

BAB 7

SIMPULAN DAN SARAN

7.1. Simpulan

1. Kadar *25-hydroxyvitaminD* pada anak yang menderita tumor *solid* dengan dugaan sepsis lebih rendah dibandingkan tanpa sepsis
2. Kadar *25-hydroxyvitaminD* pada anak yang menderita kanker darah dengan dugaan sepsis lebih rendah dibandingkan tanpa sepsis
3. Terdapat perbedaan kadar *25-hydroxyvitamin D* pada pasien anak yang menderita kanker dengan dan tanpa dugaan sepsis.
4. Tidak ada perbedaan status vitamin D antara anak yang menderita kanker dengan dugaan sepsis maupun tanpa sepsis karena sama-sama berstatus defisiensi vitamin D yaitu < 20 ng/mL.

7.2. Saran

1. Mempertimbangkan asupan makanan dan paparan sinar matahari yang dapat menyebabkan bias pada penelitian.
2. Dilakukan penelitian lebih lanjut dengan pasien sepsis kultur bakteri positif sebagai *gold standard* untuk mencari nilai prognostic kadar vitamin D pada pasien sepsis.
3. Melakukan pemeriksaan kadar *25-hydroxyvitamin D* pada pasien kanker untuk mengetahui nilai *baseline*.
4. Dilakukan penelitian lebih lanjut dengan waktu pemeriksaan kadar vitamin D yang seragam.

DAFTAR PUSTAKA

- Abe, E., Miyaura, C., Sakagami, H., Takeda, M., & Konno, K. (1981). Differentiation of mouse myeloid leukemia cells induced by 1 alpha,25-dihydroxyvitamin D₃. *Proc Natl Acad Sci USA*, 78, 4990–4994.
- Ahmed, N., Yadav, V., Soni, R. K., Nagaraj, N., Berwal, P. K., & Sengar, G. S. (2016). A study of association between vitamin d deficiency in sepsis. *International Journal of Contemporary Pediatrics*, 3(4), 1419–1421.
- Angus, D., & van der poll, T. (2013). Severe sepsis and septic shock. *N Engl J Med*, 29(7), 1303–1310.
- Aydemir, G., Cekmez, F., Kalkan, G., Fidanci, M. K., Kaya, G., Karaoglu, A., ... Gunduz, R. C. (2014). High Serum 25-Hydroxyvitamin D Levels Are Associated with Pediatric Sepsis. *Tohoku J. Exp. Med*, 234, 295–298. <https://doi.org/10.1620/tjem.234.295>.
- Battault, S., Whiting, S. J., Peltier, S. L., Sadrin, S., Gerber, G., & Maixent, J. M. (2013). Vitamin D metabolism, functions and needs: From science to health claims. *European Journal of Nutrition*, 52(2), 429–441. <https://doi.org/10.1016/j.anireprosci.2012.12.003>
- Beker, B., Training, S. E., & Ozkan, A. (2013). Vitamin D in Childhood Cancer : A Promising Anticancer Agent? *Pediatric Endocrinology Reviews (PER)*, 10(April), 485–493.
- Bellasi, A., Lullo, L. Di, Bellasi, A., Barbera, V., Russo, D., Russo, L., ... Ronco, C. (2017). Pathophysiology of the cardio-renal syndromes types 1 – 5 : An uptodate. *Indian Heart Journal*, (January). <https://doi.org/10.1016/j.ihj.2017.01.005>
- Bikle, D. D. (2014). Vitamin D metabolism, mechanism of action, and clinical applications. *Chemistry and Biology*, 21(3), 319–329. <https://doi.org/10.1016/j.chembiol.2013.12.016>
- Cekmez, F., Aydemir, G., Yildirim, S., Bulut, O., Tung, T., Kul, M., ... Coban, A. (2014). Diagnostic Value of 25-hydroxyvitamin D level and New Cytokines in Neonatal Sepsis. *European Journal of Inflammation*, 12(2), 297–304. <https://doi.org/10.1177/1721727X1401200209>
- Coussens, L. M., & Werb, Z. (2010). Inflammation and cancer. *Nature*, 420(6917), 860–867. <https://doi.org/10.1038/nature01322>.Inflammation
- Culic, S., Markic, J., & Konjevoda, P. (2018). Vitamin D Status in Pediatric Patients with Newly Diagnosed Malignant Disease : Preliminary Results. *Central Eur J Paed*, 14(2), 160–166. <https://doi.org/10.5457/p2005-114.215>
- Danai, P. (2006). The epidemiology of sepsis in patients with malignancy. *Chest*, 126, 1432–1440.
- de Souza, A., & Bonorino, C. (2012). The immune system : Endogenous anticancer mechanism. *Front Biosci (Elite Ed)*, 4, 2354–2364.

