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Clinical Pearl: Clinical Pearl: Evaluation of Stillbirth Among Pregnant People with Sickle Cell Trait

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Stillbirth remains a devastating pregnancy complication for many families, with an estimated incidence of about 1 in 160 births and approximately 24,000 cases each year in the United States (1). Although the direct cause is not always identified, some well-known risk factors include obesity, diabetes, and hypertension. There is also abundant data on persistent racial, ethnic, and socioeconomic disparities for stillbirth.

"Universal newborn screening for sickle hemoglobinopathies has been introduced to identify individuals with sickle cell disease (SCD) that has, by default, identified individuals with sickle cell trait (SCT). While the diagnosis of SCD comes with extensive counseling and follow-up, patients with SCT are not reliably notified, and genetic counseling may be minimal (2)."

Universal newborn screening for sickle hemoglobinopathies has been introduced to identify individuals with sickle cell disease (SCD) that has, by default, identified individuals with sickle cell trait (SCT). While the diagnosis of SCD comes with extensive counseling and follow-up, patients with SCT are not reliably notified, and genetic counseling may be minimal (2). Although SCT is not broadly perceived as a disease state, SCT can increase the risk for complications such as exertion-related injury, venous thromboembolism, renal medullary carcinoma, and chronic kidney disease (3). There is particularly limited literature looking into the impact of SCT on reproductive health and pregnancy-associated complications. While some studies have shown an increased risk of stillbirth in those with SCT, work to date has led to conflicting results, likely due to limitations that include small sample size, limitation of analysis to one race or ethnicity, and presence of confounding variables (4-6).

In a recent retrospective cohort study by Canelon et al., authors assessed the association between SCT and stillbirth outcome in patients at Penn Medicine between 2010 and 2017 (7). Of the 63,334 deliveries that occurred during this time, 2482 newborns had SCT, and 215 newborns had SCD. 0.8% of deliveries in the general population resulted in stillbirth. While of the deliveries in patients with SCT, the prevalence of stillbirth was 1.1% and 2.3% in patients with SCD. After adjusting for additional risk factors, patients with SCT were still at increased risk for delivery resulting in stillbirth relative to those without SCT (adjusted odds ratio, aOR 8.94; 95% CI, 1.05-75.79; p = 0.045). Stillbirth did not show predominance in those with SCT from any specific race or ethnicity. Multiple gestation deliveries were also associated with stillbirth (aOR, 4.68; 95%CI, 3.48-6.29; P < .001).

Many studies on sickle cell hemoglobinopathies in the United States have isolated analysis to African American populations only, leading to limitations on the applicability of data and assumptions of disease prevalence. This may be because SCD and SCT are most commonly diagnosed amongst African American patients. By including all patients who experienced stillbirth, the authors could provide a comprehensive assessment of SCT's impact on stillbirth. Further, the authors were the first to consider each racial and ethnic identity independently to gauge the role of racism in stillbirth. In doing so, the authors could not find an association between SCT and stillbirth among Black or African American patients. Given conflicting information with previous studies and the presence of confounding factors that are difficult to separate, the data can be challenging to interpret. The authors emphasize the importance of looking at diverse patient populations and the need for further studies on the role of racism in stillbirth.

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In conclusion, this study used data from a large population to show that, in addition to patients with SCD, SCT also confers a higher risk for stillbirth than the general population. The authors identify a need for increased support for genetic counseling that could be provided during prenatal gynecologic and the postnatal period. It would also be of interest to identify the mechanistic role

of SCT in its various associated disease processes. Further work should include all patients with SCT instead of isolating studies to one race or ethnicity.

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