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COVID-19

COVID-19 infection and Down syndrome—challenges and future directions for care in children

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To the Editor-in-Chief,

We have read with immense interest the article entitled "COVID-19 in patients with Down Syndrome" by Emami et al. [1]. We thank the authors for their valuable contributions regarding directing more care to those with Down syndrome. However, the article fails to provide insight on how we can specifically help children in the post-lockdown era.

Down syndrome (trisomy 21) is one of the commonest genetic disorders worldwide with a prevalence of around 3.3–6.7 per 100,000 population [2]. Children with Down syndrome (DS) are more susceptible to infectious diseases increasing their chances of being infected with COVID-19 [3]. Though there is a huge amount of work done on children, studies understanding the impact of this infection on the population of intellectually disabled children and particularly on DS children are limited. In this article, we will present the unique challenges this population faces and provide suggestions for families, friends, caregivers and healthcare workers to improve their well-being.

Children with DS are prone to develop COVID-19 infection due to multiple factors:

1. Pro-inflammatory status — Multiples of the triple gene dose of four interferon (IFN) receptor transcripts when infected with COVID-19 lead to hypersensitivity of the macrophage activation pathway in pulmonary tissue with the subsequent stimulation of immune cells increasing cytokine production. Overexpression of four of the six IFN receptors creates a pro-inflammatory milieu in these children [3].
2. Unique genetics — Children with DS have poor anti-inflammatory response at baseline with reduced IL-6 and TNF-alpha levels and higher levels of anti-inflammatory cytokines IL-10 and IL-4 which leads to an immunodeficient state making them susceptible to infections [3]. In adults, higher levels of TNF-alpha, IL-beta and IL-gamma predispose them to develop cytokine storm post-infection. Increased neuroinflammation in DS brains is postulated to be related with the macrophage activation state due to tripling of genes like ADAMTS1, RCAN 1 and ADAMTS5 among others [3].
3. Prone to intubation and death — A case-controlled study on 18 patients with DS revealed higher risk of intubation and death [1].
4. Response to vaccination — The suboptimal primary and secondary immune response together with chances of overactive innate immune cell function and destruction of phagocytosed immune complexes leads to ineffective protection [4].

Beyond physical health, strict social distancing measures and the lockdown have disproportionately affected children with DS psychosocially as they have been deprived of going to their usual therapeutic settings and school environment. Physical distancing has also reduced social support to their caregivers negatively impacting their way of life. An important study assessing caregivers tending for children with special needs revealed higher levels of caregiver strain and depression with lack of tele-rehabilitation and a negative perception of it playing an important role in their poor mental health during the pandemic [5]. Additionally, the mental

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health of these children has suffered due to the added burden of their family's emotional stress during the pandemic.

Social interaction continues to be crucial for children with DS, even after the pandemic, as sudden changes in routine can increase their level of anxiety and worsen their behavioural issues especially when curtailing their limited freedoms [4].

It is imperative to work on the physical, psychosocial and mental well-being of children with DS. Healthy lifestyle and immunization with influenza and pneumococcal vaccines are recommended along with teaching them hand hygiene. It is imperative that children with risk factors for sleep apnoea and severe lung infections are routinely monitored via teleconsultation. Caregivers can play an important role by learning and providing tele-rehabilitation to these kids [4].

Thus, it is important to understand and shield both children with DS who were not included in the UK shielding list and US Centre for Disease Control (CDC) list of "increased risk" which was followed in the majority of developing nations. A worldwide registry containing details of hospitalization, Intensive Care Unit (ICU) admission, intubation and mortality of children and adults with DS is necessary to understand and tailor our efforts for this group [4]. It is imperative to implement novel teleconsultation and tele-rehabilitation strategies along with providing enough state-sponsored financial, emotional and supportive assistance to the caregivers and family members of children and adults with DS.

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Declarations

Conflict of interest The authors declare no competing interests.

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