

Relation of the 25 (OH) D Levels and Preterm Labour

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ABSTRACT

Pregnant women are a risk group vitamin D insufficiency found among greater than 50% of pregnant females. Actually, there few researches and knowledge which associate the Maternal 25(OH) D level and premature labour, and no one carried in Iraq. The aim of this research is to find out any relation between the maternal plasma 25(OH) D levels of females who have gave birth to premature (< 36 weeks) in comparison to females with full-term neonates in both groups . The current study is a case control research was carried out between January-August 2020, at the department of gynecology and obstetrics at Azadi Teaching Hospital in Kirkuk Governorate. A convenient sample was randomly selected consist of 30 Mothers with premature delivery, compared with 30 mothers term pregnancy delivery, the newborns were weighing >2500g and appropriate for gestational age. Revision of maternal ANC cards were carried out for investigations, ultrasonography, date of LMP of mothers', as well as fetal anthropocentric measurements through the conception period. The mean Vitamin D level was (18.6±6.7) among preterm deliveries, which is lower significantly from those with full term delivery (27.5±6.2), P value < 0.0001, as represented in figure 1. Deficient vitamin D level was reported among 15(50%) of preterm delivered mothers versus 6(20%) of full term mothers. insufficient vitamin D level was reported among 12(40%) of preterm delivered mothers versus 9(30%) of full term mothers. sufficient vitamin D level was reported among 3(10%) of preterm delivered mothers versus 15(50%) of full term mothers. The low levels Vitamin D level is significantly associated with premature deliveries.

Keywords: Vitamin D deficiency, Preterm Labor prematurity, vitamin D level

DOI: <https://doi.org/10.32441/kjps.04.01.p4>

علاقة مستويات 25 D (OH) والولادة المبكرة

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الملخص

تعتبر النساء الحوامل من الفئات المعرضة لنقص فيتامين (د) الموجود بين أكثر من 50٪ من النساء الحوامل. هناك القليل من الأبحاث والمعرفة التي تربط بين مستوى 25 D (OH) للأم والولادة المبكرة ، ولم يتم إجراء أي بحث في العراق. الهدف من هذا البحث هو معرفة أي علاقة بين مستوى بلازما الأم 25 D (OH) للإناث اللائي ولدن ولادة مبكرة (أقل من 36 أسبوعًا) مقارنة بالإناث ذوات الولادة التامة. الدراسة الحالية عبارة عن بحث حالة شواهد أجريت في الفترة ما بين كانون الثاني وآب 2020 ، في قسم أمراض النساء والتوليد في مستشفى آزادي التعليمي في محافظة كركوك. تم اختيار عينة ملائمة بشكل عشوائي تتكون من 30 أم مع ولادة مبكرة (أقل من 36 أسبوعًا) ، و 30 أمًا ولادات حمل كاملة المدة (37-41 أسبوعًا) ، والذين كانوا مناسبين لعمر الحمل ووزن الولادة < 2500 جم . تم إجراء مراجعة لبطاقات ما قبل الولادة من أجل الفحوصات المخبرية ، والتصوير بالموجات فوق الصوتية ، وتاريخ آخر دورة شهرية للأم ، والقياسات البشرية للجنين من خلال المراقبة التوليدية للحمل. كان متوسط مستوى فيتامين د (6.7 ± 18.6) بين الولادات المبكرة ، وهو أقل بكثير من أولئك الذين لديهم ولادة كاملة المدة (6.2 ± 27.5) ، قيمة $P < 0.0001$ ، كما هو موضح في الشكل 1. تم الإبلاغ عن مستوى نقص فيتامين د بين 15 (50٪) من الأمهات المولودين قبل الأوان مقابل 6 (20٪) من الأمهات الناضجات. تم الإبلاغ عن عدم كفاية مستوى فيتامين (د) بين 12 (40٪) من الأمهات المولودات قبل الأوان مقابل 9 (30٪) الأمهات الناضجات. تم الإبلاغ عن مستوى كاف من فيتامين د بين 3 (10٪) من الأمهات المولودات قبل الأوان مقابل 15 (50٪) من الأمهات الناضجات. ترتبط المستويات المنخفضة من فيتامين د بشكل كبير بالولادات المبكرة.

