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Clinicolaboratory Profile and Treatment Outcome Within Ninety Days After Discharge During Second Wave of Pediatric COVID-19

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ABSTRACT

Background: The second wave of COVID-19 pandemic hit all age groups with different presentations and outcomes. This study aimed to explore the clinical characteristics, investigational findings, hospital outcomes along with a ninety days telephonic follow-up of COVID-19 infection in children.

Methods: A longitudinal descriptive study among COVID-19 RT-PCR positive hospital-admitted children was conducted during the second wave of the pandemic from 15 Mar 2021 to 15 Oct 2021 at Kanti Children's Hospital. Demographics, clinical characteristics, oxygen saturation, comorbidities, need of oxygen, need of ventilator, laboratory investigations, admission to intensive care unit, duration of hospital stay and patient's outcome (improved and discharged or death) were recorded. A follow up at ninety days from discharge was also done via telephonic call to inquire for any illness and hospital admission.

Results: Among the 156 admitted children, males and females were 54.5% and 45.5% with a median age of 15 months and Inter quartile range (IQR) of 63. Thirty-six (23.1%) were underweight and 31 (19.9%) had comorbidities. The most common presenting symptoms were fever 115 (73.7%), cough 50 (32.1%) and vomiting 38 (24.4%). The median (IQR) length of hospital stay was 15 (range of 11–20) days. Oxygen use was seen among 35 (22.4%) cases and 36 (23.1%) cases were admitted to the ICU. Ventilator was required for 7 (4.5%) cases. The number of deaths was 9 (5.8%) during hospital stay. After discharge from the hospital during the ninety days follow-up, 117 children had no health problems while 42 reported having some health problems and 5 died after discharge.

Conclusions: In the second wave of the pandemic, only symptomatic children were admitted. Respiratory and gastrointestinal symptoms were common among the admitted cases. The majority of admitted cases had a good outcome and had no other health problems attributable to COVID-19 till ninety days of follow-up.

Keywords: Pediatric COVID-19; RT-PCR; SARS-CoV-2; second wave

INTRODUCTION

Severe acute respiratory syndrome-coronavirus-2 (SARS-CoV-2) causing coronavirus disease (COVID-19) has spread globally, posing immense challenges to every country's healthcare system. Epidemiologic studies have consistently demonstrated that children are at lower risk of developing severe symptoms or critical illness compared to adults.[1, 2] Globally, children are less frequently affected by the disease. As per WHO- China joint mission report, children <18 years of age accounted for only 2.4% of 55,924 laboratory confirmed cases of COVID-19 till February 2020 in China, most of whom were household contacts of COVID-19 positive cases.[3] The clinical presentation and outcomes of patients with COVID-19 have been variable in different countries.[4, 5]

The presentation and outcome were different in the second wave as compared to the first wave. There is insufficient pediatric data related to clinical presentations and outcomes from our part of the world. The aim of our study was to find out the presenting clinic-laboratory characteristics, hospital course and outcomes in a cohort of 156 children admitted with COVID-19 infection during the second wave of COVID-19 in a tertiary care pediatric hospital in Kathmandu, Nepal

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with a telephonic follow-up ninety days after discharge.

METHODS

This retrospective chart review with prospective follow up study was undertaken at a tertiary care pediatric government hospital in Nepal. The study was conducted during the second wave of SARS-CoV-2 outbreak from 15 Mar 2021 to 15 Jul 2021, with follow-up until 15 Oct 2021 after taking ethical approval from the Institutional Ethics Committee of Kanti Children's Hospital.

