

A study on risk factors and disease profile with analysis of prescription pattern in post Severe Acute Respiratory Syndrome-Coronavirus 2 infection among Pediatric population

Saba Farheen¹, GuruPrasad C¹, Sachhidananda R Adiga¹, Ammar Fadhl¹, Ashik Jose,¹ Vipin Babu¹, Dr.Basavanna P L², Dr.Rajendra Kumar³, Dr.Sudha RudrappaL⁴,

¹Pharm-DIntern, Sarada Vilas College of Pharmacy, Mysuru

²Professor and Head, Department of Pharmacology, Mysore Medical College and Research Institute, Mysuru

³Associate Professor, Department of Pediatrics, Mysore Medical College and Research Institute, Mysuru

⁴Medical Superintendent, Department of Pediatrics, Mysore Medical College and Research Institute, Mysuru
Corresponding Author: Dr. Basavanna P.L

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ABSTRACT: Coronaviruses (CoVs) are a wide family of zoonotic RNA viruses that are enclosed and single-stranded. CoVs have the ability to rapidly mutate and recombine, resulting in unique CoVs that can be transmitted from animals to humans. In 2002, the novel CoVs severe acute respiratory syndrome coronavirus (SARS-CoV) and Middle East respiratory syndrome coronavirus (MERS-CoV) developed, and in 2012, the novel CoVs Middle East respiratory syndrome coronavirus (MERS-CoV) emerged. The 2019 new coronavirus (SARS-CoV-2) is now producing a serious disease outbreak (titled COVID-19) across the globe, posing a worldwide pandemic risk. CoVs primarily induce respiratory and gastrointestinal problems in humans. Clinical signs range from a simple cold to more serious illnesses such as bronchitis, pneumonia, and Acute respiratory distress syndrome, multi-organ failure, and even death are all possible outcomes. SARS-CoV-2 appear to infect children less frequently than adults, and to cause fewer symptoms and less severe disease in this age group, as well as lower case fatality rates. Children are just as likely as adults to become infected with SARS-CoV-2, but they are less likely to be symptomatic or develop severe symptoms, according to preliminary findings. However, the role of children in the virus's transmission is unknown. When compared to adults, children suffer more Pulmonary issues. The majority of children infected with SARS-CoV have a fever, but this is not the case with the other new CoVs. Many children infected with MERS-CoV show no signs or symptoms. The majority of

children infected with novel CoVs have a recorded household contact, and many of them exhibit symptoms before they become infected. Adults, on the other hand, are more likely to be exposed in a hospital setting. We describe the risk, clinical symptoms, and treatment options for prevalent and novel CoVs infections in humans, with a focus on infections in children, in this article.

KEYWORDS: Coronavirus(CoV), severe acute respiratory syndrome coronavirus(SARS).

I. INTRODUCTION

According to the European Union (EU) and India, the paediatric population is defined as group of population between birth and 18 years of age. The paediatric population has several subsets. Present age classification is as follows

- preterm newborn neonates: from day of birth through the expected date of delivery plus 27 days;
- term and post-term neonates: from day of birth plus 27 days;
- infants (or toddlers): from 1 month (28 days) to 23 months;
- children: from 2 years to 11 years; and
- adolescents: from 12 years to less than 18 years.

However, in US paediatric patients are classified into broader categories up to 16 years only, which are:

Neonates are 0 to 1 month; infants are 1 month to 2 years; children are 2 to 12 years; and adolescents fall under age groups 12 to 16 years.

Coronavirus disease 2019 (COVID-19) is an illness caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), which has

resulted in global healthcare crises and caused morbidity and mortality at an unprecedented scale globally.

Throughout the world, fewer cases have been reported in children. Most cases in children are mild, and treatment consists of supportive care. Children who have a history of medical complexity (e.g., due to neurologic impairment, developmental delays, or genetic syndromes including trisomy), obesity, chronic cardiopulmonary disease, or who are immunocompromised.^[3]

Dexamethasone was recommended by the COVID-19 Treatment Guidelines Panel for hospitalized children with COVID-19 who require oxygen therapy or treatment. And Remdesivir was recommended by the FDA for only Hospitalized children aged above 12 years with COVID-19 who have risk factors for severe disease have an increasing need for supplemental oxygen regardless of whether they have risks factors for severe disease.

