***Open Access Maced J Med Sci*** **electronic publication ahead of print,**
**published on March 07, 2018 as https://doi.org/10.3889/oamjms.2018.125**

ID Design Press, Skopje, Republic of Macedonia
Open Access Macedonian Journal of Medical Sciences.
https://doi.org/10.3889/oamjms.2018.125
eISSN: 1857-9655
***Clinical Science***

# Thyroid Function and 25 (OH) Vitamin D Level among Sudanese Women in Early Pregnancy

Imad R. Musa[1*], Duria A. Rayis[2], Mohmamed A. Ahmed[2], Ammar H. Khamis[3], Abubakr M. Nasr[2], Ishag Adam[2]

*[1]King Abdu Aziz Armed Forces, Hospital at Air Base, Dhahran, Kingdom of Saudi Arabia; [2]Faculty of Medicine, University of Khartoum, Khartoum, Sudan; [3]Hamdan Bin Mohammed College of Dental Medicine (HBMCDM), Mohammed Bin Rashid University of Medicine and Health Sciences, Dubai, United Arab Emirates*

**Citation:** Musa IR, Rayis DA, Ahmed MA, Khamis AH, Nasr AM, Adam I. Thyroid Function and 25 (OH) Vitamin D Level among Sudanese Women in Early Pregnancy. Open Access Maced J Med Sci. https://doi.org/10.3889/oamjms.2018.125

**Keywords:** Vitamin D; Thyroid function; Pregnancy; Sudan

***Correspondence:** Imad R Musa. King Abdu Aziz Armed Forces Hospital at Air Base, Dhahran, Kingdom of Saudi Arabia. E-mail: irthesudanese@hotmail.com

**Received:** 06-Nov-2017; **Revised:** 19-Nov-2017; **Accepted:** 08-Feb-2018; **Online first:** 07-Mar-2018



**Funding:** This research did not receive any financial support

**Competing Interests:** The authors have declared that no competing interests exist

**Abstract**

**AIM:** A cross-sectional study was conducted at Saad Abualila Hospital (Khartoum, Sudan) to evaluate the vitamin D levels and thyroid function among pregnant Sudanese women (132) in early pregnancy.

**METHODS:** A cross-sectional study was conducted at Saad Abualila hospital (Khartoum, Sudan) during the period from March to July 2015. Women who were in early pregnancy with a singleton pregnancy were approached to participate in the study after signing informed consent. A sample size of 132 participants was calculated guided by the normal interval of thyroid function in Sudanese women in the first trimester and not the level of 25(OH) vitamin D. The 25 - hydroxyvitamin D (25 (OH) vitamins levels were measured using an electrochemiluminescence immunoassay on an Elecsys 2010 Analyzer (Roche Diagnostics, Mannheim, Germany).

**RESULTS:** The mean (SD) of age, gravidity and gestational age was 27.6 (5.5) years, 2.2 (1.6) and 10.4 (2.2) weeks, respectively. The mean (SD) of the body mass index (BMI) and haemoglobin was 27.1 (5.2) kg/m$^2$ and 10.8 (1.1) g/dl, respectively. Median (interquartile) values of TSH, FT3, and FT4 were 1.164 IU/ml (0.079 - 2.177 IU/ml), 4.639 nmol/l (3.843 - 6.562 nmol/l), and 16.86 pmol/l (13.02 - 31.48 pmol/l), respectively. There was no significant correlation between vitamin D levels and TSH, FT3 and FT4

**CONCLUSION:** There is no correlation between 25 (OH) vitamin D levels and thyroid function during early pregnancy among Sudanese pregnant women, despite prevalent vitamin D deficiency among these women.

## Introduction

Vitamin D is a fat-soluble vitamin and a steroid hormone precursor, which is primarily synthesized in the skin after exposure to ultraviolet B radiation. The liver is the first organ where hydroxylation occurs to produce 25 - hydroxyvitamin D (25(OH) D). Further hydroxylation continues mainly in the kidneys to produce the active form 1, 25 - dihydroxy vitamin D (1, 25(OH) 2D), besides the placenta and several other target organs [1]. In fact, less than 10% of vitamin D is derived from main dietary sources such as dairy, eggs, fish and meat [2] [3] [4]. Moreover, vitamin D has relatively durable stability over several weeks, and approximately 99% of circulating 25(OH) D3 is bound to vitamin D - binding proteins. Interestingly, its gradual oscillation depends on solar radiation rather than on vitamin D precursors that are gained from food items [5].

