

Current Management of Children with COVID-19 in Hospitals in India; Pilot Study and Findings

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Abstract

Introduction: To date, the focus on COVID-19 among children, especially in low- and middle-income countries, has been to address key issues including poor vaccination rates. However, the focus is changing with new variants and concerns regarding the development of hyperinflammatory syndromes. There have also been concerns with the overuse of antibiotics to treat patients with COVID-19, with the Indian Government developing guidelines, including those for children, to improve patient care. Consequently, a need to document the current management of children with COVID-19 in India and use the findings for future guidance. **Materials and Methods:** Pilot study assessing the management of children with COVID-19 among five hospitals in India using purposely developed case report forms, which had been piloted in Bangladesh. **Results:** Low numbers of children in hospital with COVID-19 (11.9% of in-patient beds). The majority were boys (58.3%) and between 11 and 18 years (55.5%). Reasons for admission were in line with previous studies and included respiratory distress/breathing difficulties. 69.4% of children with COVID-19 were prescribed antibiotics empirically, typically those on the Watch list, and administered parenterally, with only limited switching to oral therapy. A minority were prescribed antimalarials, antivirals and anti-parasitic medicines. There was appreciable prescribing of immune boosters and steroids. **Conclusion:** It was encouraging to see low hospitalisation rates. However, concerns with high empiric use of antibiotics and limited switching to oral formulations need to be addressed potentially, by instigating antimicrobial stewardship programmes. Similarly, other antimicrobials where these are not recommended.

Keywords: Antimicrobials, children, COVID-19, guidelines, hospitals, India, stewardship, vitamins

INTRODUCTION

COVID-19 was first identified in Wuhan, China, in December 2019 and by 8 November 2021, there were 249.7 million recorded cases worldwide with just over 5.0 million recorded deaths, giving a case fatality ratio (CFR) of 2.02%.^[1] This includes India where 34.4 million cases had been recorded by 8 November 2021, with over 460,000 deaths, giving a CFR of 1.34%.^[1]

Since COVID-19 is principally spread through physical contact and airborne transmission, the key stakeholder focus in the early stages of the pandemic was on its prevention,

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especially with an appreciable number of patients being asymptomatic.^[2-4] Preventative strategies adopted across countries included lockdown measures incorporating the closure of borders and schools as well as encouraging social distancing and hygiene measures including regular hand hygiene.^[2,3,5] However, there were varying degrees regarding the extent of the implementation and timing of preventative measures, resulting in appreciable differences in prevalence and mortality rates among different countries including different African, Asian and Western European countries as well as with the United States of America.^[3,6,7]

Various re-purposed medicines were suggested to reduce morbidity and mortality in patients with COVID-19. These include hydroxychloroquine, lopinavir/ritonavir and remdesivir, which are no longer recommended to manage patients with COVID 19 following large extensive trials, although this may vary at a national level.^[2,4,8-13] There is also ongoing controversy surrounding the potential use of ivermectin, which is an anti-parasitic medicine.^[2,14,15] However, both hydroxychloroquine and ivermectin were being recommended for managing patients with COVID-19 in the national Indian management guidelines issued in May 2021.^[13] This though did not include children in specific paediatric guidelines for India.^[16] This is important given for instance that misinformation on hydroxychloroquine has increased morbidity, mortality and costs.^[3,17-19] However, there is greater evidence for the role of dexamethasone among hospitalised patients following the publication of the UK Recovery trial results as well as new oral antiviral medicines including molnupiravir.^[19,20]

Concerns regarding the level of misinformation for suggested approaches to prevent and treat COVID-19 has led to bodies such as the British Medical Journal and the World Health Organisation (WHO) providing guidance as more data becomes available.^[6,11] As a result, encouraging the implementation of evidence-based approaches.^[4,18,19] This was helped in India by the Ministry of Health and Family Welfare making national guidelines available for both adults and children including discouraging the prescribing of antibiotics unless there is clinical suspicion of a bacterial infection due to few patients with COVID-19 developing secondary bacterial infections^[13,16] These build on published guidelines in the Indian Journal of Paediatrics for children.^[21]

