

## ASSOCIATION BETWEEN MATERNAL SERUM VITAMIN D AND EARLY PREGNANCY SPONTANEOUS ABORTION IN IRAQI WOMEN

ASHWAQ KADHIM MOHAMMED\*, VIAN HUSSAM ALMANSI ALQANI

Department of Obstetrics and Gynecology, College of Medicine, University of Al-Qadisiyah, Iraq. Email: ashwaqalshemeri@gmail.com

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### ABSTRACT

**Background:** Spontaneous pregnancy loss is seen in approximately 10–15% of clinically observed pregnancies.

**Objective:** This study was aimed to estimate the Vitamin D serum concentration in a cohort of women with a history of recurrent spontaneous abortion.

**Methods:** The current cross-sectional study was conducted at Al-Diwaniya maternity and child teaching hospital, Al-Diwaniya province, Iraq. Data collection, lab work, and procedures related to the study extended from August 2016 to August 2017. The study enrolled 42 women of childbearing age who have a history of spontaneous early pregnancy loss. From each woman, a venous sample was obtained and sent to a lab to assess serum Vitamin D concentrations using standard routine biochemical methods.

**Results:** Assessment of mean maternal serum Vitamin D concentration revealed that the mean was  $21.48 \pm 11.82$  (ng/ml) and the range was from 5 to 50 (ng/ml). The number of women with low serum Vitamin D (<20 ng/ml) was 25 (approximately 60%), the results also revealed a highly negative correlation was obtained between number of abortions and maternal serum Vitamin D ( $r = -0.717$ ,  $p < 0.001$ ) and that the value of  $R^2$  was 0.514 which indicated that the level of Vitamin D alone can act as an independent predictor to explain 51.4% of spontaneous abortions in the participating women.

**Conclusion:** Vitamin D level is a strong predictor of pregnancy loss in early pregnancy, and that correction of Vitamin D status among Iraqi pregnant ladies may substantially reduce the frequency of spontaneous abortion.

**Keywords:** Early pregnancy abortion, Vitamin D deficiency, Serum vitamin.

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### INTRODUCTION

One of the major pregnancy adverse outcomes is baby loss before completion of natural pregnancy period, and when conception does not end with a live born child this is termed pregnancy loss; when it happens before 28 weeks gestation, it is called abortion [1]. Spontaneous pregnancy loss is seen in approximately 10–15% of clinically observed pregnancies. Early pregnancy loss (spontaneous abortion) is assigned when the loss occurs before completion of 12 weeks gestation [2] because the majority of spontaneous pregnancy loss happens early (before 12 weeks gestation), a thorough study of the pathophysiology behind this adverse pregnancy outcome is of great importance. A lot of mechanisms have been proposed with this regard, including hormonal derangements, chromosomal anomalies, intrauterine infections, uterine abnormalities, thrombophilia, and autoimmune disorders; in approximately 50% of cases with early pregnancy loss, the causes remain enigmatic in which the loss is termed unexplained pregnancy loss [3].

Vitamin D3 (1,25 dihydroxy Vitamin D3) is a hormone that is water soluble and well known to function in promoting bone mineralization and maintaining calcium homeostasis [4]. Moreover, it-D3 plays a major role in contorting cell proliferation and maturation and in modulating immune response both innate and adaptive form [5,6].

A lot of epidemiological published literature refers to the global occurrence of Vitamin D deficiency and insufficiency. Mitchell *et al.* [7] recorded the Vitamin D deficiency incidence (a serum level of <20 ng/mL) in women during reproductive age to be 31%. Reports from the "National Health and Nutrition Examination Surveys" described that the problem is variable between racial and ethnic categories, "with non-Hispanic blacks possessing a higher rate of Vitamin D deficiency and"

insufficiency when compared to white ethnic groups [8] these results were supported "by Forrest and Stuhldreher, who registered" that blacks had the highest incidence of Vitamin D insufficiency (82.1%) and then followed by Hispanics (69.2%) [9]. In spite of its global prevalence, wide geographical screening for vitamin insufficiency has not been adopted because of the expensive serum assays. For that reason, screening has been carried out only for groups at great risk for Vitamin Deficiency [10].

Recently, a great deal of attention has been focused on vitamin status during pregnancy. Evidence about the role of Vitamin D in human reproduction has been proved in a number of researchers [11]. Globally, vitamin deficiency is a frequent problem among women at the age of childbearing [12,13] among obstetric complications that have been reported to be associated with Vitamin Deficiency are gestational diabetes [14], pre-eclampsia [15] impaired intrauterine growth [16], and bacterial vaginosis [17]. Despite that, the association between poor Vitamin D status and spontaneous early pregnancy loss is less well defined.

A number of studies showed an association between pregnancy loss and vitamin deficiency that is probably mediated by "effector CD4+ T helper (Th) cellular responses in the innate (Th1) and adaptive (Th2) immune systems." Vitamin D is proposed to promote the Th2 effect by increasing interleukin (IL-5), (IL)-4, and IL-13 and preventing the Th1 response of IL-2, IL-1, tumor necrosis factor- $\alpha$  (TNF- $\alpha$ ), and interferon- $\gamma$  (IFN- $\gamma$ ) [18]. "In a study including 133 women with recurrent pregnancy loss, Ota *et al.* showed that 63 out of 133 women (47.4%) had Vitamin D deficiency and a significant association with natural killer cell activity with Vitamin D deficiency" [19]. Moreover, in another study of 115 female patients with antiphospholipid syndrome

(APS), Vitamin D concentrations in APS women were significantly less as compared to healthy control group [20]. Tavakoli *et al.* observed same cytokine profiles and Vitamin D expression in endometrial cells taken from female patients having unexplained recurrent pregnancy loss as compared to healthy control group [21]. Hence, the aim of the present study was to estimate the Vitamin D serum concentration in a cohort of women with a history of recurrent spontaneous abortion.