Vitamin D has many vital functions such as endocrine, autocrine (the activity of vitamin $D_3$ arises from 1,25D synthesized within those cells), paracrine (1,25D is synthesized in one cell type and acts within adjacent cells), regulation of gene expression (it shares many pathways with p53), cell differentiation and proliferation [6] [7] [8]. Vitamin D receptors are found in many cells and tissues of the human body that are responsible for regulating the expression of more than 1000 genes in humans [9]. Allelic variants of the vitamin D - binding protein (DBP) gene enhance susceptibility to Graves' disease but not to Hashimoto's thyroiditis, which expresses the

endocrine role of vitamin D [10]. In contrast to this, some studies proposed an association between vitamin D deficiency and Hashimoto's thyroiditis where a higher prevalence of vitamin D deficiency was reported among these patients [11] [12] [13]. At the same time, a significantly higher prevalence of vitamin D deficiency has been reported among patients with autoimmune thyroid disorders, hypothyroidism, overt hypothyroidism and Graves' disease [14]. However, another study showed no significant relationship between non - autoimmune thyrotoxicosis and vitamin D status during pregnancy [15].

Mazokopakis *et al.* observed an inverse correlation between low serum 25(OH) D levels in euthyroid patients with Hashimoto's thyroiditis who had high serum anti-thyroid peroxidase (TPO) antibodies [16]. Despite the fact that many studies have evaluated the role of vitamin D in thyroid diseases, few studies explored the effects of 25 (OH)D in association with thyroid function in pregnancy and maternal and foetal outcomes [17] [18]. Some data focused on the adverse events of the coincidental findings of both vitamin D deficiency and thyroid disorders during pregnancy: increased risk of preeclampsia, gestational hypertension, gestational diabetes mellitus, premature delivery and low birth weight [19] [20] [21] [22]. In vitro and in vivo studies propose an increased response to 1, 25(OH) 2D in the presence of T3 in cultured anterior pituitary cells.

Moreover, an increased level of TSH is observed after acute administration of 1, 25(OH) 2D [23]. One study focused on this relationship and documented that high vitamin D status was associated with low circulating TSH in a younger group of patients [24]. On the other hand, Glinoer noted the enhancement of thyroid hormones and induced partial suppression of serum TSH in response to the sharp increase of human chorionic gonadotropin in the 1st trimester [25]. Another study from Sudan reported a suppressive effect of pregnancy on thyroid parameters TSH, FT4 and T3(26).

Due to a higher global prevalence of vitamin D deficiency, increasing concern has been raised on maternal vitamin D deficiency and possible maternal and perinatal adverse effects [18] [27] [28]. There is a high prevalence of vitamin D deficiency (vitamin D level ≤ 20 ng/ml) among pregnant women in some tropical areas, e.g., 29% and 18.9 of women in Nigeria and southern China, respectively [29] [30]. There is no published data on vitamin D and thyroid function in Sudan. Hence, the current study was conducted to assess the association of thyroid function and vitamin D levels among Sudanese women in early pregnancy.

## Method

A cross-sectional study was conducted at Saad Abualila hospital (Khartoum, Sudan) during the period from March to July 2015. Women who were in early pregnancy with a singleton pregnancy were approached to participate in the study after signing informed consent. A sample size of 132 participants was calculated guided by the normal interval of thyroid function in Sudanese women in the first trimester and not the level of 25(OH) vitamin D (no previous data). This sample size has over 80% power to detect a difference of 5% at $\alpha = 0.05$. We assumed that 10% of the women might not respond or might have incomplete data. Exclusion criteria included chronic diseases of the liver and kidney, previous gastrointestinal surgery, pulmonary tuberculosis, lymphoma, primary hyperparathyroidism, hyperthyroidism, epilepsy on anticonvulsants therapy, intake of vitamin D within the last six months or on medications that could interfere with its metabolism such as glucocorticoids, and current anticonvulsant therapy.

