Abstrak

Latar belakang: Hipertensi menjadi penyebab kematian terbesar di dunia saat ini. Hipertensi terjadi hampir pada sepertiga usia muda dan meningkatkan risiko stroke. Salah satu penyebab hipertensi adalah kenaikan tekanan darah akibat hipertiroidisme. Penyakit hipertensi dan hipertiroid lebih sering terjadi pada wanita dan terkait dengan faktor lingkungan dan genetik. Gaya hidup dan faktor genetik seperti tiroid hormon reseptor (HTR), adrenergic reseptor beta (ADRB) dan *renin-angiotensin aldosteron sytem* (RAAS). Penelitian ini bertujuan untuk menganalisis variasi gen THR, ADRB, dan RAAS dan gaya hidup terhadap kejadian hipertensi.

Metode: Penelitian ini merupakan penelitian observasional dengan desain kasus-kontrol dengan total subjek penelitian 124 orang penderita hipertiroid. Kadar TSH dan fT4, dan tekanan darah diperiksa sebelum menentukan kelompok kasus dan kelompok kontrol. Kadar renin diukur pada kedua kelompok penelitian. Variasi genetik THR (THRA rs939348, THRB exon 10); ADRB (Ser49Gly, Arg16Gly, Gln27Glu) dan RAAS (ACE I/D, AGT M235T) dianalisis dengan PCR-RFLP dan Sequencing. Kadar hormon tiroid dan renin diperiksa dengan metode Elisa.

Hasil: Subjek penelitian 87% adalah wanita dengan usia rata-rata 39,66 tahun. Kondisi hipertiroid ditunjukkan dengan nilai TSH rata-rata 0,05 µIU/mL dan fT4 diatas nilai normal dengan rata-rata 5,12 ng/dL. Tekanan darah sistolik 152,59 mmHg pada kelompok kasus, lebih tinggi daripada kelompok kontrol dan berbeda secara bermakna. Tekanan darah diastolik kelompok kasus lebih tinggi dari kelompok kontrol dan berbeda secara bermakna. Genotip CT pada THRA rs-939348 memiliki frekuensi terbesar dan merupakan faktor risiko hipertensi ($p<0,05$). Individu yang membawa genotip DD pada ACE I/D memiliki risiko 3 kali untuk menderita hipertensi dan yang memiliki alel D memiliki risiko menderita hipertensi 18,408 kali (95%CI:7,252-46,727; $P<0,05$). Penelitian ini menunjukkan individu yang membawa alel Gly pada Ser49Gly memiliki risiko 4,885 kali untuk menderita hipertensi ($p<0,05$). Alel Gly pada Arg16Gly memiliki risiko 5,121 untuk menderita hipertensi $p<0,05$). AGT M235T genotip MT memberikan risiko 4,375 kali untuk menderita hipertensi. Individu yang membawa alel T memiliki risiko 6,508 dan bermakna secara statistik. Konsumsi masakan dengan cara digoreng dan kurangnya aktivitas fisik merupakan faktor risiko hipertensi pada penelitian ini.

Kesimpulan: Kelompok dengan hipertiroid dan hipertensi memiliki tekanan darah sistolik dan diastolik lebih tinggi dibandingkan dengan kelompok kontrol. Variasi genetik THRA rs939348, ACE I/D, ADRB Ser49Gly, ADRB Arg16Gly dan AGT M235T, konsumsi makanan dengan digoreng dan aktivitas fisik merupakan faktor risiko hipertensi.

Kata kunci: Hipertiroid, hipertensi, Variasi genetik, THR, ADRB, RAAS

Abstract

Background: Hypertension is the biggest cause of death in the world at present. Hypertension occurs almost in one third of young aged people and increases the risk of stroke. One of the causes of hypertension is an increase in blood pressure due to hyperthyroidism. Hypertension and hyperthyroidism diseases are more common in women and are related to environmental and genetic factors. Lifestyle and genetic factors include the Thyroid Hormone Receptors (*HTR*), Adrenergic Receptors Beta (*ADRB*) and Renin-Angiotensin Aldosteron System (*RAAS*). This study aimed to analyze variations of *THR*, *ADRB*, and *RAAS* genes and lifestyle in the incidence of hypertension.

Methods: This study was an observational study with case-controls with a total subject of 124 people with hyperthyroidism. TSH and FT4 levels, and blood pressure were checked before determining case and control groups. Renin levels were measured in both research groups. Genetic variations of *THR* (THRA RS939348, THRB Exon 10); *ADRB* (Ser49Gly, Arg16Gly, Gln27Glu) and *RAAS* (ACE I/D, AGT M235T) were analyzed by PCR-RFLP and genetic sequencing. The levels of thyroid hormones and renin were examined by the ELISA method.

Results: Subjects of this study 87% were women with an average age of 39.66 years old. The hyperthyroid condition was indicated by an average TSH value of 0.05 μIU / mL and FT4 with an average of 5.12 ng/dl. Mean systolic blood pressure was 152.59 mmHg in the case group, which was higher than the controls group and statistically different. Mean diastolic blood pressure in the case group was higher than controls and significantly different. The CT genotype in *THRA* RS-939348 has the largest frequency and is considered a risk factor for hypertension ($p<0.05$). Individuals carrying DD genotypes on ACE I/D have 3 times higher risk to suffer from hypertension and those who have alleles have 18.408 times higher risk to suffer hypertension (95% CI: 7.252-46.727; $p<0.05$). This research identified individuals who carry allele Gly at Ser49Gly have 4.885 times higher risk to suffer hypertension ($p<0.05$). Carriers of allele Gly in Arg16Gly have 5.121 higher risk of to suffer hypertension ($p<0.05$). AGT M235T genotype MT has 4.375 times higher risk to suffer hypertension. Individuals who carry T allele have 6.508 higher risk and the difference was statistically significant. The consumption of fried foods and lack of physical activity are the main risk factors for hypertension identified in this study.

Conclusion: Groups with hyperthyroidism and hypertension have higher systolic and diastolic blood pressure compared to controls. *THRA* rs939348, ACE I/D, *ADRB* Ser49Gly, *ADRB* Arg16Gly and *AGT* M235T, fried food consumption with low physical activity are identified as significant risk factors for hypertension.

Keywords: hyperthyroid, hypertension, genetic variation, THR, ADRB, RAAS