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Relation of maternal 25 (OH) D Concentration and preterm labour

ABSTRACT

Background:

WHO reported that about 15 million neonates are born preterm, with about million deaths occurring during infancy PTB infants who survive frequently suffer from chronic pulmonary diseases and learning deficits, causing heavy burdens for society and family. This study aimed at finding the relation between preterm labour and maternal (25(OH) D blood level.

Subject and Methods

A prospective cohort study, conducted in obstetric department in Salah Al-Deen general hospital from 31st Jan to the 11st July 2021. A convenient sample of 154 pregnant women in the 2nd trimester were taken and followed up for assessment of pregnancy outcome. Inclusion criteria include all pregnant women aged 18-45 years, and planned delivery at Salah Al-Deen general Hospital. Data collection done through: standardized questionnaire. Blood samples were collected from the mothers on 13-24 week and ≥32 week and followed to report the prevalence of preterm delivery.

Results:

Deficient vitamin D3 found among 40 (27%) of the total pregnant women, insufficient level found among 110 (73%) of the women while none of the pregnant women had sufficient vitamin D3 at 32 week of gestation. Vitamin D3 deficiency found among 3 (12%) of the preterm labour and 2(1.2%) of the full term labour group, while insufficient vitamin D3 found among 21 (84%) of the preterm labour and 108 (83.7 %) full-term labour in a statistically significant relation. The correlation of the vitamin D3 level at 13-24 week of gestation and gestational age show significant linear (r= 0.426). The correlation of the vitamin D3 level at 24 - 32 week of gestation and gestational age show significant linear (r= 0.449).

Conclusions:

Vitamin D3 deficiency found significantly among women of the preterm labour than the full term labour group.

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Introduction:

Preterm labor is labor that starts before 37 weeks of pregnancy. Preterm labour is of multifactorial etiology in which maternal & fetal medical conditions (vaginal bleeding, multiple pregnancy, and hormonal changes) are included, in addition to socioeconomic situation (1) but a syndrome of spontaneous preterm labour results in 70% of all preterm labour (2). One of the fat soluble essential vitamins is vitamin D because of its important role in calcium metabolism (3). Pregnancy is a critical time in the lifecycle of a woman where she is responsible not only for her own well-being, but also that of her developing fetus, a process that continues during lactation. Until recently, the impact of vitamin D status during this period had not been fully appreciated. Data regarding the importance of vitamin D in health have emerged to challenge traditional dogma, and suggest that vitamin D – through its effect on immune function and surveillance – plays a role beyond calcium and bone metabolism on the health status of both the mother and her fetus. Following birth, this process persists; the lactating mother continues to be the main source of vitamin D for her infant. Thus, during both pregnancy and lactation, maternal deficiency predicts fetal and infant deficiency; the significance of this is just beginning to be understood and will be highlighted in this review. (4) During pregnancy, maternal serum level of vitamin D increases considerably and the placenta is a major site of activation of vitamin D. During pregnancy the maternal metabolism undergoes multiple alterations of physiological processes to ensure a healthy development of the fetus. A close relationship between maternal and fetal vitamin D status during pregnancy underscores the importance of an optimal supply in this critical time. Maternal supply status could significantly affect the development and health of the offspring in utero and in later life. The extent the problem Vitamin D deficiency during pregnancy has been documented in many populations across the globe and

is often associated with adverse maternal and birth outcomes. (2, 3) In fact, observational studies from all over the world show a link between low vitamin D levels and adverse pregnancy related outcomes for mother and child [4]. The reference range of the total 25(OH)D level is 25-80 ng/mL. In a combined post hoc analysis of two studies, maternal 25(OH) D <50 nmol/l was associated with increased risk of preterm birth. Interestingly, this association was stronger near the delivery date, indicating that optimization of maternal vitamin D levels in the third trimester of pregnancy might be beneficial. [5]

Aim of the study: This study aims to find the relation between preterm labor and maternal (25(OH)D blood level.

