RELATIONSHIP BETWEEN VITAMIN-D DEFICIENCY AND PRE-ECLAMPSIA

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ABSTRACT

Background

Pre-eclampsia is a pregnancy-specific syndrome that affects virtually every organ system, characterized by the new onset of hypertension and proteinuria after 20th week of gestation. The exact cause of pre-eclampsia is not known. Recent epidemiological studies have emphasized the role of vitamin D deficiency in immunomodulation and placental development and thus, they put the emphasis on vitamin D deficiency, regarding its possible role in the pathophysiology of pre-eclampsia.

Objectives

To assess the frequency of vitamin D deficiency among pregnant women in the study groups and to find any relationship between vitamin D deficiency and pre-eclampsia.

Patients and Methods

A case -control study conducted at Sulaimani Maternity Teaching Hospital. A total of one hundred primigravid women with singleton pregnancy without any medical problem were included in the study, fifty women with pre-eclampsia (the study group) and the other fifty women with healthy pregnancy without preeclampsia (the control group). Serum vitamin D level estimation was done for all women in the study and comparison done between the two groups. Vitamin D level < 20 ng/ml. were considered insufficient, while level < 10ng/ml considered significant deficiency.

Results

All women who participated in the study had vitamin D level below normal (< 20 ng/ml). With the majority of women in both groups have significant deficiency (level <10ng/ml) which was 45 (90%) women in the study group compared to 40 (80 %) women in the control group with a P- value = 0.6. The mean vitamin D level was not statistically different between the pre-eclampsia group and healthy women (5.87± 3.37 versus 6.5± 3.67) with P- value =0.25.

Conclusion

Vitamin D deficiency was very common among the studied women. No statistical significant association between vitamin D deficiency and pre-eclampsia was found in this study.

Keywords: *Vitamin D deficiency, Pre-eclampsia.*

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INTRODUCTION

Pre-eclampsia is a pregnancy-specific syndrome that affect virtually every organ system, characterized by the new onset of hypertension and proteinuria after 20th week of gestation in a woman whose blood pressure was previously normal [1, 2]. Pre-eclampsia may also occur up to six weeks post-partum [3]. The disease can occur in the absence of fetal tissue (molar pregnancy), and in the absence of a uterus (abdominal pregnancy), suggesting that it is the trophoblastic tissue that provide the stimulus for the disorder [4]. Pre-eclampsia complicates 3-5% of all pregnancies and more than 10% of women will develop pre-eclampsia in their first pregnancy [5]. Although the majority of these will have successful pregnancy outcomes, the condition can give rise to severe multisystem complications including seizure, cerebral haemorrhage, hepatic and renal dysfunction, respiratory compromise, fetal growth restriction and even death. The development of strategies to prevent and treat the disorder has been challenging due to an incomplete understanding of the underlying pathogenesis [5].

Hypertension in pregnancy defined as either, diastolic BP > 110mmHg on any one occasion or diastolic BP ≥90 mmHg on two or more consecutive occasions > 4 hours apart. Proteinuria in pregnancy defined as either one 24-hour collection with total protein excretion> 300 mg/24 hour or two, clean-catch-midstream, or catheter specimens of urine collected > 4 hours apart with ≥2+ on reagent strip [6].

The exact nature of primary event causing pre-eclampsia is not known, pre-eclampsia is a disease of theories, because genetic, immunologic, vascular, hormonal, nutritional, and behavioral factors have all been proposed as causes. No single definitive cause has been identified and the origin of the disease is considered to be multifactorial [2]. Maternal diet is among the factors that are related to the etiology of pre-eclampsia; an insufficient diet, especially in terms of calcium, magnesium, selenium and vitamin A and C, is a contributing factor to pre-eclampsia [7, 8].

Recent epidemiological studies have emphasized the role of vitamin D deficiency in the development of pre-eclampsia. Recent in vitro studies have demonstrated the improvement of angiogenesis and inhibition of release of adhesion molecules from endothelial cells by vitamin D [9, 10]. The role of vitamin D deficiency in immunomodulation and placental development has been emphasized in various studies and thus, they put the emphasis on vitamin D deficiency, regarding its possible role in the pathophysiology of pre-eclampsia. [11-13].

