



Review Article

The Association between Serum Vitamin D Levels and Male Fertility: A Systematic Review and Meta-Analysis

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Objective. The probable relationship between serum vitamin D levels and male fertility is being increasingly investigated; however, the findings have been controversial. This review dealt with assessing the relationship between serum vitamin D levels and male fertility and sperm quality by executing systematic review and meta-analysis of the published data. **Methods.** The meta-analysis was executed as per the PRISMA 2020 statement. The protocol was registered with PROSPERO (CRD42022327583). Relevant literature was retrieved by searching online databases, including Embase, Scopus, PubMed, Web of Science, and the Cochrane Library, up to December 1st, 2022. Additionally, Google Scholar was searched to assess relevant articles. To ensure a more comprehensive review, unpublished articles, gray literature, and references of suitable articles were also assessed to find additional eligible publications. The articles that satisfied the inclusion criteria were evaluated for their quality using the Joanna Briggs Institute Critical Appraisal Tool. Meta-analysis was conducted through STATA 12. **Results.** Twenty-four articles, comprising 7,345 participants in total, were chosen for the systematic review and meta-analysis. The resulting data indicated that serum vitamin D levels in infertile males were remarkably elevated compared with that in fertile males (weighted mean difference (WMD) = 7.06, 95% confidence interval (95% CI) = 2.51–11.62, $P = 0.002$), and its deficiency (<20 ng/mL or 50 nmol/L) significantly reduced sperm concentration (WMD = 8.54, 95% CI = 4.01–13.06, $P < 0.001$), total sperm count (WMD = 14.43, 95% CI = 1.30–27.55, $P = 0.031$), sperm motility (WMD = 6.40, 95% CI = 3.15–9.64, $P < 0.001$), sperm progressive motility (WMD = 5.00, 95% CI 1.09–8.92, $P = 0.012$), and altered sperm morphology (WMD = 0.74, 95% CI = 0.20–1.27, $P = 0.007$). The data analysis determined that vitamin D did not remarkably influence sperm volume (WMD = 0.17; 95% CI = –0.00–0.34; $P = 0.050$). **Conclusion.** The acquired data implied that serum vitamin D is significantly associated with male fertility and sperm quality. This finding holds crucial implications for patients suffering from male infertility.

1. Introduction

Infertility, defined as being unable to conceive after 1 year of regular unprotected sexual intercourse, impacts around 15% of newly married couples [1]. It was noted that male causative factors account for almost 50% of these cases [2]. While comprehensive prevalence data on male infertility are not readily available, it remains a significant global issue affecting 72.4 million people [3]. Moreover, emerging research indicates that male infertility could be linked to an increased risk of developing chronic medical conditions [4]. Additionally, men with abnormal semen parameters may face a higher susceptibility to malignancy [5]. Even more concerning is the

mounting evidence of declining semen parameters worldwide [6, 7]. Infertility exerts a remarkable and adverse impact on various aspects of the life of an individual, including psychological well-being and the dynamics of sexual and interpersonal relationships among couples. Additionally, fertility treatments, while offering hope, often introduce additional stress, and pressure on infertile couples. As a result, infertility has emerged as a critical concern both in terms of public health and social implications worldwide [8, 9].

The causes of male infertility are complex and encompass a wide range of risk factors including age [10], body mass index [11], smoking [12], alcohol [13], varicocele [14],

mobile phone usage [15], and nutritional elements [16]. The relationship between male infertility and vitamin D has been increasingly investigated. The steroid hormone, vitamin D, mainly plays a role in maintaining bone health by mediating calcium and phosphate metabolism [17, 18]. In addition to its well-established role in bone health, vitamin D has recently attracted much attention for its effect on the male reproductive system. Various animal experiments have revealed that vitamin D supplementation can restore fertility in vitamin D deficient rats [19]. Furthermore, vitamin D receptors and metabolic enzymes are present in the reproductive system of males. The presence of these elements suggests that vitamin D may exert a crucial role in the reproductive system of males [20].

Male reproductive function is mainly assessed through semen examination. Numerous experiments have explored the potential effect of vitamin D levels in the serum on male fertility. Some of the data documented that the quality of the sperm was positively linked to vitamin D levels. For instance, various investigations reported that men that were deficient in serum vitamin D showed a reduced sperm concentration and total sperm count and abnormal progressive motility, total motility, and sperm morphology [19, 21, 22]. Nonetheless, some studies were unable to find any impacts of vitamin D levels on semen parameters [23, 24]. The correlation of serum vitamin D with male fertility was further assessed through a recent meta-analysis [25]. Nonetheless, the limited studies conducted and the inappropriate assessment of the study quality suggest that these findings should be interpreted with caution. Despite the limitations of the previous meta-analysis, the importance of serum vitamin D in male fertility has garnered considerable interest, leading to a growing body of research in this area. As more studies have been published, both shortcomings and advancements have been identified in the existing literature. In light of the increasing interest and the need for further evidence to guide clinical applications, a comprehensive systematic review and meta-analysis was conducted. The primary objective of this research was to provide more clarity on the association of vitamin D serum levels with semen quality in males.