Patients and Methods

Data collection done by1- Questionnaire: Data collection done by face to face interview with the pregnant women attending the gynecology and obstetrics out patient, using the structured questionnaire developed by the researcher include the following information: Information regarding the pregnant women demographic variables [Age, Educational level], obstetrical history (parity, gravity, abortion, , history of pregnancy induced illness like hypertension, Diabetes mellitus, and urinary tract infection), history of receiving supplements like Vitamin D, Folic acid and iron during pregnancy. Antenatal care visits, if regular or not and number of visits. History of sunscreen use, sun exposure and duration of sun exposure. 2- Clinical examination and laboratory investigations done: Chronic hypertension or gestational hypertension (pregnancy induced hypertension in whom blood pressure 140/90 in 2nd half of pregnancy, or systolic blood pressure increased 30mmHg and or diastolic increased 15 mmHg over baseline on two occasions in addition to edema and confirmed albuminuria. Gestational diabetes mellitus (DM) was diagnosed by oral glucose tolerance test (with 75 g glucose, with two or more positive values of plasma glucose; fasting ≥95

mg/dL, 1 hour ≥180 mg/dL, 2 hours ≥155 mg/dL). Anemia was considered present when Hb <11gm/dl till 12 wk of gestation or <10.5 gm/dl and clinical features afterwards). Preterm was diagnosed as gestational age at delivery < 37 completed weeks. 4- Body mass index counted according to formula of [kg /(height in m^2) categorized as (underweight BMI<18.5, normal weigh BMI 18.5–24.9, over weight BMI 25.0–29.9, obese BMI >30) [62] 5-Serum vitamin D level (in the form of 25(OH)D), were divided into four stages in accordance with international standards [6] normal (equal or higher than 30 ng/mL), insufficient (between 20 and 30 ng/mL), mild deficiency (between 10 and 20 ng/mL), and moderate to severe deficiency (less than 10 ng/mL). The IOM standard stipulates that higher than 20 ng/mL of 25(OH)D is sufficient for body metabolism. We used 20 ng/mL as the cut-off point for analyzing the correlation between vitamin D deficiency and PTB. [7] 3- Laboratory examination: Blood samples were collected from the mothers on 13-24 week and follow up examination at ≥ 32 week and followed to report the prevalence of preterm delivery. 10 mL of the mother's blood were drawn by arm venipuncture. Ethical Considerations, at the beginning of the interview, verbal informed consent was obtained individually from all participants after clearly explaining the purpose of the study and the type of data required, and respondents were assured of data confidentiality and privacy. The statistical analysis done by questionnaire forms that checked at the end of the interview to avoid missing data. SPSS Software version 25.0 was used to perform statistical analysis for this study. Qualitative data were presented as numbers and percentages, while continuous data were presented as mean ± standard deviation. To establish the relation of vitamin D level with preterm labour, the linear regression and odd ratios (OR) was calculated. Comparison of study groups was carried out using chi-square test for categorical data, and Student's t-test for

continuous data. P-value of < 0.05 was considered statistically significant.

Results

Total pregnant women enrolled in the study was 154 women 25(16.23%) ended with preterm labour while 129 (83.77%) had full-term labour. Those aged < 20 years and 31-40 years among preterm labour group 5(20%), 7(28%) respectively were higher than full term group 23(17.8%), 31(24%), this relation was statistically not significant as shown in table 3.1. pregnancy weight gain was low among 7(28%) of the preterm labour group while it was low among 6(4.7%) of the full term group, this relation was statistically significant as shown in table 1. It is very important to know that the gaining the right amount of weight during pregnancy can help protect your health and the health of your baby. If you gain too little weight during pregnancy, you're more likely than other women to: Have a premature baby. A premature baby is born too early, before 37 weeks of pregnancy.

Table 1. Distribution of study sample according to gestational length & general characteristics.

	Preterm labour		**Full-term labour**		**Total**		**P value**
	No.	%	No.	%	No.	%	
Age							
< 20 Years	5	20.0%	23	17.80%	28	18.20 %	0.23
20-30 Years	12	48.0%	75	58.10%	87	56.50 %	
31-40 Years	7	28.0%	31	24.00%	38	24.70 %	

> 41 years	1	4.0%	0	0.00%	1	0.60%	
Education							
Illiterate	8	32.0%	40	31.0%	48	31.2%	0.96
1ry school	10	40.0%	48	37.2%	58	37.7%	
2ndry school	6	24.0%	37	28.7%	43	27.9%	
high education	1	4.0%	4	3.1%	5	3.2%	
Pregnancy weight gain							
High	7	28.0%	14	10.9%	21	13.6%	0.0023 *
Adequate	11	44.0%	109	84.5%	120	77.9%	
Low	7	28.0%	6	4.7%	13	8.4%	
Smoking							
No	19	76.0%	112	86.8%	131	85.1%	0.16
Yes	6	24.0%	17	13.2%	23	14.9%	
BMI							
18.5-24.9	7	28.0%	32	24.8%	39	25.3%	0.8
25-29.9	14	56.0%	70	54.3%	84	54.5%	
>30	4	16.0%	27	20.9%	31	20.1%	

