

## Genetic determinants of obesity heterogeneity in type II diabetes

### ABSTRACT

Background: Although obesity is considered as the main cause of Type II diabetes (T2DM), non-obese individuals may still develop T2DM and obese individuals may not. Method: The mRNA expression of PI3K/AKT axis from 100 non-obese and obese participants with insulin sensitivity and insulin resistance states were compared in this study toward the understanding of obesity heterogeneity molecular mechanism. Result: In present study, there was no statistically significant difference in gene expression levels of IRS1 and PTEN between groups, whereas PI3K, AKT2 and GLUT4 genes were expressed at a lower level in obese diabetic group compared to other groups and were statistically significant. PDK1 gene was expressed at a higher level in non-obese diabetic group compared to obese diabetic and non-obese non-diabetics groups. No statistically significant difference was identified in gene expression pattern of PI3K/AKT pathway between obese non-diabetics and non-obese non-diabetics. Conclusion: The components of PI3K/AKT pathway which is related to the fasting state, showed reduced expression in obese diabetic group due to the chronic over-nutrition which may induced insensitivity and reduced gene expression. The pathogenesis of insulin resistance in the absence of obesity in non-obese diabetic group could be due to disturbance in another pathway related to the non-fasting state like gluconeogenesis. Therefore, the molecular mechanism of insulin signalling in non-obese diabetic individuals is different from obese diabetics which more investigations are required to study insulin signalling pathways in greater depth, in order to assess nutritional factors, contribute to insulin resistance in obese diabetic and non-obese diabetic individuals.

**Keyword:** Obesity paradox; PI3K/AKT pathway; PDK1; Non-obese diabetic; Type II diabetes; Gene expression; RT-PCR