2. Methods

2.1. Search Strategy. The following databases: Web of Science, Embase, PubMed, Scopus, and the Cochrane Library, were searched up to December 1st, 2022 to retrieve relevant articles. Google Scholar was investigated as well. The following search strategy was run in PubMed and tailored to each database when necessary: “vitamin D” OR “25-OH-Vitamin D” OR “vitamin D” OR “cholecalciferol” OR “ergocalciferol” OR “calcitriol” OR “alphacalcidol” AND “fertility” OR “infertility” OR “male fertility” OR “male infertility” OR “asthenozoospermia” OR “oligozoospermia” OR “oligoasthenozoospermia” OR “oligoasthenoteratozoospermia” OR “teratozoospermia” OR “semen quality” OR “sperm quality” OR “sperm analysis” OR “sperm volume” OR “sperm count” OR “sperm concentration” OR “sperm motility” OR “sperm morphology.” To ensure a more comprehensive analysis, unpublished and gray literature

was searched using Google Scholar and World Health Organization databases. The references of suitable articles were examined to determine other eligible publications. The search for relevant literature was executed with no language restriction. The search and collection processes of relevant literature were performed by two independent authors (FL and TFY). The PICO method was used: Population (*P*) = Men with serum vitamin D level, Intervention (*I*) = Serum vitamin D deficiency, Comparison (*C*) = Men with normal serum vitamin D level, and Outcome (*O*) = The results of male fertility status and sperm parameters. The inclusion criteria were: (1) the study investigated the presence of any possible link between vitamin D and male fertility, (2) semen analysis was undertaken according to the WHO criteria, (3) it was an observational study (cross-sectional and case-control study), and (4) the participants in the study were male adults. The exclusion criteria were: (1) the study could not extract relevant data and (2) it was a duplicated study.

2.2. Data Extraction. The analysis was carried out with reference to the PRISMA 2020 Checklist [26]. The protocol was registered with PROSPERO (CRD42022327583). Two of the authors (FL, TFY) independently reviewed the articles and extracted the data appropriately as per the criteria set for the inclusion and exclusion of data. Any discrepancies were dealt with via arbitration by a third reviewer (JJQ). The information below of every article was examined: first author, year of publication, date of sample collection, location, sample size, age of participants, abstinence time, study design, health status, and quality assessment score.

2.3. Quality Assessment. Independent assessments of the quality of the filtered articles were executed through two reviewers (FL, TFY) as per the Joanna Briggs Institute (JBI) Critical Appraisal Checklist [27]. The resolution of any disagreement via arbitration was by a third reviewer (JJQ). The checklist for cross-sectional studies comprised eight questions, and that for case-control studies comprised 10 questions. A response of “clear” to each question received two points, while a response of “unclear” received one point. No point was given if a question was not answered. Scores of <30%, 30%–70%, and >70% were categorized as low, moderate, and high quality, respectively.

2.4. Statistical Analysis. Microsoft Excel 2007 (Microsoft©) was used for data collection and recording, and meta-analysis was conducted through STATA (STATA Corp. LLC, version 12). The weighted mean difference (WMD) and corresponding 95% confidence interval (95% CI) with a random effect model were undertaken to evaluate the association of vitamin D in the serum with male fertility. The variation in the level of vitamin D among fertile and infertile male participants as well as the association between these vitamin levels and the quality of sperm (volume, total counts, concentration, motility, progressive motility, and morphology) were assessed. The statistic I^2 test was employed to evaluate heterogeneity, with the respective low, moderate, and high heterogeneity defined as an I^2 index of 25%, 50%, and 75% [28]. Subgroup analysis was performed if the heterogeneity was high. The stability of the resulting data was assessed through

