Oncology
and Radiotherapy©
18(7) 2024: 001-004 • REVIEW ARTICLE

Vitamin D and lymphoid cancers: A review

Akaba kingsley[1], Marcus Inyama[1], Edakabasi Akaba[2], Theophilus Ugbem[2], Ofem Enang[3]

[1] Department of Hematology, University of Calabar, Nigeria
[2] Department of Histopathology, University of Calabar teaching Hospital, Nigeria
[3] Department of internal medicine, University of Calabar, Nigeria

ABSTRACT

Background: Lymphoid Cancers (LC), is a heterogeneous monoclonal group of disorder with accumulation of abnormal of lymphocytes in the blood, bone marrow and reticule-endothelia tissue. LC is the commonest hematological cancers and constitutes the 5th most common cancer. Vitamin D, is crucial with respect to outcome and prognosis. However, there is death and inconsistency of data on Vitamin D in LC.

Aim: The aim of this review is to determine the role and level of Vitamin D in Lymphoid cancers.

Method: A vigorous search was run via various academic search engine, such as Ebsco, Hinari, google scholar, Scopus etc.

Conclusion: The role of vitamin D in lymphoid malignancies has been underscore; this review will help to awaken health practioner with bias for lymphoid cancers on the importance of vitamin D with the insight into further research for development of therapeutic intervention.

Keywords: lymphoid, cancers, vitamin D

Address for correspondence:

Akaba kingsley,

Department of Haematology, University of calabar, cross river state, Nigeria

E-mail: akaba_kingsley@yahoo.com

Word count: 2395 **Tables:** 00 **Figures:** 02 **References:** 40

Received: 05 April, 2024, Manuscript No. OAR-24-133546
Editor Assigned: 10 May, 2024, Pre-QC No. OAR-24-133546(PQ)
Reviewed: 19 June, 2024, QC No. OAR-24-133546(Q)
Revised: 23 June, 2024, Manuscript No. OAR-24-133546(R)
Published: 29 June, 2024, Invoice No. J-133546

INTRODUCTION

Lymphoid Cancer (LC) is heterogeneous spectrum of monoclonal disorder with accumulation of abnormal of lymphocytes in the blood, bone marrow and reticuloendothelial This ranges from the B and T -cell, Hodgkin to Non-Hodgkin Lymphomas disorders, and its spectrum [1-3].

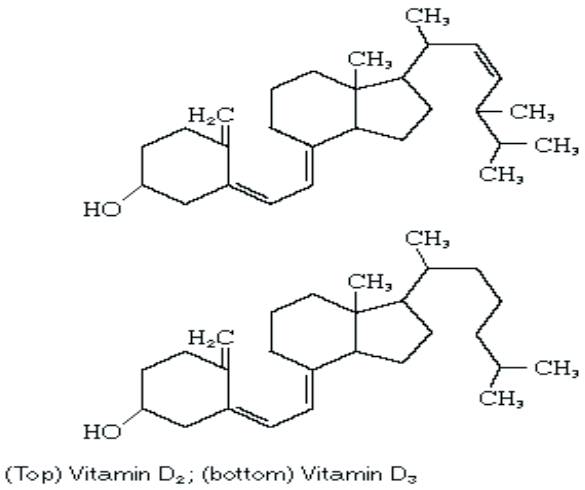
Epidemiologically lymphoid malignancies differ from one geographical region to another. Jaffe et al in iss tudy on understanding the new WHO classification reported, that the most common hematological malignancies were Non-Hodgins's Lymphoma (NHL) and it makes up 3% of cancer diagnoses and deaths [4]. Another study by Omoti et al reported a high prevalence of 61.1% of NHL in an oil rich region of Niger-delta [5]. Furthermore, another study, reported a prevalence of 76.81% of lymphoid malignancies at cross river state, south-south of Nigeria [6]. Similarly, salawu in ife southwest of Nigeria reported a high prevalence of 69% moreso another study by Mounia et al in morocco North Africa, reported predominantly NHL with a prevalence of 29.7% [7, 8]. Vitamin D is a fat-soluble vitamin and plays a majorly role in calcium homeostasis, and mineralization of the bone [8, 9]. It can be acquired through exposure to sunlight, ingestion of vitamin D rich diets and other supplement. Several studies have reported low level of vitamin D in high grade B- lymphoma and chronic lymphocytic leukemia, patients, treated with immunotherapy [10, 11]. Similarly, a nest case-controlled study conducted in Finland by Lim U et al, show no likely relationship between serum vitamin D and lymphoid malignancies, rather provides a potential protective risk of non-Hodgkin Lymphoma (NHL) [12]. However similar studies conducted by Kricker et al., reported no statistically significant change with the downtrend in risk with total sun exposure and Vander Rhee et al., respectively reported no changes in the level of vitamin D level among lymphoid malignancies [13, 14]. This shows that there is dearth and inconsistency of information on vitamin D in lymphoid cancer. Hence this study seeks to review the role and level of vitamin D in lymphoid cancer.

