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Long COVID Among the Children Admitted to the Department of Pediatrics in a Tertiary Care Centre

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ABSTRACT

Introduction: Long COVID is described as signs and symptoms that continue or develop after acute COVID-19. In most cases, long COVID symptoms resolve within 1-5 months. Long-term health sequels of the COVID-19 are a major public health concern. However, evidence on post-acute COVID-19 syndrome is still limited, particularly for children and adolescents.

Objectives: To investigate the prevalence, symptoms, duration and risk factors of long COVID.

Methodology: A prospective, observational, longitudinal study was done in BMCTH, a tertiary care centre. Sixty children up to the age of 14-year, diagnosed as COVID-19 by RT-PCR and antibody were included. Follow-up of children were done within 1-3 months and 3-5 months after the treatment of acute COVID-19. Symptoms and duration of symptoms were noted on follow-up after the treatment of acute COVID-19.

Results: Out of 60 children, 45 (75%) children were followed within 1-3 months and 3-5 months. Among them, 14 (31.11%) developed long-COVID symptoms. Long COVID symptoms were common in children of one year 5 (33.33%) with predominance of male 9 (36%) compared to female children 5 (25%). The long COVID symptoms were mostly respiratory and neuropsychiatric like cough 7 (50%), difficulty in breathing 5 (35.71%), fever 3 (21.43%), headache 2 (4.28%) fatigue2 (14.28%), Chest/ abdomen pain 2 (14.28%), loss of appetite 1 (7.28%). Severity of acute COVID-19 and multisystem inflammatory syndrome in children were risk factors for long COVID. The symptoms subsided mostly within 3 months.

Conclusion: Thirty-one percent hospitalized children developed long COVID; mostly respiratory and neuropsychiatric symptoms. Long COVID symptoms subsided within three months after treatment.

INTRODUCTION

Corona virus disease 2019 (COVID-19) is an acute respiratory infection caused by SARS-CoV-2. Children are affected less frequently as compared to adults. They are mostly asymptomatic (40-80%) or experience clinically mild disease. Severe COVID-19 is less common in children than in adults. COVID-19 survivors have reported ongoing persistent symptoms long after recovery from the acute phase of COVID-19. They reported a wide variety of somatic and mental health issues that were either persisting, recurring, or newly occurring beyond the four week of acute COVID-19. Clinical studies of hospitalized patients for COVID-19 have also reported that high proportions of patients continue to suffer from one or more health complaints for months after discharge.

Long COVID is described as signs and symptoms that continue or develop after acute COVID-19.6 To date, there is no clear agreement on the definition or

duration for this syndrome. According to National Institute of Health and Care Excellence (NICE) guidelines, long COVID includes both on-going symptomatic COVID-19 (from 4 to 12 weeks after acute COVId-19) and post COVID-19 syndrome (12 weeks or more after acute covid-19).6 The prevalence of long COVID symptoms ranges from 1.6 to 70%.7,8 The most common long COVID symptoms are headache, fatigue, muscle weakness, chest pain, cough, fever and depression, anxiety.9,10 The long COVID in children and adolescent involve multiple systems, including respiratory, neurological, cardiovascular systems and gastroenterology. Several factors such as demographic information, clinical characteristics, multisystem inflammatory syndrome in children (MIS-C), hospitalization and severe acute initial infection have been found to be associated with long COVID.

In most cases, long COVID symptoms resolve within 1-5 months.11 Long-term health sequels of the COVID-19 are a major public health concern. However, evidence on long COVID is still limited, particularly for children and adolescents. Still the potential range of signs, symptoms and their frequency of occurrence in children and adolescents remains unclear. There is a need to create awareness among parents, physicians, and for the health system to better understand the sequelae in order to provide targeted medical attention and treatment. The study was done to investigate the prevalence, symptoms, duration and risk factors of long COVID among children admitted to the Department of Pediatrics in a tertiary care centre.

METHODOLOGY

This observational, descriptive, longitudinal study was conducted in Birat Medical College Teaching Hospital (BMCTH), Morang, Nepal from February to July 2022. Ethical clearance was obtained from the Institutional Review Committee (Reference number: IRC-PA-192-2078-79). Sixty-three children were admitted in pediatric intensive care unit (PICU) and COVID ward. Among them 60 survived and 3 died. The survived 60 children with positive RT-PCR and antibody were included in the study. Children who lost to follow up and three-died were excluded from study and remaining 45 children were followed. Consent was taken from the parents. Pulse oximetry, arterial blood as (ABG) analysis, compete blood count (CBC), Coagulation profile, renal function test (RFT), liver function test (LFT), C-reactive protein (CRP), Chest X-ray and other investigations like serum ferritin level, pro-calcitonin, blood culture and urine examination were done for the management of the disease during hospital admission. Consecutive sampling method was used for data collection. Data were collected by using specifically designed proforma after taking written and oral consent from the parents. Demographic and medical information was collected from parents' interviews and medical records during the hospital stay. Among sixty children enrolled in the study, forty-five children came for follow up. Follow up was done within 1-3 months and 3-5 months after the treatment of acute COVID-19. Parents were contacted via phone and asked if their child had any persistent, new, or returning symptoms or health problems that may have been associated with the COVID-19. Face, Leg, Activity, Cry, Consability (FLACC) scale was used for pain assessment for less

