

# Peran inflamasi dan apoptosis terhadap jejas jantung pembuluh darah pada Preeklamsia Awitan Dini dan lanjut: Kajian terhadap NF- KB, PARP-1, TUNEL dan Cyclophilin A. The Role of Inflammation and Apoptosis Impact on Cardiovascular Injury in Early Onset and Late Onset Preeclampsia: Study on NF- KB, PARP-1, TUNEL assay and Cyclophilin A

Novi Resistantie, author

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## Abstrak

Preeklamsia merupakan salah satu penyebab kematian utama ibu dan perinatal di dunia. Inflamasi disertai tingginya indeks apoptosis di syncytiotrophoblast dan ekspresi Cyclophilin A diduga berperan pada preeklamsia. Faktor tersebut diasumsikan menyebabkan jejas jantung/pembuluh darah yang meningkatkan risiko morbiditas dan mortalitas ibu dan perinatal. Tujuan penelitian ini adalah menganalisis peran inflamasi, indeks apoptosis dan Cyclophilin A terhadap jejas jantung/pembuluh darah pada preeklamsia awitan dini, lanjut dan kehamilan normal.

Sebanyak 47 wanita hamil yang terpilih dilakukan pemeriksaan hematologi, ekokardiografi dan ultrasonografi Doppler. Plasenta diperiksa secara histopatologis untuk mengukur ekspresi NF-KB dan PARP-1, indeks apoptosis berdasarkan pemeriksaan TUNEL, ekspresi Cyclophilin A dan pemeriksaan ultrastruktur mikroskopik pada syncytiotrophoblast. Analisis Anova digunakan untuk mengidentifikasi perbedaan antara ketiga kelompok, sedangkan regresi linier digunakan untuk mengetahui korelasi faktor yang diduga terhadap jejas jantung/pembuluh darah menggunakan SPSS 20.

Usia ibu, indeks massa tubuh (IMT), hitung trombosit, NF- KB dan indeks apoptosis lebih tinggi disertai Cyclophilin A lebih rendah pada preeklamsia awitan dini dibandingkan preeklamsia awitan lanjut dan kehamilan normal. Hitung leukosit lebih tinggi pada preeklamsia awitan lanjut dibandingkan awitan dini dan normal. Total peripheral resistance (TPR) paling tinggi pada kelompok awitan dini dibandingkan awitan lanjut dan kehamilan normal, sedangkan cardiac index (CI) tidak berbeda bermakna pada ketiga kelompok. Resistensi indeks (RI) lebih tinggi pada preeklamsia awitan dini dibandingkan awitan lanjut dan kehamilan normal.

Berdasarkan analisis regresi linier multivariat, membuktikan indeks apoptosis dan Cyclophilin A memiliki hubungan dengan jejas jantung/pembuluh darah. Hal tersebut menunjukkan inflamasi, indeks apoptosis, Cyclophilin A disertai pemeriksaan ekokardiografi dan ultrasonografi Doppler merupakan metode yang cepat, tepat dan noninvasif faktor risiko terhadap jejas jantung/pembuluh darah pada preeklamsia. Penelitian yang dianjurkan di masa datang adalah menilai geometri jantung dengan ekokardiografi dan volumetri plasenta dengan ultrasonografi.

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Preeclampsia is one of the leading cause of maternal and perinatal death in the world. Inflammation accompanied by a high apoptotic index of syncytiotrophoblast and Cyclophilin A were speculated to play a role in preeclampsia. Those response were assumed to cause cardiovascular injury which lead to the risk of maternal and perinatal morbidity and mortality in preeclampsia. The objective of the study was to investigate the role of inflammation, apoptotic index and Cyclophilin A in cardiovascular injury in early and

late onset preeclampsia compared to normal pregnancy.

A total of 47 pregnant women were selected, consisting almost the same size of each group (30%) and assessed for maternal hematology, echocardiography and Doppler ultrasound. Placentae were assessed histopathologically by measuring nuclear factor kappa-light-chain-enhancer of activated B cells (NF- $\kappa$ B) and Poly (ADP-ribose) polymerase 1 (PARP-1) expression for inflammation marker, terminal deoxynucleotidyl transferase dUTP nick end labeling (TUNEL) assay for apoptotic index and Cyclophilin A. Confirmation by transmission electron microscopy (TEM) was done. Anova analysis was used to identify the differences between the three groups while linear regression was employed to assess the correlation between factors on cardiovascular injury using SPSS 20.

Maternal age, body mass index (BMI), platelet count, NF- $\kappa$ B and apoptotic index, resistance index (RI) were higher supported by low Cyclophilin A in early onset preeclampsia (EOP) than in late onset preeclampsia (LOP) and normal pregnancy. Leukocyte count was higher in late onset preeclampsia than in early and normal pregnancy. Total peripheral resistance (TPR) was highest in the EOP compared to LOP and normal pregnancy, while the cardiac index (CI) was not significantly different in all groups.

Based on multivariate linear regression analysis, the apoptotic index and Cyclophilin A correlated to cardiovascular injury. Assessing inflammation, apoptotic index, Cyclophilin A, echocardiography examination and Doppler ultrasound examination might indicated timely and non-invasive detection as an alarm entry point for cardiovascular injury in both early and late onset preeclampsia. Cardiac geometry by echocardiography and placental volumetry by Doppler ultrasound should be performed in future research.