

# Evaluation of the Relationship between Maternal Serum Vitamin D Level and Abortion in Patients Referred to Ali Ibn Abitaleb Hospital in Zahedan in 2018

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## ABSTRACT

**Background and Aim:** Due to the increasing prevalence of vitamin D deficiency, there is concern about the effects of the high prevalence of vitamin D deficiency in the entire population of the world, including pregnant women. Therefore, the aim of this study was to determine the relationship between maternal serum vitamin D levels and abortion in patients referred to Ali Ibn Abitaleb Hospital in Zahedan.

**Materials and Methods:** In this case-control study, 50 mothers who were admitted to the gynecology ward of Ali Ibn Abitaleb Hospital in Zahedan due to abortion were included in the case group, and 50 healthy pregnant women with normal gestational age and no history of abortion were considered as controls. Serum levels of vitamin D less than 10 ng/ml were considered as vitamin D deficiency and 10 to 30 ng/ml were considered as inadequate levels. Then, information such as maternal vitamin D level as the main target and maternal age, paternal age, and fetal age as the secondary target of the study were determined.

**Results:** The subjects were in the age range of 17 to 35 years with an average of  $26.27 \pm 4.84$  years. The results showed that the frequency of severe vitamin D deficiency was 34% in the case group and 12% in the control group. Based on the results of this study, it was found that the mean serum level of vitamin D and gestational age in the group of mothers with abortion were significantly lower than the control group ( $P < 0.05$ ).

**Discussion and Conclusion:** In our study, it was found that mothers with abortions have low levels of vitamin D. Also, the frequency of severe deficiencies in these people was higher than those without abortion, and vitamin D deficiency in people under 30 years of age was more important than people over 30 years of age; In addition, the levels of this vitamin was not affected by gestational age.

## KEYWORDS

Vitamin D, Abortion, Vitamin D Deficiency.

## Introduction

One of the most important consequences of pregnancy is the loss of the fetus before the end of the normal pregnancy and when it occurs before 22 weeks of pregnancy, it is referred as abortion [1]. Spontaneous abortion is seen in approximately 10-15% of pregnancies. Spontaneous abortion is determined when the fetal loss occurs before the end of 12 weeks of gestation [2]. Many mechanisms have been proposed in the field of abortion, including hormonal disorders, chromosomal abnormalities, intrauterine infections, uterine abnormalities, thrombophilia, and autoimmune disorders [3].

Vitamin D or 1,25 dihydroxyvitamin D<sub>3</sub> is a hormone that is fat soluble and its function is to strengthen bone mineralization and maintain calcium homeostasis [4]. Factors such as age, season, latitude, sun exposure, skin type, type of coverage and use of sunscreen can affect the production of vitamin D [5]. Vitamin D has been shown to play an important role in a wide array of diseases by regulating hormone secretion, regulating immune function, differentiation and cell proliferation [6-9]. Vitamin D receptors are found throughout the genitals including the ovaries, endometrium, and placenta [10]. Vitamin D deficiency is widespread throughout the world and serum levels of vitamin D are higher in summer. The causes of this pervasive deficiency are a combination of behavioral factors

(staying indoors for a long time, using sunscreen, and wearing thick clothing) and internal factors (vitamin destruction in the skin and melanin of the skin) [11]. Obesity is also associated with vitamin D deficiency, which may be due to the fat-soluble nature of this vitamin and consequently more uptake by adipose tissue [12].

