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A possible explanation for the existence of multisystem inflammatory syndrome in children (MIS-C) only in the pediatric population

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Abstract: **Multisystem inflammatory syndrome in children (MIS-C) is a relatively new disease that came into existence after the COVID-19 pandemic. It is defined as a multisystem inflammatory condition post-COVID-19 infection due to an immune-mediated reaction of the body toward coronavirus. It is especially seen and defined in children, but this disease's underlying cause affecting a particular population is yet to be determined. Several hypotheses have been postulated which explain this disease as a result of immune dysregulation. The immune system responds to any infection by the B and T-cell response systems. This leads to antibody formation and cytokine production respectively. Some of the studies in the past have shown that the intensity of cytokines response in different age groups is different. The number of T-cells producing IL-2 and NK cells producing IFN-Y plays a huge role in an inflammatory response. Age group 1-21 yrs has shown to induce maximum cytokine response in studies which might be a possible explanation for the occurrence of MIS-C mostly in the children population.**

Keywords: **Multisystem inflammatory syndrome in children (MIS-C), cytokines, COVID-19.**

1. INTRODUCTION

Multisystem inflammatory syndrome in children (MIS-C) is a disease condition that is usually seen to appear weeks after COVID-19 infection. Most of the patients have only a mild disease process but some tend to have a severe course of the disease as well. This is a rare complication of the COVID-19 infection. This disease's exact incidence and pathophysiology are unknown, and studies are still going on the proposed hypothesis for the exact cause (1) The disease has a clinical picture of a viral infection, to begin with, and presents as fever followed by involvement of multiple organs like the gastrointestinal tract, central nervous system, cardiorespiratory system, etc. The presentation is more like that of Kawasaki disease, toxic shock syndrome, MAS, and other multisystem inflammatory diseases (2). Once there is suspicion of the MIS-C the diagnosis begins with an algorithm of lab work and imaging to identify different organ involvement. The treatment guidelines depend upon the clinical status. Other than symptomatic treatment, the other modalities are intravenous immunoglobulin, steroids, and antithrombotic agents (3)

There are proposed hypotheses to explain the underlying pathophysiology of MIS-C but the exact mechanism is still unknown. It happens after COVID-19 infection when most patients have COVID-19 RT-PCR negative and positive COVID-19 IgG antibodies. Most of the cases are seen between the age group of 1-21 years with a median age of 9 and almost half of the cases occur between ages 5-13 years as per CDC reports (5).

A probable explanation for the MIS-C disease process and its occurrence in a particular age group is how strongly the immune system responds to the infection. The immune system responds to any infections by producing a cytokine

response. This response induces the production of interleukins, TNF alpha, and IFN-Y (4). The immune system develops as we grow and starts to fade away as we age and this phenomenon is known as immunosenescence or aging of the immune system (9). COVID-19 infection leads to immune suppression and dysregulation (6, 8). The cytokines response post-infection leads to activation of inflammation and the underlying MIS-C disease process. Some of the studies have shown that the cytokine response generated by the body varies with the age. There is an increase in the IL-2 and IFN-Y as we grow with a peak seen around the teenage group followed by a decline (7). This can explain why such a dysregulated immune response is generated and with the cytokine, the storm body develops a clinical picture of MIS-C.

2. HYPOTHESIS DISCUSSION & PROBABLE CONCLUSIONS

COVID-19 infection affects the immune system and weakens it. As the body fights the virus and the infection resolves the body tries to build an immune response against the novel coronavirus. The response is dysregulated leading to a surge of cytokines in the body. Interleukins, interferons, and other inflammatory cytokines lead to a vicious circle of inflammation leading to a picture of MIS-C. Since cytokine response is at its peak in the first 2 decades of life this possibly explains why MIS-C is seen in the first 2 decades of life.

3. COMPLIANCE WITH ETHICAL STANDARDS

Conflict of interest: The authors Ashish Shrivastava declare that they have no conflict of interest.

Ethical approval: This article does not contain any studies with human participants or animals performed by any of the authors.

Informed consent: No informed consent was required.

Figure legend

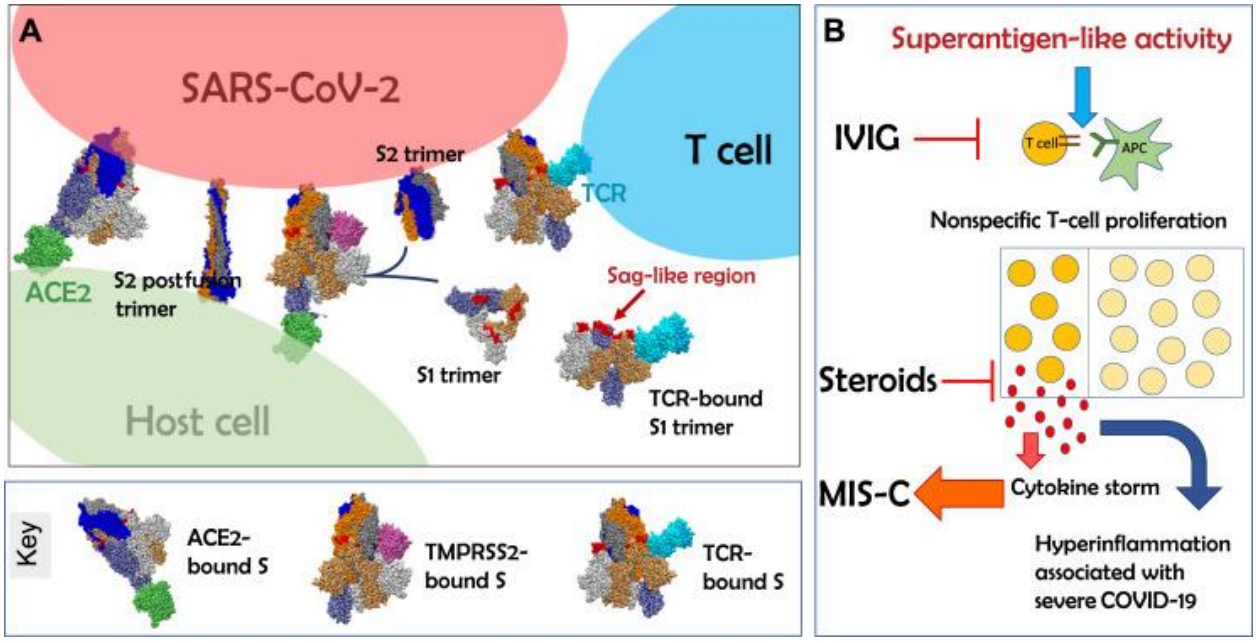

Figure 1: Image with possible pathogenesis of MIS-C post-COVID-19 infection (10).

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