

Correlation of serum 25-hydroxyvitamin d and thyroid hormones in pregnant women in amman-jordan

Abstract

Aim: The aim of this study is to investigate changes of vitamin D and thyroid hormones levels during pregnancy to maintain normal fetus development and growth.

Method: Serum hydroxyl vitamin 25(OH)D and thyroid levels were measured in 109 pregnant women referred to our laboratory from prenatal clinic during the period of May to October 2015. Blood samples were detected for 25 (OH) vitamins D, TSH, FT4 and FT3 by chemiluminescent (Tosoh A1A, Japan).

Results: Pregnant women aged 19-45 years (18.2 years age average) were examined. The mean 25(OH) D was 21.7 ± 5.6 ng/ml (range 8.7 to 47.2). The mean levels of Serum Free T3, FT4 and TSH were 1.61 ± 0.21 , ng/dl, 0.86 ± 0.23 ng/dl and $1.56 \pm .9$ μ IU/ml respectively, results for 25(OH) D mean values were 29.5 ng/ml (27.9%), 33.2 ng/ml (49.6%) and 37.3 ng/ml (22.5%) for vitamin D deficiency, insufficiency and sufficiency respectively. No correlation was found between vitamin D, TSH, FT4 and FT3 however, there was statistical significant correlation between the vitamin D and TSH ($p < 0.05$), level especially in patients with sufficient vitamin D level.

Conclusion: Association between higher vitamin D (>30.0 ng/ml) and lower TSH in pregnant was observed ($P < 0.005$). However, no correlation between 25-Hydroxyvitamin D FT4 and FT3 hormone was observed.

Keywords: 25-hydroxy vitamin d, thyroid stimulating hormone (tsh), thyroxin (ft4), triiodothyronine (ft3), vitamin d (25-(oh))d

Volume 4 Issue 1 - 2017

Battikhi Mohammed Nizar, Zqlam W
Battikhi, Banat E Battikhi
Battikhi central Laboratories, Jordan

Correspondence: Battikhi Mohammed Nizar, Battikhi central Laboratories 149 Ibn Khaldon Street, Amman 11183, 1017-1645 De Maisonneuve O, Montreal H3H 2N3, QC Canada, Email m_nizar11@hotmail.com

Received: May 02, 2016 | **Published:** January 31, 2017

Introduction

Vitamin D is important for fetus good health, growth and strong bones.¹ Vitamin D deficiency (VDD) is a global and public health problem in many countries.^{1,2} Vitamin D deficient or insufficient have been reported in many people and pregnant women are not exceptional. Vitamin D deficiency in pregnancy is still a public health issue³ and increasing evidence shows that vitamin D deficiency/insufficiency leads to a series of adverse outcomes for pregnant women and their offspring. They have been identified as a high-risk group, among whom the prevalence of VDD ranges between 20 and 40%¹. Deficiency in vitamin D was linked to a variety of different health problems, from depression to cancer, and osteoporosis to Parkinson's disease. Risk of heart disease and diabetes and their diseases. Vitamin D deficiency and/or VDRs gene polymorphism were associated with many kinds of autoimmune disorders, including type 1 diabetes mellitus, erythematosus systemic lupus, multiple sclerosis rheumatic arthritis.^{4,7} It was reported that vitamin D deficiency associated with autoimmune diseases necessary and supplementation prevents the onset and/or development of these autoimmune diseases^{10,11} which is needed for development of skeletal muscle due to involvement in calcium homeostasis.^{2,12} Therefore understanding sources of vitamin D supplementation is vital to reduce risk on mother and fetus. Major vitamin D sources is cutaneous synthesis via exposure to sunlight (95%) and dietary intake account for 5%.¹² Moreover vitamin D is a fat-soluble which is stored in body fat and liver^{11,12} through complex pathway involve kidney.^{1,2,12} The ultimate conversion of supplemented Vitamin D occurs in the liver to 25-Hydroxyvitamin D which is the most widely accepted indicator of vitamin D because serum 25(OH) D has longer half-life of approximately two to three weeks than 1, 25-(OH)₂ D with a shorter circulating half-life of fifteen hours^{2,13}

