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Clinico-etiological profile of COVID- 19 positive paediatrics patients in a tertiary care hospital: A retrospective study

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***Abstract*---**With the sudden outbreak of corona virus pandemic in 2019, there is a paucity of data on the clinical and epidemiological profile of COVID positive paediatric patients. Objective of the study was a retrospective analysis of clinico-etiological profile of COVID-19 paediatric patients admitted to a tertiary care centre Karad. A retrospective cross-sectional study was conducted in the Paediatric Department of tertiary care hospital Krishna Institute of medical sciences deemed to be university, Karad, from 22 March 2020 till 30 November 2020. A total of 154 children were enrolled. Among neonates, all were born to COVID-19 positive mothers and were asymptomatic and SARI in children less than 1 year (excluding neonates) (33%) and in the 1-5 years age group (15.8%). In children more than 5 years, acute febrile illnesses were the main admitting diagnosis (27.5%). Asymptomatic children (33.7%) dominated the COVID19 positive group. The most common symptom included fever (35.7%) with no reported mortality. Atypical symptoms (64.3%) were more common than respiratory symptoms. The majority of children had mild COVID-19 symptoms (67%). The unusual presentation of COVID-19 was in the form of diarrhoea (9.7%) in the symptomatic group. The majority of children infected with COVID-19 were infected through family clustering, were asymptomatic, and had minor symptoms with a favourable prognosis. In rare circumstances, a strong suspicion of COVID-19 associated multisystem inflammatory syndrome should be kept in mind for early identification.

***Keywords*---**COVID-19, SARS-CoV-2, risk factors, severity, clinico-etiological profile, asymptomatic patients.

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Introduction

Corona virus disease 2019 (COVID-19) is a pandemic that originated in Wuhan, China in December 2019 and then spread globally. Despite the terrible implications of COVID-19 infection, it is more of an adult disease than a childhood illness, as evidenced by the documented number of cases globally. On the 3rd of January 2020, the Chinese Centre for Disease Control and Prevention confirmed that the disease is caused by a novel member of enveloped RNA corona virus.The name of this novel corona virus has been formally proclaimed as "Severe Acute Respiratory Syndrome Corona virus 2" by the International Committee on Virus Taxonomy (SARS-CoV-2).The sickness caused by SARS-CoV 2 has been dubbed Corona Virus Disease 19 by the World Health Organization (WHO) (COVID-19). Despite the terrible implications of COVID19 infection, it is more of an adult disease than a Juvenile sickness, as evidenced by the documented number of cases globally. The disease affects all age groups and its spectrum varies from mild fu-like illness to severe pneumonia with complications like acute respiratory distress syndrome (ARDS), shock, multiorgan dysfunction, myocardial injury and acute kidney injury (AKI) [1]. Worldwide surveillance data have reported children typically to account for 13 percent of laboratory-confirmed cases. Herein, we will be reviewing the characterisation of COVID-19 infections in the Paediatric age group.

Mode of transmission

The first infections were tracked to China's Huainan Seafood Market, and were largely caused by animal interaction. The virus is transmitted between humans through respiratory droplets. However, as demonstrated by a study evaluating the aerosol and surface stability of SARS-CoV-2, the authors investigated the survivability of the virion particles on various surfaces, including stainless steel, plastic, cardboard, and copper, as well as in aerosol particles (5 μm). It was found that the virus remains viable in aerosol particles for up to 3 hours with a median half-life of 1.2 hours. The virus is more stable on plastic and stainless- steel surfaces than on copper and cardboard. The viability of the virus was found to be up to 3 days on plastic and stainless-steel, 24 hours on cardboard, and 4 hours on copper surfaces. Direct contact is another source of virus transmission via touching the mouth, nose or conjunctiva with contaminated fingers. Feco-oral transmission could be an alternative route of transmission as several studies have reported positive stool samples, even after nasopharyngeal/throat swabs were COVID-19 negative.

Pathogenesis

SARS-CoV-2 is primarily a lung pathogen. The attachment of S protein to angiotensin-convertingenzyme 2 (ACE2) receptors facilitates its entry into the lung, which may be the same as SARS-CoV-2, which also enters cells via ACE2 receptors[26.] Moreover, it uses the host Transmembrane protease serine 2 (TMPRSS2) for S protein priming and fusion of viral and host cell membranes. ACE2 receptor binding can be shown by two lines of evidence: (1) sequence analysis of the receptor binding motif, which is the part of receptor binding

domain hat comes into direct contact with ACE2 receptor, which has revealed extensive similarities between SARS-CoV and SARS-CoV-2, and
(2) The blockade of SARS-2-S driven cell entry by using human ACE2 antisera.

