



A STUDY OF CLINICAL PROFILE OF PEDIATRIC COVID 19 PATIENTS IN A GOVERNMENT TERTIARY CARE HOSPITAL IN INDIA

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ABSTRACT

BACKGROUND AND OBJECTIVES: After two stormy waves in adults, epidemiologists are predicting third wave to be more severe in vulnerable pediatric population which is yet to be vaccinated. Therefore, to address this issue we aim to present clinical characteristics and outcome of children with COVID-19 infection admitted to a government tertiary care hospital during first and second COVID-19 pandemic wave which can help in planning clinical services to manage these children in face of escalating pandemic.

METHOD: This was a cross-sectional observational study of 94 children admitted with COVID-19 infection between April 2020 and March 2021 who were tested positive by RTPCR or Rapid antigen test for COVID-19.

RESULTS: In the study population of 94 children, the Median age was 4 years with Age group ranging from 3 days -12 years consisting of 28.7% infants. 53.2% were males and 81.9% had history of exposure in family. Out of total admissions, 25(26.6%) were asymptomatic, 48 (51.1%) had mild symptoms, 7.4% had moderate illness and 14.9% were severely ill. Fever (54.3%), cough 26.6%, and cold 21.3% were the most common presenting complaints. 22(23.4%) had co morbidities with SAM being most common. Amongst the inflammatory markers, it was noticed that, 27(28.7%) had raised CRP levels, 36(38.3%) had raised d dimer levels, 69(73.4%) had raised ferritin levels and 28(29.8%) had raised LDH levels. 9 patients required non-invasive support and 11 needed invasive oxygen support. Out of total 94 patients, 10(10.6%) did not survive.

CONCLUSIONS- Most children acquired infection through household contacts. Although lower incidence than adults, children too have severe COVID-19 infections. The presence of a comorbid illness in pediatric patients with COVID-19 did not impact the severity in our study.

KEYWORDS : COVID-19, outcome, pediatric, SAM

INTRODUCTION

The new coronavirus, a single-stranded, zoonotic RNA virus was initially named 2019-nCoV but was later renamed as Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2).^[1] WHO declared COVID-19 caused by SARS CoV-2 as a public health emergency of international concern on 30th January 2020 and subsequently declared it to be a Pandemic on 11th March 2020.^[2,3]

Coronavirus disease 2019 (COVID-19) caused by SARS-CoV-2 has spread around the world, and reports of children with COVID-19 are increasing. The major reasons for the huge impact of COVID-19 are lack of preparedness for exceptional and unforeseen spread, intrinsic virulence of the pathogen and its contagiousness, asymptomatic carriers, lack of immunity and effective vaccination, and unavailability of proven and effective antiviral drugs.

Multiple reports have demonstrated that children and young adults have a milder form of the disease compared to adults.^[4] Asymptomatic, mild and moderate infections comprise over 90% of all children who are tested positive for COVID-19 with fewer severe and critical cases (5.9%) compared to adults (18.5%).^[4] Moreover, there is limited literature on the spectrum of pediatric comorbidities and their outcome in association with SARS-CoV-2 infection from our country, which tends to be entirely different from those observed in the children from developed countries.^[5]

In India, there were 1,17,34,058 cases of COVID-19 infections, and 1,60,441 patients succumbed to death till 24th march 2021. In Maharashtra, 25, 33,026 cases were diagnosed while 53,589 patients (2.12%) had died. Out of total cases in the state, 81,188 cases (3.22%) were in age 0-10 years, (6.63%) cases in age 11-20 years.^[6] Since symptomatology, severity and outcome of COVID-19 have been variable in different countries local data on epidemiology, clinical presentation, investigations, treatment modes and outcomes will be helpful to plan clinical services including screening, testing, isolation and intensive care facilities to manage these children in face of escalating pandemic.

At present, it is uncertain how long the pandemic may continue and what would be its long-term effects. After two stormy waves in adults, epidemiologists are predicting third wave to be more severe in vulnerable pediatric population which is yet to be vaccinated. Therefore, to address this issue, authors aimed to present the clinical, demographic profile, risk factors, associated co-morbidities, course of illness, complications and outcome of children with COVID-19 infections admitted to their tertiary care government hospital during first two waves of pandemic.