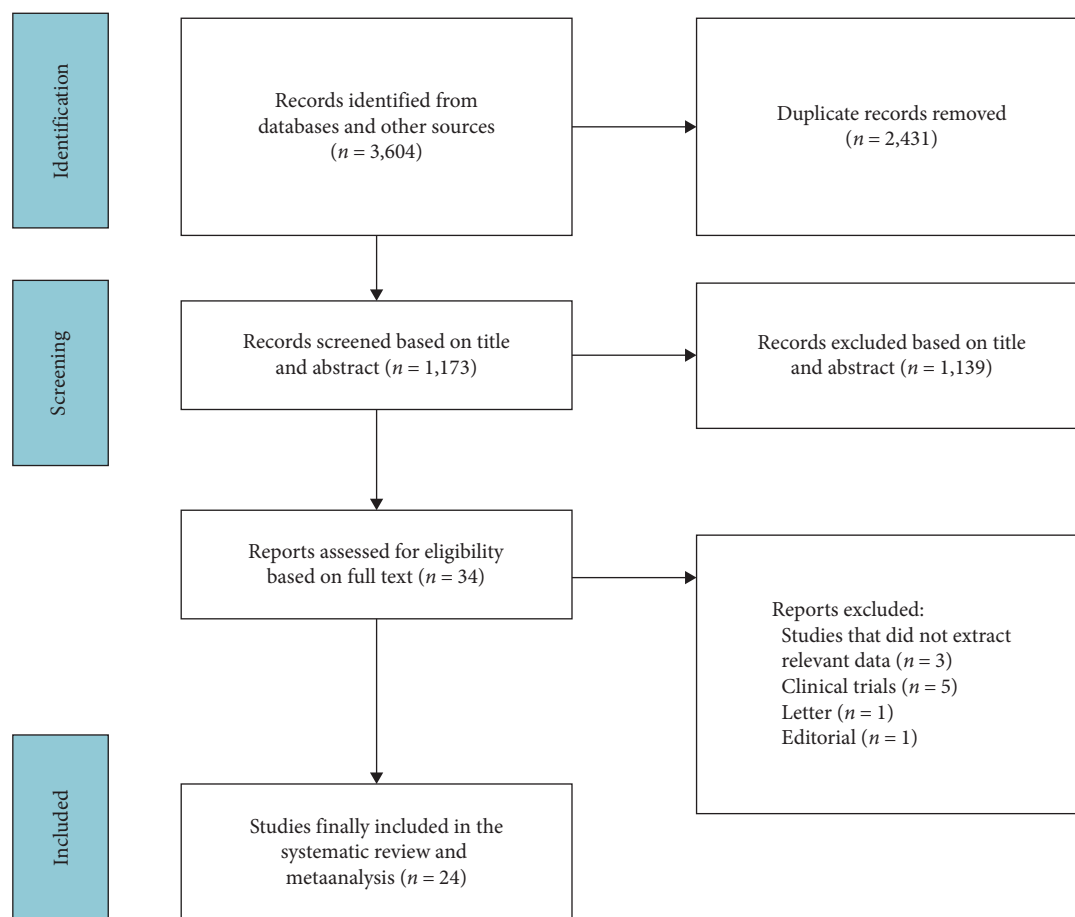


FIGURE 1: Flow diagram depicting article selection for the systematic review.

sensitivity analyses by utilizing the leave-one-out method. This process involves the exclusion of each study from the analysis one at a time. Egger's and Begg's tests were employed to test potential publication bias.

3. Results

3.1. Study Selection. In total, 3,604 studies were initially included through a systematic exploration of the databases. After removing duplicate studies, 1,173 studies were reviewed by initially assessing the title and abstract. Among these, 34 reports were considered eligible for a review of the full text. After evaluation of the full texts, 10 papers were excluded (3 studies were unsuitable for extracting relevant data, 5 were clinical trials, 1 was a letter, and 1 was an editorial article). Finally, 24 studies that conformed to the specific criteria were subjected to systematic review and meta-analysis. A diagrammatic presentation of PRISMA illustrating the selection of the included articles is shown in Figure 1.

3.2. Characteristics of the Included Studies. In total, 24 articles satisfied the set criteria for this review and meta-analysis and comprised 7,138 participants. Among the 24 articles, 18 were cross-sectional (75%) [19, 20, 22, 29–43], and 6 were case-control studies (25%) [21, 44–48]. Furthermore, 4 studies were from Denmark [20, 31, 32, 46], 4 from Iran [29, 30, 36, 44], 4 from China [22, 33, 39, 42], 2 from Turkey [43, 47], 2 from

Pakistan [19, 48], and the remaining 8 were from Iraq [45], the USA [37], Jordan [21], Spain [41], Brazil [34], Egypt [38], India [40], and Italy [35]. The participants were all fertile in 3 of the studies [20, 31, 37], subfertile in 11 [19, 29, 30, 32–34, 36, 39–41, 43], and both fertile and infertile in 10 studies [21, 22, 35, 38, 42, 44–48]. Among the articles, the study quality was determined to be high for 15 articles [20, 21, 29, 31–34, 36, 37, 39, 41–44, 47] and nine studies were of moderate quality [19, 22, 30, 35, 38, 40, 45, 46, 48] according to the JBI Critical Appraisal Checklist. *Supplementary 1* presents a summary of the included articles.

3.3. Assessment of Serum Vitamin D Levels and Fertility. The 15 high-quality studies (8 cross-sectional and 7 case-control studies) comprised a total of 2,981 participants and documented the association of vitamin D levels with fertility. Pooled results retrieved from these data implied remarkably diminished levels of vitamin D in infertile individuals in comparison with fertile individuals (WMD = 7.06; 95% CI = 2.51–11.62; $P = 0.002$) and the heterogeneity of this result was high ($I^2 = 98.5%$, $P < 0.001$) (Supplementary 2).

Subgroup analysis as per the quality of the selected studies (high quality vs. moderate) was executed. The resulting data indicated the presence of remarkably lowered levels of vitamin D in infertile individuals compared with fertile individuals in both high-quality studies (WMD = 2.58; 95%

CI = 0.79–4.37; $P = 0.005$) with moderate heterogeneity ($I^2 = 58.9\%$, $P = 0.033$) and in studies of moderate quality (WMD = 10.25; 95% CI = 5.27–15.23; $P < 0.001$) with high heterogeneity ($I^2 = 98.1\%$, $P < 0.001$) (Supplementary 2).

A lack of publication bias was revealed by Begg's test ($P = 0.692$), whereas Egger's test reported the opposite ($P = 0.001$). Upon applying the trim-and-fill technique, no articles were corrected and added to the articles originally included. This indicates that, despite the potential presence of publication bias, the overall analysis results remained unchanged (WMD = 7.06; 95% CI = 2.51–11.62; $P = 0.002$) and unaffected after the trim-and-fill method.

3.4. Examining the Relationship between Serum Vitamin D Levels and Sperm Volume. Eight studies, all cross-sectional studies, with a total of 4,116 participants, suggested the relationship between vitamin D levels and sperm volume. The pooled results suggested that these two elements lacked any remarkable correlation (WMD = 0.17; 95% CI = -0.00–0.34; $P = 0.050$). However, it is important to note that there was evidence of heterogeneity among the included research. ($I^2 = 63.0\%$, $P = 0.008$) (Supplementary 2). Begg's test ($P = 0.063$) and Egger's test ($P = 0.140$) reported the absence of publication bias.

