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VITAMIN D AND INFERTILITY: A CASE-CONTROL STUDY CONDUCTED IN BAGHDAD CITY

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ABSTRACT

Background: Vitamin D plays an important role in reproductive physiology through its effects on endocrine, metabolic, and immunological pathways. Despite abundant sunlight, vitamin D deficiency is highly prevalent among women of reproductive age in the Middle East and may contribute to infertility. **Objectives:** To assess serum vitamin D levels in infertile women compared to fertile controls and to evaluate the association between vitamin D status, infertility and selected metabolic parameters. **Methods:** A hospital-based case–control study was conducted in Baghdad from March 2024 to February 2026, including 200 women (100 infertile cases and 100 fertile controls). Serum 25-hydroxyvitamin D levels were measured and classified as deficient (<20 ng/mL), insufficient (20–29 ng/mL), or sufficient (≥30 ng/mL). Fasting glucose, insulin, and insulin resistance (HOMA-IR) were also assessed. Statistical analysis included group comparisons, correlation analysis, and multivariate logistic regression. **Results:** Infertile women had significantly lower mean vitamin D levels compared to controls (17.2 ± 6.8 vs 26.5 ± 7.4 ng/mL, $p < 0.001$). Vitamin D deficiency was more prevalent in cases (68%) than controls (32%) ($p < 0.001$). Vitamin D deficiency was strongly associated with infertility (OR = 4.25, 95% CI: 2.20–8.21, $p < 0.001$) and remained an independent predictor after adjustment (adjusted OR = 3.87, 95% CI: 1.95–7.68, $p < 0.001$). Infertile women also exhibited significantly higher fasting glucose, insulin levels, and HOMA-IR ($p < 0.001$). Serum vitamin D levels showed significant negative correlations with HOMA-IR ($r = –0.41$, $p < 0.001$), insulin ($r = –0.36$, $p < 0.001$), BMI ($r = –0.28$, $p = 0.004$), and fasting glucose ($r = –0.25$, $p = 0.009$). **Conclusion:** Vitamin D deficiency is significantly associated with infertility and may contribute to reproductive dysfunction through metabolic pathways, particularly insulin resistance. Screening and correction of vitamin D deficiency may represent a simple and cost-effective strategy in the management of infertility.

KEYWORDS: Infertility, Insulin resistance, Reproductive health, Vitamin D.

1-INTRODUCTION

Infertility is a serious global public health concern, impacting an estimated 10-15% of couples globally and having significant psychosocial and economic consequences.[1] Infertility is caused by a complicated and multifaceted process that includes changes in ovulatory function, endocrine regulation, metabolic balance, tubal patency, and uterine receptivity.[2] In recent years, there has been a growing focus on the impact of micronutrients and endocrine modulators in reproductive physiology, with vitamin D emerging as a crucial determinant of interest.[3]

Vitamin D is a fat-soluble secosteroid hormone that is largely produced in the skin after UVB exposure and then hydroxylated in the liver and kidneys to its biologically active form, calcitriol (1,25-dihydroxyvitamin D).[4] Aside from its traditional involvement in calcium and phosphate metabolism, vitamin D has pleiotropic effects via the vitamin D receptor (VDR), a nuclear transcription factor found in a variety of tissues such as the ovaries, endometrium, placenta, hypothalamus, and pituitary gland. This extensive distribution implies an important involvement in reproductive endocrinology.[5,6] Accumulating evidence suggests that vitamin D has a role in several

important processes required for female reproduction. It has been demonstrated to control ovarian follicular growth, impact steroidogenesis via aromatase activity, and improve endometrial receptivity by increasing decidualization and implantation.[7] Furthermore, vitamin D possesses immunomodulatory and anti-inflammatory characteristics, which may influence implantation success and early pregnancy survival. It also influences glucose metabolism and insulin sensitivity, making it linked to metabolic illnesses like polycystic ovarian syndrome (PCOS), the major cause of anovulatory infertility.[8]