LITERATURE REVIEW

Vitamin D structure, source, function and metabolism

It regulates calcium metabolism; it is one of the fat-soluble vitamins. It is synthesized from the skin.

Vitamin D is derived from its precursor cholesterol. It exists in two forms: vitamin D_2, (Ergocalciferol) which is synthesize from plants, while the second form is vitamin D_3, and derive from animal tissues and also termed cholecalciferol. These inactive precursors are converted to active precursor in the liver which is termed calcidiol (25-hydroxyvitamin D) (Figure 1). Calcitriol, transported to the renal tubules, where it is converted to the active and potent calcitriol, via vitamin D binding proteins in the blood [15].



(Top) Vitamin D_2; (bottom) Vitamin D_3

Fig. 1. Calcitriol x (1,25 dihydroxyvitamin D)

Vitamin D is essential in so many physiological activities in the body such as immune modulation, calcium regulation and cell differentiation [16, 17]. Calcitriol gets activated through the attachment to the vitamin D receptor, a receptor located in nuclear and it is found in most organs [18]. During activation, the vitamin D receptor heterodimerize with retinoid x receptor, there by stimulating the target genes to regulate their transcription, increasing the concern of the potential biological impact of vitamin D in cancer prevention and treatment [19-22].

Vitamin D is synthesis mainly from the skin with dietary contributing less because foods rich in vitamin D are not routine dietary pattern. Hence supplementation of vitamin D to persons with its deficiency because of inadequate sun exposure is important (Figure 2).

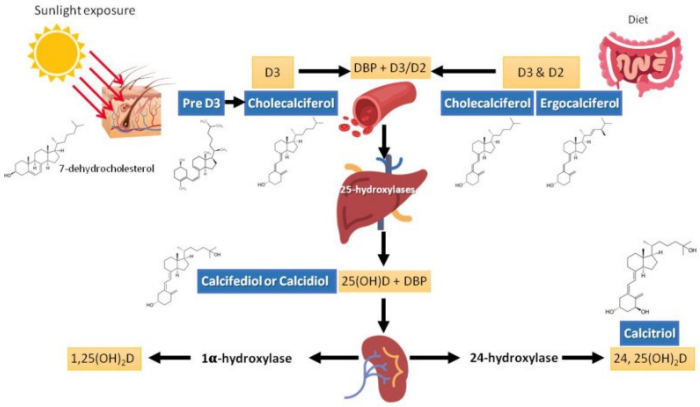


Fig. 2. Calcidiol (25-hydroxyvitamin)

Vitamin D and lymphoid cancer

Vitamin D, regulate several cancers associated cellular processes, which include differentiation, proliferation, angiogenesis, apoptosis and spread of cancer cells [23, 24]. Calcitriol impaired the growth of cancer cells by activating cell cycle arrest through the stimulation of cyclin-dependent kinase inhibitors, such as p21 and p27, and the downregulation of cyclins, thereby impairing the progression of the cell cycle [25, 26]. Furthermore, vitamin D causes continuous and uncontrolled differentiation of cancer cell [27, 28]. Moreso in many cancer cell lines, calcitriol has shown to increase the expression of markers of differentiation and activate morphological changes. Also, its merit in the treatment of acute myeloid leukaemia with analogues of vitamin D [21, 29].