3.5. Examining the Relationship between Sperm Concentration and Serum Vitamin D Levels. Thirteen studies, including 11 cross-sectional and two case-control studies, with 4,954 participants, reported the impact of serum vitamin D levels on sperm concentration. Pooled results suggested remarkably lower levels of vitamin D in infertile individuals in comparison with fertile individuals (WMD = 8.54; 95% CI = 4.01–13.06; $P < 0.001$). Additionally, the analysis was indicative of the presence of heterogeneity ($I^2 = 57.0\%$, $P = 0.006$) (Supplementary 2).

Begg's test showed no evidence of publication bias ($P = 0.855$), however, Egger's test yielded the opposite results ($P = 0.018$). The trim-and-fill method was utilized, and five articles were corrected and added to the originally included articles. The results of the original 13 papers (WMD = 8.54; 95% CI = 4.01–13.06; $P < 0.001$) and the corrected 18 papers (WMD = 6.03; 95% CI = 1.95–10.12; $P = 0.004$) were both confirmed to be statistically significant. The presence of publication bias in the study did not alter the overall conclusion, as both the original and corrected results demonstrated a remarkable relationship between vitamin D serum levels and the outcome.

3.6. Assessing the Relationship between Total Sperm Count and Serum Vitamin D Levels. Eight studies, all cross-sectional studies, with overall 4,172 participants, reported a relationship between the level of vitamin D and total sperm counts. Pooled results suggested that the deficiency of vitamin D in the serum of men significantly reduced the total sperm count (WMD = 14.43, 95% CI = 1.30–27.55, $P = 0.031$) and the data were indicative of the presence of heterogeneity ($I^2 = 66.4\%$, $P = 0.004$) (Supplementary 2). An absence of publication bias was revealed by Begg's test ($P = 0.711$) and Egger's test ($P = 0.419$).

3.7. Correlation between Serum Vitamin D Levels and Sperm Motility. Twelve studies, including 11 cross-sectional studies and one case-control study, with a total of 5,267 participants, indicated that the levels of vitamin D were remarkably linked to sperm motility. Pooled results suggested that the deficiency of this vitamin in men significantly reduced sperm motility (WMD = 6.40, 95% CI = 3.15–9.64, $P < 0.001$), and the heterogeneity of this result was high ($I^2 = 84.4\%$, $P < 0.001$) (Supplementary 2).

Subgroup analysis was executed based on the mean age (<30 vs. 30–35 vs. >35 years) and the resulting data indicated that serum vitamin D deficiency remarkably reduced sperm motility in the <30 years group (WMD = 4.38; 95% CI = 0.98–7.79; $P = 0.012$) with moderate heterogeneity ($I^2 = 49.5\%$, $P = 0.138$), the 30–35 years group (WMD = 4.47; 95% CI = 0.61–8.33; $P = 0.023$) with high heterogeneity ($I^2 = 81.1\%$, $P < 0.001$) and the >35 years group (WMD = 16.99; 95% CI = 3.98–30.01; $P = 0.011$) with high heterogeneity ($I^2 = 85.9\%$, $P = 0.008$) (Supplementary 2).

Begg's test provided no evidence for publication bias ($P = 0.193$), but Egger's test reported the opposite results ($P = 0.007$). The trim-and-fill method was utilized, and no articles were corrected and added to the articles originally included. There was no change after the trim-and-fill method (WMD = 6.40, 95% CI = 3.15–9.64, $P < 0.001$) suggesting that although this study did have publication bias, it did not affect the analysis result.

3.8. Examining the Relationship between Sperm Progressive Motility and Vitamin D Levels. Ten studies, including eight cross-sectional and two case-control studies, with 3,976 participants, assessed the association of vitamin D levels in the serum with the progressive motility of the sperm. Pooled results suggested that vitamin D deficiency in men significantly reduced sperm progressive motility (WMD = 5.00, 95% CI = 1.09–8.92, $P = 0.012$) and the heterogeneity of this result was high ($I^2 = 84.6\%$, $P < 0.001$) (Supplementary 2).

Subgroup analysis took into account the quality of the selected studies (high vs. moderate quality), and the results did not indicate any correlation of the serum vitamin D levels with the sperm progressive motility in the high-quality studies (WMD = 2.75; 95% CI = -0.43–5.93; $P = 0.090$) with moderate heterogeneity ($I^2 = 67.4\%$, $P = 0.003$). Additionally, serum vitamin D deficiency significantly reduced sperm progressive motility in the moderate-quality studies (WMD = 11.65; 95% CI = 8.41–14.89; $P < 0.001$), and the data indicated the absence of any remarkable heterogeneity ($I^2 = 0.00\%$, $P < 0.865$) (Supplementary 2). No publication bias was documented by Begg's test ($P = 0.592$) and Egger's test ($P = 0.130$).

3.9. Association between Serum Vitamin D Levels and Sperm Morphology. Thirteen studies, including 11 cross-sectional and two case-control studies, with 5,370 participants, documented the influence of vitamin D levels on the morphology of sperms. Pooled results suggested that the deficiency of this vitamin in men significantly reduced normal sperm morphology (WMD = 0.74, 95% CI = 0.20–1.27, $P = 0.007$) and the data indicated the presence of heterogeneity ($I^2 = 73.1\%$, $P < 0.001$) (Supplementary 2). No publication

bias was indicated by Begg's test ($P = 0.583$) and Egger's test ($P = 0.332$).