and it is the best indicator of total vitamin D status which is restored from sunlight exposure, diet and conversion from adipose stores in the liver.^{14,15} International vitamin D Levels of 30 to 32 ng/ml, 20 to 29 ng/mL and <12 ng/ml are considered to be sufficient, insufficient and deficient respectively.¹⁶ There are other factors reported to affect vitamin D status such as, geographic zone, season, dietary habits, race/ethnicity, cultural and religious factors, smoking and drinking, supplementation, sunscreen use, education and body mass index (BMI).^{17,28} To date, vitamin D deficiency in pregnancy is still a public health issue.³ Our interest in this study rises from the documented link between vitamin D and thyroid hormone since both are bind to similar receptors⁹ and both vitamin D deficiency and thyroid dysfunction/autoimmunity can cause different diseases such as preeclampsia, gestational hypertension, gestational diabetes mellitus, premature delivery, low birth weight, and impaired neurodevelopment of offspring.^{29,37} Therefore to maintain healthy pregnancy and fetus skeletal development and to prevent pre-eclampsia optimum level of Vitamin D should be maintained to ensure fetus health.¹⁰ Many studies have shown the role of vitamin D in autoimmune thyroiditis however, few studies examined the role of 25 (OH)D in association with thyroid hormones in pregnancy and conflict results reported on the association of 25(OH)D levels in pregnancy and adverse effects on maternal and fetal health.^{11,37,38} Thus, it is advisable to review VDD in mothers and their children so that strategies can be implemented to prevent VDD in pregnancy and lactation, in order to prevent impact on the fetus, newborn and in childhood, aiming at a possible reduction in the future development of chronic diseases in adulthood.^{38,39} The aim of this study is to investigate the relationship between 25-Hydroxyvitamin D status and circulating TSH, FT4, FT3 levels in pregnant women live in sunny Jordan.

Materials and methods

One hundred and nine pregnant women were referred to laboratory for vitamin D and thyroid levels tests from prenatal clinic during the period May to September 2015. Blood samples were analyzed within two hours using (Tosoh A11, Japan). Patients were not on rehabilitation drug therapy, neither on vitamin D supplement. Patients were tested for Thyroid Peroxides Antibody (TPOAb) and Thymoglobulin Antibody (TgAb) to exclude the presence of autoimmune thyroid disease (AITD) and the elevated antibody peroxides or thymoglobulin.² Blood samples were tested for FT3, FT4, TSH and 25 (OH) vitamins D. Reference range (1.2-4.4 pg/ml for FT3), (0.8–2.0 ng/dl for FT4) and (0.5–5.0 mU/l for TSH).⁴⁰ Vitamin D serum level was defined as deficiency, insufficiency and normal for serum level of 25 (OH) D of <=20 ng/ml, between 20 ng/ml and <30 ng/ml and normal >or=30 ng/ml respectively.¹⁶

Statistical analysis

Results were statistically analyzed by SPSS 11.5 for Windows. The mean and the standard deviation (SD) for all the variables were calculated. Analysis of variance F test (ANOVA) was used to compare

Table 1 Mean level of vitamin 25 (OH) D to age and number of patients

25(OH)D Range	No and % of Patients	Age Mean (Y)	Mean 25(OH)D ng/ml
<20	30(27.5%)	29	17.4
21-30	54(49.5%)	33	28.3
>30	25 (23.0%)	27	34.7
Total	109	29.7	

Table 2 Correlation between vitamin 25 (OH) D levels, TSH, FT4 and FT3

25(OH)D Range	No of Patients	Age Mean (Y)	FT3 pg/ml	FT4 ng/dl	TSH ulu/ml	r FT4	r TSH	r FT3	p FT4	p FT3	PTSH
<20	30(27.5%)	29	1.11	0.91	1.33	0.004	-0.11	0.005	<0.01	<0.01	<0.01
21-30	54(49.5%)	33	1.63	0.84	1.59	-0.17	0.019	-0.31	<0.01	<0.01	<0.01
>30	25(23.0%)	27	2.1	0.83	1.76	-0.06	-0.51	-0.042	<0.01	<0.01	<0.005
Total	109	29.7	1.61	0.88	1.58	-0.23	-0.067	-0.28	<0.01	<0.01	<0.015

