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Full Length Research Paper

Vitamin D deficiency and recurrent pregnancy loss in Iranian women

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Vitamin D deficiency is a common problem worldwide. Recurrent Pregnancy Loss (RPL) is considered as a controversial subject in reproductive medicine and is unexplained in half of the cases. The immunological factors may play a role in failure of pregnancy in women with RPL. The role of this vitamin D has also been proved in the immune system. The present study aimed to investigate vitamin D deficiency with some factors in the women with the history of RPL and those with the history of Sporadic Pregnancy Loss (SPL). This cross-sectional study was conducted on 120 pregnant women with gestational age below 20 weeks (60 women with RPL and 60 women with SPL) who had referred to the clinics affiliated to Shiraz University of Medical Sciences within the past 6 months. The participants' serum vitamin D levels were measured. Low vitamin D levels (<8 ng/ml) were observed in 20 out of the 60 women with RPL (33.3%) versus 9 out of the 60 ones with SPL (15%) that revealed an association between the women with RPL and those with SPL regarding vitamin D deficiency ($P=0.038$). Also the median serum level of vitamin D was 9.20 ng/ml in the women with four or more abortions, 10.85 ng/ml in those with three abortions, and 11.50 ng/ml in the women with two abortions. It seems that vitamin D deficiency plays a role in miscarriage in the women with RPL by defect of the immune inflammatory response. Thus, routine request of 25-hydroxy vitamin D test and prescription of vitamin D supplements are important in these women.

Keywords: Recurrent pregnancy loss, Vitamin D, Immune inflammatory response

INTRODUCTION

Recent reviews have indicated that the 25(OH)D level was much less than the amount required to maintain health. The prevalence of vitamin D deficiency in Europe

had vary 2-30% and in some countries is 75% (Mithal et al., 2009). Despite frequent exposure to ultraviolet radiation in tropical countries, some studies have shown vitamin D deficiency in these areas. The prevalence of vitamin D deficiency is especially in the Middle East (Azai et al., 2000; Norval and Wulf, 2009; Matsuoka et al., 1988; Marks et al., 1995; Hennie et al., 2002). Vitamin D, a steroid hormone, is well known to be involved in

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calcium phosphate homeostasis and bone metabolism (Kuniaki et al., 2013). vitamin D metabolites include genomic and non-genomic effects. Genomic effects on the classical target organs, bone, skeletal muscle, parathyroid glands, intestine, and kidney have been known for many years. In the meantime, vitamin D receptors have been demonstrated in most 'non-classical' target tissues of the body, including smooth muscle, heart muscle, thyroid, cells of the immune system, brain, liver, lung, colon, gonads, prostate, and skin (Mizwicki and Norman, 2009). Also, presence of Vitamin D Receptor (VDR) and the enzymes involved in hydroxylation of vitamin D and identification of localized vitamin D synthesis in human placenta and decidua implicate the importance of this hormone in reproductive function and is so as a risk factor of recurrent pregnancy loss (Tavakoli et al., 2011). Recurrent Spontaneous Abortion (RSA) is defined as three or more consecutive pregnancy losses prior to the 20th week of gestation. Recently, many specialists agree that at least after two consecutive abortions, the cause should be investigated because epidemiological studies have suggested that the risk of subsequent pregnancy loss is approximately 24% after two and 30% after three consecutive clinical pregnancy losses (Cunningham et al., 2010). Approximately one case of Recurrent Pregnancy Loss (RPL) is detected in every 300 pregnancies (Berek, 2006). Multiple causes of RPL are charged alone or in combination with each other (Norval and Wulf, 2009). over half of the cases remain unexplained (Kwak-Kim et al., 2009; Berkane et al., 2003; Laird et al., 2003). Among the diverse causes of RPL, the role of immunological factors should be considered more than the other factors (Laird et al., 2003). in reviews hypothesized that endometrial cells of women with unexplained recurrent spontaneous abortion (URSA) have impaired capacity to produce or respond to vitamin D. therefor Evidence has revealed that vitamin D deficiency is identified as risk factor in RPL (Tavakoli et al., 2011). according imonological of activity vitamin D and the prevalence high vitamin D dificiendy the present study counducted, to investigate vitamin D dificiency between two groups of the iranian women with a history of RPL and a history of Sporadic Pregnancy Loss (SPL).

