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## MIR-146A AND MIR-21 FROM PBMCs AND EXTRACELLULAR VESICLES IN GESTATIONAL DIABETES: A COMPARISON OF PAIRED SAMPLES FOR THE ANALYSIS OF POTENTIAL INDICATORS OF THE REDOX STATUS

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Dysregulation of the redox system and the interconnected low-level inflammation (LLI) act as a driving force of damaging mechanisms in gestational diabetes mellitus (GDM) and are strongly related to severe obstetric and neonatal complications of hyperglycaemic pregnancies. Major disturbances in microRNA-based mechanism accompany (glyco)oxidative stress ((g)OS), for which reason we hypothesized that microRNAs may serve as sensors and/or effectors of (g)OS/LLI in GDM and we chose candidates for GDM biomarker analysis among known (g)OS/LLI-associated microRNAs. The aim of the study was to analyze the properties of miR-146a-5p and miR-21-5p as redox status indicators in GDM, as well as to compare two different biological samples as sources of potentially relevant GDM biomarkers. miR-146a-5p and miR-21-5p were quantified by real-time polymerase chain reaction in peripheral blood mononuclear cells of patients with GDM and normoglycaemic pregnant controls (n=40 each), as well as in paired samples of extracellular vesicles (EVs) extracted from serum. Correlation analysis was conducted for the expression levels of tested microRNAs and the activities of glutathione reductase (GR), total superoxide dismutase (SOD), catalase (CAT), concentration of serum thiol groups and the level of Nrf2 mRNA. In both samples, tested microRNAs were upregulated in GDM group, with a more pronounced increase in expression in EVs, compared to peripheral blood mononuclear cells (PBMCs) (1.81 vs. 1.52 fold for miR-146a-5p and 1.98 vs. 1.58 fold for miR-21-5p). There was a significant positive correlation between the expression of miR-21-5p from PBMCs and Nrf2 in both GDM patients and controls, as well as a positive correlation with the activity of total SOD in GDM patients. On the other hand, miR-146a-5p from EVs demonstrated negative correlation with Nrf2 expression and the activity of total SOD. These data demonstrate the potential of (g)OS/LLI-related microRNAs miR-146a-5p and miR-21-5p to serve as indicators of GDM and the associated (g)OS-related changes.

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