Discussion

Significant of vitamin 25(OH) D was reported as a common condition throughout the world⁴¹ and deficiency/insufficiency range from 5% to 83.6%.^{29,43} During pregnancy can cause a series problems for pregnant women and their offspring.² Recent studies have shown an increase of vitamin D insufficiency in the Mediterranean region.² Jordan is close to that region and comparative study could lead to a significant outcome. Results in our study revealed 49.0% prevalence of 25 hydroxyvitamin D insufficiency in pregnant subjects who lived mainly in sunny zone which agree with other study² indicating that high levels of sunshine in Jordan might not necessarily compensate for vitamin D deficiency. Therefore, other factors should be investigated to understand the cause of vitamin D depletion during pregnancy so the right vitamin D concentration could be achieve. Hejlab might have negative effect on vitamin D cutaneous synthesis.⁴⁴ Many studies have shown significant relationship between serum 25-Hydroxyvitamin D and thyroid hormones during pregnancy due to the role of vitamin D in the function of cardiac, skeletal muscles, immune cell proliferation and differentiation.² As mentioned previously 25(OH) D status is Influenced by many factors^{2,11,44} one of these factor is thyroid hormones changes by fetus action causing depletion of TSH, FT4 and FT3 leading to various problems such as placental abruption, miscarriage, fetal growth retardation.⁴⁹ Other studies recommended vitamin D supplementation during pregnancy.^{8,12,25}

Many studies showed role of vitamin D on thyroid hormone due to its activity in thyroid gland^{2,11} and even in patients with thyroid

the results of all examined cases in all studied groups. The differences between mean values for each tested variable have been tested by student's "t" test. The correlations between serum Vitamin D and TSH were presented by correlation coefficient (r^2). Results considered non-significant or significant when $P >$ or $<$ 0.05, respectively.¹¹

Results

One hundred and nine pregnant women aged 19-45years (18.2 years age average) were examined. The mean 25(OH) D was 21.7±5.6 ng/ml (range 8.7 to 47.2). The mean level of serum Free T3, FT4 and TSH was 1.61 ± 0.21, ng/dl, 0.86 ± 0.23 ng/dl and 1.56 ± .91 μIU/ml respectively, number of patients showing vitamin D deficiency, insufficiency and sufficiency were 30 (27.5%), 54 (49.5%) and 25 (23.0%) respectively, with mean concentration of 25(OH) D serum of 17.4ng/ml,28.3 ng/ml and 34.7 ng/ml respectively, Table1. No significant correlation was found between vitamin D, TSH, FT4 and FT3 Table2. No correlation was observed between vitamin D and FT4 ($r = -0.064$ $p < 0.01$) and between vitamin D and FT3 ($r = -0.071$ $p < 0.01$) however, vitamin D sufficient group showed significant correlation with TSH($r = 0.51$ $p < 0.005$).

diseases and thyroid autoantibody.^{46,47} However, few studies focus on the link between 25-(OH)D and thyroid hormones during pregnancy. Therefore this study was conducted on group of pregnant women who lives in sunny Jordan and Hejlab is prevailing. The significant correlation between high vitamin D and low TSH ($p < 0.005$) in pregnant women with a sufficient level of vitamin D (> 30 ng/ml) revealed in our study which agrees with other study.² Meanwhile no significant statistical variation was found ($p < 0.01$) between vitamin D level and FT4 which agree with other studies^{2,9,11} adding to that correlation between vitamin D and FT3 ($p < 0.01$) was not clear suggesting further work is needed^{9,11} including larger study sample of pregnant women divided according to weeks of pregnancy, age and those wearing Hejlab.⁴⁴ Meanwhile if the responsible factors for vitamin D deficiency could not be revealed so that the correct concentration of vitamin D could maintain in pregnant women public health awareness should be reused and recommendation for vitamin D supplementation before and after pregnancy is extremely important.

Conclusion

Our results indicated that slight correlation between vitamin D insufficiency and low TSH level during pregnancy was observed however, no evidence was provided on the correlation between vitamin D, FT3 and FT4 therefore more research must be conducted on group of pregnant women divided according weeks of pregnancy, age and Hejlab meanwhile, recommendation for vitamin D supplementation is recommended.

Acknowledgments

None.

Conflicts of interest

None.

Funding

None.