Programmed cell death, also called apoptosis is a mechanism in the body for removal of abnormal cells, such as cancer cells. Calcitriol turn-on apoptosis via the appearance of antiapoptotic and proapoptotic proteins, such as B-Cell Leukaemia/Lymphoma 2 protein (BCL-2) family members and caspases [30, 31]. Thus, apoptosis generated by vitamin D may contribute to its antitumor activity and hamper angiogenesis in developing tumours by obstructing the production of proangiogenic molecules, such as matrix metalloproteinase and vascular endothelial growth factors [32]. Calcitriol has anti-inflammatory effects, which is significance for cancer prevention by hampering the production of chemokines and proinflammatory cytokines, which may accord to its anticancer properties [32]. Another study also reported a lower level in follicular lymphoma and it is associated with inferior survivor [33]. Furthermore, another study by Nath K et al, also reported that vitamin D insufficiency is associated with an inferior outcome with chimeric antigen receptor in diffuse Large B-cell lymphoma [34]. Moreso, Bitten bring et al also reported reduce of vitamin D level in patients among Diffuse Large B Cell Lym-

phoma (DLBCL) and reduce rituximab activity mediated [35]. Drake et al., also reported that in insufficient level of Vitamin D is associated with inferior event free survival and T cell Lymphoma [36]. Furthermore, another study conducted by Vasko and Veselin also reported a low of serum vitamin D level in Non–Hodgkin lymphomas and multiple myeloma [37]. However, Tracy et al, reported a clinical failure and adverse outcome with vitamin D insufficiency among those treated with therapies other than im-munochemotherapy [38]. Furthermore, similar studies with slight variation by Vasko and Veselin, show that there was reduce level of vitamin D in Non-Hodgkin Lymphoma except Burkitt Lym-phoma [37]. Renne et al also reported an upward regulation of vi-tamin D receptor in Hodgkin's Lymphoma but reduce in B-NHL subtype [39]. Another study by Luczynska showed association between increase Vitamin D level and lower risk of Chronic Lymphocytic Leukaemia (CLL) however does not adduce to it protec-tive role in lymphoid cancers [40].

CONCLUSION

The role of Vitamin D, in lymphoid cancer has been underscore with so paucity and inconsistency of information, this calls for further research to bridge the gaps of the so many unanswered questions on its role in lymphoid cancers. Authors declared that there is no conflict of interest.

ETHICAL ISSUE

Not applicable.

