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Gestational Diabetes Mellitus as a Herald of Type 2 Diabetes Mellitus: An Opportunity for a Lifetime

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Gestational diabetes mellitus is defined as carbohydrate intolerance of any degree that begins or is first recognized during pregnancy.¹ It complicates approximately 4% of all pregnancies in the United States¹ and 3-5% in the United Kingdom.² Notably, variable prevalence rates between 1-14%¹ have been reported due to factors including differences in the diagnostic criteria used to define both gestational diabetes and Type 2 diabetes mellitus,³⁻⁶ as well as the heterogeneous racial/ethnic populations studied.⁷

Despite controversy over diagnostic criteria, the risks associated with gestational diabetes in pregnancy have been well-recognized. These have included neonatal risks such as macrosomia, maternal risks such as increased Cesarean delivery rate,⁸ and their respective comorbidities. Additionally, the impact of gestational diabetes after the pregnancy has been appreciated. The incidence rate of Type 2 diabetes after a pregnancy complicated by gestational diabetes has ranged from 2.6% to over 70% in studies examining women from 6 weeks to 28 years postpartum.⁹ Difficulty in precisely defining the incidence of Type 2 diabetes in women with a history of gestational diabetes has been attributed to factors such as varied diagnostic criteria for both gestational diabetes and Type 2 diabetes,³⁻⁶ insulin use during pregnancy, longer periods of postpartum follow-up,⁹ as well as missed opportunities in identifying and diagnosing these women through education and screening efforts.¹⁰

In today's *Lancet*, Leanne Bellamy and colleagues¹¹ report findings from their meta-analysis of cohort studies examining the correlation between gestational diabetes and subsequent development of Type 2 diabetes. Their analysis included 20 studies representing 675,455 women and 10,859 cases of Type 2 diabetes. They observed a nearly 7.5 fold increased risk of developing Type 2 diabetes for women who had gestational diabetes during pregnancy. Moreover, when considering the duration of follow-up, women within 5 years of a pregnancy complicated by gestational diabetes had a relative risk of 4.69 which more than doubled to 9.34 among women who were examined more than 5 years postpartum.

Because of differences in diagnostic criteria for both gestational diabetes and Type 2 diabetes across studies, as well as variable distributions of gestational diabetes risk factors among the studies, the authors conducted several subgroup analyses in order to discover

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I confirm that I have seen and approved the submitted version of this comment.

potential sources of heterogeneity. They did not uncover heterogeneity resulting from duration of follow-up, ethnicity, maternal age, maternal BMI during pregnancy or postpartum, or diagnostic criteria for gestational diabetes and Type 2 diabetes.

However, other potential sources of heterogeneity were not examined in subgroup analyses, possibly due to an inability to gather complete data in the setting of a meta-analysis. Parity is potentially a risk factor for both gestational diabetes¹² and Type 2 diabetes¹³ and is often handled as an adjusted covariate in the setting of a multivariate analysis. Therefore, dichotomizing this parameter, if parity data could indeed be captured from the relevant studies, may provide insight into sources of heterogeneity. Additionally, lifestyle information, which cannot always be gleaned from study descriptions of patient characteristics, would also provide beneficial information when considering sources of heterogeneity. For example, lactation has been demonstrated to decrease the risk of developing Type 2 diabetes among women with a history of gestational diabetes.¹⁴ Nevertheless, I recognize that a meta-analysis is inherently limited by the data contained in the studies under examination and, given the significant multicollinearity among risk factors for gestational diabetes and Type 2 diabetes, teasing out specific attributable risk will prove challenging if not impossible.

Sufficient evidence has been accumulated to support the assertion that gestational diabetes is a harbinger of Type 2 diabetes in women who are presumably predisposed to Type 2 diabetes and are faced with the metabolic challenges of pregnancy. The current task is to ensure that this information is disseminated to clinicians, and that they use this information to target women who have experienced gestational diabetes for Type 2 diabetes prevention efforts. Consequently, future studies should address how the progression from gestational diabetes to Type 2 diabetes can be arrested in order to develop evidence-based approaches to the health care of this population. Given the compelling data evidencing the link between gestational diabetes and the development of Type 2 diabetes, we as clinicians are afforded the rare opportunity to alter the natural course of disease and impact a woman's future health today. *Carpe diem!*

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