UNIVERSITI TEKNOLOGI MARA

NEUROCOGNITIVE IMPAIRMENT IN GESTATIONAL DIABETES MELLITUS: OXIDATIVE STRESS AND INFLAMMATION AS POSSIBLE MECHANISM

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AUTHOR'S DECLARATION

I declare that the work in this thesis was carried out in accordance with the regulations of Universiti Teknologi MARA. It is original and is the results of my own work, unless otherwise indicated or acknowledged as referenced work. This thesis has not been submitted to any other academic institution or non-academic institution for any degree or qualification.

I, hereby, acknowledge that I have been supplied with the Academic Rules and Regulations for Post Graduate, Universiti Teknologi MARA, regulating the conduct of my study and research.

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ABSTRACT

The correlation between gestational diabetes mellitus (GDM) and cognition is modest. Some individuals remain cognitively intact during the gestational period despite the presence of GDM, whereas others show cognitive impairment and dementia in the same milieu. The aim of the present study was to examine the cognitive functions and evaluate the oxidative/inflammatory parameters in early and late stages of gestation in a GDM rat model. GDM has been associated with cognitive impairment as insulin receptors in the brain are located in the hippocampus, which is responsible for memory. Impaired insulin signaling in the brain may induce oxidative stress and inflammation, causing nerve damages and consequently cognitive impairment. In this study, we looked at the oxidative and inflammatory status in the brain of GDM rats on day 14 (D14) and 21 (D21), in addition to brain histology and cognitive function through Morris Water Maze (MWM) test. Gene expression of oxidative stress (SOD, CAT, GPX, p53, Hao-1) and inflammatory markers (IL-6, NF-Kb, IFN-γ, TNF-α, PPAR-γ, Vegf) were evaluated using quantitative RT-PCR analysis. The result showed that GDM group had a lower expression of antioxidant enzymes (SOD, CAT, GPX) on D14 and D21, and higher expression of Hao-1 and p53 than control. These indicate oxidative stress in brain of GDM rats. High expression of pro-inflammatory genes (IL-6, NF-Kb, IFN-γ, TNF-α) and low expression of anti-inflammatory genes (PPAR-γ, Vegf) were observed in the GDM group. Furthermore, disruption of normal layer organization, darkened and shrunken nuclei were observed in the hippocampus of GDM group, indicating apoptosis. GDM rats also showed impaired learning and memory function in the MWM test, where GDM rats clocked a longer escape latency time and shorter time spent in target quadrant than control. These findings provide evidence on the impairment of cognitive functions in GDM, which may be due to oxidative stress and inflammation in the brain.

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