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The Cardiac Effects of Severe Acute Respiratory Syndrome Corona virus 2 (SARS-CoV-2) [COVID-19] Infection in Children and Young Adults

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Abstract

SARS-COV-2, although it causes less serious infection in children and young adults than in older adults, it does trigger morbidity and mortality. SARS-COV-2 can present in one of the two ways, either as an acute infection or as Multi System Inflammatory Syndrome in children (MIS-C). Both scenarios can be differentiated on clinical grounds. MIS-C also must be differentiated from Kawasaki disease (KD). A few children require hospitalization, some even require care in the critical care unit. Vaccination helps to prevent serious infection and hospitalization.

Keywords: COVID-19, MIS-C, KD, inflammation, vaccination, pharmacological agents

Introduction

As per the CDC, COVID-19 infection in the pediatric age group of 18 years and below afflicted 17.6% of the total cases with a mortality rate of 0.1%. On the other hand, young adults made up 21% of total cases with a mortality rate of 0.8%.[1] Those children with comorbid conditions such as obesity, an immunocompromised state, and chronic pulmonary disease are at risk for increased hospitalization, admission into critical care unit, and death.[2]

MIS-C is an inflammatory disorder that follows 2-6 weeks after COVID-19 infection[3] and affects multiple organs, occurring in 1 in 3164 cases of COVID-19 infection.[4] It is seen more in non-Hispanic black children, Hispanic children and less in non-Hispanic white and Asian children.[5]

Pathogenesis:

SARS-COV-2 is an RNA virus whose spike protein (S-protein) has a great affinity for Angiotensin Converting Enzyme-2 receptor (ACE-2) which is found on the surface of the host cell and therefore can easily binds to the S-protein.[6] The virus entry into the type-2 alveolar epithelial cell is facilitated by the host's serine protease which cleaves ACE-2 and thus activates the viral protein.[7]

The mechanism of cardiac injury[6] is due to

1. Direct injury by the virus,
2. Severe proinflammatory response leading to injury by cytokines generated because of inflammation,
3. Hypoxic-ischemic damage.

However certain factors such as lower ACE-2 receptor in the heart, frequent viral infections, immunizations, and different cytokine response in children act as a protective influence for less severe infection following SARS-COV-2

exposure.[8] SARS-COV-2 produces different infective phases in affected individuals, namely, the acute phase when the virus infects type-2 epithelial cells of the lung, activation of macrophages in the lung which induces an inflammatory response, severe proinflammatory response leading to excessive cytokine generation and resulting in multiple organ injury.[6]

MIS-C results from an overactive immune responseto the SARS-COV-2 virus. It involves robust $CD8^+$ (cytotoxic cells) T-cell activation.[9]

Symptoms and signs of infection:

SARS-COV-2 can appear in two different ways, namely, as an acute illness or as MIS-C. The differences between the two are shown in table 1.

Table 1: Comparison of clinical presentation of acute illness from SARS-COV-2 and MIS-C

	Type of SARS-COV-2 presentation	
Clinical presentation	**Acute illness**	**MIS-C**
General symptoms	No symptoms[10] or	Symptomatic
	Symptoms of fever and cough[10] with rare loss of taste & smell.[11]	Fever.[20]
Systemic manifestations	GI, resp. including ARF in (<2%), neurologic: less commonly TE, DVT, PE, enceph., stroke, sz.[12] CVS: less commonly arrhy., pericar.,& myocard.[13]	skin: rash, eyes: conjunctivitis, oral: mucosal alteration,[20] neurological: headache, altered sensorium,[21] GI: abd. pain, vomiting, & diarrhea.
Co-morbidities	In three-fourths, CHD, CM, hypertension, obesity, CNS, asthma, less frequently prematurity, genetic, immunodef., diabetes, cancer.[14]	CLD, asthma, & obesity.[20]
Mortality	16% in severely affected & 0.3% in infected.[15]	1.4-1.9%.[20]
Therapy	Supportive, mab for post exposure prevention & treatment,[16] Remdesivir for children >12 years of age early in infection,[17] dexamethasone for those on HFNC, NIV, IMV, & ECMO.[17]	Rx for HF with inotropes & vasoactive agents, IMV for ARF, & ECMO for ARF & HF.[20,22] 1st line of Rx is IVIG & judiciously used in CHF [20]. TNF-α antagonist, IL-1R antagonist, & glucocorticoids in children with coronary artery dilatation or LV dysfunction.[20] Low dose Aspirin in children with coronary artery involvement.[23]
Hospitalization	Moderate-severe infection, comorbid conditions, and suspected progression.[18]	Suspected MIS-C with fever, pain, diarrhea, & organ dysfunction.[24]
Complications	Secondary bacterial infection, sepsis, neurological, cardiac, renal, & coagulopathy.[19]	Cardiac (CA dilation), ARF, abdominalpain, & shock.[25]