*significant

Vitamin D supplementation was reported among 6(24%) of the preterm group and 69(53.5%) of the full term group, this relation was statistically significant (P value <0.05). Folic acid supplementation was reported among 17(32%) of the preterm group and 103 (79.8%) of the full term group, this relation was statistically not significant (P value >0.05). Iron supplementation was reported among 23(92%) of the preterm group and 124 (96.1%) of the

full term group, this relation was statistically not significant (P value >0.05). Frequent use of sun screen (because it is related with diminished skin sun exposure that affect vitamin D) was reported among 3(12%) of the preterm group and 18 (14%) of the full term group, this relation was statistically not significant (P value >0.05). Regular exposure to sun light was reported among 9 (36%) of the preterm group and 77 (59.7%) of the full term group, this relation was statistically significant (P value <0.05) as shown in table 2.

Table2. Distribution of preterm & full term labour based to supplement in pregnancy

	Preterm labour		**Full-term labour**		**Total**		**P value**
Vit. D supplement	6	24.0%	69	53.5%	75	48.7 %	0.007 *
folic Acid supplement	17	68.0%	103	79.8%	120	77.9 %	0.19
Iron supplement	23	92.0%	124	96.1%	147	95.5 %	0.36
Frequent use of sunscreen	3	12.0%	18	14.0%	21	13.6 %	0.79
Regular exposure to sun light	9	36.0%	77	59.7%	86	55.8 %	0.029 *

*significant

Pregnancy induced illness (Hypertension, diabetes mellitus, & UTI that chosen as common causes of preterm labour) found among 25

(100%) of the preterm labour, while found among 91(70.5%) of the full term group, this relation was statistically significant. Irregular prenatal care found among 19 (76 %) of the preterm labour, while found among 81(62.8%) of the full term group, this relation was statistically significant. Small for GA found among 15 (60%) of the preterm labour, while found among 0(0%) of the full term group, while the adequate for GA was found among 8 (32%) of the preterm labour, while found among 110(85.3 %) of the full term group this relation was statistically significant as shown in table 3.

Table 3. Pregnancy related conditions among prterm and full term group.

		Preterm labour		**Full-term labour**		**Total**		**P value**
pregnancy induced illness	yes	25	100.0 %	91	70.5%	116	75.3 %	
	Non	0	0.0%	38	29.5%	38	24.7 %	0.002 *
prenatal care	Regular	5	20.0%	48	37.2%	53	34.4 %	0.044 *
	irregular	19	76.0%	81	62.8%	100	64.9 %	
	Non	1	4.0%	0	0.0%	1	0.6 %	
Gender of the baby	Female	13	52.0%	53	41.1%	66	42.9 %	0.330
	Male	12	48.0%	76	58.9%	88	57.1 %	
Mode of	VD	1	76.0%	97	75.2%	11	75.3	0.9

delivery		9				6	%	
	C/S	6	24.0%	32	24.8%	38	24.7 %	
size for gestational age	Adequate for GA	8	32.0%	110	85.3%	118	76.6 %	0.0001*
	Small for GA	15	60.0%	0	0.0%	15	9.7 %	
	Large for GA	2	8.0%	19	14.7%	21	13.6 %	

*significant, GA; gestational age

Gestational Diabetes mellitus was found among 5 (20%) of the preterm labour group while it found among 6(4.7%) of the full term labour group, this relation was statistically significant. Pregnancy induced HT was found among 9(36%) of the preterm labour group while it found among 11(8.5 %) of the full term labour group, this relation was statistically significant. Urinary tract infection was found among 9(36%) of the preterm labour group while it found among 11(8.5 %) of the full term labour group, this relation was statistically significant as shown in table 4. Hypertension, diabetes mellitus, & UTI were chosen as common causes of preterm labour.