Despite having plenty of sunlight, vitamin D deficiency is very common around the world, especially in the Middle East. This contradiction is exacerbated by cultural behaviors, limited solar exposure, inadequate nutrition, and increased obesity.[9] Several studies have found a significant frequency of hypovitaminosis D among women of reproductive age in Iraq and nearby regions, raising concerns about the potential link to reproductive failure.[10] Low serum vitamin D levels have been linked in observational studies to decreased fertility, poorer ovulation, lower success rates in assisted reproductive procedures, and an increased risk of pregnancy problems.[11,12] The interaction of maternal systemic illness and placental insufficiency emphasizes the significance of a comprehensive maternal-fetal assessment.[13]

Furthermore, there is a paucity of locally collected data investigating the association between vitamin D level and infertility among Iraqi women. Understanding this relationship is critical, as vitamin D insufficiency is a potentially modifiable risk factor that can be addressed by supplementation and public health measures. As a result, the current study aims to compare serum vitamin D levels in infertile women to those in fertile controls, as well as to evaluate the relationship between vitamin D status and specific clinical, hormonal, and metabolic markers.

2-PATIENTS AND METHODS

This was a hospital-based case-control study conducted at Um Al-Baneen private Hospital in Baghdad during the period from March 2024 to February 2026. A consecutive sampling technique was employed to recruit participants who met the eligibility criteria until the required sample size was achieved.

The study population consisted from 200 cases and it was divided into two groups. The case group (100 cases) included women aged 18 to 45 who had been diagnosed with infertility, which is defined as the inability to conceive after at least 12 months of regular unprotected sexual intercourse. Both primary and secondary infertility cases were considered. The control group (100 controls) consisted of age-matched fertile women who visited the same hospital for routine gynecological treatment or antenatal follow-up and had at least one previous spontaneous pregnancy but no prior diagnosis of infertility.

Eligible participants were to be of reproductive age (18-45 years), not pregnant at the time of recruitment, and willing to give informed permission. Women were excluded if they had a known endocrine disorder such as thyroid dysfunction, hyperprolactinemia, or Cushing's syndrome, chronic systemic diseases such as renal, hepatic, or autoimmune conditions, or if they had used vitamin D supplementation, calcium therapy, or hormonal medications in the previous three months. Furthermore, women with verified male factor infertility or known anatomical reasons of infertility were excluded where such information was available.

Data were collected by a structured modified questionnaire submitted by direct interview. Demographic factors such as age were collected, as well as clinical variables such as body mass index (BMI), type and duration of infertility, menstrual history, and relevant medical history. Standardized protocols were used to conduct anthropometric measurements.

Venous blood samples (5-10 mL) were drawn from all participants under aseptic circumstances, ideally in the morning after an overnight fast, to reduce diurnal variation. Serum levels of 25-hydroxyvitamin D [25(OH)D], the major biomarker of vitamin D status, were determined using an enzyme-linked immunosorbent assay (ELISA) or chemiluminescent immunoassay, depending on laboratory availability. Vitamin D levels were classified as deficient (< 20 ng/mL), insufficient (20-29 ng/mL), or sufficient (≥30 ng/mL). Additional biochemical investigations were carried out where possible, including fasting blood glucose, serum insulin levels for calculating insulin resistance using the Homeostatic Model Assessment (HOMA-IR), lipid profile, and selected reproductive hormones such as follicle-stimulating hormone (FSH), luteinizing hormone (LH), prolactin, and estradiol.

Statistical analysis involved descriptive statistics. Continuous variables were expressed as mean ± standard deviation for normally distributed data or median with interquartile range for non-normally distributed data, while categorical variables were presented as frequencies and percentages. Comparisons between groups were performed using the independent sample t-test or Mann–Whitney U test for continuous variables, as appropriate, and the chi-square test or Fisher's exact test for categorical variables. Correlation analysis was conducted using Pearson or Spearman coefficients to assess the relationship between vitamin D levels and clinical or biochemical parameters. Multivariate logistic regression analysis was applied to identify independent predictors of infertility while controlling for potential confounding variables such as age, BMI, and metabolic parameters. A p-value of less than 0.05 was considered statistically significant.

3- RESULTS

A total of 200 women were enrolled, including 100 infertile women (cases) and 100 fertile women (controls). There were no statistically significant differences between the two groups regarding baseline characteristics such as age and body mass index (BMI), ensuring comparability. Moreover, among case group, primary infertility was prevalent among 62 (62%) patients while secondary infertility was prevalent among 38 (38%) patients. As shown in table 1.