MATERIALS AND METHODS

The Ethics Committee of Shiraz University of Medical Sciences approved the study(6758). Besides, written informed consents for taking part in the study were obtained from all the participants upon recruitment. This cross-sectional study was conducted on 120 healthy women with gestational age below 20 weeks. Among the participants, sixty had RPL and sixty had Sporadic Pregnancy Loss (SPL). The study women were selected from Motahari, Hafez, and Zainabiyeh clinics, Shiraz, Iran. The exclusion criteria of the study were suffering

from known cardiac disease, renal dysfunction, kidney stones, rheumatoid arthritis, arteriosclerosis, thyroid, parathyroid, or adrenal disorders, type 1 diabetes, infertility, known malignancy, malabsorption syndrome, and Cushing syndrome. All the subjects had regular menstrual cycles and had not used hormones or vitamin D for at least 3 months. For all the women under study, Body Mass Index (BMI) was obtained from their weight and height recorded by midwives during the first prenatal consultation at the beginning of the first trimester of pregnancy. Moreover, a general questionnaire including the participants' socio-demographic characteristics and information about prior abortion, smoking, alcohol consumption, sunscreen usage, diseases, medications, and use of food supplements was completed through a face-to-face interview conducted by the researchers. Furthermore, approximately 5 ml whole blood was collected by venipuncture in a non-heparinized tube. The samples were centrifuged and serum extraction was done in the field. Then, the samples were sent to Namazi hospital's medical researches laboratory for analysis and were frozen immediately. Afterwards, 25-hydroxy vitamin D (25(OH) D) level was measured using High Performance Liquid Cromatogheraphy (HPLC). The normal range for serum vitamin D (25(OH) D) was 20-80 ng/ml. Thus, 8-20 ng/ml and less than 8 ng/ml 25(OH)D levels were considered as severe vitamin D inadequacy and vitamin D deficiency, respectively.

All data analyses were performed using the SPSS statistical software. The results were expressed as mean \pm SD or median (IQR). Mann-Whitney and Kruskal-Wallis tests were used to determine the significance of differences between the study groups.

RESULTS

The study participants' characteristics have been presented in Table 1. The mean age of all participated women was 29.291 ± 5.213 while the mean age of the women with SPL and those with RPL was 28.1 ± 4.74 and 30.43 ± 5.44 years Based on the results, 42.5% of the women with RPL and 41.7% of those with SPL had average education. Considering occupation, 80% of the women with SPL and 86.7% of those with RPL were homemakers. Moreover, 58.3% of the women with RPL and 66.7% of those with SPL had normal BMI. the mean gestational age was in RPL 11.48 ± 5.53 and in SPL 13.51 ± 4.33 . the median gravida was 4.00 in RPL and 2.00 in SPL. Additionally, 38.3% of the women in the SPL group and 43.3% of those in the RPL group used sunscreen. The cause of abortion was unknown in 85% of the women with SPL and 91.7% of those with RPL. Vitamin D deficiency was detected in 15% of the women with SPL and 33.3% of those with RPL (Table 2). our study showed that vitamin D deficiency was associated in two groups ($p=0.038$) (Table 3). The median serum level

