Journal of Women's Health Care

OPEN ACCESS Freely available online

Research Article

A Study of Vitamin D Level in Pregnancy and the Effect of its Deficiency on Pregnancy Outcome

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ABSTRACT

Background: From conception, the embryo is dependent on the mother for all nutritional requirements until birth. Vitamin D deficiency or insufficiency is thought to be common among pregnant women and have an adverse effect on pregnancy outcome.

Objectives: To study the prevalence of vitamin D deficiency among pregnant women attending Al-Mawaani Teaching Hospital and to assess the correlation with maternal complications and evaluate the perinatal outcome.

Material and Methods: A prospective hospital-based cross-sectional observational study undertaken at the Obstetrical Department at Al Mawani Teaching Hospital in Basra. A total of 100 pregnant women who attended the labor word in active labor were studied to determine the serum level of 25-hydroxyvitamin D and assessment of the associated obstetrical complications and risk factors for one year.

Results: Of the studied pregnant women about 87% were deficient in vitamin D levels. The majority of patients were less than 30 years of age (68.97%) with vitamin D deficiency. Vitamin D deficiency was more in the housewife (89.66%), multigravida (67.81%), those with primary education (65.52%) and less exposure to the sun (83.91%).33 pregnant women had vitamin D deficiency with complications, like pre-eclampsia 4(12.12%), gestational diabetes mellitus 4(12.12%), PROM 9(27.27%), preterm labor 13(39.39%), chronic hypertension 3(9.09%). Neonatal outcome in deficient group was: Birth weight >2.5kg (95.23%), Birth weight <2.5kg (4.76%), Apgar score >7(79.76%), Apgar score <7(20.23%), admitted to Neonatal Intensive Care Unit (25%) compared to (75%) not admitted. The Mode of delivery by caesarean section in 52% and by vaginal delivery in 35% of the deficient group.

Conclusions: Our study shows a high prevalence of vitamin D deficiency in pregnant women. A complication in pregnancy like hypertension disorder, gestational diabetes, caesarean section, PROM and preterm labor were less predominantly seen in vitamin D deficiency group and fails to show a causal relationship between low maternal vitamin D level and adverse maternal and fetal outcome.

Keywords: Vitamin D Level, Pregnancy Outcome, Risk Factors

INTRODUCTION

During the past decade, vitamin D has received increasing attention and has been associated with health benefits, in addition to its recognized effects on bone health. One of these areas of interest is vitamin D status during pregnancy. The pregnant women's vitamin D status determines the vitamin D status of her new-born infant [1]. Vitamin D is a fat-soluble vitamin obtained mainly from diet and can be produced endogenously in the skin with exposure to sunlight. It plays a role in calcium metabolism, bone growth, and mineralization [2]. Various researches have studies the influence of season and sunlight exposure on vitamin D concentration in pregnancy. The average daily exposure to sunlight was higher in women with higher vitamin D concentration [3]. The major source of vitamin D is cutaneous synthesis following sunlight exposure, several factors can affect the synthesis of vitamin D including the use of sunscreen, age, skin pigmentation, clothing, and season [4]. Vitamin D is synthesized in the skin during summer under the influence of ultraviolet light of the sun or it is obtained from food, especially fatty fish, first hydroxylation in the liver into

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Received: August 29, 2020; **Accepted:** September 14, 2020; **Published:** September 21, 2020

Citation: Faik Al Mahfooth W, Lafta RA, Khuoo AN (2020) A Study of Vitamin D Level in Pregnancy and the Effect of its Deficiency on Pregnancy Outcome. J Women's Health Care 9:500. doi:10.35248/2167-0420.20.9.500.