3.10. Sensitivity Analyses. Sensitivity analyses were performed to estimate the robustness of the outcomes of this study. Results showed that all of the outcomes in this study were very stable.

4. Discussion

This research dealt with investigating the correlation of serum vitamin D levels with male fertility and sperm quality. The serum vitamin D deficiency was remarkably linked to reduced total sperm count and sperm concentration and abnormal morphology. However, no remarkable correlation was noted between the levels of vitamin D and sperm volume. It should be noted that the relationship between vitamin D levels and male fertility, sperm motility, and progressive motility needs to be considered with caution because the acquired data implied high heterogeneity or opposite results after subgroup analysis.

Many studies have focused on the possible processes governing the relationship between serum vitamin D levels and male fertility. In the human reproductive field, vitamin D receptors and metabolizing enzymes have been primarily found in the prostate, seminal vesicles, epididymis, and germ cells (esp., spermatocytes, spermatogonia, and Sertoli cells). Thus, vitamin D could be related to spermatogenesis and maturation of human spermatozoa [49–51]. As per the data acquired by Blomberg Jensen et al. [49], vitamin D is critically involved in trans-epithelial calcium transfer in the epididymis to improve the status of male reproduction. Vitamin D may improve sperm motility through elevating adenosine triphosphate synthesis via both cyclic adenosine monophosphate and the activity of the protein kinase A pathway [31, 39]. Furthermore, some studies reported a positive correlation between vitamin D and sex hormone-binding globulin [20, 52, 53] and total or free testosterone [54–56]. Hence, vitamin D may indirectly modulate the bioavailable fraction of testosterone to influence male fertility.

A meta-analysis by Arab et al. [25] indicated remarkably elevated serum levels of 25(OH)D₃, a form of vitamin D, infertile men than in fertile men. Moreover, a significant association between serum vitamin D levels, sperm motility, and sperm progressive motility was noted as well. Our study found that serum vitamin D deficiency could also reduce sperm concentration and total sperm counts and induce abnormal sperm morphology. The current study includes seven additional newer studies with 2,572 participants compared to the previous study, suggesting that the results of our pooled quantitative assessment may be more robust and reliable than the previous report. The Newcastle–Ottawa Quality Assessment Scale (NOS) was utilized for assessing study quality in the meta-analysis by Arab et al. [25]. Although the NOS value was the best for case–control and cohort studies [57], most of the studies included were cross-sectional studies. In this meta-analysis, the JBI Critical Appraisal Checklist was adopted to examine the quality more accurately [27]. The

above differences may explain the different results obtained between our study and the previous report.

The present meta-analysis has some limitations. Significant heterogeneity was observed among the selected studies. Differential inclusion and exclusion criteria, ethnicities, serum vitamin D detection method, age, body mass index, lifestyle, season, and polymorphisms in the vitamin D receptor could have contributed to this heterogeneity. Seven studies [20, 29, 31–33, 37, 41] reported analysis results after adjusting for potential confounders. However, different studies were adjusted for different confounders, and many studies included in our meta-analysis did not report any potential confounders associated with serum vitamin D levels. This led to calculations being done for only unadjusted pooled values for this meta-analysis. Hence, owing to this lack of complete data, the appropriate subgroup analysis could not be performed to identify the precise reason for heterogeneity across different studies. The sperm DNA fragmentation index (DFI) appears to be an important parameter of semen quality and has been widely used in Andrology Laboratories [58]. However, a majority of the selected literature included in this analysis did not analyze this factor. Hence, more studies on the correlation between serum vitamin D levels and DFI are needed in the future. Nonetheless, this meta-analysis provides some insights into the correlation between vitamin D levels in the serum and male fertility, which could help reproductive medicine doctors to initiate more appropriate treatment.

In conclusion, the present meta-analysis revealed the vulnerability of semen quality to serum vitamin D deficiency. However, the findings concerning the impact of serum vitamin D on male reproduction should be interpreted with caution. To strengthen the evidence base and gain a more comprehensive view of the association between vitamin D in the serum and male fertility, further investigations are warranted. It is recommended to conduct research in diverse countries to account for potential regional confounders. Additionally, evaluating all relevant semen parameters in future studies will provide a more comprehensive assessment of this process.

Conflicts of Interest

The authors declare that they have no conflicts of interest.

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Supplementary Materials

Supplementary 1. Characteristics of the included articles.

Supplementary 2. Association of serum vitamin D level with fertility illustrated through forest plot. Forest plot displaying the results of subgroup analysis examining the association between serum vitamin D level and fertility. Forest plot presenting the association of serum vitamin D level with sperm volume. Forest plot illustrating the association between serum

vitamin D level and sperm concentration. Forest plot illustration of the association between vitamin D serum level and total sperm count. Forest plot presenting the association between serum vitamin D level and sperm motility. Forest plot of subgroup analysis results of the association between serum vitamin D level and sperm motility. Forest plot of the association between vitamin D level in the serum and sperm progressive motility. Forest plot of subgroup analysis results of the association between vitamin D level in the serum and sperm progressive motility. Forest plot illustration of the association between serum vitamin D level and sperm morphology.