Sociodemographic and obstetric history were gathered using a questionnaire. The height and weight were measured using conventional methods and were used to calculate the body mass index (BMI) by using the formula: weight in kilograms (kg) divided by the square of the height in metres ($m^2$). A blood sample was collected in a gold - top serum separator tube and allowed to clot. The samples were centrifuged at 1100 - 2000 g for 10 minutes. Serum then was separated from cells immediately and refrigerated at temperature 2 to 8°C before processing it. Grossly haemolysed, lipemic or samples containing particulate material were rejected. The 25 - hydroxyvitamin D (25 (OH) vitamins levels were measured using an electrochemiluminescence immunoassay on an Elecsys 2010 Analyzer (Roche Diagnostics, Mannheim, Germany). The normal level of 25 (OH) D is 20 ng/ml or above [31]. Thyroid function tests (TSH, T3and T4) were obtained using commercially available kits by Roche Elecsys Modular Analytics Cobas e411 utilising electrochemiluminescence immunoassay (Roche Diagnostics, Mannheim, Germany). Complete blood count was checked to assess haemoglobin (Hb) levels.

### *Ethics*

The study received ethical approval from the board of the Department of Obstetrics and Gynaecology, Faculty of Medicine, University of Khartoum, Sudan.

### *Statistics*

Data were entered into a computer and SPSS for Windows was used for data analyses. Continuous data were checked for normality using the Shapiro - Wilk test. Data were expressed as proportions: mean (SD) and median (interquartile). Correlation (Pearson and Spearman) were performed. $P < 0.05$ was considered statistically significant.

## Results

One hundred – thirty - two women were enrolled in the study. The mean (SD) of age, gravidity and gestational age was 27.6 (5.5) years, 2.2 (1.6) and 10.4 (2.2) weeks, respectively. The majority (81.8%) of these women had urban residence and were housewives (75.8). The mean (SD) of the BMI and haemoglobin were 27.1 (5.2) kg/m$^2$ and 10.8 (1.1) g/dl, respectively. The mean (SD) or median (interquartile) of TSH, FT3, FT4 and vitamin level are shown in Table 1.

**Table 1: The level of thyroid hormones and 25 (OH) vitamin D level in Sudanese women in early pregnancy**

| Variables | |
|---|---|
| *5-95%, mean (SD) of* | |
| FT3, pmol/l | 1.483–2.670, 2.022 (0.339) |
| FT4, pmol/l | 0.760–1.390, 1.072(1.972) |
| *5-95%, median (interquartile) of* | |
| TSH, m iU/l | 0.579–3.424, 1.684 (1.163–2.104) |
| 25 (OH) vitamin D, ng/ml | 5.3–16.1, 8.4(7.2– 11.1) |

Except for one woman, all the participants (99.2%) demonstrated vitamin D deficiency. There is no correlation between 25 (OH) vitamin D, thyroid functions and BMI, Table 2.

**Table 2: Correlations between thyroid functions, BMI and 25 (OH) vitamin D**

| Variable | FT3 | | FT4 | | TSH | | BMI | |
|---|---|---|---|---|---|---|---|---|
| | *r* | *P* | *r* | *P* | *r* | *P* | *r* | *P* |
| FT3 | | | 0.001 | 0.992 | 0.128 | 0.144 | 0.043 | 0.620 |
| FT4 | | | | | - 0.122 | 0.202 | -0.059 | 0.502 |
| TSH | | | | | | | 0.033 | 0.711 |
| 25 (OH) vitamin D | 0.010 | 0.910 | 0.133 | 0.129 | - 0.003 | 0.970 | - 0.156 | 0.075 |

## Discussion

The current study showed no significant association between vitamin D levels and thyroid functions among pregnant Sudanese women during the 1st trimester. This is in concordance with a previous study that was conducted among pregnant women in Northern China [32]. In the latter study, a high prevalence (96%) of vitamin D deficiency during the 1st trimester was reported [32]. Likewise, a non - significant difference between vitamin D deficiency and thyroid antibodies status was reported in a case-control study that recruited 531 pregnant women and 238 age-matched, non - pregnant women as a control group [33]. Another study showed no correlation between 25 – Hydroxyvitamin D, FT4 and FT3 hormone during pregnancy, but a significant correlation was observed among pregnant women with higher and sufficient levels of vitamin D (> 30.0 ng/ml) and lower TSH [34]. These may be explained by the specific course of pregnancy that reflects the state of immune tolerance as the antithyroid autoantibody titers reduce by at least 50% from the 1st to the 3rd trimester [35].