الكلمات الدالة: نقص فيتامين د والولادة المبكرة ، ومستوى فيتامين د.

Introduction

A secosteroid hormone that its main role is calcium and phosphorus homeostasis regulation called Vitamin D (25 (OH. Actually, vitamin D body's requirement is taken through its synthesis in the skin during sun light exposure and then transformed to active form in liver & kidney. [1] Vitamin D deficiency prevalence is globally wide spread, Asian and the Middle East females have elevated risks of 25(OH) D deficiency: in Turkey 50%, in Pakistan 45%, and in India 60%. [2] Severe vitamin D deficiency in Iraq was documented among reproductive aged females at (76%) and 25 (OH) D insufficiencies (18%), and only 7% had sufficient serum level. [3] Pregnant women are a risk group vitamin D insufficiency found among greater than 50% of pregnant females [4]

Vitamin D concentration level of the mother has an impact on its concentration in fetus, 25(OH) D, the calcium and phosphorus placental transfer, also had a role in as well as equilibrium of hormones & well-functioning immune system, the later were important in skeletal system development and feto-placental solidity.[5] Several researches associate reduced Maternal concentration of 25(OH) D and preeclampsia, gestational diabetes, [6, 7], and intrauterine growth restriction [8]. Actually, there few researches and knowledge which associate the Maternal 25(OH) D level and premature labour, and no one carried in Iraq. The aim of this research is to find out any relation between the Maternal plasma 25(OH)D level of females who have gave birth to premature (< 36 weeks) in comparison to females with full-term neonates in both groups.

Patients & Methods

The current study is a case control research was carried out between January-August 2020, at the department of gynecology and obstetrics at Azadi Teaching Hospital in Kirkuk Governorate. A convenient sample was randomly selected consist of 30 Mothers with premature delivery (< 36 weeks), and 30 mothers full term pregnancy deliveries and their neonates (37- 41 weeks), who were appropriate for gestational age and with a birth weight > 2500 g. Exclusion criteria encompass the following: Mothers with type 1 DM, rheumatic disease, kidney disease, and those using immunosuppressant were excluded. The mothers included in the study answered questions in a standardized questionnaires, that encompass questions about their socioeconomic situations, medications, education, pre-existing problems

and/or obstetric disease, mineral supplements or vitamin utilization (iron, folic acid, and vitamin D), sunlight exposure, and the regular sunscreen utilization .

Revision of the maternal cards of antenatal care carried out for lab investigations, ultrasonography, dating of LMP of mothers', and recorded measurement's of fetus thorough the conception. Mother baseline height and weight in Pre-pregnancy, along with weight gain per week during conception. BMI (kg/m²) were based on the height and weight measurements. Blood samples of 10 mL from mother's blood on delivery in the obstetrics center. At once blood placed in EDTA and dry then send for lab for measure the level of 25(OH) D. The vitamin 25(OH) D cutoff points were as follows: sufficient > 30 ng/mL, insufficient 20-30 ng/mL and deficiency < 20 ng/dL [9]. Advised levels for pregnant females were > 30 ng/mL. enroled mothers were informed about the study and their acceptance for participation in the research that showed the agreement to undergo the procedures of the research..

Results

The greatest frequency of full term & premature delivered mothers has primary education 12 (40%), 14 (46.7%), respectively. Most of the premature and full term delivered mothers were multigravida 16 (53.3%), 19 (63.3%) respectively in a statistically no one significant relation. Higher percentages of Full term mothers had folic acid supplementation 26 (86.7%) than those with premature pregnancy 17 (56.7%), this variation was statistically significant. There were equal percentage regarding iron supplementation among premature and full term delivered mothers 23(76.7%), 26(86.7%), respectively this relation was statistically not significant. None significant difference was shown in table 1 between premature and full term delivered mothers regarding vitamin D supplementation 3 (10%), 2 (6.7%) respectively. Conception complications of gestational hypertension UTI, was significantly higher among those with preterm delivery 12(40%), 13(43.3%)) than those with full term delivery 5(16.7%), 6(20%) respectively. Antenatal care visits was irregular among 24(80%) of those with preterm delivery group while only 7(23.3%) of those with full term pregnancy had irregular visits.

