"PERBANDINGAN KADAR *25-HYDROXYVITAMIN D* PADA ANAK YANG MENDERITA KANKER DENGAN DAN TANPA DUGAAN SEPSIS"

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ABSTRAK

PENDAHULUAN. Vitamin D diketahui berperan penting dalam berbagai fungsi fisiologis tubuh dan melawan infeksi melalui sistem kekebalan bawaan dan adaptif. Anak dengan kanker memiliki risiko lebih tinggi untuk menderita sepsis dan kekurangan vitamin D. Berbagai penelitian tentang kadar vitamin D pada pasien anak yang menderita kanker dengan sepsis memberikan hasil yang bervariasi dan masih kontroversi. Tujuan penelitian untuk menganalisis kadar 25-hydroxyvitamin D pada anak yang menderita kanker dengan dugaan sepsis dan tanpa sepsis.

METODE. Penelitian bersifat analitik observasional dengan rancangan *cross sectional* dilakukan di Ruang rawat inap dan rawat jalan Hematologi-Onkologi Anak RSUD Dr. Soetomo pada periode April-September 2019. Sampel dibagi 2 kelompok yaitu kelompok kanker dengan dugaan sepsis 41 anak dan kanker tanpa sepsis 41 anak. Masing-masing kelompok diukur kadar 25(OH)D, kemudian dinilai perbedaan antar kelompok. Pemeriksaan vitamin D menggunakan metode *antibody competitive immunoassay chemiluminesence* dengan alat ADVIA Centaur.

HASIL. Kedua kelompok memiliki kadar *25-hydroxyvitamin D* yang rendah dengan status defisiensi pada kelompok dugaan sepsis 92,7% dan tanpa sepsis 78%. Terdapat perbedaan kadar *25-hydroxyvitamin D* pada anak yang menderita kanker dengan dugaan sepsis dan tanpa sepsis (p = 0,002).

PEMBAHASAN. Kadar vitamin D lebih rendah ditemukan pada kelompok kanker dengan dugaan sepsis. Kadar vitamin D yang rendah menurunkan aktivitas T helper 2 dan menurankan imunitas seluler yaitu penurunan fagositik makrofag sehingga patogen lebih mudah masuk ke dalam tubuh dan mengalami bakteremia.

SIMPULAN. Terdapat perbedaan kadar *25-hydroxyvitamin D* pada anak kanker dugaan sepsis dengan anak kanker tanpa sepsis.

KATA KUNCI. *25-hydroxyvitamin D*, kanker anak, sepsis.

"COMPARISSON OF 25-HYDROXYVITAMIN D LEVELS IN PEDIATRIC CANCER WITH AND WITHOUT SUSPECTED SEPSIS "

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ABSTRACT

Introduction. Vitamin D is known to play an important role in a variety of physiological functions of the body and in fighting infections though the innate and adaptive immune system. Children with cancer have a higher risk of suffering sepsis and vitamin D deficiency. Some studies on vitamin D levels in pediatric cancer with sepsis have varied results and are still controversial.The objective of the study was to analyze 25-hydroxyvitamin D levels in pediatric cancer with and without suspected sepsis.

Method. The was an observational analytical study with cross sectional design. Samples were collected during April – September 2019 from Inpatient and Outpatient Pediatric Clinic of the Dr. Soetomo Hospital Surabaya. The samples were divided into 2 groups, a group of pediatric cancer with suspected sepsis of 42 and pediatric cancer without sepsis of 42. Each group was measured 25-hydroxyvitamin D levels, then differences in levels of 25-hydroxyvitamin D between groups were assessed. Vitamin D examination was performed using the antibody competitive immunoassay chemiluminesence method with ADVIA Centaur.

Results. Both groups had low 25-hydroxyvitamin D levels with a deficiency state in the suspected sepsis group of 92.7% and without sepsis 78%. There were differences in levels of 25-hydroxyvitamin D in pediatric cancer with and without suspected sepsis ($p = 0.002$).

Discussion. Lower vitamin D levels were found in the cancer group with suspected sepsis. Low vitamin D levels reduce T helper 2 activity and decrease cellular immunity, a decrease in phagocytic macrophages so that pathogens enter the body more easily and become bacteremia.

Conclusion. There were significant differences in levels of 25-hydroxyvitamin D in pediatric cancer with suspected sepsis and pediatric cancer without sepsis.

Key words : 25-hydroxyvitamin D, pediatric cancer, sepsis

RINGKASAN

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Sepsis adalah salah satu komplikasi yang sering terjadi pada pasien anak dengan kanker bahkan menyebabkan kematian. Daya tahan tubuh pada anak kanker sangat menurun karena penyakitnya sendiri maupun karena perawatan yang harus dijalani. Defisiensi *25-hydroxyvitamin D* pada anak yang menderita kanker dihubungkan dengan peningkatan kejadian sepsis, dimana peran vitamin D yang penting dalam sistem kekebalan tubuh. Anak dengan kanker sendiri memiliki risiko yang tinggi untuk mengalami defisiensi vitamin D karena berbagai faktor. Berbagai penelitian tentang defisiensi vitamin D pada sepsis memberikan hasil yang bervariasi, sehingga masih kontroversi.