MATERIALS AND METHODS:

Study population and settings- This is a prospective cross-sectional observational study conducted in children aged 0-12 years at a dedicated COVID-19 tertiary care referral government hospital, in Central Maharashtra with a definitive diagnosis of COVID-19 infection confirmed either by Rapid Antigen Test-(RAT) or Real Time Reverse Transcriptase Polymerase Chain Reaction (RT-PCR) assay for SARS-CoV-2 on throat or/and nasopharyngeal swab between April 2020 till March 2021. As our Centre was a designated referral Centre for adults and children, patients >12 years of age and suspected cases of COVID-19 infection without positive RT-PCR were excluded. Institutional ethics committee approval was taken before starting this study.

A written informed consent was taken in person from parents of admitted children by the treating team. Data was collected by the doctors attending pediatric patients and from the prerecorded case forms. Information regarding Age, sex, pre-existing co-morbidity (Heart Disease, Developmental Delay, Diabetes, Immunocompromised State, Obesity, Haemolytic Anaemia, Aplastic Anaemia, Nephrotic Syndrome, Severe Acute Malnutrition), mode of presentation, sociodemographic profile, setting of exposure, vital parameters at admission, laboratory investigations, treatment given, clinical course and outcome was collected.

Case definitions and classification: A standard protocol which included case definitions for categorization of SARS-CoV-2 infection, detailed management plan, baseline and follow up investigations and

treatment according to clinical severity was devised by a group of experts of tertiary care center. This consensus treatment algorithm was developed after reviewing the guidelines of various international societies and Revised National Clinical Management guidelines for COVID-19 by the MoHFW, Government of India, dated March 31, 2020.¹⁷

Symptomatic patients were categorized to have mild, moderate or severe disease. Patients with uncomplicated upper respiratory tract infection or non-specific symptoms such as fever, cough, sore throat, nasal congestion, malaise and headache were classified to have Mild disease. Patients with radiologically proven pneumonia but without the signs of severe pneumonia were categorized as Moderate disease. Severe pneumonia included patient with fever, along with one of the following, tachypnea (RR ≥60 in age less than 2 months, RR ≥50 in age 2-12 months, RR ≥40 in age 1-5 years) severe respiratory distress and SpO₂ <90% on room air. Standard criteria for defining, ARDS and MODS were used.^{18,91} Critically ill patients included those who had severe pneumonia, shock and organ dysfunction syndrome at admission or during hospital stay.

The ICMR guidelines were followed to discharge the patients from the hospital. Initially, till May 8, 2020, all the admitted patients were discharged only after two consecutive nasopharyngeal swabs (done after 14th day of stay) tested negative on RT-PCR. After May 8, 2020, with a change in the national guidelines, asymptomatic and mild patients were discharged after 10 days of symptom onset and being afebrile for three consecutive days. The discharge guidelines for severe pneumonia were also revised and mandated oxygen-free period of three days and a negative RT-PCR result as against the two samples previously.^{10a,11}

Statistical Analysis:

Data was analyzed using SPSS version 24.0th. Normality of data was assessed by Shapiro-Wilk test for quantitative variable and for some parameters data was found to be not normally distributed. So, for this non-normal data Mean & IQR was calculated and the Kruskal-Wallis H test applied to check significant difference of different laboratory investigation between Asymptomatic, mild, moderate & severe groups. Also, for normal data Mean and SD were calculated for quantitative variables & ANOVA was applied and proportions were calculated for categorical variables. Chi-square test was applied to check significant association between attributes. P- Value of <0.05 was considered statistically significant.

RESULTS:

In our cross-sectional study over 12 months, we had 94 pediatric patients from age group 3 days -12 years. Median age was 4 years. There were 27 (28.7%) infants. Of total, 50 (53.2%) were male, 72 (76.6%) were from urban area. It was observed that 45 (47.9%) were from joint family. In this study, 77 (81.9%) had history of exposure to COVID-19 in family. Out of total admissions 25(26.6%) were asymptomatic, 48 (51.1%) had mild symptoms, 7.4% had moderate illness and 14.9% were severely ill. Average duration of hospital stay was 8.79±2.56 days. (Table 1)

Table 1: Demographic Data and Clinical Characteristics of Pediatric COVID-19 patients