The mean Vitamin D level was (18.6±6.7) among preterm deliveries, which is lower significantly from those with full term delivery (27.5±6.2), P value < 0.0001, as represented

in figure 1. Deficient vitamin D level was reported among 15(50%) of preterm delivered mothers versus 6(20%) of full term mothers. insufficient vitamin D level was reported among 12(40%) of preterm delivered mothers versus 9(30%) of full term mothers. sufficient vitamin D level was reported among 3(10%) of preterm delivered mothers versus 15(50%) of full term mothers. This relation was statically significant as shown in table 2.

Table 1. The distribution of study sample according to multiple risk factors and type of delivery

Variable		preterm delivery		full term delivery		P value
		F	%	F	%	
Age		25.8±5.4		26.4±6.3		
Education	Illiterate	7	23.3	6	20.0	>0.05 ^{NS}
	1ry	12	40.0	14	46.7	
	2ndry	7	23.3	5	16.7	
	high education	4	13.3	5	16.7	
Parity	Primigravida	14	46.7	11	36.7	>0.05 ^{NS}
	Multigravida	16	53.3	19	63.3	
supplementation during pregnancy	folic acid	17	56.7	26	86.7	<0.05 S
	Iron	23	76.7	26	86.7	>0.05 ^{NS}
	Calicum	4	13.3	3	10.0	>0.05 ^{NS}
	Vit D	3	10.0	2	6.7	>0.05 ^{NS}
pregnancy complication	gestational HT	12	40.0	5	16.7	<0.05 S
	UTI	13	43.3	6	20.0	<0.05 S
ANC	Regular	6	20.0	23	76.7	<0.05 S
	Irregular	24	80.0	7	23.3	

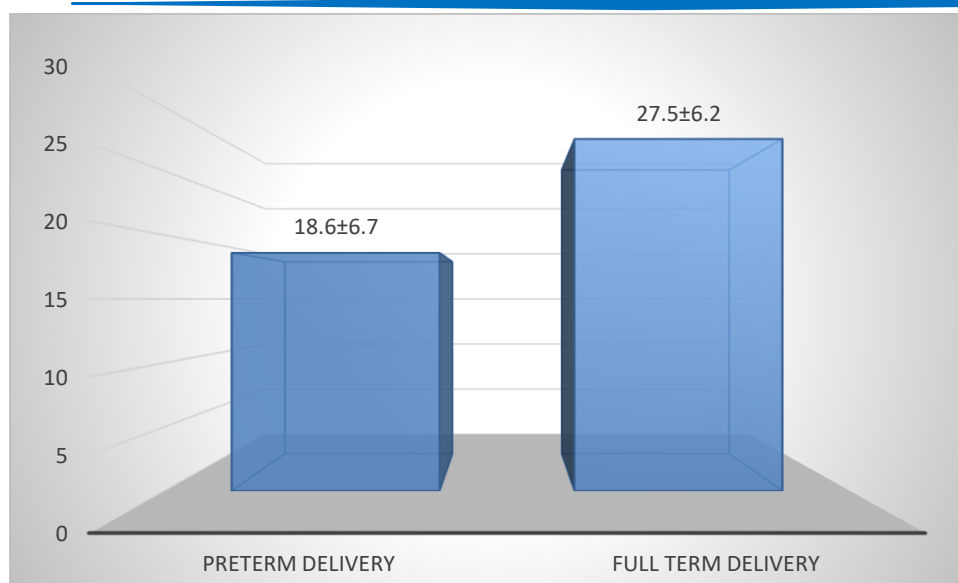


Figure 1. The mean vitamin D level among preterm and full term delivered mothers.

