

Clinical Profile and Short-term Outcome of Paediatric COVID-19 in the First, Second and Third Wave of the Pandemic in India- An Observational Study

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ABSTRACT

Introduction: There has been adequate evidence that children are less likely to contract the Coronavirus Disease-2019 (COVID-19) infection and less likely to experience a deadly course of the disease in the paediatric group. The majority of the time, they exhibit moderate respiratory symptoms, like fever, dry cough and exhaustion. They were all free of COVID-19 pneumonia.

Aim: To compare the clinical features and short-term outcomes of COVID-19 in children during May 2020 to April 2022.

Materials and Methods: The present analytical observational study was conducted in the Department of Paediatrics, Chettinad Hospital, Chennai, Tamil Nadu, India, from March 2020 to March 2022. The study population included Reverse Transcription-Polymerase Chain Reaction (RT-PCR) positive COVID-19 children between age groups of one month and 18 years age. A sample size of 102, 90 and 98 were included from first, second and third wave, respectively. Kruskal-Wallis test and Analysis of Variance (ANOVA) test were used for statistical analysis.

Results: In the study population, the mean age in the wave 1, wave 2 and wave 3 was 9.1 ± 5.25 years, 9.3 ± 4.99 years and 9.2 ± 5.12 years, respectively. Males were more affected in all the phases than females. The most common symptoms in all the three waves were cough, myalgia and fever. Fever was the predominant symptom reported in all three waves (74.8% in wave 1, 80.6% in wave 2 and 75% in wave 3). Between the COVID-19 waves, baseline investigations such as Alanine Transaminase (ALT) and Aspartate Transaminase (AST) (p -value=0.001, 0.02) showed significant differences. C-reactive Protein (CRP) was non reactive in (81.55%) in wave 1, (85.07%) in wave 2 and (65.3%) in wave 3. (p -value=0.029).

Conclusion: The present study results conclude that the presenting features of COVID-19 in children were mild, and the outcome was good. The first, second and third waves had considerable differences in clinical findings and short-term outcomes among COVID-19-affected children.

Keywords: Capillary refilling time, Coronavirus disease-2019, Fever, Myalgia

INTRODUCTION

The risk of COVID-19 infection is universal. Based on previous literature, there does not appear to be an age limit for COVID-19 susceptibility. According to recent research, children represent for a tiny percentage of COVID-19 occurrences as compared to adults [1,2]. Although COVID-19, Severe Acute Respiratory Syndrome (SARS), and Middle East Respiratory Disease (MERS) are all caused by a coronavirus and can cause severe respiratory distress, COVID-19 has its unique epidemiological and clinical characteristics. COVID-19 has a prolonged incubation time, high infectivity, unusual clinical signs, and a significant fatality rate in elderly adults [3,4].

According to some reports, children are at higher risk to contract SARS-CoV-2, although they had minimal symptoms and a milder sickness, as well as a lesser case-fatality rate compared to adults [5-7]. Because many of the early investigations in China were conducted in adult facilities, the number of children reported was limited [8]. The number of paediatric children infected with COVID-19 is expected to grow rapidly, if it has not already, due to the fast global spread of SARS-CoV-2 infection [9]. The report by Max Planck Institute for Demographic Research (MPIDR) coverage database suggested that among 3.7 million deaths, over 13,400 (0.4%) were recognised in paediatrics and adolescents under 20 years of age. Specifically, the epidemiological and clinical manifestations of COVID-19 in the 0-14-years paediatric population until now are not completely described [10]. The devastating second wave of COVID-19 in India peaked during the May 2021 primary, fueled

by B.1.617 lineage variations, particularly the delta variant [5]. It is probable that the clinical aspects of each wave will alter based on the variants that dominate the waves [11,12]. The current research was conducted to compare the clinical manifestations and short-term aftermaths of COVID-19 in children during the first wave, second wave and third wave.

MATERIALS AND METHODS

The present analytical observational study was conducted in the Department of Paediatrics, Chettinad Hospital, Chennai, Tamil Nadu, India, from March 2020 to March 2022. The Institutional Ethics Committee had approved the study (IEC number: IHEC-II/0437/22).

