



INTISARI

Latar belakang: Defisiensi besi merupakan gangguan nutrisi yang umum terjadi dan dapat memengaruhi berbagai populasi, termasuk mahasiswa kedokteran sebagai kelompok berisiko. Faktor risiko mencakup asupan zat besi yang rendah, gangguan absorpsi, kehilangan besi, dan peningkatan kebutuhan. Pemeriksaan laboratorium untuk mendeteksi defisiensi besi meliputi parameter hematologi dan biokimia. Feritin serum merupakan indikator terbaik cadangan besi pada kondisi tanpa inflamasi, namun nilainya dapat meningkat sebagai respons fase akut. Sebaliknya, *Reticulocyte Hemoglobin Expression* (RHE) merefleksikan status besi fungsional untuk eritropoiesis dan relatif tidak dipengaruhi oleh infeksi atau inflamasi.

Tujuan: Mengevaluasi validitas RHE untuk skrining defisiensi besi.

Metode: Penelitian ini adalah penelitian observasional analitik potong lintang dengan desain uji diagnostik. Subjek penelitian adalah calon mahasiswa PPDS dan koas yang berusia ≥ 18 tahun dan menjalani pemeriksaan kesehatan di Departemen Patologi Klinik dan Kedokteran Laboratorium FK-KMK UGM Yogyakarta. Kriteria inklusi meliputi kondisi sehat dan kesediaan menjadi partisipan, kriteria eksklusi mencakup menstruasi, kehamilan, sedang/riwayat terapi besi, riwayat transfusi dalam tiga bulan terakhir, kadar CRP > 5 mg/L, dan hasil HbA₂ $> 3,5\%$. Pemeriksaan *Reticulocyte Hemoglobin Expression* (RHE) dilakukan dengan metode *flow cytometry*, feritin serum dianalisis menggunakan metode imunoturbidimetri. Analisis statistik deskriptif disajikan dalam bentuk rerata \pm simpangan baku atau median (min–maks) sesuai distribusi data. Uji beda dilakukan dengan *independent t-test* atau *Mann–Whitney*, dan analisis ROC digunakan untuk mengevaluasi validitas RHE berdasarkan standar rujukan feritin serum ≤ 15 ng/mL.

Hasil: Penelitian ini melibatkan 640 subjek berusia ≥ 18 tahun yang memenuhi kriteria inklusi, dieksklusi 296 karena memenuhi kriteria eksklusi. Subjek kelompok defisiensi besi sebanyak 17 orang dan tidak defisiensi besi sebanyak 327 orang. Hasil analisis ROC menunjukkan *area under the curve* (AUC) 0,852 (95%CI: 0,779-0,924), $p = 0,001$, RHE dengan *cut off* terpilih berdasarkan standar rujukan feritin serum 15 $\mu\text{g/L}$ adalah $\leq 28,65$ pg, memiliki sensitivitas 76,4%, spesifisitas 81,96%, akurasi 81,69%, LR(+) 4,24, dan LR(-) 0,29.

Simpulan: *Reticulocyte hemoglobin expression* (RHE) memiliki validitas 81,69% untuk skrining defisiensi besi. Nilai RHE dengan *cut off* $\leq 28,65$ pg memiliki sensitivitas 76,5%, spesifitas 81,96%, nilai ramal positif 18,06% dan nilai ramal negatif 98,53%.

Kata kunci: defisiensi besi, anemia defisiensi besi (ADB), *reticulocyte hemoglobin expression* (RHE)



ABSTRACT

Background: Iron deficiency is a common nutritional disorder that can affect various populations, including medical students, who are considered a high-risk group. Risk factors include inadequate iron intake, impaired absorption, iron loss, and increased physiological demand. Laboratory evaluation for detecting iron deficiency includes both hematological and biochemical parameters. Serum ferritin is the best indicator of iron stores in the absence of inflammation, although its levels may increase as part of the acute-phase response. In contrast, Reticulocyte Hemoglobin Expression (RHE) reflects functional iron status for erythropoiesis and is relatively unaffected by infection or inflammation.

Objective: To evaluate the validity of RHE for iron deficiency screening.

Method: This study was an analytical observational cross-sectional study with a diagnostic test design. Subjects were individuals aged ≥ 18 years undergoing health examinations at the Department of Clinical Pathology and Laboratory Medicine, Faculty of Medicine, Public Health, and Nursing, Universitas Gadjah Mada (FK-KMK UGM), Yogyakarta. Inclusion criteria included being in healthy condition and willing to participate, while exclusion criteria included menstruation, pregnancy, current or prior iron therapy, history of blood transfusion within the past three months, CRP level >5 mg/L, and HbA₂ level $>3.5\%$. Reticulocyte Hemoglobin Expression was measured using flow cytometry, while serum ferritin was analyzed using the immunoturbidimetric method. Descriptive statistics were reported as mean \pm standard deviation or median (min–max) based on data distribution. Comparative analysis used the independent t-test or Mann–Whitney test, and ROC analysis was performed to assess the validity of RHE using serum ferritin ≤ 15 ng/mL as the reference standard.

Result: This study included 640 subjects aged ≥ 18 years who met the inclusion criteria; 296 were excluded based on the exclusion criteria. Among the remaining participants, 17 were classified as iron deficient, and 327 were non-deficient. Analysis of ROC yielded an AUC of 0.852 (95% CI: 0.779–0.924, $p = 0.001$). Using a cut-off value of RHE ≤ 28.65 pg (based on the serum ferritin reference of ≤ 15 ng/mL), the test demonstrated sensitivity of 76.4%, specificity of 81.96%, overall accuracy of 81.69%, positive likelihood ratio [LR(+)] of 4.24, and negative likelihood ratio [LR(-)] of 0.29.

Conclusion: Reticulocyte hemoglobin expression (RHE) has a validity of 81.69% for screening iron deficiency. An RHE value with a cut-off of ≤ 28.65 pg has a sensitivity of 76.5%, specificity of 81.96%, positive predictive value of 18.06%, and negative predictive value of 98.53%.

Keywords: iron deficiency, iron deficiency anaemia (IDA), reticulocyte hemoglobin expression (RHE)