There was a dedicated 25 bedded COVID ward established for screening and triaging of patients with suspected COVID-19 illness as well as a general ward having facilities of monitoring oxygen saturation, IV fluids and oxygen facemask. An intermediate ward with monitor, CPAP, infusion sets and Pediatric Intensive Care Unit (PICU) with mechanical ventilators and other facilities was also available. These wards were managed round the clock by nurses, medical doctors and consultant pediatricians. The criteria for admission of suspected COVID-19 illness included any of the following: respiratory distress, SpO_2 on room air < 94%, shock/poor peripheral perfusion, poor oral intake or lethargy, presence of seizures or encephalopathy. Furthermore, the presence of comorbidities and/or age < 1 year in COVID-suspected children were other indications for admission. The RT-PCR sample for novel COVID-19 virus was sent on admission in accordance with WHO guidelines.[6] Patients admitted to non-COVID wards of the hospital who developed suspicious symptoms, patients who came from containment zones/hotspots or with a history of contact with COVID-19 cases (which was previously undisclosed during time of admission) were also screened. The confirmed cases were classified as mild, moderate, severe and critical as per the published guidelines.[1] Severe and critical cases requiring intensive monitoring, ventilation and organ support therapy were managed in the HDU/ICU of COVID ward. The mild and moderate cases were admitted in general/ intermediate ward and patients who improved after intensive care were stepped down to general/intermediate wards. The patients were subjected to investigations including complete blood count, serum biochemistry (liver and kidney function test, electrolytes), and chest radiograph as per need. All the patients were managed as per the hospital protocol made for management of COVID-19.[6]

Children who were below 14 years of age and tested positive RT-PCR test for novel COVID-19 virus were included in the study. The case record files of COVID-19 positive patients admitted in COVID wards were reviewed. Variables like demographic data, clinical signs and symptoms at presentation, laboratory and radiologic results, and severity of disease, comorbidities if any present, treatment given in hospital, and outcomes on all COVID-19 positive patients admitted to the hospital during the study period were collected in an Excel sheet. Ninety days follow-up call was made for discharged children and the health problems they had if any were recorded by medical doctors.

Discharged from hospital and mortality in hospital and mortality within ninety days of discharge were the primary outcomes. The duration of hospital stay, need of PICU care, need of oxygen support and need of ventilatory support were other variables of interest to be observed.

Data was entered in the Excel sheet. Clinical data were presented as counts and percentage, mean and SD, and median and IQR. Comparison of means and median was performed using the 2-sample Student t test or Wilcoxon rank-sum test, respectively. Categorical data were compared using Pearson c2 or Fisher exact test if any expected cell size numbered <5. All tests were 2-tailed with a level of significance of P <0.05.

RESULTS

A total of 156 children were included in our study. In our study, we found that children of all ethnic groups had COVID-19. There was male predominance in the number of admitted cases with males 54.5% and females 45.5%. The mean and median age of admitted children was 42.65 months and 15 months respectively with Inter quartile range (IQR) of 63. Among the admitted children, 36 (23.1%) were found to be underweight and 31 (19.9%) had comorbidities. The mean duration of hospital stay was 15 days where 74 (47.4%) of the children stayed less than 5 days while 82 (52.6%) of children stayed more than 5 days in hospital.

The results are shown in Table 1.

Table 1. Epidemiological and Clinical Profile of the children with COVID-19 infection (n=156).

	Variables	Frequency	percent
Ethnicity	Janajati	65	41.7
	Brahmin/ Chhetri	57	36.5
	Madhesi	22	14.1
	Dalit	12	7.7
Religion	Hindu	128	82.1
	Buddhist	22	14.1
	Christianity	2	1.3
	Muslim	1	.6
	Not mentioned	3	1.9

Gender	Male	85	54.5
	Female	71	45.5
Age	Less than 1 month	16	10.3
	1-24 months	78	50.0
	25-59 months	23	14.7
	5-14 years	39	25.0
Age mean/ Median age	42.65 months/ 15 months (IQR 63)		
Comorbid condition	No	125	80.1
	Yes	31	19.9
Nutritional status	Normal	120	76.9
	Underweight	36	23.1
Length Hospital stay	Up to 5 days	74	47.4
	More than 5 days	82	52.6

The most common presenting symptoms were fever 115 (73.7%), cough 50 (32.1%) and vomiting 38 (24.4%) followed by other symptoms seen in lesser percentages. At presentation, 24 (15.4%) had SpO_2 less than 90% in room air requiring SpO_2 monitoring. The most common system involved was respiratory system 66 (42.3%) followed by central nervous system (CNS) 20 (12.8%) and surgical cases 10 (6.4%). The results are shown in Table 2.

Table 2. Presenting symptoms and Clinical Findings in Children with COVID-19 (n=156).

