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EDITORIAL COMMENT

Is the Placenta Inflamed in Cardiovascular Disease?*

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Cardiovascular disease complicates 1%-4% of pregnancies, and it is the leading cause of maternal death in developed countries[1]. Little is known about the effect of cardiovascular disease on the placenta itself and the implications it may have on fetal development. Recent research has predominantly focused on the association of placental pathology with future development of cardiovascular disease as well placenta-preeclampsia pathophysiology; however, the findings from Wu et al[2] are the first to report the association of cardiovascular disease with placental inflammation.

In this issue of *JACC: Advances*, Wu et al[2] describe placenta pathology in 264 pregnancies complicated by maternal cardiovascular disease encompassing a wide variety of maternal diagnosis such as congenital heart disease, arrhythmias, cardiomyopathy, valvular and acquired heart disease. Not surprisingly, compromised maternal hemodynamics may lead to a decrease in the placental perfusion with subsequent growth restriction in the fetus. In addition to the findings such as placental weight being lower in 45% with vascular pathology noted in 41%, acute chorioamnionitis was seen in 23% of the placentas. Interestingly, they also found villitis of unknown etiology (VUE) in 11% of the placental specimens.

VUE is a rare maternal T-cell-mediated placental inflammation that is destructive to the placenta as maternal T cells (CD8+ cytotoxic T cells) infiltrate into the chorionic villi[3]. Independently, VUE has been shown to be associated with poor obstetrical outcomes including gestational hypertension, preeclampsia, fetal growth restriction, and preterm birth, with predisposing factors being certain races, autoimmune disease, increasing body mass index, and multigravidity and possibly also linked to increasing maternal age, seasonal variation, and viral infection[4-6]. The findings from Wu et al. are unique to report the association of VUE with maternal cardiovascular disease which suggest additional mechanisms that may influence adverse pregnancy outcomes in this population.

These findings are suggestive of the complex nature of the immune modulatory effects generated by the underlying cardiovascular disease promoting inflammation in the maternal compartment that targets placenta with potential impact on placental development. Currently, VUE can only be diagnosed after delivery of the fetus by placental histology; however, there is need for an earlier diagnosis and therapeutic options during an ongoing pregnancy to impact outcomes. Future research may lead to insights into the intricate fetal-placental unit as it relates to altered maternal hemodynamics and mechanisms leading to maternal inflammation. The inflammatory nature of placental pathology, diagnosis, and immunomodulatory therapy to alter the course of inflammatory pathway is an area of future research that may impact maternal and fetal outcomes.

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The authors attest they are in compliance with human studies committees and animal welfare regulations of the authors' institutions and Food and Drug Administration guidelines, including patient consent where appropriate. For more information, visit the Author Center.

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