Vitamin D is important for overall health and scientists are getting closer to knowing how exactly vitamin D keeps us healthy. The classic function of vitamin D is to increase the intestinal absorption of calcium for proper mineralization of bone [14]. The active form of vitamin D, 1,25-dihydroxyvitamin D (1,25 $(OH)_2D$), acts as a steroid hormone by binding to the vitamin D receptor (VDR) which is present in many cells throughout the body including cardiomyocytes [15], vascular smooth muscle [16] and endothelium [17]. Recent evidence has demonstrated that individuals deficient in vitamin D are more likely to have cardiovascular disease or are at risk of developing incident cardiovascular disease. The mechanism for how vitamin D may protect individuals from cardiovascular disease has not been fully elucidated. Several mechanisms have been proposed including negatively regulating renin to lower blood pressure, improving vascular compliance, decreasing parathyroid hormone levels and improving glycemic control [18].

Recent research reports that vitamin D has a hand in how the immune system works, which also plays a role in the risk of developing pre-eclampsia. In some women with pre-eclampsia, their immune system responds against the placenta and baby, as if they're foreign invaders. It has been found that vitamin D influences the immune system by affecting the balance between helpers T cells, which are essential for a healthy pregnancy so vitamin D's positive effect on the immune system may potentially help prevent pre-eclampsia [19].

A number of studies have suggested that the season of the year is linked to pre-eclampsia. Vitamin D levels are generally highest during summer months and lowest during winter months. These studies suggest that the link between season and risk of pre-eclampsia, may be related to vitamin D deficiency . Researchers have found that vitamin D deficiency during the second trimester increases the chance of developing pre-eclampsia [20, 21].

This study aimed to investigate the serum vitamin D level in pre-eclampsia and healthy pregnant women in order to assess the frequency of vitamin D deficiency among pregnant women in the study groups and to find

any relationship between vitamin D deficiency and pre-eclampsia

PATIENTS AND METHODS

This study is a case -control study conducted at Sulaimani Maternity Teaching Hospital over a period of 6 months starting from the 1st of January 2015. A total of one hundred primigravid women with singleton pregnancy without any pre-existing medical problem were included in the study, fifty pregnant women with pre-eclampsia (the study group) and the other fifty pregnant women with healthy pregnancy without pre-eclampsia (the control group). The pre-eclampsia group were taken from the out- patient clinic or patients who admitted to the hospital with preeclampsia. While the control group selected from pregnant women with apparently healthy pregnancy who admitted to give birth of their baby.

The diagnosis of pre-eclampsia was based on the following criteria: patients with systolic blood pressure ≥140 mmHg and/or diastolic blood pressure ≥90 mmHg (measured twice after a period of rest of four hours) and proteinuria (≥300 mg protein/24 h) or two, clean-catch-midstream, or catheter specimens of urine collected > 4 hours apart with ≥2+ on reagent strip .

A verbal consent was obtained from the patients included in the study and the study was approved by the scientific and ethical committee of School of Medicine /Sulaimani University.

Blood samples were taken from all women included in the study for evaluating the serum vitamin D level. After aspiration, the blood allowed to clot and then centrifuged for 10 minutes to separate the serum, then the sera were stored at -70°C until the time of analysis which was done at the same time for all samples and in the same laboratory. Then comparison between the two groups was done. Vitamin D level ≥ 20ng/ml was considered normal, levels less than 20ng/ml but more than 10ng/ml. were considered insufficient , while level < 10ng/ml. were considered significant deficiency [22].

Statistical analysis was carried out using the SPSS version 19 for windows software program. Data expressed in frequency and percentage, mean and standard deviation. Student's t-test was used to evaluate the difference between values. A P value ≤ 0.05 was considered significant.

RESULTS

This study included 100 pregnant women, fifty women with pre-eclampsia (the study group) and fifty women with apparently healthy pregnancy without pre-eclampsia (control group).

Table (1) showed the demographic characteristics of women in both groups.The mean maternal age± slandered deviation for the study group(women with pre-eclampsia) was 30.2±4.4 years as compared to the control groups which was 29.3±4.4 years. There was no statistically significant difference as the P- value was 0.213. The mean BMI for the study group was 23.9±1.7 Kg/m2 as compared to the control groups which was 23.7±2.9 Kg/m2 also statistically no significant difference as the P value was (0.650).Seventy two percent of the study group and 78 % of the control group were house wives, the difference in percentage was also statistically not significant.

Regarding the vitamin D level, all women who participated in the study have vitamin D level below normal (< 20ng/ml) with the majority of women in both groups have significant deficiency of vitamin D (level <10ng/ml) which was 45 (90%) women in the study group compared to 40 (80 %) women in the control group with a P value = 0.6 which is statistically not significant, as shown in Table (2).