Table 2. Frequency distribution of vitamin D level among both study groups

Vitamin D level	preterm delivery		full term delivery	
	F	%	F	%
Deficiency	15	50.0	6	20.0
insufficiency	12	40.0	9	30.0
sufficiency	3	10.0	15	50.0
Total	30	100.0	30	

P value <0.005 significant Discussion

Discussion

Throughout conception, the only source of fetal vitamin D is the maternal vitamin D which spreads across the placenta. Elevated production of hepatic vitamin D binding protein (DBP) in relation with decreased in levels of albumin, through conception alter the metabolism of maternal vitamin D. resulting from this is decreased free vitamin D level, and elevated placental 1, 25(AH) 2 D3 production. [10] In the current research, there was a significant

elevated percentages of Full term mothers had folic acid supplementation (86.7%) than those with premature conception (56.7%), this goes with a study carried out Papadopoulou, E et al (2013) that the folic acid daily intake of a dose of 5 mg supplemental was related with a 31% reduction in the risk of premature delivery (RR, 0.69; 95 % CI, 0.44, 0.99), [11] A research of a meta-analysis type carried out by Li Bingbing et al, revealed that the higher is the folate levels and the supplementation of the folic acid is significantly correlated with a reduced general risk of whole PTB. [12]

While a research achieved by Rolschau et al. have shown a reduced risk for premature deliveries and SGA neonates in females receiving folic acid pre-pregnancy or in the first half of conception in affluent Northern worlds. [13] No relation was found by Timmermans et al. between the impacts of folic acid supplementation on gestational age. [14]

The gestational hypertension was considerably higher among those with premature delivery 12 (40%), than those with full term delivery 5 (16.7%) UTI, was considerably higher among those with preterm delivery (43.3%) than those with full term delivery (20%) the mean Vitamin D level was (18.6 ± 6.7) among preterm deliveries In this study, this goes Letícia VD et al who found vitamin D level among preterm mothers 20.8 ± 11.8 , full term mothers was 26.5 ± 9.7 . [15] But was higher than reported in Egypt by Tahoun AM et al 2018 that PTB (16.15 ± 8.63) , PTB (10.93 ± 4.40) [16]. In the current, it was found a considerable reduced mean vitamin D level among premature deliveries than full term deliveries this was in line of other researches carried out by Letícia VD et al (2020), Tahoun AM et al (2018), Burris HH et al (2012), Kim MS et al (2007) [16, 17, 18]. On the other hand Lixia Yang et al found a non-significant effect of vitamin D deficiency on PTB for OR was 0.78 [19].

In the current research the Deficient vitamin D level was documented among 15 (50%) of premature delivered mothers versus 6 (20%) of full term mothers, insufficient vitamin D level was documented among 12 (40%) of preterm delivered mothers versus 9 (30%) of full term mothers, sufficient vitamin D level was documented among 3(10%) of premature delivered mothers versus 15(50%) of full term mothers.

This finding goes with Tahoun AM et al found that 93% of cases having preterm labor had abnormally low 25 (OH) D levels. Where 60% of patients showed deficient 25 (OH) D (<12

ng/ml), 33% of patients showed insufficient 25 (OH) D (>20 and <30 ng/ml), while 7% of cases showed normal vitamin D level. [16] In another study done by Burris HH et al 2012 found, 98.9% of preterm infants had vitamin D insufficiency or deficiency, and 51.1% of preterm infants were severely vitamin D deficient. [17] Chen Yuan-Hua et al 2018 China followed large number of mothers found that 8.23% of those mothers with sever vitamin D deficiency, (RR: 3.28) and 3.81% of those mothers with insufficient vitamin D level (RR: 1.45) had preterm delivery [20] Levels of vitamin D concentration in premature delivered females was considerably reduced in association to its concentration in the full-term delivered females, and vitamin deficiency was documented in around 50% of the females affected by PTN. [15]

Flood-Nichols SK et al 2015 found in a retrospective study 235 patient studied the relation of vit d level and pregnancy complications found that 10% of preterm deliveries had deficient, 60% insufficient level and 30% had sufficient level, the study concluded that there is no relation between 1st trimester vit d level and pregnancy complication. The mean vit D was 28.4 rang (19.9-72.3) [21]

