

Association between periodontitis and sperm quality: a systematic review and meta-analysis

Authors: F. M. Ridho^{1,*}; R. Alfatah²; S. M. Cahyani³; V. A. Tasyah⁴; R. S. Rahmawati⁵

Affiliations: ¹Department of Dental Medicine, Faculty of Dental Medicine, Universitas Airlangga, Surabaya 60132, Indonesia; ²Faculty of Medicine, Universitas Islam Negeri Walisongo, Semarang 50185, Indonesia; ³Doctor of Dental Surgery, Faculty of Dental Medicine, Universitas Brawijaya, Malang 65145, Indonesia; ⁴Department of Medicine, Faculty of Medicine and Health Sciences, Universitas Bengkulu, Bengkulu 38119, Indonesia; ⁵Department of Periodontology, Faculty of Dental Medicine, Universitas Airlangga, Surabaya 60132, Indonesia.

ABSTRACT

INTRODUCTION: The present study was conducted to evaluate the association between periodontitis and sperm quality.

METHODS: A systematic review and meta-analysis of any observational studies published from inception to August 2024 in Scopus, PubMed, ScienceDirect, EBSCO, and Google Scholar was performed. A JBI checklist was used to assess the risk of bias. Statistical analysis was performed using Stata version 17. Fixed- or random-effects model meta-analyses were used and reported as pooled odds ratio (OR) and 95% confidence interval (CI).

RESULTS: Six studies involving 987 men aged ≥ 21 years were included in the systematic review, and four of them were included in the meta-analysis. Periodontitis was significantly associated with any sperm abnormalities (OR = 1.86; 95% CI = 1.32-2.60; $p = 0.0003$). In subgroup analysis, significant associations were found between periodontitis and sperm quality in Asian populations (OR = 2.13; 95% CI = 1.48-3.07; $p = 0.0001$) and subnormal sperm count (OR = 2.08; 95% CI = 1.03-4.23; $p = 0.04$). When stratified by the severity, moderate-to-severe periodontitis was associated with sperm quality (OR = 2.76; 95% CI = 1.78-4.26; $p = 0.0000$).

CONCLUSION: This study shows that periodontitis is associated with any sperm abnormalities.

Keywords: Infertility, Periodontal Disease, Periodontitis, Semen, Sperm

INTRODUCTION

Periodontitis is a chronic, multifactorial inflammatory disease that affects the periodontium, the tissue supporting tooth

structure [1]. In general, periodontitis is caused by plaque and pathogens, which subsequently lead to uncontrolled inflammation [2,3], resulting in the destruction of periodontal tissues and inhibition of effective bacterial clearance [4]. Periodontitis is

***Corresponding author:** Fiki Muhammad Ridho, Faculty of Dental Medicine, Universitas Airlangga, Jl. Prof. Dr. Moestopo No. 47, Mojo, Tambaksari, Surabaya 60132, Indonesia, Email: fiki.muhammad.ridho-2020@fkg.unair.ac.id, Tel: +62 81393617683; **Potential Conflicts of Interest (Col):** All authors: no potential conflicts of interest disclosed; **Funding:** All authors: No funding was sought for this study; **Academic Integrity:** All authors confirm that they have made substantial academic contributions to this manuscript as defined by the ICMJE; **Ethics of human subject participation:** The study was approved by the local Institutional Review Board. Informed consent was sought and gained where applicable; **Originality:** All authors: this manuscript is original has not been published elsewhere; **Review:** This manuscript was peer-reviewed by three reviewers in a double-blind review process; **Type-editor:** King (USA).

Received: 24th February 2025; **Initial decision given:** 20th April 2025; **Revised manuscript received:** 22th April 2024; **Accepted:** 4th June 2025.

Copyright: © The Author(s). This is an Open Access article distributed under the terms of the Creative Commons Attribution License (CC BY-NC-ND) ([click here](#)) which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited. **Publisher:** Rwanda Biomedical Centre (RBC)/Rwanda Health Communication Center, P. O. Box 4586, Kigali. ISSN: 2079-097X (print); 2410-8626 (online)

Citation for this article: F. M. Ridho; R. Alfatah; S. M. Cahyani, et al. Association between periodontitis and sperm quality: a systematic review and meta-analysis. Rwanda Medical Journal, Vol. 82, no. 2, p. 41-52, 2025. <https://dx.doi.org/10.4314/rmj.v82i2.5>

one of the most common diseases and has become a global public health concern [5]. Between 2011-2020, periodontitis was estimated to affect 62% of the global adult population, with 23.6% having severe periodontitis [6]. Furthermore, periodontitis has significantly contributed to the global disease burden over the past three decades, with 1.1 billion cases of severe periodontitis reported in 2019 and continuing to increase [7]. Numerous studies have also reported an association between periodontitis and various systemic diseases [8–12]. Therefore, periodontitis must be addressed due to its detrimental effects on general health.

