



## Effect of Vitamin D on Placenta Accreta

Ashraf Jamal<sup>1</sup>, Farnaz Sahhaf<sup>2\*</sup>, Rita Dousti<sup>3</sup>, Somaiyeh Saiyarsarai<sup>3</sup>

### Abstract

**Objectives:** Vitamin D receptors exist in the reproductive system of women. Vitamin D is a fat-soluble vitamin that plays a double role as vitamin and hormone. Vitamin D deficiency is a major health problem around the world. The prevalence of vitamin D deficiency is high worldwide. The morbidly adherent placenta is now a significant obstetric challenge. Therefore, we decided to conduct a study on the effects of vitamin D deficiency on placenta accreta to help identify high-risk women.

**Materials and Methods:** This analytical cross-sectional study was conducted from August 2016 to February 2017 at Alzahra hospital affiliated to Tabriz University of Medical Sciences, Tabriz, Iran. In our study, we had 2 groups of women who referred to the high risk pregnancy clinic in Alzahra hospital.

**Results:** According to the results obtained from independent samples *t* test, serum level of vitamin D was lower than 30 ng/mL in 97% of the participants.

**Conclusions:** Based on the results of the present study, since the diagnosis of placenta accreta was made earlier in the pregnancy, it can be determined simultaneously with an anomaly scan during pregnancy to prevent the possible complications of placenta accreta. We hope that with this study we can help prevent and reduce the occurrence of placenta accreta in order to prevent the psychiatric and surgical complications of hysterectomy caused by placenta accreta.

**Keywords:** Placenta accreta, Vitamin D deficiency, Pregnancy complication

### Introduction

The existence of vitamin D receptors in women's reproductive system including the uterus, endometrium, ovary, and placenta suggests that vitamin D is involved in women's fertility (1). Vitamin D and its receptors facilitate the implantation in fertility techniques such as in vitro fertilization (IVF) by regulating an endometrial immune response and stimulating endometrial decidualization (2).

Vitamin D is a fat-soluble vitamin that plays a double role as vitamin and hormone (3). Recent studies have shown that the amount of vitamin D synthesis is not adequate for daily requirements and that several factors contribute to the deficiency of this vitamin (4). Among the micronutrient deficiencies, vitamin D deficiency is now considered a pandemic (5).

In addition to classical functions of vitamin D in calcium homeostasis and bone metabolism (6), recent studies have also reported non-classical functions of vitamin D which include anticancer activity (7) and cardiovascular effects (8), and immune regulation (9).

Vitamin D deficiency causes disorders in women of reproductive age including gestational diabetes, endometriosis, polycystic ovaries, bacterial vaginosis, preterm labor, and preeclampsia (10).

People at risk for vitamin D deficiency are those who

have darker skin, less exposure to sunlight, and a body mass index (BMI) greater than 30 (11-16).

The level of vitamin D is determined by measuring the serum levels of 25-hydroxy (25-OH) vitamin D (17). The Institute of Medicine defined the adequate level of vitamin D for pregnant women as having serum 25-OH vitamin D concentrations greater than 50 nmol/L (20 ng/mL) (18).

Serum 25-OH Vitamin D level below 50 nmol/L is a sign of vitamin D deficiency. Accordingly, the serum levels of 25-75 nmol/L are moderate and below 25 nmol/L are severe deficiencies. Based on these definitions, the estimates show that around one billion people worldwide are moderately or severely impaired (19,20).

Vitamin D deficiency is a major health problem around the world (21). On the other hand, it is possible to prevent and remedy the situation on the basis of appropriate measures, especially in high risk groups (22,23).

Vitamin D deficiency is highly prevalent in the world. In 195 studies in 44 countries with more than 168 000 cases, the mean vitamin D level was lower than 20 ng/mL in 37.3% of the studies (25). The prevalence of vitamin D deficiency was 42.4% in African-American women (26), 81.4% in Turkish pregnant women (27), 79.7% in some regions of China (28) and 87.3 in Saudi Arabia (29). In 1047 studies conducted in Iranian schools, the



mean serum level of vitamin D was  $14.7 \pm 9.4$  ng/mL (30). Placenta accreta-related mortality is currently a big challenge. Late diagnosis of placenta accreta may lead to postpartum hemorrhage and hysterectomy during pregnancy (31). The prevalence of placenta accreta has increased to 1 in 533 pregnancies in the last 20 years (32). Given that placenta accreta and cesarean hysterectomy are among the most threatening problems for women of reproductive age and cause mortality, psychological complications, and economic consequences in the society and the health system, we decided to conduct a study on the effects of vitamin D deficiency on placenta accreta to help identify high-risk women and prevent the physical, psychological, and financial consequences of this incident through evaluations and follow-ups.

