Commentary: COVID-19 and ocular inflammation: Where do we stand and where are we headed?

The ongoing coronavirus disease 2019 (COVID-19) pandemic, caused by the severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2), is an unprecedented health crisis gripping the world. It has infected more than 120 million people and caused more than 2.66 million deaths despite the most aggressive efforts to contain and treat the disease.[1] Epidemiological evidence has undoubtedly shown that the elderly and those with comorbid conditions are at a higher risk of severe COVID-19 and deaths than children.[2] In a systemic review of 45 publications, Ludvigsson has shown that children account for only 1% to 5% of the detected COVID-19 cases, with a milder disease course compared with adults, and deaths being extremely rare.[3] However, although children are usually spared of severe disease and/or death, reports of a multisystem inflammatory syndrome in children (MIS-C) or Kawasaki-like disease secondary to COVID-19 are an emerging cause of concern.[4] Presence of ocular inflammation can also be a part of this altered systemic immune response.[5] In cases with MIS-C, elevated levels of the inflammatory cytokine interleukin-6 have been demonstrated,[6] suggestive of a full-body immune response to the SARS-CoV-2. Such kind of robust immune response is potentially protective for children against disease severity, but at the same time makes them highly vulnerable to inflammatory sequelae such as MIS-C.

Currently, there is an unprecedented effort to control the COVID-19 pandemic. A significant step toward achieving this is the initiation of the COVID-19 vaccination drive on a global scale. Currently, more than 200 vaccine candidates are in various stages of development around the world.[7] The basic platform for vaccine development includes live attenuated virus, recombinant viral-vectored vaccines, inactivated or killed virus, protein subunit vaccines, virus-like particles, and nucleic-based (DNA or mRNA) vaccines.[7] Although the vaccines are developed using various components of the SARS-CoV-2, the primary aim of each one of them is to achieve a long-lasting immune response against the virus. Unfortunately, the durability of the immune response secondary to the vaccine or the natural infections remains unknown. Furthermore, the safety and efficacy of the vaccine in the pediatric population remain unexplored. There are multiple issues in evaluating the COVID-19 vaccine in children, including the medicolegal aspect with the consent, difficulty in assessing the adverse reactions, and the need for a higher number of study participants to reach a level of statistical significance since children are infrequently affected by the disease. Additionally, as COVID-19 poses a life-threatening risk of MIS-C, a similar fatal immune response triggered by the vaccine cannot be completely negated. This can potentially place hitherto normal children at an increased risk of severe adverse immunological reaction after vaccination, which is essentially intended to prevent COVID-19. In fact, MIS-C-like syndrome involving ocular tissue has even been reported in adults older than 40 years of age.[5] Thus, there is a potential risk of ocular inflammation that can be a part of the systemic immune response post-COVID-19 vaccination for all age-groups. Benage and Fraunfelder have reported 289 cases of vaccine-associated uveitis between 1984 and 2014.[8] Among the vaccines, hepatitis B was the commonest cause with a vast majority of affected patients being females (199/289 patients).[8] The median age of the affected patients was 30 years, ranging from 2 months to 86 years.[8]

Based on the current literature related to inflammation associated with COVID-19,[2,3,5] we can postulate that MIS-C and related ocular inflammation can occur more frequently in children than in adults. So it is vital to further explore the pathogenesis and mechanisms related to the deranged immune response and development of MIS-C in COVID-19. With this background, we will be able to effectively evaluate the role and potential risks of COVID-19 vaccines in a pediatric population. At the same time, the vaccination drive is well underway on a global scale in adults and the elderly population. Hence, with

a background of SARS-CoV-2-related immune modulation and associated uveitis, as ophthalmologists, we need to be vigilant regarding any potential vaccine-mediated ocular inflammation. In the presence of symptoms of COVID-19 or a recent history of COVID vaccination in a patient with ocular inflammation, we can provide timely advice related to the early detection of systemic inflammatory markers to abort MIS-C and other COVID-related ocular and systemic complications.

***Jay U Sheth*[1,2]**

[1]Vitreo-Retina Consultant and Head of Research, Surya Eye Institute and Research Centre, Mumbai, Maharashtra, [2]Clinical Research Lead, Chaitanya Eye Hospital and Research Institute, Trivandrum, Kerala, India

Correspondence to: Dr. Jay U Sheth, Surya Eye Institute and Research Centre, Mumbai - 400 080, Maharashtra, India.
E-mail: drjay009@gmail.com

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