

# Views and insights into the remdesivir study for the treatment of severe pediatric COVID-19 cases

Dear Sir,

I am writing to share my thoughts and address the recent study "Remdesivir therapy for severe pediatric COVID-19 in Singapore: A single-center retrospective observational cohort study" that was published in your prestigious journal.<sup>1</sup> The study concentrated on the administration of remdesivir (RDV) to treat severe pediatric COVID-19 cases at Singapore's KK Women's and Children's Hospital. In the framework of the ongoing international effort to manage the COVID-19 epidemic, particularly, among vulnerable populations like children, I find as an internist that this study is not only timely but also vital.

The meticulous methodology of the study, in particular, its retrospective observational cohort design, offers a thorough understanding of the use and results of RDV treatment in pediatric patients. The strict selection criteria that concentrated on children with severe COVID-19 who needed to be admitted to the high-dependency unit (HD)/intensive care unit (ICU) and get oxygen supplementation made sure that the effects of RDV on critical cases were thoroughly examined. This specificity is praiseworthy since it fills in a major study void on pediatric COVID-19, particularly, in Asian settings.

RDV has been used in cases and observational studies involving children infected with COVID-19. Seven of the eight children under the age of 16 who got compassionate treatment with RDV in a multicenter observational study conducted in Spain saw satisfactory clinical outcomes without experiencing any adverse events.<sup>2</sup> Another observational study that involved 77 children with severe COVID-19 who were treated with RDV revealed that the majority of patients had a full recovery and that the incidence of major side effects was minimal.<sup>3</sup> An interesting study on RDV use in pediatric immunocompromised patients with mild infection found that there were no adverse effects, but it did not lead to early clearance of SARS-CoV-2.<sup>4</sup>

RDV has demonstrated a strong safety profile in pediatric patients. However, bradycardia occurrences in pediatric children have been reported.<sup>5</sup> Adverse events included acute renal injury (11%) and a rise in alanine transaminase (8%), which occurred in 53 hospitalized children under the age of 12 years and weighing between 3.5 and 40 kg, as part of a phase 2/3 research assessing the safety, tolerability, and pharmacokinetics of RDV. Because there was no control group, no judgments about efficacy could be drawn.<sup>6</sup> An additional study by Schulz et al. found

that 29% of patients on RDV experienced mild-to-moderate adverse events, but these did not require discontinuation except for one patient who developed premature ventricular contractions.<sup>7</sup>

The absence of a significant difference in the rate of de-escalation from HD/ICU care between children treated with RDV and those who were not is one of the pivotal findings by Seah et al. This data raises crucial questions regarding the role of RDV in pediatric care. It is also interesting to note that kids in the RDV group had median HD/ICU care days that were longer. It implies that although RDV may be beneficial in treating COVID-19, patient-specific factors including the severity of the illness and the timing of treatment may have an impact on how successful RDV is. Romani et al. also alluded to delaying RDV after a more severe presentation (pneumonia) may be associated with longer duration of therapy, especially if comorbidities are present.<sup>8</sup>

The discussion section of the study thoughtfully interprets these findings, acknowledging the complexity of pediatric COVID-19 presentations and the challenges in managing them. The study rightly points out that although no clear benefit of RDV in reducing HD/ICU duration was observed in this cohort, the potential benefits of early RDV intervention in more severe cases should not be overlooked. This balanced view is essential for clinicians and healthcare providers who are at the forefront of treating pediatric COVID-19 cases.

The study recognizes its limitations, such as the limited sample size and absence of a randomized control group, even if it provides important new insights. This frank evaluation highlights the need for additional study in this area. Subsequent research, especially those with a bigger sample size and a randomized control group, would be crucial in confirming the inclusion of RDV in pediatric COVID-19 treatment regimens. Furthermore, given the development of several COVID-19 variations, future studies ought to investigate how these variants affect the effectiveness of therapies such as RDV.

To sum up, this research constitutes a noteworthy advancement in our comprehension of managing severe COVID-19 in children. The results lay the groundwork for additional investigation and debate within the medical community. We must stick to evidence-based treatments and stay open to new information as we work through the difficulties presented by the COVID-19 epidemic, particularly, when it comes to vulnerable groups like children. These kinds of studies are crucial for directing our actions and guaranteeing the finest results for every patient.

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children, pediatric, remdesivir, SARS-CoV-2, severe COVID-19

**AUTHOR CONTRIBUTIONS**

**Taige Cao:** Conceptualization; writing—review and editing; writing—original draft; formal analysis. The author has read and approved the final version of the manuscript.

**CONFLICT OF INTEREST STATEMENT**

The author declares no conflict of interest.

**DATA AVAILABILITY STATEMENT**

Taige Cao had full access to all of the data in this study and takes complete responsibility for the integrity of the data and the accuracy of the data analysis.

**TRANSPARENCY STATEMENT**

The lead author Taige Cao affirms that this manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned (and, if relevant, registered) have been explained.

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