Impact of COVID-19 on Children: A Study from Tertiary Level Hospital in Bangladesh. *European Journal of Pharmaceutical and Medical Research*, 8, 128-134.
- [11] Hossain, Md.A. and Laila, K. (2022) Fighting against COVID 19: A 7 Days Experience of a Resident Physician from Bangladesh. *European Journal of Pharmaceutical and Medical Research*, 9, 81-86.
- [12] BSMMU COVID 19 Clinical Case Management Guideline https://internalmedicine.bsmmu.edu.bd/notice/253/bsmmu-covid-19-clinical-casemanagement-guidance
- [13] Deville, J.G., Song, E. and Ouellette, C.P. (2022) COVID-19: Management in Children. https://www.uptodate.com/contents/covid-19-management-in-children
- [14] World Health Organization (2021) WHO Coronavirus (COVID-19) Dashboard.
- [15] Siam, M.H.B., Hasan, M.M., Raheem, M.E., Khan, H.R., Siddiqee, M.H. and Hossain, M.S. (2020) Insights into the First Wave of the COVID-19 Pandemic in Bangladesh: Lessons Learned from a High-Risk Country. *Heliyon*, 7, E07385. https://doi.org/10.1016/j.heliyon.2021.e07385
- [16] IEDCR (2022) COVID-19 Dynamic Dashboard of Bangladesh. Institute of Epidemiology Disease Control and Research, Dhaka. <u>http://103.247.238.92/webportal/pages/covid19.php</u>
- [17] Masum, O. (2021) Declining Infection Rate Drives Hopes of Curbing COVID Spread in Bangladesh. Official Reports Show Daily Lab-Tested COVID-19 Infection Rate in Bangladesh Below 5 Percent over the Last 13 days. <u>https://bdnews24.com/bangladesh/2021/02/01/declining-infection-rate-drives-hope s-of-curbing-covid-spread-in-bangladesh</u>
- [18] Dhaka Tribune (2021) Daily Deaths Hit Record High of 119 as Covid Engulfs Bangladesh.
- [19] Hussain, M., Abdullah, M. and Mamun, A. (2020) COVID-19 in Children in Bangladesh: Situation Analysis. *Asia Pacific Journal of Pediatric and Child Health*, 3, 59-65.
- [20] Benelli, G., Buscarini, E., Canetta, C., La Piana, G., Merli, G., Scartabellati, A. and Lauria, G. (2021) SARS-COV-2 Comorbidity Network and Outcome in Hospitalized Patients in Crema, Italy. *PLOS ONE*, **16**, e0248498. <u>https://doi.org/10.1371/journal.pone.0248498</u>
- [21] Cowling, B.J., Fang, V.J., Nishiura, H., Chan, K.H., Ng, S., Ip, D.K. and Peiris, J.M.

(2012) Increased Risk of Noninfluenza Respiratory Virus Infections Associated with Receipt of Inactivated Influenza Vaccine. *Clinical Infectious Diseases*, **54**, 1778-1783. https://doi.org/10.1093/cid/cis307

