Original Article

Problems of Vitamin D Deficiency Associated with Women's Infertility

Asawer Kareem Alsadoon, Hayder Sudan Abbas Obaid[1], Nariman Abdulhassan Karbul[2]

Department of Basic Science, College of Dentistry, Wasit University, Wasit, [1]Department of Physiology and Medical Physics, Hammurabi College of Medicine, University of Babylon, Hillah, Iraq, [2]Department of Obstetrics and Gynecology, Hammurabi College of Medicine, University of Babylon, Hillah, Iraq

Abstract

Background: When exposed to UV radiation, the skin produces vitamin D, a lipid-soluble vitamin. Because of the receptors of vitamin D are located in reproductive organs such as the endometrium, ovary, and uterus, researchers can develop theories about its role in reproduction. The role of vitamin D in fertility has been shown in a variety of animal experiments. However, human studies have not consistently confirmed vitamin D's effect on infertility. **Objectives:** The major goal of this research was to define the prevalence of vitamin D deficiency among Wasit women and its effect on infertility, with a focus on those who were experiencing primary or secondary infertility. **Materials and Methods:** Samples were collected from 60 females with primary infertility, 60 women with secondary infertility, and 60 fertile women with at least one child, and were recruited from February to May 2023, then divided into three age groups, the first group (15-25 years), the second group (26-35 years), and the third group (>35 years). The levels of vitamin D were measured using the enzyme-linked immunosorbent assay. **Results:** It was found that vitamin D deficiency was rather common, with the greatest rates occurring in those aged 35 and older (40% for women with primary infertility and 53% for those with secondary infertility). Primary and secondary infertility rates were each 20% lower in the second age group (26-35 years). **Conclusion:** The current study found a high prevalence of vitamin D deficiency in women suffering from primary and secondary infertility in Wasit Governorate. Therefore, women who suffer from infertility may benefit from examining their levels of vitamin D because it may be one of the causes of infertility, which can be easily treated by taking vitamin D supplements.

Keywords: Infertile women, primary infertility, secondary infertility, VD supplementation; vitamin D Deficiency

Introduction

Infertility is defined as the failure to conceive during regular sexual activity for 12 months or more.[1] Primary infertility is when a woman does not give birth to a live child, while secondary infertility is when a female is unable to develop pregnant during a certain period even though she was previously pregnant and gave birth or lost the pregnancy.[2] Infertility is a public health problem, and the causes vary and are numerous, some of which are direct and widely studied as endocrine disorders, some sexually transmitted diseases, congenital malformations of the uterus, and autoimmune diseases, and some are indirect, such as anemia, poverty, stress, malnutrition, lifestyle, obesity, and many other unknown causes. More than one cause may occur at the same time, and primary infertility is more common than secondary infertility.[3]

Infertility is a fast-developing global health concern that affects 15% of the world's population and has a high prevalence rate.[4] Infertility may be caused by a wide variety of causes, ranging from poor reproductive health in either spouse to a lack of essential biological components such as vitamins and hormones, both of which can go unrecognized or untreated, and it is

Access this article online

Quick Response Code:

Website: https://journals.lww.com/mjby

DOI: 10.4103/MJBL.MJBL_877_23

Address for correspondence: Mrs. Asawer Kareem Alsadoon, Department of Basic Science, Wasit University, College of Dentistry, Wasit 52001, Iraq.
E-mail: a.hami@uowasit.edu.iq

Submission: 01-Jul-2023 **Accepted:** 18-Dec-2023 **Published:** 23-Jan-2026

How to cite this aritlce: Alsadoon AK, Obaid HSA, Karbul NA. Problems of vitamin D deficiency associated with women's infertility. Med J Babylon 2025;22:1251-5.

believed that there are between 60 and 80 million cases globally. Ovulatory dysfunction, tubal disease, and endometriosis are the most common reasons for female infertility.[5]

Vitamin D is synthesized in the body in reply to exposure to ultraviolet radiation, while only a small portion of it comes from dietary sources. Its deficiency may be the result of several reasons, including living in high latitudes, aging, certain diseases or genetic defects, diabetes or kidney disease, as well as the use of certain medications. Vitamin D is critical for overall health, including bone health and the ability to become pregnant. Its deficiency is linked to a wide range of gynecological problems, including polycystic ovary syndrome and uterine fibroids.[6,7]