The World Health Organization (WHO) defines male infertility as the inability of a man to impregnate a fertile woman for at least one year with regular sexual frequency without using contraception [13,14]. Analysis of reported data from the 2019 global burden of disease on male infertility globally showed a 19% increase compared to 1990. The article also reported that male infertility increased the most in the 30-34 age range [15]. In general, the causes of male infertility include endocrine/hormonal disorders, sperm duct abnormalities, idiopathic, and primary defects in testicles. Problems in the testicles are the most common in male infertility, 65-80% of all cases. This is related to abnormalities in sperm parameters even without other underlying causes [13]. Inadequate sperm quality, including low sperm production, poor motility, and abnormal sperm morphology, are the main causes of male infertility that have been widely described in several publications. Bacterial or viral infections are believed to be one of the direct causes of male infertility. Infectious agents can directly damage the seminiferous tubules of the testis. Swelling of the testicles due to local infection by these infectious agents increases intratesticular pressure, leading to decreased blood flow and, subsequently, tissue ischemia. Lack of oxygen disrupts cell metabolism, and most cannot carry out the spermatogenesis

process properly. Chronic infection has also been reported to cause testicular atrophy in adults [16–18]. Additionally, an unhealthy lifestyle, including smoking, excessive alcohol intake, and obesity, can further worsen sperm quality [19,20].

Previous studies have reported a possible link between periodontal disease and male infertility [21–23]. These findings are supported by evidence suggesting shared risk factors between periodontitis and male infertility, including smoking/tobacco use, alcohol consumption, diabetes, psychological stress, and obesity [20,24–27]. Systemic inflammation and periodontal pathogens are recognized as mechanisms explaining the association between periodontitis and impaired sperm quality [28]. Furthermore, a systematic review suggested a possible relationship between periodontitis and sperm quality [29]. However, so far, no meta-analysis has been conducted on the relationship between periodontitis and decreased sperm quality. In addition, a systematic review conducted by Lecaplain and colleagues [29] concluded that this relationship remains unclear and requires further evidence. Therefore, the present study aims to conduct a systematic review with meta-analysis to provide a comprehensive understanding of the relationship between periodontitis and sperm quality.

METHODS

Study design

This study was a systematic review and meta-analysis following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines [30]. It was registered with PROSPERO under the registration number: CRD42024625340.

Research question

The research question in this study was “What is the association between periodontitis and sperm

Table 1: PECOS framework.

| Element | Details |
|------------|---|
| Population | Adult male population |
| Exposure | Clinically diagnosed periodontitis |
| Comparison | Men without periodontitis or healthy controls |
| Outcomes | Sperm parameters |
| Study | Cross-sectional, cohort, and case-control studies |

quality?". In addressing the research questions, we used the population, exposure, comparison, outcomes, and study (PECOS) framework described in Table 1.

Search strategy

Five electronic databases, including Scopus, PubMed, ScienceDirect, EBSCO, and Google Scholar, and citation search, were used in the study for literature search. A literature search was performed using the following keyword combinations: periodontitis, periodontal, periodontal disease, sperm, semen, male infertility, infertility, fertility, and sexual, and using Boolean operators (AND, OR) to combine relevant keywords. All studies published from inception to August 2024 were considered in this study.

Eligibility criteria

Studies included in this research had to meet the established inclusion criteria, including 1) any observational studies (cross-sectional, case-control, or cohort studies), 2) participants were those diagnosed with periodontitis, 3) study controls were those who were periodontally healthy, 4) studies reporting estimates with 95% confidence intervals (CI), and 5) peer-reviewed and full-text. In contrast, studies that were review articles, commentaries, editorials, experimental studies, case reports, case series, and studies that only published abstracts were excluded. There were no other restraints in study selection, including publication year and language; therefore, all articles published until August 2024 were considered for inclusion.

