

Clinical Profile and Outcome of COVID -19 in Children with Pre-Existing Renal Disease

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Abstract

Background and Aim: Despite several studies about COVID-19, many factors remain unknown. Apart from pulmonary involvement, the other systemic association needs to be explored. Since information is lacking this study was conducted to see the impact of COVID-19 infection in children with kidney diseases.

Methods: This retrospective study was carried out at Dhaka Shishu (children) Hospital and Square Hospitals Ltd from April 2020 to August 2020. All the admitted children below 18 years who had renal diseases and tested RT PCR positive for the SARS-COV-2 virus were included in the study. Data regarding patient's demography, clinical presentation, hospital course, and outcome were collected from the hospital database and were analyzed.

Results: Among the COVID-19 positive pediatric patients, the proportion of patient with a history of kidney disease were 12%. The commonest age group belongs to 6 -10 years with a female predominance. Nephrotic syndrome (50%) was the commonest primary renal etiology followed by acute kidney injury (26%). Along with COVID-19 related symptoms like fever (38%) and respiratory tract infection (31%), a good number of them remain asymptomatic (27%) during diagnosis. Hypertension (50%) and hematuria (35%) were the two prevailing clinical findings. Moreover, anemia (65%), and elevated creatinine (50%) were found surprisingly higher irrespective of the primary etiology. A better outcome was observed in children under 5 years.

Conclusion: Covid -19 is frequent in patients with a history of kidney diseases and it may present with an atypical presentation like hypertension and or hematuria. Hence, clinicians should increase their awareness and concern to deal with COVID-19 infection among renal patients.

Keywords: COVID-19; Nephrotic Syndrome; Acute Kidney Injury; Hypertension; Anemia.

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Introduction

The noble coronavirus disease is caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). It was first reported in Wuhan, Hubei province, China in December 2019 and gradually spread into all over the world (1, 2). On 11th March 2020, the World Health Organization (WHO) declared the disease as a pandemic (3). Epidemiological studies showed that the elderly and

patients with co-morbidities are becoming severely ill and ended up with poor prognosis and higher mortality rates (4). Children are less prone to develop severe disease manifestations though there are reports of multisystem inflammatory syndrome (MIS-C) and Kawasaki like manifestation. According to the earlier meta-analysis, the predominant clinical manifestations are fever and

cough followed by dyspnea, myalgia (or fatigue) in children (5). The picture is also similar in a recent meta-analysis (6). There are few reports on children with kidney diseases and one of the reports from the European Rare Kidney Disease Reference Network (ERKNET) which showed that the commonest presenting feature was fever (72%) in children with kidney diseases who were on immunosuppressive therapy (7). Bangladesh is a country of 165 million population, and the COVID-19 situation has been closely monitored by WHO from the beginning. Since the detection of the first case of COVID-19 in Bangladesh on 8th March 2020, it was found that children are less affected and have mild symptoms than an adult. According to the WHO report of WHO, a total of 312,966 cases of COVID-19 confirmed by RT-PCR assay, and among them, 4281 reported death by 31st August 2020. Pediatric patients comprise 8% of total positive cases and the mortality rate was 0.3% in the less than 10 years age group and 0.7% in older children aged 11-20 years (8, 9). Although few studies were reported COVID-19 in children from Bangladesh, there is a scarcity of studies related to this infection in children with a kidney problem.

Methods

This retrospective observational study was carried out in two hospitals in Dhaka city, Bangladesh (Dhaka Sishu Hospital and Square Hospitals Ltd), where advanced pediatric nephrology supports are available. This study includes children younger than 18 years with kidney disease, who were admitted between 1st April 2020 to 31 August 2020 into the study centers and found to be SARS-CoV-2 positive. After a child becomes test positive, they were sent to a COVID dedicated unit. Patients were followed up to 14 days for the immediate outcome either in the hospital or over the telephone after discharge. Nasopharyngeal specimens were collected by a trained physician, nurse or medical technologist which was immediately transferred to the laboratory. Viral RNA was extracted from the nasopharyngeal specimen within 24-48 hours of collection and tested for presence of SARS-CoV-2 using the – COVID 19 RT PCR Kit (S3104E; Sansure Biotech Inc, Changsha, Hunan, China). Information regarding demographics, clinical presentations, hospital course, and the outcome were collected from the departmental record book and laboratory test results were extracted from the

laboratory database. Finally, all the data were analyzed using a statistical package for social science (SPSS) version 24. Continuous variables were presented as mean (SD) and categorical variables were expressed as frequency rates and percentages.