REFERENCES

1. Chen C, Gu YD, Geskin LJ. A Review of Primary Cutaneous CD30+ Lymphoproliferative Disorders. Hematol Oncol Clin North Am. 2019;33:121-134.
2. Sawada A, Inoue M. Hematopoietic Stem Cell Transplantation for the Treatment of Epstein-Barr Virus-Associated T- or NK-Cell Lymphoproliferative Diseases and Associated Disorders. Front Pediatr. 2018;6:334.
3. Litz CE, Brunning RD. Chronic lymphoproliferative disorders: classification and diagnosis. Baillieres Clin Haematol. 1993;6:767-83.
4. Jaffe ES, Barr PM, Smith SM. Understanding the New WHO Classification of Lymphoid Malignancies: Why It's Important and How It Will Affect Practice. Am Soc Clin Oncol Educ Book. 2017;37:535-546.
5. Omoti CE, Nwannadi AI, Obieche JC, Olu-Eddo AN. The epidemiological features of lymphoid malignancies in Benin City, Nigeria: a 15 years study. Pan Afr Med J. 2012;11:10.
6. Kingsley A, Benedict N, Idongesit A, Bassey BO, Effiong OE, et al. Epidemiological Pattern of Adult Haematological Malignancies in a Tertiary Hospital in Cross River State. Int Res J Oncol. 2019;2:1-9.
7. Salawu L, Bolarinwa RA, Durosinmi MA. Chronic lymphocytic leukaemia: A-twenty years experience and problems in Ile-Ife, South-Western Nigeria. Afr Health Sci. 2010;10:187-192.
8. Mounia EE, Manal EE, Redouane B, Meryem O, Mohammed B. Distribution and features of haematological malignancies in Eastern Morocco: A retrospective multicenter study over 5 years. BMC Cancer. 2016;16:159-169.
9. Postlethwaite AE, Tuckey RC, Kim TK, Li W, Bhattacharya SK, et al. 20S-Hydroxyvitamin D3, a Secosteroid Produced in Humans, Is Anti-Inflammatory and Inhibits Murine Autoimmune Arthritis. Front Immunol. 2021, 12, 678487.
10. Cesari M, Incalzi RA, Zamboni V, Pahor M. Vitamin D hormone: A multitude of actions potentially influencing the physical function decline in older persons. Geriatr Gerontol Int. 2011, 11, 133–142.
11. Hohaus S, Tisi MC, Bellesi S, Vitamin D deficiency and supplementation in patients with aggressive B-cell lymphomas treated with immunochemotherapy. Cancer Med 2018; 7: 270–281.
12. Lim U, et al. A prospective investigation of serum 25-hydroxyvitamin D and risk of lymphoid cancers. Int J Cancer. 2009;124:979–86.
13. Molica S, Digiesi G, Antenucci A, Vitamin D insufficiency predicts time to first treatment (TFT) in early chronic lymphocytic leukemia (CLL). Leuk Res 2012; 36: 443–447.
14. Kricker A, Armstrong BK, Hughes AM, Personal sun exposure and risk of non Hodgkin lymphoma: a pooled analysis from the InterLymph Consortium. Int J Cancer 2008; 122: 144–154.
15. Jarrett RF. Risk factors for Hodgkin's lymphoma by EBV status and significance of detection of EBV genomes in serum of patients with EBV-associated Hodgkin's lymphoma. Leuk Lymphoma. 2003;44: 27-32.
16. Vanderschueren D, Pye SR, O'Neill TW, Lee DM, Jans I, et al. Active vitamin D (1,25-dihydroxy vitamin D) and bone health in middle-aged and elderly men: The European Male Aging Study (EMAS). J Clin Endocrinol Metab. 2013, 98, 995–1005.
17. Pike JW, Meyer MB. The vitamin D receptor: New paradigms for the regulation of gene expression by 1,25-dihydroxyvitamin D(3). Endocrinol Metab Clin N Am. 2010, 39, 255–269.
18. Krishnan AV, Trump DL, Johnson CS, Feldman D. The role of vitamin D in cancer prevention and treatment. Endocrinol. Metab Clin N Am. 2010, 39, 401–418.
19. Holick MF. Vitamin D: Its role in cancer prevention and treatment. Prog Biophys Mol Biol. 2006, 92, 9–59.