Parameter		Value
Age	Mean±SD	5.01±3.92 years
	Range	[3 Days-12 years]
	Median	4.00 years
	≤ 1 year	27(28.7%)
	>5-12 years	40(42.5%)
Gender	Male	50(53.2%)
	Female	44(46.8%)
Area	Urban	72(76.6%)
	Rural	22(23.4%)
Family type	Nuclear	49 (52.1%)
	Joint	45 (47.9)
Exposure setting	Household	77(81.9%)
	Unknown	17(18.1%)
Severity of illness	Asymptomatic	25(26.6%)

	Mild	48(51.1%)
	Moderate	7(7.4%)
	Severe	14(14.9%)
Average Length of hospital stay		8.79±2.56
Symptoms	Fever	51(54.3%)
	Cold	20(21.3%)
	Cough	25(26.6%)
	Sore Throat	09(9.6%)
	Breathlessness	15(16.0%)
	Fatigue	7(7.4%)
	Pain in abdominal	5(5.3%)
	Loss of test or Smell	09(9.6%)
	Nausea & Vomiting	12(12.8%)
	Convulsion	08(8.5%)
	Other	6(6.8%)
	Asymptomatic	25(26.6%)
	Clinical signs	Febrile
Tachycardia		25(26.6%)
Tachypnoea		11(11.7%)
Hypotension (BP less than -2 SD)		07(7.4%)
Hypoxemia Spo2 less than 94 on room air on admission		10(10.6%)
Pallor		23(24.5%)
Icterus		2(2.1%)
Cyanosis		2(2.1%)
Lymphadenopathy		1(1.1%)
Oedema		2(2.1%)
Conjunctival congestion		2(2.1%)
Rash		2(2.1%)
Ecchymosis, Petechiae		1(1.1%)
Nutrition status	Moderate acute malnutrition	5(5.3%)
	SAM	12(12.8%)
	Stunted	9(9.6%)
	Microcephaly	1(1.1%)
Co morbidities	Total	22(23.4%)
	Severe acute Malnutrition	12(12.8%)
	Post operative/post surgery	2(2.1%)
	Thalassemia	1(1.1%)
	Juvenile Diabetes mellitus	1(1.1%)
	Obesity	1(1.1%)
	Congenital heart disease	2(2.1%)
	Chronic kidney disease	1(1.1%)
	Hydrocephalous	1(1.1%)
Burns	1(1.1%)	

(BP=blood pressure, SAM=Severe acute malnutrition)

Clinical symptoms: Fever (54.3%), cough 26.6%, cold 21.3% and breathlessness 16% were the most common presenting complaints and 23.4 % had comorbidities. 12(12.8%) patients in our study group had severe acute malnutrition. On admission, fever 14.9%, tachycardia 26.6%, tachypnea 11.7%, hypotension 7.5, hypoxemia 10.6% were common clinical findings. Pallor was seen in 24.5%. Table 1 shows clinical findings of patients in details.

Table .2 Treatment given, Complications and Outcome:

Oxygen therapy	Non-invasive o2	07(7.4%)
	Invasive o2 support	11(11.7%)
Dialysis	Haemodialysis	1(1.1%)
Drugs therapy	Antibiotics	37(39.4%)
	Oseltamivir	36(38.3%)
	HCO	03(3.2%)
	Favipiravir	19(20.2%)
	Lopinavir/Ritonavir	15(15.9%)
	Anticonvulsants	11(11.7%)
	Doxycycline	2(2.1%)
Steroids	13(13.8%)	

	LMWH	22(23.2%)
	IVIG	6(6.4%)
	Inotropes	10(10.6%)
Blood products		10(10.6%)
Complications	Respiratory failure requiring mechanical ventilation	11(11.7%)
	Shock	10(10.6%)
	DIC	6(6.6%)
	ARDS	8(8.5%)
	Multiorgan failure	7(7.4%)
	Kidney failure	1(1.06%)
	Cardiac	4(4.3%)
	MISC	00
Outcome	Survival	84(89.4%)
	Non-Survive	10(10.6%)

(HCQ=hydroxychloroquine, LMWH=low molecular weight heparin, DIC=Disseminated intravascular coagulation, ARDS= Acute respiratory distress syndrome, MISC= multisystem inflammatory syndrome in children)

Patients' therapy: As shown in above table 2, 39.4% received antibiotics while targeted antiviral therapy was given in the form of Favipiravir in 20.2%, Lopinavir/ritonavir 15.9%, Oseltamivir 38.3% and HCQ 3.2%.6 patients received IVIG and 10.6% required blood products. 9 patients required noninvasive support and 11 needed invasive oxygen support. We observed that 10.6% patients had shock and 8.5% landed up in ARDS. Out of total 94 patients, 10(10.6%) did not survive.