There are concerns about the effects of the high prevalence of vitamin D deficiency worldwide in the general population, including pregnant women. Changes due to maternal calcium metabolism and vitamin D concentration have been shown to be transmitted to the fetus through the placenta during pregnancy [13]. On the other hand, vitamin D deficiency is associated with preeclampsia and high blood pressure, preterm labor, gestational diabetes, and other problems during pregnancy, also, it is a risk factor for bacterial vaginosis; therefore, vitamin D deficiency in pregnancy is a very important problem and for this reason, the treatment of this complication is very important for mother and baby [14-17]. The prevalence of vitamin D deficiency is estimated to be 20-85% depending on the geographical location and other related factors [18]. The prevalence of Vitamin D deficiency is also high in Iran and it has been reported to be 26-86% in different studies and cities [19, 20]. According to studies, insufficient levels of vitamin D during pregnancy and lactation has been identified as a major problem. In a study by Azar Pirdehghan et al. on the prevalence of vitamin D deficiency and its effect on pregnancy complications, it was shown that the mean levels of vitamin D in people undergoing normal delivery or elective cesarean section were higher, in comparison with people undergoing an abortion and emergency cesarean section [21]. Therefore, the aim of this study was to investigate the relationship between maternal serum vitamin D levels and abortion in patients referred to Ali Ibn Abitaleb Hospital in Zahedan in 2018.

## Materials and Methods

In this cross-sectional case-control study, mothers who were admitted to the gynecology ward of Ali Ibn Abitaleb Hospital in Zahedan, Iran in 2018 due to abortion were studied. Inclusion criteria were mothers with abortion for no apparent reason and were satisfied with the study. Exclusion criteria included pregnant women with recurrent miscarriages and infectious miscarriages, age over 35 years, Mullerian anomalies, renal disorders, metabolic disorders, bone problems, diabetes and preeclampsia, lupus and antiphospholipid syndrome, and dissatisfaction with the study, or defect in the file and lack of access to the patients. Accordingly, 50 pregnant women with abortion were considered as the case group and 50 pregnant women who were in the first and second trimesters of pregnancy (less than 22 weeks) and had no history of abortion were considered as the control group. Also, serum levels of vitamin D less than 10 ng/ml were considered as vitamin D deficiency and 10 to 30 ng/ml were considered as inadequate levels. In this study, all Helsinki principles were observed and after approval of the ethics committee of Zahedan University of Medical Sciences (code: IR.ZAUMS.REC.1397.041), individuals were examined for the purposes of the study.

The information was collected through the patient's medical records, interview with the mother, and paraclinical results. Then, information such as maternal vitamin D level as the main target and maternal age, paternal age, and fetal age as the secondary target of the study were determined.

## Data Analysis

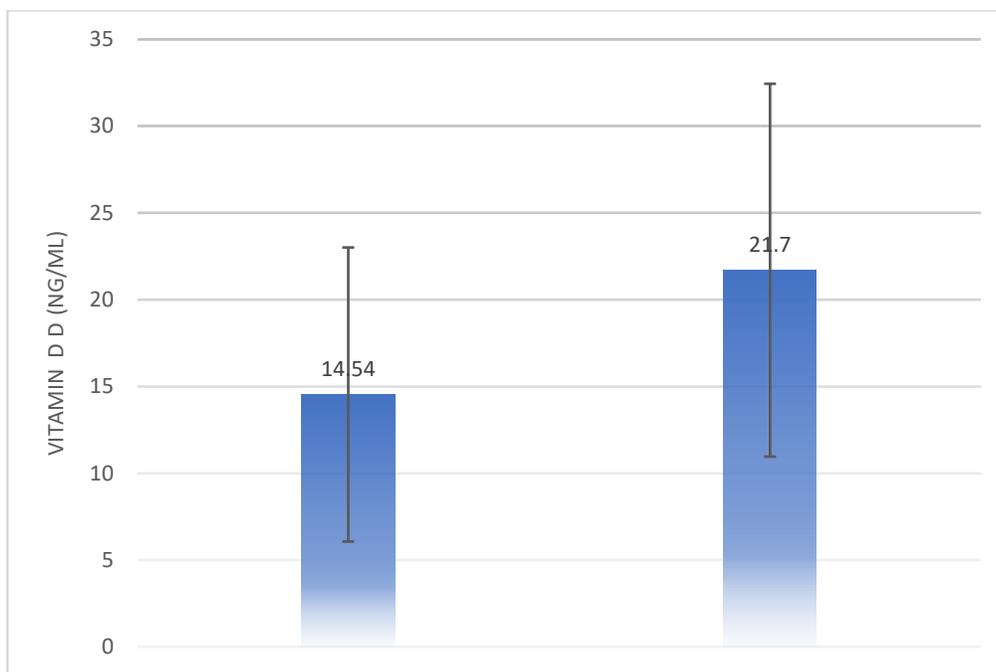
Data were analyzed using SPSS ver.24 software; in order to perform analytical and inferential analyses, independent t-test (comparing the mean of the two groups), Chi-square, and analysis of covariance, and to examine the quantitative variables, t-test and Mann-Whitney U test were used. Significance level was also considered  $P < 0.05$ .

