

To Estimate the Prevalence of Extra-Pulmonary Symptoms of COVID-19 in Children

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Abstract:

Background: The COVID-19 pandemic, initiated by SARS-CoV-2, has posed an unparalleled global health emergency since its emergence. Initially, respiratory symptoms predominated, but understanding has broadened to encompass diverse clinical presentations. Children, previously deemed less vulnerable, are now recognized as potential carriers and victims. Emerging evidence indicates extra-pulmonary manifestations in pediatric COVID-19 cases, underscoring the need for prevalence assessment. Such insights facilitate prompt diagnosis, inform pathophysiological understanding, and guide public health strategies to contain viral spread and protect children's health.

Methods: This prospective observational study, conducted at the Department of Paediatrics, aimed to investigate extra-pulmonary symptoms in pediatric COVID-19 cases. Over 10 months, children aged 1 month to 18 years with laboratory-confirmed COVID-19 were recruited. Clinical evaluations and baseline samples were obtained, documenting symptoms and conducting laboratory investigations. Data were analyzed using SPSS version 20.0, employing descriptive statistics to summarize demographic characteristics and symptom prevalence, including multisystemic involvement and post-COVID effects.

Results: Our study on pediatric COVID-19 cases revealed a predominance of male participants (60.2%) with a mean age of 8.2 years. Among 113 participants, one had malnutrition (0.9%), and none had positive parental COVID-19 status or tested positive for HIV, HBV, or HCV. Common clinical features included fever (41.6%), cough (10.6%), diarrhea (6.2%), skin rash (7.1%), and loss of taste/smell (2.7%). Laboratory investigations indicated normal hemoglobin, leukocyte count, and platelet count. No abnormality was noted in liver, kidney, or electrolyte function. Proteinuria was absent, and no participant required ICU admission.

Conclusion: In conclusion, our study provides valuable insights into the clinical and laboratory characteristics of COVID-19 in children, highlighting the importance of vigilance for extra-pulmonary symptoms and the need for tailored management strategies in this population.

Keywords: COVID-19, Diarrhea, Loss of smell, Neurological, Hepatic injury.

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Introduction

The COVID-19 pandemic caused by the novel coronavirus SARS-CoV-2 has presented an unprecedented global health crisis since its emergence in late 2019. Initially characterized primarily by respiratory symptoms such as fever, cough, and shortness of breath, the understanding of COVID-19 symptomatology has evolved to encompass a wide range of clinical presentations [1]. While considerable attention has been focused on the respiratory manifestations of the disease, emerging evidence suggests that COVID-19 can also affect various organ systems beyond the lungs, including the gastrointestinal, cardiovascular,

neurological, and dermatological systems [2,3]. Children, initially thought to be less susceptible to severe illness from COVID-19 compared to adults, have increasingly been recognized as potential carriers and victims of the virus [4]. Despite a generally milder clinical course in pediatric populations, there is growing recognition of extra-pulmonary manifestations of COVID-19 in children. These manifestations, which may present in isolation or in conjunction with respiratory symptoms, encompass a diverse array of clinical features, ranging from gastrointestinal disturbances

to dermatological manifestations and neurological symptoms [5,6].

Understanding the prevalence of extra-pulmonary symptoms of COVID-19 in children is crucial for several reasons. Firstly, it aids in the identification of atypical presentations of the disease, facilitating prompt diagnosis and appropriate management. Secondly, it provides insights into the pathophysiology of COVID-19, shedding light on the mechanisms underlying its multi-organ involvement. Moreover, knowledge of the spectrum of clinical manifestations in pediatric patients informs public health strategies, including surveillance efforts and vaccination campaigns, aimed at controlling the spread of the virus and mitigating its impact on children's health [7,8].

There has been substantial evidence on respiratory symptoms of covid-19 in children as well as in adults. While there is a scarcity of data regarding the extra-pulmonary manifestations. There are few case reports and reviews regarding the multisystemic manifestations of covid-19 and gap of knowledge exists regarding the subject [8,9,10]. Hence, the present study was conceptualized to estimate the prevalence of possible extra-pulmonary symptoms of covid-19 in children based on clinical and laboratory parameters. It is important to know the pulmonary as well the extra-pulmonary symptom associated with the disease so as to identify it early and manage effectively with proper precautions.

