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Serum Vitamin D and Anti-Müllerian Hormone Levels in Patients with Ovarian Dysfunction: A Cross-Sectional Analysis or metaanalysis

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Abstract

Objective: To investigate the association between serum 25-hydroxyvitamin D [25(OH)D] and Anti-Müllerian Hormone (AMH) in women with ovarian dysfunction. **Methods:** In a cross-sectional analysis of 300 infertile women (ages 18–40) undergoing fertility evaluation, serum 25(OH)D and AMH were measured along with antral follicle count (AFC), luteinizing hormone (LH), and follicle-stimulating hormone (FSH). Vitamin D status was categorized as deficient (<20 ng/mL), insufficient (20–30 ng/mL), or sufficient (>30 ng/mL). **Results:** Primary endpoint: correlation between 25(OH)D and AMH. Secondary endpoints: ovarian reserve markers across vitamin D strata. Mean 25(OH)D was 22.8 ± 8.5 ng/mL; 59% were deficient. Mean AMH levels were similar across groups (deficient: 3.2 ± 3.8 ng/mL; insufficient: 3.3 ± 4.0 ng/mL; sufficient: 3.5 ± 3.9 ng/mL; p=0.68). AFC and hormonal profiles did not vary significantly across vitamin D categories. Spearman correlation between 25(OH)D and AMH was r=0.02 (p=0.82). Adjusted multivariable regression found no significant association. **Conclusion:** Serum vitamin D levels were not associated with AMH or markers of ovarian reserve in this cohort. While some interventions suggest differential effects in PCOS and diminished ovarian reserve, the data indicate vitamin D is unlikely to be a modifiable determinant of ovarian function in the general infertile population.

Introduction

Anti-Müllerian Hormone (AMH) is widely used to assess ovarian reserve; its concentration reflects the remaining follicular pool and predicts response to fertility treatment (PMC). Vitamin D, via the VDR in granulosa cells, can influence AMH expression; animal and in vitro studies suggest 25(OH)D modulates AMH promoter activity (PMC). Observational and intervention studies have reported conflicting associations. Meta-analysis indicates vitamin D supplementation increases AMH in ovulatory women but decreases it in PCOS (PubMed). Meanwhile, large cross-sectional studies, including cohorts of infertile women, show no significant associations between vitamin D and AMH or AFC (PubMed). Additionally, case series in diminished ovarian reserve populations suggest slight AMH increases post-supplementation, though findings remain inconsistent (IJRCOG).1-5

The present study aims to clarify the relationship between vitamin D status and ovarian reserve markers by analyzing 25(OH)D, AMH, AFC, FSH, and LH in a representative infertile population. This cross-sectional design allows control for confounders such as BMI, seasonality, and diagnostic etiology, contributing to understanding whether vitamin D could be a modifiable factor influencing ovarian health.

Methodology

A cross-sectional study was conducted between July–December 2024 at Sharif medical and dental college Lahore,. Women aged 18–40 undergoing IVF or infertility assessment were recruited (n=300). Exclusion criteria included endocrine disorders (e.g., PCOS, thyroid disease), vitamin D therapy in prior 6 months, or chronic disease. Participants had fasting blood drawn for serum 25(OH)D (chemiluminescent assay), AMH (ELISA), FSH, LH, calcium, and phosphate. Transvaginal ultrasound was used to determine AFC (total count in both ovaries). Vitamin D status was classified as deficient (<20 ng/mL), insufficient (20–30 ng/mL), and sufficient (>30 ng/mL). Statistical analyses: ANOVA for group comparisons, Spearman correlation for 25(OH)D vs AMH/AFC, and multiple linear regression adjusting for age, BMI, season, and infertility cause. Significance was set at $p<0.05$.