Table 1. Comparison of the descriptive characteristics of the two groups

Group	Women with RPL	Women with SPL	
Descriptive characteristics	Mean ± SD	Mean ± SD	p-value
Age (years)	30.43±5.44	28.15±4.74	0.000
BMI (kg/m ²)	N(%)	N(%)	0.000
Underweight	2(3.3)	2(3.3)	
Normal	35(58.3)	40(66.7)	
Overweight	11(18.3)	9(15)	
Obese	12(20)	9(15)	
Total	60(100)	60(100)	
GA (weeks)	11.48±5.53	13.51±4.33	0.000
Occupation			0.000
Homemaker	52 (86.7%)	48 (80%)	
Employed	8 (13.3%)	12 (20%)	
Total	60 (100%)	60 (100%)	
Education level	22 (36.7%)	17 (28.3%)	0.062
Below diploma	26 (43.3%)	25 (41.7%)	
Diploma	12 (20%)	18 (30%)	
Academic	60 (100%)	60 (100%)	
Gravida	Median	Median	0.000
	4.00	2.00	
Use of sunscreen	26 (43.3)	23 (38.3)	0.045
Non-use of sunscreen	34 (56.7)	37 (61.7)	
Etiology of abortion	55 (91.7)	51 (85)	0.000
Unknown	5 (8.3)	9 (15)	
Other			

Table 3. Descriptive statistics of vitamin D levels in the women with SPL and RPL

Group	Vitamin D levels		Deficiency		Inadequate		Normal	
	N	%	N	%	N	%	N	%
RPL (60)	9	15	31	51.7	20	33.3		
SPL (60)	20	33.3	26	43.3	14	23.3		

Table 4. Comparison of vitamin D levels in the women with RPL and SPL

Group	Vitamin D levels Median (IQR)	P-value
PRL	14.60 (10.57- 23.70)	0.038
SPL	10.9 (6.70-17.10)	

Non-parametric Mann-Whitney test

Table 4. Comparison of vitamin D levels and number abortion in RPL

Number abortion	N	Vitamin D levels	P-value
two abortion	35	11.50(17.10 –7.20)	0.836
Three abortion	18	10.85(6.32- 18.22)	
Four and more abortion	7	9.20 (6.50-28.30)	

Non-parametric Kruskal-Wallis test

of vitamin D was 9.20 ng/ml in the women with four or more abortions, 10.85 ng/ml in those with three abortions, and 11.50 ng/ml in the women with two abortions. (Table 4)

DISCUSSION

Vitamin D deficiency during pregnancy is a common problem worldwide (Lips, 2010; Dent and Gupta, 1975; Vandevijvere et al., 2012). Vitamin D deficiency in pregnant women is associated with increased risk of obstetrical complications, such as preeclampsia, bacterial vaginosis and the associated preterm delivery, gestational diabetes mellitus, and small-for-gestational age births (Trixie et al., 2013; Bodnar et al., 2007; Bodnar et al., 2009; Bodnar and Simhan, 2010). It seems that vitamin D induces the necessary immunological changes to prevent pregnancy loss (Maghbooli et al., 2008). In our study Vitamin D deficiency was detected in 20 out of the 60 women with RPL (33.3%) and 9 out of the women with sporadic abortion (15%) ($p=0.03$). In the study by Kota et al. (2012), 29 out of the 58 women with PRL (41.4%) were vitamin D deficient (Ota et al., 2012). In the study by Kuniakiota et al. (2013) also, among the 133 women with recurrent miscarriage, 63 (47.7%) had vitamin D deficiency (Kuniaki et al., 2013). In addition, the results of the study conducted by Maryam Tavakoli et al. (2011) indicated that endometrial cells in women with recurrent spontaneous abortion were deficient in production of or response to vitamin D (Tavakoli et al., 2011), which were in agreement with the results of this study.

Based on the results in our study, the median serum level of vitamin D was 9.20 ng/ml in the women with four or more abortions, 10.85 ng/ml in those with three abortions, and 11.50 ng/ml in the women with two abortions. Thus, the women with higher number of abortions had lower vitamin D serum levels. However, no association was found between the serum vitamin D levels and number of abortions in the women with RPL ($p=0.836$).

In Conclusions The prevalence of vitamin D deficiency was high in the women with RPL (33.3%) and with higher number of abortions had lower vitamin D serum levels. Thus, routine request of 25-hydroxy vitamin D test and prescription of vitamin D supplements are important in these women.

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