GAD Antibodies in Women With Hyperglycemia in Pregnancy: No Association With Large-for-Gestational-Age Birth Weight

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Hyperglycemia in pregnancy (HIP) in women with no known diabetes before pregnancy includes gestational diabetes mellitus and diabetes in pregnancy, which is defined as a glycemic level similar to that for diabetes outside pregnancy (1). Type 1 diabetes may be discovered during pregnancy, and one way to screen for it is to evaluate the presence of β-cell–specific autoantibodies. Up to 10% of women with HIP have these autoantibodies (2). As type 1 diabetes is associated with a very high rate of large-for-gestational-age (LGA)–birth-weight infants (i.e., 44% in France [3]), we hypothesized that women with HIP and GAD antibodies (GADAs) may have a higher prevalence of LGA-birth-weight infants than women with HIP but no GADAs because of higher glucose levels during pregnancy and a decrease in insulin secretion (4). In this context, we investigated through a multiethnic, observational, prospective cohort whether HIP pregnancies had a poorer prognosis in terms of LGA infants according to different GADA categories, after adjusting for confounders.

The study was conducted at Jean Verdier University Hospital in Bondy, a suburb of Paris, France, with a high rate of social inequities. Analyses of routine hospital electronic medical records of maternal and neonatal data at birth between 2012 and 2017 were performed. The methodology was recently described elsewhere (4,5). At the hospital, we use French recommendations for HIP screening and care and the International Association of Diabetes Pregnancy Study Group's criteria for diagnosis (2). We calculated that a study sample of 1,200 women would be needed to provide a power of 80% in order to detect a 10% difference in LGA birth weight using a χ^2 test at a two-sided significance level of 5%. We included consecutive women ≥18 years old with a single-fetus pregnancy who had no known diabetes before pregnancy or personal history of bariatric surgery and who had HIP and a GADA measurement. LGA birth weight was defined as a birth weight greater than the 90th percentile for the standard French population (4,5). We measured GADA (dedicated Wizard Gamma Counter radioimmunoassay; PerkinElmer-cisbio) on the day of hospitalization dedicated to providing initial education for HIP. Of note, no woman had clinical signs of diabetes, such as polyuria, weight loss, or ketonemia. We considered that women with a GADA level <1 IU/mL (the threshold for positivity according to the assay manufacturer) were GADA negative (i.e., no GADA), that those with a level between 1 and 2.99 IU/mL were moderately GADA positive, and that those with a GADA ≥3.0 IU/mL were clearly GADA positive. The coefficient of variation was 4.9% at 6.1 IU/mL and 7.0% at 43 IU/mL, with a limit of detection of 0.11 IU/mL.

The study sample comprised 1,182 women with both HIP (7% with diabetes in pregnancy and 93% with gestational diabetes mellitus) and GADA measurements. GADAs were present in 87 (7.4%), including 56 (4.7%) moderately GADA positive and 31 (2.6%) clearly GADA positive. Table 1

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Table 1—Metabolic characteristics according to GADA rates

	Women with available data, *n*	No GADA (*n* = 1,095)	Moderately positive GADA (*n* = 56)	Clearly positive GADA (*n* = 31)	*P*
Metabolic characteristics					
Age (years)	1,182	32.8 ± 5.4	33.6 ± 6.0	33.4 ± 6.0	0.45
Prepregnancy obesity	1,170	339 (31.2)	11 (20.4)	9 (30.0)	0.24
Family history of diabetes	1,182	395 (36.1)	14 (25.0)	15 (48.4)	0.08
Previous pregnancy(ies)					
History of HIP	1,182				0.23§
First child		328 (30.0)	23 (41.1)	13 (41.9)	
No		589 (53.8)	22 (39.3)	12 (38.7)	
Yes		178 (16.2)	11 (19.6)	6 (19.4)	
History of macrosomia	1,182				0.7§
First child		328 (30.0)	23 (41.1)	13 (41.9)	
No		707 (64.6)	30 (53.6)	16 (51.6)	
Yes		60 (5.5)	3 (5.4)	2 (6.5)	
Ethnicity*	1,179				0.3
Sub-Saharan African		165 (15.1)	11 (20.4)	6 (19.4)	
North African		408 (37.3)	12 (22.2)	11 (35.5)	
Caribbean		50 (4.6)	5 (9.3)	1 (3.2)	
European		213 (19.5)	9 (16.7)	6 (19.4)	
Indian, Pakistan, or Sri Lankan		182 (16.6)	9 (16.7)	6 (19.4)	
Other		76 (6.9)	8 (14.8)	1 (3.2)	
Neonatal outcomes					
Birth weight (g)	1,182	3,340 ± 523	3,230 ± 524	3,290 ± 500	0.24
LGA birth weight	1,182	155 (14.2)	5 (8.9)	3 (9.7)	0.51

Data are *n* (%) or mean ± SD unless otherwise indicated. *Ethnicity was self-identified. §Yes vs. no (no history possible if first child).

shows the study sample's characteristics; no difference was observed according to GADA category.

The rates of LGA birth weight were 14.2, 8.9, and 9.7% in women with no, moderately positive, and clearly positive GADA, respectively (P = 0.55). After adjustment for age, BMI, ethnicity, smoking during pregnancy, and glycemic status in a multivariable logistic regression, there was still no association between LGA birth weight and GADA category (moderately positive vs. no GADA, P = 0.38; clearly positive vs. no GADA, P = 0.58).

The reasons for why our initial hypothesis was unconfirmed are unclear. For example, we were not able to evaluate glycemic control during pregnancy. Study limitations are the lack of a control group of pregnant women with no HIP and that we did not measure other β-cell antibodies. One of the study's strengths is that we included a large prospective cohort of women from various ethnicities, which suggests that our results are transferrable to various populations, especially since globally, our main result was adjusted for this confounder.

To conclude, using universal testing, we found that 7.4% of our study sample of women with HIP in France were positive for GADA. However, these women were not identified as having a higher risk of LGA-birth-weight infants.

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