20. Fleet JC, DeSmet M, Johnson R, Li Y. Vitamin D and cancer: A review of molecular mechanisms. Biochem J. 2012, 441, 61–76.
21. Malloy PJ, Feldman D. Inactivation of the human vitamin D receptor by caspase-3. Endocrinology 2009, 150, 679–686.
22. Moukayed M, Grant WB. Molecular link between vitamin D and cancer prevention. Nutrients 2013, 5, 3993–4021.
23. Bhoora S, Punchoo R. Policing Cancer: Vitamin D Arrests the Cell Cycle. Int J Mol Sci. 2020, 21, 9296.
24. Díaz L, Díaz-Muñoz M, García-Gaytán AC, Méndez I. Mechanistic Effects of Calcitriol in Cancer Biology. Nutrients 2015, 7, 5020–5050.
25. Asunción FB. Vitamin D Effects on Cell Differentiation and Stemness in Cancer. Cancers 2020, 12, 2413.
26. Jeon SM, Shin EA. Exploring vitamin D metabolism and function in cancer. Exp Mol Med. 2015, 50, 1–14.
27. Hughes PJ. Marcinkowska E, Gocek E, Studzinski, GP, et al. Vitamin D3-driven signals for myeloid cell differentiation—Implications for differentiation therapy. Leuk Res. 2013, 34, 553–565.
28. Marcinkowska E. Vitamin D Derivatives in Acute Myeloid Leukemia: The Matter of Selecting the Right Targets. Nutrients 2022, 14, 2851.
29. El-Sharkawy A, Malki A. Vitamin D Signaling in Inflammation and Cancer: Molecular Mechanisms and Therapeutic Implications. Molecules 2020, 25, 3219.
30. Irani M, Seifer DB, Grazi RV, Irani S, Rosenwaks Z, et al. Vitamin D Decreases Serum VEGF Correlating with Clinical Improvement in Vitamin D-Deficient Women with PCOS: A Randomized Placebo-Controlled Trial. Nutrients 2017, 9, 334.
31. Roffe-Vazquez DN, Huerta-Delgado AS, Castillo EC, Villarreal-Calderón JR. et al. Correlation of Vitamin D with Inflammatory Cytokines, Atherosclerotic Parameters, and Lifestyle Factors in the Setting of Heart Failure: A 12-Month Follow-Up Study. Int J Mol Sci. 2019, 20, 5811.
32. Rizzoli R. Vitamin D supplementation: upper limit for safety revisited? Aging Clin Exp Res. 2021;33:19-24.
33. Kelly JL, Salles G, Goldman B, Fisher RI., Brice P, et al. Low serum vitamin D levels are associated with inferior survival in follicular lymphoma: A prospective evaluation in SWOG and LYSA Studies. J Clin Oncol. 2015, 33, 1482–1490.
34. Nath, K. Vitamin D Insufficiency and Clinical Outcomes with Chimeric Antigen Receptor T-Cell Therapy in Large B-cell Lymphoma. Transpl Cell Ther. 2022, 28, 7511–7517.
35. Bittenbring JT, Neumann F, Altmann B, Achenbach M, Reichrath J, et al. Vitamin D deficiency impairs rituximab-mediated cellular cytotoxicity and outcome of patients with diffuse large B-cell lymphoma treated with but not without rituximab. J Clin Oncol. 2014, 32, 3242–3248.
36. Drake MT, Maurer MJ, Link, Bk. Vitamin D insufficiency and prognosis in non-Hodgkin's lymphoma. J Clin Oncol. 2010, 28, 4191–4198.
37. Graklanov V, Popov V. Vitamin D levels in patients with non-Hodgkin lymphoma/diffuse large B-cell lymphoma, chronic lymphocytic leukemia and multiple myeloma. J Int Med Res. 2020;48.
38. Tracy SI, Maurer MJ, Witzig TE. Vitamin D insufficiency is associated with an increased risk of early clinical failure in follicular lymphoma. Blood Cancer J. 2017, 7, 595.
39. Renne C. Benz AH. Hansmann, M.L. Vitamin D3 receptor is highly expressed in Hodgkin's lymphoma. BMC Cancer, 2012:12,1-7.
40. Luczynska A, Kaaks R, Rohrmann S, Becker S, Linseisen J, et al. Plasma 25-hydroxyvitamin D concentration and lymphoma risk: results of the European Prospective Investigation into Cancer and Nutrition. Am J Clin Nutr. 2013; 98:827-838.