Profile and Outcome of Children with COVID-19 Attending Bangabandhu Sheikh Mujib Medical University

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Abstract: Background: Coronavirus disease 2019 (COVID-19) caused by SARS-CoV-2 is a global pandemic. Covid-19 has spread around Bangladesh and children are also being infected with comparatively fewer symptoms and lower case-fatality rates. Objectives: To assess the clinical profile, disease severity, presence of co-morbidities and outcome of pediatric COVID-19 patients. Methods: This prospective observational study was conducted in the fever clinic and the Department of Pediatrics, Bangabandhu Sheikh Mujib Medical University (BSMMU). Data were collected from the confirmed cases by using a structured questionnaire by face to face interview and also over telephone at 1st visit and at 2nd and 8th week of disease course. Collected data were analyzed using appropriate statistical tests. Result: Among 2091 suspected COVID-19 cases attending fever clinic and department of Pediatrics, 462 (22.09%) were real time polymerized chain reaction (RT PCR) COVID-19 positive. Of them 377 (81.60%) responded to the questionnaire and subsequent follow up. Highest numbers of cases were found in June 2020. More than 60% of cases were within the age group of 10 to 18 years and 3.44% were infants. Male: female ratio was 1.04:1. Associated co-morbid conditions were present in 21.48% patients. Fever was the most common (72.67%) clinical feature followed by others. Incidences of severe and critical illness were more in older children. Most of the moderate cases and all of the severe and critical COVID cases were managed in the inpatient department including Pediatric intensive care unit. Among them, 100% required oxygen therapy, 72.41% needed oral or IV steroids, 8.6% and 6.9% needed intravenous immunoglobulin and biological agents (Tocilizumab) respectively. Seventeen patients (4.5%) recovered with some complications. Conclusions: Among suspected cases 22% were RT-PCR positive. Majorities were in the older age group and most of the moderate and all the severe and critical cases also belonged to older age group. Most of the cases (94.42%) recovered without complication and 4.5% recovered with some complications. Mortality was 1.06%.

Keywords: COVID 19, RT PCR, Disease Severity, Outcome

1. Introduction

Coronaviruses comprise a large family of enveloped, single-stranded, zoonotic RNA viruses belonging to the family Coronaviridae. [1] A novel coronavirus was discovered in December 2019 in Wuhan, Hubei Province, China, following a series of pneumonia cases of unknown etiology in people with a history of exposure to the Huanan seafood market. [2, 3] The World Health Organization (WHO) announced that the outbreak constituted a public health emergency of international concern and named the disease COVID-19, short for “coronavirus disease 2019”. [4] Soon after, the virus was officially named as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) by the International Committee on Taxonomy of Viruses (ICTV). [4] The World Health Organization declared the outbreak as a ‘pandemic’ on 11 March. [5] In Bangladesh first case of COVID 19 was identified on 8th March, 2020. [6] Since then the number of infected persons in Bangladesh were increasing day by day with a significant mortality rate. The number of daily new cases reached a peak in May and June...
2020 and maintained the same rate till August 2020 then was gradually declining over September and October 2020 and reached a plateau. Again in November, there was another peak though the incidence was lower than the previous one. This peak was declining over subsequent 3 months and came down to less than 5%. In March 2021, the number of new cases and the number of death again started to increase.\cite{6} Reports from different countries show that children might be immune from the worst part of it.\cite{7, 8} The clinical features, disease course and outcome in children and young adults so far appeared milder compared to older patients although the scenario are still evolving. Pediatric patients with COVID-19 mostly have family clustering or a close contact history.\cite{7, 8} The majority (>90%) of pediatric patients experienced asymptomatic, mild or moderate presentation during their disease course, and recovery occurred within 1 -2 weeks of onset.\cite{9} Two initial observational studies from Wuhan province, China, reported that infants and children infrequently experienced severe disease from COVID-19 compared with adults.\cite{10, 11} The CDC morbidity and mortality weekly report, published in April 6, 2020, reported that 1.7% of known cases of COVID-19 infection in the United States were in children. Of the 2572 pediatric cases, 15 were admitted to ICU, and 3 children died.\cite{12, 13} At the same time, children with other co-morbidities such as congenital heart, lung and airway diseases, malnutrition, malignancy etc. were more vulnerable to infection with SARS CoV2.\cite{14} Neonatal COVID 19 infection has also been reported in different countries.\cite{4} However some studies from Italy, France, UK and US identified quite good number of severe diseases in the form of Kawasaki Disease, Kawasaki Disease Shock Syndrome or other manifestations of severe inflammatory response of cytokine storm.\cite{15} In Bangladesh there are documented pediatric COVID 19 patients with low mortality rate.\cite{16} Reports of pediatric vulnerability are increasing day by day.\cite{17-21} In comparison to China and Western countries, incidence of COVID 19 in children are much more in our country, which is 3% of total affected population in case of children less than 10 years of age, and 7% in the age group of 10 to 18 year.\cite{22} To address these issues, this study was carried out to determine the socio-demographic and clinical data of pediatric COVID 19 patients as well as their clinical outcomes. The study findings may help in managing COVID 19 affected children effectively and to raise awareness among pediatricians for early diagnosis of suspicious cases.