Results

Over the outbreak of the COVID-19 pandemic, a total 7255 number of patients were admitted [7104 patients from Dhaka Shishu (Children's) Hospital and the remaining 149 from Square Hospitals Ltd] during the study period. RT PCR for COVID-19 was tested positive in 226 patients (3%). Among them, 26 (12%) children had renal diseases (Figure

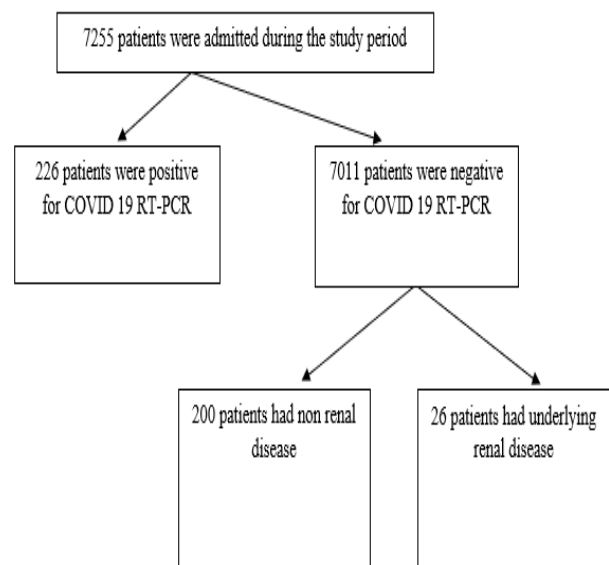


Figure 1. Flow diagram of patient admission from 1st April to 31st August in study centers

1).

In this study the mean age \pm SD of the study patients were 6.36 ± 4.4 years and most of the patients belonged from the 6-10 years age group (38%). Male Female ratio was 1:1.2.

Nephrotic syndrome (NS) was the commonest underlying renal disease found among 13 (50%). The next predominant renal etiology was acute kidney injury (AKI) in 7(27%) children. Out of the two patients had septicemia induced AKI and the other 5 patients had AKI associated with other underlying disease (Table 1). Out of 26 children, 7 (27%) of study patients did not have any COVID-19 related symptoms. Hypertension 13 (50%) and hematuria 9 (35%) were two common non-COVID

clinical manifestations found in COVID-19 positive renal patients. Among the systemic features, fever was found in 10 (38%) followed by respiratory symptoms in eight (31%) patients (Table 1).

Table1. Demographics of the study participants.

Patients Characteristics	Number (%) [n=26]
Age in years	
Less than 1 year	4 (15)
1- 5years	7 (27)
6-10years	10 (38)
11-15 years	5 (19)
Sex	
Female	14(54)
Underlying kidney disease	
Nephrotic syndrome	13(50)
Acute kidney injury(AKI)	2 (8)
AKI with pre-existing kidney disease*	5 (19)
Chronic kidney disease (CKD)	3 (12)
Congenital anomaly of kidney and urinary tract (CAKUT)	3 (12)
Rapidly Progressing Glomerulo Nephritis (RPGN)	2 (8)
Lupus nephritis	1 (4)
Haemolytic uremic Syndrome (HUS)	1 (4)
Transient Glomerulopathy	1 (4)
Clinical presentation	
Asymptomatic	7 (27)
Hypertension	13 (50)
Hematuria	9 (35)
Fever	10 (38)
Cough and cold	5 (19)
Breathing difficulty	3 (12)
Diarrhea or abdominal pain	3 (12)
Others	5 (19)

*Raised creatinine from baseline with underlying kidney disease.

Regarding hematological parameters of the study participants, mild to moderate grades of anemia was present in 17(65%) of patients with a mean± SD hemoglobin value were 9.92± 2.4g/dl. Among the biochemical parameters, hypoalbuminemia was found significantly in 21 (81%) patients and raised

creatinine was found in 13 (50%) patients. A total of 6 (23%) of the study patients had an abnormality in the chest X-ray either pneumonia or pneumonia with pleural effusion (Table-2). Besides this, it was found that 19% of patients required hospitalization for more than 2 weeks. The reason behind prolonged hospital stay was attributed to non-responsive to immunosuppressive therapy, multiple infections, and vascular access-related complications.

After COVID-19 infection, the majority of the patients 18 (69%) were able to discharge to home and unfortunately, 3 (12%) patients died and the reason behind their death was pulmonary edema with sepsis in two patients and septic shock in one patient (Table 2). The overall mortality of the children with kidney disease was 12% and they belonged to the 6- to 10year age group.

Table2. Laboratory parameter, Hospital course, and outcome of the study children.