### Materials and Methods

This analytical cross-sectional study was conducted from August 2016 to February 2017 at Alzahra hospital, Tabriz, Iran. In our study, we had 2 groups of women who referred to the high-risk pregnancy clinic in Alzahra hospital. The first group included pregnant women who had no complication caused by pregnancy and the second group included pregnant women with placenta previa and accreta diagnosed in the first 20 weeks of pregnancy. We measured the serum level of 25(OH)D in both groups and compared them. Women in the 2 groups did not use any vitamin D supplement in peripartum. The diagnosis of placenta accrete was performed by sonography at 25 to 34 weeks of gestation. In some cases, MRI was requested for verification of diagnosis. To ensure the accuracy of the findings, sonography was performed in all cases at Alzahra hospital.

The level of vitamin D was measured in Tabriz Laboratory in Abbott Machine through electrochemical method. The collected data were analyzed in Excel using Independent samples *t* test with a significance level of  $P < 0.05$ .

### Results

In this study, 34 patients were enrolled in placenta previa accreta group (group A) and 12 patients in placenta previa without infiltration (group B) and 75 patients in normal pregnancy group (group C).

Based on the results obtained from all 3 groups: The median age of mothers was 30-32 years; 100% of the cases were from East Azerbaijan; and 100% of the cases had experienced more than 1 pregnancy (Table 1).

Serum levels of vitamin D were lower than 30 ng/mL in 97% of groups A and B and 24% of group C. In groups A and B, 47.6% had 1 previous cesarean section, 42.8% had two, 4.7% had 3, and 4.7% had no cesarean section. Additionally, 83.3% had placenta accreta and underwent cesarean hysterectomy and 16.6% had no penetration and underwent cesarean section without any complication (Table 2).

The mean gestational age for diagnosis of placenta previa was 20 weeks and the mean gestational age for the diagnosis of placenta accreta was 28 weeks.

In 9.5% of the cases, the cause of cesarean hysterectomy was placental abruption which led to the termination of pregnancy at <32 weeks of gestation.

The cause of previous cesarean was elective cesarean delivery in 57.14%, parturition pain with absence of progress in delivery in 21.42%, fetal bradycardia at delivery in 4.76%, fetal bradycardia with placental abruption in 9.52%, meconium and birth pain in 2.38%.

Serum levels of vitamin D were lower than 30 ng/mL in 97%. There was no difference between groups A and B.

### Discussion

The findings of this study showed that vitamin D deficiency is significantly associated with placenta previa accreta.

The first model described for the effect of vitamin D on implantation is that cytokines produced at the embryonic level stimulate the development of CYP27B1 (6).

As a result, active vitamin D has an important effect on implantation, which may be different in various ways. Researchers have found new effects of vitamin D on the *HOXA10* gene, which is effective in the development of the embryo (16).

To date, no studies have been conducted on the relationship between vitamin D deficiency and placenta accreta. However, studies on the role of vitamin D in infertility and the success of IVF show that women with higher levels of vitamin D have had more successful embryo transfer and IVF (33).

On the other hand, the immunological activity of the placenta depends on vitamin D. Placental cells are immunological targets for the effect of vitamin D and thus have an effect on the oocyte implantation.

**Table 1.** Comparison of 3 Study Groups

	Groups		
	A	B	C
Maternal age	30-32	30-32	30-32
Location	East Azerbaijan, Iran	East Azerbaijan, Iran	East Azerbaijan, Iran
Gravidity	>1	>1	>1
Vitamin D deficiency	97%	100%	24%

**Table 2.** The Results of Groups A and B

	A, B
C/S hysterectomy	83.3%
GA-placenta previa	20 weeks
GA-placenta accreta	28 weeks
No complication	16%
History of elective cesarean	57.14%

In a study conducted on mice, it has been concluded that the absence of vitamin D receptors can cause developmental disorder, gonadal dysfunction, decreased aromatase activity, pregnancy complications, uterine hypoplasia, and infertility (17, 34).

According to the above-mentioned studies and the results found in this study, it can be hypothesized that vitamin D deficiency is one of the factors associated with defects in the placenta.

### Conclusions

Based on the results of the present study, since the diagnosis of placenta accreta was made earlier in the pregnancy, it can be determined simultaneously with an anomaly scan during pregnancy to prevent the possible complications caused by placenta accreta.

The number of samples in our study was low. For more accurate results, it is recommended to carry out studies with more samples. It seems the results of this study can help prevent and reduce the occurrence of placenta accreta in order to prevent the psychiatric and surgical complications of hysterectomy caused by placenta accreta.

### Conflict of Interests

Authors have no conflict of interests.

### Ethical Issues

This study has been done according to the ethical policies of Tabriz University of Medical Sciences.

### Financial Support

We do not have any financial support.

### Acknowledgement

This study has been done as a thesis for perinatology fellowship degree in Tabriz University of Medical Sciences in 2018 (5/34002).

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