International Journal of Science and Research (IJSR)
ISSN: 2319-7064
SJIF (2022): 7.942

Assessment of Serum Vitamin D in Patients with Hypothyroidism in a Nigerian Tertiary Hospital

Dalili; M. S[1], Hadiru G. M[2], Dungus M. M[3], Aisha S. K[4], Amali A. O[5], Hassan A. A[6], Gademi F. M[7], Fatima M. L[8], Halima M. A[9], Musa A. H[10], Mshelia D. S[11]

[1]Department of Chemical Pathology, Federal University of Health Sciences, Azare, Bauchi State.

[2]Department of Chemical Pathology University of Maiduguri Teaching Hospital, Maiduguri, Borno State.

[3]Department of Chemical Pathology University of Maiduguri Teaching Hospital, Maiduguri, Borno State.
Corresponding Author Email: *musadungus[at]yahoo.com*

[4]Department of Chemical Pathology University of Maiduguri Teaching Hospital, Maiduguri, Borno State.

[5]Department of Internal Medicine, University of Maiduguri Teaching Hospital, Maiduguri, Borno State

[6]Department of Internal Medicine, University of Maiduguri Teaching Hospital, Maiduguri, Borno State

[7]Department of Chemical Pathology, University of Maiduguri Teaching Hospital, Maiduguri, Borno State.

[8]Department of Chemical Pathology, University of Maiduguri Teaching Hospital, Maiduguri, Borno State.

[9]Department of Chemical Pathology, University of Maiduguri Teaching Hospital, Maiduguri, Borno State.

[10]Department of Medical Laboratory Sciences, Faculty of Allied Health Sciences, University of Maiduguri, Borno State.

[11]Department of Chemical Pathology, Faculty of Basic Clinical Sciences, University of Maiduguri, Borno State, Nigeria.

Abstract: ***Introduction: Hypothyroidism is said to be associated with Vitamin D deficiency which is not routinely assessed in hypothyroid patients. The serum level of 1, 25 - dihydroxycholecalciferol and its link to hypothyroidism was assessed. Material and Methods: A total of 70 males and 90 females aged 20 - 60 years were assessed for the study. Evaluation of serum 1, 25 - dihydroxycholecalciferol was done on ELISA monobind Inc. CA 92630, immuno - assay analyzer. Serum fT_3, fT_4 and TSH were also evaluated by enzyme linked immunosorbent assay (ELISA) technique using stat - fax - 2100. Result: In our study, we have found the values of fT_3 in the subjects as 1.21+ 0.89pg/ml lower than controls values of 1.92+0.66pg/ml, values of fT_4 in subjects as 0.60+0.53ng/dl as compared to control group value of 1.40+0.30ng/dl, values of TSH as 2.07+1.19miU/L higher than the control group of 0.48+1.67 miU/L. The mean values of 1, 25 - dihydroxycholecalciferol for subjects as 25.80+4.20 nml/L lower than the control group with 35.70+6.30. Conclusion: Our study findings suggest that patients with hypothyroidism also have low serum levels of 1, 25 - dihydroxycholecalciferol (Vitamin D) which can have implications related to numerous organ systems, such as the Bones, Kidneys, Cardiovascular, and Immunological systems.***

Keywords: fT_3, fT_4, TSH, 1, 25 - dihydroxycholecalciferol (Vitamin D), Hypothyroidism and Vitamin D deficiency

1. Introduction

Hypothyroidism defined as plasma levels of thyroid stimulating hormone (TSH) of > 5.0miU/L, free tri - iodothyronine (fT_3) of <1.4pg/ml and tetra - iodothyronine (fT_4) of <0.8ng/dl is common thyroid disease associated with decrease activity of the thyroid gland. The predominant features include: Cold intolerance, Weight gain, dry skin, hair loss, menstrual abnormalities, fatigue and constipation. Leg swelling, myoxoedema, pallor and brittle nails are other features associated with hypothyroidism [1].

It is a common endocrine disorder worldwide with a prevalence rate of 2.4% in Nigeria, 0.3% - 3.7% in United States and between 0.2% and 5.3% in Europe [2, 3, 4].