Thus, a weak association between 25(OH) D and thyroid antibodies may result, leading to a non - significant relationship [32]. Hence, researchers speculated that both 25(OH) D and thyroid dysfunction might work independently and contribute to some of the same adverse effects during pregnancy [32]. We also propose that a higher level of human chorionic gonadotropin in the 1st trimester that influences TSH may be considered another contributing factor to weaken such coincidental effects. Moreover, no association was reported between vitamin D deficiency in non - pregnant women in both cases and control group, the hypothyroid and euthyroid subjects [36]. On the other hand, a significant correlation between vitamin D deficiency and all thyroid parameters (TSH, T4 and T3) have been documented among pregnant women in Italy [37].

Furthermore, a significant correlation between vitamin D and TSH has been observed among pregnant women with a sufficient level of vitamin D (> 30 ng/ml) [34]. A recent population-based health survey reported a higher prevalence of vitamin D deficiency and insufficiency in thyroglobulin antibodies (TgAb) positive cases which were 78.3% and 20% respectively [38]. Vitamin D deficiency has been reported as a risk factor for autoimmune thyroiditis and thyroid hypofunction [6] [39]. This may be explained by the unique immunomodulatory effect of 1, 25 - (OH) 2D3 which is observed on T - lymphocyte function, antigen presenting cells and stimulated phagocytosis. It, therefore, inhibits the cytodestructive ability of T helper type - 1(Th1) lymphocytes, and enhances T helper type - 2(Th2) cytokine (Interleukin - 4) production [40]. Both vitamin D and thyroid hormone share the same steroid hormone receptors [5].

Nevertheless, there is some evidence that links vitamin D receptor gene polymorphisms with autoimmune thyroid diseases (AITD) [6]. The mutation of genes encoding for tissue hydroxylases and Vitamin D receptor additionally carries a potential risk of developing thyroid cancer [41]. In a case-control study, 53 patients with gestational transient thyrotoxicosis and 35 healthy pregnant women were recruited, and vitamin D levels were significantly lower

in cases when compared to the controls (11.1 ± 7.7 and 16.5 ± 0.5 ng/mL, respectively) [42]. A previous study documented an association between pronounced decreased levels of 25(OH) D3 and Graves' disease, in addition to an inverse correlation between 25(OH) D3 levels and thyroid gland volume [43]. Being a female may harbour a genetic risk for thyroid dysfunction, and global vitamin deficiency may influence the outcome of some studies. This is supported by a recent study that enrolled a total number of 1714 subjects (females = 1197 and males = 517) and showed significantly higher serum TSH levels, higher thyroid antibodies titers and lower serum 25(OH) vitamin D levels in females compared to males [38].

The active calcitriol is promoted as a translocation regulator for T3 in the cerebellum by improving the binding capacity of the cytosolic T3 - binding protein [44]. Moreover, it enhances TSH secretion of thyrotropin at the pituitary level [45]. The placental oestrogen stimulates Thyroxine Binding Globulin (TBG) synthesis [6]. The role of thyroid hormones is to stimulate intrauterine foetal growth, which is evident during the second half of gestation and has an influence on foetal metabolism [37]. Vitamin D deficiency has negative effects on thyroid functions, and when both coincide together during pregnancy, imminent harm may come to both mother and her foetus; hence, correction of both disorders is recommended to minimise risk. The limitations of this study are the seasonal variation for vitamin D levels and some laboratory tests that are not included, e.g., calcium, phosphorous, parathyroid hormones and thyroid antibodies.

In conclusion, our study showed no significant association between vitamin D deficiency and thyroid function during the 1$^{st}$ trimester among Sudanese pregnant women despite the higher prevalence of vitamin D deficiency. We recommend further studies in this area.

