Multisystem Inflammatory Syndrome in Children: How to Live with COVID-19?

Sir,

Shankarraman et al., in their interesting letter,[1] suspected SARS-CoV-2 to cause direct cytopathic effect for the aggravation of inflammation; as the presence of SARS-CoV-2 in the appendix and stool is well documented. Multisystem inflammatory syndrome in children (MIS-C) is rare, and COVID-19 is less common as compared to SARS-CoV-2 positivity in children (akin to HIV positivity vs. AIDS) as well as compared to the adult.

Why This Discrepancy Is?

I would like to add a few points in an attempt to clarify as well as to hint management for COVID-19. Living cells are essentially necessary for the replications of virus. Keratin layer on the skin and mucus gel on mucosa are nonliving. They are natural defense and coat ACE2 to prevent SARS-CoV-2 to enter the cells. The thickness of nasal and intestinal mucus gel layer is around 15 and 50 µ, respectively, and the size of SARS-CoV-2 is around 0.1 µ. Hence, the gel layer is 150–500 times wider than the size of SARS-CoV-2; comparable to a six feet nonswimmer trying to cross a lake, width matches to 3–9 football ground, respectively!

So, how the SARS-CoV-2 viruses would overcome the natural defense?

They get a chance with Brownian movement to cross that “vast lake” and to stroke on ACE2 receptors. Understandably, the enormous number of virus is necessary to increase the chance. Each droplet (size ~15 µ) contains ~60,000 virions and chances are directly proportional to the number of droplets dropped on mucus gel. Children are protected with thicker mucus gel compared to almost dry mucosa in the elderly. Following the success of the hurdle, SARS-CoV-2 replicates and sheds progeny virus to contaminate mucus gel. Mucus contaminated with SARS-CoV-2 (MCS) glides toward the lung and alimentary system as microaspiration.[2,3] However, at the same time, MCS might also be washed off by the excessive watery nasal secretion, which is common in children and Omicron infection. Along with this, children and younger population have got another natural defense of young, moist, vibrant mucociliary conveyor that sweeps away MCS from the lower respiratory tract toward the oropharynx to protect the lung from pneumonia.

Mucosal immune systems are compartmentalized and get stimulated one by one following cellular invasion by the viruses in the respective compartment. The initial invasion of SARS-CoV-2 in nasal epithelium stimulates nasopharynx-associated lymphoid tissue (NALT). Hence, the reactive interleukin-6 and other pro-inflammatory cytokines are produced to be poured in blood to spread in other organs. In this regard, gut-associated lymphoid tissue (GALT) is the largest mass of lymphoid tissue in the body. Hence, if GALT is provoked by SARS-CoV-2, it would secret a considerable amount of pro-inflammatory cytokines to cause MIS-C even without pneumonia and respiratory distress. Stimulation of broncho alveolar lymphoid tissue (BALT) following microaspiration would discharge further cytokines in circulation.

Plausibly NALT and GALT with or without BALT would be pouring an enormous amount of cytokines in circulation following stimulation from SARS-CoV-2 to cause MIS-C.

Nevertheless, MIS-C is rare in children due to its natural defenses. The incidence of lower respiratory tract infection is less, compared to elderly people, as nasal secretion washes off MCS outside and/or delivers toward the alimentary system.

In our study, we found SARS-CoV-2 as a “surface virus”[4] as it has got no hematogenous spread.[5] Hence, it can be washed off with nasal saline nasal spray and gargle (NSNSG) or with Jal Neti (Google search) to prevent further spread into the lower respiratory tract. Similarly, steam inhalation and drinking warm water (as expectorant) keep the mucociliary conveyor vibrant and active to prevent or to minimize pneumonia.

Plausibly, MIS-C following SARS-CoV-2 infection is due to the discharge of cytokines into circulation from NALT, GALT, and/or BALT without the cytopathic effect of SARS-CoV-2.

What Have we Achieved from This Information?

Thick nasal mucus gel and young vibrant mucociliary conveyor in children and younger people protect lower tract invasion of SARS-CoV-2 by preventing microaspiration, compared to elderly people. Mucus secretion is a continuous process. NSNSG washes off MCS, i.e., contaminated mucus gel which might be harmful to the lower respiratory tract. On the other hand,
the moisturizing effect of normal saline and water vapor inhalation rejuvenates the mucociliary apparatus and that is essential, particularly in elderly people. Saline is also a nonliving substance. Hence, it also acts as a temporary barrier during and after wash.

**How to live with COVID-19?**

Severity and fatality occur following migration (as microaspiration) of upper respiratory tract infection of SARS-CoV-2 toward the lower respiratory tract. Otherwise, it is like “simple influenza.” From our study, we knew that SARS-CoV-2 is a surface virus and SARS-CoV-2 could be kept restricted in the upper respiratory tract with NSNSG by preventing microaspiration. In our study, we found that ground-glass opacity following a lower respiratory tract infection decreased significantly ($P = 0.028$) by preventing further microaspiration compared to patients in control. Oxygen support and hospitalization might be necessary following infection of SARS-CoV-2 in the lower respiratory tract.

COVID-19 is here to stay and we have to “live with COVID-19” with logical confidence to stay safe and to maintain our national gross domestic product. We have to consider NSNSG for prevention, for therapeutic purpose, and to “live with COVID-19” with confidence. However, further study would strengthen the concept of a surface virus, microaspiration, and NSNSG.

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There are no conflicts of interest.

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