Table 3: Baseline Laboratory and radiologic parameters at Admission in Pediatric COVID-19 patient :

	Parameter	Median (IQR)	Normal Range
Complete blood count	HB	11.90 (10.67-12.85)	11.5-14.5
	<11.5	39(41.5%)	
	TLC	7550.0(5475-9800.0)	4000-12000
	Increased	12(12.8%)	
	Decreased	04(4.2%)	
	Platelets	2.58(2.10-3.26)	1.5Lakh-4.5 lakh
	<1.5 lakh	09(9.6%)	
	>4.5 lakh	06(6.3%)	
Liver and renal function tests	N:L Ratio	1.1(0.90-2.00)	<3.5
	>3.5	08(8.5%)	
	BUN	14.00(10.20—18.69)	5.00-18.0
	>18	25(26.6%)	
	Serum Creatinine	0.60(0.48-0.80)	0.22-0.59
	>0.59	59(62.8%)	
	Serum Billirubin	0.80(0.60-0.90)	<1.00
	>1.0	04(4.2%)	
	PT	13.0(13.0-14.0)	11.9-14.4
	>14.4	14(14.9%)	
Inflammatory markers	PTTK	30.0(26.0-34.0)	23.9-34.7
	>34.7	20(21.3%)	
	CRP	3.1(3.00-10.05)	0.6-7.9
	>7.9	27(28.7%)	
	D-Dimer	257.5(149.2-832.0)	<400
	>400	36(38.3%)	
	LDH	416.0(226.2-560.2)	150-500
Blood culture positivity	>500	28(29.8%)	
	Ferritin	99.45(53.75-243.5)	10-60
	>60	69(73.4%)	
Chest Xray findings (n=69)	Normal	51	
	diffuse opacities bilaterally	11(15%)	

	unilateral patchy infiltrates	4(5.7%)
	Cardiomegaly	2(2.9%)
	Pleural effusion	1(1.44%)
	Peumoperitoneum	1(1.44%)

(HB=Hemoglobin, TLC=Total Leucocyte count, N:L ratio= neutrophil and lymphocyte ratio, BUN= Blood urea nitrogen, PT Prothrombin time, INR= International normalized ratio, PTTK= Partial thromboplastin time, CRP=C reactive protein, LDH=lactate dehydrogenase)

Out of 94 children, 39(41.5%) had anemia,12(12.8%) had leukocytosis, 4.2 % had leucopenia and N/L ratio (> 3.5) was seen in 8.5%. 9(9.6%) patients had thrombocytopenia while thrombocytosis was seen in 6.3% patients. 4(4.2%) had serum bilirubin more than 1.0mg/dl. Prothrombin time was deranged in 14(14.9%) children.Amongst the inflammatory markers, it was noticed that, 27(28.7%) had raised CRP levels, 36(38.3%) had raised D-dimer levels, 69(73.4%) had raised ferritin levels and 28(29.8%) had raised LDH levels. Culture positive sepsis was noted in only 3 patients. We did X-ray chest of all symptomatic patients. Among the 69 children, 15% had diffuse bilateral opacities and 4(5.7%) had unilateral patchy infiltrates. (Table 3).

Table 4: Difference between asymptomatic, mild and moderate-severe cases:

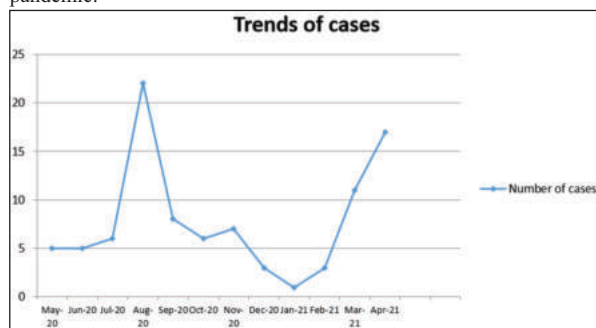
	Asymptomatic	Symptomatic			p-value
		Mild	Moderate-	Severe	
Gender					
Male	13	27	4	6	P=0.840
Female	12	21	3	8	NS
Age-Group					
≤ 1 year	3	17	1	6	P=0.101
1-5 years	12	9	3	3	NS
>5-12 years	10	22	3	5	
BCG Immunisation history					
Immunised	25	46	7	13	P=0.591
Unimmunised	0	2	0	1	NS
+ Co morbidities					
Present	3	10	3	5	P=0.191
Absent	22	38	4	9	NS
D DIMER	198.50(121.12-304.0)	245.0(146.1-615.50)	245.0(120.0-2934.0)	1561.0(772.5-4150.0)	P<0.000 1 S
LDH	415.5(126.25-487.75)	386.0(124.25-580.0)	486.0(230.0-568.0)	496.0(261.2-690.0)	P=0.235 NS
FERRITIN	67.50(26.5-114.5)	88.0(54.9-214.5)	137.0(89.0-221.0)	435.50(158.2-582.7)	P<0.000 1 S
CRP	3.0(2.25-3.0)	4.2(3.0-11.1)	4.0(3.0-12.0)	11.75(4.94-53.25)	P<0.000 1 S
AST	29.32±7.26	28.58±8.30	26.0±8.28	56.35±25.22	P=0.002 S
ALT	30.64±7.43	30.29±9.27	32.14±9.47	28.57±15.69	P=0.879 NS
Sr Bili	0.67±0.29	0.71±0.19	0.71±0.18	1.35±1.55	P=0.007 S
PT	13.60±1.73	13.46±1.33	13.87±2.30	16.10±5.12	P=0.006 S
INR	1.03±0.07	1.06±0.08	1.09±0.25	1.35±0.58	P=0.001 S
APTT	30.00±4.14	33.57±4.50	32.07±8.56	32.07±8.56	P=0.260 NS
Sodium	137.16±3.38	138.41±3.25	137.42±4.46	138.57±3.97	P=0.447 NS
Potassium	4.01±0.42	3.98±0.39	3.92±0.26	3.89±0.59	P=0.855 NS

AST= Aspartate transaminase, ALT= Alanine transaminase

D dimer, serum ferritin and CRP was statistically significant in moderate and severe cases when compared to asymptomatic, mild

and moderate symptomatic cases. (P value < 0.05)(Table 4).

Graph-1- Distribution of cases during first and second wave of pandemic.



DISCUSSION:

This is a prospective observational study on epidemiological and clinical characteristics of pediatric COVID-19 patients admitted to a government referral tertiary care hospital in central Maharashtra during first and second outbreaks, between April 2020 to March 2021. We hereby report total 94 cases with COVID-19 infection and present their clinical and demographic profile, outcome, laboratory and imaging data.

During this period our hospital had total 10,310 COVID-19 positive admissions, out of which 94 admissions were in pediatric age group. Being a government referral tertiary care hospital, we had considerable referrals of moderate and severe cases but simultaneously mild and asymptomatic cases were admitted along with the family members who were admitted with COVID-19 infection.

The median age of children in our study was 4 years (range 3 days to 12 years) and slightly more number of boys (53.2%) were affected than girls, which was similar to other studies^[12, 13]. The difference in gender was statistically insignificant. The median age of patients in a systemic review done by Hensel Hoang in 7780 patients was 8.9±0.5years.^[14] Most of our patients (81.9%) acquired COVID-19 infection through household settings which was comparable to the study done in China.^{[15][16]}

We noticed that out of total admissions, 26.6% were asymptomatic and 51.1% mildly affected, 7.4% had moderate symptoms and 14.9% had severe symptoms. Our findings were similar to a Italian study^[17] in which the percentage of severe cases was high. In a study done in china^[15], asymptomatic were 5.9%, mild and moderate group consisted 99.3% of study population and only 0.9 % were severe and critical. Similarly, study done by Dong et al^[12] found that 5.3% of study population was having severe symptoms. This high percentage of moderate and severe cases in our study could be explained by fact that our institute being the regional government tertiary care and referral center for Marathwada region in India. The average duration of stay in hospital in our study was 8.79±2.56 days compliant with ICMR guidelines^[10, 11] which was also similar to systemic review^[14]. In a study done in New York^[18], most patients were discharged (38 [76%]) with a median length of stay of 3 days (range, 1-30 days).