Risk of bias assessment

Risk of bias assessment in included studies was performed using the Joanna Briggs Institute (JBI) critical appraisal tool. In this study, we used JBI for cross-sectional consisting of eight questions and JBI for case-control with 10 questions, with green, yellow, and red indicating low, moderate, and high risk of bias, respectively. The assessment was performed by two reviewers (FMR and RA). If there was any disagreement, we discussed carefully to reach a consensus with a third author (SMC).

Data pre-processing

Given the varying definitions of periodontitis across studies, we determined the definition of periodontitis so that the combined effect size

would provide reasonable results. Periodontitis was defined as probing depth (PD) ≥ 4 mm or clinical attachment loss (CAL) ≥ 1 mm in at least one tooth. If the periodontitis examination did not involve CAL but involved radiographic alveolar bone loss (ABL), then a radiographic ABL of at least $<15\%$ or approximately coronal third is considered periodontitis [31]. In diagnosing periodontitis using the community periodontal index of treatment need (CPITN), we defined codes 3 and 4 as periodontitis, according to research conducted by Nwhator et al. [32]. Furthermore, to determine sperm abnormalities, we used the standard definition by WHO regarding sperm abnormalities [33].

Data extraction

Data on both studies included in the qualitative and quantitative synthesis were extracted in tables consisting of references/authors, country, study design, sample size, age, periodontitis diagnostic method, semen analysis method, and study results.

Statistical analysis

Stata version 17 (StataCorp LLC, College Station, Texas, USA) was used for the statistical analysis. Study heterogeneity was analyzed with the provisions of low and high heterogeneity if the I^2 values were $\leq 50\%$ and $>50\%$, respectively. In cases of low heterogeneity ($I^2 \leq 50\%$ or $p \geq 0.1$), a fixed-effects model was used. Conversely, a random-effects model was used when heterogeneity was high ($I^2 > 50\%$ or $p < 0.1$) [34]. All findings were reported as odds ratios (OR) with 95% CI and presented in pooled OR and 95% CI with forest plots, with a p-value of < 0.05 defined as statistically significant. A funnel plot was not used in this study because the number of studies included in this meta-analysis was less than 10 studies [35]. A sensitivity analysis was carried out to determine the robustness of the results of the meta-analysis. It was performed using the leave-one-out method by removing each study sequentially and reanalyzing the remaining data set to determine whether there was a significant difference in OR and 95% CI [36].

RESULTS

Study selection

A literature search in electronic databases identified

800 articles. Any duplicates were removed using Mendeley reference manager software, leaving 748 records. In the initial screening, we excluded 669 articles, resulting in 79 studies. In further evaluation of titles and abstracts, 66 papers were excluded due to irrelevance to this study, leaving 13 articles for eligibility assessment. Of the 13 articles, two were excluded due to the irrelevance of the research objectives. Five others were review studies, and one was due to the same dataset use. This resulted in five remaining studies from electronic databases. We also identified studies through citation searches and found one study. Finally, a total of six studies were included in the qualitative review, and four of those included were retrieved in the meta-analysis. The entire flow of this study selection is depicted in Figure 1.

Characteristics of included studies

Six articles involving 987 male participants aged ≥21 years were finally included in this study. They consisted of five cross-sectional studies [32,37–40] and one case-control study [41]. The studies were conducted in several countries, including China [40,41], Hungary [39], Israel [38], Nigeria [32], and India [37]. However, only four studies [32,39–41] were included in the meta-analysis. The rest were excluded from the meta-analysis

because the studies did not compare periodontitis and periodontally healthy groups [37], and did not report data clearly or estimate with 95% CI [38]; however, they were included in the qualitative synthesis because of the relevance of their findings to the research questions that will support the results of this meta-analysis. All characteristics of eligible studies are summarized in Table 2.

Risk of bias assessment of included studies

We further evaluated the included studies for their risk of bias using the JBI checklist. Based on the risk of assessment, all studies showed a low to moderate risk of bias. No questions in the JBI checklist were considered high risk for all studies. The risk of bias summary is shown in Figure 2.