References

- Urrutia Periria M, Sole D. Vitamin D deficiency in pregnancy and its impact on the fetus, the newborn and childhood. *Rev Paul Pediatr.* 2015;33(1):104-113.
- Lavalle G, Onori ME. Relationship between serum 25-Hydroxy vitamin D and Thyroid hormones during pregnancy in the North of Rome. *International Journal of Science and Research.* 2012; 3(10):358.
- McAree T, Jacobs B, Manickavasagar T, et al. Vitamin D deficiency in pregnancy - still a public health issue. *Matern Child Nutr.* 2013;9(1):23-30.
- Zipitis CS, Akobeng AK. Vitamin D supplementation in early childhood and risk of type 1 diabetes: a systematic review and meta-analysis. *Arch Dis Child.* 2008;93(6):512-517.
- Van Belle TL, Gysemans C, Mathieu C. Vitamin D in autoimmune, infectious and allergic diseases: a vital player? *Best Pract Res Clin Endocrinol Metab.* 2011;25(4):617-632.
- Lapillonne A. Vitamin D deficiency during pregnancy may impair maternal and fetal outcomes. *Med Hypotheses.* 2010;74(1):71-75.
- Merlino LA, Curtis J, Mikuls TR, et al. Vitamin D intake is inversely associated with rheumatoid arthritis: results from the Iowa Women's Health Study. *Arthritis Rheum.* 2004;50(1):72-77.
- Tamer G, Arik S, Tamer I, et al. Relative vitamin D insufficiency in Hashimoto's thyroiditis. *Thyroid.* 2011;21(8):891-896.
- Yamashita H, Noguchi S, Murakami T, et al. Seasonal changes in calcium homeostasis affect the incidence of postoperative tetany in patients with Graves' disease. *Surgery.* 2000;127(4):377-382.
- Mulligan ML, Felton SK, Riek AE, et al. Implications of vitamin D deficiency in pregnancy and lactation. *Am J Obstet Gynecol.* 2010;202(5):429.
- Mackawy AMH, Bushra Mohammed AM, Al rashidi BM. Vitamin D Deficiency and Its Association with Thyroid Disease. *Int J Health Sci (Qassim).* 2013;7(3):267-275.
- Zhao Y, Miao W, Li C, et al. "Dynamic changes in serum 25-hydroxyvitamin D during pregnancy and lack of effect on thyroid parameters". *PLoS One.* 2014;9(3):e 90161.
- Holick M. Vitamin D: photobiology, metabolism, mechanism of action and clinical applications. (5th edn), Humana Press , Washington DC, USA. 2003. p.1160.
- Heaney RP. The vitamin D requirement in health and disease. *J Steroid Biochem Mol Biol.* 2005. 97(1-2):13-19.
- Institute of Medicine. Dietary reference intakes for calcium and vitamin D. *Institute of Medicine website.* 2010.
- Qamar J Khan MD, Carol J Fabian MD. How I Treat Vitamin D Deficiency. *J Oncol Pract.* 2010; 6(2):97-101.
- Tsiaras WG, Weinstocks MA. Factors influencing vitamin D status. *Acta Derm Venereol.* 2011; 91(2):115-124.
- Andersen R, Broth C, Jacobsen J, et al. Seasonal changes in vitamin D status among Danish adolescent girls and elderly women: the influence of sun exposure and vitamin D intake. *Eur J Clin Nutr.* 2013;67(3):270-274.
- Andersen S, Jakobsen A, Laurberg P. Vitamin D status in North Greenland is influenced by diet and season: indicators of dermal 25-hydroxy vitamin D production north of the Arctic Circle. *Br J Nutr.* 2013;110(1):50-57.
- Bodnar LM, Simhan HN, Powers RW, et al. High prevalence of vitamin D insufficiency in black and white pregnant women residing in the northern United States and their neonates. *J Nutr.* 2007;137(2):447-452.
- van der Meer IM, Karamali NS, Boeke AJ, et al. High prevalence of vitamin D deficiency in pregnant non-Western women in The Hague, Netherlands. *Am J Clin Nutr.* 2006;84(2):350-353.
- Ojah RC, Welch JM. Vitamin D and musculoskeletal status in Nova Scotian women who wear concealing clothing. *Nutrients.* 2012;4(5):399-412.
- Tsur A, Metzger M, Dresner Pollak R. Effect of different dress style on vitamin D level in healthy young Orthodox and ultra-Orthodox students in Israel. *Osteoporos Int.* 2011;22(11):2895-2898.
- Datta S, Alfaham M, Davies DP, et al. Vitamin D deficiency in pregnant women from a non-European ethnic minority population—an interventional study. *BJOG.* 2002;109(8):905-908.
- Vandevijvere S, Amsalkhir S, Van Oyen H, et al. High prevalence of vitamin D deficiency in pregnant women: a national cross-sectional survey. *PLOS ONE.* 2012;7(8):e43868.
- Hedlund L, Brembeck P, Olausson H. Determinants of vitamin D status in fair-skinned women of childbearing age at northern latitudes. *PLOS ONE.* 2013;8(4):e60864.
- Charatcharoenwitthaya N, Nanthakomton T, Somprasit C, et al. Maternal vitamin D status, its associated factors and the course of pregnancy in Thai women. *Clin Endocrinol (Oxf).* 2013;78(1):126-133.
- Thuesen B, Husemoen L, Fenger M, et al. Determinants of vitamin D status in a general population of Danish adults. *Bone.* 2012;50(3):605-610.
- Bodnar LM, Catov JM, Simhan HN, et al. Maternal vitamin D deficiency increases the risk of preeclampsia. *J Clin Endocrinol Metab.* 2007;92(9):3517-3522.
- Negro R, Mestman JH. Thyroid disease in pregnancy. *Best Pract Res Clin Endocrinol Metab.* 2011; 25:927-943.
- Krassas GE, Poppe K, Glinooer D. Thyroid function and human reproductive health. *Endocr Rev.* 2010;31(5):702-755.
- Alzaim M, Wood RJ. Vitamin D and gestational diabetes mellitus. *Nutr Rev.* 2013;71:158-167.
- Karakosta P, Alegakis D, Georgiou V, et al. Thyroid dysfunction and auto antibodies in early pregnancy are associated with increased risk of gestational diabetes and adverse birth outcomes. *J Clin Endocrinol Metab.* 2012;97(12):4464-4472.
- Urrutia RP, Thorp JM. Vitamin D in pregnancy: current concepts. *Curr Opin Obstet Gynecol.* 2012;24(2):57-64.
- Aghajafari F, Nagulesapillai T, Ronksley PE, et al. Association between maternal serum 25-hydroxyvitamin D level and pregnancy and neonatal outcomes: systematic review and meta-analysis of observational studies. *BMJ.* 2013;346.
- Levenson CW, Figueiroa SM. Gestational vitamin D deficiency: long-term effects on the brain. *Nutr Rev.* 2008;66(12):726-729.
- Li Y, Shan Z, Teng W, et al. Abnormalities of maternal thyroid function during pregnancy affect neuropsychological development of their children at 25–30 months. *Clin Endocrinol (Oxf).* 2010; 72(6):825-829.