References

- [1] Q. Q. Meng, Y. L. Zhang, and A. G. Ren, "Infertility rate in married couples of reproductive age in China: a systematic review and meta-analysis," *Zhonghua Liu Xing Bing Xue Za Zhi*, vol. 34, no. 8, pp. 826–831, 2013.
- [2] A. Arab, N. Rafie, M. Mansourian, M. Miraghajani, and H. Hajianfar, "Dietary patterns and semen quality: a systematic review and meta-analysis of observational studies," *Andrology*, vol. 6, no. 1, pp. 20–28, 2018.
- [3] J. Fainberg and J. A. Kashanian, "Recent advances in understanding and managing male infertility," *F1000Research*, vol. 8, 2019.
- [4] M. L. Eisenberg, S. Li, M. R. Cullen, and L. C. Baker, "Increased risk of incident chronic medical conditions in infertile men: analysis of United States claims data," *Fertility and Sterility*, vol. 105, no. 3, pp. 629–636, 2016.
- [5] T. J. Walsh, "Male reproductive health and prostate cancer risk," *Current Opinion in Urology*, vol. 21, no. 6, pp. 506–513, 2011.
- [6] H. Levine, N. Jørgensen, A. Martino-Andrade et al., "Temporal trends in sperm count: a systematic review and meta-regression analysis of samples collected globally in the 20th and 21st centuries," *Human Reproduction Update*, vol. 29, no. 2, pp. 157–176, 2023.
- [7] H. Levine, N. Jørgensen, A. Martino-Andrade et al., "Temporal trends in sperm count: a systematic review and meta-regression analysis," *Human Reproduction Update*, vol. 23, no. 6, pp. 646–659, 2017.
- [8] B. H.-K. Luk and A. Y. Loke, "The impact of infertility on the psychological well-being, marital relationships, sexual relationships, and quality of life of couples: a systematic review," *Journal of Sex & Marital Therapy*, vol. 41, no. 6, pp. 610–625, 2015.
- [9] B. H. K. Luk and A. Y. Loke, "Sexual satisfaction, intimacy and relationship of couples undergoing infertility treatment," *Journal of Reproductive and Infant Psychology*, vol. 37, no. 2, pp. 108–122, 2019.
- [10] R. N. Calonge, J. A. Guijarro, C. Andrés et al., "Relationships between lipids levels in blood plasma, follicular fluid and seminal plasma with ovarian response and sperm concentration regardless of age and body mass index," *Revista Internacional de Andrología*, vol. 20, no. 3, pp. 178–188, 2022.
- [11] M. Hudnall, B. Goyette, S. Ambulkar et al., "Self-reported race/ethnicity is not associated with abnormal semen parameters after accounting for body mass index and socioeconomic status," *Journal of Urology*, vol. 208, no. 1, pp. 164–170, 2022.
- [12] D. Daumler, P. Chan, K. C. Lo, J. Takefman, and P. Zekowitz, "Men's knowledge of their own fertility: a population-based survey examining the awareness of factors that are associated with male infertility," *Human Reproduction*, vol. 31, no. 12, pp. 2781–2790, 2016.
- [13] E. Ricci, S. Al Beitawi, S. Cipriani et al., "Semen quality and alcohol intake: a systematic review and meta-analysis," *Reproductive BioMedicine Online*, vol. 34, no. 1, pp. 38–47, 2017.
- [14] X. Zhang, C. Deng, W. Liu et al., "Effects of varicocele and microsurgical varicocelectomy on the metabolites in semen," *Scientific Reports*, vol. 12, no. 1, Article ID 5179, 2022.
- [15] S. Kim, D. Han, J. Ryu, K. Kim, and Y. H. Kim, "Effects of mobile phone usage on sperm quality—no time-dependent relationship on usage: a systematic review and updated meta-analysis," *Environmental Research*, vol. 202, Article ID 111784, 2021.
- [16] X. Zhou, H. Shi, S. Zhu, H. Wang, and S. Sun, "Effects of vitamin E and vitamin C on male infertility: a meta-analysis," *International Urology and Nephrology*, vol. 54, no. 8, pp. 1793–1805, 2022.
- [17] R. Al Khalifah, M. H. Hamad, A. Hudairi et al., "Prevalence and related risk factors of vitamin D deficiency in Saudi children with epilepsy," *Children*, vol. 9, no. 11, Article ID 1696, 2022.
- [18] O. Feehan, P. J. Magee, L. K. Pourshahidi, D. J. Armstrong, and E. M. McSorley, "Vitamin D deficiency in nursing home residents: a systematic review," *Nutrition Reviews*, vol. 81, no. 7, pp. 804–822, 2023.
- [19] R. Rehman, S. Lalani, M. Baig, I. Nizami, Z. Rana, and Z. J. Gazzaz, "Association between vitamin D, reproductive hormones and sperm parameters in infertile male subjects," *Frontiers in Endocrinology*, vol. 9, Article ID 607, 2018.
- [20] C. H. Ramlau-Hansen, U. K. Moeller, J. P. Bonde, J. Olsen, and A. M. Thulstrup, "Are serum levels of vitamin D associated with semen quality? Results from a cross-sectional study in young healthy men," *Fertility and Sterility*, vol. 95, no. 3, pp. 1000–1004, 2011.
- [21] A. Alzoubi, H. Mahdi, S. Al Bashir et al., "Normalization of serum vitamin D improves semen motility parameters in patients with idiopathic male infertility," *Acta Endocrinologica (Bucharest)*, vol. 13, no. 2, pp. 180–187, 2017.
- [22] C.-L. Zhu, Q.-F. Xu, S.-X. Li et al., "Investigation of serum vitamin D levels in Chinese infertile men," *Andrologia*, vol. 48, no. 10, pp. 1261–1266, 2016.
- [23] R. Shetty, S. Sethu, R. Deshmukh et al., "Corneal dendritic cell density is associated with subbasal nerve plexus features, ocular surface disease index, and serum vitamin D in evaporative dry eye disease," *BioMed Research International*, vol. 2016, Article ID 4369750, 10 pages, 2016.
- [24] C.-H. Yang, J. Albietz, D. G. Harkin, M. G. Kimlin, and K. L. Schmid, "Impact of oral vitamin D supplementation on the ocular surface in people with dry eye and/or low serum vitamin D," *Contact Lens and Anterior Eye*, vol. 41, no. 1, pp. 69–76, 2018.
- [25] A. Arab, A. Hadi, S. P. Moosavian, G. Askari, and M. Nasirian, "The association between serum vitamin D, fertility and semen quality: a systematic review and meta-analysis," *International Journal of Surgery*, vol. 71, pp. 101–109, 2019.
- [26] M. J. Page, J. E. McKenzie, P. M. Bossuyt et al., "The PRISMA 2020 statement: an updated guideline for reporting systematic reviews," *BMJ*, vol. 372, Article ID n71, 2021.
- [27] S. Moola, Z. Munn, C. Tufanaru et al., "Chapter 7: systematic reviews of etiology and risk," in *Joanna Briggs Institute Reviewer's Manual*, vol. 5, The Joanna Briggs Institute, 2017.
- [28] M. Cumpston, T. Li, M. J. Page et al., "Updated guidance for trusted systematic reviews: a new edition of the Cochrane Handbook for Systematic Reviews of Interventions," *Cochrane*