Regarding the mean vitamin D level, it was 5.87± 3.37 in the study group compared to 6.5± 3.67 in the control group, although the mean level was higher in the control group but statistically it was not significant with a P value =0.25, as shown in Table (3).

Table 1. Demographic characteristics of women in both groups.

Characteristics		Study group	Control group	P- value
Age(years) (mean± SD)		30.2±4.4	29.3±4.4	0.213
BMI (Kg/m2) (mean± SD)		23.9±1.7	23.7±2.9	0.650
Occupation No(%)	House wives	36 (72)	39 (78)	0.46
	Employee	14 (28)	11 (22)	

Table 2. The frequency distribution of women in both groups according to vitamin D level.

Vitamin D level (ng/ml)	Study group No (%)	Control group No (%)	P-value
10-20	5 (10)	10 (20)	0.06
< 10	45 (90)	40 (80)	
Total	50 (100)	50 (100)	

Table 3. The mean vitamin D level in both groups.

Vitamin D level	Study group (pre-eclampsia)	Control group (healthy women)	P -value
(Mean ± SD)	5.87± 3.37	6.5± 3.67	0.25

DISCUSSION

Pathogenesis of pre-eclampsia is complex and a vitamin D deficiency is one of the factors in the etiology of pre-eclampsia. Vitamin D is considered as having a major role in the synthesis and regulation of genes that are effective in the early developmental phase of the placenta [11, 12] .Vitamin D deficiency has been suggested to be a predisposing factor in the peripheral vascular phase modulation, which will result in inadequate placental development and the development of pre-eclampsia during the early weeks of pregnancy [23].

This study has been conducted to evaluate the frequency of vitamin D deficiency among women in the study groups and its relationship with pre-eclampsia. Regarding the frequency of vitamin D deficiency , all women who participated in this study have vitamin D level below normal (<20ng/ml), with the majority of women in both groups have significant deficiency (level <10ng/ml) which was 45 (90%) women in the study group compared to 40 (80 %) women in the control (table 2).

This high prevalence of vitamin D deficiency in our study may be related to two facts, first, data were collected during winter months were vitamin D deficiency known to be high, second, most of women in this study were house wives (72% in the study group and 78% in the control group, table1) so they are not going outdoors and not exposed adequately to sunlight during the day time.

Our result agrees with other studies carried out in the USA, Australia, the Middle East and South Asia,

where vitamin D deficiency was detected in 26-98% of pregnant women. Vitamin D deficiency is around 66-100% in women with a dark skin color [24-26].

The mean vitamin D level among pre-eclampsia group in this study was not found to be statistically different from the mean vitamin D level of the control group (5.87± 3.37 versus 6.5± 3.67, p value=0.25).

This result disagree with study done by Singla R et al, 2015 [27] in India who found that the mean serum vitamin D was significantly lower among cases (9.7 Â± 4.95 ng/ml) as compared to controls (14.8 Â± 6.68 ng/ml); p = 0.0001. In a meta-analysis of this issue, Tabesh et al 2013 [28], established the association of low 25(OH) D level and pre-eclampsia. Also, in a prospective cohort study, maternal vitamin D concentration during the 24-26th week of pregnancy was found to be 14% lower in the patient group with pre-eclampsia compared to the group of healthy pregnant women [29].

However, many other studies like our study have not supported the association between vitamin D and pre-eclampsia . In one study, vitamin D levels were found to be similar in patients with and without development of pre-eclampsia during the first and second trimester [30]. Also Wetta et al., in their case control study, demonstrated that serum 25 (OH) D levels measured at the 15th and 21st week of pregnancy were statistically similar in their two groups that comprised of 89 cases with diagnosed pre-eclampsia at the 37th week of pregnancy and 177 controls [31]. In a randomized controlled trial conducted by Marya et al., no significant difference was found in the incidence of pre-eclampsia between cases with or without vitamin D (1,200 IU/daily) and calcium (375 mg/daily) support during the 20th and 24th week of pregnancy in 400 patients [32].

In conclusion, vitamin D deficiency was very common among the studied women.No statistical significant association between vitamin D deficiency and pre-eclampsia was found in this study.

Recommendation

Since vitamin D deficiency is very common among pregnant women, we recommend screening for and supplementation with vitamin D during pregnancy.

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