EDITORIAL

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INFLAMMATION IS THE COMMON MECHANISM OF DISEASES (CMD) IN COVID-19 DISEASE DURING PREGNANC AND IN GESTATIONAL DIABETES MELLITUS

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The Regional Cooperation for Health, Science and Technology (RECOOP HST) Consortium, led by Cedars-Sinai Medical Center was formed in 2006, was transformed into an Association in 2012 and includes 17 universities and academic organizations from eight countries: seven in Central and Eastern Europe (Croatia, Czech Republic, Hungary, Poland, Romania, Slovakia, Ukraine) and the United States. RECOOP builds multinational, multidisciplinary collaborations, and assists as well as coordinates the research activities of the sixteen research groups that are the Cedars-Sinai Medical Center – RECOOP Research Centers (CRRCs). https://www.cedars-sinai.org/research/administration/recoop.html.

Implementations of RECOOP's strategic goals enable diverse talents geared towards integration of new knowledge derived from multiple specialties to investigate Common Mechanism of Diseases (CMD). While some may consider *RECOOP's CMD research strategy unorthodox*, recent and timely scientific evidence shows that inflammation is the triggering event in the change of vascularization and it is the common mechanism of these two diseases: COVID-19 disease during pregnancy and gestational diabetes mellitus (GDM).

Binding of the SARS-CoV-2 virus to the ACE2 receptor and its entrance into endothelial cells plays a role in vascular thrombosis but has a lesser effect placental endothelial dysfunction. The latter is induced by inflammation and exacerbated by proinflammatory cytokines, resulting in ischemic events and creating an upward spiral of an inflammatory reaction in pregnant women, accompanied by similar conditions in the placenta that will ultimately affect fetal development. In mild or moderate COVID-19 disease, changes in placental vascularization and blood flow have similarities to comorbidities in pregnancy such as GDM. However, during severe or critical stages of COVID-19 Disease, the changes could be harsher than those observed in GDM. In COVID-19 disease and GDM the immune status of pregnant women and consequently the newborn is altered due to inflammation and characterized by changes in levels of C-reactive protein (CRP), immunoglobulins (IgG, IgM, IgA) and proinflammatory cytokines that are detectable in maternal and umbilical cord blood and in mother milk.

To examine changes and monitor placental angiogenesis it is necessary to measure *Vascular Endothelial Growth Factor (VEGF), Placental Growth Factor (PLGF), and Umbilical Cord Blood Sclerostin (UCBS)* in maternal and umbilical cord blood serum. The angiogenic activity of sclerostin must be validated with the well-known marker VEGF, which is a proven indicator for changes in vascularization. The morphology of the vascular tree and blood flow in the placenta could be evaluated with three-dimensional power Doppler. The proinflammatory and ischemic effects in the placenta should be quantified with histopathology and immunohistochemistry. Changes in blood flow in the placenta and the morphology of the vascular tree in COVID-19 Disease during pregnancy may have similarities to those observed in GDM.

In summary, to improve maternal and fetal outcomes it is imperative to formulate better strategies for managing pregnancies during COVID-19 disease and comorbidities like GDM. *VEGF*, *PLGF* and *UCBS* could be predictors of placental weight, birth weight, and fetal outcomes. In addition, further studies are needed to investigate the effects, if any, of proinflammatory and anti-inflammatory cytokines on postnatal development.

K e y w o r d s: pregnancy, COVID-19 disease, comorbidities, immunoglobulins, cytokines, inflammation, pathophysiology, placenta, vascularization.