- Equils, O., Naiki, Y., Shapiro, A. M., Michelsen, K., Lu, D., Adams, J., & Jordan, S. (2005). activation in human endothelial cells. *Clinical and Experimental Immunology*, (II), 58–64. <https://doi.org/10.1111/j.1365-2249.2005.02961.x>
- Fleet, J. C. (2009). Molecular Actions of vitamin D contributing to cancer prevention. *NIH Public Access*, 29(6), 388–396. <https://doi.org/10.1016/j.mam.2008.07.003>.Molecular
- Gitto, E., Karbownik, M., Reiter, R. J., Tan, D. U. N. X., Cuzzocrea, S., Chiurazzi, P., ... Barberi, I. (2001). Effects of Melatonin Treatment in Septic Newborns, 50(6), 756–760.
- Goldstein, B., Giroir, B., & Randolph, A. (2005). International pediatric sepsis consensus conference: Definitions for sepsis and organ dysfunction in pediatrics*. *Pediatr Crit Care Med*, 6(1). <https://doi.org/10.1097/01.PCC.0000149131.72248.E6>
- Haan, K. De, Groeneveld, A. B. J., Geus, H. R. H. De, Egal, M., & Struijs, A. (2014). Vitamin D deficiency as a risk factor for infection , sepsis and mortality in the critically ill : systematic review and meta-analysis. *Critical Care*, 18(660), 1–8. <https://doi.org/10.1186/s13054-014-0660-4>
- Hewison, M. (2011). Antibacterial effects of vitamin D. *Nature Publishing Group*, 7(6), 337–345. <https://doi.org/10.1038/nrendo.2010.226>
- Hewison, M. (2012). An update on vitamin D and human immunity, 315–325. <https://doi.org/10.1111/j.1365-2265.2011.04261.x>
- Higgins, D. M., Wischmeyer, P. E., Queensland, K. M., Sillau, S. H., Sufit, A. J., & Heyland, D. K. (2014). Journal of Parenteral and Enteral Nutrition. *Journal of Parenteral and Enteral Nutrition*, 36(6), 713–720. <https://doi.org/10.1177/0148607112444449>
- Holick, M. F. (2008). Sunlight, vitamin D and skin cancer. *Advances in Experimental Medicine and Biology*, 1–14.
- Holick, M. F. (2012). Vitamin D : A D-Lightful Vitamin for Health Vitamin D : A D-Lightful Vitamin for Health. *Endocrinol Metab*, 27(4), 255–267. <https://doi.org/10.3803/EnM.2012.27.4.255>
- Holick, M. F., Binkley, N. C., Bischoff-ferrari, H. A., Gordon, C. M., Hanley, D. A., Heaney, R. P., ... Weaver, C. M. (2012). Deficiency and Insufficiency Revisited. *J. Clin Endocrinol Metab*, 97(4), 1153–1158. <https://doi.org/10.1210/jc.2011-2601>
- Hu, Y., Jahangiri, A., Delay, M., & Aghi, M. (2012). Tumor cell autophagy as an adaptive response mediating resistance to treatments such as antiangiogenic therapy. *Cancer Res*, 72, 4294–4299.
- Huerta, S., Irwin, R. W., Heber, D., Go, V. L. W., Koeffler, H. P., Uskokovic, M. R., & Harris, D. M. (2002). 1 α , 25- (OH) 2 -D 3 and Its Synthetic Analogue Decrease Tumor Load in the APC Mouse. *The Journal of Cancer Research*, 62(27), 741–746.
- Ikatan Dokter Anak Indonesia. (2016). Diagnosis dan Tata Laksana Sepsis pada Anak.