## References


1. Holick MF. Sunlight, ultraviolet radiation, vitamin D and skin cancer: how much sunlight do we need? Adv Exp Med Biol. 2014; 810:1–16. https://doi.org/10.1007/978-1-4939-0437-2_1

2. Green RJ, Samy G, Miqdady MS, El-Hodhod M, Akinyinka OO, Saleh G, et al. Vitamin D deficiency and insufficiency in Africa and the Middle East, despite year-round sunny days. S Afr Med J. 2015; 105(7):603–5. https://doi.org/10.7196/SAMJnew.7785

3. Jakobsen J, Knuthsen P. Stability of vitamin D in foodstuffs during cooking. Food Chem. 2014; 148:170–5. https://doi.org/10.1016/j.foodchem.2013.10.043 PMid:24262542

4. Liu Y, Jin Q, Bao Y, Li S, Wang J, Qiu L. Investigation of the vitamin D nutritional status in women with gestational diabetes mellitus in Beijing. Lipids Health Dis. 2017; 16(1):22. https://doi.org/10.1186/s12944-017-0412-y PMid:28129773 PMCid:PMC5273824

5. Vondra K, Stárka L, Hampl R. Vitamin D and thyroid diseases. Physiol Res. 2015; 64(Suppl 2): S95–100. PMid:26680495

6. Bizzaro G, Shoenfeld Y. Vitamin D and autoimmune thyroid diseases: facts and unresolved questions. Immunol Res. 2015; 61(1–2):46–52. https://doi.org/10.1007/s12026-014-8579-z PMid:25407646

7. van Driel M, Koedam M, Buurman CJ, Hewison M, Chiba H, Uitterlinden AG, et al. Evidence for auto/paracrine actions of vitamin D in bone: 1 -hydroxylase expression and activity in human bone cells. FASEB J. 2006; 20(13):2417–9. https://doi.org/10.1096/fj.06-6374fje PMid:17023519

8. Pols HAP, Birkenhäger JC, Foekens JA, van Leeuwen JPTM. Vitamin D: A modulator of cell proliferation and differentiation. J Steroid Biochem Mol Biol. 1990; 37(6):873–6. https://doi.org/10.1016/0960-0760(90)90435-N

9. Ginde AA, Sullivan AF, Mansbach JM, Camargo CA, Jr. Vitamin D insufficiency in pregnant and nonpregnant women of childbearing age in the United States. Am J Obstet Gynecol. 2010; 202(5):436.e1-436.e8. https://doi.org/10.1016/j.ajog.2009.11.036 PMid:20060512 PMCid:PMC3784988

10. Pani MA, Regulla K, Segni M, Hofmann S, Hüfner M, Pasquino AM, et al. A Polymorphism within the Vitamin D-Binding Protein Gene Is Associated with Graves' Disease but Not with Hashimoto's Thyroiditis. J Clin Endocrinol Metab. 2002; 87(6):2564–7. PMid:12050214

11. Tamer G, Arik S, Tamer I, Concert D. Relative Vitamin D Insufficiency in Hashimoto's Thyroiditis. Thyroid. 2011; 21(8):891–6. https://doi.org/10.1089/thy.2009.0200 PMid:21751884

12. Arslan MS, Topaloglu O, Ucan B, Karakose M, Karbek B, Total E, et al. Isolated vitamin D deficiency is not associated with nonthyroidal illness syndrome, but with thyroid autoimmunity. Scientific World Journal. 2015; 2015:239815.

13. Mackawy AMH, Al-Ayed BM, Al-Rashidi BM. Vitamin d deficiency and its association with thyroid disease. Int J Health Sci (Qassim). 2013; 7(3):267–75. https://doi.org/10.12816/0006054

14. Kim D. Low vitamin D status is associated with hypothyroid Hashimoto's thyroiditis. Hormones. 2016; 15(3):385–93. https://doi.org/10.14310/horm.2002.1681

15. Yorulmaz G, Gönüllü Emel, Akalin Aysen, Senol Murat, Yildiz Pinar, Tomus Narguler, et al. The effect of non-autoimmune thyrotoxicosis to vitamin D status during pregnancy; Biomedical Research. 2015; 27(1):225-4.

16. Mazokopakis EE, Papadomanolaki MG, Tsekouras KC, Evangelopoulos AD, Kotsiris DA, Tzortzinis AA. Is vitamin D related to pathogenesis and treatment of Hashimoto's thyroiditis. Hell J Nucl Med. 2015; 18(3):222-7. PMid:26637501

17. DeLuca HF. Evolution of our understanding of vitamin D. Nutr Rev. 2008; 66(10 Suppl 2):S73–87. https://doi.org/10.1111/j.1753-4887.2008.00105.x PMid:18844850