Table 4. The pregnancy induced illness among preterm and full term labour

Pregnancy induced illness		**Preterm labour**		**Full-term labour**		**Total**		**P value**
		No.	%	No.	%	No.	%	
Gestational DM	Yes	5	20%	6	4.7%	11	7.1 %	0.006*

	No	20	80%	123	95.3%	143	92.9 %	
Pregnancy induced HT	yes	9	36%	11	8.5%	20	13.0 %	0.001 *
	No n	16	64%	118	91.5%	134	87.0 %	
UTI	yes	21	84%	82	63.6%	103	66.9 %	0.047 *
	No n	4	16%	47	36.4%	51	33.1 %	

*significant, DM; Diabetes mellitus, HT, Hypertension, UTI; Urinary tract infection

The percentage of vitamin D3 deficiency was 5(3.25%), insufficiency 20-30ng/ml found among 129 (83.77%) of the pregnant women in the study. Vitamin D3 deficiency found among 3(12%) of the preterm labour and 2(1.6%) of the full term labour group, while sufficient vitamin D3 found among 1(4%) of the preterm labour and 19(14.7%), this relation was statistically significant as shown in table 5.

Table 5. Vitamin D3 level in preterm & full-term labour at 13-24 week gestation.

Vit D3 level at 13- 24 week	**Preterm labour**		**Full-term labour**	
	No.	%	No.	%
< 20 ng/mL	3	12 %	2	1.6%
20-30 ng/mL	21	84 %	108	83.7%
> 30 ng/mL	1	4 %	19	14.7%
Total	25	100 %	129	100 %

X^2=8.89, df=2, P value <0.05 (significant)

Deficient vitamin D3 found among 40(27%)of the total pregnant women , insufficient level found among110(73%) of the women while none of the pregnant women had sufficient vitamin D3 at 32 week of gestation. The correlation of the vitamin D3 level

at 13-24 week of gestation and gestational age show significant linear (r= 0.426), as shown in Figure 1.

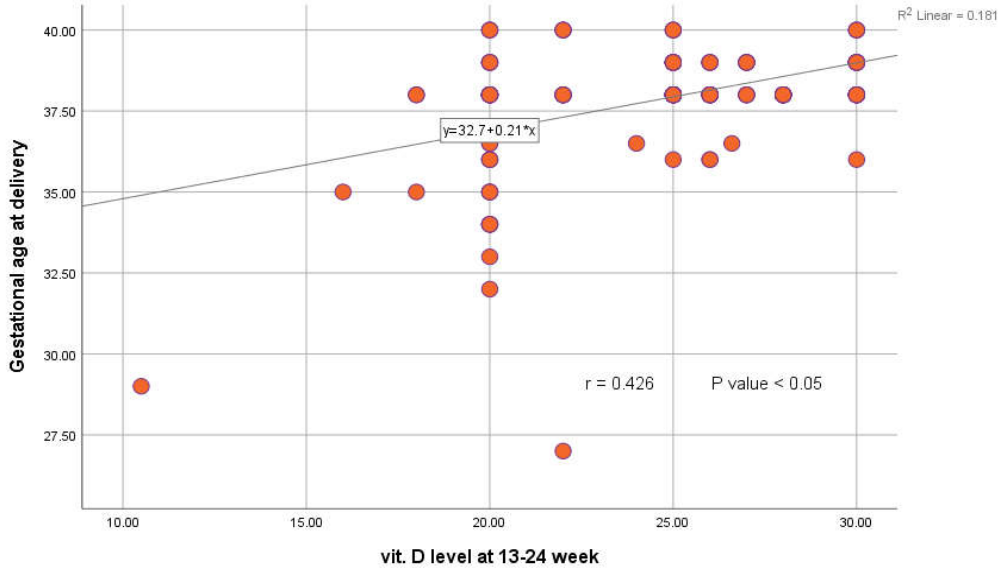

Figure 1. The correlation between vitamin D3 level at 13-24 week and gestational age at labour

The correlation of the vitamin D3 level at 24 - 32 week of gestation and gestational age show significant linear (r= 0.449), as shown in Figure 2.