&: and, GI: gastrointestinal, Resp.: respiratory, ARF: acute respiratory failure, TE: thromboembolism, DVT: deep vein thrombosis, PE: pulmonary embolism, enceph.: encephalitis, seizures, CVS: cardiovascular system, arrhy.: arrhythmia, pericar.: pericarditis., myocard.: myocarditis, abd.: abdominal, CHD: congenital heart disease, CM: cardiomyopathy, CNS: central nervous system, immunodef.: immunodeficiency, CLD: chronic lung disease, mab: monoclonal antibodies, HFNC: high frequency nasal cannula, NIV: noninvasive ventilation, IMV: intermittent mandatory ventilation, ECMO: extracorporeal membrane oxygenator, HF: heart failure, CHF: congestive heart failure, TNF-α : tumor necrosis factor, IL-1R: interleukin-1 receptor, LV: left ventricular, CA: coronary artery.

Table 2: MIS-C versus typical and atypical KD

Clinical	Typical KD	Atypical KD	MIS-C
Criteria	Fever > 5 days, 4 of the 5 signs: rash, cervical lymphadenopathy of at least 1.5 cm in diameter, bilateral conj. Injection, oral mucosal changes, periph. extremity changes	Defined as those who do not fit criteria for typical KD but have fever & coronary artery abnormalities. Fever for >5 days or more, meeting 2 or 3 diagnostic criteria or fever for >7 days with no other reason for the fever. If CRP is <3 mg/L & ESR is <40 mm/hr., serial clinical & lab assessment. Skin peeling: ECHO if CPR>3 & ESR is ≥40 & 3 or more lab findings: anemia, plat. >450 K after 7th day of fever, albumin<3 g//dL, ↑ALT, WBC ≥15K, urine wbc≥ 10/hpf, or +ve ECHO.	<21 years with fever*, lab evidence of inflammation**, clinical illness requiring hospitalization, multisystem organ dysfunction (≥2) [Cardiac, renal, resp., heme., GI, skin, or CNS]. And: No other possible diagnosis, and +ve or recent COVID-19 inf. by RT-PCR, serology, or ag test; or exposure to a suspected or confirmed COVID-19 case within the 4 weeks prior to the onset of symp.

*Fever ≥38^{0}C for ≥24 hrs., or report of subjective fever lasting ≥24 hrs., **including but limited to one or more of the following: ↑CRP, ESR, fibrinogen. procalcitonin, d-dimer, ferritin, LDH, or IL-6, ↑neutrophils, ↓lymphocytes, and low albumin.

Note: some children may display full or partial criteria for KD, and it must be reported if they meet the case definition for MIS-C. MIS-C must be considered in any pediatric death with evidence of SARS-COV-2 infection.[26]

Conj.: conjunctival, periph.: peripheral, ECHO: echocardiography, CRP: C-reactive protein, mg/L: milligram per liter, ESR: erythrocyte sedimentation rate, mm/hr: millimeter per hour, plat.: platelet, K: thousand, ↑ increased, ALT: alanine transaminase, WBC: white blood cell, hpf: high power field, heme.: hematology, inf.: infection, ag.: antigen, symp.: symptoms.

Conclusion

Although SARS-COV-2 is a less serious infection in children, clinicians need to be aware of the complications resulting from it. The use of vaccination must be encouraged in children and young adults. As well, any concerns of the family regarding vaccination and its side effects must be addressed. The vaccine side effects include seizures, myocarditis, stroke, MIS-C, menstrual disorder, appendicitis albeit the prevalence of these complications is low (0.2%).[27] Treatment is supportive and the availability of pharmacological agents has led to good outcomes.

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Conflicts of Interest

The authors declare that there are no conflicts of interest.

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