We are aware that children have a lower risk of infection with COVID-19 and milder clinical manifestations when they become infected than adults.^[2,6,21-24] Generally, respiratory infections, cough, fever, nausea and diarrhoea are the most frequent clinical characteristics of children with COVID-19;^[6,22-24] however, an appreciable number of children remain asymptomatic.^[6,22] Overall, only a small minority of children infected with COVID-19 experience severe disease compared with adults, especially unvaccinated adults,^[22,23,25] which could be due to elevated antibodies compared with adults as well as other factors.^[6,26] Consequently, the focus on children in low- and middle-income countries (LMICs) during

the pandemic, including India, has typically been addressing key concerns including poor vaccination rates as well as other issues including the education and mental wellbeing of children during the pandemic with fears of increasing suicide rates.^[2,6,27,28]

However, the focus on the optimal management of children with COVID-19 is changing, especially with new variants and the increasing number of cases in children,^[6] reflected by national guidelines for children launched in May 2021.^[16] In addition, we are aware of the high use of antimicrobials in hospitals to treat patients with COVID-19, including children, despite only a very limited number of patients having concomitant bacterial infections.^[6,29] This is a concern as inappropriate use of antibiotics drives up antimicrobial resistance (AMR) rates with an associated increase in morbidity, mortality and costs.^[6,30,31] We also see that children diagnosed with COVID-19 do develop Kawasaki Disease-like symptoms/hyperinflammatory syndromes, which increases the need for intensive care.^[6]

As a result of growing concerns with the number of children with COVID-19 in India, especially those with symptoms, coupled with concerns with the potential overuse of antimicrobials, we believed it was important to document the current management of children hospitalised in India as a result of COVID-19 to provide future direction. This builds on preliminary studies including those of Banerjee *et al.*, Ramteke *et al* and Dash *et al.*^[24,26,32]

MATERIALS AND METHODS

A rapid analysis was undertaken among five hospitals across India with a range of in-patient paediatric beds treating children with COVID-19. The paper-based CRFs that were used for data collection were based on a recent study in Bangladesh as well as previous publications discussing the management of COVID-19 in children in India.^[6,25,26] The study was undertaken in August 2021.

Data collection took place on a single day, similar to other prevalence studies. However, medical records could be viewed up to the previous 10 days. Ten days were chosen for this study by the principal investigators due to the envisaged low numbers of children with COVID-19 admitted to hospitals in India on any specific day, with, as mentioned, children with COVID-19 generally asymptomatic or with milder clinical manifestations than adults.^[6,22,23] Table 1 contains the key data sets collected.

We also assessed antibiotic prescribing against the WHO Access, Watch or Reserve list, which is increasingly being used to assess the quality of antimicrobial prescribing among children.^[33] In addition, where documented, whether clinicians believed they were following recent guidance from the Ministry of Health and Family Welfare Government of India [Table 2].^[16]

Cost data were typically not requested as most of the surveyed hospitals were Government hospitals where care is provided free of charge.

Table 1: Key data sets collected in the case report forms**Key data sets**

Number of paediatric patients typically being treated in the hospital
Percentage of children with COVID-19 in the hospital
Patient's ages in years (3 bands: 0-5 years; 6-10 years; 11-18 years) and gender
Principal reasons for admittance (3 principal reasons – drop-down menu) including
Breathing difficulties/respiratory distress
Prolonged fever
Cough
Diarrhoea
Feeding difficulty/vomiting
Comorbidities (mention top 3)
Percentage of children with COVID-19 admitted to PICU and the reasons – taken from
Severe respiratory distress/low O ₂ saturation; shock
Coagulation disorders/thromboembolic manifestations
Extensive lung involvement in high-resolution CT scan (HRCT)
Percentage prescribed antibiotics (which key ones) and percentage empiric
Route of administration of antibiotics
Whether prescribing of antibiotics was re-assessed and total length of prescription
Whether any antivirals (e.g., remdesivir), antimalarials (e.g., hydroxychloroquine), anti-parasitics (e.g., ivermectin) and anti-inflammatories (e.g., dexamethasone) or supplements/immune boosters such as Vitamins C or D or zinc were prescribed
Outcome – mortality, morbidity or recovery
HRCT: High-resolution computed tomography, PICU: Paediatric intensive care unit

The co-authors orchestrated ethical approval for their hospitals building on the initial approval orchestrated by the lead co-author (SK– KSDEC/21-22/Apr/001). No parents or guardians were approached for consent since this was a retrospective study based on data collated from patients' medical records with no direct contact with children, their parents or guardians. This is in line with previous point prevalence studies undertaken by the co-authors across countries.^[6,34-37]

RESULTS

The key characteristics of children admitted to the five pilot hospitals with COVID-19 are depicted in Table 3. Overall, 11.9% of in-patient children had COVID-19, mainly males (58.3%) and aged between 11 and 18 years (55.5%). The principal reasons for admission to the hospital with suspected COVID-19 included prolonged fever, breathing difficulties/respiratory distress and a cough. There were also feeding difficulties/vomiting and diarrhoea in a minority of admitted patients.