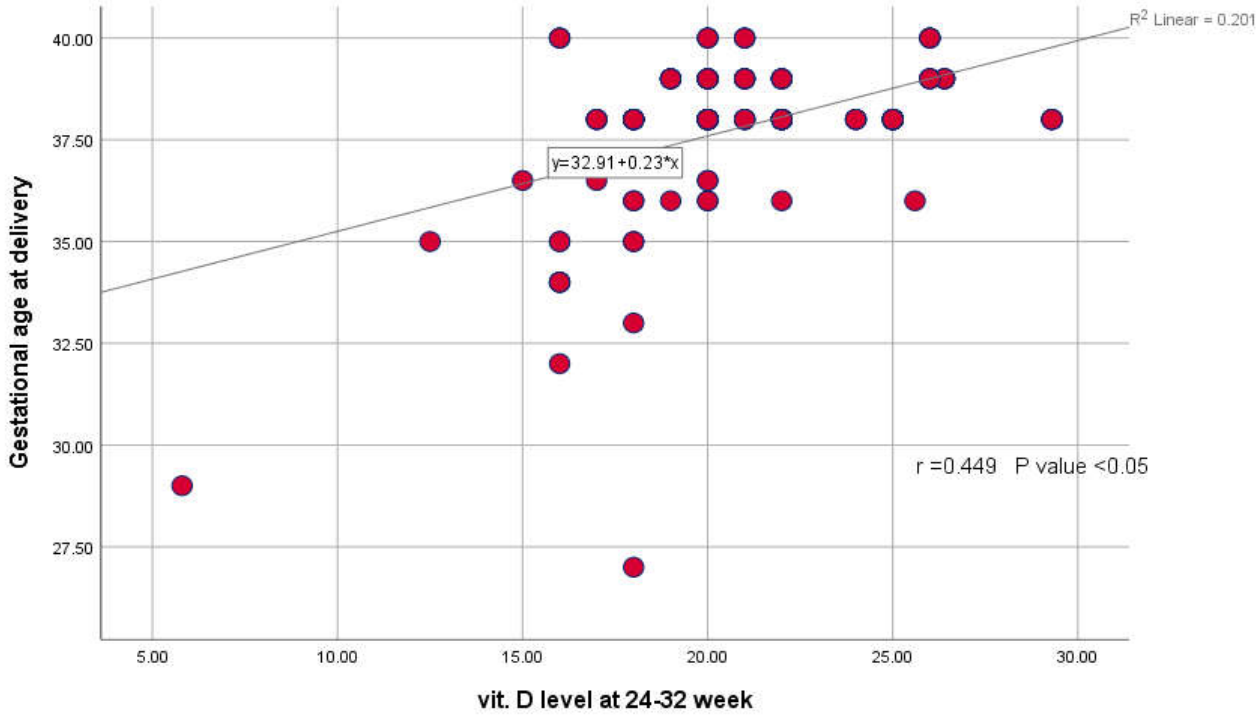

Figure 2. Correlation between vitamin D3 level at 24 - 32 week & gestational age at labour

Discussion

In the current study, vitamin D3 deficiency found significantly among women of the preterm labour than the full term labour group. Also the current study revealed that, the deficient vitamin D3 found among (27%) of the total pregnant women, insufficient level found among (73%) of the women while none of the pregnant women had sufficient vitamin D3 at 32 week of gestation. Different results reported by Samira S Hussien 2020 found that significantly lower level of the mean Vitamin D level was (18.6±6.7) among preterm deliveries in comparison to those with full term delivery (27.5±6.2). Samira S Hussien 2020 also reported that deficient vitamin D level was reported among (50%) of preterm delivered mothers versus (20%) of full term mothers. [8] Dhillon GK *et al* 2020 found that (18.45%) of pregnant mothers had Vitamin D deficiency (VDD) levels (<30 ng/ml), and that (17.14%) of them had preterm labour. [9]

Jyoti Singh *et al* 2015 found that (74%) of pregnant women were found vitamin D deficient (<30 nmol/l), 12% were having inadequate vitamin D levels (30-49.99 nmol/l). also found that it was found that (8%) women had delivered preterm vaginally in cases as compared to (38%) in control group in a statistically significant (P = 0.001) relation. Jyoti Singh *et al* 2015 found that a significant (P = 0.001) increase number of preterm birth were found among control group who were vitamin D deficient with mean vitamin D levels <50 nmol/l as compare to study group who were supplemented with vitamin D and had sufficient vitamin D with mean vitamin D levels >50 nmol/l. [10] As compare to present study Shibata M *et al.* (2011) also found high prevalence hypovitaminosis D in pregnant Japanese women with serum concentration of vitamin significantly low in women with preterm labour (11.2 ± 3.2 ng/ml) in comparison with term controls, (15.6 ± 5.1 ng/ml). [11]

