Vitamin D3 deficiency and early pregnancy loss

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Abstract

Vitamin D is important for reproductive health, and healthy pregnancy; its deficiency is related to many obstetrical complications. This study aimed to study the relation of Vitamin D deficiency and early pregnancy loss.

Subject and methods: A Retrospective Case control study was done in Azadi teaching Hospital during the period 1st January 2019-1st May 2019. Inclusion criteria was any pregnant women with singleton pregnancy in the 1st trimester;106 women with miscarriage in 1st trimester were enrolled and compared with 106 normal pregnancies enrolled as control. Exclusion criteria were any women with recurrent miscarriage, multiple pregnancy, TORCH infection, anemic patient, patients with medical diseases like diabetes, thyroid disease, antiphospholipid syndrome or any congenital abnormality of the uterus.

Results: The total sample showed that 186 (79.2%) were fully covered 182 (85.8%) with Vitamin D3 deficiency, 16 (7.5%) with insufficiency, and 14 (6.6%) had a normal level of Vitamin D3.

There are significant differences among both study groups regarding Gestational age in weeks, and 25-hydroxivitamin D levels. 25- hydroxivitamin D level was lower among those with miscarriage 11.3±5.3, than normal pregnancy 15.9±11.2. Gestational age (GA) among the miscarriage group was 8.6±2.1 lower than those with normal pregnancy 9.4±2.4.

Those with deficient 25- hydroxivitamin D level mostly had miscarriage 96 (52.7%), versus normal pregnancy 86 (47.3%); those with insufficient 25- hydroxivitamin D were commonly missed 10 (62.5%); those with normal level mostly had a normal pregnancy 14 (100%). Most of the covered women had miscarriage 140 (83.3%), which is lower than the deficiency level among uncovered women 42(95.5%).

Conclusion: Vitamin D deficiency was associated with early pregnancy loss. Sufficient vitamin D is important for healthy pregnancy.

Key words: Vitamin D, 25- hydroxivitamin D, early pregnancy loss

Introduction

Pregnancy loss (miscarriage) is a common complication of pregnancy. It has both a psychological and physical impact on the patient. The incidence of miscarriage is about 10-15% with the highest risk being in the first trimester of pregnancy [1].

The definition of spontaneous miscarriage is the loss of a pregnancy prior to viability. This is legally regarded in the United Kingdom as a gestation of 23 weeks and 6 days.[2]

However miscarriage has been defined by the World Health Organization, and the Center for Disease Control and prevention as any pregnancy loss before 20 weeks gestation, or a miscarried fetus less than 500 g weight [3]. Three or more consecutive miscarriages is defined as recurrent miscarriage and affects 1% of women and is regarded as predictive of high rates of future miscarriage [4].

Many causes have been identified for miscarriage; chromosomal anomaly accounts for about 50% of miscarriages, other risk factors that have been associated with miscarriage include: maternal and paternal age, congenital abnormality of uterus, history of infections, increase in body mass index, medical diseases like diabetes mellitus, thyroid disease, epilepsy, anti-phospholipid syndrome and heart disease, excess alcohol and caffeine consumption [5,6,7,8].

Because miscarriage has great psychological and physical impact on the health of women [9] it is important to look for other risk factors that may affect the rate of miscarriage in the first trimester of pregnancy when miscarriage is the commonest.

Vitamin D is important for normal reproductive health; Vitamin D receptors have been found in the ovary, uterus, placenta, hypothalamus, and pituitary gland [10].

Poor vitamin D status during pregnancy has been associated with preeclampsia, [11] gestational diabetes, [12] bacterial vaginosis, and compromised intrauterine growth [13]. Little has been reported in Iraq about the association of vitamin D deficiency and miscarriage in the 1st trimester. This study aimed to study the association of spontaneous pregnancy loss in the 1st trimester and Vitamin D deficiency.

Subjects and method

A retrospective Case control study was done in Azadi Teaching Hospital during the period 1st January 2019-1st May 2019.

Inclusion criteria was any pregnant woman with singleton pregnancy with gestational age from 6 weeks till 13 completed weeks in the 1st trimester. 106 women with miscarriage in 1st trimester were enrolled and compared with 106 normal pregnancies enrolled as control.
Exclusion criteria were any women with recurrent miscarriage, TORCH infection, anemic patient, medical disease such as diabetes and thyroid disease, antiphospholipid syndrome, multiple pregnancy and congenital anomaly of uterus.

Measurement of serum 25(OH) D
Blood samples from fasting women were collected from women with normal pregnancy at 1st trimester, as well as from women with spontaneous miscarriage in 1st trimester. After centrifugation for 10 minutes at 3000r.p.m. at room temperature, the serum specimens were stored at −80°C. Before assaying, all samples were thawed to room temperature and assayed on the same day to avoid inter-assay variation. Quantitation of serum 25(OH)D was performed using commercial ELISA kits.

The intra-assay and inter-assay precision for the ELISA were less than 10% and 15% for 25(OH)D. All the assays were performed according to the manufacturer's instruction. Biological samples were blinded prior to analyses.
Serum levels of 25- hydroxivitamine D is defined as: sufficient = 30 ng/ml 25(OH), values between insufficiency= 29 and 20 ng/ml, deficiency= less than 20 ng/ml, severe deficiency= below 7 ng/ml. [14]

Results

In analyzing samples of 106 women with miscarriage compared with 106 women with normal pregnancy, the total sample showed that 186 (79.2%) were covered women, 182 (85.8%) with Vit D3 deficiency, 16 (7.5%) with insufficiency, and 14 (6.6%) had normal level of Vit D3.