Diagnostic tools

- Laboratory diagnosis
  The real-time reverse transcriptase-polymerase chain reaction (RT-PCR) test is the gold standard for SARS-CoV-2. It is thought to be highly specific, with a sensitivity of 91 percent [95 percent CI: 83-97 percent] reported for first RT-PCR. RT-PCR sensitivity has been found to be as high as 95-97 percent in other studies.
- Radiology
  Chest radiography is the first-line imaging modality utilised to scan patients with suspected COVID-19, although being less sensitive than chest computed tomography (CT). Consolidation or ground-glass opacity (GGO), which is more often bilateral and peripheral, and has lower zone predominance, is among the anomalies. Lung ultrasonography may also be beneficial in the evaluation of COVID-19 patients who are critically unwell. The use of CT radiological results to diagnose or test for COVID-19 has sparked debate. CT findings were not included in the diagnostic criteria for COVID-19, according to an American-Singaporean panel. Others, on the other hand, have employed CT findings as a surrogate diagnostic test.

Aim and Objective

Aim and objective of the study was to evaluate clinic- etiological profile of hospitalized COVID-19 positive paediatric cases, admitted in the Paediatric Department of tertiary care hospital Krishna Institute of medical sciences deemed to be university, Karad, from July 2021 till 7th January 2022.

Methods

This was a retrospective cross-sectional study, conducted in the Paediatric Department of tertiary care hospital, Krishna Institute of medical sciences deemed to be university, Karad, during the lockdown period from July 2021 till 7th January 2022. The sample size was selected based on the total admissions that took place in the Paediatric department during the study period. 324 paediatric patients who were admitted to the hospital during this time period had their medical records reviewed, and those who met the following inclusion criteria were enrolled in the study: Children aged 0-14 years who arrived in a paediatric emergency, were admitted and hospitalised for at least 24 hours, and those who left hospital against medical advice were suspected COVID-19 hospitalised paediatric patients.Any of the following were considered admission criteria for probable COVID-19 illness: respiratory distress, SpO2 94% on room air, shock/poor peripheral perfusion, low oral intake or lethargy, convulsions or encephalopathy [9, 10]. Further, presence of co morbidities and/or age <1 yr in COVID-suspect children were other indications for admission.

The children with COVID19-suspected illness and requiring admission were shifted to suspected COVID 19 ward from emergency. The RT-PCR sample for novel COVID-19 virus was sent at admission in accordance with WHO guidelines9. Some children from non-COVID areas of the hospital were also screened for COVID-19 illness, if they developed suspicious symptoms after admission, came from containment zones/hotspots or had a history of contact with COVID-19 cases (undisclosed before). Based on the results of confirmatory RT-PCR and clinical assessment, hospital treatment or home isolation measures were instituted with contact tracing measures as applicable (in accordance with the local prevailing guidelines). The children who had a positive COVID-19 test and met the admission requirements were transferred to the COVID ward. Patients were initially assessed based on their appearance, respiration, and circulation after admission, and were then classified as stable, unstable and not life threatening, or unstable with life threatening disorders. Patients with confirmed COVID-19 were also classified as having mild, moderate, or severe disease, according on the severity of their admitting complaints. At the time of admission, temperature, oxygen saturation, and other vitals were documented. The baseline studies were completed after a thorough history and examination. COVID-19 RT-PCR was performed on throat and nasal swabs in patients with severe acute respiratory infections (SARI).

According to WHO recommendations, SARI is characterised as a temperature (>38 °C), cough, and increased labour of breathing that requires hospitalisation. Eligible candidates for COVID-19 testing were chosen in accordance with timely criteria given by the Indian Council of Medical Research (ICMR), Department of Health, Government of India, which were updated as the COVID-19 situation in India and hospital testing policies changed. Patients who were admitted were treated according to regular procedures. The patients were subjected to investigations including complete blood count, serum biochemistry (liver and kidney function test, electrolytes), and chest radiograph. The coagulation profile, arterial blood gases, markers of inflammation including C-reactive protein, procalcitonin, serum ferritin, and CPK-MB were evaluated in those with severe COVID. All the patients were managed as per the standard WHO protocol [9].

Paracetamol for fever control and intravenous or oral fluids to maintain adequate hydration and to maintain fluid electrolyte balance was administered as required. Early initiation of nutrition was also considered in non critically sick children. The patients developing respiratory distress or hypoxemia on room air were given oxygen whenever indicated as per the prevailing guidelines. n situations of suspected sepsis or shock, empirical antibiotics were given and the patient was managed according to the Surviving Sepsis Campaign Guidelines [11]. Children with multisystem inflammatory syndrome (MIS-C) were treated with intravenous immunoglobulin (IVIG) and methylprednisolone, as recommended by the Centres for Disease Control and Prevention (CDC). Clinico etiological profile and outcome of the patients were documented. Statistical analysis for the study period, the variables of interest was extracted manually by the study authors. For the first dataset, relevant data was entered into a Microsoft Excel (version 2013) spreadsheet. Following that, standardised response codes for all variables were generated in order to arrive at the final data set that was used for statistical analysis using SPSS version 23.0. (IBM, USA). Patient confidentiality was

preserved by the use of anonymised data with unique identifiers and a password-protected dataset with limited access.

