



Hubungan Polimorfisme Gen Methylenetetrahydrofolate Reductase (MTHFR) Varian C.677C>T terhadap Kejadian Stroke Associated Infection (SAI) pada Pasien Stroke Iskemik Akut (SIA) pada Populasi Jawa di Daerah Istimewa Yogyakarta

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HUBUNGAN POLIMORFISME GEN METHYLENETETRAHYDROFOLATE REDUCTASE (MTHFR) VARIAN c.677C>T TERHADAP KEJADIAN STROKE ASSOCIATED INFECTION (SAI) PADA PASIEN STROKE ISKEMIK AKUT (SIA) PADA POPULASI JAWA DI DAERAH ISTIMEWA YOGYAKARTA

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ABSTRAK

Latar Belakang: Stroke iskemik akut sering disertai komplikasi infeksi (*stroke-associated infection*/SAI) yang meningkatkan morbiditas dan memperpanjang lama rawat. Polimorfisme gen *methylenetetrahydrofolate reductase* (MTHFR) varian c.677C>T berpotensi memodulasi respons inflamasi-imunitas melalui hiperhomosisteinemia, sehingga diduga berhubungan dengan kerentanan SAI. Penelitian ini bertujuan untuk menganalisis hubungan polimorfisme gen *MTHFR* varian c.677C>T terhadap kejadian SAI pada pasien stroke iskemik akut pada populasi Jawa di Daerah Istimewa Yogyakarta.

Metode: Penelitian *cross-sectional* dilakukan pada pasien stroke iskemik akut suku Jawa yang dirawat di Unit Stroke RSUP dr. Sardjito Yogyakarta periode Mei 2023-Juni 2024. Genotipe MTHFR c.677C>T (rs1801133) diperiksa menggunakan PCR-RFLP dan dikategorikan polimorfisme bila CT/TT. *Outcome* adalah SAI yang terjadi ≤ 7 hari pasca onset (pneumonia, infeksi saluran kemih, sepsis, atau ulkus dekubitus). Analisis bivariat dilakukan untuk kandidat perancu, kemudian regresi logistik multivariat digunakan untuk menentukan prediktor independen SAI.

Hasil: Sebanyak 219 pasien disertakan dalam penelitian ini. Genotipe CC 69%, CT 26%, dan TT 5% (polimorfisme 31%). Kejadian SAI ditemukan pada 70 pasien (32%). Analisis bivariat menunjukkan polimorfisme tidak berhubungan signifikan dengan SAI (25% vs 35,1%; $p=0,138$; OR 0,62), tetapi berhubungan dengan risiko infeksi saluran kemih yang lebih rendah (11,8% vs 25,2%; $p=0,024$; OR 0,39). Variabel yang berkaitan dengan SAI pada analisis bivariat meliputi usia lebih tua, penyakit jantung, NIHSS admisi lebih tinggi, ketergantungan fungsional lebih berat, leukositosis, neutrofil lebih tinggi, limfosit lebih rendah, glukosa puasa lebih tinggi, serta profil lipid lebih rendah. Pada regresi logistik multivariat, polimorfisme MTHFR menjadi prediktor independen SAI (OR 4,593; 95%CI 1,658–12,723; $p=0,003$) bersama usia (OR 1,042; $p=0,031$), NIHSS admisi (OR 1,129; $p=0,010$), dan lama rawat (OR 1,192; $p=0,003$).

Kesimpulan: Polimorfisme MTHFR c.677C>T berhubungan secara independen dan signifikan dengan peningkatan risiko SAI pada pasien stroke iskemik akut populasi Jawa setelah pengendalian faktor klinis utama.

Kata Kunci: Stroke iskemik akut; Stroke-associated infection (SAI); Polimorfisme MTHFR c.677C>T; Hiperhomosisteinemia



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THE METHYLENETETRAHYDROFOLATE REDUCTASE (MTHFR) GENE POLYMORPHISM VARIANT c.677C>T AND THE INCIDENCE OF STROKE ASSOCIATED INFECTION (AIS) IN ACUTE ISCHEMIC STROKE (AIS) PATIENTS IN THE JAVANESE POPULATION IN THE SPECIAL REGION OF YOGYAKARTA

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ABSTRACT

Background: Acute ischemic stroke is often accompanied by infectious complications (*stroke-associated infection* / SAI), which increases morbidity and prolongs the length of stay. *The methylenetetrahydrofolate reductase* (MTHFR) gene polymorphism variant c.677C>T has the potential to modulate the inflammatory-immune response through hyperhomocysteinemia, thus suspected to be associated with SAI susceptibility. This study aims to analyze the relationship of the *MTHFR gene polymorphism* variant c.677C>T to the incidence of SAI in acute ischemic stroke patients in the Javanese population in the Special Region of Yogyakarta.

Methods: A *cross-sectional study* was conducted on Javanese acute ischemic stroke patients treated at the Stroke Unit of Dr. Sardjito General Hospital Yogyakarta from May 2023 to June 2024. The MTHFR c.677C>T (rs1801133) genotype was examined using PCR-RFLP and categorized as a polymorphism if CT/TT. *The outcome* was AIS occurring ≤ 7 days after onset (pneumonia, urinary tract infection, sepsis, or pressure ulcer). Bivariate analysis was performed for potential confounders, and multivariate logistic regression was used to determine independent predictors of AIS.

Results: A total of 219 patients were included in this study. The CC genotype was 69%, CT 26%, and TT 5% (polymorphism 31%). The incidence of SAI was found in 70 patients (32%). Bivariate analysis showed that polymorphism was not significantly associated with SAI (25% vs. 35.1%; $p=0.138$; OR 0.62), but was associated with a lower risk of urinary tract infection (11.8% vs. 25.2%; $p=0.024$; OR 0.39). Variables associated with SAI in bivariate analysis included older age, heart disease, higher admission NIHSS, more severe functional dependence, leukocytosis, higher neutrophil count, lower lymphocyte count, higher fasting glucose, and lower lipid profile. In multivariate logistic regression, MTHFR polymorphism was an independent predictor of SAI (OR 4.593; 95%CI 1.658–12.723; $p=0.003$) along with age (OR 1.042; $p=0.031$), admission NIHSS (OR 1.129; $p=0.010$), and length of stay (OR 1.192; $p=0.003$).

Conclusion: The MTHFR c.677C>T polymorphism is independently and significantly associated with an increased risk of SAI in acute ischemic stroke patients in the Javanese population after controlling major clinical factors.

Keywords: Acute ischemic stroke; Stroke-associated infection (SAI); MTHFR c.677C>T polymorphism; Hyperhomocysteinemia