2. Materials and Methods

It was a prospective observational study conducted in the fever clinic and the department of Pediatrics of BSMMU over a period of four months (April 2020 – July 2020). All the RT – PCR positive COVID 19 confirmed pediatric cases (1day to18 years) who attended BSMMU during the study period were taken as samples by purposive sampling method. After taking ethical clearance from the institutional review board of BSMMU, data of initial visit were collected by using a structured, predesigned and pre-tested questionnaire by face to face interview from the parents/guardians of confirmed COVID 19 pediatric cases attending the general pediatrics outdoor, fever clinic and admitted patients in the Corona Unit of BSMMU with all personal protective measures.

Collected data included necessary socio-demographic and clinical information. Socio-demographic variables included age, gender, residence, family income, maintenance of social distancing practice, maintenance of personal hygiene measures, travel history, history of contact with COVID-19 positive patients, history of BCG vaccination and number of family members affected.

Typical or atypical clinical symptoms and signs, disease duration, disease severity and presence of any co-morbidity such as bronchial asthma, cystic fibrosis, chronic kidney disease, chronic liver disease, congenital/acquired heart disease, hemoglobinopathies, rheumatological conditions, malnutrition, malignancies etc. were searched for. Clinical course of each of the admitted patients were monitored during their hospital stay. If the clinical course was complicated with pneumonia, acute respiratory failure, acute respiratory distress syndrome, multisystem inflammatory syndrome, disseminated intravascular coagulation, septic shock, acute liver/cardiac/renal injury etc., the disease was considered as severe COVID 19.\cite{23}

Admitted patients were followed up daily. For outdoor cases, after providing appropriate management during the initial visit and after discharge (in case of hospitalized patients), subsequent follow up were done during the 2nd and 8th weeks over telephone to investigate the outcome. During each follow up, disease severity and clinical outcome were looked for.

Collected data were recorded in the case record forms and analyzed. Appropriate statistical tests were applied for statistical analysis.

![Figure 1. Monthly Distribution of Study Population for the year 2020.](image-url)
Among the 462 RT PCR positive cases, 377 responded to the questionnaire and subsequent follow up. More than 60% of positive cases were in the age group of 10 to 18 years and 3.44% were infants. No neonatal case was found in the study. Male female ratio was 1.04:1. Quite a good number of patients (21.48%) had associated co-morbid conditions such as bronchial asthma, thalassemia, chronic liver disease, chronic kidney disease, malignancy, congenital heart disease and rheumatological conditions. History of contact with known COVID-19 cases were present in 84.08% cases and among them 98.7% children had household contact. No children had history of travelling abroad (Table 1).

Table 1. Demography of RT PCR for COVID 19 Positive Children (n=377).

| Age Group         | Frequency | Percentage |
|-------------------|-----------|------------|
| 1 month- 1 year   | 13        | 3.44       |
| >1 year - 5 year  | 50        | 13.26      |
| >5 year - 10 year | 87        | 23.07      |
| >10 year - 18 year| 227       | 60.21      |
| Mean age          | 10.8 years|            |

Gender
- Male: 193 (51.19)
- Female: 184 (48.80)

Presence of co-morbid conditions: 81 (21.48)
History of contact with known COVID-19 cases: 317 (84.08)
Family history of positive cases: 313 (83.02)
History of Travel: 0 (0)

Among the 377 RT PCR positive cases, 82.23% were symptomatic. Fever was the most common (72.67%) clinical feature followed by headache, anosmia, dysguesia, cough and runny nose. 17.77% patients were asymptomatic. Sore throat, nasal congestion, conjunctivitis and loose motion were also the presenting features. Breathing difficulty was found in 11.93% of cases (Table 2).