An early report showed that the active hormone circulating 25(OH)D is transformed to 1,25(OH)2D3 to 40 ng/ml [22] in an optimal way. Several researches of vitamin D supplementation showed that preterm delivery rates for women with vitamin D ≤ 20 ng/ml are substantially higher compared to those with serums vitamin D ≥ 40 ng/ml, concluding a decreased PTD with increasing maternal vitamin D level .[23]

The low level of vitamin D among both groups preterm and full term could be explained by the finding in previous results in Karbala in Iraq about the prevalence of vitamin D among women in reproductive age found that (87%) of the females had low level of vitamin D in front of only 13% of them had sufficient vitamin D females conducted in the study and economic status of them, amount of milk taking per week, parity and with the duration of sun exposure. [24] The etiology of women's decreases in vitamin D is likely to be multi-stakeholders, but partially due to the increased BMI and protection of the sun combined with a reduced consumption of vitamin D, such as milk or other dairy products. Sadly, an increase in the use in younger and older adults of multivitamins and dietary supplements appears not to be associated with a related increase in the serum 25-OH vitamin D levels. [25, 26] In recent randomized controlled studies, loading doses as high as 1000–4000 IU/day were needed

before adequate vitamin D plasma concentrations were measured [23,26] In most of geographical regions, where sunshine enough for the proper photo-cutaneous synthesis of vitamin D; however, the greater number of Middle East women who spend most of their time indoors cannot benefit from this source through cultural practices, such as clothing and veiling among Muslim women.[27]

Conclusions

The low levels Vitamin D level is significantly associated with premature deliveries. More researches needed to explore the benefit of vitamin D supplementation in preventing preterm labors.

References

- [1] Holick, M. F. “*Resurrection of vitamin D deficiency and rickets*”, J. Clin. Invest 116, 2062–2072. (2006).
- [2] C. Palacios & L Palacios,” *Gonzalez. Is vitamin D deficiency a major global public health problem?* “J. Steroid Biochem. Mol. Biol 144: 138–145. (2014).
- [3] H A Hantoosh , MH Mahdi, BW Imran, AA Yahya. “*Prevalence of vitamin D deficiency in Iraqi female at reproductive age*”. Medical Journal of Babylon,16 (2),119,(2019)
- [4] S. Rajneeta, Susan M.B. C A Morton . Jr Camargo. C. G Cameron, “*Global summary of maternal and newborn vitamin D status - a systematic review*”. Matern Child Nutr;12:647–68. .(2016)
- [5] Olmos-Ortiz A, Avila E, Durand-Carbajal M, Díaz L. “*Regulation of calcitriol biosynthesis and activity: focus on gestational vitamin D deficiency and adverse pregnancy outcomes*”. Nutrients, 7, 443–80. (2015)
- [6] SS Zhou, YH Tao, K Huang, BB Zhu, FB Tao. “*Vitamin D and risk of preterm birth: up-to-date meta-analysis of randomized controlled trials and observational studies*”. J Obstet Gynaecol Res, 43,247–56, (2017)