18. Li Y, Shan Z, Teng W, Yu X, Li Y, Fan C, et al. Abnormalities of maternal thyroid function during pregnancy affect neuropsychological development of their children at 25-30 months. Clin Endocrinol (Oxf). 2009; 72(6):825–9. https://doi.org/10.1111/j.1365-2265.2009.03743.x PMid:19878506

19. Bodnar LM, Catov JM, Simhan HN, Holick MF, Powers RW, Roberts JM. Maternal vitamin D deficiency increases the risk of preeclampsia. J Clin Endocrinol Metab. 2007; 92(9):3517–22. https://doi.org/10.1210/jc.2007-0718 PMid:17535985 PMCid:PMC4288954

20. Negro R, Mestman JH. Thyroid disease in pregnancy. Best Pract Res Clin Endocrinol Metab. 2011; 25(6):927–43. https://doi.org/10.1016/j.beem.2011.07.010 PMid:22115167

21. Krassas GE, Poppe K, Glinoer D. Thyroid Function and Human Reproductive Health. Endocr Rev. 2010; 31(5):702–55. https://doi.org/10.1210/er.2009-0041 PMid:20573783

22. Alzaim M, Wood RJ. Vitamin D and gestational diabetes mellitus. Nutr Rev. 2013; 71(3):158–67. https://doi.org/10.1111/nure.12018 PMid:23452283

23. Smith MA, McHenry C, Oslapas R, Hofmann C, Hessel P, Paloyan E. Altered TSH levels associated with increased serum 1,25-dihydroxyvitamin D3: a possible link between thyroid and parathyroid disease. Surgery. 1989; 106(6):987–91. PMid:2511635

24. Chailurkit L, Aekplakorn W, Ongphiphadhanakul B. High Vitamin D Status in Younger Individuals Is Associated with Low Circulating Thyrotropin. Thyroid. 2013; 23(1):25–30. https://doi.org/10.1089/thy.2012.0001 PMid:22931506

25. Glinoer D. The Regulation of Thyroid Function in Pregnancy: Pathways of Endocrine Adaptation from Physiology to Pathology. Endocr Rev. 1997; 18(3):404–33. https://doi.org/10.1210/edrv.18.3.0300 PMid:9183570

26. Elhaj ET, Adam I, Ahmed MA, Lutfi MF. Trimester-specific thyroid hormone reference ranges in Sudanese women. BMC Physiol. 2016; 16(1):5. https://doi.org/10.1186/s12899-016-0025-0 PMid:27795209 PMCid:PMC5087113

27. Ponsonby A-L, Lucas RM, Lewis S, Halliday J. Vitamin D status during Pregnancy and Aspects of Offspring Health. Nutrients. 2010; 2(3):389–407. https://doi.org/10.3390/nu2030389 PMid:22254029 PMCid:PMC3257641

28. Karras SN, Anagnostis P, Annweiler C, Naughton DP, Petroczi A, Bili E, et al. Maternal vitamin D status during pregnancy: the Mediterranean reality. Eur J Clin Nutr. 2014; 68(8):864–9. https://doi.org/10.1038/ejcn.2014.80 PMid:24824015

29. Xiao J-P, Zang J, Pei J-J, Xu F, Zhu Y, Liao X-P. Low Maternal Vitamin D Status during the Second Trimester of Pregnancy: A Cross-Sectional Study in Wuxi, China. PLoS One. 2015; 10(2):e0117748. https://doi.org/10.1371/journal.pone.0117748 PMid:25659105 PMCid:PMC4320063

30. Gbadegesin A, Sobande A, Adedeji O, Disu E, Korede O, Dosunmu A, et al. Maternal serum vitamin D levels and pregnancy outcomes: from Lagos, Nigeria. J Obstet Gynaecol (Lahore). 2017; 37(1):25–8. https://doi.org/10.1080/01443615.2016.1196483 PMid:27760474

31. Holick MF, Binkley NC, Bischoff-Ferrari HA, Gordon CM, Hanley DA, Heaney RP, et al. Evaluation, Treatment, and Prevention of Vitamin D Deficiency: an Endocrine Society Clinical Practice Guideline. J Clin Endocrinol Metab. 2011; 96(7):1911–30. https://doi.org/10.1210/jc.2011-0385 PMid:21646368