Laboratory test	Number (%) [n=26]
Hemoglobin	9 (35)
>11g/dL	
9-11g/dL	8 (31)
<9 g/dL	9 (35)
Decreased Lymphocyte	7 (27)
Increased Lymphocyte	9 (35)
Raised C-reactive protein (> 6)	14 (54)
Raised Creatinine (mg/dl)	13 (50)
Hypoalbuminemia (< 25g/L)	21 (81)
Chest radiograph	
Pneumonia	5 (19)
Pneumonia and Pleural effusion	1 (4)
Adjunctive therapy/ intervention during hospitalization	
Oxygen inhalation	8 (31)
Vasopressor therapy	3 (12)
Renal replacement therapy	3 (12)
Hospital stay	
< 2 weeks	21(81)
>2weeks	5 (19)
Hospital outcome	
Discharge to home	19 (73)
Death	3 (12)
Remain in the hospital at the time of reporting this study	4 (15)

Discussion

In this study, among the COVID-19 affected children, 12% have kidney involvement, which is very high among the reported studies (9, 10). A similar prevalence was found in another study among adult patients in China (11). One possible explanation of this high prevalence of kidney involvement is that most of the kidney patients had chronic disease processes that create a pro-inflammatory state with functional deficits in innate and adaptive immune cell populations that have a high risk of infection (12). In the current study, there was a female predominance, whereas in other meta-analysis depicted a male predominance (9, 13, 14). However, the reason for this female predominance remains unknown. Among hospitalized children with COVID-19, the nephrotic syndrome was the most common etiology 13(50%) and among them, eight children were on immunosuppressant previously. A recent report published in Lancet showed few children who were on immunosuppressive therapy due to nephrotic syndrome and kidney transplantation were tested COVID-19 positive (7). However, the influence of immunosuppressive therapy needs to be evaluated by large multicentric studies. AKI was observed in a large number of patients (26%) in comparison to other studies. This study was done in two tertiary care hospitals where the patient may come in advance stage could explain the fact. Possible causes considered were tubular injury due to cytokine storm, a direct cytopathic effect, and immune-mediated glomerulonephritis (11).

Hypertension was a common presenting feature in our study. Among them, a third of the children had new-onset hypertension with nephrotic etiology. Other etiology of hypertension were glomerulonephritis and CKD. The reason behind new-onset hypertension may be either fluid overload or glomerular involvement during COVID-19 infection. Further studies should be elucidated to find the association. In this current study hematuria was another predominant feature of glomerular injury and present in 35% of the patient. Almost similar involvement was observed in another study done among adults with kidney disease, where hematuria was suggestive of an independent marker of poor prognosis (11).

In this present study, fever (38%) and respiratory symptoms (30%) were seen insignificant in comparison to other studies (7, 15, 16). Another

study by Bai K et al. stated 32% of children remain asymptomatic who previously were on immunosuppressive therapy, which was similar to the current study (17). However, 3 (12%) of our study children had gastrointestinal manifestation but most of them have a less severe clinical course that showed similarities with other study results (18-20).

Anemia was an important finding present in 65% of the study participants. The presence of anemia can be multifactorial such as secondary to the primary disease, due to the viral infection, although the rare possibility of nutritional anemia could not be ruled out in this study; which needs subsequent evaluation. A recent article by Tao et al. showed anemia was associated with more severe inflammatory responses, coagulation disorders, and organ injuries and associated with comorbidities and severity of COVID-19 among the adult population (21). In this study, hypoalbuminemia was present in a significant number of patients other than nephrotic etiology, which might be secondary to tubular injury in the form of acute tubular necrosis (ATN) or acute interstitial nephritis (22). This study revealed normal and elevated lymphocyte count as a common finding which was alike most of the studies in children with COVID-19 (10, 16, 23). Alteration of acute-phase reactants in our study was also similar to other pediatric studies as well as adult studies (24- 27). This study found a higher mortality rate among the kidney patients with COVID-19 infection (12%) in children, which is higher in relation to total pediatric mortality 1% until 31st August 2020 (8). The reason for higher mortality could be delayed presentation to the hospital, presence of sepsis and associated comorbidities of the patients. However, a recent study in the adult population showed kidney disease was associated with mortality among hospitalized COVID-19 patients (11). Therefore, further study should be performed to find out the poor prognostic markers among COVID-19 positive children with renal disease.

Conclusion

The incidence of COVID-19 in children with kidney disease is high. They can present with a new onset of hypertension and may have significant renal involvement. A significant number of children may be asymptomatic; hence, the careful evaluation of kidney involvement and co-morbidities are

necessary. However, further multicenter studies are needed to enrich knowledge about the spectrum of kidney involvement by COVID-19.

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Conflict of Interest

The author declares no conflicts of interest.

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Ethics

The ethic committees of Dhaka Sishu Hospital and Square Hospitals Ltd were approved this study.

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