Symptoms of COVID-19 are nonspecific with asymptomatic or mildly symptomatic to severe pneumonia and death.^[4] Covid 19 is considered milder disease in children and some asymptomatic cases, but with evidence of radiological lung changes. The Report of the WHO-China Joint Mission on COVID-19 stated that 2.5% of the cases among those under 19 years old were severe and 0.2% were critical. Although with limited and missed evidence it was suggested that children with underlying conditions are at greater risk of infection or more severe disease.^[1]

Common symptoms include - fever, cough, breathlessness, shortness of breath, fatigue, myalgia, rhinorrhea, sore throat, diarrhea, loss of smell, loss of taste etc. and also may have many non-specific symptoms, and few were having symptoms like only upper respiratory symptoms or only gastrointestinal symptoms.^[5] It was also observed that the signs and symptoms of COVID-19 in children are similar to those of other infections and noninfectious processes, including influenza, streptococcal pharyngitis, and allergic rhinitis, and also a new syndrome named multi system inflammatory syndrome (MIS-C) has been described in children with epidemiological linkage to SARS CoV-2.^[2]

Because there are no specific signs or symptoms and most cases reported were asymptomatic. The screening for identification of SARS-CoV-2 based on symptoms was challenging. Apart from that it was also observed in some recent studies, children with severe COVID-19 may

develop respiratory failure, coagulopathy, myocarditis, diabetic ketoacidosis, acute renal failure, shock, intussusception and multi-organ system failure.

The hospital burden was also high in cases of children who are hospitalized as it was a burden on the whole family, as once the child is admitted or known to have Covid-19, the whole family had to be extra cautious and it affected the family even emotionally. Economic burden was also observed to be high when compared to only one adult being suffering while in the case of children the complete family was required to take care the patient.

As we have observed from previous data very few paediatric cases of COVID-19 have been reported. We have limited pathogenesis and clinical spectrum data and very little is known about the epidemiology in children. Our study is aimed to understand the infection rate based on symptoms, clinical presentation, clinical outcomes, difference between other similar diseases and transmission dynamics of SARS-CoV-2, in order to inform clinical and public health measures.

We have also noticed that there is no paediatric data from placebo-controlled randomized clinical trials and very limited data from observational studies which can help in recommending a specific treatment for COVID-19. We have observed that a systematic study of followup after recovery from acute COVID-19 is needed. It was also noted that there is limited evidence about which underlying medical conditions in children might increase the risk for severe illness.

Hence this observational study was conducted to understand the age group that is getting affected most and the time duration required for different age group of paediatric to get back to normal post covid and also understand and evaluate the socio economic burden on the families of the affected age groups

II. NEED FOR THE STUDY

To develop a more comprehensive description of complications linked to post covid-19, by conducting systematic observational study on its symptoms, analysis of prescription pattern and prognosis. As Children are on verge of getting infected with SARS-CoV-2 and with no vaccination yet, it was important to analyse the complications linked with covid-19 in children.

III. RESEARCH METHOD

Research Ethic

The study protocol was approved by the Institutional Ethical Committee, MMC&RI Mysore. The research has been carried out in compliance with the ethical principles outlined in the Declaration of Helsinki of 1964 and its subsequent modifications.

Study Site:

The study was conducted in Cheluvamba Hospital attached to Mysore Medical College and Research Institute(MMCRI), Mysore

Study Design

The study was a Prospective observational study and was carried out from May until September 2021.

Study Population and Sample Size Determination

The study was carried out among sample population presented to Cheluvamba hospital in Mysuru taluk. A total of 149 patients were included in the study. Out of which 17 patient's data were incomplete, 6 patients didn't give the consent for the study and 34 subjects didn't meet the study requirements. As a result, they were deemed ineligible for the study due to the study's requirements. The study enlisted 92 patients as per the inclusion criteria.

Inclusion criteria:

1. Patient of age < 18 years
2. Patient who has tested positive for RT/PCR Covid-19
3. Patient admitted or discharged with case data in pediatric ward.

Exclusion criteria:

1. Patients whose data is incomplete.

2. Patients who are not ready to cooperate and not willing to participate

Instrument for data collection

Data collection was carried out in two phases. In first phase data were collected through medical records of the patient. The observations were recorded in both paper CRF as well as electronic-CRF(Excel). In second phase patient's parents/legal guardians were interviewed for pharmaco-economic data and recorded the

Study protocol and Informed consent

Each patient and their parents/legal guardian were approached and the purpose of the study was explained. The consent of the subject was taken for their inclusion in the study and subjects cooperation and participation was overwhelming.

