

INTISARI

Latar Belakang: Skizofrenia merupakan gangguan mental kronis yang ditandai dengan gejala positif dan negatif, serta menyebabkan disabilitas fungsional jangka panjang. Klozapin dikenal efektif sebagai antipsikotik atipikal pada kasus refrakter, namun penggunaannya berisiko memicu peningkatan tekanan darah dan peningkatan kadar glukosa melalui mekanisme antagonisme reseptor dopamin, serotonin, adrenergik, dan muskarinik. Polimorfisme gen *LEP* rs7799039 diduga berperan dalam regulasi kadar leptin, tekanan darah, dan resistensi insulin, namun belum diteliti hubungannya dengan respons klozapin di Indonesia. Penelitian ini bertujuan mendukung pengembangan kedokteran presisi guna meningkatkan efektivitas dan keamanan terapi skizofrenia.

Tujuan Penelitian: Penelitian ini bertujuan untuk mengetahui distribusi polimorfisme *LEP* rs7799039 serta hubungannya dengan tekanan darah dan glukosa darah sewaktu pada pasien skizofrenia yang mendapatkan klozapin.

Metode: Penelitian observasional dengan rancangan potong lintang melibatkan 130 pasien skizofrenia yang menerima terapi klozapin di Rumah Sakit Soerojo Magelang. Data demografi, tekanan darah, gula darah sewaktu, dan variabel klinis dikumpulkan retrospektif dari rekam medis. Identifikasi polimorfisme *LEP* rs7799039 dilakukan melalui isolasi DNA dan *TaqMan real-time PCR*. Distribusi genotip menggunakan *Hardy-Weinberg*, hubungan genetik dinilai dengan uji *Chi-Square*, *OR*, dan regresi logistik multivariat untuk prediktor independen.

Hasil Penelitian: Dari 130 subjek penelitian, distribusi frekuensi gen *LEP* rs7799039 alel A pada pasien skizofrenia di Indonesia yaitu 26 % dan alel G 74% (MAF = 0,26). Genotipe GG merupakan yang paling dominan 55,4%, diikuti oleh GA 37,7% dan AA 6,9%. Varian *LEP* rs7799039 berhubungan signifikan dengan profil tekanan darah yang tinggi (AA/GA) $OR = 5,769$ $p=0,000$ CI: 2,315-14,378) dan meningkatkan risiko lima kali lipat, namun tidak berhubungan signifikan dengan profil tekanan darah diastolik maupun profil glukosa darah sewaktu.

Kesimpulan: Polimorfisme gen *LEP* rs7799039 berhubungan dengan profil tekanan darah sistolik yang tinggi, namun tidak pada profil tekanan diastolik dan profil glukosa darah sewaktu.

Kata kunci: Skizofrenia, Klozapin, Polimorfisme gen *LEP* rs7799039, Tekanan darah, Glukosa darah sewaktu.

ABSTRACT

Background: Schizophrenia is a chronic mental disorder characterized by positive and negative symptoms, leading to long-term functional disability. Clozapine is known to be effective as an atypical antipsychotic for treatment-resistant cases; however, its use carries the risk of increasing blood pressure and glucose levels through antagonistic mechanisms involving dopamine, serotonin, adrenergic, and muscarinic receptors. The LEP gene polymorphism rs7799039 is suspected to play a role in the regulation of leptin levels, blood pressure, and insulin resistance, but its association with clozapine response has not yet been studied in Indonesia. This study aims to support the development of precision medicine to improve the effectiveness and safety of schizophrenia therapy.

Objective: This study aimed to determine the distribution of *LEP* rs7799039 polymorphism and its association with blood pressure and random blood glucose levels in patients with schizophrenia receiving clozapine therapy.

Methods: This observational cross-sectional study involved 130 patients with schizophrenia receiving clozapine therapy at Soerojo Hospital, Magelang. Demographic data, blood pressure, random blood glucose levels, and clinical variables were retrospectively collected from medical records. *LEP* rs7799039 polymorphism was identified through DNA isolation and TaqMan real-time PCR. Genotype distribution was assessed using Hardy-Weinberg equilibrium, while genetic associations were analyzed using Chi-square test, odds ratio (OR), and multivariate logistic regression for independent predictors.

Results: Among 130 study subjects, the allele frequency of the *LEP* rs7799039 A allele was 26%, and the G allele was 74% (MAF = 0.26). The GG genotype was the most prevalent (55.4%), followed by GA (37.7%) and AA (6.9%). The *LEP* rs7799039 variant was significantly associated with elevated blood pressure profiles (AA/GA) (OR = 5.769, $p = 0.000$, 95% CI: 2.315–14.378), indicating a fivefold increased risk. However, it was not significantly associated with diastolic blood pressure or random blood glucose levels.

Conclusion: The *LEP* rs7799039 gene polymorphism is associated with elevated systolic blood pressure profiles but not with diastolic blood pressure or random blood glucose levels.

Keywords: Schizophrenia, Clozapine, *LEP* rs7799039 polymorphism, Blood pressure, Random blood glucose.