- Database of Systematic Reviews*, vol. 10, Article ID Ed000142, 2019.
- [29] S. Abbasihormozi, A. Kouhkan, A. R. Alizadeh et al., "Association of vitamin D status with semen quality and reproductive hormones in Iranian subfertile men," *Andrology*, vol. 5, no. 1, pp. 113–118, 2017.
- [30] E. Azizi, M. Najji, M. Shabani-Nashtaei, A. Aligholi, A. Najafi, and F. Amidi, "Association of serum content of 25-hydroxy vitamin D with semen quality in normozoospermic and oligoasthenoteratozoospermic men," *International Journal of Reproductive BioMedicine*, vol. 16, no. 11, pp. 689–696, 2018.
- [31] M. Blomberg Jensen, P. J. Bjerrum, T. E. Jessen et al., "Vitamin D is positively associated with sperm motility and increases intracellular calcium in human spermatozoa," *Human Reproduction*, vol. 26, no. 6, pp. 1307–1317, 2011.
- [32] M. Blomberg Jensen, J. Gerner Lawaetz, A.-M. Andersson et al., "Vitamin D deficiency and low ionized calcium are linked with semen quality and sex steroid levels in infertile men," *Human Reproduction*, vol. 31, no. 8, pp. 1875–1885, 2016.
- [33] Y. Chen, D. Liu, L. Zeng et al., "Effect of serum 25-hydroxyvitamin D levels on sperm quality and assisted reproductive technology outcomes for men of infertile Chinese couples," *Andrology*, vol. 8, no. 5, pp. 1277–1286, 2020.
- [34] I. M. Ciccone, E. M. F. Costa, J. R. Pariz et al., "Serum vitamin D content is associated with semen parameters and serum testosterone levels in men," *Asian Journal of Andrology*, vol. 23, no. 1, pp. 52–58, 2021.
- [35] C. Foresta, G. Strapazzon, L. De Toni et al., "Bone mineral density and testicular failure: evidence for a role of vitamin D 25-hydroxylase in human testis," *The Journal of Clinical Endocrinology & Metabolism*, vol. 96, no. 4, pp. E646–E652, 2011.
- [36] H. Hajianfar, E. Karimi, N. Mollaghasemi, S. Rezaei, and A. Arab, "Is there a relationship between serum vitamin D and semen parameters? A cross-sectional sample of the Iranian infertile men," *Basic and Clinical Andrology*, vol. 31, no. 1, p. 29, 2021.
- [37] A. O. Hammoud, A. W. Meikle, C. M. Peterson, J. Stanford, M. Gibson, and D. T. Carrell, "Association of 25-hydroxyvitamin D levels with semen and hormonal parameters," *Asian Journal of Andrology*, vol. 14, no. 6, pp. 855–859, 2012.
- [38] T. M. Hussein, N. Eldabah, H. A. Zayed, and R. M. Genedy, "Assessment of serum vitamin D level and seminal vitamin D receptor gene methylation in a sample of Egyptian men with idiopathic infertility," *Andrologia*, vol. 53, no. 9, Article ID e14172, 2021.
- [39] K. Jueraiteitbaike, Z. Ding, D.-D. Wang et al., "The effect of vitamin D on sperm motility and the underlying mechanism," *Asian Journal of Andrology*, vol. 21, no. 4, pp. 400–407, 2019.
- [40] S. Kumari, K. Singh, S. Kumari, H. Nishat, and B. Tiwary, "Association of vitamin D and reproductive hormones with semen parameters in infertile men," *Cureus*, vol. 13, no. 4, Article ID e14511, 2021.
- [41] A. Rudnicka, E. Adoamnei, J. A. Noguera-Velasco et al., "Vitamin D status is not associated with reproductive parameters in young Spanish men," *Andrology*, vol. 8, no. 2, pp. 323–331, 2020.
- [42] B. Yang, H. Sun, Y. Wan et al., "Associations between testosterone, bone mineral density, vitamin D and semen quality in fertile and infertile Chinese men," *International Journal of Andrology*, vol. 35, no. 6, pp. 783–792, 2012.
- [43] E. Ozdemir, A. Tokmak, S. Erklm, H. B. Yakut, and N. Ylmaz, "Association between vitamin D levels and semen parameters in infertile males," *Journal of Clinical and Analytical Medicine*, vol. 6, pp. 765–769, 2015.
