

ABSTRAK

Latar Belakang : Pasien penyakit ginjal kronik (PGK) yang menjalani hemodialisis selalu menderita anemia yang disebabkan defisiensi eritropoetin. Resistensi terhadap *Erythropoiesis-Stimulating Agent* (EPO) terjadi pada 5-12% pada pasien hemodialisis. Terapi EPO membutuhkan pembiayaan yang besar. Pada keadaan tertentu misal hiporesponsif (resisten EPO) yaitu tidak tercapainya target Hb. Banyak faktor yang terkait dengan resistensi EPO, misal defisiensi besi, inflamasi, inadekuat dialisis, dan faktor variasi gen yaitu ORAI1. Penelitian tentang variasi gen ORAI1 (rs12313273 dan rs6486795) masih dapat dikembangkan untuk memperbaiki manajemen PGK agar tercapai terapi yang presisi dan menekan pembiayaan dari pemberian EPO.

Tujuan: Menganalisis hubungan antara variasi gen ORAI1 (rs12313273 dan rs6486795) dengan terjadinya resistensi EPO.

Metode: Penelitian observasional dengan desain *case control*. Subjek penelitian adalah penderita PGK dari Unit Hemodialisis PKU Muhammadiyah Bantul yang memenuhi kriteria inklusi, yaitu : pasien PGK yang menjalani dialisis rutin dengan frekuensi dua kali (2x) dalam 1 pekan minimal 3 bulan, usia lebih dari 18 tahun. Kriteria eksklusi yaitu kehamilan, keganasan, riwayat transfusi dalam 2 pekan terakhir. Sampel berupa darah vena sebanyak 5cc untuk mengukur variabel variasi gen ORAI1. Pemeriksaan genotip berbasis RT-PCR terhadap variasi alel rs12313273 dan rs6486795 pada gen ORAI1.

Hasil: Subjek penelitian sebanyak 180 orang, dieksklusi 33 orang, total subjek penelitian 147 orang. Responden yang resisten eritropoetin (n=68) dan tidak resisten (n=79). Variasi gen ORAI1 rs6486795 berhubungan dengan terjadinya resistensi eritropoetin, memiliki peluang 3,23 kali (OR 1,06-9,87) untuk terjadinya resistensi eritropoetin dengan mempertimbangkan variabel indeks masa tubuh (IMT), hemeoglobin (Hb), ureum post hemodialisis, kreatinin post hemodialisis, ferritin, *C Reactive Protein*, Retikulosit Hemoglobin, dosis Eritropoetin, pemakaian obat *Angiotensin Receptor Blocker* (ARB), vitamin B12, asam folat. Variasi gen ORAI1 rs6486795 model aditif TT memiliki peluang 3,63 kali (CI 1,15-11,45) untuk terjadinya resistensi eritropoetin dengan mempertimbangkan banyak variabel. Variasi gen ORAI1 rs12313273 tidak memiliki hubungan dengan terjadinya resistensi eritropoetin.

Kesimpulan: Variasi gen ORAI1 rs6486795 memiliki peluang terjadinya resistensi Eritropoetin sebanyak 3,23 kali pada pasien penyakit ginjal kronik yang menjalani hemodialisis

Kata Kunci: resisten EPO, penyakit ginjal kronik, dialisis, gen ORAI1 (rs12313273 dan rs6486795)

ABSTRACT

Background: Chronic kidney disease (CKD) patients undergoing hemodialysis often suffer from anemia caused by erythropoietin deficiency. Resistance to erythropoiesis-stimulating agents (EPO) occurs in 5–12% of hemodialysis patients. EPO therapy is costly, and in certain cases—such as EPO hyporesponsiveness, where the target hemoglobin (Hb) level is not achieved—treatment becomes more complicated. Various factors are associated with EPO resistance, including iron deficiency, inflammation, inadequate dialysis, and genetic variations, particularly in the ORAI1 gene. Study on ORAI1 genetic variation (rs12313273 and rs6486795) can be further developed to improve CKD management, enabling more precise therapy and reducing the financial burden of EPO administration.

Objective: To analyze the relationship between ORAI1 genetic variations (rs12313273 and rs6486795) and the occurrence of EPO resistance.



Hubungan Variasi Gen ORAI (rs12313273 dan rs6486795) dengan Resisten Eritropoetin pada Pasien Penyakit Ginjal Kronik yang Menjalani Hemodialisis

Linda Rosita, Prof. Dr. dr. Nyoman Kertia, Sp.PD (KR); Dr. dr. Tri Ratnaningsih, M.Kes, Sp.PK (K)

Universitas Gadjah Mada, 2025 | Diunduh dari <http://etd.repository.ugm.ac.id/>

UNIVERSITAS
GADJAH MADA

Methods: *This observational study employed a case-control design. The subjects were CKD patients undergoing hemodialysis at the PKU Muhammadiyah Bantul Hemodialysis Unit who met the inclusion criteria: patients undergoing routine dialysis twice per week for at least 3 months, aged over 18 years. Exclusion criteria included pregnancy, malignancy, and a history of blood transfusion within the last two weeks. A 5 cc venous blood sample was collected from each participant. Genotyping was conducted using real-time PCR for the ORAI1 genetic variation (rs12313273 and rs6486795), followed by sequencing to identify allele variations.*

Result: *Initial subject of this study was 180 individual, in which 33 individual were then excluded, resulting in a final sample size of 147. It consists of 68 patients were resistant to erythropoietin and 79 were non-resistant. The ORAI1 rs6486795 TT genotype is associated with a 3.23-fold increased likelihood of EPO resistance (OR 3.23; 95% CI: 1.06–9.87), after considering several factors such as urea, creatinine, CRP, Ret-He, ferritin, Hb, use of ARB drugs, folic acid, vitamin B12, EPO dose, and body mass index. Similarly, in the additive model, the ORAI1 rs6486795 TT genotype shows a 3.63-fold increased likelihood (OR 3.63; 95% CI: 1.15–11.45), after considering the same factors. However, no significant association is found between the ORAI1 rs12313273 polymorphism and EPO resistance.*

Conclusion: *The ORAI1 genetic variant rs6486795 is associated with an increased (3.23) likelihood of erythropoietin resistance in chronic kidney disease patients undergoing hemodialysis.*

Keywords: *EPO-resistant, chronic kidney disease, dialysis, ORAI1 gene (rs12313273 and rs6486795)*