25-hydroxyvitamin D (25(OH)D), the second hydroxylation to active form 1.25-dihydroxyvitamin D $1.25(OH)_2D$ occurs mostly in the kidney. The active metabolite can enter the cell bind to vitamin D receptor and subsequently to a responsive gene such as that of calcium-binding protein, mediates calcium absorption from the gut. The production of $1.25(OH)_2D$ is stimulated by parathyroid hormone and decreased by calcium [5]. Risk factors for vitamin D deficiency are premature birth, skin pigmentation, low sunshine exposure, obesity, mal-absorption, advanced age. Maternal vitamin D metabolism is altered during pregnancy leading to increase the circulating level of both vitamin D binding protein (VDBP) and active metabolite $1.25(OH)_2D$ at term, expectant mothers have almost twice the concentration of $1.25(OH)_2D$ compared to non-pregnant of which at least 50% is thought to be contributed by the placenta and decidual tissue [6]. The surge in $1.25(OH)_2D$ is a physiological response induced to permit immune tolerance through vitamin D pathways at maternal-fetal interface thereby supporting proper placentation [7]. The concentration of 25(OH)D is relatively constant throughout pregnancy. The mother is the only source of vitamin D for the fetus [8]. Vitamin D concentrations in the umbilical cord are usually (60-89%) of the values in the mother's blood. The active form of vitamin D does not cross the placenta. However, its concentration in the mother's blood is double in pregnancy probably because of its production in fetal tissue and placenta [9]. The abnormalities of the action of vitamin D receptor could manifest in signs and symptoms of vitamin D deficiency during pregnancy, this may present as gestational diabetes mellitus, pre-eclampsia, and preterm birth [10]. Maintaining optimum vitamin D nutrition during pregnancy is essential for the prevention of hypovitaminosis D in the fetus and vitamin D deficiency at birth and in early infancy [11]. There is a lack of consensus regarding the need for vitamin D supplementation during pregnancy in the UK. The Food Standards Agency recommends that pregnant women should take supplements containing 10mg vitamin D/day [12]. In the USA and Canada, the adequate intake for the general population aged (0-50) years including pregnant women is set at 5mg vitamin D/day [13]. However, in recent years, it has been suggested that recommended intakes for an adult should be much higher than the current recommendation. American College of obstetrician and gynaecologist (ACOG) propose 1000-2000 IU per day of 25(OH) D when the deficiency is identified (less than 20ng/ml) [14]. Many studies have shown a positive effect of the intake of nutritional supplements on vitamin D concentration in pregnant women. Another suggested the supplement dose of 400 I.U. of vitamin D as the one which enables pregnant women to achieve optimal vitamin D concentration [15]. In summary, the observational and randomized clinical trials present a clear message that 4000 I.U/day vitamin D3 supplementation is beneficial to both mother and her developing fetus through optimization of vitamin D metabolism that goes beyond calcium and bone haemostasis [16]. Identifying vitamin D deficiency by the circulating concentration of 25(OH)D, the indicator of nutritional vitamin D status. There is no consensus about the optimal 25(OH)D level, but many experts accept a range 75nmol/L (more than 30ng/ml) as optimal and serum vitamin D level below 50nmol/L (20ng/ml) represent deficiency [17]. Maternal vitamin D deficiency may be an independent risk factor for pre-eclampsia. Vitamin D supplementation in early pregnancy should be explored for preventing pre-eclampsia and promoting neonatal well-being. The pathogenesis of pre-eclampsia may involve a number of biological processes that may be directly or indirectly affected by vitamin D including immune dysfunction, placental implantation, abnormal angiogenesis, excessive inflammation, and hypertension [18]. There many ways through which vitamin D could affect glucose metabolism and maintain glucose tolerance through its influence on insulin secretion and sensitivity. Vitamin D deficiency in pregnant women with gestational diabetes increases the risk of poor neonatal outcomes such as neonatal hypoglycemia and small for gestational age [19]. Vitamin D could influence the pathophysiology of preterm labor as it affects the processes of inflammation and immunomodulation. The susceptibility to infection is increased in the case of vitamin D deficiency because of impairment of toll-like mediated induction of antimicrobial peptide cathelicidin from macrophages [20]. The objective of the study was to determine the prevalence of vitamin D deficiency in pregnancy and assess the correlation with maternal complications and perinatal outcome.

