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Letter to the Editor

Opportunities for preventing further endothelial dysfunction in pregnant COVID-19 patients with familial hypercholesterolemia



Patients with heterozygous familial hypercholesterolemia (FH) with COVID-19 are at increased risk for acute myocardial infarction (AMI) as shown in a recent report from a very large United States national database of over 300 000 individuals which showed an absolute risk for AMI in those with COVID-19 of approximately 0.3% for non-FH patients, 0.5% for probable FH patients without prior atherosclerotic cardiovascular disease (ASCVD), and 2% for probable FH patients with prior ASCVD.¹

The heightened risk is probably a result of the lifelong elevated serum low-density cholesterol (LDL-C) as well as lipoprotein(a) [Lp(a)] levels in FH patients.² During normal pregnancy, serum LDL-C increases by about 30% and serum triglycerides (TG) can double.³ Additionally, serum Lp(a) levels rise.⁴ As LDL-C levels are already elevated in FH patients, levels can rise substantially. During pregnancy, the vascular endothelium of pregnant FH mothers is therefore under further endogenous stress from three fronts, namely elevated serum LDL-C, Lp(a) as well as TG. If a pregnant mother with FH were to contract SARS-CoV-2, the infection could potentially worsen endothelial dysfunction even further.^{5,6} Whilst our knowledge of the risk factors or markers for COVID-19 severity among pregnant women is incomplete it is very likely that changes in the lipid profile in FH mothers are undesirable and that these changes need to be minimized by treatment with lipid-modifying drugs.

Unfortunately, lipid-modifying drug treatment in pregnant FH mothers remains controversial.⁷ Currently, only bile acid sequestrants and/or lipoprotein apheresis are considered safe and are recommended for use in severe FH during pregnancy.^{8,9} While lipoprotein apheresis is an option in severe FH patients with COVID-19¹⁰ the role of bile acid sequestrants remains uncertain.¹¹ In addition, if bile sequestrants are used, vitamin D and K levels need to be monitored.⁷

There is little evidence to show that statins are teratogenic during pregnancy.¹² The FDA has recently removed the contraindication for statins in pregnant females with established ASCVD or at very high risk for ASCVD, such as patients with homozygous FH, which will enable health care pro-

fessionals and patients to make individual decisions about the benefit and risk of ongoing statin therapy during pregnancy.¹³ As evidence-based guidelines on the use of statins in pregnant FH patients who are at increased risk for ASCVD are lacking, an individual approach considering the pros and cons of statin use needs to be entertained and the use of statins is therefore, at least in some cases, justified.⁷ Currently, risk factors for pregnancy complications in mothers with SARS-CoV-2 infection have only just begun to be identified.¹⁴ However, it is reasonable to assume that pregnant FH mothers with SARS-CoV-2 infection are at heightened risk and the role of ongoing statin use, or even the escalation of statin dosage, is paramount.¹⁵ Pravastatin is probably a particularly suitable statin because it does not affect fetal cholesterol metabolism.¹⁶ However, the risk of harm with any statin during pregnancy is probably minimal and outweighed by the potential benefits. Preliminary results have also suggested that lipid-modifying therapy could have a beneficial impact in patients with COVID-19.¹⁷ Current knowledge on the safety of other lipid-modifying drugs such as ezetimibe, PCSK9-inhibitors, and bempedoic acid is scanty and these drugs are not recommended during pregnancy. In summary, the treatment of a pregnant FH mother with SARS-CoV-2 infection should include a case-by-case assessment of the potential benefit of ongoing statin therapy or the introduction of statin therapy as the benefits may well outweigh the risks.

Declaration of Competing Interest

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