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Analysis of clinicolaboratory profile and outcome in COVID-19 positive pediatric patients

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***Abstract*---**COVID-19 infection in children has important public health, social, and economic implications, and even though children may have considerably milder symptoms than individuals >18 years of age, those infected seem to have the same levels of circulating virus in their body and may be as infectious as adults. The objective is to study clincolaboratory profile and outcome in COVID-19 positive pediatrics patients. This hospital based prospective observational study was conducted in the department of Pediatrics , Government Medical College , Haldwani Uttarakhand. COVID 19 Positive Pediatric patient from birth to 18 years from September 2020 to September 2021 were enrolled in the study. Referred patients were 1 in moderate, 3 in severe and 1 in MIS-C group. Expired patients mostly belong to severe category. 1 patient expired due to celphos poisoning and was diagnosed as covid-19 on routine sampling. In conclusion these laboratory findings and clinical features should raise strong suspicion of COVID-19 infection and severity and could be used as a useful predictor for planning treatment in children with moderate to severe illness.

***Keywords*---**COVID-19, clincolaboratory profile, pediatrics patients.

Introduction

Coronavirus disease (COVID-19), a global pandemic challenging modern medicine in many aspects. Coronavirus have been long known as causing disease in both

mammals and birds. They are enveloped viruses with positive sense RNA causing respiratory and GI symptoms. Coronaviruses are capable of recombination's and rapid mutations leading to newer coronavirus strain [1]. COVID 19 is one such infection, caused by SARS CoV 2 (severe acute respiratory distress syndrome coronavirus which is responsible for current global pandemic [2].

COVID-19 infection in children has important public health, social, and economic implications, and even though children may have considerably milder symptoms than individuals >18 years of age, those infected seem to have the same levels of circulating virus in their body and may be as infectious as adults[3]. However, other studies suggest that children have a small role in the spread of COVID-19. Previous studies suggest that COVID infection in pediatric age group tends to be milder form then in adults. The disease burden seems to be significantly lower in the pediatric population, with many children being completely asymptomatic or mildly affected but the cases tends to increase [4]. Pediatric patients acquired COVID-19 by clear transmission that included close contact with family members with COVID-19 or the history of exposure to epidemic area, or both. The previous study also indicate that source of infection could not be traced for some cases of pediatric COVID-19. [5]

Patients in the MIS-C group were less likely to receive invasive ventilation but were more often treated with vasoactive drugs, corticosteroids and immunoglobulins. It was concluded that the MIS-C seems to be the most frequent presentation among critically ill children with SARS-CoV-2 infection [6]. A meta-analysis on 49 studies with a total of 1667 pediatric COVID-19 patients, where in most of the children had mild symptoms only. They concluded that the characteristics of COVID-19 differ between adults and children [7]. In December 2019, a cluster of patients with pneumonia of unknown cause which was linked to a seafood wholesale market in Wuhan, China. Different from both MERS-CoV and SARS-CoV, 2019-nCoV is the seventh member of the family of coronaviruses that infects humans [8]. Rao S K et al (2021)[9]described the clinical profile, risk of infection and outcome of coronavirus disease-19 in immuno-compromised children and found that children on immuno-suppressant medication have 2.89 times increased risk of infection. Disease manifestation was asymptomatic or mild with predominant gastrointestinal symptoms without alteration in immunosuppressive treatment regimen [10].

The various studies in the literature shows that the percentage of children amongst the total number of COVID-19-affected patients was quite small and most of them developed milder form of illness. As the pandemic continues, the number of paediatric patients with COVID-19 is expected to increase significantly [11]. Since there is difference in the respiratory structural characteristics as well as immune response system among children and adults, therefore, it may be not be appropriate to follow the diagnostic criteria and management according to recommendations targeting adults. Also, several studies have also reported the clinical profile of COVID-19 infection in children; however, since the sample size of most of the studies was not big, there is a need to pool data from such studies and to deduce meaningful results [12]. In view of the above, the main aim is to

study clincolaboratory profile and outcome in COVID-19 positive pediatrics patients.

