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Genome Wide Association Study of Patients with History of Postpartum Hemorrhage

Abstract

Postpartum hemorrhage (PPH) is the leading cause of maternal morbidity and mortality worldwide. Uterine atony is the most common etiology, contributing to 80% of PPH cases. While a number of clinical risk factors have been identified (i.e., preeclampsia, chorioamnionitis), PPH remains difficult to predict and the molecular mechanisms are not well delineated. A portion of PPH risk is heritable, with both maternal and fetal genetic contributions. Oxytocin is a hormone, neuromediator and uterotonic and multiple genetic variants in the oxytocin signaling pathway have been described; however, there are no studies in patients with PPH. In this proposal, we aim to identify maternal genetic variants in the oxytocin signaling pathway that contribute to PPH risk. In addition, we will identify new genetic variants by performing the first large genome-wide association study (GWAS) of PPH. We have access to several large biobanks with PPH cases, including the UK Biobank (n=1,636), Vanderbilt BioVU, (n=499), Partners Biobank (n=564) and Michigan Genomics Initiative (n=233), which contain patient genotyping linked to medical records of 2,932 patients with PPH and more than 300,000 healthy controls. We will perform a GWAS on the European patients and seek to replicate our results in other ethnicities and cohorts. Using existing analytic tools, we will further functionally characterize the pathways and gene sets to define the role of the identified genetic variants in PPH pathogenesis. We anticipate that these results will significantly advance our understanding of the pathophysiology of PPH, and ultimately aid obstetric anesthesia care of pregnant patients by identifying novel biologic targets for PPH prediction and pharmacotherapy.