Data Analysis

Statistical analysis and descriptive analysis were carried out using IBM SPSS Software for Windows version 22

IV. RESULTS

From table 1 the mean age of the patients were 8 years 1 month with SD of 5.88 and age group of children and adolescents were tend to be affected frequently with covid-19 infection with frequency of 36(39.10%) and 29(31.50%) respectively. Proper covid protocol were followed in case of neonates and infants which resulted in less frequency of infection.

Age Group Classification	FREQUENCY
Neonates (birth to 1 month)	10 (10.9%)
Infants (1 month to 2 years)	17 (18.5%)
Children (2 to 12 years)	36 (39.1%)
Adolescents (12 years to 18 years)	29 (31.5%)
Total	92 (100%)

Table 1: Age group classification

From table 2 and 3 it demonstrates that out of 92 patients, 59 (64.1%) were boy and 33 (35.9%) were girl. The patients age ranged from 1 - 18 (in years). The patient gender data only revealed the twice the number over girl's population in the overall covid infected sample population. The maximal number of subjects affected with Covid-19 infection were in children(2-12years) age

group in which boys tend to get more affected for the same (n=25)

The mean length of stay in the hospital isolation ward was 8.64 ± 3.73 days, with a median of 8 days. Half number of sample population were subjected for treatment in hospital for 5-10 days (n=46), while 31.5%(n=29) were stayed 10-15days in hospital for better patient care

GENDER	FREQUENCY
BOY	59 (64.1%)
GIRL	33 (35.9%)
Total	92 (100%)

Table 2: Gender Distribution

Table 3: Duration of hospital stay along with Economic burden

AGE GROUP	GENDER		TOTAL
	BOY	GIRL	
NEONATES (BIRTH TO 1 MONTH)	7	3	10

DURATION OF HOSPITAL STAY		ECONOMIC BURDEN		
		BOTH	DIRECT COST	INDIRECT COST
0 - 5 DAYS	17(18.5%)	9	3	5
11-15 DAYS	29(31.5%)	18	6	5
6-10 DAYS	46(50%)	32	8	6
TOTAL		59(63.1%)	17(18.5%)	16(17.4%)

INFANTS (1 MONTH TO 2 YEARS)	11	6	17
CHILDREN (2 TO 12 YEARS)	25	11	36
ADOLESCENTS (12 YEARS TO 18 YEARS)	16	13	29
Total	59	33	92

Table 4: Age Group with gender distribution

Economic constraints	Yes	No
Is there any Economic burden	87(94.6%)	05(5.4%)
Was treatment funded by Government	72(78.3%)	20(21.7%)
Was amount reimbursed	63(68.5%)	29(31.5%)

Table 5: Pharmacoeconomic data

From table 3 and 4 The mean length of stay in the hospital isolation ward was 8.64 ± 3.73 days, with a median of 8 days. Half number of sample population were subjected for treatment in hospital for 5-10 days (n=46), while 31.5%(n=29) were stayed 10-15days in hospital for better patient care

When we analyzed the cost of 92 COVID-19 patients who received health care services in hospital wards, we identified the economic burden

were due to cost item of bed charges followed by laboratory tests, medications, interventions, imaging tests, medical supplies and outsourced physician costs, and only 68.5% total cost was reimbursed through various government scheme and policy insurance. A total of 94.6%(n=87) patients were reported with economic burden in which 78.3% patients got advantage of treatment funded by government under Ayushman bharath scheme.

From table 5, out of 92 patients reported to the hospital with illness 88%(n=81) were of symptomatic to covid19 infection, were 11.9%(n=11) subjects presented covid19 infection asymptotically and only diagnosed after routine

check-up done on admission and 89.1%(n=82) of them were newly infected followed by 10.8%(n=10) of the sample population were previously diagnosed with covid19 infection.