than children of one year. Age, sex, weight, symptoms and duration of symptoms were noted at the time of follow up. Data was entered using Microsoft Excel and analyzed using IBM SPSS Statistics version 26.0. Mean, median, mode and standard deviation were used for descriptive study while chi square test for analytic study.

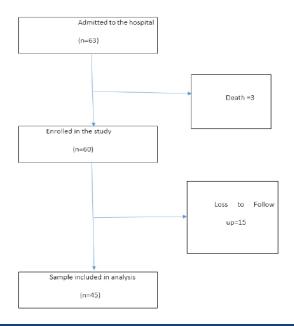


Figure 1: Flow diagram of children with COVID-19.

RESULTS

Out of 60 survived children, 45 (75%) children were followed at 1-3 and 3-5 months. Among them, 14 (31.11%) children developed long-COVID symptoms. Long COVID symptoms were common in children of less than one year 5 (35.71%) followed by children of 10-14 years 4 (28.58%), predominantly male 9 (64.28%) compared to female children 5 (35.71%) as shown in table 1. Demography of children with acute COVID-19 were shown on the table 2. Fever 37 (77.8%), cough 23 (51.1%), dyspnea 19 (42.2%) and noisy breathing 5 (11.1%) were the most common presenting symptoms at the time of hospital admission. Out of them, 27 (60%) children needed PICU admission and 18 (40%) were managed in COVID ward. Similarly, 26 (57.8%) children needed respiratory support in the form of oxygen via nasal prongs, face mask, non-rebreathing mask (NRM), heated humidified high flow nasal cannula (HFNAC) and mechanical ventilator (MV). The average length of hospital stay (LOS) was 5.2 days (median; 4 days). Similarly, 4 (8.9%) children had developed multisystem inflammatory syndrome (MIS-C). [Table 2] The long covid-19 symptoms were cough 7 (50%), difficulty in breathing 5 (35.71%), fever 3 (21.43%), headache 2 (14.28%), fatigue 2 (14.28%), Chest/abdomen pain 2 (14.28%), loss of appetite 1 (7.28) as shown in Table 1. Severity of acute COVID-19 and multisystem Inflammatory syndrome in children (MIS-C) were risk factor for long COVID while age, sex, admission pattern and need of respiratory supports were not associated with long covid as shown in table 3. The symptoms had subsided mostly within 3 months and in some cases, it took 5 months to resolve. The health status of children who lost to follow up was

unknown.

Table 1: Demography and symptoms of long COVID (N= 14)

Characteristics	n (%)
Age <1year 1-5 year 5-10 year 10-14 year	5(33.3) 3(30) 2(25) 4(33.3)
Sex Male Female	9(36) 5(25)
Symptoms of Long COVID Cough Difficulty in breathing Fever Headache Fatigue Pain abdomen/Chest Convulsion Anxiety Suicidal attempt Loss of taste/appetite	7(50.00) 5(35.71) 3(21.43) 2(14.28) 2(14.28) 2(14.28) 1(7.14) 2(14.28) 2(14.28) 2(14.28)

Table 2: Demography of children with acute COVID-19 (n=45)

Characteristics	n (%)
Age <1 year 1-5 year 5-10 year 10-14year	15(33.33) 10(22.2) 8 (17.8) 12(26.7)
Sex Male Female	25(55.6) 20(44.4)
System Involved Respiratory Gastrointestinal Neuromuscular	29(64.4) 20(44.4) 9(20)
Symptoms Fever Cough Shortness of Breath Noisy Breathing Seizure Throat Pain Others	35(77.8) 23 (51.1) 19 (42.2) 5(11.1) 4(8.9) 2(4.4) 18(40)
Severity Mild Moderate Severe to Critical	9(20) 24(53.3) 12(26.7)
Admission Pattern PICU Covid Ward	27(60) 18(40)
Length of hospital Stay	5.2days(Median=4 days)
MIS-C	4(8.9)
Respiratory support Needed Not needed	26(57.8) 19(42.2)

Table 3: Risk factor for long COVID (n=45)

Characteristics	Long COVID	No Long COVID	Total	Chi square test
Sex Male Female	9	16 16	25 20	0.239
Age <1 year 1-5 year 5-10 year 10-14 year	5 3 2 4	10 7 6 8	15 10 8 12	0.901
Severity Mild Moderate Severe	0 8 5	9 16 7	9 24 2	0.027*
MIS-C Yes No	3 11	1 30	4 41	0.047*
Respiratory support Needed Not needed	8 5	18 14	26 19	0.745
Admission Pattern PICU Ward	7 7	20 11	27 18	0.357

^{*} Significant at p<0.05

DISCUSSION

Long-term health sequels of the COVID-19 are a major public health concern. However, evidence on long COVID is still limited, particularly for children and adolescents. The potential range of signs, symptoms and their frequency of occurrence in children and adolescents remains unclear.