Presenting symptoms	Fever	115	73.7
	Cough	50	32.1
	Vomiting	38	24.4
	Pain abdomen	22	14.1
	Abnormal body movement	20	12.8
	Noisy breathing	16	10.3
	Fast breathing	16	10.3
	Diarrhea	15	9.6
	Decreased feed	14	9.0
	Oedema	11	7.1
	SOB	11	7.1
	Lethargy	9	5.8
	Irritability	6	3.8
	Rash on the body	5	3.2
	Headache	2	1.3
Clinical findings			
SpO_2	More than 94%	116	74.4
	91 to 94 %	12	7.7
	Less than 90%	24	15.4
	Not mentioned	4	2.6
Systemic diagnosis	Respiratory	66	42.3
	CNS	20	12.8
	Surgical	10	6.4
	Gastrointestinal	6	3.8
	Renal	4	2.6

The laboratory findings showed that 67 (42.9%) had abnormal CBC range and 42 (26.9%) had lower haemoglobin levels. There were 17 (10.9%) COVID-19 positive children with raised ESR and 95 (60.9%) children with positive CRP. The Serum Urea was abnormal in 5 (3.25) while 9 (5.8%) had abnormal sodium and 7 (4.4%) had abnormal potassium. This is shown in Table 3.

Table 3. Laboratory Investigations of Children with COVID-19 Infection (n=156).

Variables		Frequency	Percent
Complete blood count	WBC less than 4000	32	20.5
	WBC 4000 to 11000	86	55.1
	WBC greater than 11000	35	22.4
	Not mentioned	3	1.9
Hemoglobin	Less than 10	42	26.9
	Greater than 10	111	71.2
	Not mentioned	3	1.9
CRP	Positive	95	60.9
	Negative	48	30.8
	Not mentioned	13	8.3
ESR	Less than 20	19	12.2
	More than 20	17	10.9
	Not mentioned	120	76.9
Sodium	Normal	142	91.0
	Abnormal	9	5.8
	Not mentioned	5	3.2
Potassium	Normal	144	92.3
	Abnormal	7	4.4
	Not mentioned	5	3.2
Urea	Normal	146	93.6
	Abnormal	5	3.2
	Not mentioned	5	3.2
Creatinine	Normal	151	96.8
	Abnormal	0	0
	Not mentioned	5	3.2

There were 31 (19.8%) children who had comorbidities during presentation. Most of the COVID-19 infected children had CNS related comorbidities n=10 (6.4%) followed by cardiac n=6 (3.8%). In this study, we found that oxygen use was seen among 35 (22.4%) cases and 36 (23.1%) cases were admitted to the ICU. Ventilator was used for 7 (4.5%) cases. One hundred thirty-five cases (86.5%) were discharged while 12 (7.7%) left against medical advice and 9 (5.8%) cases expired. This is shown in Table 4.

Table 4. Comorbidities, Management and Outcome of Children with COVID-19 (n=156).

	Variables	Frequency	Percent
Comorbidities	CNS	10	6.4
	Cardiac	6	3.8
	Oncology	6	3.8
	Renal	3	1.9
	Skeletal deformity	1	0.6
	Surgical	1	0.6
	Others	4	2.5
	No comorbidity	125	80.2
Use of oxygen	Yes	35	22.4
	No	121	77.6
Admission in ICU	Yes	36	23.1
	No	120	76.9
Use of ventilator	Yes	7	4.5
	No	149	95.5
Outcome	Discharged	135	86.5
	Leave against Medical advice	12	7.7
	Mortality during Hospital Stay	9	5.8

The ninety days follow-up was done for 147 children (excluding 9 in-hospital mortality cases) among which 30 (20.2%) children reported having some health problem, 8 (5.4%) were readmitted and 5 (3.2%) had mortality within ninety days of discharge.

Table 5. Ninety days Follow-up of Children with COVID-19 Infection (n=147).

