

INTISARI

Latar belakang: Hipertensi dalam kehamilan sangat berperan dalam angka kesakitan dan kematian ibu. Faktor genetik dan nutrisi merupakan faktor penting dalam etiologi hipertensi dalam kehamilan. Beberapa studi sebelumnya menunjukkan hubungan polimorfisme gen *Vitamin D Receptor* (VDR) dengan hipertensi dalam kehamilan. Konsentrasi vitamin D serum yang rendah pada ibu juga dapat meningkatkan risiko preeklamsia dan suplemen vitamin D dapat menurunkan risiko tersebut. Vitamin D mungkin memainkan peran penting dalam perubahan kekebalan tubuh dan kardiovaskular yang diperlukan untuk kehamilan yang sehat. Namun jumlah studi masih sangat terbatas dan hasilnya berbeda satu sama lain. Oleh karena itu dibutuhkan kualitas bukti yang memadai untuk menentukan hubungan sebab akibat.

Tujuan penelitian adalah menganalisis status vitamin D, *plasma renin activity* (PRA), polimorfisme rs2228570 dan rs731236 gena VDR dan polimorfisme rs4646994 gena *Angiotensin Converting Enzyme* (ACE) pada subyek dengan hipertensi dalam kehamilan (HDK) dan non hipertensi dalam kehamilan pada etnis Madura.

Metode: Subyek penelitian terdiri dari 105 subyek ibu hamil dengan hipertensi dan 105 subyek ibu hamil non hipertensi dari etnis Madura. Teknik sampling yang digunakan dalam penelitian ini adalah *consecutive sampling*. Kadar vitamin D dan PRA ditentukan menggunakan ELISA kit. Polimorfisme rs2228570 (T>C) dan rs731236 (T>C) dideteksi dengan *Polymerase Chain Reaction – Restriction Fragment Length Polymorphism* (PCR-RFLP). Polimorfisme rs4646994 gena ACE dideteksi dengan PCR. Seluruh data dianalisis secara statistika dengan *T-Test* dan *Chi-Square*.

Hasil: Tidak ada perbedaan nilai rerata kadar vitamin D yang signifikan antara kelompok HDK ($37,87 \pm 6,32$ ng/mL) dengan kelompok non HDK ($37,89 \pm 7,04$ ng/mL) ($p = 0,984$). Perbedaan nilai rerata kadar PRA yang signifikan ditemukan antara kelompok HDK ($3,96 \pm 2,75$ ng/mL) dengan kelompok non HDK ($1,84 \pm 0,70$ ng/mL) ($p < 0,001$). Frekuensi genotip TT dari rs2228570 (15,2%) pada kelompok HDK lebih tinggi dari pada kelompok non HDK (6,7%) ($p = 0,047$). Frekuensi alel T dari rs2228570 (40,5%) pada kelompok HDK lebih tinggi dari pada kelompok non HDK (30,5%) ($p = 0,032$). Genotip TT pada rs2228570 menunjukkan risiko 3,048 kali lebih besar untuk menderita HDK dibandingkan genotip CC (OR = 3,048 (1,135-8,183), $p=0,023$). Alel T memberikan risiko 1,551 kali lebih besar untuk menderita HDK. Tidak ada perbedaan yang bermakna pada genotip dan alel rs731236 dan rs4646994 antara subyek HDK dengan kontrol.

Simpulan: Nilai rerata kadar PRA pada kelompok HDK lebih tinggi dibandingkan kelompok non HDK. Genotip TT dan alel T dari rs2228570 pada kelompok HDK menjadi faktor risiko HDK pada studi ini. Genotiping polimorfisme gena VDR pada wanita hamil diharapkan dapat berguna dalam strategi penanganan hipertensi dalam kehamilan.

Kata kunci: gena reseptor vitamin D, gena *Angiotensin Converting Enzyme*, hipertensi kehamilan, *plasma renin activity*, polimorfisme, vitamin D, wanita hamil

ABSTRACT

Background: Hypertension in pregnancy plays a very important role in maternal morbidity and mortality. Genetic and nutrition factors are important considerations in the etiology of gestational hypertension. Several previous studies have shown an association of Vitamin D Receptor (*VDR*) gene polymorphisms with hypertension in pregnancy. Low maternal serum vitamin D concentrations may also increase the risk of preeclampsia and vitamin D supplementation may reduce this risk. Vitamin D may play an important role in the immune and cardiovascular changes necessary for a healthy pregnancy. However, the number of studies is still very limited and the results differ from one another. Therefore, sufficient quality of evidence is needed to determine a causal relationship.

This study aimed to analyze vitamin D status, plasma renin activity, the polymorphisms of rs2228570 and rs731236 of the *VDR* gene and the polymorphism of rs4646994 of the angiotensin converting enzyme (*ACE*) in subjects with hypertension in pregnancy and non-hypertension in pregnancy in Madura ethnicity.

Methods: The researchers conducted tests for two polymorphisms in the *VDR* gene among 210 subjects consisting of 105 pregnant women with hypertension and 105 non-hypertension pregnant women from Madura ethnicity. The sampling technique used in this research was consecutive sampling. Vitamin D and PRA levels were determined using the ELISA kit. The rs2228570 (T>C) and rs731236 (C>T) polymorphisms were detected by Polymerase Chain Reaction - Restriction Fragment Length Polymorphism. The rs4646994 polymorphism was detected by Polymerase Chain Reaction. All data were analyzed by T-tests and Chi-Square tests.

Results: There was no significant difference in the mean value of vitamin D levels between the hypertension group (37.87 ± 6.32 ng/mL) and the non hypertension group (37.89 ± 7.04 ng/mL) ($p = 0.984$). A significant difference in the mean PRA levels was found between the hypertension group (3.96 ± 2.75 ng/mL) and the non hypertension group (1.84 ± 0.70 ng/mL) ($p < 0.001$). The TT genotype frequency of rs2228570 (15.2%) in the hypertension group was higher than in the non-hypertension group (6.7%) ($p=0.047$). The T allele frequency of rs2228570 (40.5%) in the hypertension group was higher than in the non-hypertension group (30.5%) ($p=0.032$). Subjects with the TT genotype at rs2228570 showed a 3.048 times greater risk of developing hypertension than the CC genotype (OR = 3.048: 1.135-8.183, $p=0.023$). Subjects with the T allele had 1.551 times greater risk of developing hypertension. There was no significant difference in genotype and allele of rs731236 between hypertension subjects and controls.

Conclusion: The mean value of PRA levels in the hypertension group was higher than the non-hypertension group. The frequency of the TT genotype and T allele of rs2228570 in the hypertension group were risk factors for hypertension in this study. Genotyping of *VDR* gene polymorphisms in pregnant women is expected to be useful in strategies for treating hypertension in pregnancy.

Keywords: vitamin D receptor gene, angiotensin converting enzyme gene, hypertension in pregnancy, polymorphism, pregnant women, plasma renin activity, vitamin D