Due to the attendance of vitamin D receptors (VDR) in more cells such as ovarian cells, fallopian epithelial cells, endometrial glandular epithelial cells, and granulosa cells, vitamin D has a substantial influence on a variety of biological systems, including the reproductive system. Studies have revealed that vitamin D protects against uterine fibroids and women with myomas have lower vitamin D levels. additionally, patients who take vitamin D supplements have a lower incidence of muscle tumors.[8,9]

The vitamin D receptors are a kind of steroid receptor involved in mediating vitamin D's actions. The vitamin D receptor (VDR) is found not just in the brain and pituitary gland, but also in the ovary, placenta, uterus, and testicles, all of which play a role in reproduction. It is fair to suppose that vitamin D has a role in reproductive physiology, due to the broad expression of VDR.[10,11] The study aimed to determine the prevalence of vitamin D deficiency in women in the governorate and its impact on infertility, with a focus on those suffering from primary or secondary infertility.

Materials and Methods

Research design and sampling

Patients in this study included infertile women who sought treatment at Al-Kut Hospital for Gynecology Obstetrics and Pediatrics. It included 60 women with primary infertility, sixty women with secondary infertility, and sixty healthy women who had previously given birth to at least one child, as the Control group, with an average age between 15 and 50 years, blood samples were collected from February to May 2023, then divided into three age groups: the first group (15-25 years), the second group (26-35 years), and the third group (>35 years to measure the level of vitamin D in the serum.

Selection and exclusion criteria

Blood samples were collected from infertile women who were 15 years old or older and did not suffer from chronic diseases such as diabetes, kidney disease, and high blood pressure. Those with chronic diseases, and who take vitamin D and calcium supplements were excluded from the study.

Data collection and diagnosis

General information was collected from all patients and control group in a special questionnaire, such as age, body mass index, marital status, genetic diseases, history of infertility, and regular or irregular menstrual cycle, (5 cc) of venous blood was taken from all patient and biochemical parameters were measured, for measurement vitamin D level. ELISA (Dynex, Chantilly, Virginia, USA) system used to evaluate the level of vitamin D. ELISA test kit was used for *in vitro* determination of 25-OH vitamin D in (Abcam, England, UK, Germany). The reference range for vitamin D was: (<10 ng/mL (deficiency)), (10-30 ng/mL (sufficiency)), and (30-100 ng/mL (Adequate)).

Statistical methods

Patient and control groups of the same age were compared to identify significant differences; these comparisons were made using the SPSS program for statistical analysis of variance (ANOVA), and the LSD was determined by determining whether or not the *t* test criterion for the examinations studied was less than the probability level of 0.05.[12]

Ethical approval

The Declaration of Helsinki served as a framework for all research. Patients gave us both verbal and written consent before we obtained any samples from them. A local ethics committee accepted the study methodology, subject data, and permission form in Document 3/2023 (January 2, 2023).

Results

The results of this study showed a difference in vitamin D levels for the three age groups (were divided into three age groups: the first group (15-25 years), the second group (26-35 years), and the third group (more than 35 years)) as shown in the tables below: Table 1 showed that 20% of the women in first age group, as well as 13% of the females in the second group and 7% of women in the third group were vitamin D deficiency. In Table 2, in primary infertility, the percentage of people suffering from vitamin D deficiency was 20% in the first and second age groups, but it increased to 40% among those over 35 years old. Table 3 shows that in women with secondary infertility, vitamin D deficiency levels were only 7% in the first age group, while in the second age group, the percentage of deficiency reached 20%, and the highest percentage of deficiency was in the last group, where it reached 53%. Tables 4 and 5 show that the *P* value increased significantly when comparing control with women with primary and secondary infertility. As in the following tables:

Table 1 : The effect of age on vitamin D in control women

Age	Control Women						Total N.	Chi-Square	*P*-Value
	D Deficient		D Insufficient		D Adequate				
(15-25) Years	0	0%	0	0%	16	27%	**16**	**1.667**	**0.435**
(26-35) Years	0	0%	8	13%	16	27%	**24**		
More 35 Years	0	0%	4	7%	16	27%	**20**		