Materials and Methods

Study Design

This study is a prospective observational study was conducted at the Department of Paediatrics, School of Medical Sciences and Research, Sharda University, Greater Noida, Uttar Pradesh, India. The study was conducted in accordance with the principles outlined in the Declaration of Helsinki and approved by the institutional review board.

Participants

Children aged 1 months-18 years with laboratory confirmed COVID-19 diagnosis were recruited for a period of 10 months (March 2020 to December 2020) from General pediatric ward and ICU dedicated for COVID-19.

The laboratory confirmed cases were either rapid antigen test COVID-19 RT-PCR or COVID-19 antibodies testing. Informed consent was obtained from parents or legal guardians prior to enrollment. Children with laboratory confirmed cases of malaria, typhoid, dengue and hepatitis were excluded from the study.

Sample Size Calculation

The sample size was calculated assuming prevalence of extra-pulmonary symptoms of COVID-19 in children as 50% as there is lack of

previous studies. With a desired confidence level of 95% and a margin of error of 5%, the minimum required sample size was determined to be 96 participants.

Clinical Evaluation

Participants underwent a comprehensive clinical evaluation to assess for the presence of extra-pulmonary symptoms associated with COVID-19. Symptoms assessed included but were not limited to Gastrointestinal symptoms (e.g., diarrhea, vomiting, abdominal pain), Neurological symptoms (e.g., headache, dizziness, altered consciousness), Dermatological manifestations (e.g., rash, skin discoloration), and Cardiovascular symptoms (e.g., chest pain, palpitations), etc. Weight at admission was taken for every child. To reduce the exposure risk additional parameters like height and head circumference were taken in suspected cases of malnutrition or endocrinal problems. Temperature was recorded by a digital thermometer for all the children in Fahrenheit.

Laboratory parameters

Baseline samples were collected from each participant for comprehensive laboratory investigations including complete hemogram, erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), liver function tests (LFTs), kidney function tests, urine routine microscopy, and urine for protein and red blood cells (RBCs).

Data Collection

Clinical presentation and symptoms were documented by trained healthcare providers using standardized data collection forms. Severity and duration of symptoms were also recorded. During the entire stay of the child in the hospital, any development of new symptoms or any aberration in the laboratory parameters was also looked for and accordingly managed. Once the child was discharged from the hospital, a telephonic follow-up was conducted regarding any persisting or new symptoms or any other query related to COVID from the child or the parent was also addressed. In the event of mortality, the standard hospital procedure was followed for every patient. Along with the biochemical parameters, other available information from chest radiographs, CT scans, or ultrasound was also recorded and analyzed.

Statistical Analysis

The collected data was entered in MS excel spread sheet and analysed using SPSS version 20.0. Descriptive statistics were used to summarize the demographic characteristics of the study population and the prevalence of extra-pulmonary symptoms. Continuous variables were presented as means \pm standard deviations or medians with interquartile ranges, while categorical variables were presented as frequencies and percentages. In data analysis, we

also aimed to assess multisystemic involvement caused by SARS-CoV-2, and evaluate after-effects of COVID infection in children.

Ethical Considerations

This study was conducted in accordance with ethical standards outlined in the Declaration of Helsinki. Informed consent was obtained from parents or legal guardians of all participants. Confidentiality of participants' information was maintained throughout the study.

Results

In our study, conducted on children diagnosed with COVID-19, revealed that among the participants,

39.8% were female, while 60.2% were male. The mean age of the children was 8.2 years with a standard deviation of 3.9 years, in addition, it was found that 6 children, were below one year of age, with their ages ranging from 2 to 11 months (2, 6, 7, 8, 10, and 11 months).

