

DISERTASI

**HUBUNGAN POLIMORFISME LOKUS P352L, R538G GEN
COL4A1, RS9521733 GEN COL4A2, KADAR IFN- γ ,
IL-17, DAN VE-CADHERIN DENGAN KEJADIAN
PERDARAHAN INTRASEREBRAL SPONTAN
NON LOBAR PENDERITA HIPERTENSI**



Oleh

TONDI MASPIAN TJILI

NIM. 2030312004

Pembimbing

- 1. Prof. Dr. dr. Yuliarni Syafrita, Sp.N(K)**
- 2. Prof. Dr. dr. Eryati Darwin, PA(K)**
- 3. Prof. Dr. dr. Julius July, Sp.BS(K), M.Kes, JFAANS**

**PROGRAM STUDI ILMU BIOMEDIS PROGRAM DOKTOR
FAKULTAS KEDOKTERAN UNIVERSITAS ANDALAS
PADANG**

2025

ABSTRAK

HUBUNGAN POLIMORFISME LOKUS P352L, R538G GEN COL4A1, DAN RS9521733 GEN COL4A2, KADAR IFN- γ , IL-17, VE-CADHERIN DENGAN KEJADIAN PERDARAHAN INTRASEREBRAL SPONTAN NON LOBAR PENDERITA HIPERTENSI

Perdarahan intraserebral spontan non lobar paling sering didapatkan dengan hipertensi sebagai faktor resiko utama. Pecahnya pembuluh darah otak sering dihubungkan dengan disfungsi endotel yang mengganggu sawar darah otak. Disfungsi endotel tersebut dapat disebabkan oleh gangguan pada membran basal, proses inflamasi, ikatan adhesi endotel, dan karakteristik yang melekat pada pasien hipertensi. Penelitian ini bertujuan untuk menganalisis hubungan polimorfisme lokus P352L, R538G Gen Col4A1, RS9521733 Gen Col4A2, kadar IFN- γ , IL-17, dan VE-Cadherin dengan perdarahan intraserebral spontan non lobar penderita hipertensi.

Penelitian ini adalah penelitian dengan pendekatan *cross-sectional comperatif*. Penelitian ini membandingkan dan menganalisis 40 sampel darah darah tepi dari penderita hipertensi yang mengalami perdarahan intraserebral spontan non lobar dan 40 sampel darah tepi dari penderita hipertensi tanpa perdarahan intraserebral spontan non lobar. Masing-masing sampel darah dilakukan pemeriksaan laboratorium kimia, ELISA, dan PCR. Pemeriksaan tersebut untuk memeriksa karakteristik, kadar IFN- γ , IL-17, VE-Cadherin, dan polimorfisme lokus P352L, R538G Gen Col4A1, RS9521733 Gen Col4A2. Selanjutnya dilakukan uji bivariate dengan uji Chi-square, uji eksak Fisherl, uji t, dan uji Mann-Whitney. Bermakna jika $p < 0,05$. Semua variabel yang memiliki nilai $p < 0,25$ ini selanjutnya dilanjutkan dengan analisis multivariabel dengan regresi logistik ganda.

Perbedaan data karakteristik pada kedua kelompok yang menunjukkan perbedaan yang bermakna ($p < 0,05$) adalah jenis kelamin, umur, merokok, kadar gula darah sewaktu, dan ureum. Hasil *genotype* variasi genetik Gen Col4A1 lokus P352L, R538G menunjukkan hasil yang sama, sedangkan gen Col4A2 lokus RS9521733 tidak menunjukkan perbedaan yang bermakna ($p > 0,05$). Kadar IFN- γ memiliki perbedaan bermakna secara statistik dengan nilai $p = 0,018$ ($p < 0,05$). Nilai kadar VE-Cadherin memiliki perbedaan bermakna secara statistik dengan nilai $p = 0,001$ ($p < 0,05$). Hasil analisis regresi logistik ganda terdapat dua variabel yang berhubungan secara multivariabel dengan kejadian perdarahan intraserebral spontan non lobar pada penderita hipertensi yaitu kadar VE-Cadherin dan IFN- γ .