Various epidemiological studies indicate that women are more predisposed to hypothyroidism than men [5]. Deficiency of iodine is said to be the commonest cause of hypothyroidism worldwide, the iodine sufficient population on the other hand, suffer from hypothyroidism as a result of autoimmune thyroiditis as in Hashimoto thyroiditis, cancer and thyroidectomies [6]. Normal free tetra - iodothyronine (fT_4) and elevated serum thyroid stimulating hormone (TSH) has been recognized as subclinical hypothyroidism in an intact hypothalamic - pituitary - thyroid axis [6].

The interest in the study of thyroid disorder has risen in recent times due to their role in masking cardiovascular diseases causing increase mortality in many low-income countries. The reported relative survivals after five years of diagnosis was 12.5% in contrast to what is obtained in the United States where the cure rate is high [7].

Treatment of hypothyroidism includes the use of oral administration of Levothyroxine (L4) that is well tolerated with minimal side effects and less expensive [8].

Vitamin D is a fat - soluble secosteroid that exist in different forms (D1 - D5). The most important type of Vitamin D in humans is cholecalciferol (D3) and ergocalciferol (D2) found

in plants. Most Vitamin D is synthesized in the skin after exposure to ultraviolet light (D3), while dietary sources provide only about 5 - 10% [9].

Exposure of skin to sunlight causes the transformation of 7 - dehydrocholesterol in to Vitamin D3 which is then transformed in the liver by the action of the enzyme hepatic 25 - hydroxylase in to 25 - hydroxyvitamin D (Calcidiol). The active form of Vitamin D (1, 25 - dihydroxycholecalciferol) also called Calcitriol is produced in the kidney by the action of an enzyme 1α - hydroxylase encoded by the CYP27B1 gene [10]. The main role of calcitriol is the regulation of calcium and phosphate concentrations in plasma. It increases intestinal and renal absorption of calcium and phosphate. It is also important in bone mineralization [11]. Other functions of calcitriol include regulation of cell growth, immune, neuromuscular and immunosuppressive effects [12].

Calcitriol binds to Vitamin D receptor (VDR) which belongs to the nuclear receptor superfamily. This is followed by binding to the retinoid X receptor (RxR) which translocate in to the nucleus and binds to Vitamin D response elements within DNA [13].

Hypothyroidism is said to be associated with Vitamin D deficiency as seen in a study conducted by Mackawy et al. which revealed that hypothyroid patients had hypovitaminosis D with hypocalcemia that was thought to be associated with the degree and severity of hypothyroidism [14]. There is also evidence of Vitamin D effects on cardiometabolic disease through modulation of endothelial and smooth muscle cell activity, renin - angiotensin - aldosterone system, nitric oxide, oxidative stress. An inflammatory response and associated Vitamin D deficiency, autoimmune thyroid diseases, and relationship between Vitamin D concentration in serum and titres of antibodies and thyroid autoimmunity replacement [15].

Experimental data indicates a direct effect of Vitamin D on Type 2 deiodinase expression causing sub sequential peripheral conversion of T_4 into T_3. However, the functional links among thyroid hormones, Vitamin D and the cardiovascular system, and clinical effects of coexisting abnormalities have limited attention by researchers.

Studies find that people with Hashimoto's and non - autoimmune hypothyroidism have low serum level of Vitamin D and calcium and taking Vitamin D supplement may improve serum TSH levels and decrease the severity of thyroid dysfunction [14]. The possible explanation why patients with hypothyroidism have low Vitamin D include inadequate intestinal absorption of Vitamin D from diet, decrease activation of Vitamin D due to decrease exposure of hypothyroid patients to sun light, or as a result of decrease basal metabolic rate leading to inactivity [14].

Vitamin D has anti - inflammatory, anti - oxidant, anti - fibrotic properties and modulation of immune system. However, the underlying mechanisms by which Vitamin D impacts autoimmune disease remain unclear [15].

Vitamin D supplementation to patients with both overt and subclinical hypothyroidism could go a long way in reducing symptoms and possible complications associated with hypothyroidism.

