

KADAR HIGH MOBILITY GROUP BOX-1 DALAM SIRKULASI SEBAGAI FAKTOR RISIKO DERAJAT AKTIVITAS DAN KEPARAHAN OFTALMOPATI GRAVES'

Mohammad Robikhul Ikhsan^{1,2}, Nyoman Kertia², Supanji³, Bambang Udji Djoko Rianto⁴

¹Program Doktor Ilmu Kedokteran dan Kesehatan, ²Departemen Ilmu

Penyakit Dalam, ³Departemen Ilmu Kesehatan Mata, ⁴Departemen Ilmu Telinga, Hidung, Tenggorok-
Kepala Leher

Fakultas Kedokteran, Kesehatan Masyarakat, dan Keperawatan, Universitas Gadjah Mada,
Yogyakarta;

Abstrak

Latar belakang : Penyakit Graves' merupakan penyakit tiroid autoimun. Respon autoimunitas ini menyebabkan terjadinya oftalmopati yang hingga saat ini faktor risikonya belum sepenuhnya diketahui. *High Mobility Group Box-1* (HMGB1) merupakan salah satu penanda hayati dari *Damage-associated molecular patterns* (DAMPs) diduga berperan dalam perjalanan oftalmopati Graves'.

Tujuan: membuktikan perbedaan kadar HMGB1 antara subjek penyakit Graves' dengan oftalmopati dibandingkan tanpa oftalmopati, serta menentukan apakah kadar HMGB1 merupakan faktor risiko munculnya oftalmopati dan pengaruhnya terhadap derajat aktivitas dan keparahan oftalmopati.

Metode : Penelitian kasus kontrol pasien penyakit Graves' baru terdiagnosis yang berkunjung ke RSUP Dr Sardjito dengan kelompok kasus 22 subjek penyakit Graves' dengan oftalmopati dan kelompok kontrol 22 tanpa oftalmopati. Dilakukan pemeriksaan kadar HMGB1 dan dilakukan analisis meliputi perbedaan rerata kadar HMGB1 dan melakukan analisis kadar HMGB1 sebagai faktor risiko munculnya oftalmopati serta dengan derajat aktivitas dengan nilai CAS dan derajat keparahan oftalmopati dengan nilai EUGOGO. Analisis data dengan uji *Mann-Whitney*, uji korelasi *Spearman*, uji regresi *logistic biner* dan *multinomial*

Hasil : Didapatkan perbedaan bermakna ($p < 0,001$) kadar HMGB1 pada kelompok kasus dengan median 15,49 pg/mL (5,12 pg/mL-47,59 pg/mL) dibanding kelompok kontrol dengan nilai median 2,33 pg/mL (0,82 pg/mL-15,66 pg/mL). Terdapat hubungan kuat kadar HMGB1 dengan CAS ($r = 0,779$; $p < 0,001$) dan nilai EUGOGO ($r = 0,781$; $p < 0,001$). Analisis faktor risiko didapatkan subyek penyakit Graves' dengan kadar HMGB1 $\geq 8,86$ (pg/mL). memiliki peningkatan risiko 12 kali kejadian oftalmopati, dan 5,1 kali penyebab oftalmopati aktif. derajat keparahan oftalmopati berdasarkan nilai EUGOGO tidak dipengaruhi oleh kadar HMGB1

Simpulan : Terdapat perbedaan kadar HMGB1 antara kelompok subjek penyakit Graves' dengan oftalmopati dibandingkan tanpa oftalmopati. Kadar HMGB1 $\geq 8,86$ pg/mL memiliki peningkatan risiko 12 kali terjadinya oftalmopati dan 5,1 kali oftalmopati aktif.

Kata kunci : penyakit Graves', oftalmopati, *High Mobility Group Box-1*, faktor risiko

CIRCULATION LEVELS OF HIGH MOBILITY GROUP BOX-1 AS A RISK FACTOR FOR DEGREE OF ACTIVITY AND SEVERITY IN GRAVES' OPHTHALMOPATHY

Mohammad Robikhul Ikhsan^{1,2}, Nyoman Kertia², Supanji³, Bambang Udji Djoko Rianto⁴

¹Doctorate Program ²Department of Internal Medicine, ³Department of Ophthalmology, ⁴Department of Ear, Nose and Throat-Head and Neck

Faculty of Medicine, Public Health, and Nursing, Universitas Gadjah Mada, Yogyakarta

Abstract

Background : Graves' disease is an autoimmune thyroid disease and causes the occurrence of ophthalmopathy. The risk factors for ophthalmopathy have not been fully known. High Mobility Group Box-1 (HMGB1) molecule is one of the biomarkers of Damage-associated molecular patterns (DAMPs) have play role in autoimmune disease and may a risk factor of Graves' ophthalmopathy.

Objectives: To determine the difference HMGB1 level between Graves' disease patients with ophthalmopathy compared to without ophthalmopathy, and determined levels of HMGB1 is risk factor for the occurrence of ophthalmopathy and its effect on the degree of activity and severity of ophthalmopathy

Method : Case control study of newly diagnosed Graves' disease patients who visited Dr Sardjito Hospital with the case group being 22 Graves' disease subjects with ophthalmopathy and the control group of 22 Graves' disease subjects without ophthalmopathy. An examination levels of HMGB1 and analysis was carried out between the group of cases and controls including differences of mean, correlation and determine as risk factors for occurrence, degree of activity with CAS score and degrees of ophthalmopathy severity with EUGOGO score. Data analysis with Mann-Whitney test, Spearman correlation test, binary and multinomial logistic regression test

Result : There was a significant difference ($p < 0.001$) in levels of HMGB1 in the case group with a median score 15.49 pg/mL (5.12 pg/mL-47.59 pg/mL) compared to the control group with a median score 2.33 pg/mL (0.82 pg/mL-15.66 pg/mL). There was a strong relationship between levels of HMGB1 and the degree of ophthalmopathy activity based on cas score ($r = 0.779$; $p < 0.001$) and degrees of ophthalmopathy severity based on EUGOGO score ($r = 0.781$; $p < 0.001$). Analysis of risk factors obtained by Graves' disease subjects with levels of HMGB1 with a cut-off point score of > 8.86 (pg/mL) causing an increased risk of 12 times the incidence of ophthalmopathy, and 5.1 times causing active ophthalmopathy. The severity of ophthalmopathy based on EUGOGO score is not affected by levels of HMGB1

Conclusion : There were differences in levels of HMGB1 between Graves' disease subjects with ophthalmopathy compared to Graves' disease without ophthalmopathy. The levels of HMGB1 > 8.86 pg/mL caused a 12 times increase in the risk of ophthalmopathy and 5.1 times the risk of active ophthalmopathy.

Keywords : Graves' disease, ophthalmopathy, High Mobility Group Box-1, risk factor