Al Janaby S in Karbala in Iraq 2017 found that (87%) of the females had low level of vitamin D [12] This can be

explained by multifactorial etiology of women's deficiency in vitamin D, 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. Unfortunately, the elevated rate of utilization of multivitamins and dietary supplements looks not to elevate the serum 25-OH vitamin D levels. [13, 14] 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. [15]

There is a wide range of the prevalence of Vitamin D deficiency in the Indian subcontinent extending from 50% to 90% [16-18]. This could be attributed to the socioeconomic status of the study sample & cultural practices such as purdah and hijab and also had free access to a tertiary care center; thus, more likely to be taking a balanced diet and nutritional supplements. There is a wide range of the prevalence of Vitamin D deficiency in the Indian subcontinent extending from 50% to 90% [16-18] which is not in consonance with the current study population (18.45% Vitamin D deficiency). This could be attributed to the study sample in current study being from upper middle socioeconomic status without any malnutrition or indulgence in cultural practices such as purdah and hijab and also had free access to a tertiary care center; thus, more likely to be taking a balanced diet and nutritional supplements.

Only a research done by Hossain *et al.* [19] reported that higher maternal and cord blood Vitamin D status to be associated with shorter gestational periods ($r = 0.33$, $P = 0.003$) [20]. This result disagrees to the current as well as greater number of researches which could be explained by relatively small sample size. The probable causes for the contrasting rates in the association between Vitamin D and gestational age may be due to certain reasons like the

followings; pre-pregnancy BMI, arbitrary cut off values for Vitamin D, smoking status (including secondhand smoke), socioeconomic status, physical activity (pre-pregnancy as well as during pregnancy), ethnicity, geographical location, season of birth, and emotional distress. [21] The current study, revealed correlation of the vitamin D3 level at 13-24 week of gestation and gestational age show significant linear (r= 0.426), reported that the correlation of the vitamin D3 level at 24 - 32 week of gestation and gestational age show significant linear (r= 0.449). This in summary, means that increased level of vitamin D associated with increased the gestational age. A research carried out by Wagner C *et al.* 2012 reported the efficacy of vitamin D supplementation in reducing preterm birth risk in pregnant women and revealed similar results with inverse relation between vitamin D supplementation and preterm birth. Preterm labour/birth was inversely associated with initial (P = 0.001) and month prior to delivery 25(OH) D (P = 0.008). [22] The rate of preterm delivery was 1.59 times higher in mothers with Vitamin D deficiency.

Mehrdad Shakiba *et al.* Yazd, Iran (2009) 32 a total of 51 healthy, pregnant women in, were recruited and supplemented vitamin D and results were a low rate of prematurity among neonates born to women who have been supplemented with vitamin D. Among the 51 women who received vitamin D-supplementation, only 1 (2%) neonate was delivered prematurely [95% Confidence Interval (CI) 1.3-5.5][23]. In the current study, vitamin D supplementation & regular sun exposure reported among (24%), (36%) of the preterm, in comparison to (53.5%),(59.7%) of the full term group in a statistically significant (P value <0.05) relation respectively. These results were found similar to other researches in association to vitamin D supplementation and reducing the risk for preterm birth. Bruce H *et al.* (2011) also studied that vitamin D sufficiency may protect against preterm birth from preliminary analysis of a large cohort of

pregnant females supplemented with vitamin D and their initial findings show that the risk of preterm birth at 37 and 32 weeks was reduced among women taking vitamin D. They also reported mean gestational age at delivery among women with 2000 IU vitamin D supplementation was 38.8 ± 1.8 weeks. [24]

References

1.Alison L. Park, Marcelo L. Urquia and Joel G. ray: Risk of Preterm Birth according to Maternal and Paternal Country of Birth: A Population-Based Study. Journal of obstetrics and Gynaecology Canada, 2015 Dec;37(12):p.1053-1062.

2.Roberto Romero, Sudhansu K. Dey and Susan J. Fisher: Preterm labor: One syndrome, many causes. Science, 2014 Aug;345(6198):pp.760-765.

3. Wagner C, L, Hollis B, W: Early-Life Effects of Vitamin D: A Focus on Pregnancy and Lactation. Ann Nutr Metab 2020;76:16-28.

4-J.-P. Xiao, J. Zang, J.-J. Pei, F. Xu, Y. Zhu, X.-P. Liao, Low maternal vitamin D status during the second trimester of pregnancy: a cross-sectional study in Wuxi, China, PLoS ONE. 10 (2015) e0117748.

