Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Hydroxychloroquine at usual doses as an option for coronavirus disease 2019 treatment

Check for updates

TO THE EDITORS: We read with great interest the article by Dashraath et al.[1] During pregnancy, the onset of severe acute respiratory syndrome (SARS) can jeopardize both mother and fetus and may cause extreme prematurity, as in previous coronavirus outbreaks.

Considering the promising chloroquine treatment, the authors focus on the side effects of high doses, mainly on the basis of the report of higher volumes of distribution of chloroquine during pregnancy in a small series of women.[2] However, their deduction of an assumed need for higher doses against coronavirus disease 2019 ("at least 500 mg twice daily") raises the question of the rationale for such doses.

In actuality, the authors of this pharmacokinetic study[2] only hypothesized that reduced concentrations of chloroquine in pregnancy "could compromise its curative antimalarial efficacy."

Besides, the 90% effective inhibitor concentration of chloroquine against SARS coronavirus 2 in Vero E6 cells is low[3] and easily achievable in vivo. Another pharmacokinetic study confirms that clearance and total drug exposure of the widely used variant hydroxychloroquine does not change during pregnancy,[4] which does not support using higher doses during pregnancy.[4,5]

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The authors report no conflict of interest.

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Coronavirus disease 2019 and obesity: one pandemic meets another

Check for updates

TO THE EDITORS: Recent publications on the novel coronavirus disease 2019 (COVID-19) regarding the high-risk populations have focused on the elderly, those with cardiovascular disease, diabetes, and, women during pregnancy. An important article by Dashraath et al[1] that was recently published in the *American Journal of Obstetrics & Gynecology* provided a thorough summary of the factors that need to be considered for pregnancy, maternal health, and postpartum care during the time of COVID-19, and guidelines on how these factors should be addressed and monitored.[1] However, the factors of overweight and obesity as critical preexisting health conditions, which are growing risk factors in pregnancy, are missing from this important discussion. With the ever-changing global mortality rates associated with COVID-19, which thus far seem to have regional variations, we implore researchers to collectively investigate and consider whether these regional variations in the mortality rates and the severity of COVID-19 could have any links to the prevalence of overweight and obesity. These factors should be investigated because most of the nations with the highest confirmed COVID-19 cases (the United States, Italy, Spain, Germany, France, and Iran; according to data at the time of submission April, 2020) are on the higher end of the overweight and obesity prevalence rates (ranges: 56%–68% overweight and 20%–36% obese according to the 2016 World Health Organization rates).

The alarming rise in the rates of overweight and obesity is a public health challenge that is causing a shift in chronic disease rates and health complications,[2] especially in pregnancy with or without gestational diabetes. During this time

of COVID-19, overweight and obese populations could have a higher susceptibility to develop severe complications, especially linked to respiratory illness. Studies have shown that obesity is associated with pulmonary complications such as pneumonia.[3,4] Obesity has a negative effect on both the respiratory function (eg, owing to reduced lung expansion and narrowing airways) and on the immune function and host defense,[4] both of which are specifically under threat during the time of COVID-19 and during pregnancy. Adipose tissue dysfunction in overweight and obesity can act as a diseased organ (eg, chronic inflammation). Moreover, much is still unknown about how the severity of respiratory viral infections is compounded by overweight or obesity when coupled with other risk factors or pregnancy. This fast spreading virus could highlight the dire consequences of the rise in the rates of overall compromised health compounded by the exploding overweight and obesity rates.

It is important to consider whether the severity of COVID-19 and the associated mortality rates could increase because of a spread into regions with a higher prevalence of overweight and obesity, which may also be applicable to children (areas where childhood overweight and obesity is high). To best support the mandatory global efforts in identifying and defining the most relevant at-risk populations, we strongly suggest that overweight and obesity should be considered as a high potential variable and a comorbidity or risk factor in the general population. ■

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REPLY

Check for updates

We thank Carbillon and coworkers for their perspectives on the optimal dose of chloroquine in pregnancy. The novel use of chloroquine phosphate and hydroxychloroquine in the management of coronavirus disease 2019 (COVID-19) is an area of evolving research. Our rationale for high-dose chloroquine was based, at the time, on expert consensus from the Chinese Ministry of Health and data from the interim analysis of a study by the Health Commission of Guangdong province, China, which supported the use of a twice-daily 500-mg regimen in the clinical management of COVID-19.[1]

However, important findings from a subsequent double-masked, randomized phase IIb clinical trial from Brazil (ClinicalTrials.gov number, NCT 04323527) of adults with severe COVID-19 have since demonstrated that high-dose chloroquine is associated with greater toxicity and mortality from QTc prolongation.[2] Although these results are not generalizable across the COVID-19 disease spectrum, we now caution against the use of high-dose regimens and advise providers to consult their institutional protocols when considering these drugs as a treatment option in pregnancy.

Rancourt and colleagues astutely highlight the influence of body mass index (BMI) on disease outcomes. Although anthropometric data of pregnant women with COVID-19 were not available during the initial stages of the pandemic, obesity is now a well-recognized risk factor for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection.[3] Cohort studies of nonpregnant adults with COVID-19 and a BMI >35 kg/m^2 have demonstrated a higher risk for admission to critical care and the need for invasive mechanical ventilation. Similar trends are observed in pregnancy; our recent systematic review of 637 pregnant women with laboratory-confirmed SARS-CoV-2 infection demonstrated a 40% prevalence of obesity and diabetes mellitus among COVID-19—related maternal mortalities reported between December 2019 and May 2020.[4] Prospective data from the United Kingdom Obstetric Surveillance System in addition reveal that overweight and obese pregnant women with COVID-19 were at least twice as likely to require admission to hospital when compared with those with a BMI <25 kg/m^2.[5]

It is believed that obesity attenuates cardiorespiratory reserves and amplifies circulating serum interleukin-6 levels; the latter, by instigating a cytokine storm, results in a significantly elevated risk of severe disease and mortality from COVID-19.[3,4] Pregnant women who are obese and battling COVID-19 would therefore find themselves between Scylla and Charybdis, where gravid physiology and disease pathology collide to encourage progression to critical illness. ■

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