P value- < 0.05 (significant)

Table 2: The effect of age on vitamin D in women with primary infertility

Age	Women with primary infertility						Total N.	Chi-Square	*P*-value
	D Deficient		D Insufficient		D Adequate				
(15-25) Years	12	20%	4	7%	0	0%	**16**	**2.946**	**0.567**
(26-35) Years	12	20%	4	7%	0	0%	**16**		
More 35 Years	24	40%	0	0%	4	7%	**28**		

(*P* value < 0.05 significant)

Table 3: The effect of age on vitamin D in Women with secondary infertility

Age	Women with secondary infertility						Total N.	Chi-Square	*P*-value
	D Deficient		D Insufficient		D Adequate				
(15-25) Years	4	7%	0	0%	12	20%	**16**	**10.313**	**0.006**
(26-35) Years	12	20%	0	0%	0	0%	**12**		
More 35 Years	32	53%	0	0%	0	0%	**32**		

P value < 0.05 (significant)

Table 4: The difference in vitamin D concentrations between control and primary infertility women

Groups	Mean	SD	*T*-test	*P*-value
Control	32.07	2.94	**9.587**	**0.000**
Primary Infertility	10.27	8.30		

(*P* value < 0.05 significant)

Table 5: The mean concentration of vitamin D levels between control and secondary infertility women

Groups	Mean	SD	*T*-test	*P*-value
Control	32.07	2.94	**8.371**	**0.000**
Secondary Infertility	13.87	7.89		

P value < 0.05 significant

Discussion

Infertility is the inability of a woman to become pregnant after a year of trying, or after 6 months if she is 35 years old or older. The percentage of infertile women is thought to be between 25% and 30% of childbearing age and declines rapidly after the age of 37 years. A woman's chances of getting pregnant are less than 10% in each menstrual cycle when she reaches 40 years old. Our study makes a significant contribution in this regard, although few studies have investigated the relationship between vitamin D levels and female infertility. According to previous studies, loss of fertility and reproductive ability in female rats has been linked to vitamin D deficiency. Moreover, some Iranian research has shown that the use of vitamin D supplements may enhance fertility.[13,14]

Table 1 shows the proportion of vitamin D in the control group which is healthy women, who were chosen at random for our study and acted as the control group. The findings show that there is no association between age and the percentage of vitamin D. According to the findings, 20% of women of generative age, 13% of women in the second group (26-35 years), and 7% of women in the third group (more than 35 years) were vitamin D deficient. These percentages offer compelling proof of the widespread vitamin D deficiency among fertile women. Our results are similar to Saudi Arabian research that found that women aged 30-49 are likely to be vitamin D deficient than older women (aged 50-65). This could be a result of elderly women ingesting more vitamin-rich meals and vitamin D supplementation.[15]

According to Table 2, 80% of women with primary infertility were vitamin D deficient. These results are similar to those found in studies conducted in Basra, where the infection rate reached 76%.[16] When we studied vitamin D levels in these individuals. We found that the percentage of women with primary infertility increased in their vitamin D deficiency with age. Their percentage reached 20% in the first and second age groups, but it rose to 40% among those over 35 years of age. These results are consistent with the results of another study that found that 88.5% of infertile females suffer from vitamin D deficiency. A cross-sectional study of 388 premenopausal females detected a positive significance between 25(OH)D and AMH levels in 40-year-old females.[17] This is in contrast to another study,[18] which showed that vitamin D deficiency in women with infertility due to (polycystic ovary syndrome) was significantly younger, in addition to the results of other studies that indicated no significance between vitamin D and infertility.[19]

Table 3 shows the vitamin D status of women with secondary infertility, with varying levels between normal and deficient levels. In the first category, only 7% were deficient. In the second category, the percentage of deficiency reached 20%, and the highest percentage of deficiency was in the last category, which amounted to 53%. It is widely known that fertility decreases with age, making it an important factor in female infertility. A woman's fertility reaches its peak between the ages of 18 and 24, after which it gradually declines. However, this decline accelerates after the age of 35, making age the most important factor in infertility in women.[20]