Association between periodontitis and any sperm abnormalities

Four studies [32,39–41] met the criteria for inclusion in the quantitative synthesis. The results of the fixed-effects model meta-analysis showed that periodontitis was significantly associated with any sperm abnormalities (OR = 1.86; 95% CI = 1.32-2.60; p = 0.0003) (Figure 3). Clinically, this finding suggests that men with periodontitis have approximately 86% higher odds of experiencing sperm abnormalities compared to men with

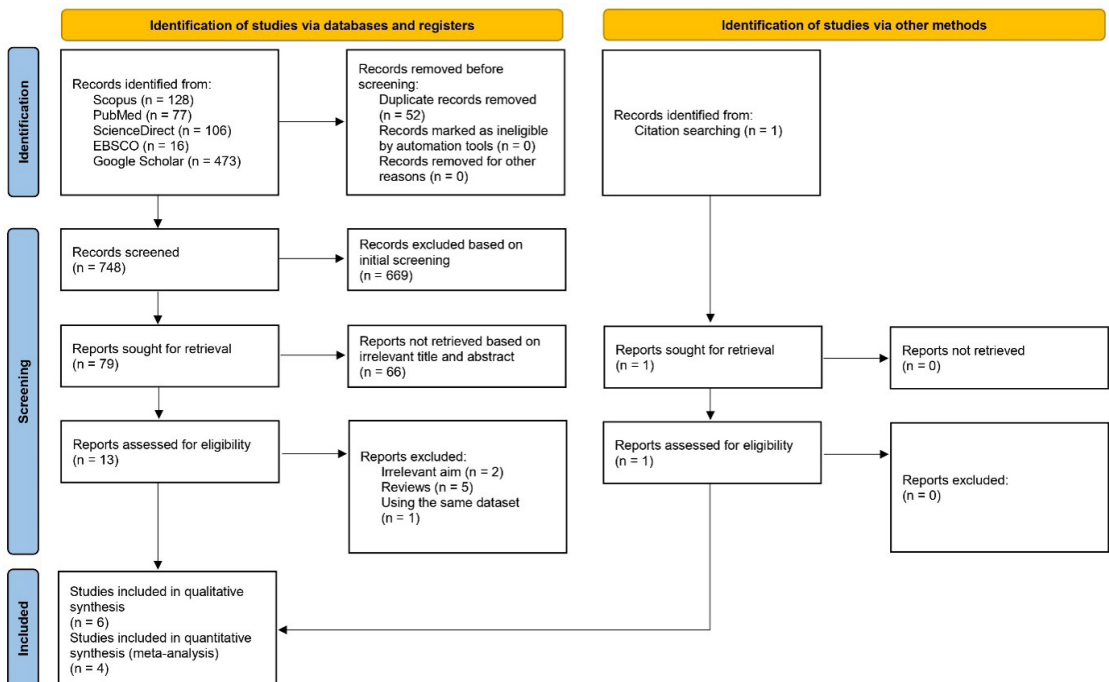


Figure 1: PRISMA flowchart

Table 2: Characteristics of included studies.

| Authors | Country | Study design | Sample size | Age (years) | Periodontitis diagnosis | Sperm analysis parameters | Results |
|-----------------------|---------|-----------------|---|-------------|---|---|--|
| Zhu et al. [40] | China | Cross-sectional | 360 | 22-46 | PD \geq 4 mm, CAL \geq 1 mm, radiographic ABL not exceeding 1/3 of the root length (mild), exceeding 1/3 but not exceeding 1/2 of the root length (moderate) or exceeding 1/2 or 2/3 of the root length (severe). | Sperm concentration, motility, viability, and deformity | Chronic periodontitis was significantly associated with male infertility, characterized by deterioration in sperm quality. |
| Klinger et al. [38] | Israel | Cross-sectional | 75 | Mean: 32.7 | PD \geq 4 mm, CAL \geq 1 mm. | Ejaculate volume, sperm concentration, overall and progressive motility, morphology, and white cells presence | There was a possible relationship between infertility and decreased semen quality, and periodontal infection. |
| Nwhator et al. [32] | Nigeria | Cross-sectional | 76 | 27-56 | CPITN score with codes 3 and 4. | Sperm count and motility | Chronic periodontitis and poor oral hygiene were significantly associated with subnormal sperm count. |
| Práger et al. [39] | Hungary | Cross-sectional | 199 | | PD \geq 4 mm, BOP \geq 50% of teeth. | Sperm morphology, motility, progressive and non-progressive motility, concentration, and total count | Some clinical features of poor periodontal disease were associated with abnormalities in sperm count. |
| Chidambar et al. [37] | India | Cross-sectional | 85 | 21-45 | PD \geq 4 mm, CAL \geq 1 mm. | Ejaculate volume, sperm concentration, motility, morphology, and the white cell presence. | There was a link between decreased sperm quality and infertility and periodontal disease. |
| Tao et al. [41] | China | Case-control | 192 (125 men in the case group and 67 men in the healthy control group) | | PD \geq 4 mm, CAL \geq 3 mm. | Sperm concentration, count, and progressive and non-progressive motility | Periodontitis was associated with abnormalities of semen and sperm motility. |