Penelitian ini bertujuan untuk membandingkan kadar *25-hydroxyvitamin D* pada anak yang menderita kanker dengan sepsis dan tanpa sepsis di RSUD Dr. Soetomo Surabaya. Penelitian bersifat analitik observasional dengan rancangan penelitian *cross sectional.* Pemeriksan *25-hydroxyvitamin D* menggunakan metode *antibody competitive immunoassay chemiluminesence* dengan alat Advia Centaur® xpt vitamin D total (VitD) dari Siemens. Sampel dikumpulkan selama 5 bulan yaitu April-September 2019 di Ruang Rawat Inap dan Rawat Jalan Hematologi-Onkologi Anak RSUD dr. Soetomo Surabaya. Sampel dibagi menjadi 2 kelompok yaitu kelompok dugaan sepsis dan tanpa sepsis. Masing-masing kelompok diukur kadar *25-hydroxyvitamin D*, kemudian dinilai perbedaan kadar *25-hydroxyvitamin D* antar kelompok.

Hasil penelitian menunjukkan kedua kelompok memiliki status defisiensi vitamin D. Pada kelompok kanker dengan dugaan sepsis ditemukan lebih banyak yang yang menderita defisiensi vitamin D yaitu 92,7% dan tanpa sepsis 78%. Kekurangan vitamin D pada pasien anak kanker dapat disebabkan karena *intake* yang berkurang, kurangnya paparan sinar matahari, gangguan ginjal dan hati karena pernyakitnya dan obat-obatan kemoterapi yang harus dijalani.

Terdapat perbedaan bermakna antara kadar *25-hydroxyvitamin D* pada anak yang menderita kanker dengan dugaan sepsis dan tanpa sepsis (p = 0,002). Anak yang menderita kanker dengan dugaan sepsis memiliki kadar *25-hydroxyvitamin D* yang jauh lebih rendah dibandingkan tanpa sepsis. Penelitian oleh Moromizato et.al. di Boston mengatakan bahwa nilai ambang kadar 25-hydroxyvitamin D lebih kecil atau sama dengan 16 ng/mL berhubungan dengan kejadian sepsis dan didukung oleh

penelitian metaanalisis di seluruh dunia oleh Haan, et. al yang mengatakan bahwa kekurangan vitamin D dikaitkan dengan kejadian infeksi dan sepsis.

Anak dengan kanker cenderung memiliki kadar vitamin D yang rendah karena berbagai faktor risiko seperti memiliki tubuh yang lemah sehingga lebih sering berada di dalam ruangan sehingga paparan sinar UV berkurang, nafsu makan yang menurun juga menyebabkan *intake* sumber vitamin D berkurang. Kanker itu sendiri juga dapat mengakibatkan perubahan VDR yang mengakibatkan berkurangnya aktivitas transkripsi tergantung $1\alpha,25(OH)_2D_3$. Aktivitas enzim CY27B1 yaitu suatu enzim yang diperlukan untuk konversi $25(OH)D_3$ menjadi $1\alpha,25(OH)_2D_3$ juga menurun. Berkurangnya kadar *25-hydroxyvitamin D* ini akan menurunkan aktivitas T-helper 2 dan menurunkan imunitas seluler yaitu penurunan fagositik makrofag, AMP dan LL 37 yang mengakibatkan perlawanan terhadap patogen terganggu sehingga patogen lebih mudah masuk ke dalam tubuh dan mengakibatkan bakteremia.

SUMMARY

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Sepsis is one of the complications that often occurs in pediatric cancer patients and even causes death. The immune system in children with cancer greatly decreases due to the disease itself and because of the treatment that must be undertaken. 25 hydroxyvitamin D deficiency in pediatric cancer is associated with an increase incidence of sepsis, where the important role of vitamin D is in the immune system. Children with cancer themselves have a high risk for vitamin D deficiency due to various factors. Some studies on vitamin D deficiency in sepsis gave various results, so that it is still controversial.

This study aimed to compare the levels of 25 hydroxyvitamin D in pediatric cancer with sepsis and without sepsis in Dr. Soetomo Hospital Surabaya. This was an observational analytical study with cross sectional study design. The examination of 25 hydroxyvitamin D level was performed using the antibody competitive immunoassay method with Advia Centaur total vitamin D (VitD) from Siemens. Samples were collected during April – September 2019 from the Outpatient and Inpatient Care of Pediatric Hematologi Oncology Clinic Dr. Soetomo Hospital. Samples were divided into 2 groups : suspected sepsis group and without sepsis. Each group were measured for 25-hydroxyvitamin D levels, then the differences between group were assessed.

The results showed that both groups had a vitamin D deficiency state. In the cancer group with suspected sepsis, there were more children suffering from vitamin D deficiency, 92% and without sepsis 78%. Vitamin D deficiency in pediatric cancer patients can be caused by reduced intake, lack of sun exposure, kidney and liver disorders due to illness and chemotherapy drugs.

There was a significant difference between 25-hydroxyvitamin D level in pediatric cancer with suspected sepsis and without sepsis ($p = 0.002$). Pediatric cancer with sepsis have much lower 25 hydroxyvitamin D levels than without sepsis. Study by Moromizato et. al. in Boston explained that the 25 hydroxyvitamin d level threshold was less than to 16 ng/mL associated with the incidence of sepsis and was supported by metaanalysis studies worldwide by Haan, et. al who explained vitamin D deficiency due to infection and sepsis.

Children with cancer tend to have low levels of vitamin D due to various risk factors such as having a fatique leading to more indoor activities and decreased sun exposure, loss of appetide with consequent decreased oral intake of dietary vitamin D. Cancer itself can also cause changes in VDR that result in reduced transcription activity depending on $1\alpha,25(OH)_2D_3$. The enzyme activity of CY27B1, as enzyme needed for the conversion of $25(OH)D_3$ to $1\alpha,25(OH)_2D_3$ also decreases. The decreament levels of 25 hydroxyvitamin D will reduce T helper 2 activity and decrease cellular immunity as phagocytic reduction of macrophages, AMP and LL37 that cause the pathogens more easily to infected and become bacteremia.