- [22] Kopel, J., Perisetti, A., Roghani, A., Aziz, M., Gajendran, M. and Goyal, H. (2020) Racial and Gender-Based Differences in COVID-19. *Frontiers in Public Health*, 8, Article No. 418. <u>https://doi.org/10.3389/fpubh.2020.00418</u>
- [23] Faure, E., Kipnis, E., Bortolotti, P. and Salik, J. (2020) Clinical Characteristics of Covid-19 in New York City. *The New England Journal of Medicine*, 29, 2016-2017.
- [24] Onder, G., Rezza, G. and Brusaferro, S. (2020) Case-Fatality Rate and Characteristics of Patients Dying in Relation to COVID-19 in Italy. *JAMA*, **323**, 1775-1776. <u>https://doi.org/10.1001/jama.2020.4683</u>
- [25] Shim, E., Tariq, A., Choi, E., Lee, Y. and Chowell, C. (2020) Transmission Potential and Severity of COVID-19 in South Korea. *International Journal of Infectious Diseases*, **93**, 339-344. <u>https://doi.org/10.1016/j.ijid.2020.03.031</u>
- [26] De La Vega, R., Ruíz-Barquín, R., Boros, S. and Szabo, A. (2020) Could Attitudes toward COVID-19 in Spain Render Men More Vulnerable than Women? *Global Public Health*, 15, 1278-1291. <u>https://doi.org/10.1080/17441692.2020.1791212</u>
- [27] Bwire, G.M. (2020) Coronavirus: Why Men Are More Vulnerable to Covid-19 than Women? SN Comprehensive Clinical Medicine, 2, 874-876. <u>https://doi.org/10.1007/s42399-020-00341-w</u>
- [28] Tsankov, B.K., Allaire, J.M., Irvine, M.A., Lopez, A.A., Sauve, L.J., Vallance, B.A. and Jacobson, K. (2021) Severe COVID-19 Infection and Pediatric Comorbidities: A Systematic Review and Meta-Analysis. *International Journal of Infectious Diseases*, 103, 246-256. <u>https://doi.org/10.1016/j.ijid.2020.11.163</u>
- [29] Gaythorpe, K.A., Bhatia, S., Mangal, T., Unwin, H.J.T., Imai, N., Cuomo-Dannenburg, G. and Ferguson, N.M. (2021) Children's Role in the COVID-19 Pandemic: A Systematic Review of Early Surveillance Data on Susceptibility, Severity, and Transmissibility. *Scientific Reports*, **11**, Article No. 13903. <u>https://doi.org/10.1038/s41598-021-92500-9</u>
- [30] Liguoro, I., Pilotto, C., Bonanni, M., Ferrari, M.E., Pusiol, A., Nocerino, A., Vidal, E. and Cogo, P. (2020) SARS-COV-2 Infection in Children and Newborns: A Systematic Review. *European Journal of Pediatrics*, 179, 1029-1046. https://doi.org/10.1007/s00431-020-03684-7 https://www.uptodate.com/contents/covid-19-clinical-manifestations-and-diagnosis -in-children/abstract/5
- [31] Stokes, E.K., Zambrano, L.D., Anderson, K.N., Marder, E.P., Raz, K.M., El Burai Felix, S., Tie, Y. and Fullerton, K.E. (2020) Coronavirus Disease 2019 Case Surveillance—United States, January 22-May 30, 2020. *Morbidity and Mortality Weekly Report*, 69, 759-765. <u>https://doi.org/10.15585/mmwr.mm6924e2</u> <u>https://www.uptodate.com/contents/covid-19-clinical-manifestations-and-diagnosis</u> <u>-in-children/abstract/83</u>
- [32] Li, Y., Tong, C.H., Bare, L.A. and Devlin, J.J. (2021) Assessment of the Association of Vitamin D Level with SARS-CoV-2 Seropositivity among Working-Age Adults. *JAMA Netw Open*, 4, e2111634. https://doi.org/10.1001/jamanetworkopen.2021.11634
 https://www.uptodate.com/contents/covid-19-clinical-manifestations-and-diagnosis -in-children/abstract/136
- [33] Ben-Tov, A., Lotan, R., Gazit, S., Chodick, G., Perez, G., Mizrahi-Reuveni, M. and Patalon, T. (2022) Dynamics in COVID-19 Symptoms during Different Waves of

the Pandemic among Children Infected with SARS-CoV-2 in the Ambulatory Setting. *European Journal of Pediatrics*, **181**, 3309-3318. <u>https://doi.org/10.1007/s00431-022-04531-7</u> <u>https://www.uptodate.com/contents/covid-19-clinical-manifestations-and-diagnosis</u> <u>-in-children/abstract/139</u>

- [34] Esper, F.P., Adhikari, T.M., Tu, Z.J., Cheng, Y.W., El-Haddad, K., Farkas, D.H., Bosler, D., Rhoads, D., Procop, G.W., Ko, J.S., Jehi, L., Li, J. and Rubin, B.P. (2022) Alpha to Omicron: Disease Severity and Clinical Outcomes of Major SARS-CoV-2 Variants. *The Journal of Infectious Diseases*, 2022, jiac411. <u>https://doi.org/10.1093/infdis/jiac411</u> <u>https://www.uptodate.com/contents/covid-19-clinical-manifestations-and-diagnosis</u> <u>-in-children/abstract/140</u>
- [35] Forrest, C.B., Burrows, E.K., Mejias, A., Razzaghi, H., Christakis, D., Jhaveri, R., Lee, G.M., Pajor, N.M., Rao, S., Thacker, D. and Bailey, L.C. (2022) Severity of Acute COVID-19 in Children<18 Years Old March 2020 to December 2021. *Pediatrics*, 149, e2021055765. <u>https://doi.org/10.1542/peds.2021-055765</u> <u>https://www.uptodate.com/contents/covid-19-clinical-manifestations-and-diagnosis</u> <u>-in-children/abstract/141</u>
- [36] Singh, P., Attri, K., Mahto, D., Kumar, V., Kapoor, D., Seth, A. and Goel, A. (2022) Clinical Profile of COVID-19 Illness in Children—Experience from a Tertiary Care Hospital. *Indian Journal of Pediatrics*, 89, 45-51. https://doi.org/10.1007/s12098-021-03822-5

