Vitamin D Deficiency and its Impact on Thyroid Disorder - A Computational Analysis

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Abstract

The requisite level of Vitamin D presence in a human body is important for maintaining the proper immunity system and associated health benefits in an individual. Sufficient level of Vitamin D in humans plays multiple body growth related aspects such as ensuring the one's teeth and bones to stay stronger, helps for the support of good immune system, also takes care of the brain and nervous system, balances the hormone levels and so on. It has been reported in the literature that lower levels of Serum Vitamin D are closely associated with Thyroid and its associated diseases. In some other published reports, their association is not clearly spelt. In the light of this, the present study is aimed at investigating the impact/consequence in the TSH levels due to the effect of Serum Vitamin D levels. For this purpose, some statistical analyses are carried out and the results are discussed.

Keywords Serum Vitamin D, Thyroid Simulating Hormone (TSH), Statistical Analyses

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INTRODUCTION

Bioinformatics has emerged as one of the popular and effective scientific disciplines giving solutions to the unsolved problems in life sciences. The bioinformatics tools effectively handle tasks such as biological information acquisition, data processing, data storage, data allocation, data scrutiny and elucidation of unique data features. The tools are created using the confluence of mathematics, biology and computer science with the objective of understanding the biological significance of the analyzed data. For the purpose of studying and understanding very large biological databases and to understand the disease origins by analyzing their genomics and proteomics bioinformatics use computational techniques and tools by relating all of them with healthcare data [1]. This has become a very useful aspect in medicine, drug discovery and in another related research. The process of gathering large healthcare data electronically helps in easy and effective data analytics in the healthcare system. The proficiency of data analytics is reflected in the progress of healthcare system, diminution of cost and

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thus improves the life safety of individuals [2].

One of the major health related concerns among the majority of the present human population all over the globe is the deficiency of Vitamin D in their bodies. Changing life styles and lack of opportunities at the workplaces to get enough insolation leads to the reduction in Vitamin D levels naturally. Deficiency of vitamin means that human body does not have enough Vitamin D in blood levels as Vitamin D is the crucial one which controls the calcium levels and maintains the phosphorus level at prescribed ranges in the body. A 25-hydroxy Vitamin D (which is also referred as calcidiol) blood test is considered as the most exact approach to find out Vitamin D levels in a human body. Having the calcidiol level of less than 20ng/ml indicates Vitamin D deficiency. Levels from 21–29 ng/mL are deemed to be insufficient while a level of 30-60 ng/ml is considered as sufficient for a healthy Vitamin D profile [3].

The widely prevalent health disorders viz. anemia, Type-1 diabetes, rheumatoid arthritis, chronic lymphocytic thyroiditis, cardiovascular syndrome and cancer are attributed to fallen Vitamin-D levels in the human body. Some studies have recently revealed that a deficiency in Vitamin D causes Basedow's disease and chronic lymphocytic thyroiditis [4], [5]. Hence it has become the cynosure of researchers involved in biomedical investigations to investigate the correlation among Vitamin D Deficiency and hypothyroidism.

Many findings proved that an early detection of decreasing Vitamin D levels in the body would help for the prevention of Autoimmune Thyroid Disorder (AITD) and other kinds of disorders closely associated with it [6]. With these observations, the present study focuses in examining the relationship between the deficiency of Vitamin D with hypothyroidism.

In general, the methods in statistical analyses help to carry out studies which contain various chores pertinent to data collection, analysis of the collected data, figuring out significant interpretation and exploring the outcome of the research findings. To derive accurate inferences and for finding out the exact results, proper statistical tests have to be done [7]. An appropriate recommendation of a study, an exact choice of the model of a study and choosing correct statistical tests are required for the above purposes which will help in producing accurate results of the tests that are being carried out.

LITERATURE SURVEY

Yasin Simsek and Ilkay Cakir [8] aimed to observe whether there exist a relationship between Thyroid and autoimmunuity. This was done by looking at the effects of dealing both serum levels of TPO-Ab and anti-TgAb levels in the blood. In their work, they found that deficiency of vitamins might play a major cause for the origin and development of AITD and that supplementing with thyroid antibodies reduced thyroid antibody titers.