Material and Methods

This hospital based prospective observational study was conducted in the department of Pediatrics , Government Medical College , Haldwani Uttarakhand. COVID 19 Positive Pediatric patient from birth to 18 years from September 2020 to September 2021 were enrolled in the study. The study subjects were all patients from birth to 18 years, from the screening area, was enrolled in the study who were RT- PCR/ Rapid Antigen / True Net Positive. The participants who refused of consent for participation were excluded from the study. All pediatric patients were diagnosed as COVID-19 on the basis of Rapid Antigen/True Nat/RT-PCR positive and was subjected to above investigations and Chest X-ray and CT Thorax (if required). The patients were classified as asymptomatic, mild symptomatic, moderately symptomatic and severely symptomatic. Patient and attendants were explained the same, and an informed written consent was obtained. The treatment was included Oxygen support, Ventilation (NIV/ Invasive) IV/ Oral antibiotics (Azithromycin/ Doxycycline), LMWH, Inj Dexamethasone, Inj Remdesivir, Ivermectin, HCQ Supportive Care, Multivitamins, Vitamin C, Vitamin D and Zinc depending on the degree of symptoms and other clinic laboratory Derangements. After approval from the Institutional Ethical Committee all patients were selected as per inclusion and exclusion criteria. A detailed history, complete physical examination and routine & appropriate investigations were done for all patients.

Data analysis

The data was entered into the Microsoft excel and the statistical analysis was performed by statistical software SPSS Version 25.0. The variables were present in the frequency with percentage. The chi square test was used to find the association. The p-value less than 0.05 is considered to be significant.

Results

From *Table 1*, it is observed that majority of the study population belonged to 11-15 years (32.2%) and > 15 years (20.0%). The study population consisted of 52 (57.8%) males and 38 (42.2%) females. History of Contact was reported among 34.4%and History of Travel among 2.2% Fever (66.7%), Cough (41.1%) and Breathing difficulty (33.3%) were the predominant symptoms reported followed by Running nose (21.1%), Vomiting (17.8%), Sore throat (16.7%) and headache (12.2%) Seizures were reported in 10 (11.1%), out of which 4 had underlying previous CNS abnormality. GI symptoms comprised of vomiting (17.8%), abdominal pain (10%) and diarrhea (6.7%) Hypotension was present in 16 (17.8%), Pallor in 46 (51.1%), Icterus in 3 (3.3%), Oedema in 9 (10.0%), LAP in 2 (2.2%) and Rash in (4.4%). Asymptomatic cases were 8 (20.0%), Mild COVID-19 were 25 (28.9%), Moderate COVID-19 were 26 (27.8%), Severe COVID-19 were 17 (18.9%) and MISC were 4 (4.4%). Improvement occurred in 85.6%, 5.6% were

Referred and 8.9% Expired. Referred patients were 1 in moderate, 3 in severe and 1 in MIS-C group. Expired patients mostly belong to severe category. 1 patient expired due to celphos poisoning and was diagnosed as covid-19 on routine sampling.

In *Table 2*, Underweight were more among Moderate and Severe covid-19. Normal weight comprised of 64.5% and mostly having mild infections. The most common co-morbidities were Severe Anaemia (10%) and Malnutrition (30%) which were more among moderate and severe covid-19. 2 patients were of HIE sequale, 2 were thalassemia and are asymptomatic, 3 were of Vitamin d deficiency, 2 were post-transplant both having severe covid and 2 were CKD having moderate and severe covid CT thorax showed Abnormal (Associated with Covid) (CORADS>3) among 21.1% patients which were more among moderate and severe covid-19. X-ray findings showed that Consolidation/ Pneumonia was found among 53.3%, ARDS picture among 35.6% and Pleural Effusion among 5.6% patients. Consolidation/Pneumonia findings are more associated with moderate and severe covid. ARDS picture was seen mostly in severe covid and was more associated with mortality Cadiomegaly was present in 1 patient of thalassemia Hyperinflation was seen in a patient of hyperactive airway disease