Table 2. Clinical Profile among RT PCR for COVID19 Positive Children (n=377).

| Clinical Features | Frequency | Percentage |
|-------------------|-----------|------------|
| Symptomatic       | 310       | 82.23      |
| Fever             | 274       | 72.67      |
| Anosmia           | 124       | 32.89      |
| Headache          | 122       | 32.36      |
| Cough             | 120       | 31.83      |
| Runny nose        | 119       | 31.56      |
| Dysgeusia         | 119       | 31.56      |
| Body ache         | 114       | 30.23      |
| Sore Throat       | 89        | 23.60      |
| Nasal Congestion  | 86        | 22.81      |
| Loose motion      | 51        | 13.52      |
| Conjunctivitis    | 50        | 13.26      |
| Breathing difficulty | 45    | 11.93      |
| Chest Pain        | 35        | 9.28       |
| Nausea, Vomiting  | 27        | 7.31       |
| Abdominal Pain    | 24        | 6.36       |
| Chills and Rigor  | 15        | 3.97       |
| Rash              | 15        | 3.97       |
| Asymptomatic      | 67        | 17.77      |

Personal protective measures such as use of mask, social distancing, frequent hand washing, avoidance of unnecessary roaming was not well maintained by many of the cases and their care givers (Table 3).

Table 3. Personal Hygiene among RTPCR Positive Cases (n=377).

| Variable                  | Patient |  |  |  |  |  |  |  |  |  |
|---------------------------|---------|---|---|---|---|---|---|---|---|---|
|                           | Frequency | Percentage | Frequency | Percentage | Percentage |
| Use of Mask               | Yes     | 115 | 30.50 | 196 | 51.99 |
|                           | No      | 262 | 69.49 | 181 | 48.01 |
| Social Distance           | Yes     | 287 | 76.12 | 277 | 73.47 |
|                           | No      | 90  | 23.87 | 100 | 26.52 |
| Hand Washing              | Yes     | 223 | 59.15 | 276 | 73.20 |
|                           | No      | 154 | 40.84 | 101 | 26.79 |
| Leaving Home without      | Yes     | 03  | 0.79  | 37  | 9.81  |
|                           | No      | 374 | 99.20 | 340 | 90.18 |

Incidences of severe and critical illness were more in older children. Severe cases in the 5 to 10 years age group were 36.84%, whereas 47.36% above 10 years had severe illness. Critically ill children were 2 and both were above 10 years.

Table 4. Severity of presentation in children in different age groups (n=377).

| Age group               | Mild cases (%) | Moderate cases (%) | Severe cases (%) | Critical cases (%) | P value  |
|-------------------------|----------------|--------------------|------------------|--------------------|----------|
| 1 month- 1 year         | 8 (2.68)       | 5 (8.62)           | 0                | 0                  |          |
| >1 year - 5 year        | 37 (12.41)     | 10 (17.24)         | 3 (15.78)        | 0                  |          |
| >5 year - 10 year       | 66 (22.14)     | 14 (24.13)         | 7 (36.84)        | 0                  | 0.170919 |
| >10 year - 18 year      | 187 (62.75)    | 29 (50)            | 9 (47.36)        | 2 (100)            |          |
| Total                   | 298 (100%)     | 58 (100%)          | 19 (100%)        | 2 (100%)           |          |

*Chi-square test

All children having mild illness and few cases with moderate illness (11 out of 58) were managed in the outdoor with anti-pyretic (100%), anti-histamine (38.83%), bronchodilators (15.21%) and oral steroids (7.11%). Most of the moderate cases and all of the severe and critical COVID cases were managed in the inpatient department and in pediatric ICU. Among them, 100% required oxygen therapy, 72.41% children needed oral or IV steroids, 8.6% needed
intravenous immunoglobulin and 6.9% children needed biological agents (Tocilizumab). No patient received anti-viral drugs or thrombembolic prophylaxis (Table 5).

After management, most of the patients (94.42%) improved without any complication or residual illness. Seventeen patients (4.5%) recovered with some complications such as acute disseminated encephalomyelitis, ventricular dysfunction, dilatation of major coronary vessels, severe gastro-intestinal involvement, persistent pneumonia, pneumothorax etc. (Table 5).