The study population included RT-PCR positive COVID-19 children between age groups from one month to 18 years age. The children with incomplete record of data were excluded. First COVID-19 wave was from March 2020 to October 2020, second wave was from April 2021 to September 2021 and third wave was from December 2021 to March 2022 [13,14]. The sample included in the first wave was 103 subjects and 90 subjects in the second wave and 98 subjects in the third wave. The data was collected regarding demographical, clinical symptoms and signs, including daily vital parameters, laboratory measurements, imaging findings, management, and outcome.

All children were monitored for their vitals from admission till discharge and parameters includes temperature, heart rate, respiratory rate and Capillary Refilling Time (CRT). A complete haemogram, CRP,

liver function tests (AST, ALT), D-dimer, serum electrolytes, and urea creatinine at admission is done for all cases and second-line additional tests like Prothrombin Time (PT), Activated Partial Thromboplastin (aPTT), ferritin, Fibrinogen Degradation Products (FDPs) were ordered based on the severity progression of the disease. Ultrasonogram (USG), Computed Tomography (CT) scan and Chest X-ray (CXR) were requested only for children admitted to Intensive Care Unit (ICU) care.

Nasal and throat samples were collected and transported in viral transport media. During the procedure, appropriate Personal Protective Equipment (PPE) for specimen collection was used. Visitors were strictly restricted from entering the sample collection areas. RT-PCR was considered as positive with a Cycle threshold (Ct) value of 36 and below for the E gene and confirmed after RdRp gene detection with recommended SD Biosensor kit for Rotor Gene Q(Qiagen) machine in all the three waves.

In the present study COVID-19 patients meeting any of the following criteria were diagnosed as severe: 1) respiratory distress, higher respiratory rate (age specific criteria as per IMNCI); 2) oxygen saturation $\leq 93\%$ at rest; and 3) Partial pressure of Oxygen (PaO₂)/Fraction of Inspired Oxygen (FiO₂) ≤ 300 mmHg. COVID-19 patients with any of the following criteria were diagnosed as critical: 1) respiratory failure and mechanical ventilation needed; 2) shock; or 3) organ failure and ICU admission needed for monitoring and treatment [15].

Management of the COVID-19 patients was based on the existing guidelines issued by Indian Council of Medical Research (ICMR). On the third defervescence day or after clinical improvement is attained, the study participants were discharged from the hospital. The parents of the children were instructed to report through telecommunication, if there were general red flag signs. Follow-up of the participants and enquiry about the wellbeing was done through a telephonic conversation after 14 days of discharge.

STATISTICAL ANALYSIS

All quantitative variables were inspected for normal distribution. The quantitative variables like age (in years), serum electrolytes like (Na, K, Cl, and HCO₃), etc., were compared between the 3-study groups and reported as mean \pm Standard Deviation (SD) using the Analysis of Variance (ANOVA) test. For non normally distributed quantitative parameters, Interquartile Range (IQR) and Median were compared using the Kruskal-Wallis test. While the categorical variables like gender, symptoms, treatment, etc., were reported as percentages and counted between the three study groups. The test statistic used was Chi-square or Fisher's-exact test. The p-value < 0.05 defined as statistically significant. Statistical Package for the Social Sciences (SPSS) software version 22.0 was utilised for statistical analysis.

RESULTS

A total of 291 subjects were involved in the final analysis. Mean age was slightly less in COVID-19 first wave (p-value=0.621), males were more affected in all the waves compared to females (p-value=0.71). All vitals were reported to be normal in the majority of study participants and no statistically significant difference was found between the three phases. Vomiting, diarrhoea and pain abdomen were reported by a very few participants in all the three waves [Table/Fig-1].

Fever was the predominant symptom reported in all three waves (74.8% in wave 1, 80.6% in wave 2 and 75% in wave 3). On comparison of COVID-19 waves 1, 2, and 3 no significant difference was found in majority of laboratory parameters including D-dimers (p-value=0.338). CRP was non reactive in 84 (81.55%) in phase 1, 76 (84.44%) in phase 2 and 64 (65.3%) in phase 3. The difference in CRP was found to be statistically significant (p-value < 0.05). AST

and ALT levels were found to be higher in wave 3 compared to wave 1 and wave 2 (p-value < 0.05). D-dimer levels were comparable in all three waves [Table/Fig-2].