Table 1: Basic characteristics of the study patients (number = 200).

Diagnosis	Case = 100	Controls = 100	P value
Age (years), mean ± SD	29.8 ± 5.6	30.4 ± 5.2	0.412
BMI (kg/m²), mean ± SD	27.6 ± 4.3	26.9 ± 4.1	0.238
Duration of infertility (years), mean ± SD	4.2 ± 2.1	—	—
Primary infertility, number (%)	62 (62%)	—	—
Secondary infertility, number (%)	38 (38%)	—	—

Table 2 shows comparison between cases and controls regarding their biochemical parameters. Statistically significant difference between the two groups regarding their means of Vitamin D levels, fasting glucose, insulin and HOMA-IR.

Table 2: Comparison between cases and controls regarding their biochemical parameters (number = 200).

Biochemical parameters	Case = 100	Controls = 100	P value
Vitamin D (ng/mL), mean ± SD	17.2 ± 6.8	26.5 ± 7.4	**<0.001**
Fasting glucose (mg/dL), mean ± SD	98.6 ± 12.3	91.4 ± 10.2	**<0.001**
Insulin (µIU/mL), mean ± SD	14.8 ± 5.6	10.2 ± 4.1	**<0.001**
HOMA-IR, mean ± SD	3.6 ± 1.4	2.3 ± 1.1	**<0.001**

Table 3 shows comparison between cases and controls regarding their Vitamin D status. Vitamin D deficiency was significantly more prevalent among infertile women (case group).

Table 3: Comparison between cases and controls regarding their vitamin D status (number = 200).

Vitamin D status	Case = 100	Controls = 100	P value
Deficient (<20 ng/mL)	68 (68%)	32 (32%)	**<0.001**
Insufficient (20–29 ng/mL)	22 (22%)	38 (38%)	**<0.001**
Sufficient (≥30 ng/mL)	10 (10%)	30 (30%)	**<0.001**

Table 4 shows association between Vitamin D levels and infertility. Statistically significant association was found between Vitamin D deficiency and infertility.

Table 4: Association between Vitamin D level and infertility.

Variables	Odds ratio	95% Confidence interval	P value
Deficient (<20 ng/mL)	**4.25**	**2.20 – 8.21**	**<0.001**
Insufficient (20–29 ng/mL)	1.74	0.92 – 3.29	0.084

Table 5 shows multivariant logistic regression analysis of factors associated with infertility. Infertility was significantly associated with Vitamin D and insulin resistance.

Table 5: Association between Vitamin D level and infertility.

Variables	Adjusted Odds ratio	95% Confidence interval	P value
Vitamin D deficiency	**3.87**	**1.95 – 7.68**	**<0.001**
BMI	1.08	0.99 – 1.17	0.072
Age	0.97	0.92 – 1.02	0.211
HOMA-IR	**1.56**	**1.21 – 2.01**	**0.001**

Table 6 shows correlation between serum Vitamin D levels and clinical/biochemical parameters. Vitamin D had significant moderate negative correlation with HOMA-IR, serum insulin. To less extend Vitamin D had significant weak correlation with BMI and fasting glucose level.

Table 6: Correlation between serum Vitamin D levels and clinical/biochemical parameters.

Variables	Correlation Coefficient (r)	P value
HOMA-IR	**-0.41**	**<0.001**
BMI	**-0.28**	**0.004**
Age	-0.12	0.118
Fasting glucose	**-0.25**	**0.009**
Serum insulin	**-0.36**	**<0.001**