Zhao et al. [9] explored into the immune modulating function and its role in AITD. The risk of AITD is increased when there is a deficiency. This study also suggested that medication can help patients with AITD to feel better. However, whether it can be prevented or not remains a contentious issue.

The prediction and cure for Thyroid disorders was investigated using Machine Learning Approaches by Aversano et al. [10]. Their work focused on a number of machine learning algorithms that could be used to predict thyroid illness. They reported a method based on machine learning techniques that take advantage of parametric measurements thyroid hormone as well as other clinical data. The approach mostly focused on detecting the condition

as well as the clinical history of hypothyroidism patients.

AITD's cause and consequences was reported by Vieira et al. [11]. The research looked into search whether there exist a link between Vitamin D and AITD and the part of Vitamin D in the progress of AITD. It also looked into whether supplementation can aid with the prevention or therapy of AITD.

Mangaraj et al. [12] proposed a study to determine the status of new Onset Graves Disease patients and their impact on thyroid-related parameters. They found that levels were much lower in new-onset Graves' disease, but there was no link between thyroid hormone and the condition.

Talael et al. [13] reported on the influences of thyroid supplementation on hypothyroid patients' function. The goal of that study was to see how supplementation helps to improve the regular function of thyroid in hypothyroid patients. The study found that they could find the improvement of the levels of calcium and serum TSH than the control group after the supplementation for 12 weeks. However, it was discovered that serum T3 and T4 levels were unaffected.

Kirsten et al. [14] developed a model for determining the influence of thyroid autoimmune disease. The primary goal of this study was to see the chances of diminishing thyroid auto antibodies with therapeutics in comparison to a placebo.

Chaudhary et al. [15] investigated antibody levels in autoimmune thyroid disease patients by studying the effect of supplementations lowering thyroid Peroxidase through randomized controlled experiments. Finally, they discovered that deficit and insufficiency are far more common in AITD patients.

A review on the meta-analysis of the association between and AITD was reported by Wang et al. [16]. Their study examined to detect whether a link between thyroid disorder and AITD prevails.

MATERIALS AND METHODS

Observational studies investigating relevance usually include Vitamin D levels reported with clinical investigations. Danilovic et al. [17] in their study reported 25-Hydroxyvitamin D and TSH as risk factors in Thyroid carcinoma. For the present investigation of finding the presence of possible correlation between Vitamin D levels and degree of Thyroid problem, the opensource dataset [18] used by Danilovic et al. [17] has been used. In the present work, the two significant parameters viz. Vitamin D (Serum 25OHD) and TSH (Thyroid Simulating Hormone) along with the regular parameters like Age, Height, Weight and BMI of the patients have been considered. The dataset records are classified into four categories for carrying out the investigations using Serum 25OHD and TSH levels. The levels of Serum 25OHD and their causes are well known in medical terms which state that having Serum 25OHD < 12nmol/L is risk for a human and it is considered as Vitamin D Deficiency. Likewise, the level between 12 to 30 nmol/L is measured as Vitamin D Insufficient. Serum 25OHD level in the range of 30-50 nmol/L are considered as healthy with sufficient level of Vitamin D in the blood. Higher level of Serum 25OHD(>50nmol/L) are regarded as toxic.

The usual range of TSH hormone is in the range between 0.4 mU/L to 4.2 mU/L. For the analysis, these two parameters are segregated into four categories and the details are given in Table 1.

Table 1: The categorizations of Vit. D and TSH levels

Category	Serum 25OHD and TSH Levels
Category -I	Vit. D < 20 ng/ml and TSH <4.2 mU/L
Category-II	Vit. D < 20 ng/ml and TSH >=4.2 mU/L
Category-III	Vit. D >= 20 ng/ml and TSH < 4.2 mU/L
Category-IV	Vit. D >= 20 ng/ml and TSH >=4.2 mU/L

The performed statistical tests included the following:

(i) Analysis Of Variance (ANOVA)
(ii) Correlation test and
(iii) Linear Regression test

The tests are carried out to verify the proposed null hypothesis that a strong internal and mutual association/dependence exists between Serum 25OHD and TSH levels in Thyroid disorders induced by low Vitamin D levels in females. From the dataset [18], the mean values of age, weight, height and Body Mass Index (BMI) of the population (females only) are computed for the defined four categories and the computed results are shown in Table 2.