2. Materials and Methods

2.1 Patients

A total of 160 individuals consisting of 70 males and 90 females patients age 20 – 60 years comprising 80 hypothyroids as cases and 80 euthyroids as controls were consecutively recruited at the metabolic clinic of the University of Maiduguri Teaching Hospital. Euthyroidism was defined as fT_3 of 1.4 – 4.2pg/mol, fT_4 of 0.8 – 2.0ng/dl and TSH of 0.28 – 0.53 miU/ml [16]. Patients are hypothyroids if their serum levels of fT_3 is <1.4pg/ml, fT4 of <0.8ng/dl and TSH of >0.53miU/ml (>5miU/L). Patients were excluded if they are hypertensive, diabetic or pregnant. Liver, Kidney and heart diseases, previous history of thyroid disease as well as patients on medications that affect thyroid hormone levels were also excluded.

Informed consent was obtained from all participants and the study was approved by the ethical committee of the University of Maiduguri Teaching Hospital.

2.2 Measurements

Measurements of weight, height, body mass index (BMI) and blood pressure were done. Weight was estimated using a weighing scale (OHAUS pioneer PA413) with subjects putting on thin cloths and without shoes.

The height was measured by stadiometer and BMI was extrapolated by calculation using weight (kg) divided by height (m2). The blood pressure was measured twice in the sitting position on the left arm using an accuson's sphygmomanometer.

About 5ml of venous whole blood specimens were collected from the antecubital vein in a plain vacutainer bottle after an overnight fast observing the aseptic procedures for measurement of fT_3, fT_4, TSH and Vitamin D. Serum was separated from cells using Pasteur pipette and spun at 3, 000 rpm for 10 minutes using swinging bucket centrifuge and stored - frozen at - 200c until time of analysis.

fT_3, fT_4 and TSH levels were analyzed by enzyme linked immunosorbent assay (ELISA) kit Perkins Elmer. The serum Vitamin D was evaluated quantitatively using ELISA monobind Inc. CA 92630. USA product code: 9425 – 300 (measurement range is > 50nmol/L) [16]. Patients are considered to be vitamin D deficient if their serum level is <30nmol/L.

3. Statistics Analysis

Analysis of statistical data was carried out using SPSS version 16. Evaluation of variance software package was used in determination of significance between the mean of the two groups. Results were presented as means + standard deviation (SD). Differences in between were measured by independent sample test for the two groups. *p* - values of <0.05 were considered as statistically significant.

4. Result

The mean age distribution for both cases and control was found to be 40.10 + 4.3 years, 42.3 + 4.8 years with predictive value of 0.17 are not statistically significant. On the other hand the body mass index (BMI) of cases and controls was found to be 24.1+ 4.5 kg/m2, 21.3 + 2.4 kg/m2 were also not statistically significant (*p* - 0.09). The mean values of systolic blood pressure of both groups were 125.30 + 1.42 mmHg, 121.25 + 2.10 mmHg and their diastolic blood pressure counterparts were 78.4 + 2.13 mmHg, 73.58 + 1.40 mmHg with predictive values of 0.07 and 0.05 respectively were also not statistically significant (Table 1).

Table 1: Mean Values of Age, BMI and Blood Pressure

S/No	Parameters	Cases	Control	*p* - Values
1	Age (Years)	40.10 ± 4.3	42.3 ± 4.8	0.17
2	BMI (kg/m2) (Body Mass Index)	24.1 ± 4.5	21.3 ± 2.4	0.09
3	Systolic Blood Pressure	125.30 ± 1.42	121.25 ± 2.10	0.07
4	Diastolic Blood Pressure	78.40 ± 2.13	73.58 ± 1.40	0.05

$p<0.05$ is considered Significant

The mean values of free T_3 (fT_3) in both cases and controls were found to be 1.21 +0.89 pg/ml and 1.92 + 0.66 pg/ml with the predictive value of 0.001 were statistically significant.

The mean values of free T_4 (fT_4) for the cases and controls were 0.60 + 0.53ng/dl, 1.40 + 0.30 ng/dl respectively were statistically significant (p=0.001). the thyroid stimulating hormone (TSH) mean values for both cases and controls were found to be 2.07 + 1.19 miU/L and 0.48 + 1.67 miU/L were also statistically significant (p=0.003). The mean values of calcitriol for cases and control respectively were 25.80 + 4.20nmol/L, 35.70 + 6.30nmol/L were statistically significant (p=0.004)

Table II.