Hasil penelitian ini menyimpulkan bahwa kadar VE-Cadherin dan IFN- γ mempunyai hubungan terhadap kejadian perdarahan intraserebral spontan non lobar penderita hipertensi. Variabel yang menjadi prediktor utama untuk dapat

terjadinya perdarahan intraserebral spontan non lobar penderita hipertensi adalah kadar VE-Cadherin.

Kata kunci : Perdarahan intraserebral non-lobar, hipertensi, polimorfisme, Col4A1, Col4A2, IFN- γ , IL-17, VE-Cadherin



ABSTRACT

CORRELATION BETWEEN POLIMORPHISMS OF THE P352L, R538G LOCI OF THE COL4A1 GENE, AND THE RS9521733 LOCUS OF THE COL4A2 GENE, LEVEL OF IFN- γ , IL-17, VE-CADHERIN, AND THE OCCURENCE OF SPONTANEOUS NON-LOBAR INTRACEREBRAL HEMORRHAGE IN HYPERTENSIVE PATIENS

Tondi Maspian Tjili

Spontaneous non-lobar intracerebral hemorrhage is most often associated with hypertension as the primary risk factor. The rupture of brain blood vessels is frequently linked to endothelial dysfunction, which disrupts the blood-brain barrier. This endothelial dysfunction can be caused by abnormalities in the basement membrane, inflammatory processes, endothelial adhesion junctions, and characteristics inherent in hypertensive patients. This study aims to investigate the relationship between polymorphisms at the P352L and R538G loci of the Col4A1 gene, the RS9521733 locus of the Col4A2 gene, and levels of IFN- γ , IL-17, and VE-Cadherin with spontaneous non-lobar intracerebral hemorrhage in hypertensive patients.

This study employs a comparative cross-sectional approach. It compares and analyzes 40 peripheral blood samples from hypertensive patients with spontaneous non-lobar intracerebral hemorrhage and 40 peripheral blood samples from hypertensive patients without spontaneous non-lobar intracerebral hemorrhage. Each blood sample undergoes laboratory tests including chemical assays, ELISA, and PCR. These tests are conducted to examine laboratory characteristics, levels of IFN- γ , IL-17, VE-Cadherin, and polymorphisms at the P352L and R538G loci of the Col4A1 gene and the RS9521733 locus of the Col4A2 gene. Numeric data are first tested for normality using the Shapiro-Wilk test, with data considered normally distributed if $p > 0.05$. Subsequently, they are analyzed using bivariate tests such as the Chi-square test, Fisher's exact test, t-test, and Mann-Whitney test, with significance set at $p < 0.05$. Variables with $p < 0.25$ are further analyzed using multivariate analysis with multiple logistic regression.

Characteristics showing significant differences ($p < 0.05$) between the two groups were gender, age, smoking, random blood sugar levels, and urea levels. Genetic variation results for the Col4A1 gene at loci P352L and R538G were similar between groups, while the Col4A2 gene at locus RS9521733 did not show significant differences ($p > 0.05$). The median level of IFN- γ have difference was statistically significant with a p-value of 0.018 ($p < 0.05$). VE-Cadherin levels have. difference was statistically significant with a p-value of 0.001 ($p < 0.05$). The results of the multiple logistic regression analysis showed that there were two variables that were independently associated with the occurrence of spontaneous

non-lobar intracerebral hemorrhage in hypertensive patients, namely VE-Cadherin and IFN- γ levels.

The results of this study conclude that VE-Cadherin and IFN- γ levels are associated with the occurrence of spontaneous non-lobar intracerebral hemorrhage in hypertensive patients. The main predictors for spontaneous non-lobar intracerebral hemorrhage in hypertensive patients is VE-Cadherin level.

Keywords : *Non-Lobar intracerebral hemorrhagic, hypertension, polymorphism, Col4A1, Col4A2, IFN- γ , IL-17, VE-Cadherin*