Table 2: Computed averages of physique parameters of patients spreading over the four categories

Parameters	25OHD<20, TSH<4.2	25OHD<20, TSH>=4.2	25OHD>=20, TSH<4.2	25OHD>=20, TSH>=4.2
Mean Age (Years)	56.4	48.2	51.1	39.51
Mean Weight (kg)	71	67	69	64.96
Mean Height (m)	1.6	1.6	1.6	1.6
Mean BMI (kg/m^2)	29.0	26.7	27.7	25.45

RESULTS AND DISCUSSION

A perusal of Table 2 shows that younger women are more susceptible to enhanced levels of 25OHD and TSH in spite of maintaining a healthy BMI. On the other extreme, the elderly women with higher BMI possessed least levels of both 25OHD and TSH values among the four categorized groups. It is a usual supposition that younger population are healthy and agile compared to the older ones. But the observance of these two parameters at higher levels, in younger females leading to thyroid related complications, intrigues to explore further the interdependence between them.

The test of ANOVA compares the means of different groups and helps to find the presence of any statistical differences between the means. The sample means need to be from different populations and the observations within each sampled

population need to be normally distributed. The p-value in the ANOVA output determines whether there is statistical significant exist among the means. It is a probability measure giving indication against the null hypothesis. Low probabilities provide powerful evidence against it. A significance level (denoted as α or alpha) of 0.05 indicates a 5% risk of concluding that a variation exists when there is no actual dissimilarity occurs between the groups. If the p-value is less than or equal to the significance level, then the null hypothesis could be rejected. Otherwise, evidences for the validity of the null hypothesis could be explored further.

The p-values computed from the ANOVA tests for all possible categories (groups listed in Table 2) are shown in Table 3. The p-value being above 94 % in those tests which essentially included either Category-II or Category-III or both strongly indicate the presence of a definite associateship between 25OHD and TSH levels. The two groups test results between II and III and that between I and IV giving the p-values 94.4% and 75.5% respectively leads to conclude more in favor of the supposition that enhanced/ adequate Vitamin D level is prone to reduce Thyroid complications.

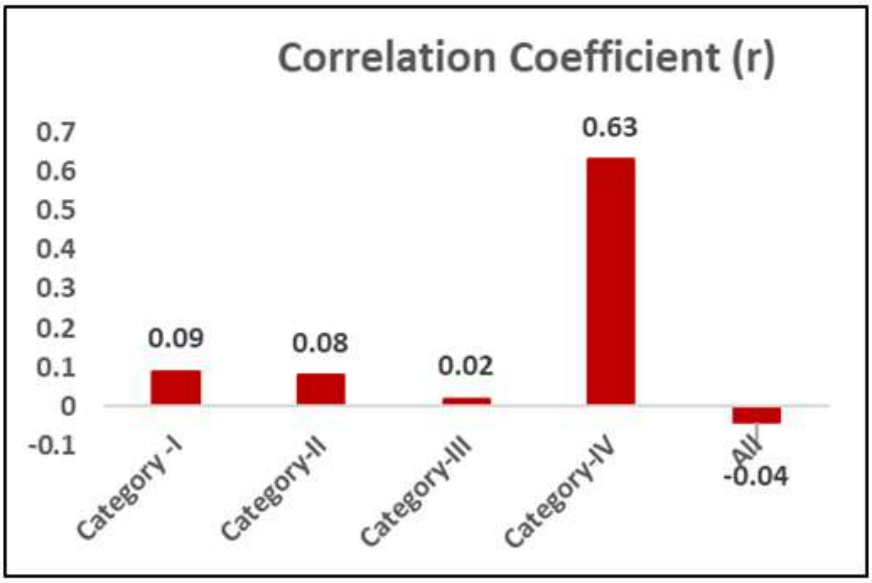
Further to explore the dependence between the 25OHD and TSH levels correlation studies are made between the above two factors for all the 384 patients and as well between the four categories and the Pearson correlation coefficient values obtained are illustrated in Fig.1.

