## UNIVERSITI TEKNOLOGI MARA

# UNRAVELLING THE MECHANISMS UNDERLYING THE IMMUNOMETABLIC CHANGES IN GESTATIONAL DIABETES MELLITUS ANIMAL MODEL THAT IS INDUCED THROUGH BIOCHEMICAL, PHARMACOLOGICAL AND LIFESTYLE FACTORS

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#### ABSTRACT

Gestational diabetes mellitus (GDM) is defined as diabetes that is not clearly apparent diabetes, diagnosed in the second or third trimester of pregnancy. Women diagnosed with diabetes during gestation have an increased incidence of complications during and after pregnancy. Thus, this study attempts to develop a GDM animal model in female Sprague-Dawley rats. This study comprises of two phases; first phase showed comparison between four groups with different diets with GDM fed with high fat sucrose diet group was chosen in GDM animal model in Phase 2 of this study, as the group show the relative elevated level of glucose and lipid profiles. Rats were fed with high fat sucrose diet, impregnated, and induced with Streptozotocin and Nicotinamide on (D0). Sleeping patterns of the rats were also manipulated to induce stress, a lifestyle factor that contributes to GDM. Rats were tested for glycaemic parameters, lipid profiles, genes affecting glucose transporters, pro-inflammatory cytokines, antioxidants and immune parameters on D6 and D21. GDM rats showed possible insulin resistance as evidenced by high expression of pro-inflammatory cytokines, PCK-1 and CRP. Furthermore, low levels of IRS-2 and AKT-1 genes and downregulation of GLUT-4 from the initial to final phases indicate possible defect of insulin signaling. GDM rats also showed an impairment of antioxidant status and a hyperlipidemic state. Percentages of T cells and NK cells were significantly higher in GDM group compared to control. Based on the findings outlined, the current GDM animal model closely replicates the disease state in human and can serve as a reference for future investigations.

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