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Assessing the Link between Vitamin D Levels and Miscarriage Risk in Women

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Author's contribution

The sole author designed, analysed, interpreted and prepared the manuscript.

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ABSTRACT

Background: The issue of miscarriage, sometimes known as missed abortion, is a contemporary concern in the field of obstetrics and gynecology. This condition is characterized by a cluster of clinical symptoms, one of which is the inability of the embryo to survive. Through the process of its metabolism of 1.25(OH) vitamin D, vitamin D has a significant role in promoting the reproductive health of women.
Aim of the Study: This study aims to investigate the correlation between Vitamin D deficiency and idiopathic miscarriage in women.
Materials and Methods: There were 180 miscarriage survivors who took part in this study.; and only forty-three women with idiopathic miscarriage included in this study. They were attended to private clinics in Karbala Province from the period of May-August/ 2024, and their ages range between (17- 43) years. The confident diagnosis was confirmed according to examination by gynaecologists.
Results: The female patients with miscarriage were evaluated to exclude all other potential reasons of miscarriage, including age, body mass index, hypertension, endometrial abnormalities, and smoking. Out of 180 women who experienced miscarriage, only 43 were included in the current study. The study assessed infectious agents and other autoimmune disorders in all

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participating women to eliminate those with Toxoplasma gondii, Rubella, Chlamydia, Herpes (TORCH), and autoimmune diseases. The findings revealed that only 43 women experienced idiopathic miscarriage, and no women exhibited a significant correlation or positive outcomes for any of the aforementioned characteristics. The study revealed a strong association between the trimester of pregnancy and miscarriage among the patients, indicating notable fetal losses In the first and second trimesters, a substantial association was identified; however, no such relationship was evident in the third trimester. The findings indicated that Vitamin D insufficiency was substantially correlated with miscarriage in all women experiencing miscarriage in the research.
In conclusion: The role of Vitamin D deficiency significantly affected the losses of pregnancy in women with idiopathic miscarriage.

Keywords: Vitamin D deficiency; miscarriage; idiopathic loses of pregnancy.

1. INTRODUCTION

The 15.3% of recognized pregnancies that end in miscarriage suffer physical and psychological harm. On a global scale, 10.8% of women experience one miscarriage, 1.9% have two, and 0.7% have three (Quenby et al. 2021). An adverse event that can impact reproductive health is a miscarriage, which can develop during pregnancy. The embryo dies before the 20th week of gestation, which is the name used to describe this phenomenon (Hu et al. 2018, Kasim 2022). Medical professionals use the phrase "spontaneous abortion" to describe a miscarriage, which can occur at any point throughout the pregnancy. Miscarriage may result from multiple circumstances, including as chromosomal abnormalities, uterine anomalies, hormonal imbalances, thrombophilia, immunological problems, infections, and as many as half of all cases lacking identifiable causes. Many of these factors are challenging to rectify; nevertheless, there are some modifiable elements whose adverse effects can be entirely alleviated prior to conception, such as dietary deficiencies, particularly vitamin D insufficiency (Petrushkina et al. 2019).

Vitamin D, a steroid hormone, is recognized for its function in bone metabolism and the regulation of calcium and phosphate levels (Al-Berry et al. 2022). Vitamin D exhibits non-genomic effects in various organs, including the brain and reproductive tissues, the heart and cardiovascular system, pancreatic β-cells, The adaptive and innate immune systems, along with the non-skeletal skeletal system, are influenced by Vitamin D, which is essential for sustaining reproductive health in women via its metabolism of 1.25(OH)D. The endometrium, placenta, decidual cells, ovarian granulosa cells, uterine tube epithelium, pituitary gland, and hypothalamus are all sites of vitamin D receptors (VDR) (Radzinsky et al. 2021).

Pregnant women and those trying to conceive are especially vulnerable to vitamin D deficiency, a significant global public health issue. Contrary to popular belief, vitamin D insufficiency is more prevalent among women who suffer from serious obstetric and reproductive issues like preeclampsia, gestational diabetes, and premature birth (Tamblyn et al. 2022). This condition has long been associated with problems with the bones of both mothers and newborns. Additionally, it is essential for the endometrium's functional differentiation, which is linked to the calibre of implantation procedures throughout the initial phases of gestation (Du et al. 2005). To survive, the semi-allograft human embryo must rely on the immunological tolerance of the mother. An increased risk of miscarriage may be linked to vitamin D, which acts as an immune modulator and may be essential for the maternal-foetal immunologic response (Parvez 2024). 25, hydrochloride It is reasonable to assume that increased vitamin D levels during the first trimester of pregnancy encourage healthy embryonic and foetoplacental development since vitamin D controls an enzyme that is crucial for fertility and embryo implantation (Wei et al. 2013).