Table 3: Results of the ANOVA experiments

Categories	p-value
I, **II, III** and IV	**0.98976**
I, **II, III**	**0.98474**
I, **II,** IV	**0.94763**
I, **III**, IV	**0.94700**
II, III, IV	**0.97393**
I, II	0.86754
I, III	0.92248
I, IV	0.75509
II, III	**0.94442**
II, IV	0.88198
III, IV	0.82824

The moderate correlation between Serum 25OHD and TSH in category-IV could be due to relatively lesser number of sample size when compared to the rest of the categories. Generally, a near zero correlation coefficient is a measure of statistical insignificance between the explored parameters. However, r being -0.04 when computed for the entire test set of 384 female patients could be highly significant and needs further experimentation. This is evident from the correlation coefficient from getting reversed from positive insignificance to negative insignificance when computed for the entire data set.

Figure 1.Pearson correlation analysis between 25OHD vs TSH levels



Regression analysis helps in understanding the strength of relationships between variables and is used to evaluate trends and make estimates or forecasts. The statistical measurements like R-squared/ adjusted R-squared facilitate to understand how much of the total variability in the data is explained. The R value signifies that there is a strong linear relationship between the variables taken into consideration. It is the correlation between the predicted values and the observed values of TSH for given 25OHD. The R square parameter is known as the coefficient of determination and its value if equals unit would indicate the regression predictions perfectly fitting the data. It is a goodness of fit indicator conveying the percentage of points that fall on the regression line. The results of the linear regression analysis performed between 25OHD and TSH levels are shown in figures 2(a) to (c).

