Title: Association of Single Nucleotide Polymorphism of Leptin Receptor Gene with Metabolic Parameters in Gestational Diabetes Mellitus

Abstract:

Background: Genetics plays a major role in the pathophysiology of GDM. Leptin and its receptor genes might have a significant contribution in the disease. Objective of the study is to find the association of leptin gene polymorphism with gestational diabetes mellitus (GDM) and its role in altered leptin levels, insulin resistance and dyslipidemia in GDM.

Methods: Hundred GDM patients fulfilling the study criteria, hundred gestational age and BMI matched normal glucose tolerant pregnant women were considered as control group was recruited and five milliliters of venous blood samples were drawn from them for biochemical and genetic analysis. Genotyping of leptin receptor (LEPR)Gln223Arg was performed by PCR-RFLP. Fasting blood sugar, leptin, insulin-peptide and lipid profile were done. Various insulin resistance models were constructed using suitable formulae. The statistical analysis was carried out with SPSS 23.0. Hardy-Weinberg Equilibrium (HWE) for the LEPR gene variant among cases was performed and comparisons of the distribution of the allele frequencies between different variants were carried out using chi-square test. Chi-square test was used to investigate the association between genotypes distribution and serum concentration of leptin and insulin resistance. Mann Whitney U test was used to compare biochemical parameters between cases and controls. Spearmann's correlation test was used to find the correlation between biochemical parameters. ROC curves were constructed to assess whether leptin levels and IR models can be used as markers to predict GDM.

Results: There was no significant association found between leptin receptor gene polymorphism and leptin levels, insulin resistance in GDM. However, Odd's ratio showed that individuals with A allele were at 1.25 times higher risk of developing GDM. HOMA B cell significantly varied among LepR genotypes ($p<0.0001$), values being double in AA genotype, compared to AG ($p<0.05$), 10 times higher in AA compared to GG ($p<0.0001$).The value was four times higher in AG compared to GG ($p<0.01$). None of the genotype frequency distributions for rs7799039 and rs1137101 variants deviated significantly from HWE in GDM cases ($P>0.05$), suggesting that alleles were in equilibrium.

Conclusion: It could be concluded from the study that, there is no significant association between leptin receptor, LEPR Gln223Arg alleles and gestational diabetes, leptin levels and insulin resistance. However, subjects with 'G' allele for LEPR at higher risk of hyperleptinemia. C –peptide based insulin resistance models were elevated in GDM patients

The study is able to establish a cycle of gene polymorphism altering leptin levels which in turn can alter insulin secretion and insulin resistance, contributing for dyslipidemia of pregnancy as well as gestational diabetes