MATERIAL AND METHOD

This study was a prospective hospital-based cross-sectional observational study that was carried out in the Obstetrics and Gynaecology Department of Al Mawani teaching hospital in Basra/Iraq. 100 pregnant women in 3rd trimester in active labor admitted to the labor ward were enrolled in this study. The study period was from January 2019 to December 2019. All pregnant women were subjected to testing serum vitamin D during labor after counselling and informed consent.

Data collection

100 patients were included in the study from 28 weeks to 40 weeks of gestation. Information on age, education, parity, occupation, and exposure to the sun, obstetric history was obtained from the mother using a questionnaire. Gestational age (in weeks) was calculated from 1st day of the last menstrual period. History of iron, calcium, and vitamin D intake was also taken, blood investigation like haemoglobin and serum vitamin D level was done for all women included in the study. High-risk factors like anaemia, hypertensive disorder (pre-eclampsia), and diabetes were identified. Patients were followed up for mode of delivery weather, vaginal delivery, caesarean section, and birth outcome, birth weight, APGAR score, and admission to neonatal intensive care unit (NICU) were recorded. The analysis study carried out according to serum vitamin D value. The deficiency value of vitamin D was less than 30ng/ml, the sufficient value of vitamin D was more than 30ng/ml.

Statistical analysis

Data were collected through specially designed proforma. Data were expressed as numbers and percentages (%). Association between categorical data, vitamin D category, and demographic variable, mode of delivery, maternal outcome, and neonatal outcome were assessed by the chi-square test/Fisher exact test. A P-value of 0.05 or less was considered statistically significant.

RESULTS

The present study was undertaken among 100 pregnant women admitting in the labor ward at the obstetrics and gynaecology department of Al Mawani Teaching Hospital. These were subjected to assess serum vitamin D levels, 87%were deficient in vitamin D level (Table 1).

Table 2, shows the socio demographic characteristics of patients according to vitamin D status. The majority of patients aged below 30 years (64%), those with low education (primary school) (65.52%)

and housewives 88% were significantly more likely to have vitamin D level deficiency. Regarding exposure to the sun, 74% of pregnant women were exposed less to the sun, those without vitamin D supplementation were 80%, multigravida was 64% and the patient lived in the urban area 88% were significantly more likely to have vitamin D deficiency (Table 2).

Table 3, shows the total number of vaginal delivery 44%, 35% of this had vitamin D deficiency, and the total number of patients with caesarean section was 56%, about 52% had vitamin D deficiency (Table 3).

Table 4, shows the total number of pregnancies without complications 63%, from these 54% had vitamin D deficiency. Pregnancy with complications 37%, from these 33% had vitamin D deficiency, these include: preterm labor 13(39.39%), PROM 9(27.27%), gestational diabetes 4(12.12%), pre-eclampsia 4(12.12%), chronic hypertension 3(9.09%) (Table 4).

Table 5, shows neonatal outcome, live birth (84%) had vitamin D deficiency. Only 4% of total neonatal outcome with intrauterine death, 3(3.4%) had vitamin D deficiency. The outcome of live birth in pregnant women with vitamin D deficiency, birth weight <2.5kg(4.76), birth weight >2.5kg(95.23%). Apgar score <7 in deficient group (20.23%) and Apgar score >7 in deficient group (79.76%). Neonatal intensive care unit (NICU) admission in vitamin D deficiency (25%) and vitamin D sufficient (16.66%) (Table 5).

Table 1: Vitamin D status.

Vit D status	Number	Percentage
<30ng/ml	87	87%
>30ng/ml	13	13%

Table 2: Demographic factor.