Results

A total of 154 children, that were admitted in the paediatric department of our hospital, during this time period were enrolled in the study. Table 1 shows the demographic profile of hospitalised paediatric patients over the study period. As compared to 2019, (480 paediatric emergency admissions during 2019), the hospitalization rate dropped to around 50% in lockdown period. Majority of admitted children had unstable and not life-threatening medical condition at the time of admission (64.6%). Among neonates, all were born to COVID-19 positive mothers (5.8%) and were asymptomatic, as shown in Table 1. The clinical features of children of all other age groups (excluding neonates) are shown in Table 2. SARI was the most common diagnosis at the time of admission among children under the age of one year (excluding neonates) and children aged one to five years (33 percent and 15.8%, respectively). At discharge, majority of admitted SARI cases in children less than 1 year (7.3%) and more than 5 years (10.3 %) had pneumonia (both bacterial and viral), however in children of age group between 1-5 years, diarrhoea was the main diagnosis. In all age groups years, acute febrile illnesses, were the main presenting diagnosis, among which dengue fever was predominantly seen during the study period (8.4%).With respect to COVID-19 testing, initially all suspected cases were evaluated by the RT-PCR method.

Among the tested children154 were found to be positive. The clinical characteristics of COVID-19 positive hospitalized paediatric patients are shown in Table 2. Almost one-third (33.7%) of the tested children were asymptomatic, had normal chest X-ray and were home quarantined with close supervision of any danger signs. Among the symptomatic patients (66.6%), the most common symptoms include fever with body temperature ranging from 37.3 to 40°C (41%). Atypical symptoms were more common than the respiratory symptoms, such as acute diarrhoea, altered sensorium, and abdominal pain. Overall, majority of hospitalized COVID-19 positive children had mild symptoms with a benign course and a decent recovery. As far as the treatment was concerned, all symptomatic children with normal chest X-ray were given supportive therapy and atypical cases given the established evidence-based care with no antiviral therapy or steroids given to any of them. Severe respiratory complications were rare in the paediatric COVID-19 positive patients. Only one child, aged four, was admitted to the hospital in a state of shock, requiring ionotropes and ventilator support.

The affected youngster experienced no serious respiratory issues as a result of COVID, but became critically ill when the underlying core illness worsened. One COVID positive children had diabetic ketoacidosis and had acute renal failure further requiring renal replacement therapy. Both of these children were treated and discharged with full recovery. In the neonatal age group, a preterm baby born at 34 weeks to a COVID-19 positive mother was admitted with neonatal respiratory distress (distress resolved within 48 hours of admission) and had a positive COVID-19 RT-PCR. With limited breathing support and intravenous antibiotics, the baby recovered and was treated conservatively due to a negative septic workup and a normal chest X-ray. As far as the outcome of the admitted

children was concerned, Table 3 shows that, out of 154 children, a substantial proportion got discharged (98%), 2% children who took DAMA (discharge against medical advice), and there was no mortality COVID-19 cases that was reported in this timeframe in our hospital.

Discussion

Although there is a vast amount of information for adult COVID-19 patients, our knowledge of the clinical characteristics and epidemiology of COVID-19 in children is limited. We conducted a retrospective study of COVID-19 positive children under the age of 14 who were admitted to the Paediatric Department of the tertiary care hospital Krishna Institute of medical sciences declared to be university, Karad, between July 2021 and January 7th, 2022, in order to assess the clinico-etiological profile of hospitalised paediatric patients.. Our paediatric emergency hospitalizations decreased by 50% as a result of the lockdown limitations. As the Government of India loosened the restrictions on lockdown, the strain on the health-care system increased. In a resource-constrained underdeveloped country, the COVID-19 outbreak was difficult to contain. Limited health-care facilities and a large vulnerable population, many of whom were already suffering from comorbid diseases,caused problems on all fronts. The majority of the kids were either asymptomatic contacts or had minimal signs of fu. Fever was the most prevalent symptom, followed by cough and rapid breathing, but many people also had gastrointestinal issues. A large number of children needed to be admitted to the hospital due to co-morbidities and acute illness.

