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Editorial

Gestational diabetes and maternal obesity suggestively priming children's premature atherosclerosis: Is it the mother fault?

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In the last four decades, an increase of gestational diabetes mellitus [1] as well as maternal obesity was observed. The increase of gestational diabetes mellitus was, however, not found to be related to body-mass-index, ethnicity or family history [1]. Various explanations were discussed: most likely, a genetically different response to weight gain, which is a normal physiologic reaction in pregnancy, is responsible, why some others might develop gestational diabetes and/or a non-physiologic weight gain – maternal obesity. Nevertheless, gestational diabetes mellitus as well as (maternal) obesity shares a common link with type 2 diabetes mellitus – insulin resistance [2]. Thus, it is clear that gestational diabetes and maternal obesity are associated not only with a high rate of a later development of full-blown type 2 diabetes mellitus, but also later more frequent (early) atherosclerosis and associated events [3,4] in those past pregnant women.

The association of the complex interrelation of obesity, gestational diabetes mellitus, later type 2 diabetes mellitus and vascular disease with the children of those mothers is even more complex [5]. We, as scientific community, had to realize that offspring exposed even to mild hyperglycemia during pregnancy has increased obesity and is also at an increased risk of later diabetes and vascular disease [6,7]. Not a few scientists even anticipate that a part of today's increase in obesity and type 2 diabetes mellitus might be a “self-feeding” negative back loop, of increasing maternal obesity/gestational diabetes mellitus, resulting in more obese off-spring, resulting in more obese mothers with more gestational diabetes mellitus and so on. Mothers, however are not to blame, since we do not have a clear association of those findings with the individual weight gains in the mothers. Known and unknown genetic and epigenetic associations seem to be dominantly responsible.

A major problem in the assessment of early atherosclerotic disease in this young population is the lack of data. Intima-media thickness as a surrogate marker of subclinical atherosclerosis was shown to be associated with cardiovascular risk factors in children [8,9], but long-term outcome data on cardiovascular events is limited. Furthermore, arterial wall examination in children is challenging due to structure size, and suitable intima-media thickness values can only be acquired by very-high resolution ultrasound [10].

In this issue of *Atherosclerosis*, Sundholm and colleagues [11] reported an analysis of body size and composition, blood pressure, arterial morphology and stiffness in 201 pairs of obese mothers and their children at 6.1 years. Child obesity is higher among boys (5.4% *vs.* 2.5%, $p = 0.05$), but not among girls (4.3% *vs.* 4.4%, $p = 0.95$), and child carotid intima-media thickness (mean 0.16, SD 0.75, $p = 0.003$) were increased in comparison to a healthy Finnish reference population. In contrast, no associations with gestational diabetes mellitus were found. Impaired glucose balance at the first and second maternal trimester related to a minor increase in child carotid stiffness. However, the absolute predictive value remained low with an R^2 of about 4.8–6.2%.

In summary, the findings of Sundholm et al. are modest. Most likely, the obtained associations were small, since the sample size was (too) small. Based on the small dimensions and the high technical variability reducing the strength of the biological association, the chance of failure was statistically high. But the authors did obtain, weak, but significant associations, of e.g. a prediction of later child carotid stiffness, with maternal glucose imbalances in the first and second trimester.

So, the authors, did set up a new field of research, the transgenerational research of not only genetically but also epigenetically inherited early vascular disease (onset), as suggested by the authors.

This theory must be tested in future large studies, to allow to draw clear conclusions and to elucidate possible confounding factors.

Conflict of interest

The authors declared they do not have anything to disclose regarding conflict of interest with respect to this manuscript.

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