Genetic Association Study and Development of Genetic Risk Score for Obesity in Thai Adults

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Background: Several studies have demonstrated evidence for genetic predisposition to obesity in other populations; however, the significance of this finding among Thais remains unclear.

Objective: To explore the association between genetic variants and obesity, as well as to develop a genetic risk score (GRS) for obesity in Thai adults.

Methods: Obese (BMI ≥30 kg/m²) and lean adults (BMI 18–23 kg/m²) were enrolled in this case-control study. All participants were subjected to careful evaluation including personal and family history, anthropometry, and biochemical profiles. Thirteen common variants of BMI-associated loci were screened by high resolution melting (HRM) analysis. Genetic risk score (GRS) was calculated by summing the number of risk alleles that presented in each of the obesity-associated loci (0, 1, or 2) in each subject.

Results: The study consisted of 302 obese subjects (aged 39.5±13.0 years, 62% female, BMI 40.2±6.7 kg/m²) and 306 lean controls (aged 31.9±7.1 years, 86% female, BMI 19.5±1.5 kg/m²). Logistic regression analysis using codominant models demonstrated that homozygous genotypes of 5 out of 13 loci, including BDNF rs6265 (G/G), FTO rs17817449 (G/G), GNPDA2 rs10938397 (G/G), TFAP2B rs4715210 (T/T), and CDKAL1 rs9356744 (T/T) were significantly associated with obesity with odds ratios (ORs) of 1.70 (95%CI: 1.08-2.68, p=0.023), 2.43 (95%CI: 1.34-4.40, p=0.004), 3.54 (95%CI: 2.04-6.14, p< 0.001), 2.31 (95%CI: 1.13-4.73, p=0.022), and 3.06 (95%CI: 1.79-5.22, p<0.001), respectively. GRS combining these 5 SNPs was significantly higher in the obese than the lean group (mean 4.3±1.6 vs. 3.5±1.4, p<0.001) and correlated significantly with BMI (r=0.256, p<0.001). Using subjects with GRS≤2 as the reference group (n=106, 17.4%), ORs for obesity in subjects with GRS of 3 (n=148, 24.3%), 4 (n=144, 23.7%), 5 (n=113, 18.6%), and ≥6 (n=97, 16.0%) were 0.91 (95%CI:0.54-1.52, p=0.722), 1.27 (95%CI:0.76-2.11, p=0.361), 2.78 (95%CI:1.61-4.81, p<0.001), and 4.33 (95%CI:2.39-7.75, p<0.001), respectively. In a multivariate model adjusted for age and sex, an increase of 1 point in GRS corresponded to an adjusted OR of 1.38 (95%CI:1.23-1.56, p<0.001) for obesity.

Conclusion: Our findings confirm significant polygenic contribution in development of obesity among Thais. The proposed GRS significantly correlated with obesity risk in a dose-dependent manner. Whether this GRS would be clinically useful for obesity prevention or treatment requires further investigation.

Keywords: Obesity, Body mass index (BMI), Genotype, High-resolution melting analysis (HRM), Genetic risk score (GRS)
Figure Distribution of the genetic risk score in the case and control samples and relationship between genetic risk score categories to mean BMI of the overall population