Abbreviation: ABL, alveolar bone loss; CAL, clinical attachment loss; CPITN, community periodontal index of treatment need; GI, gingival index; NA, unavailable; PD, probing depth.

healthy periodontal tissue. This pooled effect size may have important implications in clinical practice, especially in populations where periodontitis

is prevalent, highlighting the potential role of oral health screening as part of male infertility evaluation.

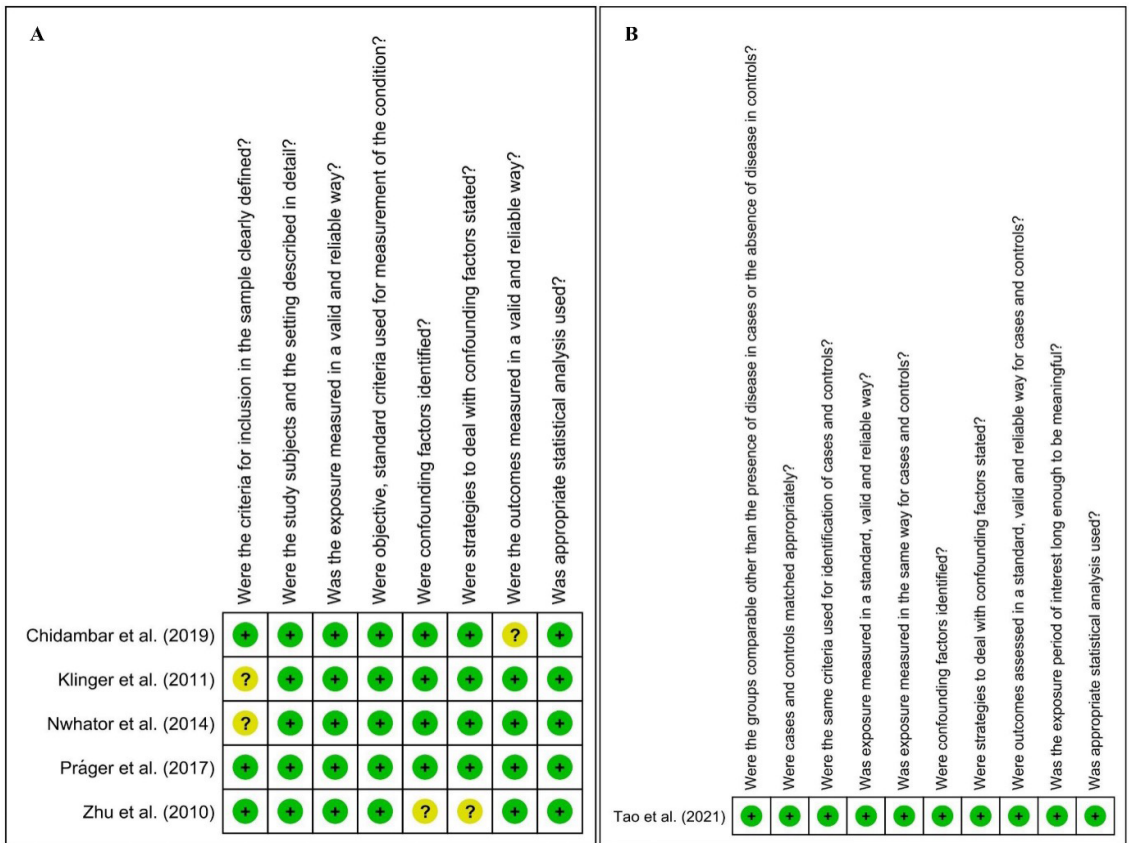


Figure 2: Risk of bias summary using JBI checklist: cross-sectional studies (A) and case-control study (B).

Subgroup analysis

Subgroup meta-analyses were performed stratified by country region, study design, periodontitis severity, and sperm abnormality parameters. All subgroup analyses are described in Table 3.

