Genetic polymorphisms in neuroendocrine disorder-related candidate genes associated with pre-pregnancy obesity in gestational diabetes mellitus patients by using a stratification approach

ABSTRACT

Background: Certain candidate genes have been associated with obesity. The goal of this study is to determine the association between thirteen neuroendocrine disorder-related candidate genes and pre-pregnancy obesity among gestational diabetes mellitus (GDM) patients using the stratification approach defined the Asian and International criteria-based body mass index (BMI). Methods: This was a post-hoc case-control exploratory sub-analysis of a cross-sectional study among GDM women to determine which candidate single nucleotide polymorphisms (SNPs) related to neuroendocrine disorders may be associated with obesity. Factors were adjusted for socio-demographic characteristics and concurrent medical problems in this particular population. Pre-pregnancy BMI and concurrent medical profiles were obtained from maternal health records. Obesity is defined as BMI of ≥ 27.5 kg/m2 for Asian criteria-based BMI and >30 kg/m2 for International criteria-based BMI. Thirteen candidate genes were genotyped using Agena® MassARRAY and examined for association with pre-pregnancy obesity using multiple logistic regression analysis. The significant difference threshold was set at P value <0.05. Results: Three hundred and twelve GDM women were included in this study; 60.9% and 44.2% of GDM patients were obese using Asian and International criteria-based BMI, respectively. GDM patients with AA or AG genotypes in specific SNP of brain-derived neurotrophic factor (BDNF) (G > A in rs6265) are more likely to be obese (adjusted odd ratio =2.209, 95% CI, 1.305, 3.739, P=0.003) compared to those who carry the GG genotype in the SNP adjusted for parity, underlying with asthma, heart disease, anaemia, education background in the International criteria-based BMI stratification group. On the other hand, there were no associations between other candidate genes (NRG1, FKBP5, RORA, OXTR, PLEKHG1, HTR2C, LHPP, SDK2, TEX51, EPHX2, NPY5R and ANO2) and maternal obesity. Conclusions: In summary, BDNF rs6265 is significantly associated with pre-pregnancy obesity among GDM patients. The exact role of BDNF adjusted for diet intake and lifestyle factors merits further investigation.

Keyword: Polymorphisms; Brain-derived neurotrophic factor (BDNF); Genetic variation; Gestational diabetes; Obesity