- [44] H. Akhavadegan and M. Karbakhsh, "Comparison of serum vitamin D between fertile and infertile men in a vitamin D deficient endemic area: a case-control study," *Urologia Journal*, vol. 84, no. 4, pp. 218–220, 2017.
- [45] M. Albaldawy and A. Alsallami, "Study of association among vitamin D, testosterone and semen quality in fertile and Iraqi infertile men," *Journal of Pharmaceutical Sciences and Research*, vol. 9, pp. 1067–1071, 2017.
- [46] M. Blomberg Jensen, A. Jørgensen, J. E. Nielsen et al., "Expression of the vitamin D metabolizing enzyme CYP24A1 at the annulus of human spermatozoa may serve as a novel marker of semen quality," *International Journal of Andrology*, vol. 35, no. 4, pp. 499–510, 2012.
- [47] K. Güngör, N. D. Güngör, M. M. Başar, F. Cengiz, S. S. Erşahin, and K. Çil, "Relationship between serum vitamin D levels semen parameters and sperm DNA damage in men with unexplained infertility," *European Review for Medical and Pharmacological Sciences*, vol. 26, no. 2, pp. 499–505, 2022.
- [48] F. Hussain, A. Malik, M. S. Qureshi et al., "Homeostatic relevance of vitamin D in maintaining male fertility in human: down-regulation of oxidative stress and up-regulation of anti-oxidative defense and steroid hormones," *Asian Pacific Journal of Reproduction*, vol. 7, no. 2, pp. 56–61, 2018.
- [49] M. Blomberg Jensen, J. E. Nielsen, A. Jørgensen et al., "Vitamin D receptor and vitamin D metabolizing enzymes are expressed in the human male reproductive tract," *Human Reproduction*, vol. 25, no. 5, pp. 1303–1311, 2010.
- [50] A. K. Nangia, O. Hill, M. D. Waterman, C. E. B. Schwender, and V. Memoli, "Testicular maturation arrest to testis cancer: spectrum of expression of the vitamin D receptor and vitamin D treatment in vitro," *Journal of Urology*, vol. 178, no. 3 Pt 1, pp. 1092–1096, 2007.
- [51] L. Zanatta, A. Zamoner, R. Gonçalves et al., "Effect of 1 α ,25-dihydroxyvitamin D₃ in plasma membrane targets in immature rat testis: ionic channels and gamma-glutamyl transpeptidase activity," *Archives of Biochemistry and Biophysics*, vol. 515, no. 1–2, pp. 46–53, 2011.
- [52] K.-Y. Chin, S. Ima-Nirwana, and W. Z. Wan Ngah, "Vitamin D is significantly associated with total testosterone and sex hormone-binding globulin in Malaysian men," *The Aging Male*, vol. 18, no. 3, pp. 175–179, 2015.
- [53] V.-V. Välimäki, H. Alftan, K. K. Ivaska et al., "Serum estradiol, testosterone, and sex hormone-binding globulin as regulators of peak bone mass and bone turnover rate in young Finnish men," *Journal of Clinical Endocrinology and Metabolism*, vol. 89, no. 8, pp. 3785–3789, 2004.
- [54] A. C. Heijboer, M. Oosterwerff, N. F. Schrotten et al., "Vitamin D supplementation and testosterone concentrations in male human subjects," *Clinical Endocrinology*, vol. 83, no. 1, pp. 105–110, 2015.
- [55] R. Rafiq, N. M. van Schoor, E. Sohl et al., "Associations of vitamin D status and vitamin D-related polymorphisms with sex hormones in older men," *The Journal of Steroid Biochemistry and Molecular Biology*, vol. 164, pp. 11–17, 2016.
- [56] Y. J. Tak, J. G. Lee, Y. J. Kim et al., "Serum 25-hydroxyvitamin D levels and testosterone deficiency in middle-aged Korean men: a cross-sectional study," *Asian Journal of Andrology*, vol. 17, no. 2, pp. 324–328, 2015.

- [57] X. Zeng, Y. Zhang, J. S. W. Kwong et al., "The methodological quality assessment tools for preclinical and clinical studies, systematic review and meta-analysis, and clinical practice guideline: a systematic review," *Journal of Evidence-Based Medicine*, vol. 8, no. 1, pp. 2–10, 2015.
- [58] World Health Organization, *WHO Laboratory Manual for the Examination and Processing of Human Semen*, World Health Organization, 2010.