Based on country region, periodontitis was

significantly associated with decreased sperm quality in Asian populations (OR = 2.13; 95% CI = 1.48-3.07; p = 0.0001); however, it was not significant in African (OR = 1.91; 95% CI = 0.11-33.35; p = 0.66) and European populations (OR = 0.81; 95% CI = 0.33-1.99; p = 0.67). Meta-analysis of subgroups stratified by study design, significant

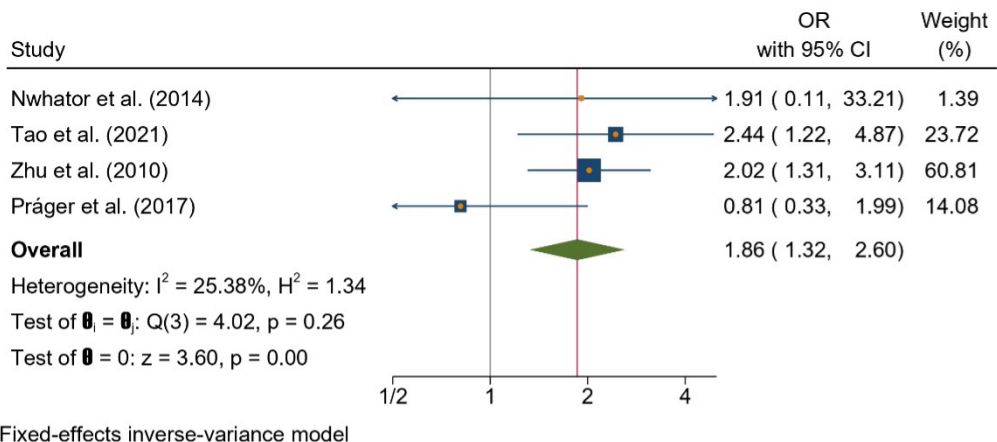


Figure 3: Forest plot of the association between periodontitis and any sperm abnormalities

Table 3: Subgroup analysis of the association between periodontitis and sperm quality

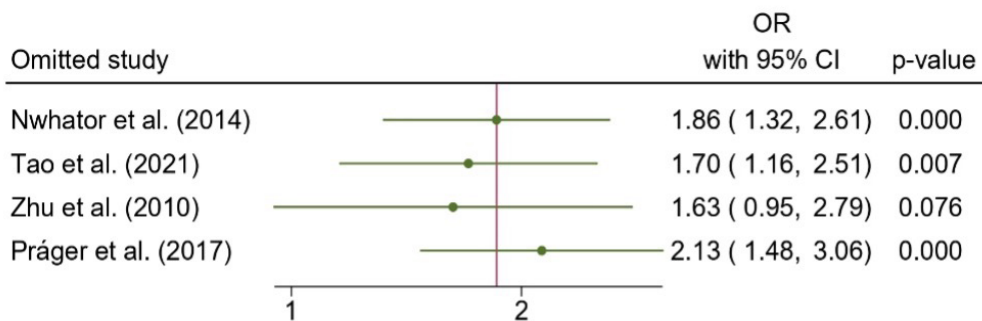
| Subgroup | Studies | OR (95% CI) | p-value | Heterogeneity | |
|---------------------------|---------|-------------------|---------|---------------|--------------------|
| | (n) | | | p | I ² (%) |
| Overall | 4 | 1.86 (1.32-2.60) | 0.0003 | 0.26 | 25.38 |
| Country | | | | | |
| Asia | 2 | 2.13 (1.48-3.07) | 0.0001 | 0.65 | 0.00 |
| Africa | 1 | 1.91 (0.11-33.35) | 0.66 | NA | NA |
| Europe | 1 | 0.81 (0.33-1.99) | 0.67 | NA | NA |
| Study design | | | | | |
| Cross-sectional | 3 | 1.71 (1.16-2.51) | 0.007 | 0.20 | 38.15 |
| Case-control | 1 | 2.44 (1.22-4.87) | 0.01 | NA | NA |
| Severity of periodontitis | | | | | |
| Mild | 2 | 1.58 (0.99-2.53) | 0.06 | 0.46 | 0.00 |
| Moderate-severe | 2 | 2.76 (1.78-4.26) | 0.0000 | 0.58 | 0.00 |
| Abnormal sperm parameters | | | | | |
| Subnormal sperm count | 3 | 2.08 (1.03-4.23) | 0.04 | 0.90 | 0.00 |
| Progressive motility | 2 | 1.34 (0.65-2.80) | 0.43 | 0.04 | 76.64 |
| Total motility | 2 | 1.00 (0.95-1.05) | 0.97 | 0.20 | 37.89 |
| Sperm concentration | 2 | 1.00 (0.99-1.01) | 0.99 | 0.20 | 38.21 |

