INTISARI

Hubungan Variasi Genetik Gen *Hepatocyte Nuclear Factor 1 Alpha* dengan Fungsi Sel β Pankreas dan Resistensi Insulin pada Penderita Sindroma Metabolik

Latar belakang: Prevalensi sindroma metabolik terus meningkat, hal ini terkait peningkatan risiko mortalitas dan morbiditas beberapa penyakit seperti diabetes melitus dan penyakit kardiovaskuler. Variasi genetik HNF1A p.I27L dan p.A98V diketahui berhubungan dengan disfungsi sel β pankreas (HOMA-β), resistensi insulin (HOMA-IR) dan meningkatkan risiko sindroma metabolik. Studi assosiasi fenotipe genotipe ini belum pernah dipublikasikan khususnya pada populasi etnis Jawa. **Tujuan:** Penelitian ini bertujuan untuk mengetahui hubungan variasi genetik HNF1A p.I27L dan p.A98V dengan fungsi sel β pankreas, resistensi insulin dan sindroma metabolik **Metode:** Penelitian ini merupakan penelitian kasus kontrol. Subjek penelitian adalah 85 kasus sindroma metabolik dan 85 kontrol etnis Jawa, yang dilakukan *matching* sesuai usia dan jenis kelamin. Diagnosis Sindroma metabolik berdasarkan IDF konsesus 2009 menggunkan lingkar pinggang untuk populasi Asia yang memenuhi minimal 3 dari 5 kriteria : obesitas sentral, hipertensi, hiperglikemia, hipertrigliseridemia dan *LowHDL*. Fungsi sel β pankreas diukur menggunakan HOMA-β, resistensi insulin menggunakan HOMA-IR. Genotiping dilakukan dengan teknik PCR-RFLP. Data dianalisis dengan *Independent Sampel T-test*, *Mann-Whitney U test, Chi-Square tes*t, *One-Way Anova* dan *binary logistik regretion* dengan nilai *p* <0,05 sebagai batas signifikansi. **Hasil:** Karakteristik lingkar pinggang, tekanan darah sitolik dan diastolik, kadar trigliserida, kadar HDL kolesterol, kadar insulin puasa dan nilai HOMA-IR antara kelompok sindroma metabolik menunjukkan perbedaan bermakna. Genotipe AC p.I27L merupakan genotipe proteksi terhadap sindroma metabolik (*p*=0,041; OR=0,48; 95% CI 0,25-0,92) daripada genotipe AA. Genotipe AC (*p*=0,020; OR=0,272; 95% CI 0,10-0,76) dan genotipe model dominan AC+CC (*p*=0,041; OR=0,390; 95% CI 0,15-0,97) merupakan genotipe proteksi terhadap sindroma metabolik pada usia ≤ 45 tahun. Tidak terdapat hubungan antara nilai HOMA-β dengan genotipe variasi genetik HNF1A p.I27L (*p*=0,687), genotipe p.A98V (*p*=0,859) dan haplotipe (*p*=0,444). Tidak terdapat hubungan antara nilai HOMA-IR dengan genotipe variasi genetik HNF1A p.I27L (*p*=0,614), genotipe p.A98V (*p*=0,607) dan haplotipe (*p*=0,515). Haplotipe ACCC merupakan haplotipe proteksi terhadap sindroma metabolik (*p*=0,030; OR=0,45; 95%CI = 0,233-0,886). **Kesimpulan**: Hasil kami menunjukkan bahwa variasi genetik HNF1A p.I27L merupakan faktor protektif terjadinya sindroma metabolik untuk usia yang lebih muda. Variasi genetik HNF1A p.I27L dan p.A98V pada penelitian ini tidak berhubungan dengan fungsi sel β pankreas dan resistensi insulin. Haplotipe ACCC merupakan haplotipe proteksi terhadap sindroma metabolik.

Kata kunci: HNF1A, variasi genetik, HOMA-β, HOMA-IR sindroma metabolik

ABSTRACT

Association of Genetic Variations Hepatocyte Nuclear Factor 1 Alpha Genes with Insulin Secretion and Insulin Resistance in Patients with Metabolic Syndrome

Background : The prevalence of metabolic syndrome continues to increase, this is associated with the risk of mortality and morbidity of several diseases such as diabetes mellitus and cardiovascular disease. Genetic variations of HNF1A p.I27L and p.A98V are known to be associated with pancreatic β cell dysfunction, impaired insulin secretion, insulin resistance and an increased risk of metabolic syndrome. This genotype phenotype association study has never been done in Javanese ethnic populations. **Objective**: This study aims to determine the relationship between genetic variations of HNF1A p.I27L and p.A98V with pancreatic β cell function, insulin resistance and metabolic syndrome..**Methods**: This research is a case control study. The research subjects were 85 cases of metabolic syndrome and 85 controls of Javanese ethnicity, which were matched according to age and sex. The diagnosis of metabolic syndrome was based on the 2009 consensus IDF using waist circumference for the Asian population, which met at least 3 of the criteria for central obesity, hypertension, hyperglycemia, hypertriglyceridemia and low HDL. Pancreatic β cell function was measured using HOMA-β, insulin resistance using HOMA-IR. Genotyping was done by PCR-RFLP technique. Data were analyzed by Independent Sample T-test, Mann-Whitney U test, Chi-Square test and One-Way Anova with p value <0.05 as the limit of significance. **Results**: The characteristics of waist circumference, systolic and diastolic blood pressure, triglyceride levels, HDL cholesterol levels, fasting insulin levels and HOMA-IR values between the metabolic syndrome groups showed significant differences. The AC genotype p.I27L was a protective genotype against the metabolic syndrome (p=0.041; OR=0.48; 95% CI 0.25-0.92) than the AA genotype. The AC genotype (p=0.020; OR=0.272; 95% CI 0.10-0.76) and the dominant model AC+CC genotype (p=0.041; OR=0.390; 95% CI 0.15-0.97) were genotype protection against metabolic syndrome at age 45 years. There was no relationship between HOMA-β values with the genetic variation genotype of HNF1A p.I27L (p=0.687), genotype p.A98V (p=0.859) and haplotype (p=0.444). There was no relationship between the HOMA-IR value and the genetic variation genotype of HNF1A p.I27L (p=0.614), genotype p.A98V (p=0.607) and haplotype (p=0.515). The ACCC haplotype was a protective haplotype against the metabolic syndrome (p=0.030; OR=0.45; 95%CI = 0.233-0.886).
Conclusion: The genetic variation of HNF1A p.I27L is associated with the incidence of metabolic syndrome at a younger age. The genetic variation of HNF1A p.I27L and p.A98V was not associated with pancreatic β cell function and insulin resistance. The ACCC haplotype is a protective haplotype against the metabolic syndrome.

Keywords: HNF1A, genetic variation, HOMA-β, HOMA-IR, metabolic syndrome