## Results

In the present study, 100 cases were studied (50 mothers with abortion in the case group and 50 mothers with a normal pregnancy in the control group). Our results showed that the mean age of patients was  $26.27 \pm 4.84$  years (17-35 years). Mean and standard deviation of maternal, paternal, and gestational age are also shown in Table 1 and there was no significant relationship between any of the mentioned variables in the two groups ( $P > 0.05$ ).

**Table 1.** The mean and standard deviation of maternal, paternal, and gestational age in the two study groups

Variable	Group	Quantity	Mean	Standard deviation	P-value
Maternal age (years)	Case	50	25.72	5.067	0.286
	Control	50	26.82	4.606	
Paternal age (years)	Case	50	30.39	5.800	0.437
	Control	50	31.30	5.289	
Gestational age (weeks)	Case	50	11	3.408	0.682
	Control	50	11.68	4.368	



**Figure 1.** Mean and standard deviation of serum vitamin D levels in the two groups

According to Figure 1. The mean serum levels of vitamin D in the group of mothers with abortion (14.54 ± 8.47) were significantly lower than the control group (21.7 ± 10.74) (P < 0.001).

Also, according to Table 2, the frequency of severe and moderate vitamin D deficiency in the two groups showed that a total of 82% of mothers had severe and moderate vitamin D deficiency, which demonstrated a significant difference from the control group. (P = 0.032).

**Table 2.** Frequency of vitamin D deficiency in the two groups

Vitamin D		Group	Mothers with abortion	Control	Total	P-value
Severe deficiency	Quantity (%)		17 (34)	6 (12)	23 (23)	0.032
	Quantity (%)		29 (58)	38 (76)	67 (67)	
Normal	Quantity (%)		4 (8)	6 (12)	10 (10)	
Total	Quantity (%)		50 (100)	50 (100)	100 (100)	

The results of Table 3 showed that the mean serum levels of vitamin D in the case group and cases under 30 years of age were significantly lower than the control group (13.52 versus 21.19 ng/ml) (P < 0.001). However, there was no

significant difference in the age group of over 30 years ( $P > 0.05$ ). On the other hand, the mean serum levels of vitamin D in the group of mothers with abortion and in both groups of gestational age were significantly lower than the control group ( $P < 0.05$ ). (Table 3).

**Table 3.** Mean and standard deviation of serum vitamin D levels in the case and control groups and different age groups of mothers

Variable	Group	Quantity	Mean	Standard deviation	P-value
Less than 30 years of age	Case	35	13.52	6.518	<0.001
	Control	33	21.19	10.301	
30 years of age or more	Case	15	16.92	11.820	0.079
	Control	17	22.69	11.816	
Less than 12 weeks	Case	25	13.75	6.79	<0.001
	Control	28	21.83	9.98	
12 weeks or more	Case	23	15.31	10.08	0.025
	Control	22	21.53	11.87	

## Discussion

Among micronutrient deficiencies, vitamin D deficiency is currently a pandemic; lower than normal levels of vitamin D are a major problem in the general population, but some people are at greater risk for developing the deficiency, the most distinct example of which is pregnant women. Therefore, vitamin D deficiency is almost common in pregnant women. Since pregnancy increases the need for vitamins, vitamin D deficiency is also considerably observed during this period [6, 22]. The aim of this study was to evaluate the level of vitamin D in women who experienced abortions.