38. Deluca HF. Evolution of our understanding of vitamin D. *Nutr Rev.* 2008;66(10 suppl 2):S73-87.
39. Dawodu A, Wagner CL. Prevention of vitamin D deficiency in mothers and infants worldwide - a paradigm shift. *Paediatr Int Child Health.* 2012;32(1):3-13.
40. Kaplan MM. Clinical perspectives in the diagnosis of thyroid disease. *Clin Chem.* 1999;45(8): 1377-1383.
41. Lippi G, Montagnana M, Meschi T, et al. "Vitamin D concentration and deficiency across different ages and genders". *Aging Clinical and Experimental Research.* 2007;24(5):548-551.
42. Brembeck P, Winkvist A, Olausson H. Determinants of vitamin D status in pregnant fair-skinned women in Sweden. *Br J Nutr.* 2013;110(5):856-864.
43. Xiang F, Jiang J, Li H, et al. High prevalence of vitamin D insufficiency in pregnant women working indoors and residing in Guiyang, China. *J Endocrinol Invest.* 2013;36(7):503-507.
44. Battikhi MN. Significant of serum 25-Hydroxyvitamin D and Thyroid Hormones levels in pregnant women in Jordan. *JMEN.* 2016;3(1):1.
45. Azizi F, Amouzegar A, Mehran L, et al. "Screening and management of hypothyroidism in pregnancy: Results of an Asian survey". *Endocrine Journal.* 2014;61(7):697-704.
46. Zhang Q, Wang Z, Sun M, et al. "Association of high vitamin D status with low circulating thyroid stimulating hormone independent of thyroid hormone levels in middle-aged and elderly males". *Int J Endocrinol.* 2014; 631819.
47. Goswami R, Marwaha RK, Gupta N, et al. Prevalence of vitamin D deficiency and its relationship with thyroid autoimmunity in Asian Indians: a community-based survey". *Br J Nutr.* 2009; 102(3):382-386.