COMMENT ON FOUSSARD ET AL.

Skin Autofluorescence of Pregnant Women With Diabetes Predicts the Macrosomia of Their Children. Diabetes 2019;68: 1663–1669

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Diabetes 2020;69:e3–e4 | https://doi.org/10.2337/db19-1120

Macrosomia is one of the most frequent complications in women with hyperglycemia in pregnancy, and advanced glycation end products (AGEs) may play a role in fetus growth. We were very interested by the article by Foussard et al. (1) reporting a positive association in women with pregestational diabetes or hyperglycemia in pregnancy between maternal skin autofluorescence (sAF), an estimate of AGE accumulation, and large-for-gestational-age (LGA) newborns or infants with birth weight >4,000 g. This association remained significant after adjustment for HbA_{1c}, suggesting that, besides hyperglycemia, other factors might be involved in the relation between sAF and macrosomia.

We had the opportunity to explore the relationship between sAF and LGA infants in 177 pregnant women. In 2015–2016, we measured sAF at 28 ± 7 weeks' gestation in 29 normoglycemic women and in 148 women with early diagnosis (before 22 weeks' gestation, $n = 58$) or later diagnosis ($n = 90$) of diabetes in pregnancy. sAF values were similar whether or not women had delivered LGA newborns (mean ± SD 2.0 ± 0.4 vs. 2.0 ± 0.5 arbitrary units). Moreover, after adjustment for age, there was no difference between women with high sAF versus lower sAF either for birth weight (3,328 ± 519 g vs. 3,372 ± 512 g, respectively, $P = 0.86$) or for LGA infants (10.0% vs. 12.9%, respectively, $P = 1.00$). The adjustment for glycemic status was crucial since we had previously shown that sAF increases progressively from normoglycemia to late-diagnosed hyperglycemia in pregnancy, early-diagnosed hyperglycemia in pregnancy, and overt diabetes in pregnancy (2); furthermore, glycemic status and gestational age at hyperglycemia diagnosis are highly determinant for fetal growth. We performed a multivariable analysis to explain LGA infants in the 148 women with hyperglycemia, including maternal sAF, BMI, gestational weight gain, history of macrosomic infant, glycemic status, and maternal HbA_{1c} as covariables. Our results showed that gestational weight gain (odds ratio [OR] 1.10 per kg, 95% CI 1.01–1.20, $P < 0.05$) and history of macrosomic infant (OR 3.25, 1.10–9.58, $P < 0.05$) were independently associated with LGA. sAF values were still not associated with LGA infants. Our results are in line with those of de Ranitz-Greven et al. (3), who showed that sAF was not related to adverse pregnancy outcomes in 79 women with hyperglycemia in pregnancy, 21 patients with preexisting diabetes, and 55 women without diabetes.

However, sAF only reflects skin accumulation of AGEs. Therefore, our results do not eliminate a role for AGEs in

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adverse events during pregnancy, eventually through acute changes. AGEs interact with their receptors (RAGEs), mainly localized in endothelium and cells from the vascular wall. RAGEs are highly expressed in the placental bed tissues during pregnancy but also in the fetal membranes (4). For example, compared with control placenta, Alexander et al. (5) observed decreased RAGE gene expression during hyperglycemia in pregnancy, increased RAGE protein in preeclampsic placenta, and decreased rates in intrauterine growth–restricted placenta. The underlying mechanisms imply inflammation and vascular damage (5). Therefore, further studies on AGEs during pregnancy remain crucial.

Duality of Interest. No potential conflicts of interest relevant to this article were reported.

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