Pharmacovigilance data	Reported	
	YES	NO
Adverse Drug Reactions(ADRs)	03(3.3%)	89(96.7%)
Drug interactions	11(1.9%)	81(88.0%)
Adverse Events	02(2.2%)	90(97.8%)
Medication Error	03(3.3%)	89(96.7%)

Table 6: Pharmacovigilance data

Covid Signs	Yes	No
Fever	81(88%)	11(11.9%)
Myalgia	58(63%)	34(36.9%)
Cough	52(56.5%)	40(43.5%)
Cold	55(59.8%)	37(40.2%)
Dyspnea	31(33.7%)	61(66.3%)
Vomiting	16(17.4%)	76(82.6%)
Sore throat	52(56.5%)	40(43.5%)

Table 7: Frequency of Signs presented by Covid19 infected Children

From table 6 it was observed that only 2.7% error from the healthcare workers were reported during the treatment protocol given to the covid19 infected sample population and good pharmacovigilance practice were followed while giving at most care for the patient health. In spite of higher workload, psychological distress and social exclusion/stigmatization 94% of patients were tend to experience a good medical practice from the hospital staffs and administration.

From table 7 it was observed that the incidence of severe COVID-19 was higher in boys than in girls (64.1%), The most common symptom was Fever (88.0%) in severe COVID-19 patients,

Myalgia being second (63.0%), followed by cold (59.8%).1/3rd of the sample population experienced dyspnoea which were treated symptomatically with O2 supplementation. A total of 191 complications were reported out of which Multisystem Inflammatory Syndrome in children were more in number (29.3%, n=56), followed by pulmonary complications (24.1%, n=46). Beyond these complications, it was observed that most of the covid19 infected children population presented with newly diagnosed Neuropsychiatric complications (19.9%, n=38) for which the effective measures have been taken to curb down its worsening.

COMPLICATIONS	FREQUENCY
CARDIOVASCULAR	08 (4.2%)
GASTROINTESTINAL	06 (3.1%)
HEMATOLOGICAL	11 (5.7%)

NEPHROLOGICAL	08 (4.2%)
ORTHOPEDIC	02 (1.0%)
MIS-C	56 (29.3%)
NEUROLOGICAL	16 (8.4%)
PSYCHIATRY	22 (11.5%)
PULMONARY	46 (24.1%)
NO COMPLICATIONS	08 (4.2%)
OTHERS	08 (4.2%)
TOTAL	191 (100%)

Table 8: Frequency of Signs presented by Covid19 infected Children

From above table a total of 191 complications were reported out of which Multisystem Inflammatory Syndrome in children were more in number (29.3%, n=56), followed by pulmonary complications (24.1%, n=46). Beyond these complications, it was observed that most of the covid19 infected children population presented with newly diagnosed Neuropsychiatric complications (19.9%, n=38) for which the effective measures have been taken to curb down its worsening.

V. DISCUSSION

Our study population exhibited a significant incidence rate of Multisystem inflammatory syndrome in children (MIS-C) when compared to previous published research. Fever was the most prevalent symptom observed in this study, followed by cold and cough. Out of 92 population included in study sample, the risk of covid 19 and complications were found more frequent in boys (n=59) than in girls (n=33).

The Pharmacovigilance data has showed only 2.7% discrepancies from a prescription analysis which was addressed on time with at-most care. The Pharmacoeconomic data revealed 94.6% population suffered from economic burden due to healthcare facilities of covid19 management

Prevention from getting infected to Covid is of prime importance and need of an hour as COVID-19 vaccines are yet to be authorized by Ministry of Health and Family welfare to be distributed on a wide scale for pediatric population immunization. Government experts are finalising a list of comorbidities that will set the stage for

making children in India eligible to take the Covid-19 vaccine, for which paediatrician's clearance could be required to take the anti-Covid shot.

VI. CONCLUSION

Because of the fact that severe COVID-19 sickness is uncommon in children, the majority of the COVID-19 pandemic has been focused on adult COVID-19 disease. Throughout the pandemic, the children voice has mainly gone ignored. However, the COVID-19 pandemic and mitigation attempts have had an impact on many aspects of child health. School closures and other social distancing tactics disproportionately impacted vulnerable children from low-income households, with troubling consequences for children's mental health. Overall, the social distancing strategies resulted in a significant reduction in acute illness in children, providing insight into how we can minimise the burden of childhood disease in the future. Furthermore, there has been no strong indication that the COVID-19 pandemic led in a shift in health-seeking behaviour, resulting in a high number of children presenting late with serious illness. Children's vaccination programmes are expanding, helping to reduce COVID transmission in the community and preventing cases of severe COVID-19, MIS-C, or extended Covid in children.

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