- [7] AK Amegah, MK Klevor, CL Wagner. “*Maternal vitamin D insufficiency and risk of adverse pregnancy and birth outcomes: a systematic review and meta-analysis of longitudinal studies*”. PLoS One.;12:e0173605. (2017)
- [8] Y Tian, C Holzman, AM Siega-Riz, MA Williams, N Dole, DA Enquobahrie, CD Ferre.” *Maternal serum 25-Hydroxyvitamin D concentrations during pregnancy and infant birthweight for gestational age: a three-cohort study*”, Paediatr Perinat Epidemiol,30,124–33. (2016)
- [9] Gel-H F, R Bouillon, B Clarke, M Chakhtoura, C Cooper, M McClung, Singh RJ. “*Serum 25-Hydroxyvitamin D levels: variability, knowledge gaps, and the Concept of a desirable range*”. J Bone Miner Res. 30,1119–33, (2015)
- [10] Larqué E, Morales E, Leis R, Blanco-Carnero JE. “*Maternal and Foetal health implications of vitamin D status during pregnancy*”. Ann Nutr Metab., 72 (3):179–92,(2018)
- [11] E Papadopoulou.,, N.Stratakis, , T Roumeliotaki,. et al. “*The effect of high doses of folic acid and iron supplementation in early-to-mid pregnancy on prematurity and fetal growth retardation: the mother–child cohort study in Crete, Greece (Rhea study)*”, Eur J Nutr 52, 327–336 (2013). <https://doi.org/10.1007/s00394-012-0339-z>.
- [12] Li Bingbing , “ *Folic Acid and Risk of Preterm Birth: A Meta-Analysis*”. Frontiers in Neuroscienc,e 13,1284, (2019)
- [13] J Rolschau, K Kristoffersen, M Ulrich, P Grinsted, E Schaumburg, N Foged .”*The influence of folic acid supplement on the outcome of pregnancies in the county of Funen in Denmark.*” Part I. Eur J Obstet Gynecol Reprod Biol, 87(2),105-10, (1999)
- [14]Timmermans S, Jaddoe VWV, Hofman A, Steegers-Theunissen RPM, Steegers EAP “*Periconception folic acid supplementation, fetal growth and the risks of low birth weight and preterm birth: the Generation R Study*”. Br J Nutr, 102(05),777–785, (2009)
- [15] Letícia VD et al.” *Association between vitamin D plasma concentrations and VDR gene variants and the risk of premature birth.*” BMC Pregnancy and Childbirth; 20,3, (2020)
- [16] AM Tahoun. “*Maternal Vitamin D Level in Preterm and Term Labouras a Risk Facto,*”. The Egyptian Journal of Hospital Medicine, 73 (6), 6818-27, (2018)

- [17] HH Burris, SL Rifas-Shiman, K Kleinman, " *Vitamin D deficiency in pregnancy and gestational diabetes mellitus*". Am J Obstet Gynecol., 207, 182.e1–8, (2012)
- [18] Kim MS et al. " *Alpha,25(OH)2D3-induced transrepression by vitamin D receptor through E-box-type elements in the human parathyroid hormone gene promoter*", Mol Endocrinol,21, 334-42,(2007)
- [19] Lixia Yang et al." *The Correlation Between Serum Vitamin D Deficiency and Preterm Birth*". Med Sci Monit, 22, 4401-5, (2016)
- [20] Chen Yuan-Hua et al. " *Influent factors of gestational vitamin D deficiency and its relation to an increased risk of preterm delivery in Chinese population*". Scientific Reports 8:3608, (2018)
- [21] SK Flood-Nichols," *Tinnemore D, Huang RR, Napolitano PG, Ippolito DL. Vitamin D deficiency in early pregnancy*". PLoS One.;10(4):e0123763. (2015)
- [22] Hollis, BW et al. " *Vitamin D supplementation during pregnancy: double-blind, randomized clinical trial of safety and effectiveness*". J. Bone. Miner. Res, 26, 2341-57,(2011).
- [23] Wagner CL, McNeil R, Hamilton SA, Winkler J, Rodriguez Cook C, Warner G, Bivens B, Davis DJ, Smith PG, Murphy M, Shary JR, Hollis BW. " *A randomized trial of vitamin D supplementation in 2 community health center networks in South Carolina*". Am J Obstet Gynecol.,208(2),137.e1-13, (2013)
- [24] Al Janaby S, Al Timimy G, Al yassery R. " *Prevalence of Vitamin D Deficiency of Females in Karbala, Iraq,2017*". Karbala Journal of Medicine, 13(1), 2319-2325(2020).
- 25-Yetley EA. Assessing the vitamin D status of the US population. Am J Clin Nutr 2008;88(2):558S–564S,
- [26] Holick MF et al. " *Evaluation, treatment, and prevention of vitamin D deficiency: an Endocrine Society clinical practice guideline*". J Clin Endocrinol Metab,96(7),1911–1930 (2011).
- [27] Aghajafari F, Nagulesapillai T, Ronksley PE, Tough SC, O'Beirne M, Rabi DM. " *Association between maternal serum 25-hydroxyvitamin D level and pregnancy and neonatal outcomes: systematic review and meta-analysis of observational studies*". BMJ, 26, 346:f1169. (2013)