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Use of unproven COVID-19 therapies by African American patients poses risks

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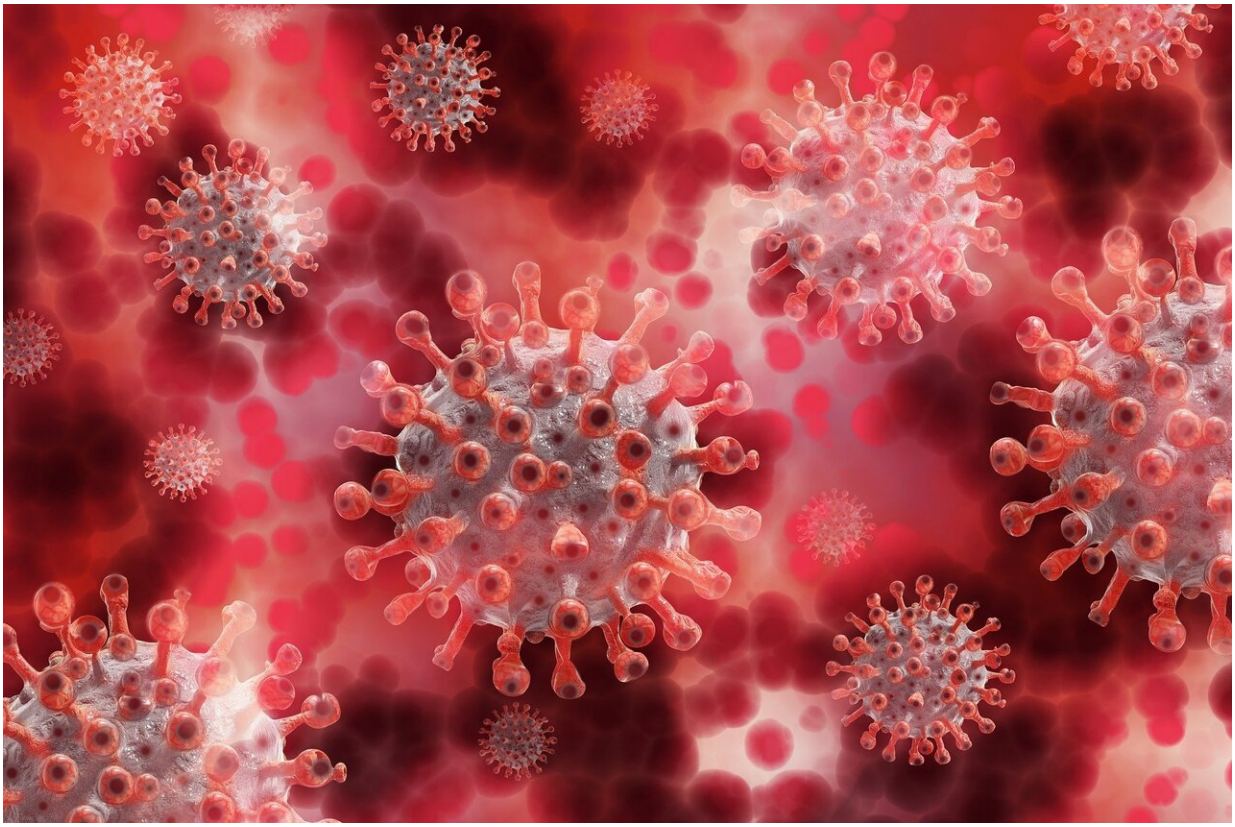

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Nearly one out of every 10 African Americans has a genetic variant that puts them inherently at an increased risk for ventricular arrhythmias and sudden cardiac death. Writing in the journal *Heart Rhythm*, the official

publication of the Heart Rhythm Society and the Cardiac Electrophysiology Society, investigators observe that along with socioeconomic and cultural factors, this genetic risk factor may contribute to the racial health disparities that have been documented in victims of the COVID-19 pandemic. They also note that the unwanted effects of therapies such as hydroxychloroquine may put African Americans with the variant at increased risk of drug-induced ventricular arrhythmias. Therefore, they urge particular caution.