Fever was the most common presenting complaint in 51(54.3%) patients followed by cold or runny nose in 21.3 % and cough in 26.6 % in our study population. Similar findings were observed by most of the studies.^[12, 14, 16]

In a systemic review^[14], twenty studies (n=655) reported that COVID-19 positive children had immunosuppressed status or a pre-existing respiratory or cardiac disease (65%). In study done in New York,^[18] the most prevalent co morbidity was obesity (22%) and overweight (16%). Though our study had only one case of obesity. Reason behind this observation might be due to our center is regional government tertiary care Centre, hence the majority population catered is from lower socioeconomic strata.

In the present study, 22.3 % of the patients were transferred to PICU. The exact PICU admission rate in children with COVID-19 remains unknown. The PICU admission rate was 8% in Europe^[13] 16% in Spain^[19] 28% in New York City.^[20] Although some of these studies show a higher rate of critical illness than previously reported, detailed clinical characteristics and multicenter longitudinal outcomes were not reported. The difference in results may be attributed to different PICU

admission policies. Also, since we are a referral hospital, all critically ill children needing PICU admission were referred late and had poor outcome. In our study, 7.4% required noninvasive oxygen support during course of admission while 11.7% required invasive ventilation. In New York study^[18], approximately one-third of the hospitalized patients (32%) required some form of respiratory support like nasal cannula, NIPPV, or mechanical ventilation and NIPPV was the maximum respiratory support used for 6% patients and mechanical ventilation was required for 18% patients. In a study done in Canadian PICU^[21], of the patients requiring any respiratory support, 38% required endotracheal or tracheostomy ventilation.

The treatment measures for pediatric COVID-19 is not as complex as that of adults and our management mainly consisted of supportive therapy, antiviral therapy (36%), antibiotics, steroids (13.8%) and oxygen. None of the patient received Remdesivir. In a systemic review^[14], out of 616 patients, 21.8 % patients received Remdesivir or other unspecified antiviral therapy while Lopinavir/Ritonavir and Oseltamivir were given in 11.2% and 8.6 % patients respectively. In a Study done in New York^[18], Hydroxychloroquine was administered to 30 % patients. Shock (10.6%), ARDS (8.5%) and respiratory failure (11.7 %) requiring mechanical ventilation were the most common complications seen in our patients. In systemic review,^[14] respiratory failure requiring mechanical ventilation in 0.54% and shock in 0.24% were the most common complications in 7780 patients. Mortality was 10.6 % in our study which was very high as compared to other western studies. This can be attributed to the reason that; all severe patients were referred and there was significant delay in referrals of the cases. Similar findings were noted in a Indian study in which mortality was as 24%^[15]. In an Iranian study,^[14] mortality was 4%. The mortality in this study was attributed to severe cases with co morbidities. Out of total number of cases in our study, only 23.4% had co-morbidities, most common being severe acute malnutrition (12.8%). We found that the presence of a comorbid illness in children with COVID-19 did not impact the illness severity, length of hospitalization, ventilation requirement and mortality as only 5 (35.7%) children with severe illness had co-morbidities. Similar findings were observed by a study done in India by Kapoor et al.^[5]

Elevated inflammatory markers, anemia and thrombocytopenia were common findings in other studies.^[14, 24, 25] As observed in New York study,^[18] patients who required mechanical ventilation were characterized by high inflammatory markers (ferritin, C-reactive protein, procalcitonin, D-dimer, and IL-6) which was similar to our study. We did X-ray chest in symptomatic patients (n= 69); it was observed that 15% had diffuse opacities bilaterally and 5% unilateral patchy infiltrates which was coherent with radiology recommendation.^[26]

Results of this study shows that COVID-19 in children is mostly a mild, asymptomatic disease however percentage of children with moderate and severe disease cannot be neglected. In our study almost 40 % of children with severe disease were infants which was consistent to Chinese case series^[12]. Our data also reflects the uncertainties regarding drug treatment options for COVID-19 in children. In some countries including Spain and Italy, National guidelines were encouraging use of HCQ for selected cases as reflected in our data while other countries recommendations were more guarded regarding use of antivirals in absence of robust human data^[22]

This study had several limitations like inability to do viral load and its correlation with severity could not be established. As it is a cross sectional study, it needs follow up evaluation. There were investigational constraints faced due to financial issues. Due to small sample size and specific cohort of pediatric patients, it might not represent the general population conclusions and multi centric studies from other government tertiary care hospitals from India are required.

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Conflict of interest- None

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