	Variables	Frequency	Percent
Ninety days follow-up	No health problem	117	79.6
	Symptoms only	17	11.6
	Readmission	8	5.4
	Mortality within 90 days	5	3.2

DISCUSSION

This study aims to highlight the clinical characteristics and outcomes at the time of discharge of COVID-19 infected children along with a telephonic follow-up ninety days after discharge. We at Kanti Children's Hospital enrolled 156 children affected by COVID-19 during the second wave of the pandemic. Only hospital admitted children were enrolled in this study so the data likely represents individuals from the moderate to severe end of the disease spectrum.

There were more children affected in the second wave of the pandemic as compared to the first wave. The second wave started from March 15 2021 to July 15 2021 in Nepal. The number of COVID-19 admissions at the hospital during the second wave was 156 which was also higher than the number of admissions in a similar study conducted during the first wave (Jun 2020 to Jan 2021).[11] However, the admission criteria was different for the first and second waves. During the first wave, all COVID-19 PCR positive children were admitted but during the second wave, only COVID-19 PCR positive children requiring hospital admission were admitted while mild cases not requiring hospitalization were kept at home or in institutional isolation. There is scarcity of publications from Nepal in relation to COVID-19 in the pediatric population. But there are a few studies from India and other neighboring countries. [7-10]

Children from all ethnicities and religions were affected by the second wave and were admitted to our hospital. Most of the admitted children were of normal weight as compared to underweight (76.9% vs. 23.1%) which is fairly the same as the prevalence of under nutrition in the community of our country.

Our study showed a male predominance compared to female (54.5% vs. 45.5%) which is contradictory to the other study of neighboring countries which found almost equal male and female distribution in first wave.[4, 13-15] However, we had reported outnumbered male compared to female (67% vs. 32%) during first wave.[11]

The mean age of hospitalized children was 42.65 months and the median age of hospitalized pediatric population was 15 months with Inter quartile range (IQR) of 63. The age range is different in different studies. During the first wave, the value was 6 years (median age) in a study conducted in Pune Maharashtra, India (N=50) by Sarangi et al and 7 years (median age) in another study by Dong et al conducted in China.[1,7] Another study showed the median age of 3 years.[9] This difference might be due to the difference in inclusion criteria and the number of children in other studies. A multicentric Italian study observed that COVID-19 infection was increased in early age groups where 39.3% cases were <1year and 78.8% of their hospitalized COVID-19 pediatric cases were infants <1 year as of Apr 2020.[12]

Nutritional status is an important factor for causing disease as well as recovery. However, only 23.1% of admitted children were underweight. There were 21.7% of normal weight children who got admitted in PICU while 27.8% were underweight children who got admitted in PICU. The result is not statistically significant (p=0.445).

The incidence of common symptoms due to COVID-19 was lower compared to adults. Among them, 59.9% (80% in adults) had fever; 55.9% (84% in adults) had cough; 20% (38.4% in adults) had runny nose.[17] We observed that majority of children had fever 73.7% along with respiratory symptoms (cough 32.1%, noisy breathing 10.3%), followed by gastrointestinal symptoms (vomiting 24.4%, pain abdomen 12.8% and diarrhea 9.6%). These findings were similar to the study done by Karthi Nallasamy et al in India and Madani et al in Iran and other observational studies across the world have reported similar frequencies of symptoms.[7,15,18] A systematic review of 27 studies showed fever to be present in half (41%–58%) followed by cough (39%–51%) and rapid breathing (6%–17%). Gastrointestinal symptoms, particularly diarrhea were noted in 6%–13% children.[16] Other symptoms included abnormal body movements, decreased feeding, oedema, lethargy, irritability, rash and headache. We observed that almost 75 (74.4%) children had oxygen saturation of more than 94% whereas 24 (15.4%) children had oxygen saturation of less than 90% at time of hospital presentation.

Regarding investigations, we observed that baseline investigations were not uniformly sent to all cases and tests were performed only as per indication. During first wave, most asymptomatic cases had not undergone investigations. Similar strategy was undertaken by other centers in India during the first wave of pandemic.[16] Around 20.6% (n=32) admitted children had leukopenia and 22.4% (n=35) had leukocytosis. Sixty nine percent (n=95) had CRP positive.