Parameters	Study group			p-value
	COVID-19 wave I (N=103)	COVID-19 wave II (N=90)	COVID-19 wave III (N=98)	
Age (in years)	9.1 \pm 5.25	9.3 \pm 4.99	9.2 \pm 5.12	0.621*
Gender				
Boys	61 (59.22%)	48 (53.3%)	55 (56.1%)	0.711†
Girls	42 (40.78%)	42 (46.7%)	43 (43.9%)	
Vitals				
Temperature ($< 100.4^{\circ}\text{F}$)	26 (25.2%)	18 (19.8%)	24 (25%)	0.343‡
Normal respiratory rate (age specific)	98 (95%)	86 (96%)	92 (94%)	0.545‡
Normal heart rate (age specific)	98 (95%)	83 (92%)	94 (96%)	0.643‡
Normal Capillary Refilling Time (CRT) (< 3 seconds)	103 (100%)	90 (100%)	98 (100%)	0.763‡
Associated symptoms				
Abdominal pain	1 (0.97%)	0 (0%)	0 (0%)	0.454†
Vomiting	6 (5.83%)	5 (5.5%)	7 (7.1%)	
Diarrhoea	1 (0.97%)	2 (2.22%)	5 (5.1%)	

[Table/Fig-1]: Comparison of baseline parameters at admission between study groups (N=291).

*ANOVA test, †Chi-square test, ‡statistical test was between wave 1 and wave 2

Parameters	Study groups			p-value
	COVID-19 wave I (N=103)	COVID-19 wave II (N=90)	COVID-19 wave III (N=98)	
Blood parameters				
AST (U/L) (n=170)	45 (24,58)	32 (26,25,34)	48 (30,7,56)	0.001*
ALT (U/L) (n=139)	41 (31,52)	32 (32,35.5)	45.5 (29,7,51)	0.020*
D-dimer (ng/mL) (n=31)	234 (190.75,336.5)	281 (221,393.5)	211 (221,393.5)	0.338*
Serum electrolytes				
NA (mEq/L)	139.82 \pm 3.42	139.49 \pm 3.28	140.19 \pm 1.18	0.542†
K (mEq/L)	3.96 \pm 0.48	3.98 \pm 0.48	4.1 \pm 0.32	0.790†
Cl (mEq/L)	104.36 \pm 3.03	104.03 \pm 2.77	102.14 \pm 4.12	0.475†
HCO ₃ (mEq/L)	22.06 \pm 0.83	22.09 \pm 0.85	21.03 \pm 0.73	0.812†
CRP (mg/L)				
Non reactive	84 (81.55%)	76 (84.44%)	64 (65.3%)	0.029§
Reactive	19 (18.45%)	13 (14.45%)	34 (34.7%)	
COVID-19 contact	94 (91.26%)	86 (95.52%)	93 (94.9%)	0.134§
Follow-up/ Complaints (at 14 days)				
Cough	1 (0.97%)	1 (1.2%)	3 (3.1%)	0.725§
Fever	4 (3.88%)	1 (1.2%)	4 (4.1%)	
Asymptomatic	98 (95.15%)	87 (96.7%)	91 (92.9%)	

[Table/Fig-2]: Comparison of laboratory parameters and follow-up between study groups (N=291).

The p-value in bold font indicates statistically significant values. Values are presented as n (%) and mean \pm SD; *Kruskal Wallis test, †Anova test, ‡Chi-square test