Variables	Total N=100	Vitamin D deficiency N= 87	Vit D sufficient N=13	P-value
		Age		
Age <30 years	64%	60(68.97)%	4(30.77)%	0.007
Age >30 years	36%	27(31.03)%	9(69.23)%	(S)
		Education		
Primary -sec	60%	57(65.52)%	3(23.03)%	0.004
>secondary	40%	30(34.48)%	10(76.92)%	(S)
		Occupation		
Housewife	88%	78(89.66)%	10(76.93)%	0.188
Working	12%	9(10.35)%	3(23.03)%	(NS)
		Exposure to sun		
Adequate	26%	14(16.09)%	12(92.31)%	0
Inadequate	74%	73(83.91)%	1(7.69)%	(S)
		Supplement		
Yes	20%	11(12.64)%	9(69.23)%	0
No	80%	76(87.36)%	4(30.77)%	(S)
		Parity		
Primigravida	36%	28(32.18)%	8(61.53)%	0.04
Multigravida	64%	59(67.81)%	5(38.46)%	(S)
		Home		
Rural	20%	14(16.09)%	6(46.15)%	0.01
Urban	80%	73(83.90)%	7(53.84)%	(S)

Table 3: Mode of delivery.

Total deliveries N=100	Vit D deficient (N=87)	Vit D sufficient (N=13)	P-value
Vaginal delivery N=44	35%	9%	0.05 (S)
Cesarean delivery N=56	52%	4%	0.049 (S)

Table 4: Maternal outcome.

Vitamin D status	Pregnancy without complication (n=63)	Pregnancy with complication (n=37)	P-value
Vitamin D sufficient (N=13)	9(9%)	4(4%)	0.618 (NS)
Vitamin D deficient (N=87)	54(54%)	33(33%)	0.614 (NS)

Pregnancy with complication (n=37)					
Vitamin D status	**Preterm labor**	**PROM**	**Diabetes**	**Pre-eclampsia**	**Chronic Hypertension**
Vitamin D sufficient (n=4)	Nill	2(50%)	Nill	Nill	2(50%)
Vitamin D deficient (n=33)	13 (39.39)%	9(27.27)%	4(12.12)%	4(12.12)%	3(9.09)%

Table 5: Neonatal outcome.

Vitamin D Status	Live birth	IUD	P-value
Vitamin D sufficient (N=13)	12(92.31)%	1(7.69)%	0.466 (NS)
Vitamin D deficient (N=87)	84(96.55)%	3(3.44)%	0.508 (NS)

Live birth (n=96)			
Neonatal Outcome	**Vitamin D sufficient (N=12)**	**Vitamin D deficient (N=84)**	**P-value**
Brith weight			
<2.5kg (n=7)	3(25%)	4(4.76%)	0.012
>2.5kg (n=89)	9(75%)	80(95.23%)	(S)
Apgar score			
<7 (n=19)	2(16.66%)	17(20.23%)	0.771
>7 (n=77)	10(83.33%)	67(79.76%)	(NS)
NICU			
Admitted (n=23)	2(16.66%)	21(25%)	0.527
Not admitted (n=73)	10(83.33%)	63(75%)	(NS)

DISCUSSION

Vitamin D deficiency is very common in pregnancy. Our study revealed that the prevalence of Vitamin D deficiency was (87%) similar to study conducted by I Pehlivan, et al [21]. While in a study conducted in South Carolina found 41% of pregnant women were deficient in vitamin D [22]. Another study found 62% of caucasian pregnant women and 96% of African American pregnant women were deficient in vitamin D [22,23]. This study shows statistically significant associated between of vitamin D deficiency and housewives women (89.66%), who were with inadequate exposure to sunlight (83.91%), no supplementation with vitamin D deficiency (87,36%), their ages <30 years (68.97%), live in the urban area (83,90%) and multiparous women (67.81%). These results go with a study done by Dipali P et al [14]. However, they found no correlation between the number of pregnancies and vitamin D deficiency.

The risk of vitamin D deficiency was higher in housewives who mostly preferred to live indoor and reduced exposure to direct sunlight. The deficiency is the sunlight exposure dependent also has a predilection with religion. The burqa practice in the Muslim community is more prone to vitamin D deficiency. In this study, we found that the rate of caesarean section 52%, P=0.049 were more than vaginal delivery 35%, P=0.05 in vitamin D deficiency group these results were similar to study conducted Dipali P. et al [14]. They show an association of vitamin D deficiency and caesarean section deliveries 23.5%, 34% respectively but this association is not statistically correlated. Segregating the vitamin D deficiency with indications of the caesarean section will be more important to understand the role of vitamin D in the initiation of labor or association with calcium metabolism [14,21]. The risk for primary caesarean section in women with vitamin D deficiency was almost four-fold times higher than women with higher vitamin D concentration. They proposed maternal vitamin D may be associated with risk for the primary caesarean section through calcium′s role in the initiation of labor, or by increasing [24].