Table II: Mean values of thyroid hormones and Vitamin D

S/No	Parameters	Cases	Control	*p* - Values
1	fT_3 (pg/ml) (Triiodothyronine)	1.21 ± 0.89	1.92 ± 0.66	0.001
2	fT_4 (ng/dl) (Tetraiodothyronine)	0.6 ± 0.53	140 ± 0.30	0.001
3	TSH (Thyroid Stimulating Hormone) (miU/L)	2.07 ± 1.19	0.48 ± 1.67	0.003
4	Vitamin D (nmol/L) (Calcitriol)	25.80 ± 4.20	35.70 ± 6.30	0.0004

$p<0.05$ is considered significant

5. Discussion

Hypovitaminosis D has been observed in the Pathogenesis of autoimmune thyroiditis (Hashimoto thyroiditis) and Grave's disease. Findings by Berg et al that the homology between Vitamin D receptor (VDR) and the thyroid hormone receptor as evidenced by VDR expression on thyroid follicular cells suggests a possible role of Vitamin D in thyroid Pathophysiology [17]. This study appears to be in agreement with our study which reveals low Vitamin D serum levels (25.80 +4.20 nmol/L) in patients with hypothyroidism compared to the control group with serum vitamin D levels of 35.70 + 6.30nmol/L.

Tamer et al reported that 1, 25 (OH) 2D3 deficiency (<30nmol/L) was more prevalent in patients with overt hypothyroidism than in subclinical hypothyroids and Euthyroids [18].

A retrospective study by Ucar et al. demonstrated that serum Vitamin D levels in elderly patients with subclinical hypothyroidism were lower than in healthy controls [19].

Aljohni et al in a cross sectional case control study, found an inverse association between Vitamin D status and fT3 [20].

A pilot study that looked at Vitamin D status in the summer months among patients on Levothyroxine treatment showed that Vitamin D sufficiency was not achieved even in the summer [21].

Mirhosseini et al. documented that serum Vitamin D values of more than 125nmol/L were associated with 30% decrease risk of hypothyroidism and a 32% reduced risk of elevated anti - thyroid antibodies [22]. Pezeshki et al. conducted a pilot randomized clinical trial in 2020 to investigate the efficacy of Vitamin D therapy on subclinical hypothyroidism. They discovered that, using Vitamin D supplements significantly reduced TSH mean levels emphasizing the need for screening and Vitamin D Treatment in subclinical hypothyroid individuals [23].

6. Conclusion/ Recommendation

In view of this study, patients with Overt hypothyroidism have been observed to also have Vitamin D deficiency that is known to complicate the thyroid disorder and its complications particularly on the cardiovascular system having in mind the obscure nature of the link between hypothyroidism and hypovitaminosis D and the need for more studies. Screening of Vitamin D and possible supplementation for all hypothyroid patients is recommended to avert the attendant consequences of both conditions.

References

[1] Afonja O. A. (2011). Hypothyroidism. In Chemical Pathology and metabolic medicine Teachers 1sted, pp289. ISBN: 978 – 2283 – 05 – 3.
[2] E. N. Okafor, M. C. ugonabo, E. E. Chukwulalu et al. Prevalence and Pattern of thyroid disorders Among

Patients attending University of Nigeria Teaching Hospital, Enugu, Nigeria. Niger Med J.2019.60 (2): 62 – 67.

[3] Aoki V. Belin RU, Clickner R, Phillips L, Mahaffey KR: Serum TSH and total T4 in the United States population and their association with participant characteristics: National Health and Nutrition Examination Survey (NHANES 1999 - 2002). Thyroid 2007, 17: 1211 – 2023.10.1089/thy.2006.0235.

[4] Garendia M. A., Santos P. S. Guillen – Grima F., Galfre J. C.: The Incidence and prevalence of thyroid dysfunction in Europe: a meta – analysis. J ClinEndocrinolMetab.2014, 99: 923 – 31.10.1210/jc.2013 – 2409.

[5] Vanderpump M. P: The Epidemiology of thyroid disease Br Med Bull.2011, 99: 39 - 51.10.1093/bmb/Idr030.