There are significant differences among both study groups regarding Gestational age in weeks, and 25- hydroxivitamin D levels. 25- hydroxivitamin D level was lower among those with miscarriage 11.3±5.3, than normal pregnancy 15.9±11.2. Gestational age (GA) among the miscarriage group was 8.6±2.1, which was lower than those with normal pregnancy 9.4±2.4, as shown in Table 1.

Table 1: The relation between different variables and type of pregnancy outcome.

	Normal pregnancy		Miscarriage		P value
	Mean	Std. Deviation	Mean	Std. Deviation	
Body mass index by Kg/square meter	26.3	3.5	26.8	4.6	NS
Gravidity	2.9	1.6	2.9	1.7	NS
Parity	1.4	1.2	1.6	1.5	NS
Miscarriage	0.5	0.7	0.4	0.6	NS
Gestational age in weeks	9.4	2.4	8.6	2.1	Significant
25- hydroxivitamin D (ng/ml)	15.9	11.2	11.3	5.3	Significant

Those with deficient 25- hydroxivitamine D level mostly had miscarriage 96 (52.7%), versus those with normal pregnancy 86 (47.3%), those with insufficient 25- hydroxivitamin D were commonly missed 10 (62.5%), those with normal level mostly had normal pregnancy 14 (100%). This relation was statistically significant (P value < 0.05), as shown in Table 2.

Table 2: The relation between Vit D level and pregnancy outcome

25- hydroxivitamin D (ng/ml)	Type of pregnancy		Total
	Missed	Normal	
8-20 ng/ml	96	86	182
	52.70%	47.30%	100.00%
20-29 ng/ml	10	6	16
	62.50%	37.50%	100.00%
>30ng/ml	0	14	14
	0.00%	100.00%	100.00%
Total	106	106	212
	50.00%	50.00%	100.00%

X2=15.5, df=2, P value <0.05 Significant

Most of the covered women had miscarriage 140 (83.3%), which is lower than the deficiency level among uncovered women 42 (95.5%). This relation was statistically not significant as shown in Table 3.

Table 3: The relation between 25- hydroxivitamin D level and women's dressing

	8-20 ng/ml	20-29 ng/ml	>30ng/ml	Total
Covered	140	16	12	168
	83.30%	9.50%	7.10%	100.00%
Uncovered	42	0	2	44
	95.50%	0.00%	4.50%	100.00%
Total	182	16	14	212
	85.80%	7.50%	6.60%	100.00%

X2=5.14, df=2, P value >0.05 not Significant

Discussion

Vitamin D has an important role in reproductive health and its deficiency is related to many obstetrical complications, such as: bacterial vaginosis, preeclampsia, gestational diabetes, small-for-gestational age births, and pregnancy loss [12,15-17].

This study revealed that most of the sample had vitamin deficiency 182(85.8%). This goes with the study of Hantoosh H. A. et al that goes with previous studies done among reproductive age group women (76%)[18], and Al-Hilali KA (65%)[19] and is supported by studies in Iran (26.1%) [20], (33%) [21].

Those with deficient 25- hydroxivitamin D level mostly had miscarriage 96 (52.7%), versus those with normal pregnancy 86 (47.3%); 25- hydroxivitamin D level was lower among those with miscarriage 11.3±5.3, than normal pregnancy 15.9±11.2. This goes with a study in Iraq that found that 60% of those with recurrent pregnancy loss had vitamin D deficiency, with a mean of 21.5±11.8.[22]

In Iran it was found that (33%) of those with recurrent pregnancy loss had Vitamin D deficiency,[21] and, in Hou W et al [23] (43.3%) women with pregnancy loss had Vitamin D deficiency, and (3.3%) in the normal pregnant group.

Mumford SL et al [24] in a prospective cohort study found that sufficient preconception serum level of Vitamin D was associated with lower rate of pregnancy loss.

In this study the mean 25- hydroxivitamin D level was lower among those with miscarriage 11.3±5.3, than normal pregnancy 15.9±11.2. This goes along with Hou W [23] that found significant lower level of Vitamin D among those with pregnancy loss than those with normal pregnancy. The mean 25(OH)D concentration was 49.32±11.65 ng/ml for the normal pregnant group, and 34.49±15.60 ng/ml for the pregnancy loss group,

Results of a study in Iraq represent that the mean serum Vitamin D level was 15.85 ± 7.69 among reproductive age women[18].

This difference in the mean levels is due to the fact that Hypovitaminosis D is prevalent in the MENA region [25]. Most of the covered and uncovered women had miscarriage rate of 140 (83.3%) and 42(95.5%) respectively. This figure shows the overall high percentage of Vitamin D deficiency among reproductive age women [2].

The explanation of high prevalence may be explained by the preference of Iraqi women to have fair skin tone, and the hot sunny weather makes them avoid exposure to sun light.

The significant association between miscarriage and serum Vitamin deficiency is understood by reviewing the results of previous studies that studied the effect of Vitamin D. Vitamin D has roles in reproductive health and pregnancy outcome. These effects are: regulation of decidualization of the uterus, by regulating HOXA10 gene responsible for endometrial development and receptivity during the window of implantation[26]. It has a role in trophoblastic invasion and angiogenesis, therefore it is responsible for embryo implantation and placenta function [27-29].

Vitamin D deficiency is associated with autoimmunity, inflammation, and intolerance of the maternal immune system to the embryo [30].

Conclusion

Vitamin D deficiency was associated with early pregnancy loss. Sufficient vitamin D is important for healthy pregnancy.

Ethical approval

Ethical clearance was taken from Kirkuk health department / research ethical committee.

This study was self-funded. No Conflict of Interest.

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