Vitamin D deficiency has been associated with several adverse health outcomes including pregnancy outcome. In this study, a maternal outcome was seen in vitamin D deficiency group 54%, (P=0.618) without complication, and this association was not statistically correlated. In the present study, vitamin D deficiency was comparable with maternal outcome regarding PROM, preterm labor, diabetes, and hypertension disorder as compared to the women with normal vitamin D levels. However, the study done by Abdulbari B. 2013 demonstrates a great risk of maternal complication in pregnant women with vitamin D deficiency compared with those with normal vitamin D levels [25]. Regarding the hypertensive disorder, this study found that maternal vitamin D deficiency in pregnancy was not significantly associated with an

elevated risk of pre-eclampsia similar to the result of a cohort study of pregnancies at high risk for pre-eclampsia in Canada [26].

Hence, the supplementation of vitamin D in pregnancy for the prevention of preeclampsia is not recommended. While in other studies, women who developed pre-eclampsia were found to have lower levels of vitamin D than women with normal levels of vitamin D, revealed a significant association between pre-eclampsia and severe vitamin D deficiency [27]. So further large studies in this perspective would be needed. In the current study, numbers of gestational diabetes were only 4 patients and all had vitamin D deficiency, this is a very small sample size to comment on the association. Vitamin D improves insulin sensitivity by enhancing insulin responses to glucose transport. In meta-analysis review of various studies reported that pregnant women with diabetes mellitus had significantly lower vitamin D levels than the comparison group [25,28]. On the contrary, no significant association was observed between vitamin D level and diabetes mellitus in the study which was similar to this result [29]. Several observational studies found no association between preterm labor and maternal vitamin D level similar to the result of this present study [30].

In contrast, Bodnar LM et al. found a significant correlation between vitamin D deficiency and preterm labor [20]. The result of some of these studies needs to be interpreted with caution as some of them focused on specific risk factors like the previous history of preterm labor, twin pregnancy, and other risk factors of preterm labor. Regarding neonatal outcome we found in the present study, maternal vitamin D level had no statistical correlation with birth weight (P=0.012), Apgar score (P=0.771), and neonatal intensive care unit (NICU) admission (P=0.527) which was similar to the study done in France [31]. In contrast, there was a study from the Netherlands, women with vitamin D deficiency had increased risk of having a small for gestation age baby. However multiple confounding factors could be implicated for vitamin D effected on gestational baby sizes such as ethnicity, nutritional status, sunlight exposure, milk, or calcium intake [32]. Vitamin D supplementation may be a simple way to reduce the risk of adverse pregnancy outcomes.

CONCLUSION AND RECOMMENDATION

In this study, we found the prevalence of vitamin D level deficiency was high in pregnant women who attended at AL-Mawani Teaching Hospital at labor word, depending partly on lifestyle factors like exposure to sunlight and no supplementation of vitamin D. After summarizing existing data, the complications of pregnancy like PROM, preterm labor, caesarean section rate, hypertension disorder, and diabetes mellitus were not prominently seen with pregnancy in vitamin D deficiency and fails to show a direct relationship between low vitamin D level and adverse neonatal outcome in the study, and thus may be related to the small size of this study while further work is needed to determine whether vitamin D level deficiency effect on pregnancy outcome. While there is some indication that vitamin D supplementation could reduce the risk of pregnancy complications, further randomized trials are required to confirm these effects. Despite these problems of interpretation recent evidence suggests that vitamin D supplementation could be of value in reducing the risk of pregnancy complications. We recommended increase supplementation or exposure to sunlight in all pregnant women to keep serum level of 25(OH)D in the normal range for adult >30ng/ml. New high-quality clinical studies are still needed to throw further light on the subject.

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