Thirty-one (19.0%) of the admitted cases had comorbidities. The commonest comorbidities were related to central nervous system (6.4%), cardiac system (3.8%) and malignancy . This is similar to the study conducted by P Singh et al in India where Tuberculosis and hematological malignancy were the most commonly observed finding.[10] This was different from the study reported by Bose SS et al in India where malignancy was the most common comorbidity followed by renal comorbidities. Congenital heart disease and central nervous system disease were also observed.[19] Harman et al found that 41% COVID-19 positive children admitted in between 25 Feb 2020 and 28 April 2020 mostly had cerebral palsy, prematurity with a single case of Wilson's disease and dilated cardiomyopathy.[20] Another multicentric study done in North America observed that 50% of cases admitted at different PICUs of the city had comorbidities.[21]

Thirty-five (22%) admitted cases required supplemental oxygen and 36 (23.1%) cases required PICU admission but only 7 (4.7%) required ventilator support. The percentages of PICU admission varied from place to place like 20% in northern India (Karthi) and 13% Pune.[19] Existing studies show that approximately 5% infected SARS-CoV-2 children can become critically ill.[22]

The average duration of hospital admission was 15 days (1 to 40 days) where 74 (47.4%) of the children stayed less than 5 days while 82 (52.6%) of children stayed more than 5 days in hospital. In an Indian study, the median length of hospital stay was 15 [11-20] days[16] and ours was eight days with a range of 1 to 44 days in first wave.[11] The hospital stay criteria in first wave was not as strict as in the second wave. During the first wave, admitted children were initially discharged after a negative RT-PCR test but later, with a change in hospital policy, children were discharged after getting medically better irrespective of the RT-PCR result. During the second wave as well, the hospital policy was to discharge the children were discharged after getting medically better irrespective of the RT-PCR result.

The mean hospital stay was longer for children requiring oxygen support. The hospital stay for children who required oxygen was 10.14±9.06 days while it was 7.96±7.023 days for those who did not require oxygen. Although it is statistically not significant (p=0.132) it is clinically shown that oxygen dependent children have a longer hospital stay. Nine percent of children who did not require oxygen got admitted in PICU while 71% of children who required oxygen got admitted in PICU which is statistically significant (p<0.001).

One hundred thirty-five cases (86.5%) were discharged while 12 (7.7%) left against medical advice and 9 (5.8%) cases expired. The mortality rate is different in different set ups. The mortality rate in a study of 191 PCR positive hospitalized Latin American children was 8.9% which is similar to ours.[23] Singh P et al in India reports higher mortality rate than ours.[10] The number is similar to the mortality rate during the first wave in our set up.[11] The possible reasons for this difference in observation are referral bias and admissions of the most critically ill children, higher transportation time due to limited means during lockdown, comorbidities, malnutrition, unproven source of infections as well as the set up present in the hospital.

There was a mortality of 6.7% for normal weight children and 16.7% mortality for underweight children which is clinically significant but statistically not significant (p=0.06). There was 4% mortality among the children who didn't require oxygen and 25.7% in children who required oxygen which was clinically and statistically

significant (p<0.001). Likewise, there was 3.3% mortality among the non PICU admitted cases while 27.8% had mortality which is statistically significant (p<0.001).

We performed a telephonic phone call ninety days after discharge from the hospital. Among them, 117 had no health related problems while 42 reported having some health related problem within ninety days of discharge. Eight cases were readmitted and 5 died after discharge within ninety days. Among the death cases, 4 were discharged from hospital after fulfilling the discharge criteria and 1 patient left the hospital against medical advice. Likewise, 4 among the 5 reported deaths were found to have comorbid conditions. This shows the gravity of care required in COVID-19 infection even after discharge.

This study had some limitations as it was conducted only at a single center. Also, as this was a retrospective chart review with telephone follow-up, some essential points might have been missed.

CONCLUSIONS

In the second wave of the pandemic, the hospital admission was increased and only symptomatic children got admitted. Respiratory and gastrointestinal symptoms were more common among the presenting symptoms. Severe and critical illnesses were few. Majority of the cases had a good outcome and had no other health problems attributable to COVID-19 till ninety days follow-up.

CONFLICTS OF INTEREST

The authors declare no conflicts of interest.

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