Table 4 compares women with primary infertility with controls, and the results show significant heterogeneity, with a *P* value of less than 0.05 indicating vitamin D deficiency in infertile women. A study comparing women with reproductive organ tumors to healthy women found that 52.36% of patients had a Vit, D deficiency. Compared to 48.70% in healthy women, vitamin D deficiency may have a serious impact on malignant tumors in the reproductive organs but is not necessarily a cause of infertility.[21]

Table 5 compares average vitamin D levels in females with secondary infertility with the control group. The results of our study show a very significant difference in vitamin D deficiency in women. This result is very similar to another study conducted in Babylon that showed the presence of the vitamin D deficiency in women. In reproductive age, the results were (VDD) in females of reproductive age, where the deficiency rate in the entire sample was 76% and the deficiency rate was 18%. While only 7% have a sufficient level of the vitamin D in serum.[22]

Although there is significant evidence supporting the role of the vitamin D levels in various aspects of human reproduction, and other studies demonstrating the importance of the vitamin D supplements in promoting fertility, vitamin D supplements are considered safe, practical, and cost-effective. In trials, vitamin D deficiency reduced the fertility of female mice by up to 75% compared to mice given vitamin D supplements.[23]

An animal study showed that the uteruses of female mice lacking the VDR gene are unusually small, and their ability to form follicles is extremely weak. On the other hand, increasing the amount of calcium in the blood or taking calcium supplements may help restore fertility and enhance hormone activity. According to one idea, vitamin D may inhibit estrogen synthesis by playing a role in regulating calcium homeostasis. This finding was made possible by the implication between low vitamin D levels and fluctuating levels of calcium and phosphorus in the blood.[24,25]

Experts in Central and Eastern Europe have produced clinical rules for predicting, diagnosing, and treating vitamin D.[26] Vitamin D deficiency includes advice that healthy adults with no additional risk factors take vitamin D supplements. This recommendation applies to females trying to get pregnant as well as anyone else who does not have any additional risk factors. Vitamin D deficiency has been linked to a significant risk of poor birth outcomes such as miscarriage, so this recommendation is based on scientific evidence. During pregnancy and lactation, a woman's vitamin D level should be maintained between 30 and 50 ng/mL (75 and 125 nmol/L 25(OH)-vitamin D).

Conclusion

This research found that vitamin D deficiency may be a significant and treatable cause of infertility among women with primary and secondary infertility in Wasit Governorate, particularly among the second (ages 26-35) and third (more than 35) age groups. Therefore, it is necessary to do a vitamin D analysis, for all women experiencing infertility or pregnancy delays. Expanding the sample size and making connections between vitamin D deficiency and other causes of infertility, such as polycystic ovarian syndrome and obesity, are important directions for future research on the topic of vitamin D and infertility.

Acknowledgments

For their assistance and support during my work, I would like to extend my sincerest gratitude and thanks to the staff and patients of Al-Kut Hospital for Gynecology Obstetric and Pediatrics, and in particular to my colleagues in the labs. I would want to extend my gratitude to the infertile ladies who worked so diligently together at the Infertility Center.

Financial source and support

Nil.

Conflicts of interest

There are no conflicts of interest.