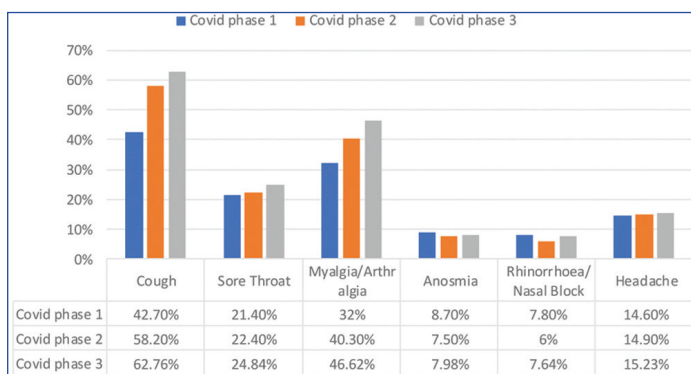
After the follow-up period, majority (95%) had no complaints in wave 1 (95%), wave 2 (97%) and wave 3 (93%). (p-value=0.725) [Table/Fig-2]. Most common presenting symptom in wave 1 (75%), wave 2 (81%) and wave 3 (75%) was fever followed by cough in 42.7%, 58% and 63% in wave 1, 2 and 3, respectively [Table/Fig-3,4].

There was no statistically significant difference in mean duration of any complaints between the waves (p-value > 0.05) [Table/Fig-3,4].

Parameter (in days)	Study groups (Mean±SD)			p-value
	COVID-19 wave I	COVID-19 wave II	COVID-19 wave III	
Duration of fever	2.35±1.14	2.33±1.1	2.2±1.3	0.931
Duration of cough	2.27±1	3.28±1.02	4.2±1.28	0.967
Duration of sore throat	1.55±0.8	1.53±0.83	2.45±0.72	0.965
Duration of myalgia/arthritis	1.79±0.82	1.67±0.73	1.27±0.32	0.553
Duration of rhinorrhoea/nasal block	4.63±0.74	3.5±0.82	4.2±0.23	0.443
Duration of headache	1.33±0.49	1.3±0.48	1.1±0.31	0.868

[Table/Fig-3]: Comparison of mean duration of complaints between study groups (N=291).

Values are presented as mean±SD



[Table/Fig-4]: Clustered bar chart for comparison of presenting complaints other than fever between three COVID-19 waves (N=291).

DISCUSSION

The present study was an attempt to compare the clinical features and outcomes of three waves of COVID-19 infection among children. The most common symptoms in all the three waves were cough, myalgia and fever. Fever was the predominant symptom among it, which was found in 74.8% of wave 1, 80.6% of wave 2 and 75% of wave three patients. This is comparable to a meta-analysis of 7780 youngsters by Hoang A et al., [16]. In a research by Li B et al., the most common clinical symptoms were fever (47%) and cough (42%) [17]. According to Tung Ho CL et al., the majority (59.3%) experienced an usual temperature, with a decreased occurrence of cough, runny nose or throat congestion, and loose stools in the study [18]. In the present study, a very uncommon symptom observed was vomiting. A meta-analysis found that (48%) of cases had fever, and (6% of cases) had diarrhoea and nausea/vomiting [19]. In a retrospective analysis of 26 children, 11 experienced fever and two experienced vomiting [20].

Less severe or mild illness affected over 90% of the children in the present study. This is comparable to the United States (US) database, where 11.7% of the youngsters needed admission [21]. None of the children in the present study required ICU admissions. However this is contrast to other studies which reported considerable proportion of ICU admissions for further management. In the Madrid research, in which 10% of their youngsters required ICU admission [22]. There was a larger proportion of infants requiring ICU hospitalisation (20.7% vs 14%), which was similar to a Chinese study where a higher proportion of infants had severe and critical disease [23].

No complications were reported by the study populations during the follow-up period in all three waves. In previous studies Multisystem Inflammatory Syndrome (MIS-C) has been reported [12,24,25]. In another study, more children were diagnosed with MIS-C in the first wave than in the second wave (2.2% vs 0.25%) [12].

Limitation(s)

The study comes from a single multispecialty tertiary care facility, which makes it susceptible to referral bias. There probably would have been a more severe end of the COVID-19 disease spectrum and more comorbidities. Smaller sample size, non inclusion of asymptomatic patients was other pitfalls.

CONCLUSION(S)

The severity of clinical presentation of COVID-19 in children was mild, and the outcome was generally good. Fever cough and myalgia were chief complaints of the study participants. There were no complications reported during the follow-up period, including mortality and ICU admissions. Hence, the study found that the three COVID-19 waves did have a considerable difference in clinical findings and short-term outcomes among COVID-19 affected children.

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