[6] Almandoz JP, Gharib H: Hypothyroidism: etiology, diagnosis, and management. Med Clin North Am.2012, 96: 203 - 21.10.1016/j. mcna.2012.01.005.

[7] Gandos A, Brenner H, Wabinga H, Parkin DM. Cancer survival in Kampala, Uganda. Br J cancer 2005; 92: 1808 - 12.

[8] Jonklaas J, Bianco AC, Baner AJ, et al: Guidelines for the treatment of hypothyroidism: Prepared by the American thyroid Association task force on thyroid hormone replacement. Thyroid.2014, 24: 1670 – 751.10.1089/thy.2014.0028.

[9] Grundmann M., von versen - Hoynck, F. Vitamin D - roles in women's reproductive health. Reprod. Biol. Endocrinol.2011, 9, 146.

[10] Bikle, D. D. Vitamin D metabolism, mechanism of action and clinical applications. Chem. Biol.2014, 21, 319 – 329.

[11] Van Driel, M,; Van Leeuwen, J. P. T. M. Vitamin D endocrinology of bone ineralization. Mol. Cell Endocrinol.2017, 453, 46 – 51.

[12] Arnson, Y.; Amtal, H,; Shoenfeld, Y. Vitamin D and autoimmunity: New aetiological and therapeutic considerations. Ann. Rheum. Dis.2007, 66, 1137 – 1142.

[13] Pike, J. W.; Meyer, M. B.; Bishop, K. A. Regulation of target gene expression by the Vitamin D receptor – An update on mechanisms. Rev. Endocr. Disord.2012, 13, 45 – 55.

[14] Mackawy AM, Al - Ayed BM, Al - Rashidi BM: Vitamin D deficiency and its association with thyroid disease. Int J Health Sci.2013, 7: 267 - 75.10.12816/0006454.

[15] C. Vasalle, A. Partanti, A. Pingitore, S. Berti, G. Lervasi L. Sabatino. Vascular Physiology, vol 12 – 2021.10.3389.2021.722912.

[16] Wada, H. G., Danisch, R. J., Baxter, S. R., Fedrici, M. M., Fracer, R. C., Brownmiller, L. J., & Lankford, J. C., (1982). Enzyme immunoassay of the glycoprotein trophic hormones - choriogonadotropin, lutropin, thyrotropin - with solid phase monoclonal antibody specific for the beta - subunit. Clinical chemistry, 28 (9), 1862 – 1866.

[17] Berg J. P., Liane K. M., Bjorhorde, S. B., Bjoro T., Torjesen, P. A., Hang, E. Vitamin D receptor binding and biological effects of cholecalciferol analogues in rat thyroid cells. J. Steroid Biochem. Mol. Biol.50, 145 – 150. Doi 10: 1016/0960 (94) 90021 – 3.

[18] Tamer G, Arik S, Tamer I, Coksert D: Relative Vitamin D insufficiency in Hashimoto's thyroiditis. Thyroid.2011, 21: 891 - 6.

[19] Ucar F, Akyol S, Ozturk G, et al: Evaluation of serum Vitamin D levels in elderly patients with subclinical hypothyroidism. J Experclin med.2014, 31: 77 – 80.

[20] Aljohni N. J. Al - Daghri NM, Al - Atlas OS, et al. Differences and associations of metabolic and vitamin D status among patients with and without suclinical hypothyroid dysfunction. BMC EndocrDisord 2013, 13: 31.

[21] Kmiec P, Minkiewic2 I, Rola R, Sworczak K, Zmijewski MA, Kowlski K: Vitamin D status including 3 – epi - 25 (OH) D3 among adult patients with thyroid disroders during summer months. Endokrynol pol.2018, 69: 653 - 60.

[22] Mirhosseini N, Brunel L, Muscogiuri G, Kimbal S, Physiological Serum 25 - hydroxyvitamin D concentrations are associated with improved thyroid function cobservations from a community - based program. Endocrine 2017, 58: 563 – 73.

[23] Pezeshki B, Ahmadi A, Karimi A: The effect of Vitamin D replacement on patient with subclinical hypothyroidism: A pilot randomized clinical trial Galen Med J.2020, 9: e1592.