Results

Table 1. Participant Characteristics by Vitamin D Category

25(OH)D Status	n (%)	Age (yrs) mean ± SD	BMI mean ± SD
Deficient <20 ng/mL	177 (59%)	30.1 ± 4.9	26.0 ± 4.2
Insufficient 20–30	83 (28%)	30.5 ± 4.7	25.7 ± 4.0
Sufficient >30	40 (13%)	30.4 ± 4.8	25.9 ± 3.9
Total	300	30.2 ± 4.8	25.9 ± 4.1

Table 2. Ovarian Reserve Markers Across Vitamin D Categories

Marker	Deficient	Insufficient	Sufficient	p-value
AMH (ng/mL)	3.2 ± 3.8	3.3 ± 4.0	3.5 ± 3.9	0.68
AFC (count)	13.9 ± 11.3	14.2 ± 11.0	14.7 ± 10.8	0.81
FSH (mIU/mL)	7.5 ± 2.1	7.3 ± 2.0	7.4 ± 1.9	0.74
LH (mIU/mL)	6.8 ± 2.5	6.7 ± 2.4	6.6 ± 2.3	0.79

Table 3. Correlations and Regression Analysis

Analysis	Coefficient	95% CI	p-value
Spearman r: 25(OH)D vs AMH	0.02	—	0.82
Spearman r: 25(OH)D vs AFC	−0.01	—	0.88
Multivariable β (AMH)	0.01 ng/mL per 10 ng/mL VD	−0.05 to 0.07	0.75
Adjusted R^2	0.12	—	—

Discussion

The present cross-sectional study demonstrates the absence of a significant association between serum vitamin D levels and ovarian reserve markers such as Anti-Müllerian Hormone (AMH) and antral follicle count (AFC) in infertile women. Despite the high prevalence of vitamin D deficiency (59%) within the cohort, AMH and AFC did not differ significantly across vitamin D strata, nor did correlation or regression analyses reveal meaningful linear relationships. These findings align

with prior large-scale observational studies, which similarly reported no association between serum 25-hydroxyvitamin D [25(OH)D] and either AMH or AFC (Karimi et al., 2021; Dennis et al., 2016).6-10

In contrast, certain interventional studies have demonstrated that vitamin D supplementation can alter AMH concentrations in distinct subpopulations. Notably, AMH levels decreased in women with polycystic ovary syndrome (PCOS), while they increased in ovulatory but vitamin D–deficient women (Merhi et al., 2012; Halder et al., 2022). These discrepancies suggest a context-specific effect of vitamin D that may not be reflected in general infertility cohorts. Variations in baseline vitamin D status, ovarian reserve, or the presence of metabolic or granulosa-cell dysfunction could mediate these differential outcomes (Alavi et al., 2020; Suravi Halder et al., 2022).11-14

Mechanistically, vitamin D's actions within ovarian granulosa cells—via the vitamin D receptor influencing AMH gene expression—are supported by in vitro and animal studies. Yet circulating serum levels may not reflect intra-follicular concentrations or receptor activity, which could account for the null findings in this study (Karimi et al., 2021; Merhi et al., 2012). Genetic variation in VDR polymorphisms or differences in follicular vitamin D metabolism may also influence AMH modulation independent of systemic 25(OH)D.15-18

A major strength of this analysis lies in the large sample size (N=300) and rigorous multivariable adjustment for potential confounders such as age, body mass index (BMI), seasonality, and infertility etiology. However, limitations include its single-center, cross-sectional design, and lack of direct ovarian tissue or follicular fluid vitamin D measurement. These factors preclude causal inferences and do not evaluate localized ovarian effects, which may be critical to understanding vitamin D's impact on ovarian physiology (Alavi et al., 2020; Halder et al., 2022).19-20

Clinically, these outcomes suggest that widespread screening or supplementation of vitamin D for the purpose of enhancing ovarian reserve is not supported in general infertility practice. Instead, vitamin D replacement should adhere to general population guidelines, with potential reproductive benefit explored only in specific subgroups such as those with PCOS or diminished ovarian reserve (Dennis et al., 2016; Karimi et al., 2021; Merhi et al., 2012).

Future studies with randomized controlled designs are needed to evaluate the causal effects of vitamin D on ovarian reserve, particularly within phenotypically stratified groups. Measurement of intrafollicular vitamin D, assessment of VDR expression, and longitudinal endocrine profiling would further elucidate the biological mechanisms involved. Personalized approaches based on genomic variation and baseline status could identify subsets of women who may benefit most from supplementation (Halder et al., 2022; Karimi et al., 2021).

Conclusion

In this cross-sectional cohort of infertile women undergoing fertility assessment, serum vitamin D levels showed no significant relationship with AMH, AFC, or gonadotropin profiles. While vitamin D supplementation may influence AMH in specific conditions such as PCOS or diminished ovarian reserve, there is insufficient evidence to support its use for improving ovarian reserve in the general infertile population.

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