Figure 2(a):Linear Regression Test for the entire data set

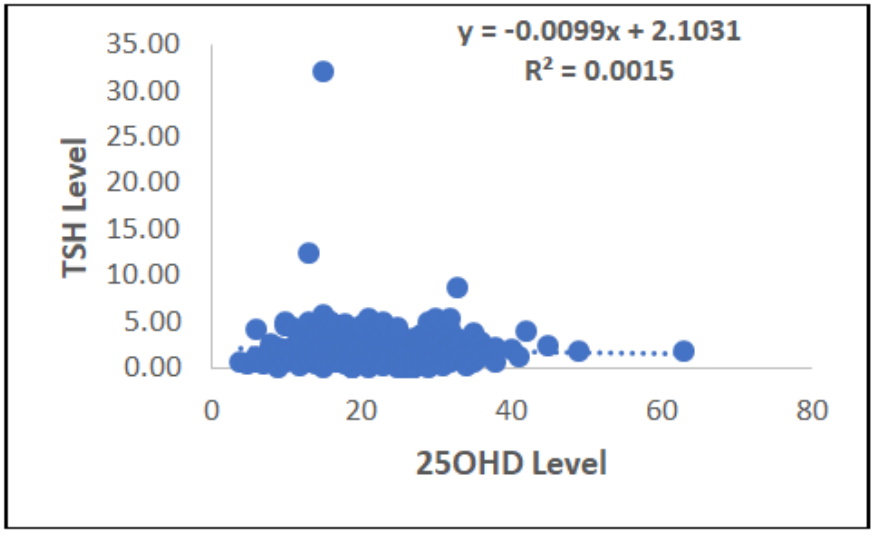


Figure 2(b):Linear Regression Test for Category-II of the data set

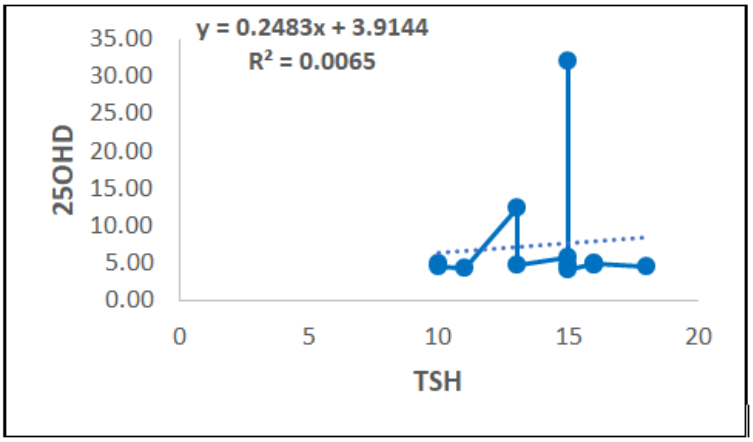
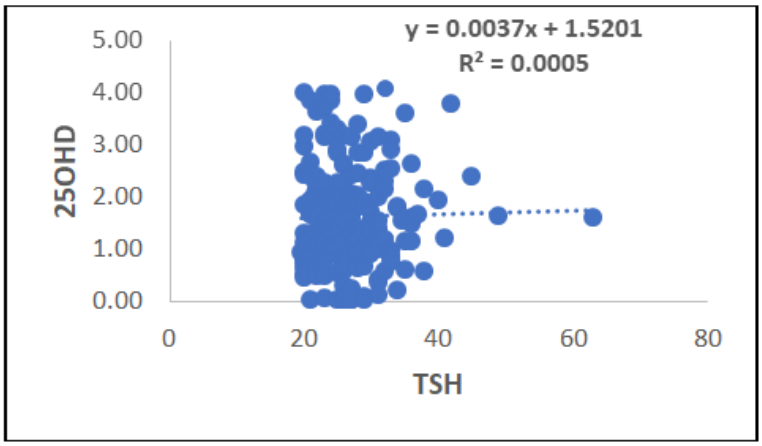


Figure 2(c): Linear Regression Test for Category-III of the data set



The simple linear regression studies between 25OHD values and TSH levels failed to bringout the incognitable relationship between them otherwise supposed to be influential in Thyroid related disorders. This is evident from the R square parameter giving nil goodness of fit for the supplied data. However, the point of concern is that both 25OHD and TSH measurements, being made from men and women with different physiological conditions, should not be stopped with a simple study of linear regression between two variables but should be extended further by including other key physiological parameters like age, BMI, other hormonal levels of immunity concern and life style conditions.

CONCLUSION

In this work, an attempt has been made to investigate the reasons for lower levels of Serum Vitamin D and its impact on Thyroid related disorders with statistical analyses. Though ANOVA tests evinced a definite relationship between the above two parameters it needs further validation from other studies. The correlation analysis also required a greater number of data and uniformity of tuples among the categories. Simple regression studies also failed to reveal the implicit association between the parameters and compel for multiple regression studies. As regression is one of the most powerful tools in statistical analysis of data, the present study could be extended by using machine learning

algorithms and with increased number of physiological parameters in the gamut of dataset.

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Reference

[1] Vinayak Majhi, Sudip Paul, Rachna Jain,"Bioinformatics for Healthcare Applications", Amity International Conference on Artificial Intelligence (AICAI),IEEE Xplore, February 2019,DIO:10.1109/AICAI.2019.8701277

[2] Jelili Oyelade, Jumoke Soyemi, Ithunuoluwa Isewon, Olawole Obembe, "Bioinformatics, HealthCare Informatics and Analytics: An Imperative for Improved Healthcare System", International Journal of Applied Information Systems,Vol 8,2015,DOI:10.5120/ijais15-451318.

[3] Michael F Holick,Tai C Chen, "Vitamin D deficiency a worldwide problem with health consequences ",American Journal of Clinical Nutrition,Vol 87,2008 pp-1080S-1086S

[4] Matthias Wacker, Michael F, Holick ,"Sunlight and Vitamin D :a global perspective for health Dermatoendocrinology",Dermato Endocrinology,Matthias Wacker,Vol 5(1),2013 pp 51-108.

