INTISARI

Artritis reumatoid (AR) merupakan penyakit autoimun yang ditandai dengan inflamasi sendi kronis. Berdasarkan Riset Kesehatan Dasar Indonesia tahun 2018, prevalensi AR di Indonesia mencapai 7,30% dan terus mengalami peningkatan. Metotreksat (MTX) merupakan disease-modifying antirheumatic drug (DMARD) lini pertama dalam terapi AR; namun, respons terapeutik terhadap MTX bervariasi antarindividu. Salah satu faktor yang dapat memengaruhi variasi respons tersebut adalah polimorfisme genetik, khususnya *SLC19A1/RFC1* G80A (rs1051266), yang berperan dalam transport MTX ke dalam sel dan berpotensi memengaruhi efektivitas terapi. Bukti mengenai hubungan polimorfisme ini dengan respons MTX pada populasi Indonesia masih terbatas. Penelitian ini merupakan penelitian observasional analitik dengan desain *cross-sectional* yang melibatkan 198 pasien AR yang menerima terapi MTX selama minimal enam bulan. Efektivitas MTX dinilai berdasarkan skor DAS28 pascaterapi dan dikategorikan menjadi kelompok efektif dan non-efektif. Genotiping *SLC19A1/RFC1* G80A (rs1051266) dilakukan menggunakan metode rhAmp SNP genotyping berbasis real-time PCR. Analisis statistik meliputi distribusi genotipe dan alel, Hardy–Weinberg equilibrium (HWE), uji Chi-square, model genetik dominan, serta analisis regresi logistik.
Genotipe GA merupakan genotipe yang paling dominan pada kedua kelompok. Analisis distribusi genotipe menunjukkan tidak terdapat hubungan signifikan antara polimorfisme *SLC19A1/RFC1* G80A dan efektivitas MTX berdasarkan DAS28 pascaterapi ($p = 0,739$). Frekuensi alel juga tidak menunjukkan hubungan signifikan ($p = 0,611$). Pada model dominan, pembawa alel varian GA + AA tidak memiliki peningkatan risiko respons non-efektif dibandingkan genotipe GG (OR = 1,060; 95% CI = 0,486–2,313; $p = 0,884$). Distribusi genotipe sesuai dengan HWE ($\chi^2 = 0,384$; $p = 0,536$). Sebaliknya, dosis kumulatif MTX selama enam bulan berhubungan signifikan dengan respons non-efektif (aOR = 5,263; 95% CI = 2,615–10,596; $p < 0,001$), yang kemungkinan mencerminkan eskalasi terapi pada pasien dengan aktivitas penyakit persisten.

Kata kunci: Artritis reumatoid, metotreksat, *single nucleotide polymorphism* (SNP), *SLC19A1, RFC1 G80A*

ABSTRACT

Rheumatoid arthritis (RA) is an autoimmune disease characterized by chronic joint inflammation. According to the 2018 Indonesian Basic Health Research, the prevalence of RA in Indonesia reached 7.30% and continues to increase. Methotrexate (MTX) is the first-line disease-modifying antirheumatic drug (DMARD) for RA treatment; however, therapeutic response varies among individuals. One factor that may contribute to this variability is genetic polymorphism, particularly *SLC19A1/RFC1* G80A (rs1051266), which is involved in cellular MTX transport and may influence treatment effectiveness. Evidence regarding this polymorphism in the Indonesian population remains limited. This analytical observational study with a cross-sectional design included 198 RA patients who had received MTX therapy for at least six months. MTX effectiveness was assessed using post-treatment DAS28 score and categorized into effective and non-effective groups. Genotyping of *SLC19A1/RFC1* G80A (rs1051266) was performed using real-time PCR-based rhAmp SNP genotyping. Statistical analyses included genotype and allele frequency distributions, Hardy–Weinberg equilibrium (HWE), Chi-square test, dominant genetic model analysis, and logistic regression. The GA genotype was the most predominant genotype in both groups. Genotype distribution analysis showed no significant association between *SLC19A1/RFC1* G80A polymorphism and MTX effectiveness based on post-treatment DAS28 score ($p = 0.739$). Allele frequency analysis also showed no significant association ($p = 0.611$). In the dominant model, carriers of the variant allele (GA + AA) did not show increased odds of non-effective response compared with the GG genotype (OR = 1.060; 95% CI = 0.486–2.313; $p = 0.884$). Genotype distribution was consistent with HWE ($\chi^2 = 0.384$; $p = 0.536$). In contrast, cumulative six-month MTX dose was significantly associated with non-effective response (aOR = 5.263; 95% CI = 2.615–10.596; $p < 0.001$), which may reflect treatment escalation in patients with persistent disease activity.

Keywords: Rheumatoid arthritis, methotrexate, single nucleotide polymorphism (SNP), *SLC19A1, RFC1 G80A*