Notably, children under the age of one year are still the most vulnerable and frequently hospitalised age group, necessitating the highest level of healthcare provider attention throughout the COVID-19 epidemic. As demonstrated in Table 2, respiratory infections and are the most common diagnoses for children under the age of five, while acute febrile illnesses are the most common reason for hospitalisation in children beyond the age of five. The majority of children with COVID19 were infected through familial clustering and had no symptoms (33.3%), which was similar to Wu et al's findings in adult patients and lower than Zimmermann et al's findings.8, 9.The age-dependent expressions of ACE2, which are lower in younger children and rise with age, appear to be the reason for the lower risk of symptomatic infection in children. COVID-19 is less symptomatic in children due to lower ACE2 expression than in adults. 10 In paediatric patients, the most common clinical symptom was fever with few concomitant illnesses and minimal serious consequences, which was similar to that seen in adult patients, as reported by Guan et al.11.

In contrast to the available literature on ventilation in SARS-CoV-2 [24], a higher proportion of children in the present study required oxygen and CPAP support. Whether the COVID-19-associated multisystem inflammatory syndrome resulted in such a presentation, as reported by Kosmeri et al, or whether the child had a pre-existing hypercoagulable condition is a topic of debate that will require further research in the future.12 Nevertheless, in severe presentation of COVID-19, a high suspicion of COVID-19 associated multisystem inflammatory syndrome need to be kept in mind for intensive monitoring, to prevent severe complications

in the affected children. Also, 9 neonates being infected with SARS-CoV-2, after the mother being tested with COVID-19 showing that irrespective of insufficient evidence of vertical transmission, there is definitely a high neonatal risk of SARS-CoV-2 infection if a mother contracted this virus during the pregnancy.3 out of 33 infants born to pregnant mothers infected with SARSCoV-2 were diagnosed with COVID-19, according to a study published by Zeng et al. Unlike Dong et al., who examined the severity of sickness by age and concluded that young children, particularly newborns, are more prone to SARS-CoV-2 infection and have more severe disease, the severe presentation was seen in children over the age of 5. 14 The overall good prognosis of COVID-19 positive children with no mortality resembled the findings reported by Wu et al.8 Only SARI cases were chosen for COVID-19 testing, according to guidelines given by the ICMR, Ministry of Health and Family Welfare, India, which could explain why only symptomatic patients or patients in contact with a COVID-19 positive close family member were tested throughout the study period. Ideally, COVID-19 testing should be done in all cases presenting with fever, diarrhoea and other systemic features as COVID-19 has variable and atypical presentation in paediatric population. Also, since inflammatory markers such as serum ferritin, LDH and d-Dimer levels were available, we could categorise the COVID-19 cases into mild, moderate and severe presentation based on the levels of inflammatory markers and treated accordingly.

Conclusion

The lockdown period witnessed 50% reduction in paediatric emergency hospitalization of our tertiary care hospital (dedicated COVID-19 health centre). During this epidemic, non-COVID-19 patients under the age of one year demand the most continuing monitoring. At the time of testing, the majority of COVID-19 positive paediatric patients were asymptomatic, with fever being the most common presenting symptom in the symptomatic group. Our institution, like the rest of the world, saw a lot of moderate COVID-19 child patients. Whether COVID-19 is linked to hypercoagulable states in children is a subject of debate that will require more research in the near future. However, to avoid the severe consequences of COVID-19 related multisystem inflammatory syndrome in children, early suspicion and intensive monitoring are essential. With that considered, considering the predominance of mild COVID-19 presentations in children, it is clear that we cannot relax the severe close monitoring of hospitalised paediatric patients in this pandemic.

Table 1
Demographic profile of hospitalized paediatric patients

Sex distribution Male	n 91	% 59
Female	63	41
Age group distribution (years) Neonates	9	5.8
Less than 1 (excluding neonates)	14	9

1-5	55	35.7
More than 5	76	49.3
Triaging at admission Stable	129	83.7
Unstable and not life threatening	23	14.9
Unstable and life threatening	2	1.2

Table 2
Etiological diagnosis of hospitalized children (excluding neonates)

	Less than 1 yr	1-5 yr	>5 yr
SARI	18 (33)	10 (15.8)	8(27.5)
Fever	22 (41)	15 (23)	18(62)
Pneumonia	4 (7.3)	6 (9.5)	3(10.3)
Severe anaemia	1 (1.8)	3 (4.7)	2(6.8)
Diarrhoeal illness	4 (7.5)	10 (15.8)	2(6.8)
Dengue fever	0 (0)	8 (12.6)	4(13.7)
Seizure disorder	5 (9.4)	1 (1.5)	2(6.8)
Meningitis	1 (1.8)	2 (3.17)	0 (0)
Asymptomatic	20 (37.7)	24 (38)	7(24.1)

Table 3
Outcome of the hospitalized paediatric patients

Complications	(N=154)	%
Acute respiratory distress syndrome	34	22
Myocarditis	5	3.2
Shock requiring vasoactive support	2	1.2
Maximal respiratory support Oxygen	84	54
NIV (CPAP)	28	18
Mechanical ventilation	4	2.5
Renal replacement therapy	1	0.6
Discharged	151	98
Referred	0	0
DAMA	3	2
Mortality	0	0

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