4. DISCUSSION

The present case-control study found a strong, statistically significant association between vitamin D deficiency and infertility in women of reproductive age. Infertile women had considerably lower serum 25-hydroxyvitamin D levels than fertile controls, indicating a higher frequency of vitamin D deficiency. Importantly, vitamin D deficiency was associated to a more than fourfold higher incidence of infertility and remained an independent predictor after controlling for age, body mass index (BMI), and insulin resistance. These findings contribute to the rising understanding of vitamin D as a key regulator of female reproductive function. The presence of vitamin D receptors (VDR) and vitamin D-metabolizing enzymes in reproductive organs such as the ovaries, endometrium, and placenta gives support to this association. Vitamin D has been demonstrated to impact important reproductive processes as folliculogenesis, steroidogenesis, and endometrial receptivity. Recent molecular data reveals that vitamin D modulates gene expression involved in hormonal production and implantation, directly influencing reproductive outcomes.[14,15] Furthermore, vitamin D has immunomodulatory and anti-inflammatory properties that may aid in successful implantation and early pregnancy maintenance. Windrim et al. found a high frequency of vitamin D insufficiency among subfertile women, which was associated with lower reproductive success.[16] Similarly, Xu et al. discovered that appropriate vitamin D levels were linked to better ovarian reserve and reproductive potential.[17] These findings reinforce the growing evidence that vitamin D status is an important determinant of female fertility.

A notable finding of this study is the strong inverse correlation between serum vitamin D levels, insulin resistance as defined by HOMA-IR, and serum insulin levels. This shows that metabolic dysfunction could be a key mechanism linking vitamin D deficiency to infertility. Vitamin D is known to improve insulin sensitivity via regulating insulin receptor expression and inflammatory pathways. Recent studies have established that low vitamin D levels are associated with increased insulin resistance and metabolic disturbances in women of reproductive age.[18,19] Furthermore, an interventional study indicates that vitamin D administration may improve metabolic indices and even reproductive results.[20]

The observed negative correlations between vitamin D levels and BMI, fasting glucose, and insulin are consistent with current literature. Obesity has been proven to lower circulation vitamin D levels by sequestering it in adipose tissue and altering metabolism. A recent regional study found that Middle Eastern women have a significant frequency of vitamin D deficiency, which is associated with metabolic risk factors.[21] These findings are particularly relevant in the present population, where lifestyle and environmental factors may contribute to hypovitaminosis D.

Interestingly, age and BMI were not independent predictors of infertility in the multivariable analysis. This could indicate that biochemical and metabolic parameters, particularly vitamin D status and insulin resistance, are more important than demographic characteristics in influencing reproductive outcomes. Similar findings have been described in recent study that highlight the significance of endocrine and metabolic pathways in reproductive dysfunction.[22]

From a clinical perspective, the high prevalence of vitamin D deficiency in infertile women (68%) emphasizes the importance of routine screening in this population. Given that vitamin D deficiency is a treatable condition, early detection and treatment may provide a straightforward and cost-effective strategy for improving reproductive results. Recent studies in assisted reproductive settings have shown that women with appropriate vitamin D levels had better pregnancy outcomes, however the results remain varied and further high-quality trials are needed.[23-25]

Despite its strengths, this study has a number of limitations. The study was conducted in a single location, which may limit the generalizability of the findings. Potential confounding factors, including dietary vitamin D consumption, sun exposure, seasonal change, and socioeconomic status, were not considered. Furthermore, despite efforts to remove male factor infertility, full partner evaluation was not consistently undertaken. Certain reproductive and inflammatory biomarkers, such as anti-Müllerian hormone (AMH) or cytokine levels, could provide more information about underlying mechanisms, but were not assessed in the study. Finally, while the sample size is sufficient for primary analysis, it may limit the capacity to identify small effect sizes in subgroup analyses.

5- CONCLUSION

In conclusion, Vitamin D deficiency is significantly related with infertility in women of reproductive age and remains an independent risk factor even after accounting for confounders. The observed association between

vitamin D deficiency and insulin resistance reveals a possible metabolic mechanism that contributes to decreased reproductive function. These data give support to the idea that vitamin D is an important and adjustable factor in female fertility. Routine vitamin D deficiency screening is suggested for women who present with infertility, especially in areas where hypovitaminosis D is common. Correction of deficiencies with supplementation and lifestyle changes may be a safe and cost-effective addition to infertility treatment. More large-scale prospective study and randomized controlled trials are required to prove causality and assess the therapeutic effect of vitamin D supplementation on reproductive outcomes.

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Conflict of intertest

About this study, the authors disclose no conflicts of interest.

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