From Table 3, Seizures was found among 8 patients out of which 4 (4.4%) had no previous CNS anomaly/Sequalae, LONS among 3 (3.3%), MISC among 4 (4.4%), AGE with severe dehydration among 1 (1.1%) and NNH among 1 (1.1%) patient.
Table 4 shows that management was done mostly with Oral Antibiotics (27.8%), IV antibiotics (55.6%), Oxygen therapy (53.3%) - Mask/ Prongs (21.1%), NIV (23.3%), Mechanical ventilation (8.9%), Steroids (IV+Inhalalational) (42.2%)- IV steroids (23.3%), Inhaled steroids (25.6%), Blood products (17.8%) and Ionotropes (12.2%). Inj Remdesivir was used only in 3 patients among severe category. Inotropes were needed severe and MISC patient and 1 asymtomatic patient (celphos poisoning)

Table 1
Frequency Distribution of the Variable

Variable	Category	Frequency	Percent
Age	< 1 year	13	14.40%
	1-5 years	20	22.20%
	6-10 years	10	11.10%
	11-15 years	29	32.20%
	> 15 years	18	20.00%
Gender	Male	52	57.80%
	Female	38	42.20%
Clinical symptoms	Fever	60	66.70%
	Headache	11	12.20%
	Running nose	19	21.10%
	Sore throat	15	16.70%
	Cough	37	41.10%
	Abdominal pain	9	10.00%

	Breathing difficulty	30	33.30%
	Altered taste	4	4.40%
	Diarrhoea	6	6.70%
	Vomiting	16	17.80%
	Seizures	8	11.10%
Clinical signs	Hypotension	16	17.80%
	Pallor	46	51.10%
	Icterus	3	3.30%
	Oedema	9	10.00%
	LAP*	2	2.20%
	Rash	3	3.30%
Severity	Asymptomatic	18	20.00%
	Mild COVID-19	26	28.9%%
	Moderate COVID-19	25	27.80%
	Severe COVID-19	17	18.90%
	MISC*	4	4.40%
Outcome	Improved	77	85.60%
	Referred	5	5.60%
	Expired	8	8.90%
History of Contact		31	34.40%
History of Travel		2	2.20%

Table 2
Association of weight with COVID-19

Variable	Category	Frequency	%	Asymptomatic	Mild	Mod	Severe	MIS-C	P value
Weight	Underweight	28	31.10%	5	4	12	6	1	0.454
	Overweight	4	4.40%	-	3	1	-	-	
	Normal Weight	58	64.50%	13	19	12	11	3	
Co-morbidities	Severe Anaemia	9	10%	1	-	4	4	-	0.244
	Vitamin D deficiency	3	3.30%	-	1	2	-	-	
	FTT/ Underweight/IUGR/PEM	28	30%	5	4	12	6	1	
	HIE	2	2.20%	-	-	1	1	-	
	Thalassemia + PEM	2	2.20%	2	-	-	-	-	
	TB meningitis	1	1.10%	-	-	-	1	-	
	Post-transplant	2	2.20%	-	-	-	2	-	
	Chronic kidney disease + Anemia	2	2.20%	-	-	1	1	-	
CT thorax (n=25)	Findings Not Related to Covid (CORADS=<3)	6	6.70%	-	2	4	-	-	0.264
	Abnormal (Associated with Covid) (CORADS>3)	19	21.10%	-	1	11	7	-	
X-ray findings	Normal	48	53.30%	15	22	7	-	3	0.315
	Consolidation/ Pneumonia	32	35.60%	2	3	15	12	-	
	ARDS picture	5	5.60%	-	-	1	4	-	
	Pleural Effusion	3	3.30%	-	-	1	1	1	
	Hyperinflation	1	1.10%	-	1	-	-	-	
	Cardiomegaly	1	1.10%	1	-	-	-	-	

Table 3
Atypical presentation

Atypical Presentation	Frequency	Percent
Seizures (without any intracranial abnormality)	4	4.40%
LONS	3	3.30%
MISC	4	4.40%
AGE with severe dehydration	1	1.10%
NNH	1	1.10%