- In *Konsensus Diagnosis dan Tata Laksana Sepsis pada Anak*.
- Jeng, L., Yamshchikov, A. V., Judd, S. E., Blumberg, H. M., Martin, G. S., Ziegler, T. R., & Tangpricha, V. (2009). Alterations in vitamin D status and anti-microbial peptide levels in patients in the intensive care unit with sepsis. *Journal of Translational Medicine*, 7(28), 1–9. <https://doi.org/10.1186/1479-5876-7-28>
- Kementerian Kesehatan. (2015). Buletin Jendela Data dan Informasi Kesehatan. Retrieved February 23, 2019, from www.depkes.go.id
- Kementerian Kesehatan. (2018). HASIL UTAMA RISKESDAS 2018. Retrieved February 23, 2019, from <https://www.depkes.go.id>
- Kofoed, K., Andersen, O., Kronborg, G., Tvede, M., Petersen, J., Eugen-olsen, J., & Larsen, K. (2007). receptor , and soluble triggering ... Use of plasma C-reactive protein , procalcitonin , neutrophils , macrophage migration inhibitory factor , soluble urokinase-type plasminogen activator receptor , and soluble triggering receptor expressed on myeloid ce. *Critical Care*, 11(2), 1–11. <https://doi.org/10.1186/cc5723>
- Lanziotti, V. S., Povoas, P., Silva, J. R. L., Barbosa, A. P., & Salluh, J. I. F. (2016). Use of biomarkers in pediatric sepsis : literature review. *Rev Bras Ter Intensive*, 28(4), 472–482. <https://doi.org/10.5935/0103-507X.20160080>
- Misra, M., Pacaud, D., Petryk, A., Solberg, P. F., & Kappy, M. (2008). Vitamin D Deficiency in Children and Its Management : Review of Current Knowledge and Recommendations. *American Academy of Pediatrics*, 122(398). <https://doi.org/10.1542/peds.2007-1894>
- Mitchell, C., Hall, G., & Clarke, R. T. (2009). Acute leukaemia in children : diagnosis and management. *BMJ*, 338, 1491–1495. <https://doi.org/10.1136/bmj.b2285>
- Moromizato, T., Litonjua, A. A., Braun, A. B., Gibbons, F. K., Giovannucci, E., & Christopher, K. B. (2014). Levels and Sepsis in the Critically Ill. *Ccmjournal*, (1), 97–107. <https://doi.org/10.1097/CCM.0b013e31829eb7af>
- Nair, S. V., Armstrong, B., & Fenech, M. (2012). Does vitamin D protect against DNA damage. *Mutat Res*, 733, 50–57.
- Naz, A., Qureshi, R. N., Shamsi, T. S., & Mahboob, T. (2013). Vitamin D levels in patients of acute leukemia before and after remission-induction therapy. *Pak J Med Sci*, 29(1), 10–14.
- Norman, A. W. (2008). From vitamin D to hormone D: Fundamentals of the vitamin D endocrine system essential for good health. *American Journal of Clinical Nutrition*, 88(2). <https://doi.org/10.1093/ajcn/88.2.491S>
- Oosterom, N., Dirks, N. F., Heil, S. G., Jonge, R. De, Tissing, W. J. E., & Pieters, R. (2018). A decrease in vitamin D levels is associated with methotrexate-induced oral mucositis in children with acute lymphoblastic leukemia. *Supportive Care in Cancer*.
- Pascale, G. De, Vallecoccia, M. S., Schiattarella, A., Gravio, V. Di, Cutuli, S. L., Bello, G., Spanu, T. (2016). Clinical and microbiological outcome in septic patients with extremely low 25-hydroxyvitamin D levels at initiation of critical care. *Clinical Microbiology and Infection*, 22(5), 456.e7-456.e13.