**METHODS**

The current cross-sectional study was conducted at Al-Diwaniya maternity and child teaching hospital, Al-Diwaniya province, Iraq. Data collection, lab work, and procedures related to the study extended from August 2016 to August 2017. The study enrolled 42 women of childbearing age who have a history of spontaneous early pregnancy loss. From each woman, a venous sample was obtained and sent to a lab to assess serum Vitamin D concentrations using standard routine biochemical methods.

**Statistical analysis**

Data were transformed into a spreadsheet of SPSS version 23. Numeric variables were expressed as mean and standard deviation whereas nominal data were expressed as number and percentage. Correlation between serum Vitamin D level and a number of abortions was evaluated using Spearman's test. The level of significance was considered at  $p \leq 0.05$ .

**RESULTS**

Then, the present study included 42 women at reproductive age and had a history of spontaneous abortions. The age was ranging from 17 to 36 years, and the mean age was  $24.95 \pm 5.09$  years. A number of spontaneous abortions were ranging from 1 to 6 and the mean was. Assessment of mean maternal serum Vitamin D concentration revealed that the mean was  $21.48 \pm 11.82$  (ng/ml) and the range was from 5 to 50 (ng/ml). The number of women with low serum Vitamin D (<20 ng/ml) was 25 (approximately 60%), as shown in Table 1.

There was no significant correlation between maternal age and serum Vitamin D concentrations ( $r=0.091$ ,  $p=0.568$ ), in other words, low level of the vitamin was evenly distributed along the scale of age and that no reproductive age is immune from having Vitamin D deficiency, as shown in Fig. 2. Nevertheless, highly negative correlation was obtained between number of abortions and maternal serum Vitamin D ( $r=-0.717$ ,  $p<0.001$ ) and that the value or  $R^2$  was 0.514 which indicated that the level of Vitamin D alone can act as an independent predictor to explain 51.4% of spontaneous abortions in the participating women, as shown in Fig. 2.

**DISCUSSION**

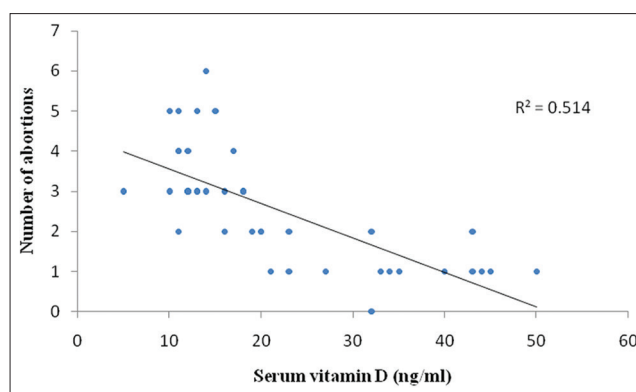
The current study showed a relatively great rate of vitamin deficiency among women with history with spontaneous early pregnancy miscarriage which was approximately 60%. Similar results were obtained by several other investigators [12,13]. "In a study including 133 women with recurrent pregnancy loss, Ota *et al.* showed that 63 out of 133 women (47.4%) had Vitamin D deficiency [19]." Moreover, a significant correlation was found between a number of abortions and serum concentration of Vitamin D.

Vitamin D status is poorly categorized as an obstetric problem in Iraqi women and little if any study has linked spontaneous abortion to recurrent spontaneous early pregnancy abortion. The cause of

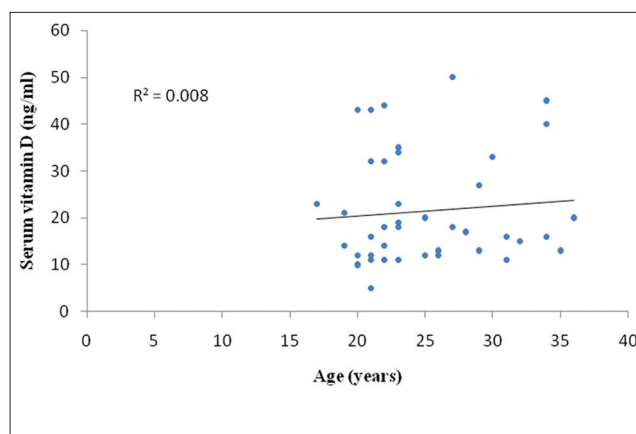
**Table 1: Characteristics of the study populations**

Characteristic	Mean±SD	Range (min-max)
Age (years)	24.95±5.09	19 (17-36)
Number of abortion	2.57±1.42	6 (1-6)
Vitamin D (ng/ml)	21.48±11.82	45 (5-50)

SD: Standard deviation



**Fig. 1: Correlation between maternal serum Vitamin D concentration and number of spontaneous abortions**



**Fig. 2: Correlation between maternal age and serum Vitamin D concentration**

pregnancy loss in women with insufficient Vitamin D levels has been investigated by several authors. It is probably mediated by "effector CD4+ T helper (Th) cellular responses in the innate (Th1) and adaptive (Th2) immune systems." Vitamin is proposed to promote them Th2 effect by increasing IL-5, (IL)-4, and-13 and preventing then Th1 response of IL-2, IL-1, TNF- $\alpha$ , and IFN- $\gamma$  [18].

**CONCLUSION**

Vitamin D level is a strong predictor of pregnancy loss in early pregnancy, and that correction of Vitamin D status among Iraqi pregnant ladies may substantially reduce the frequency of spontaneous abortion.

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