2. MATERIALS AND METHODS

This study involved 180 women with miscarriage participated in this study; and only forty-three women with idiopathic miscarriage included in this study. They were attended to private clinics in Karbala Province from the period of May-August/ 2024, and their ages range between (17-43) years. The confident diagnosis was confirmed according to examination by gynaecologists. All these women examined to exclude other causes of miscarriage like infections, autoimmune diseases, physical disorders, etc. Venous blood samples were collected and the serum separated from these

patients. Vitamin D measured ELISA technique .All the kits used in this study provided by (Elabsience/ USA company).

3. RESULTS

The patients' women with miscarriage examined to exclude all other causes that may include in miscarriage. And from 180 women with miscarriage only 43 women with miscarriage included in current study.

The determination of the physical parameters such as (Ages, Body mass index, Hypertension Endometrium abnormalities and Smoking) in 180 women with miscarriage, which may effect on the viability of fetuses in endometrium, and may causes loses of them. As shown in Table (1).

Table 1. The correlation of physical parameters and miscarriage in women included in this study

Physical Parameters	Results	Correlation (r) *P value*
Ages	17-25	0.613
	26-34	
	35-43	
	Mean 29.8± 4.31	
Body mass index (BMI)	< 20	
	20-24	0.1
	25-29	
	≥ 30	
	Mean 30.1 ± 1.02	
Hypertension	Sys 12.2 - Dys 7.8	0.42
Endometrium abnormalities	Normal	----
Smoking	Negative	----

P value ≤ 0.05 significant

Table 2. The results of infectious agents (TORCH) and autoimmune disease in women with miscarriage

Infectious agent (TORCH)	Results
Toxoplasma gondii	Negative
Rubella	Negative
Chlamydia	Negative
Herpes	Negative
Autoimmune disease	Negative

Table 3. The correlation of the number of miscarriage women with the number of live births and number of aborted fetuses

Number of miscarriage women	Number of live births	Number of aborted fetuses	Correlation (r) p value
27	1-2	1-3	
13	3-4	1-3	0.1
3	5-7	1-3	
n=43			

P value ≤ 0.05 significant

Table 4. The correlation of trimester of pregnancy with miscarriage

Trimester of pregnancy	Number of women with miscarriage	Correlation (r) *P value*
First trimester	31	0.005*
Second trimester	11	0.02*
Third trimester	1	0.6

P value ≤ 0.05 significant

Table 5. The level of Vitamin D examined in these women included in this study

Trimester of miscarriage	Number of patients	The mean of Vitamin D level (ng/ml)	Correlation (r) *P value*
First trimester	31	12.3± 0.41	
Second trimester	11	17.5± 0.24	0.002*
Third trimester	1	16.7± 0.13	

P value ≤ 0.05 significant

Also, the infectious agents and other autoimmune disorders examined to all these women under study to exclude any woman that had Toxoplasma gondii, Rubella, Chlamydia, Herpes (TORCH) and Autoimmune disease. As mentioned in Table (2).

The results obtained found that, only 43 women had idiopathic miscarriage, and any women gave significant relationship or had positive results for any of parameters in tables above excluded from current study.

The correlation between the number of miscarriages experienced by women and the number of live births and aborted fetuses, as presented in Table 3, indicates that there is no significant relationship between the frequency of miscarriages and the number of live births per woman.

The research identified a significant correlation between pregnancy trimester and miscarriage rates, revealing that fetal losses were particularly linked to the first and second trimesters, whereas no significant relationship was noted in the third trimester, as shown in Table 4.