The mean weight was 20.9 kg with a standard deviation of 8.1 kg, and weight ranged from 4.2 kg to 38.0 kg. None of the parents tested positive for COVID-19, indicating a 100.0% negative status among them. Only one participant (0.9%) had a comorbidity of malnutrition. Furthermore, none of the children tested positive for HIV, HBV, or HCV, indicating a 0% prevalence of these infections among the study participants (Table 1).

Table 1: Baseline characteristics of the study participants (N=113)

Variables	Frequency	%
Gender		
Female	45	39.8
Male	68	60.2
Mean age (in years)	8.2 ± 3.9	
Mean weight (in kg)	20.9 ± 8.1	
Parent COVID-19 status		
Positive	0	0.0
Negative	113	100.0
Comorbidity		
Malnutrition	1	0.9

Among the clinical features observed in the study participants diagnosed with COVID-19, fever was the most common, with a frequency of 47 cases, accounting for 41.6% of the cohort. Cough was reported in 12 cases (10.6%), followed by diarrhea in 7 cases (6.2%), skin rash in 8 cases (7.1%), and loss of taste or smell in 3 cases (2.7%). Additionally, vomiting, chest pain, breathing difficulty, joint pains, jaundice, and abnormal body movements were not reported among any of the participants in the study (Table 2).

Table 2: Symptoms and clinical feature among study participants (N=113)

Clinical feature	Frequency	%
Fever	47	41.6
Cough	12	10.6
Diarrhoea	7	6.2
Skin rash	8	7.1
Loss of taste/smell	3	2.7

The results of laboratory investigations among pediatric participants diagnosed with COVID-19 revealed diverse findings across various parameters. Mean hemoglobin levels were within normal range at 11.6 ± 1.3 g/dL. Total leukocyte count (TLC) showed a mean of 8050.9 ± 3523.7 cells/cumm. Polymorphs were observed at a mean of 40.3 ± 14.1 × 10³ cells/cumm, while lymphocytes exhibited a mean of 52.3 ± 12.9 × 10³ cells/cumm. Platelet count averaged 5.6 ± 3.0 lakhs/cumm. The erythrocyte sedimentation rate (ESR) averaged 21.9 ± 9.2 mm/hr. Notably, 6 cases (5.3%) demonstrated red blood cells in urine, and 46 cases (40.7%) tested positive for C-reactive protein (CRP). Renal function parameters including urea and creatinine

showed mean values of 26.7 ± 7.1 mg/dL and 0.3 ± 0.1 mg/dL, respectively. Electrolyte levels were within normal limits, with mean sodium and potassium levels at 140.3 ± 3.8 meq/L and 4.3 ± 0.5 meq/L, respectively. Serum bilirubin levels averaged 0.6 ± 0.3 mg/dL, while liver enzymes SGOT and SGPT exhibited mean levels of 52.6 ± 15.6 IU/L and 35.6 ± 16.9 IU/L, respectively. Serum albumin and globulin levels showed mean values of 3.9 ± 0.6 g/dL and 2.6 ± 0.4 g/dL, respectively. Random blood sugar levels averaged 95.4 ± 16.2 mg/dL. Protein in urine in none, none required ICU admission. Additionally, none of the participants exhibited protein in urine, indicating normal renal function among the cohort (Table 3).

Table 3: Laboratory parameters among study participants (N=113)

Parameters	Mean \pm SD (Range)
Haemoglobin (g/dL)	11.6 \pm 1.3 (8.8-16.0)
TLC (/cumm)	8050.9 \pm 3523.7 (3450-18120)
Polymorphs (x103cumm)	40.3 \pm 14.1 (15-75)
Lymphocytes (x103cumm)	52.3 \pm 12.9 (24-78)
Platelets count (lakhs/cumm)	5.6 \pm 3.0 (1.5-5.6)
ESR (mm/hr)	21.9 \pm 9.2 (6-44)
RBCs in Urine	6 (5.3)
CRP positive	46 (40.7)
Urea (mg/dL)	26.7 \pm 7.1 (5.5-43.0)
Creatinine (mg/dL)	0.3 \pm 0.1 (0.2-0.7)
Sodium (meq/L)	140.3 \pm 3.8 (134-154)
Potassium (meq/L)	4.3 \pm 0.5 (3.4-6.7)
Serum bilirubin (mg/dL)	0.6 \pm 0.3 (0.1-2.0)
SGOT (IU/L)	52.6 \pm 15.6 (22-101)
SGPT (IU/L)	35.6 \pm 16.9 (12-90)
Albumin (g/dL)	3.9 \pm 0.6 (2.7-5.2)
Globulin (g/dL)	2.6 \pm 0.4 (1.8-3.8)
Random blood sugar (mg/dL)	95.4 \pm 16.2 (65-176)

