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COMMENT ON SALOMON ET AL.

Gestational Diabetes Mellitus Is Associated With Changes in the Concentration and Bioactivity of Placenta-Derived Exosomes in Maternal Circulation Across Gestation. Diabetes 2016;65:598–609

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We read with interest the well-designed study by Salomon et al. (1) in which the authors have shown a twofold increase in placenta-derived exosomes (PdEs) in women with gestational diabetes mellitus (GDM) as compared with those in normal pregnancy at three gestational points. They have also shown the bioactivity of these exosomes in terms of increased release of proinflammatory cytokines from endothelial cells.

We believe that, along with PdEs, procoagulant microparticles (MPs) (total and placenta-derived) should also be assessed in women with GDM. Pregnancy itself is known to be a proinflammatory and hypercoagulable state, and studies now show that diabetes may also be a hypercoagulable state with a higher risk of thrombosis (2).

It is important to distinguish between MPs and exosomes as the two subpopulations are different not only in size but also in the mechanism of production, thus affecting their properties and their role in various disease processes. MPs are phospholipid vesicles 0.1 to 1 μm in size and are the basic markers of cell activation and apoptosis. The majority of them carry phosphatidylserine and tissue factor on their surface along with cell-specific antigens giving them their procoagulant attribute. Exosomes, on the other hand, are 40 to 120 nm in size, defined by an endosomal biogenesis, and regulate activities such as angiogenesis, proliferation, and metabolism. However, unlike MPs, they are not procoagulant in nature (3).

A study at our center showed elevated procoagulant MPs in women with unexplained recurrent pregnancy loss at a distance from the loss. This suggests chronic activation and vascular damage that may turn deleterious at the onset of pregnancy, assisting in uteroplacental thrombosis and subsequent recurrent pregnancy loss (4). Elevated MPs have also been reported in patients with diabetes. Endothelial dysfunction along with platelet hyperactivity is known to play a key role in the pathogenesis of diabetes (5). Thus increased endothelial and platelet MPs could be a marker of diabetes-associated endothelial dysfunction and hyperactivation of platelets, which in turn may help detect patients at risk for uteroplacental thrombosis or any adverse effects on implantation or in maternal–fetal vascular exchange. Thus we strongly believe that PdEs and procoagulant MPs as a combination may be an excellent prediction biomarker for any pregnancy-associated condition including GDM.

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

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