Table 4
Management

Management	Frequency	Percent
Oral Antibiotics	25	27.80%
IV antibiotics	50	55.60%
Oxygen therapy	48	53.30%
Mask/ Prongs	19	21.10%
NIV	21	23.30%
Mechanical ventilation	8	8.90%
IV steroids	21	23.30%
Inhaled steroids	23	25.60%
Injection Remdesvir	5	5.60%
LMWH	6	6.70%
IVIG	2	2.20%
Blood products	16	17.80%
Ionotropes	11	12.20%

Discussion

The clinical features of pediatric patients with COVID-19 have been reported to be much milder than those of adults.[1[3]] However, there is insufficient knowledge regarding the immunologic features related to the clinical outcomes of COVID-19 in pediatric patients. In this study, we describe the clinico- lab profile and outcome of children admitted in dedicated tertiary care covid hospital. As during the pandemic there was extended lockdown and closure of schools and outdoor activities, the primary source of infection in children were household contacts.

Majority of the study population belonged to 11-15 years (32.2%) and few were > 15 years (20.0%) with a male preponderance (57.8%). Majority of patients in our study were of Mild and Moderate COVID-19. We found Fever (66.7%) was the most common symptom followed by Cough (41.1%), Fast Breathing (33.3%), and Sore throat (16.7%). The common gastrointestinal symptoms in our study were Vomiting (17.8%), abdominal pain (10%) and diarrhea (6.7%). This was similar to many reviews and analysis [14,15] suggesting fever and cough were most predominant symptoms in children. These reviews[16,17] also suggest that frequency of gastrointestinal symptoms like abdomen pain, vomiting and

diarrhea are more in pediatric age group. Observational studies across the world have reported similar frequency of symptoms. [18-20]

The most common neurological manifestation in our study was seizure. Total 8 patients (11.1%) had convulsions in which 6 were febrile at the time of seizure, however COVID CSF RTPCR couldn't be done due to lab limitations. There are few case reports showing covid-19 infection is associated with febrile seizure and breakthrough seizures in a previously well controlled patient (21-22). 38 (42.2%) children had co-morbidities, in which malnutrition/undernutrition 18 (47%) and severe anemia were the most common. 2 patients were of CKD and 2 patients had bone marrow transplantation. In previous studies it has been shown that co-morbidities predispose increase severity of COVID. Current study also shows the same association(23). Studies has shown higher CRP, ESR and IL-6, Ferritin, were more in moderate to severe disease. This study also shows the same. Raised D-dimer and LDH is consistent with other studies. In conclusion these laboratory findings and clinical features should raise strong suspicion of COVID-19 infection and severity and could be used as a useful predictor for planning treatment in children with moderate to severe illness(24).

Conclusion

Pediatric patients can present with moderate and severe COVID though mortality is less as compared to adults. Major comorbidities predisposing to severity of COVID were malnutrition and anaemia. Lab parameter were suggestive of increased inflammatory markers with increased in severity. Role of TLC, ANC and N:L ratio needs to be further studied. Patients with pneumonia have more increase in inflammatory markers. Steriods both IV and inhalational, oxygen therapy along with supportive treatment are the mainstay of treatment of pediatric Covid patients. Role of remdesivir could not be assessed in our study as it was given to only 3 patients. Pediatric Covid along with MISC has a favourable outcome if managed promptly. The coagulation profile association with COVID -19 needs to be studied further. Post Covid illnesses needs further studies with a large sample size to predict better association.

Limitations of the study

Being a tertiary referral center there is greater proportion of moderate and severe covid cases in our cohort, leading to bias, hence further epidemiological studies are needed to know about the spectrum of covid-19 in paediatrics in general population. Some lab investigations and CT was not done in all patients of our study as per availability at that time hence better studies are needed to predict further association. Procalcitonin test was not available at our center so its association could not be assessed. The sample size of our study is small and better studies are needed to further strengthen our results.

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