Jumlah Dendritic Cells (DC) 10 dan Sel T Regulatorik CD4+ CD25+FoxP3 Desidua pada Preeklamsia dan Keterkaitannya dengan Kadar Seng, Vitamin A, dan Vitamin D dalam Patomekanisme Penolakan Imun = Number of Decidual Dendritic Cells (DC) 10 and Regulatoric T cell CD4+CD25+FoxP3 in Preeclampsia and Their Correlations with Decidual Levels of Zinc, Vitamin A, and Vitamin D in the Pathomechanism of Immune Rejection

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Abstrak

Preeklamsia dibagi menjadi preeklamsia awitan dini (PEAD) jika terjadi pada usia kehamilan < 34 minggu dan preeklamsia awitan lanjut (PEAL) pada kehamilan > 34 minggu. Intoleransi imun diduga menyebabkan penolakan imun terhadap fetus di plasenta. Dendritic cell 10 (DC-10) dan sel T regulator CD4+CD25+FoxP3 (Treg) di desidua berperan penting dalam menciptakan lingkungan yang tolerogenik selama kehamilan. Namun, peran spesifik dalam patomekanisme PEAD dan PEAL serta faktor-faktor nutrisi yang berperan dalam regulasi DC-10 dan Treg, yaitu seng, vitamin A, dan vitamin D belum diteliti secara jelas. Penelitian ini bertujuan untuk memahami patomekanisme penolakan imun pada preeklamsia melalui jumlah DC-10 dan sel Treg desidua serta hubungannya dengan vitamin A, vitamin D, dan seng.

Desain penelitian ini adalah studi potong lintang komparatif antara kehamilan dengan PEAD, PEAL, dan NT antara Oktober 2019 dan Desember 2021. Subjek penelitian direkrut dari RSUP Fatmawati (Jakarta), RSUPN Cipto Mangunkusumo (Jakarta), dan RSUD Karawang (Jawa Barat). Kriteria penerimaan adalah semua ibu hamil 20–40 minggu yang menjalani persalinan dengan seksio sesaria dan setuju untuk dilibatkan dalam penelitian. Kriteria penolakan meliputi pasien dengan penyulit obstetrik, plasenta previa, memiliki riwayat penyakit kronik, hipertensi sebelum kehamilan 20 minggu, terdiagnosis COVID-19, demam dan leukosit >15.000 /mL pada saat pemeriksaan dan kematian janin dalam rahim. Spesimen desidua diperoleh dengan kuretase tajam setelah seksio sesaria. Jumlah DC-10 dan sel Treg dihitung dengan flow cytometry. Konsentrasi faktor nutrisi diperiksa dengan metode ICP-MS dan LC-MS. Perbandingan median dianalisis dengan uji Kruskal-Wallis, sedangkan koefisien korelasi diperoleh dengan uji korelasi Spearman. Subjek penelitian adalah 14 ibu hamil untuk setiap kelompok (total 42 kasus). Jumlah DC-10 lebih rendah secara bermakna pada PEAD dibandingkan NT ($p < 0,001$) dan lebih rendah secara bermakna pada PEAL dibandingkan NT ($p = 0,015$). Sebaliknya, sel Treg FoxP3+CD25+ lebih tinggi secara bermakna pada PEAD dibandingkan NT ($p = 0,015$). Tidak terdapat korelasi antara faktor nutrisi dan jumlah faktor tolerogenik pada kelompok preeklamsia (PE). Namun, terdapat korelasi sedang antara konsentrasi seng desidua dan DC-10 di kelompok NT ($r = 0,656$; $p = 0,011$) dan korelasi kuat antara konsentrasi retinol desidua dan DC-10 juga di kelompok NT ($r = 0,746$; $p = 0,002$). Korelasi sedang didapatkan antara konsentrasi vitamin D dan jumlah sel Treg FoxP3+CD25+ di kelompok NT ($r = 0,590$; $p = 0,026$). Disimpulkan bahwa jumlah DC-10 pada PEAD lebih rendah dibandingkan dengan kehamilan NT, sedangkan jumlah sel Treg pada PEAD secara bermakna lebih tinggi dibandingkan dengan kehamilan NT. Konsentrasi faktor nutrisi desidua tidak berkorelasi dengan jumlah DC-10 atau Treg desidua pada

preeklamsia (PEAD dan PEAL). Namun, pada kelompok NT terdapat korelasi positif antara seng dan DC-10, retinol dan DC-10, serta vitamin D dan jumlah sel Treg desidua.
.....Preeclampsia is categorized as early-onset preeclampsia (EOPE) at < 34 week of gestation and late-onset preeclampsia (LOPE) at > 34 week of gestation. Immune intolerance is thought to be the underlying cause of immune rejection to the fetus in the placenta. Decidual dendritic cell-10 (DC-10) and T regulator cell CD4+CD25+FoxP3 (Treg) play important role to create a tolerogenic environment during pregnancy. However, the specific role in the pathomechanism of EOPE or LOPE and nutritional factors that play role in the regulation of DC-10 and Treg, i.e. zinc, vitamin A, and vitamin D have not been widely studied. This study was aimed to know the pathomechanism of immune rejection in preeclampsia through the number of decidual DC-10 and Treg cell and their correlations with vitamin A, vitamin D, and zinc.
The study design was cross-sectional comparative among EOPE, LOPE, and NT pregnancies between October 2019 and December 2021. Study subjects were recruited from Fatmawati General Hospital (Jakarta), Cipto Mangukusumo National General Hospital (Jakarta), and Karawang Regional Public Hospital (West Java). Inclusion criteria were all pregnant women between 20–40 weeks of gestation who underwent cesarean delivery and gave their written consent to be included in the study. Exclusion critera were patients with obstetric complications, placenta previa, history of chronic disease, hypertension before 20 weeks of gestation, was diagnosed with COVID-19, fever and leukocyte count of >15.000 /mL at the time of examination and presence of intrauterine fetal death. Decidual specimens were obtained by curettage after the cesarian section. The number of DC-10 and Treg cells were counted using flow cytometry. Concentrations of nutritional factors were assayed using ICP-MS and LC-MS method. Median comparison among groups was analyzed using Kruskal-Wallis test, while correlation coefficient was obtained by using the Spearman correlation test. Study subjects were 14 pregnant women for each group (42 cases in total). The DC-10 was significantly lower in EOPE compared to NT ($p < 0.001$) and significantly lower in LOPE compared to NT ($p = 0.015$). On the other hand, Treg FoxP3+CD25+ cells were significantly higher in EOPE compare to NT ($p = 0.015$). No correlation between nutritional factors and the number of tolerogenic factors in the preeclampsia group. However, there was a moderate correlation between decidual zinc concentration and DC-10 in the NT group ($r = 0.656$; $p = 0.011$) and a strong correlation between decidual retinol concentration and DC-10 also in NT group ($r = 0.746$; $p= 0.002$). A moderate correlation was found between vitamin D concentration and Treg FoxP3+CD25+ cells in the NT group ($r = 0.590$; $p = 0.026$). To conclude, the number of DC-10 in EOPE is lower than NT pregnancy, whereas the number of Treg cells in EOPE is higher than NT pregnancy. Concentrations of dedicual nutritional factors do not correlate with the number of decidual DC-10 or Treg cells in preeclampsia (EOPE and LOPE). However, in NT group, there is positive correlation between decidual zinc and DC-10, retinol and DC-10, and vitamin D and Treg cells.