Potential Heart Problems in Convalescent COVID-19 Children: Alert from a Cuban Study

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COVID-19, the disease caused by the novel coronavirus SARS-CoV-2, is present in more than 200 countries and regions and is having a devastating impact worldwide. The sheer number of critical and convalescent patients—including pediatric patients—represents a challenge to the global medical community.

Although children with COVID-19 are often asymptomatic or exhibit only mild symptoms, they can transmit the disease and suffer from serious manifestations. In Cuba, 2,932 patients ≤18 years old tested positive for COVID-19 between March 2020 and February 1, 2021. Most of these children presented few to no symptoms upon diagnosis. At the time of this writing, 82.8% of those children had recovered,[1] and there had not been a single pediatric death due to the novel coronavirus.

Nevertheless, the world has seen a significant uptick in pediatric infections linked to outbreaks following easing of restrictions designed to control transmission. Cuba is no exception: the island registered 1624 pediatric cases in a single post-holiday month (January 2021) after opening for visitors.[1]

Cuba’s COVID-19 Prevention and Control Plan applies national, multidisciplinary and intersectoral protocols to all COVID-19 patients.[2] These define care for suspected, confirmed and convalescent cases, including in pediatric ages. The therapeutic and management protocols for Cubans ≤18 years old according to national case classifications (all medications are produced in Cuba) are contained in the box below.

Pediatric COVID-19 patients tend to evolve more favorably than adults. While individual immune response depends on virus exposure and other factors unique to each patient, a child’s immune system differs from an adult’s—specifically in the angiotensin-converting enzyme 2 (ACE2), the functional receptor for SARS-CoV-2 to enter into human cells. Children also have fewer comorbidities like hypertension, cardiovascular disease and diabetes mellitus than adults.[3]

One area of growing research interest is cardiovascular damage in children and adolescents recovering from COVID-19. Recent studies indicate that long-term cardiovascular complications from SARS-CoV-2 infection may include arrhythmias, myocarditis, pericarditis, shock, multisystem inflammatory syndrome (MIS) similar to Kawasaki disease, as well as stress-induced cardiomyopathy (Takotsubo syndrome) and sudden death.[3]

Viral infection can damage heart cells in both early and late stages of infection by inducing direct myocardial damage, hyper-inflammation and an immune response causing systemic inflammation and cytokine storm—especially Interleukin-6 that directly affects the QT interval. Other relevant factors may include: vasculitis, vascular microthrombosis, disseminated intravascular coagulation, hypoxia, electrolyte imbalances, myocardial ischemia and ACE2-deficiency disorder—as ACE2 protein expression occurs in various tissues, including heart and lung, with consequences for ion channel function.[4]

Preliminary studies demonstrate myocardial inflammation and injury (without serious symptoms) in recovering COVID-19 patients two months after diagnosis.[5] Although we know that COVID-19 affects both the respiratory system and cardiovascular function over time, the actual prevalence of persistent COVID-19 heart problems is unknown. Furthermore, cardiovascular damage linked to COVID-19 is likely underreported due to low autopsy rates and suspected multi-organ failure based on clinical and radiology exams rather than systematic use of electrocardiograms, echocardiograms, Holter monitors and other measurements. Cardiovascular damage may also go under-detected as a result of low symptomology and insufficient research about subacute (5–20 days after symptom onset), medium- and long-term sequelae of the disease.[4,5] Researchers need more time to study the long-term cardiovascular manifestations of COVID-19, especially in mild pediatric cases.

In 2020, Cuba launched a nationwide study coordinated by the National Genetics Center and carried out by the National

<table>
<thead>
<tr>
<th>Case classification</th>
<th>Remitted to</th>
<th>Treatment</th>
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<tbody>
<tr>
<td>Contact of confirmed case</td>
<td>Isolation center</td>
<td>PrevengHo-Vir (homeopathic)</td>
</tr>
<tr>
<td>Suspected – mild symptoms</td>
<td>Hospital</td>
<td>Oseltamivir/Azithromycin; PrevengHo-Vir</td>
</tr>
<tr>
<td>Confirmed – PCR-positive, asymptomatic or mild symptoms w/o risk factors</td>
<td>Hospital</td>
<td>Interferon alfa-2b</td>
</tr>
<tr>
<td>Confirmed – PCR-positive, mild symptoms with risk factors</td>
<td>Hospital</td>
<td>Interferon alfa-2b; Lopinavir; Ritonavir</td>
</tr>
<tr>
<td>Confirmed – PCR-positive, moderate symptoms without risk factors</td>
<td>Hospital</td>
<td>Lopinavir; Ritonavir; Biomodulina T (immunomodulator)</td>
</tr>
<tr>
<td>Confirmed – PCR-positive, moderate symptoms with risk factors, or severe symptoms</td>
<td>Hospital</td>
<td>Steroids; anti-coagulants; Jusvinza (CIGB 258), used only in those &gt;10 years old</td>
</tr>
<tr>
<td>Critical</td>
<td>Hospital</td>
<td>Steroids; anti-coagulants; Jusvinza (CIGB 258); antibiotics (sepsis/septic shock); assisted ventilation as needed. Individualized, according to clinical status</td>
</tr>
<tr>
<td>Convalescent – PCR-negative for 14 days</td>
<td>Home</td>
<td>Comprehensive follow-up in local health area by primary healthcare teams</td>
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Researchers need more time to study the long-term cardiovascular manifestations of COVID-19, especially in mild pediatric cases. Myocardial, pericardial, electrocardiographic and vascular abnormalities are potentially reversible in children recovering from COVID-19. In our opinion, standardizing early detection and timely treatment for these patients can improve their prognosis—however reserved. We continue actively searching for cardiovascular abnormalities in COVID-19 pediatric cases using the methodology described as part of our strategy to minimize the medium- and long-term impact of the pandemic and post-infection complications among children.

It is both urgent and imperative that we continue conducting research about SARS-CoV-2 throughout every stage of the disease, from transmission to recovery and beyond. We recommend cardiovascular studies specifically for convalescent children, based on current evidence and using the latest technology. A cardiology focus should be integrated into the support and follow-up for pediatric patients, monitoring closely for subclinical abnormalities and hidden comorbidities.

REFERENCES

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Submitted: March 1, 2021
Approved for publication: April 8, 2021
Disclosures: None