References

1. Zegers-Hochschild F, Adamson GD, de Mouzon J, Ishihara O, Mansour R, Nygren K, *et al*; International Committee for Monitoring Assisted Reproductive Technology. A revised glossary of ART terminology endorsed by the International Committee for Monitoring Assisted Reproductive Technology (ICMART) and the World Health Organization (WHO). Fertil Steril 2009;92:1520-4.
2. Abdullah WH, Kadhum AJ, Baghdadi GA. Diabetic nephropathy in children with type 1 diabetes mellitus: Vitamin D deficiency and dyslipidemia as associated risk factors. Med J Babylon 2022; 19:294.
3. Magdum M, Chowdhury MAT, Begum N, Riya S. Types of infertility and its risk factors among infertile women: A prospective study in Dhaka City. J Biosci Med 2022;10:158-68.
4. Paffoni A, Somigliana E, Vigano' P, Benaglia L, Cardellicchio L, Pagliardini L, *et al*. Vitamin D status in women with uterine leiomyomas. J Clin Endocrinol Metab 2013;98:E1374-8.
5. Nasir S, Khan MM, Ahmad S, Alam S, Ziaullah S. Thyroid dysfunction in infertile women with menstrual disturbances. Gomal J Med Sci 2016;14:31.
6. Bhan A, Rao AD, Rao DS. Osteomalacia resulting from vitamin D deficiency. Rheum Dis Clin North Am 2012;38:81-91.
7. Holick MF. Approaches for the diagnosis, treatment, and prevention of vitamin D deficiency. Rev Endocr Metab Disord 2017;18:153-65.
8. Holick MF. Vitamin D deficiency in the New England Journal of Medicine. N Engl J Med 2007;357:266-81.
9. Magtooph MG. Levels of thyroid and reproductive hormones in fertile and infertile women. Univ Thi-Qar J Sci 2015;5:31-6.
10. Nemade ST, Momin AA, Naik PS, Patil YR, Nemade TV. Association between thyroid profile and primary infertility in females. Int J Health Sci Res 2012;1:90-4.
11. Lorenzen M, Boisen IM, Mortensen LJ, Lanske B, Juul A, Jensen MB. Reproductive endocrinology of vitamin D. Mol Cell Endocrinol 2017;453:103-12.
12. SAS Institute Inc. Statistical Analysis System User's Guide, Version 9. 6th ed. N.C. USA: SAS. Inst. Inc. Cary; 2018.
13. Rudick B, Ingles S, Chung K, Stanczyk F, Paulson R, Bendikson K. Influence of vitamin D levels on IVF outcomes. Hum Reprod 2012;27:3321-7.
14. Ozkan S, Jindal S, Greenseid K, Shu J, Zeitlian G, Hickmon C, *et al*. Replete vitamin D stores predict reproductive success following in vitro fertilization. Fertil Steril 2010;94:1314-9.
15. Sayed AI, Yousef AM, Aly MG. Evidence on manual therapy and its relationship with infertility. Turk J Physiother Rehabil 2022;32:19296-19301.
16. Al Faris NA, Al Kehayez NM, Al Mushawah FI, Al Naeem AN, Al Amri ND, Al Mudawah ES. Vitamin D deficiency and related risk factors in women from Riyadh, Saudi Arabia. Sci Rep 2019;9:1-8.
17. Rafique M, Nuzhat A, Al-Jaroudi D. Vitamin D deficiency in female infertility and its impact on assisted reproductive technology outcomes. J Soc Obstet Gynaecol Pak 2018;8:29-35.
18. Israel N, Shamdeen M. Polycystic ovary syndrome and vitamin D deficiency. Med J Babylon 2019;16:234.
19. Merhi ZO, Seifer DB, Weedon J, Adeyemi O, Holman S, Anastos K, *et al*. Correlation between circulating vitamin D and serum antimüllerian hormone levels in women of late reproductive age. Fertil Steril 2012;98:228-34.
20. Ameer MA, Fagan SE, Sosa-Stanley JN, Peterson DC. Uterus anatomy: Treasure Island, FL: StatPearls Publishing; 2022.
21. Mendiola J, Torres-Cantero AM, Moreno-Grau JM, Ten J, Roca M, Moreno-Grau S, *et al*. Vitamin D levels and semen parameters. Reprod Biomed Online 2008;16:842-50.
22. Hantoosh HA, Mahdi MH, Imran BW, Yahya AA. Prevalence of vitamin D deficiency in Iraqi females at reproductive age. Med J Babylon 2019;16:119-22.
23. Panda DK, Miao D, Tremblay ML, Sirois J, Farookhi R, Hendy GN, *et al*. Ablation of the 25-hydroxyvitamin D 1-alpha hydroxylase enzyme and its effects on skeletal, reproductive, and immune function. Proc Natl Acad Sci USA 2001;98:7498-503.
24. Wojtusik J, Johnson PA. Regulation of antimullerian hormone expression in granulosa cells of hens by vitamin D. Biol Reprod 2012;86:91.
25. Kwiecinski GG, Petrie GI, DeLuca HF. Restoration of fertility in vitamin D-deficient female rats by 1,25-dihydroxyvitamin D3. Am J Physiol 1989;256:E483-487.
26. Pludowski P, Takacs I, Boyanov M, Belaya Z, Diaconu CC, Mokhort T, *et al*. Clinical practice guidelines for the prevention, diagnosis, and treatment of vitamin D deficiency. Nutrients 2022;14:1483.