In our study, 14 (31.1%) children developed long COVID symptoms out of 45 children which is more than the similar cohort study by Osmanov IM, Spiridonova E, Bobkova P, et al. who reported 24.7% (128) of hospitalized children developed at least one persistent symptom. ¹² The meta-analysis also reported the prevalence of long COVID was 25.24% and 26.8%. ^{13,14} The recent systematic review showed the prevalence of long COVID symptoms ranges from 1.6 to 70%. ⁷ This finding in our study should be due to hospitalized children and low sample size.

The long COVID symptoms in hospitalized children were cough 7 (50%), difficulty in breathing 5 (35.7%), fever 3 (21.4%), headache 2 (14.28%) fatigue/ weakness 2 (14.28%), Chest/ abdomen pain 2 (14.28%), loss of appetite 1 (7.28). Luise Borch et al reported in a nationwide cohort study that the most common long COVID symptoms were fatigue, loss of smell and loss of test, dizziness, muscle weakness, chest pain and respiratory problems. This variation is due small sample size, follow up for short duration and all children were hospitalized in our study. The systemic review and meta-analysis reported that the most common long COVID symptoms are headache, fatigue, concentration difficulties sleep disturbance, abdominal pain and myalgia or arthralgia, chest tightness or pain and dyspnea. 14,15

Neuropsychiatry symptoms were headache 2 (14.28%), fatigue 2 (14.28%), and loss of appetite 1 (7.28). Anxiety/depression 2 (14.28%) and suicidal attempt 2 (14.28%), convulsion 1 (7.1%). One child was admitted with severe depression and two attempted suicide which may be a direct affect or social impact of COVID-19. Stephenson et al. in the Children and young people with long COVID (Clock) study reported that the common neuropsychiatric symptoms were tiredness, headache, shortness of breath, dizziness and anosmia.16 Cohort study conducted by Roge et al. at the Children's Clinical University Hospital in Latvia showed 70% of patients complained of at least one persistent symptom and 53% of multiple persistent symptoms. The persistent symptoms were fatigue (25.2%), irritability (24.3%), mood changes (23.3%), headaches (16.9%), rhinorrhea (16.1%), coughing (14.4%), anosmia/dysgeusia (12.3%).8 Systematic reviews by Natarajan et al showed that prevalence of neuropsychiatric symptoms was 21.26% while 27.77% and 22.44% were prevalence of anxiety and depression respectively.17

In this study, severity of acute COVID-19 and multisystem inflammatory syndrome in children (MIS-C) were risk factor for long COVID while age, sex, admission pattern and need of respiratory support were not associated with long COVID. The meta-analysis by Zheng YB, Zeng N, Yuan K et al. showed cases with multisystem inflammatory syndrome and more severe symptoms at initial infection had higher burden of long COVID.¹³ Funk AL, Kuppermann N, Florin TA et al also reported in cohort study that four or more acute symptoms were risk factor of long COVID.¹⁸

In our study, the long COVID symptoms in hospitalized children subsided mostly within 3 months and in some cases, it took 5 months to resolve. This is similar with the majority of the studies. Long COVID symptoms did not persist longer than 12 weeks. ^{19,20,21} School-aged children who experienced prolonged illness, mostly recovered by day 56. ²⁰ Similarly, the duration of post-viral cough and fatigue ranged from 3-8 weeks and 6-8 weeks from the time of symptom onset respectively. ²¹ Luise Borch et al in nationwide cohort study also reported long COVID symptoms resolved within 1-5 months in most cases. ¹¹

CONCLUSION

Almost one-third hospitalized children (31.1%) developed long COVID. Respiratory and neuropsychiatric symptoms were common. Severity of acute COVID-19 and Multisystem inflammatory syndrome in children (MIS-C) were risk factor for long COVID in our study. Long COVID symptoms mostly subsided within 3 months after treatment.

RECOMMENDATION

Follow up of the children after acute COVID should be done mandatory as significant number of children developed long COVID. Awareness regarding long COVID to the public and health workers. Policy should be made by health system of Nepal to provide targeted medical attention and treatment.

LIMITATIONS OF THE STUDY

Our study has some limitations. The sample size of the study is small and it is done in single centre. There was a bias during data collection due to telephone interview with parents during COVID pandemic as people were unable to attain hospital for follow up because of lock down in Nepal.

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