Management of paediatric patients with COVID-19 witha particular focus on Africa; findings and implications

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Introduction: The Coronavirus disease 19 (COVID-19) pandemic has had a huge impact on the global population, especially children in low- and middle-income countries (LIMCs). The African continent is plagued with inequalities and has the highest prevalence for infectious diseases globally, with COVID-19 infections rising daily. Although the rates of infection may be rising, children are seen to have lower infection rates than adults. This may be due to the way severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), the causative agent of COVID-19 manifests in paediatrics. Children present with milder manifestations of COVID-19, leading to less testing and the perception that infection rates are lower in this population. Secondly, paediatrics may be innately less susceptible to SARS-CoV-2 due to significant morphological differences such as elevated antibody levels and age-dependent lung differences. However, there are increasing infection rates among children due to the new COVID-19 variants. The paucity in information regarding the treatment regimen used in paediatrics, therefore our aim is to address the concern of limited evidence-based guidance for policy, practice, and health education for the paediatric population in COVID-19 thus leading to better informed choices and clinical guidance.

Methodology: A multifaceted approach was used to address the paucity in information. Firstly, a narrative review of published papers documenting the incidence and management of COVID-19 related hyperinflammatory state in children was completed as well as a review of the ongoing literature pertaining to paediatric patients with COVID-19 multi-inflammatory syndrome, as well as documentation of current practices across Africa. The literature search conducted through Ovid MEDLINE ® yielded 271 studies with only 15 studies being included due to relevance.

Results: The hyperinflammatory state associated with COVID-19 in children has been termed multi-inflammatory syndrome in children (MIS-C). MIS-C's pathogenesis is unknown but is seen as an excessive response to SARS-CoV-2 infection. It is characterised by an increase in inflammatory biomarkers, a characteristic it shares with Kawasaki disease (KD). Although the presentations of MIS-C and KD may be quite similar there are key differences. MIS-C tends to present in older patients (above the age of five), while those who normally present with KD are younger than the age of five. MIS-C typically has higher cardiac and gastrointestinal involvement than KD. More research needs to be done to further distinguish between the two conditions. COVID-19 infection primarily presents itself as a respiratory, cardiovascular, or gastrointestinal infection in children. Various treatments regimens have been trialed in the paediatric population to address the inflammatory state. Initial studies showing remdesivir treatment in paediatric patients above the age of 12 showed promise but more focus is needed on other age groups. The bound plasma exposures presented by hydroxychloroquine in children were seen to be too low to mediate an antiviral effect. It was also important to note that different combinations of remdesevir, hydroxychloroquine, lopinavir, ritonavir, interferon-beta and tocilizumab did not significantly impact patient recovery positively. The use of corticosteroids showed the ability to reduce mortality and decrease the need for mechanical ventilation compared to standard care of MIS-C in paediatrics. When combined with intravenous immunoglobulins (IVIG), MIS-C symptoms are seemed to be resolved. Off-label use of defibrotide, infliximab and anakinra were seen to show clinical and laboratory improvements in paediatric patients on a case-by-case basis. Regarding combination medication, the use of lopinavir-ritonavir was discontinued due to the lack of efficacy in the World Health Organisation (WHO) solidarity trial and UK recovery trial. State management of COVID-19 differs from country to country. Cameroon and Ghana had no paediatric specific guidelines at the time of this paper and used the general guidelines to successfully treat paediatric patients Namibia was one of the few countries with paediatric specific management guidelines while South Africa had a basic immunomodulatory intervention scheme. Uganda had age specific dosing guidelines while Zambia differentiates treatment according to moderate and severe COVID-19 in children.

Conclusion and recommendations: The medication used in paediatrics appears to of more of a symptomatic benefit and for the prevention of mild disease progress to severe disease. Appropriate information needs to be shared and disseminated between states to decrease the misuse of antimicrobials. The rationale behind the use of aspirin in children needs to be further studied. More research and clinical trials in paediatrics regarding the medication used for MIS-C needs to be further evaluated.

Keywords: MIS-C, Hyperinflammatory state, COVID-19, Paediatrics, SARS-CoV-2, Africa