Furthermore, none of the participants required admission to the intensive care unit (ICU), suggesting that the majority of cases were managed in non-critical care settings. These findings underscore the relatively mild presentation and favorable outcomes observed among the pediatric population diagnosed with COVID-19 in this study.

Discussion

The findings of this study shed light on the clinical characteristics and laboratory profiles of pediatric patients diagnosed with COVID-19, providing valuable insights into the disease's manifestation in this demographic. The prevalence of extra-pulmonary symptoms, diarrhea in 6.2%, followed by skin rash in 7.1%, and loss of taste or smell in 2.7%, underscores the diverse presentation of COVID-19 in children, aligning with previous reports highlighting the variability in symptomatology across different age groups. The primary extra-pulmonary symptoms identified predominantly involved the gastrointestinal (GI) system, characterized by a notable occurrence of diarrhea in the studies by Zhang et al., Dallen et al., Robbins et al., Greene et al., Tullie et al., and Wolfer et al., [11-16]. Notably, the absence of vomiting, chest pain, breathing difficulty, joint pains, jaundice, and abnormal body movements in our cohort suggests a relatively mild clinical course in most cases, corroborating observations from previous studies suggesting that severe manifestations are less common in children compared to adults. Renal manifestations were reported with hematuria, proteinuria, uremia, and increased creatinine as the main signs in the studies by Stewart et al., and Almeida et al., [17,18]. In the studies by Marhaeni et al., and Nathan et al., the presence of neuromuscular manifestations was indicated by axial hypotonia, generalized hypertonia, and muscular pain [19,20]. In terms of laboratory parameters, our results provided valuable insights

into the hematological, biochemical, and renal profiles of pediatric patients with COVID-19. While most laboratory values fell within normal ranges, abnormalities such as elevated C-reactive protein (CRP) levels were observed in a significant proportion of patients, suggesting underlying inflammatory processes and was also observed in the studies by Canarutto et al., and Olisova et al., [21,22]. Notably, none of the participants exhibited proteinuria, indicating preserved renal function in our cohort. But Acute liver injury and changes in hepatic enzyme levels were noted in the studies by Brambilla et al., Capone et al., Cui et al., and Qiu et al., [5,7,23,24].

Additionally, none of the pediatric patients included in our study required admission to the intensive care unit (ICU), highlighting the generally mild presentation and favorable outcomes observed among children with COVID-19. This finding is consistent with previous studies by Palacios et al., Riphagen et al., Pazukhina et al., Sirico et al., Sezer et al., and Patnaik et al., suggesting that severe disease and ICU admission are relatively rare in pediatric COVID-19 cases [4,25-29].

Limitations

Overall, our study contributes to the growing body of literature on COVID-19 in children by providing insights into the prevalence of extra-pulmonary symptoms and associated clinical and laboratory characteristics. However, it is important to acknowledge the limitations of our study, including its retrospective nature and the potential for

selection bias. Further prospective studies with larger sample sizes are warranted to validate our findings and elucidate the underlying mechanisms driving the clinical manifestations of COVID-19 in pediatric patients. These efforts will be crucial for informing clinical practice and guiding public health interventions aimed at mitigating the impact of the pandemic on children.

Conclusion

In conclusion, our study provides valuable insights into the clinical and laboratory characteristics of COVID-19 in children, highlighting the importance of vigilance for extra-pulmonary symptoms and the need for tailored management strategies in this population. Continued surveillance and research efforts are essential to enhance our understanding of the disease's impact on children and inform evidence-based interventions aimed at mitigating its effects on pediatric health.

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