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EDITORIAL COMMENT

When Burdened by Ischemic Heart Disease, Pregnant Individuals Lose the Advantage of Youth*

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Not all menstruating individuals are protected against cardiovascular diseases until menopause. Data indicate an even or rising incidence of coronary artery disease in people younger than 50 years, in contrast to a decline among middle-aged individuals.[1] More young people are growing up from childhood with obesity, diabetes, hypertension, and hyperlipidemia.[1] Coupled with inadequate health care and adverse environmental exposures, these risk factors accelerate the incidence of premature atherosclerosis. Thus, a subset of these young people are entering pregnancy with ischemic heart disease (IHD), when their chronologic age does not equal their biologic age.

How should we counsel individuals with IHD about their risk of morbidity and mortality in pregnancy? Common risk-stratification models for outcomes of cardiac diseases in pregnancy, like the modified World Health Organization (mWHO) classification, Cardiac Disease in Pregnancy, and Zwangerschap bij Aangeboren Hartafwijking scores, are limited in this regard. Outcomes for pregnant individuals with pre-existing IHD are unclear, and this is the gap addressed by Denoble et al[2] in this issue of *JACC: Advances*.

Denoble et al[2] compared outcomes reported in the 2015 to 2018 Nationwide Readmissions Database for those with IHD vs those with heart disease classified as mWHO I/II-IV, as well as those without cardiac diagnoses but hospitalized for obstetric delivery. Individuals with IHD were roughly 0.03% of all hospitalizations for delivery. They had a higher burden of comorbidities, socioeconomic disadvantage, and older age than those without any cardiac diagnosis. Despite this, individuals with IHD had a comparable adjusted relative risk of severe morbidity or death as those with a mWHO I and/or II classification. This adds new data that physicians can use to counsel about the low-to-intermediate risk in pregnancy for individuals with pre-existing IHD who are contemplating pregnancy or are currently pregnant. Obstetricians, anesthesiologists, and cardiologists can use these data as a reference for labor and deliver planning.

There are several strengths to the study. The analysis includes a large population of admitted patients which is likely to be representative of the U.S. birthing cohort. Patients with IHD had a highly complex medical history. They had a high proportion of mental health disorders and serious comorbidities. They were more likely to be beneficiaries of public insurance, and the burden of their care tended to fall on large, metropolitan teaching hospitals. Impressively, medical teams were able to manage the challenge of caring for these complex patients, but the results might not be generalizable to all types of hospital settings where subspecialists in cardiology and high-risk obstetric care are less accessible.

The principal limitations of the study are those that affect studies of maternal morbidity and mortality more generally; namely, the rarity of events and lack of prospective data. Investigators rely on the International Classification of Diseases (ICD) code data sets

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for these reasons. IHD is likely well defined by ICD codes, but when the diagnosis depends on a more elaborate definition, ICD codes may be less accurate. These data sets also lack imaging, medication, and laboratory data and are not linked by familial relationships. Solely restricted to pregnancy records and without linked information on neonates, we can use data from this study to counsel individuals on what they might expect for themselves but cannot counsel them on what to expect for their offspring. Rightly, the authors emphasize that the conclusions apply to those with a diagnosis of IHD alone and without knowing how their delivery risk was modified by left ventricular ejection fraction. Additionally, more people are using reproductive endocrinology and infertility assistance to achieve pregnancy later in life, but we are not able to discern specific information about this group from these data.

The results also reflect the nature of medical treatment during the time frame represented. Individuals with IHD who are considering pregnancy or are pregnant were unlikely to be prescribed statins between 2015 and 2018, but practice may be changing. In 2021, the Food and Drug Administration softened its stance on the use of statins in pregnant patients, as observational studies have not shown increase in birth defects.[3] Those with IHD, stroke, and familial hypercholesterolemia may benefit from continued treatment per the Food and Drug Administration. While the strongest warning to never use statins during pregnancy was removed, the announcement confusingly states that most should still stop statin use during pregnancy, and time will tell if physicians and others feel confident in using them. Other core components of secondary prevention like beta-blockers have been associated with small-for-gestational age infants in a dose-dependent manner, and the use of selective beta-blockers with monitoring, rather than complete withdrawal, can be an approach to balance the risk-benefit ratio.[4] Apart from the controversy of statin use and potential adverse effects of beta-blockers, aspirin is clearly recommended for prevention of preeclampsia/eclampsia in high-risk individuals.[5,6] Thus, aspirin can have a dual role in pregnant individuals with IHD, which cardiologists should be aware of.

In summary, the finding of individuals with IHD having low-to-intermediate risk of adverse events at delivery has clinical relevance to those living with stents, previous myocardial infarction, and coronary artery bypass grafting, and it may be helpful to those involved in the care of pregnant people to personalize care. With rising pregnancy-related mortality in the United States, particularly among Black and Native American individuals, it will certainly take the combined efforts of many to improve public health so that young people retain the advantage of youth in pregnancy.

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