In the present study, the mean age of the individuals was  $26.27 \pm 4.84$  years (17-35 years). The mean serum level of vitamin D in the group of mothers with abortion was significantly lower than the control group (14.54 versus 21.7 ng/ml); in other words, the frequency of severe vitamin D deficiency in mothers with abortion was equal to 34% and in the control group was equal to 12%, which showed a statistically significant difference and this difference was greater in cases aged less than 30 years. In a study by Moghadas et al., the mean concentration of D (OH) 25 in the case group was  $22.49 \pm 9.22$  and in the control group was  $30.36 \pm 10.03$  ng/ml, which demonstrated a statistically significant difference between the two groups. As a result, low levels of serum D (OH) 25 in pregnant women induced a greater risk of abortion compared to women with normal levels of vitamin D. Therefore, they reported that low serum levels of vitamin D could be a risk factor for abortion [23]. Most of the discussions about the relationship between vitamin D and implantation have originated from studies that have shown that women with higher levels of vitamin D during embryo transfer and IVF have had successful pregnancies [24]. In a review by Monastra et al., Vitamin D was defined as a steroid hormone with progesterone-like activity. Calcitriol is involved in preparing the endometrium for pregnancy. In addition, the implantation process and gestational age are supported in different ways but similar to when progesterone is used [25]. In a study on vitamin D levels in women at 7-9 weeks of gestation, Hou W et al. reported that vitamin D levels were higher in women with normal pregnancies than in women with miscarriages and that there was a strong association between low vitamin D levels and miscarriages which was consistent with the results of the present study [26].

Other findings from our study showed that vitamin D levels in mothers with abortions were significantly lower than the control group. Therefore, it can be found that vitamin D plays a significant role in the physiopathology of abortion. Also, based on the results of the present study, it was found that the incidence of abortion in the first trimester of pregnancy is significantly associated with a decrease in vitamin D levels. In 2016, Zhang et al. conducted a meta-analysis study to investigate the effect of serum vitamin D levels on pregnant women and the risk of miscarriage; by evaluating studies in line with their research objectives, they concluded that severe vitamin D deficiency can have negative effects on early fetal growth and increase the risk of abortion [27]. On the other hand, in a meta-analysis of 10,630 pregnant women, Zhang et al. reported that there was no significant association between low levels of vitamin D and an increased risk of miscarriage, but very low levels of vitamin D (less than 20 Ng/ml) were significantly associated with an increased risk of abortion in the first trimester of pregnancy. Therefore, according to their study, serum levels less than 20 ng / ml can be a risk factor for miscarriage [27]. In a study by

Bespalova O et al., which aimed to investigate the relationship between vitamin D levels and abortion, in the abortion group, morphometric results showed a lower relative level of vitamin D expression than in the control group. Also, in the abortion group, there was a significant relationship between the serum levels of vitamin D and the expression of the relative level of VDR. In the abortion group, lower levels of vitamin D and VDR were observed compared to the control group. Their results indicated the importance of vitamin D for pregnancy progression [28]. Also, in a prospective cohort study, Andersen LB et al found an association between 25 (OH) D and abortion in the first trimester of gestation, suggesting vitamin D as a modifiable risk factor for abortion. To assess this hypothesis, randomized controlled trials should be conducted to examine the potential effect of vitamin D supplementation on reducing the risk of miscarriage, by increasing 25 (OH) D concentrations in the early stages of pregnancy [29]. In our study, it was also found that the incidence of miscarriage in the first trimester of pregnancy is significantly associated with a decrease in vitamin D levels.

In general, based on the results of the present study and due to the prevalence of unwanted abortions, investigating the underlying causes in individuals, especially those at higher risk, and serum levels of vitamin D in pregnant women is necessary to reduce the number of abortions; also, studies on the physiopathology of the effect of vitamin D on abortion should be performed to further understand the exact role of vitamin D in the occurrence of abortion.

## Conclusion

The results of the present study showed that mothers with abortions had low levels of vitamin D and the frequency of severe deficiencies in these people was higher compared to those with normal pregnancy; also, vitamin D deficiency in cases under 30 years of age was more important, in comparison with people over 30 years and this deficiency was not affected by gestational age.

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