[5] Kurt A. Kennel, Matthew T. Drake, Daniel L.Hurley,"Vitamin D Deficiency in Adults:When to Test and How to Treat",Mayo clin proc.2010 Aug:85(8):752-758.

[6] Dr.Amal Mohammed Husein Mackawy ,"Vitamin D Deficiency and its Association with Thyroid Disease ",Int J Health sci(Qassim)2013 Nov,7(3):267-275

[7] Winters R,Winters A,Amerdee RG,"Statistics: A brief overview",Ochsner J.2010;10:213-216.

[8] Yasin Simsek,Ilkay Cakir,Mikail Yetmis,Oguzhan Sitki Dizdar, Osman Baspinar, and Ferhat Gokay, "Effects of treatment on thyroid autoimmunity",Journal of Research in Medical Science 2016,DOI:10.4103/1735-1995.192501.

[9] Rui Zhao, Wei Zhang,Chenghong Ma,Yaping Zhao,Rong Xiong,Hanmin Wang,Weiwen Chen,Song Guo Zheng, "Immuno madulatory Function of and its Role in Autoimmune Thyroid Disease", Frontiers in Immunology,2021,DOI:10.3389/fimmu.2021.574967.

[10] Lerina Aversano,Mario Luca Bernardi, Marta Cimitile, Martina Iammarino,Paolo , EmidioMacchia, Immacolata Cristina Nettore,ChiaraVerdone,"Thyroid Diseae Treatment prediction with machine learning approaches ",Elsevier-Vol 192,2021,pp 1031-1040.

[11] Ines Henriques Vieira,Dircea Rodrigues and Isabel Paiva,"Vitamin D and Autoimmune Thyroid Disease – Cause,Consequence, or a Vicious Cycle", Nutrients 2020 sep

11;12(9):2791.DOI:10.3390/nu12092791.

[12] Swayamsidha Mangaraj, Arun K,Choudhury, Basanta M.Swain, Pradosh K,Sarangi,Binoy K,Mohanty, and Anoj K,Baliarsinha,"Ecaluation of Status and its impact on Thyroid Related Parameters in New Onset Graves' Disease –A Cross –sectional Observational Study", Indian J Endocrinol Metab.2019 Jan-feb;23(1):35-39

[13] Afsaneh Talaei, Fariba Ghorbani, Zatollah Asemi, "The Effects of Supplementation on Thyroid Function in Hypothyroid Patients: A Randomized,Double-blind, Placebo-controlled Trial", Indian J Endocrinol Metab Sep-Oct 2018;22(5):584-588.

[14] Kristen V.Knutsen, Ahmed A,Madar, Mette Brekke, Haakon E,Meyer, Ase Ruth Eggemoen ,Ibrahimu Mdala, and Per Lagerlov,"the effect of on Thyroid Autoimmunity: A Randomized ,Double –blind ,controlled trial among Ethnic Minorities", J Endocr Soc 2017 May 1;1(5):470-479.

[15] Sandeep Chaudhary,Deep Dutta, Manoj Kumarm, Sudipta Saha,Samim Ali Mondal, Ashok Kumar, Satiath Mukhopadhyay," Vitamin D supplementation reduces thyroid peroxidase antibody levels in patients with autoimmune thyroid disease", An open-labeled randomized controlled trial-Indian J Endocrinol Metab.May-Jun 2016;20(3):391-8

[16] Jiying Wang, Shishi Lv,Guo Chen, Chenlin Geo,Jianhua He,Halihua Zhong, and Yong Xu*,Meta-Analysis of the Association between and Autoimmune Thyroid Disease – Nutrients,2015 Apr,7(4):2485-2498.

[17] Danilovic DLS, Ferraz-de-Souza B,Fabri AW,Santana NO,Kulcsar MA, Cernea CR,"25-Hydroxyvitamin D and TSH as Risk Factors or Prognostic Markers in Thyroid Carcinomat", PLOS ONE 11(10):e0164550.https://doi.org/10.1371/journal .pone.0164550

[18] Hyperlink for accessing the support information https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0164550#sec014. Downloadable data set: https://doi.org/10.1371/journal.pone.0164550.s001