Aspek mikronutrien retinol dikaitkan dengan imunitas lokal ekspresi tumor necrosis factor-alfa yang distimulasi spesifik dengan epitop E6 human papillomavirus tipe 16 dan rasio sel T CD4 /CD8 pada perjalanan alami kanker serviks = Retinol as a micronutrients related to cervical local immunity the expression of tumor necrosis factor alpha specifically stimulated with E6 epitope of human papillomavirus type 16 and ratio of CD4, CD8 T cell in natural history of cervical cancer

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Abstrak

ABSTRAK
Latar Belakang: Persistensi infeksi HPV onkogenik merupakan penyebab kanker serviks. Retinol sebagai mikronutrien antioksidan memiliki peran esensial dalam sistem imun mencegah persistensi. Retinol memodulasi sel T CD4+/CD8+ serta produksi sitokin. Tumor Necrosis Factor-Alpha (TNF-) adalah sitokin pro-inflamasi yang mampu mengendalikan HPV, namun pada infeksi persisten TNF- justru memicu karsinogenesis. Rasio sel T CD4+:CD8+ dan TNF- yang adekuat di awal infeksi HPV merupakan titik kunci klirens. Penelitian ini bertujuan untuk mengetahui tingkat kecukupan deposit retinol, ekspresi TNF-, dan rasio sel T CD4+:CD8+ pada kelompok serviks normal, infeksi subklinis HPV klirens, persisten, dan kanker serviks.

Metode: Tingkat kecukupan deposit retinol diketahui berdasarkan pemeriksaan darah perifer dengan metode ELISA. Stimulasi spesifik epitop E6 HPV tipe 16 dilakukan pada sel sekret servikovaginal yang telah diinkubasi 24 jam, diamati ekspresi TNF- secara semikuantitatif dengan metode ELISpot. Pemeriksaan sel T CD4+ dan CD8+ dari sekret servikovaginal secara kuantitatif dengan metode flowsitometri.

Hasil: Deposit retinol yang cukup pada kelompok serviks normal, infeksi subklinis HPV klirens, persisten, dan kanker serviks berturut-turut adalah 85%, 75% (OR 1,89), 33,3% (OR 11,33), dan 75% (OR 1,89). Ekspresi TNF- pada kelompok serviks normal adalah 10%, sedangkan kanker serviks 75% (OR 27,00; p<0,001). Tidak tampak ekspresi TNF- pada kelompok infeksi subklinis HPV klirens dan persisten. Rasio sel T CD4+:CD8+ yang tinggi pada kelompok serviks normal adalah 10% dan kanker serviks 25% (OR 0,33). Tidak terdapat rasio sel T CD4+:CD8+ yang tinggi pada kelompok infeksi subklinis HPV klirens (OR 1,22) dan persisten (OR 0,95). Tidak terdapat hubungan bermakna antara tingkat kecukupan deposit retinol dengan ekspresi TNF- (p=0,147), tingkat kecukupan deposit retinol dengan rasio sel T CD4+:CD8+ (p=0,726), dan rasio sel T CD4+:CD8+ dengan ekspresi TNF- (p=0,690).

Kesimpulan: Penelitian ini mampu membuktikan bahwa tingkat kecukupan deposit retinol tertinggi dijumpai pada kelompok serviks normal dan ekspresi TNF- tertinggi pada kelompok kanker serviks (OR 27,00; p<0,001). Tingkat kecukupan deposit retinol terendah bukan pada kelompok kanker serviks,

melainkan pada infeksi subklinis HPV persisten (OR 11,33). Tidak terdapat perbedaan bermakna pada tingkat kecukupan deposit retinol dan rasio sel T CD4+:CD8+. Terdapat perbedaan bermakna pada ekspresi TNF- antara kelompok kanker serviks dengan serviks normal (p<0,001), kanker serviks dengan infeksi HPV subklinis klirens (p=0,024), dan klirens dengan persisten (p=0,007). Tidak terdapat perbedaan bermakna ekspresi TNF- antara kelompok kanker serviks dengan infeksi HPV subklinis persisten (p=0,058). Tidak bermaknanya beberapa hasil terkait imunitas masih mungkin dikarenakan tingkat kecukupan deposit retinol kelompok kanker serviks pada penelitian ini sangat baik dimana bertentangan dengan kepustakaan.

<hr><i>ABSTRACT
Background: Persistency of oncogenic-HPV infection is the cause of cervical cancer. Retinol is one of antioxidant micronutrients that plays essential roles in immune system to prevent the persistency by modulating CD4+ and CD8+T cells and cytokines production. Tumor Necrosis Factor-Alpha (TNF-) is an acute pro-inflammatory cytokine which has many crucial roles in controlling HPV. In contrast, when persistent infection occurs, TNF- induces carcinogenesis. Ratio of CD4+:CD8+ T cells and adequate TNF- production in acute HPV infection are keypoints for clearance. The aim of this research is to analyze sufficency level of retinol deposit, expression of TNF-, and ratio of CD4+:CD8+ T cells in normal cervix, clearance and persistent HPV subclinical infection, and cervical cancer group.

Methods : Sufficiency level of retinol deposit was analyzed from peripheral blood by ELISA method. The cervicovaginal secretions which had 24 hours incubated were stimulated specifically by E6 epitope HPV type-16, measuring TNF- expression semiquantitatively by ELISpot method and CD4+/CD8+ T cells quantitatively by flowcytometry method.

Results: Sufficient level of retinol deposit in normal cervix, clearance HPV subclinical infection, persistent, and cervical cancer group was 85%, 75% (OR 1.89), 33.3% (OR 11.33), and 75% (OR 1.89), respectively. The expression of TNF- in normal cervix group was 10%, while in cervical cancer was 75% (OR 27.00; p<0.001). There were no expression in clearance and persistent HPV subclinical infection groups. High ratio of CD4+:CD8+ T cells in normal cervix and cervical cancer group was 10% and 25% (OR 0.33). There were no high ratio of CD4+:CD8+ T cells in clearance (OR 1,22) and persistent (OR 0.95) HPV subclinical infection groups. There was no significant correlation between sufficiency level of retinol deposit and TNF- expression (p=0.147), sufficiency level of retinol deposit and ratio of CD4+:CD8+ T cells (p=0.726), ratio of CD4+:CD8+ T cells and TNF- expression (p=0.690).

Conclusions: This study was able to prove that normal cervix group has the highest retinol deposit sufficiency level and cervical cancer group has the highest TNF- expression (OR 27,00; p<0,001). The lowest of retinol deposit sufficiency level was not in cervical cancer, but in persistent HPV subclinical infection group (OR 11.33). There was no significant correlation in sufficiency level of retinol deposit and ratio of CD4+:CD8+ T cells. There was significant correlation in TNF- expression between cervical cancer and normal cervix (p<0.001), cervical cancer and clearance subclinical HPV infection (p=0.024), and between clearance and persistent group (p=0.007). There was no significant correlation in TNF- expression between cervical cancer and persistent subclinical HPV infection group

(p=0.058). Not significant some results related immunity that might be due to retinol deposit sufficiency level in cervical cancer group in this study was very good, which conflicted with literatures.</i>