- <https://doi.org/10.1016/j.cmi.2015.12.015>
- Pazirandeh, S., & Burns, D. (2019). overview of vitamin D. *Up to Date*, 1–15.
- Permono, B., & Ratwita, M. (2010). Luaran Pengobatan Fase Induksi Pasien Leukemia Limfoblastik Akut pada Anak di Rumah Sakit Umum Dr. Soetomo Surabaya. *Sari Pediatri*, 12(2), 128–134.
- Poll, T. Van Der, & Opal, S. M. (2008). Host – pathogen interactions in sepsis. *The Lancet Infectious Diseases*, 8, 32–42. [https://doi.org/10.1016/S1473-3099\(07\)70265-7](https://doi.org/10.1016/S1473-3099(07)70265-7)
- Pound, C. M., Johnston, D. L., Armstrong, R., Gaboury, I., & Menon, K. (2008). The Morbidity and Mortality of Pediatric Oncology Patients Presenting to the Intensive Care Unit With Septic Shock, (February), 584–588. <https://doi.org/10.1002/psc>
- Priehl, B., Treiber, G., Pieber, T. R., & Amrein, K. (2013). Vitamin D and Immune Function. *Nutrients*, 25, 2502–2521. <https://doi.org/10.3390/nu5072502>
- Randolph, A. G., & McCulloh, R. J. (2014). Important considerations for diagnosing and managing severe infections in infants , children , and adolescents Pediatric sepsis. *Virulence*, 5(1), 179–189.
- Ravelti, C. G., Moura, A. D., Teixeira, A. L., & Pedroso, E. R. P. (2014). Sepsis in cancer patients admitted in the ICU : epidemiology , pathophysiology , and biomarkers. *Rev Med Minas Gerais*, 24(3), 383–389. <https://doi.org/10.5935/2238-3182.20140108>
- Rosalino, V., Rojas, O. R., Moreno, A. I., Urrutia, E., Barreto, A. P., Lizeth, G., ... Georgina, S. (2019). Antibiotic-Resistant Septicemia in Pediatric Oncology Patients Associated with Post-Therapeutic Neutropenic Fever. *MDPI*.
- Sandjaja, S., Budiman, B., Harahap, H., Ernawati, F., Soekatri, M., Widodo, Y., ... Khouw, I. (2013). Food consumption and nutritional and biochemical status of 0 · 5 – 12-year-old Indonesian children : the SEANUTS study. *British Journal of Nutrition*, 110, S11–S20. <https://doi.org/10.1017/S0007114513002109>
- Schedlich, L., Muthukaruppan, A., O’Han, M., & Baxter, R. (2007). Insulin like growth factor binding protein-5 interacts with vitamin D receptor and modulates the vitamin D response in osteoblasts. *Mol Endocrinol*, 21, 2378–2390.
- Sheikhpour, E., Sadri, Z., Heydari, S., & Ghanizadeh, F. (2018). Vitamin D Deficiency and its Relation with Cancer in Children Vitamin D and its metabolites. *Iran J Ped Hematol Oncol*, 8(3), 180–186.
- Shilpakar, R., Paudel, B. D., Neupane, P., Shah, A., Acharya, B., & Dulal, S. (2019). Procalcitonin and C-Reactive Protein As Markers of Bacteremia in Patients With Febrile Neutropenia Who Receive Chemotherapy for Acute Leukemia : A Prospective Study From Nepal original report abstract. *Journal of Global Oncology*, 1–6. <https://doi.org/10.1200/JGO.19.00147>
- Skversky, A. L., Kumar, J., Abramowitz, M. K., Kaskel, F. J., & Melamed, M. L. (2011). Association of Glucocorticoid Use and Low 25-Hydroxyvitamin D Levels : Results from the National Health and Nutrition Examination Survey (NHANES): 2001 – 2006. *J Clin Endocrinol Metab*, 96(12), 3838–3845.

- <https://doi.org/10.1210/jc.2011-1600>
- Suaini, N. H. A., Zhang, Y., Vuillermin, P. J., Allen, K. J., & Harrison, L. C. (2015). Immune modulation by vitamin D and its relevance to food allergy. *Nutrients*, 7(8), 6088–6108. <https://doi.org/10.3390/nu7085271>
- Taylor, P., Kempker, J. A., Han, J. E., Tangpricha, V., Ziegler, T. R., & Martin, G. S. (2014). Vitamin D and Sepsis An emerging relationship. *Dermato-Endocrinology*, 42, 101–108. <https://doi.org/10.4161/derm.19859>
- Tjowanta, A. S., Yoel, C., & Lubis, M. (2017). Kadar 25-Hydroxyvitamin D Sebagai Penanda Sepsis pada Anak. *Sari Pediatri*, 19(3), 150–155.
- UKK. Hematologi-Onkologi IDAI. (2013). *Panduan Protokol Leukemia Limfoblastik Akut Indonesia 2018*.
- Van der Sluis, I., & Van den Huvel, E. M. (2008). Osteoporosis in children with cancer. *Pediatr Blood Cancer*, 50, 474–478.
- WHO. (2018). Cancer in children. Retrieved October 8, 2019, from <https://www.who.int/news-room/fact-sheets/detail/cancer-in-children>
- Wieland, A., Kerbl, R., Berghold, A., Schwinger, W., Mann, G., & Urban, C. (2003). C-Reactive Protein (CRP) as Tumor Marker in Pediatric and Adolescent Patients With Hodgkin Disease. *Med Pediatr Oncol*, 41(October 2003), 21–25. <https://doi.org/10.1002/mpo.10286>
- Youssef, D. A., Miller, C. W. T., El-abbassi, A. M., Della, C., Cutchins, C., Grant, W. B., & Peiris, A. N. (2011). Antimicrobial implications of vitamin D. *Dermato-Endocrinology*, 3(4), 220–229. <https://doi.org/10.4161/derm.3.4.15027>