| Variables             | Frequency | Percentage |
|-----------------------|-----------|------------|
| Patients required admission | 58        | 15.38      |
| Oxygen therapy        | 58        | 100        |
| Steroid              | 42        | 72.41      |
| Anti-viral            | -         | -          |
| LMWH                 | -         | -          |
| Biological agents     | 4         | 6.9        |
| IVlg                  | 5         | 8.6        |
| Outdoor patients      | 309       | 81.96      |
| Anti-psyretic         | 309       | 100        |
| Antihistamine         | 120       | 38.83      |
| Bronchodilators       | 47        | 15.21      |
| Oral steroid          | 22        | 7.11       |
| Outcome               |           |            |
| Expired               | 4         | 1.06       |
| Improved              |           |            |
| Without complication  | 356       | 94.42      |
| With complication     | 17        | 4.5        |

4. Discussion

During this COVID-19 pandemic, the whole world is fighting against the invisible enemy and people are trying very hard to adopt with the new normal life. As this novel corona virus is still evolving, scientific research works are going on throughout the world to understand the disease. Though severe acute respiratory illness with fever and respiratory symptoms comprise the main clinical presentations, [24] some atypical presentations might remain undiagnosed. For this reason, understanding regional features are important. To the best of our knowledge, this prospective observational study is one of the very few initial pediatric COVID 19 reports in the country till date.

In our study, among 2091 suspected population, 22.09% became RT PCR positive for COVID 19 and met the inclusion criteria. Few similar studies have been conducted in the country in this regard. The study conducted in Dhaka medical college hospital found more than 72% RT PCR for COVID 19 positive pediatric cases among 1403 suspected population, which is far higher than our study. [25] Another study conducted in two pediatric centers in Dhaka city revealed 30.08% positivity rate among suspected pediatric population which is closer to the present study. [26] Dhaka medical college hospital study grossly differs from our study, though there was no significant socio-demographic and regional variability.

Most of the patients (60.21%) were older children (>10 years old with a mean age of 10.8 years) which is similar to the study conducted by Anwar et al. [25] where most of the patients were above 11 years. But the study conducted by Ghosh et al. [26] reported different findings and most of their cases were between 1 to 2 years. A similar retrospective study in Mainland China showed the median age as 7 years [27] which could be due to regional variation. Male: female ratio in the present study (1.04:1) which is close to the study conducted by Anwar et al. (1.53:1), [25] Ghosh et al. (1.7:1), [25] and Guo et al. (1.2:1). [27]

Eighty one children (21.48%) had different co-morbid conditions including bronchial asthma, thalassemia, chronic liver disease, chronic kidney disease, malignancies, congenital heart disease and rheumatological conditions (Table 1). The study conducted by Nallasamy et al. in Nepal found 19% patients with co-morbidities among the total study population in the form of congenital heart diseases, neuro-developmental disorders, craniofacial anomalies and nephritic syndrome. [28] Children having chronic diseases are immune-compromised and probably more vulnerable to infection including COVID 19 disease. This could be reason for the high incidence of co-morbidities with COVID 19 in different studies including the present study.

Children with COVID 19 usually acquire the disease from family members, household contacts or contacts from known surroundings. In this study, more than 84% patients had history of close contact and more than 98% of them had household contact. Ghosh et al. study reported 54.94% of patients having known home exposure to COVID 19 [26] which is much less than our study. A study from Nepal showed 74% household and 26% unknown contact [28] and the study from China showed 66% household and 28.9% endemic area contact. [27] So, it has been shown from different studies that, many children do not have known contact with a definite COVID 19 case. So avoidance of close contact with strangers should also be strongly recommended.

Pediatric COVID 19 children in this series presented predominantly with fever, anosmia, headache, cough, runny nose and others. More than 17% of patients were asymptomatic. As they had positive family history, they were tested and incidentally diagnosed. The prevalence of asymptomatic COVID 19 infection was 5.9% in the study by Guo et al. in China. [27] Different studies reported similar findings. The clinical presentation of COVID-19 in children has not yet been extensively studied. Even the available study showed contradicting findings. To mitigate this issue, a systematic review of existing literature was conducted with the hope to provide an insight into the Covid-19 disease in children. They concluded that, the clinical manifestation in children is non-specific. However, fever and cough have mostly been reported. Though the severe condition is rarely reported in children compared with adults, life-threatening complications, and death associated with COVID-19 disease have also been documented. Underlying chronic pulmonary disease, cardiovascular disease, immune-suppression, and obesity significantly contributed to the complications. [29]

Based on the clinical presentation, the COVID 19 cases were subdivided into four categories for management
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. Finally, cases of any stage presented with respiratory failure, shock, ARDS or other organ failure requiring ICU were in critical case group. [23] Incidences of severity of illness were more in older children in this study, though not statistically significant (Table 4). Children's Hospital, Colorado conducted a retrospective cohort study among positive SARS-CoV-2 PCR children. Risk factors for severe disease were analyzed and in multivariable analyses, age 0–3 months or >20 years and co-morbidities, asthma, gastrointestinal condition and diabetes were the predictors of severe disease in children. [30] In the present study more than 18 years were not included, but more than 47% of severe cases were in the age group 10 to 18 years and more than 36% were in the age group 5 to 10 years. This might reflect that chances of severe disease increase with the increasing age.