"Without a definitive explanation for the increased COVID 19-related mortality rates observed among individuals of African descent, we need to consider all potential contributors, including the possibility of genetic predispositions," explained first author John R. Giudicessi, MD, Ph.D., Department of Cardiovascular Medicine (Clinician-Investigator Training Program and Division of Heart Rhythm Services), Mayo Clinic, Rochester, MN, USA. "The African-specific p.Ser1103Tyr-SCN5A common ion channel variant is a reasonable place to start, as its proarrhythmic potential is awakened by risk factors observed in hospitalized COVID-19 patients—namely, hypoxemia, electrolyte abnormalities, and QT-prolonging drug use."

The investigators note that the proarrhythmic potential associated with p.Ser1103Tyr-SCN5A can be enhanced by drugs that can cause irregular heartbeat (QTc-prolonging medications), including some antiarrhythmic drugs but also, importantly, some antibiotics and antifungal medications.

Direct and/or indirect myocardial injury or stress has emerged as a prominent, prognostic feature in COVID-19. Acute myocardial injury in patients with COVID-19 may be caused by a direct SARS-CoV-2 myocardial infection; the exaggerated immune response known as the cytokine storm; or hypoxia, dangerously low levels of oxygen and high levels of carbon dioxide in the blood. African American infants with the p.Ser1103Tyr-SCN5A variant are over-represented in sudden infant

death syndrome, and mechanisms underlying hypoxia may be responsible. The profound hypoxia observed in many COVID-19 patients, raises reasonable concern that p.Ser1103Tyr-SCN5A could produce a similar, African-American susceptibility to ventricular arrhythmia and sudden cardiac death from the SARS-CoV-2 infection.

Taken together, the data suggest that one in 13 African Americans may be at substantially increased risk for potentially lethal ventricular arrhythmia during the COVID-19 pandemic. Whether population-specific genetic risk factors are contributing to the spike in sudden deaths and racial health disparities observed in COVID-19 epicenters remains to be proven, and given the lack of banked DNA in these epicenters, the investigators question whether the speculation may even be testable.

"The genetic variant p.Ser1103Tyr-SCN5A, is a potentially proarrhythmic, sudden cardiac death marker for African Americans, and seeking its presence and respecting it is long overdue," asserted senior author and genetic cardiologist Michael J. Ackerman, MD, Ph.D., Department of Cardiovascular Medicine (Division of Heart Rhythm Services), Department of Pediatric and Adolescent Medicine (Division of Pediatric Cardiology), and Windland Smith Rice Cardiovascular Genomics Laboratory, Mayo Clinic, Rochester, MN, USA.

As recent studies have shown that hydroxychloroquine is not effective in the treatment of sick, hospitalized COVID-19 patients, the authors advocate against its use in that setting. Nevertheless, if COVID-19-directed, QTc-prolonging agents such as hydroxychloroquine are to be used, the investigators recommend careful cardiac monitoring, preferably in a way that spares personal protective equipment.

The authors call for research into the link between p.Ser1103Tyr-SCN5A and rates of sudden death and COVID-19-related mortality,

suggesting the use of existing DNA biobanks such as the United Kingdom Biobank, a study that investigates the contribution of genetic and environmental factors to the development of disease, and the Jackson Heart Study, a large, community-based investigation into the causes of cardiovascular disease in African Americans. Point-of-care genetic testing for p.Ser1103Tyr-SCN5A should be investigated.

And finally, the authors recommend studies of medications that may better protect at-risk individuals, especially African Americans, in the context of the ongoing COVID-19 pandemic.

More information: John R. Giudicessi et al, Genetic susceptibility for COVID-19–associated sudden cardiac death in African Americans, *Heart Rhythm* (2020). DOI: 10.1016/j.hrthm.2020.04.045

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