5- Wagner, C., Baggerly, C., Mcdonnell, S., Baggerly, L., Hamilton, S., Winkler, J. Post-hoc comparison of vitamin D status at three timepoints during pregnancy demonstrates lower risk of preterm birth with higher vitamin D closer to delivery. J Steroid Biochem Mol Biol (2015) ; 148: 256–260.

6- Holick MF, Binkley NC, Bischoff-Ferrari HA et al: Evaluation, treatment, and prevention of vitamin D deficiency: An Endocrine Society clinical practice guideline. J Clin Endocrinol Metab, 2013; 96(7): 1911–30

7-Vieth R, Holick MF. Chapter 57B—The IOM—Endocrine Society Controversy on recommended vitamin D targets: in support of the Endocrine Society position. Vitamin D, 4th ed.; Feldman, D., Ed.; Academic Press: Cambridge, MA, USA. 2018:1091-107.

8-Samira S Hussien. Relation of the 25 (OH) D Levels and Preterm Labour. Al-Kitab Journal for Pure Science June 2020, 4 (1): 41-50

9- Dhillon GK, Singh S, Dhillon HS, Sasidharan S.A study of relationship between maternal serum vitamin D levels during pregnancy and risk of preterm births. J Med Soc 2020;34:25-30.

10-Jyoti Singh, Chella Hariharan, Dilip Bhaumik. Role of vitamin D in reducing the risk of preterm labour. Singh J et al. Int J Reprod Contracept Obstet Gynecol. 2015 Feb;4(1):86-93. www.ijrcog.org

11-Shibata M, Suzuki A, Sekiya T, Sekiguchi S, Asano S, Udagawa Y, et al. High prevalence of hypovitaminosis D in pregnant Japanese women with threatened premature delivery. J Bone Miner Metab. 2011 Sep;29(5):615-20.

12-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).

13-Yetley EA. Assessing the vitamin D status of the US population. Am J Clin Nutr 2008;88(2):558S–564S,

14-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).

15-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)

16-Misra M, Pacaud D, Petryk A, Collett-Solberg PF, Kappy M; Drug and Therapeutics Committee of the Lawson Wilkins Pediatric Endocrine Society. Vitamin D deficiency in children and its management: Review of current knowledge and recommendations. Pediatrics 2008;122:398-417.

17- Harinarayan CV, Joshi SR. Vitamin D status in India – Its implications and remedial measures. J Assoc Physicians India 2009;57:40-8.

18- Kamboj P, Dwivedi S, Toteja GS. Prevalence of hypovitaminosis D in India & way forward. Indian J Med Res 2018;148:548.

19-Fernández-Alonso AM, Dionis-Sánchez EC, Chedraui P, González-Salmerón MD, Pérez-López FR; Spanish Vitamin D and Women's Health Research Group: First-trimester maternal serum 25-hydroxyvitamin D_3 status and pregnancy outcome. Int J Gynaecol Obstet 2012; 116: 6–9.

20. Hossain N, Khanani R, Hussain-Kanani F, Shah T, Arif S, Pal L. High prevalence of vitamin D deficiency in Pakistani mothers and their newborns. Int J Gynaecol Obstet 2011;112:229-33.

21-Morgan C, Dodds L, Langille DB, Weiler HA, Armson BA, Forest JC, *et al*. Cord blood vitamin D status and neonatal outcomes in a birth cohort in Quebec, Canada. Arch Gynecol Obstet 2016;293:731-8.

22-Shibata M, Suzuki A, Sekiya T, Sekiguchi S, Asano S, Udagawa Y, et al. High prevalence of hypovitaminosis D in pregnant Japanese women with threatened premature delivery. J Bone Miner Metab. 2011 Sep;29(5):615-20.

23- Mehrdad Shakiba, Mohamad Reza Iranmanesh, Yazd. Vitamin D requirement in pregnancy to prevent deficiency in neonates: a randomised trial. Singapore Med J. 2013;54(5):285-8

24- Wagner CL, McNeil R, Hamilton SA, Winkler J, Rodriguez Cook C, Warner G, et al. A randomized trial of vitamin D supplementation in 2 community health center networks in South Carolina. Am J Obstet Gynecol. 2013 Feb;208(2):137.e1-13.