Appendix I. English Version of the Bengali Questionnaire

COVID-19 in Children: Experience from a Tertiary Care Hospital in Bangladesh

- A. Subject id:
- B. Date of visit:

C. Inclusion Criteria:

- Is the patient's age between 0 and 18 years? [yes = 1, no = 2]
- Does the patient have fever/cough/runny nose/others (if others, go to the Table: J for clinical features) [fever = 1, cough = 2, runny nose = 3, others = 4]

If any of this is present, go to section D

D. RT-PCR for COVID-19 [positive = 1, negative = 2]

If RT PCR positive, go to section E

E. Socio-demographic profile

- Name:
- Age (in years):
- Gender: [male = 1, Female = 2]
- Telephone no:
- Residence: [Urban = 1, Semi-urban = 2, Rural = 3]
- Father's Occupation:

[Doctor = 1, Health care worker = 2, Police = 3, Student = 4, Farmer = 5, Day Laborer = 6, Businessman = 7, Govt.

- Service = 8, Non-government Service = 9, banker = 10, Other = 11
- History of contact with COVID-19 patient [yes = 1, no = 2]

If yes, please specify [Family members = 1, Others = 2]

F. Is there any co-morbid condition

[Bronchial asthma = 1, Interstitial Lung Disease = 2, Nephrotic Syndrome = 3, Chronic kidney disease = 4, Chronic liver disease = 5, Portal Hypertension = 6, Chronic Hepatitis = 7, Undernutrition = 8, Obesity = 9, Inflammatory Bowel Disease = 10, Congential/acquired heart disease = 11, Hemoglobinopathies = 12, Malignancy = 13, Rheuma-tological conditions e.g. SLE/JIA/others = 14, Neurometabolic/Neurodegenerative disorders = 15, Cerebral palsy = 16, Epilepsy = 17, Diabetes = 18, Hypothyroidism = 19, others = 20 If others, please specify

G. Personal hygiene (Patient or caregiver): Put tick mark

Use of mask Repeated Hand wash/Sanitization Not leaving home without cause H. History of contact with anyone returning from abroad: [yes = 1, no = 2]	s Not
Not leaving home without cause	
H History of contact with anyone returning from abroad: $[yes - 1, n_0 - 2]$	
[y, y] = [y, y] = [y, y] = [y, y]	
I. History of travelling abroad [yes = 1 no = 2]	

J. Clinical features: (Put a tick mark)

a. Constitutional	Yes	No
Fever		
Headache		
Body ache		
Conjunctivitis		
Chills and rigor		
Malaise		
Weakness		
Sweating		
Others, specify		
1. Marca and a second	¥.	N
b. Muco-cutaneous	Yes	No
Cheilitis		
Conjunctivitis		
Pharyngitis		
Maculo-papular rash		
Urticarial rash		
Extremities edema		
Extremities desquamation		
Other, specify:		
c. Musculoskeletal	Yes	No
Joint pain		
Myalgia		
Muscle weakness		
Bone pain		
Joint swelling		
Others, specify		
d. Gastro-intestinal	Vac	No
	Yes	No
Abdominal pain		
Nausea Vocaitin a		
Vomiting		
Dysguesia		
Diarrhea		
GI bleeding		

	e. Cardiovascular	Yes	No
	Chest pain		
	Dyspnea		
	Syncope		
	Others, specify		
	f. Respiratory	Yes	No
	Runny nose		
	Cough		
	Anosmia		
	Nasal congestion		
	Sore throat		
	Respiratory distress		
	Pneumonia		
	Hemoptysis		
	Chest pain		
	Others, specify		
	g. Neurological	Yes	No
	Seizure		
	Cranial nerve palsy		
	Vertigo		
	Others, specify		
	h. Genitourinary	Yes	No
	Dysuria		
	Urethritis		
	Urgency		
	Increased frequency		
	Others		
H. Hospital Adm	tission: [yes = 1 no = 2]		
	Management	n	%
	Respiratory support		
	Fluid support		
	Anti-coagulant		

Continued

Continued
Aspirin
IVIG
Pulse Glucocorticoids
Oral steroids
Antiviral
Antibiotic
Others, specify
I. ICU admission [yes = 1, no = 2]
J. Outcome [Recovered without sequelae = 1, Recovered with sequelae = 2, Death = 3]
If sequelae, please specify

Name of the Interviewer: Date: **Thank you for your participation**