32. Zhao Y, Miao W, Li C, Yu X, Shan Z, Guan H, et al. Dynamic changes in serum 25-hydroxyvitamin D during pregnancy and lack of effect on thyroid parameters. PLoS One. 2014; 9(3):e90161. https://doi.org/10.1371/journal.pone.0090161 PMid:24608866 PMCid:PMC3946450

33. Moon H-W, Chung H-J, Hur M, Yun Y-M. Vitamin D status and thyroid autoimmunity in Korean pregnant women. J Matern Neonatal Med. 2015; 28(18):2210–3. https://doi.org/10.3109/14767058.2014.982530 PMid:25373429

34. Mohammed Nizar B, Battikhi ZW, Battikhi BE. Correlation of Serum 25-Hydroxyvitamin D and Thyroid Hormones in Pregnant Women in Amman-Jordan. J Microbiol Exp. 2017; 4(1):00099.

35. Smyth PPA, Wijeyaratne CN, Kaluarachi WN, Smith DF, Premawardhana LDKE, Parkes AB, et al. Sequential Studies on Thyroid Antibodies During Pregnancy. Thyroid. 2005:474–7. https://doi.org/10.1089/thy.2005.15.474 PMid:15929669

36. Musa IR, Gasim GI, Khan S, Ibrahim IA, Abo-Alazm H, Adam I. No Association between 25 (OH) Vitamin D Level And Hypothyroidism among Females. Open Access Maced J Med Sci. 2017; 5(2):126–30. https://doi.org/10.3889/oamjms.2017.029

37. Lavalle G, Onori ME. Relationship between Serum 25-Hydroxyvitamin D and Thyroid Hormones during Pregnancy in the North of Rome. Int J Sci Res. 2012; 3(10):2319–7064.

38. Wang X, Zynat J, Guo Y, Osiman R, Tuhuti A, Zhao H, et al. Low Serum Vitamin D Is Associated with Anti-Thyroid-Globulin Antibody in Female Individuals. Int J Endocrinol. 2015; 2015:1–6. https://doi.org/10.1155/2015/285290

39. Kivity S, Agmon-Levin N, Zisappl M, Shapira Y, Nagy E V, Dankó K, et al. Vitamin D and autoimmune thyroid diseases. Cell Mol Immunol. 2011; 8(3):243–7. https://doi.org/10.1038/cmi.2010.73 PMid:21278761 PMCid:PMC4012880

40. Di Rosa M, Malaguarnera M, Nicoletti F, Malaguarnera L. Vitamin D3: a helpful immuno-modulator. Immunology. 2011; 134(2):123–39. https://doi.org/10.1111/j.1365-2567.2011.03482.x PMid:21896008 PMCid:PMC3194221

41. Penna-Martinez M, Ramos-Lopez E, Stern J, Kahles H, Hinsch N, Hansmann M-L, et al. Impaired Vitamin D Activation and Association with CYP24A1 Haplotypes in Differentiated Thyroid Carcinoma. Thyroid. 2012; 22(7):709–16. https://doi.org/10.1089/thy.2011.0330 PMid:22690899 PMCid:PMC3387756

42. Küçükler Fk, Şimşek Y, Görkem Ü, Ayçiçek Doğan B, Güler S. Relationship between gestational transient thyrotoxicosis and vitamin D. TURKISH J Med Sci. 2016; 46:1374–8. https://doi.org/10.3906/sag-1507-33 PMid:27966300

43. Yasuda T, Okamoto Y, Hamada N, Miyashita K, Takahara M, Sakamoto F, et al. Serum vitamin D levels are decreased and associated with thyroid volume in female patients with newly onset Graves' disease. Endocrine. 2012; 42(3):739–41. https://doi.org/10.1007/s12020-012-9679-y PMid:22547366 PMCid:PMC3509322

44. Hashizume K, Suzuki S, Ichikawa K, Takeda T, Kobayashi M Effect of active vitamin D3 on the levels of NADPH-dependent cytosolic 3,5,3′-triiodo-L-thyronine-binding protein. Biochem Biophys Res Commun. 1991; 177(1):388–94. https://doi.org/10.1016/0006-291X(91)91995-O

45. Sar M, Stumpf WE, DeLuca HF. Thyrotropes in the pituitary are target cells for 1,25 dihydroxy vitamin D3. Cell Tissue Res. 1980; 209(1):161–6. https://doi.org/10.1007/BF00219932 PMid:7000361