Overall, 30.6% of children were admitted to the paediatric intensive care unit (PICU) with the majority (81.8%) not requiring a ventilator. The principal reasons for admittance to the PICU were severe respiratory distress/low O₂ saturation,

Table 2: Key recommendations from the ministry of health and family welfare government of India on the management of children with COVID-19 in hospital**Patient management**

- A) Moderate symptoms-management
- Check for pneumonia
 - Initiate oxygen if SpO₂ is 38°C (or 100.4°F)
 - Supportive care for comorbid conditions, if any
 - Investigations: Baseline: CBC including ESR, blood glucose and chest X-rays
 - Medicines
 - Paracetamol 10-15 mg/kg/dose; may repeat every 4-6 h
 - Antimicrobials only administered if there is evidence/strong suspicion of superadded bacterial infection
 - Remdesivir and corticosteroids not recommended
- B) Severe disease (admitted to HDU/ICU)
- a) Defined as: SpO₂ <90% on room air and any of the following: Signs of severe pneumonia/pneumonia with cyanosis, acute respiratory distress syndrome, septic shock, multi-organ dysfunction syndrome, severe retraction of the chest, grunting, lethargy, somnolence, and seizures
 - b) Management includes
 - Initiate immediate oxygen therapy and maintain a target SpO₂ 94%-96% and maintain fluid and electrolyte balance
 - In cases of ARDS or shock-initiate necessary management (ARDS and shock guidelines)
 - May need organ support in case of organ dysfunction e.g., renal replacement therapy
 - Investigations: Baseline: CBC including ESR, blood glucose, CRP, LFT, KFT, serum ferritin, and D-dimer; chest X-rays
 - c) Medicines
 - Corticosteroids therapy to be initiated (although under strict supervision)
 - Anticoagulants may also be indicated
 - Antimicrobials to be administered if there is evidence/strong suspicion of superadded bacterial infection; see antimicrobial use guide
 - Remdesivir is not recommended

ICU: Intensive care units, HDU: High dependency units, ARDS: Acute respiratory distress syndrome, ESR: Erythrocyte sedimentation rate, CBC: Complete blood count, LFT: Liver function test, KFT: Kidney function test

shock and extensive lung involvement in high-resolution computed tomography.

There was appreciable prescribing of antibiotics at 69.4% of children [Table 4], with high rates (66.7% to 100%) in four out of the five hospitals surveyed. Antibiotics were prescribed empirically among all children surveyed, typically parenterally for an average of 7 days and from the WHO Watch list of antibiotics [Table 4]. All patients were re-assessed for continued antimicrobial prescribing. This is despite four of the five hospitals confirming they follow national guidelines, which state that antimicrobials should only administered if there is evidence/strong suspicion of superadded bacterial infection [Table 2]. These was limited prescribing of antimalarial, antiviral and anti-parasitic medicines among the children in these five hospitals [Table 4]. There was greater prescribing of steroids as well as immune boosters such as Vitamin C and D [Table 4].

Table 3: Key characteristics of the children among five hospitals in the pilot study

Hospital	Date survey (2021)	Total patients childrens' wards (n)	Total with COVID-19 (n)	Percentage with COVID-19	Male (n)	Female (n)	0-5 years (n)	6-10 years (n)	11-18 years (n)
1	26.08	42	6	14.3	4	2	0	4	2
2	27.08	53	6	11.3	3	3	1	3	2
3	27.08	54	7	13.0	3	4	0	0	7
4	28.08	72	7	9.7	5	2	2	2	3
5	31.08	82	10	10.2	6	4	2	2	6
Total (%)		303	133	11.9	58.3	41.7	13.9	30.6	55.5

Table 4: Management of children with COVID-19 among the five hospitals

Hospital	Number Rx antibiotic	Percentage Rx antibiotic	Empiric or CST	Key antibiotics Rx	Antimalaria Rx (n)*	Anti-viral (n)**	Anti-parasitic (n)***	Steroid****	Supplements
1	4	66.7	100% empiric	Azithromycin (IV). Average 7 days	1	0	0	Yes	Vitamin C, D, zinc
2	6	100	100% empiric	Azithromycin (IV). Average 10 days	0	1	1	Yes	Zinc
3	2	28.6	100% empiric	Piperacillin (IV). Average 7 days	2	0	0	Yes	Vitamin C, D, zinc
4	5	71.4	100% empiric	Amikacin (IV). Average 7 days	1	1	0	Yes	Vitamin C, zinc
5	8	80.0	100% empiric	Meropenem (IV and oral). Average 7 days	3	1	2	Yes	Vitamin C, D, zinc
Total	25	69.4			7 (19.4%)	3 (8.3%)	3 (8.3%)		