The results for detecting the levels of Vitamin D indicated that a deficiency of vitamin D was significantly correlated with miscarriage in all women with miscarriages under study. As demonstrated in Table (4)

4. DISCUSSION

Previous researchers have found no significant differences between age and body mass index (BMI) in their study groups, which is consistent with the results of the current study (Samimi et al. 2016, Al-Berry et al. 2022)(. Two additional trials have investigated the relationship between preconception vitamin D levels and the risk of idiopathic miscarriage, but no association was identified (Mumford et al. 2018, Subramanian et al. 2022). Certain chemicals or medications met during the first trimester increase the probability of miscarriage or major abnormalities, and the usual half-life of vitamin D is two weeks (10). Women who sustained losses prior to 12 weeks of gestation are likely to exhibit low vitamin D concentrations, consistent with our findings, which were predominantly based on first-trimester blood samples. The current study demonstrated a correlation between first-trimester idiopathic miscarriage and vitamin D levels, but not in the second trimester. 25(OH)D may help prevent miscarriage. Vitamin D has been shown to influence both innate and adaptive immune responses. Numerous immune cells possess the vitamin D receptor, essential for regulating signaling via antigen receptors and the subsequent activation of T-cells. Active 1,25(OH)2D has been shown to downregulate Th1 cytokines, indicating its potential role as an immunotherapy for spontaneous recurrent miscarriages (Vijayendra et al. 2015). Thirty-three percent of women over 30 years old who experienced spontaneous miscarriage showed reduced serum vitamin D levels, attributed to inadequate intake of vitamin D-fortified milk and restricted outdoor activity and sun exposure. Women also utilized sunscreen, which may limit the skin's sufficient exposure to sunlight Hasan et al. 2018.

Vitamin D insufficiency in pregnant women correlates with a heightened risk of obstetric problems, including preeclampsia, bacterial vaginosis with subsequent premature delivery, newborns categorized as small-for-gestational age, gestational diabetes mellitus. Vitamin D appears to facilitate the essential immunological alterations required to avert pregnancy loss (Ghaedi et al. 2016). Andersen and his associates established that vitamin D deficiency more than doubles the chance of miscarriage. These data suggest that vitamin D deficiency is present in patients experiencing first trimester pregnancy loss (5-12 weeks), and vitamin D levels below 6.5 serve as a predictor of reproductive loss (Andersen et al. 2015).

Vitamin D may have a role before to conception and/or in the early stages of pregnancy, since it is present in the endometrium and first trimester placentas together with important vitamin D metabolic enzymes. Evidence indicates that

women exhibiting elevated VDR expression in their endometrium had a higher likelihood of achieving pregnancy (Guo et al. 2020). Research conducted in Iraq indicates that insufficient vitamin D levels are a significant factor contributing to miscarriage in pregnant women. In Iraq, 32% of women have experienced fewer than two consecutive miscarriage, while 44% have undergone more than two. Additionally, over one-third of pregnant women exhibit insufficient vitamin D levels, measured at 15 ng/mL. Vitamin D is crucial for reproductive health due to its involvement in both innate and acquired immunity, as well as its role in preventing miscarriage. Researchers looked at The relationship between vitamin D and sunlight exposure, as well as the impact of vitamin D insufficiency on the levels in women with darker skin, which tend to be lower than those in white women (Chawla et al. 2019, Borradale 2013).

A significant finding has emerged regarding a pregnancy complication, miscarriage, which results in 17% of clinically acknowledged pregnancies concluding in loss (Salim et al. 2022) Vitamin D-deficient pregnant women have a higher risk. Due to high decidua and placenta expression of CYP27B1 and VDR, miscarriage risk increases. 25(OH)-D3 must be converted to 1,25(OH)2-D3 by the placenta. Vitamin D significantly impacts trophoblastic invasion and placental artery remodeling, which are affected in miscarriage (Chan et al. 2015).

5. CONCLUSION

This review adds to the growing body of data that shows women who don't get enough vitamin D have a higher chance of miscarrying their babies and having other serious problems during pregnancy and reproduction. For idiopathic miscarriage prevention, we support using a standard set of clinically useful definitions and outcomes that are agreed upon by everyone around the world. The idea that a woman's vitamin D level before she gets pregnant might change how much weight she loses in the first and second trimesters.

Future Directions is follow up study for administration Vit.D to the women with idiopathic mischarge and detect the result.

DISCLAIMER (ARTIFICIAL INTELLIGENCE)

Author hereby declare that NO generative AI technologies such as Large Language Models (ChatGPT, COPILOT, etc) and text-to-image generators have been used during writing or editing of this manuscript.

CONSENT AND ETHICAL APPROVAL

The study adhered to ethical principles rooted in the Declaration of Helsinki. Patient written and analytical approval was obtained prior to sample collection. The local ethics committee evaluated and sanctioned the study protocol, as well as the subject information and consent form.

COMPETING INTERESTS

Author has declared that no competing interests exist.

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