All of the mild case group and 11 patients (18.96%) from moderate case group were treated in the outpatient management with anti-pyretic, anti-histamine, bronchodilators and oral steroids (in some cases). Forty seven patients from moderate case group (81.03%) and all the patients from severe and critical case groups required hospitalization. Two critically ill children developed multi-organ dysfunction and expired in ICU. All the severe cases developed multisystem inflammatory syndrome in children (MIS-C) in the form of febrile inflammatory state, Kawasaki disease like illness, shock, heart failure, pneumonia and encephalitis. These cases were managed by oxygen therapy, high flow oxygen, mechanical ventilation, intravenous steroid such as methylprednisolone or dexamethasone, intravenous tocilizumab and intravenous immunoglobulin depending on indication and clinical response. One 14 years old girl developed refractory multisystem inflammatory syndrome. Despite of management with all possible modalities, she did not survive.

It has been observed that children having pneumonia and severe or critical illness required admission and immediate management. To prevent post discharge dissemination of infection, home isolation for 1 week was advised to all.

Out of 377 children, 4 cases (1.06%) expired. Two of them were previously diagnosed as X linked agammaglobulinemia, 1 girl was a known case of systemic lupus erythematosus and 1 girl had refractory MISC (the 14 years old girl discussed above). So, it is found that, 75% of 4 death cases had prior co-morbid conditions and were immunocompromised. There is limited information on the severity of COVID-19 infection in children with comorbidities. To investigate the effects of pediatric comorbidities on COVID-19 severity, a systematic review and meta-analysis of published literature was done. Severe COVID-19 was present in 5.1% of children with comorbidities, and in 0.2% without comorbidities. The meta-analysis revealed that children with co-morbidities had a higher risk of severe COVID-19 and associated mortality. [31]

More than 94% patients in our series improved without any complication, and seventeen patients (4.5%) recovered with complications including aneurysmal dilatation of major coronary vessels (9 patients), acute disseminated encephalomyelitis (1 patient), heart failure (1 patient) and generalized weakness and myalgia in others. Recent reports from COVID-19 affected countries showed that children are hospitalized in the intensive care unit due to a rare pediatric inflammatory multisystem syndrome. A possible association with SARS-CoV-2 infection had been postulated as many of the children tested for SARS-CoV-2 infection were either positive by PCR or serology. In total, more than 2600 children with multisystem inflammatory syndrome are reported in different countries, including 33 fatalities. [32]

In this study, an attempt was also done to investigate the degree of maintenance of the personal protective measures among the study population and their caregivers. Most of the patients did not use face masks regularly, and there was no frequent hand washing practice. Most of the children were inside home for a prolonged period of time and thus maintained social distancing. Among caregivers 48.01% did not use face masks regularly. Social distancing was also not maintained properly by 26.52% of caregivers. Rate of frequent hand washing was also low. Maintenance of personal protective measures are most important for controlling Covid-19 in all including children. To prevent infection and to slow transmission of COVID-19, World Health Organization has recommended regular washing of hands with soap and water, or cleaning with alcohol-based hand rub, maintaining at least 1 meter distance between people, avoidance of touching face, covering mouth and nose when coughing or sneezing, staying home if unwell even after complete schedule of vaccination as it is not 100% protective. [33]

5. Conclusion

This study reported very early data showing the clinical profile and outcome of Bangladeshi COVID-19 pediatric patients. Majority of COVID 19 cases in this study including most of the moderate and all the severe and critical cases belonged to older age group. More than 82% cases were symptomatic and among them fever was the commonest presentation. History of contact with known COVID 19 cases was found in 84.08% cases, among them majority was household contact. Recovery without having any complications was 94.42%. Four children with COVID 19 (1.06%) expired and all of them had pre-existing co-morbidities. Personal protective measures were not given due importance by COVID 19 patients and their caregivers.

6. Recommendation

Based on the data in this study, following recommendations can be made: Further research with large
sample size is needed including long term follow up to determine the 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

The study was done in a single center within a very short time frame on a limited number of samples.

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