NB: *Antimalarial is hydroxychloroquine; **antiviral is remdesivir; ***anti-parasitic is ivermectin; ****steroids are either dexamethasone or methylprednisolone. Rx: Prescribed, CST: Culture sensitivity test

The average length of stay was 9 days with a range of 7–11 days. The vast majority of children (97.2%) made a full recovery from COVID-19, with only one child dying from COVID-19.

DISCUSSION

We believe this is one of the first studies in India to assess the characteristics and management of children with COVID-19 admitted to hospitals in India and builds on preliminary studies including those of Banerjee *et al.*, Ramteke *et al* and Dash *et al.*^[24,26,32] The percentage of children admitted with COVID-19 (11.9%) appears higher than rates discussed by Dash *et al.*,^[32] and appreciably higher than a recent pilot study in Bangladesh, which found children with COVID-19 accounted for only 4.3% of in-patients.^[6] However, this may be a reflection of the different circumstances between the countries as these rates are within reported rates of 6% to 10% of children across countries with COVID-19 experiencing severe disease.^[6,22,23] This low prevalence rate suggests that hospitals in India managing children should start to increase their other services for children which have been neglected during the early stages of the pandemic such as paediatric surgery. There were similar suggestions in Bangladesh.^[6]

More boys with COVID19 were admitted to hospitals in this pilot study [Table 3], which is similar to the findings of a recent

pilot study in Bangladesh.^[6] Similar to previously published findings, including those from Bangladesh, were that fever, breathing difficulties/respiratory distress, and cough were the principal reasons for admitting children with suspected COVID-19 to hospitals in India.^[6,22,23] Encouragingly, the high rate of recovery (97.2%) mirrors the findings in other hospitals in India as well as Bangladesh.^[6,24]

Encouragingly as well was the limited use of antimalarials, antivirals and anti-parasitic medicines for children with COVID-19 among the surveyed hospitals [Table 4]. However, any prescribing is a concern given limited endorsement for their use in the national guidelines for children [Table 2].^[6,16] Similarly, appreciable prescribing of steroids and supplements proven to benefit patients with COVID-19 [Table 4]. Of concern though is the high empiric prescribing of antibiotics among admitted children [Table 4]. However, rates are lower than in the pilot study in Bangladesh where all children were administered antibiotics.^[6] High rates of prescribing of antibiotics are a concern given the low numbers of patients with COVID-19 actually having either bacterial or fungal infections in published studies, with such over use driving up AMR rates exacerbated by the high use of Watch versus Access antibiotics.^[29,30,33] The instigation of antimicrobial stewardship programmes (ASPs) should enhance adherence to current guidelines and result in a reduction in inappropriate antibiotic

prescribing.^[30,31,38] Such programs should also enhance appropriate switching from parenteral to oral antibiotics, which can hasten early discharge,^[6,30] with costs and resources key issues in LMICs. We will be following this up in future studies.

We are aware of a number of limitations with this study. This included the fact that this was only a pilot study. In addition, this was a retrospective review of patient's notes. Consequently, physicians were not contacted regarding the rationale for their treatment approaches including the prescribing of antimicrobials despite concerns in current guidelines. Despite these limitations, we believe the findings are robust providing a basis for future direction.

CONCLUSION AND RECOMMENDATIONS

It was encouraging to see low hospitalisation rates for children with COVID-19 versus other conditions among the hospitals in India in this pilot study, mirroring the findings in other countries. There were concerns though with the high empiric use of antibiotics in the majority of surveyed hospitals and limited switching to oral formulations despite current guidelines.

Encouragingly given concerns with their effectiveness, there was limited prescribing of antimalarials, antivirals and anti-parasitic medicines. However, any prescribing is inconsistent with current guidelines. These areas need to be addressed to reduce the potential for AMR, adverse reactions and costs. Instigating or enhancing ASPs in hospitals can help improve future antimicrobial use. We will be monitoring this in the future.

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Conflicts of interest

There are no conflicts of interest.

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