associations between periodontitis and sperm quality were observed in studies with both cross-sectional (OR = 1.71; 95% CI = 1.16-2.51; p = 0.007) and case-control study designs (OR = 2.44; 95% CI = 1.22-4.87; p = 0.01). In subgroup analysis based on periodontitis severity, mild periodontitis was not significantly associated with sperm quality (OR = 1.58; 95% CI = 0.99-2.53; p = 0.06); however, moderate-to-severe periodontitis was significantly associated with any sperm abnormality (OR = 2.76; 95% CI = 1.78-4.26; p = 0.0000). Finally, when the analysis stratified by abnormal sperm parameters,

periodontitis was significantly associated with subnormal sperm count (OR = 2.08; 95% CI = 1.03-4.23; p = 0.04), but not significantly associated with sperm progressive motility (OR = 1.34; 95% CI = 0.65-2.80; p = 0.43), total motility (OR = 1.00; 95% CI = 0.95-1.05; p = 0.97), and sperm concentration (OR = 1.00; 95% CI = 0.99-1.01; p = 0.99).

Sensitivity analysis

A sensitivity analysis was performed by removing each study one by one to evaluate the robustness of the meta-analysis test results (Figure 4). The results of the sensitivity analysis showed that the



Fixed-effects inverse-variance model

Figure 4: Leave-one-out analysis of sensitivity

removal of studies conducted by Zhu et al. [40] had a significant impact on pooled OR and 95% CI. However, after considering the results of the risk of bias assessment, which showed that the study had a moderate risk of bias, we did not exclude it from the meta-analysis. The less robust sensitivity test results require this meta-analysis to be interpreted with caution.

DISCUSSION

This meta-analysis is the first study conducted to evaluate the association between periodontitis and sperm quality. Previously, there was a systematic review [29] that reported a possible relationship between periodontitis and semen quality, but a meta-analysis was needed to conclude with certainty. Therefore, this study was conducted to provide the latest systematic review with meta-analysis.

The results of this meta-analysis showed that periodontitis was significantly associated with any sperm abnormalities. Subgroup analysis showed that periodontitis was also significantly associated when stratified by study design. In addition, subgroup analysis also found that the more severe the periodontitis, the higher the incidence of any sperm abnormality, indicated by a significant association between moderate-to-severe periodontitis and any sperm abnormality. However, in subgroup analysis based on sperm quality parameters, periodontitis was found to be associated with only one parameter, subnormal sperm count, and no significant association was observed between periodontitis and other sperm quality parameters. The limited number of studies, small sample size, and high heterogeneity between studies are believed to influence the results of this subgroup meta-analysis. The heterogeneity observed among included studies in subgroup analysis may be attributed to differences in diagnostic criteria for both periodontitis and sperm abnormalities. For instance, while some studies used PD and BOP to define periodontitis, others incorporated CAL. Similarly, semen analysis protocols and classification thresholds varied slightly across studies, potentially influencing the results. These discrepancies highlight the need for standardized diagnostic protocols in future research to ensure more consistent and comparable findings.

Two other studies included in the qualitative

synthesis reported different results. A statistically significant association between periodontitis and oligospermia compared to those diagnosed with gingivitis was demonstrated in one study [37]. The study also reported statistically significant differences where periodontitis patients had higher sperm sub-motility, lower ejaculate volume, and lower sperm morphology scores. However, in contrast to previous studies, Klingers and colleagues [38] found no significant relationship between periodontitis or periodontal parameters and sperm count and motility. Although the findings from these two qualitatively reviewed studies are not completely consistent, there is preliminary evidence to suggest that periodontitis may be associated with certain aspects of impaired sperm quality.

Periodontitis is defined by CAL or radiographic ABL, PD, as well as BOP, furcation involvement, tooth mobility, and periodontitis-related tooth loss [31,42]. All included studies used standard periodontitis diagnostic methods. Five studies involved measurements of CAL, PD, and BOP [37–41]. Only one of the five studies [40] added radiographic ABL to the diagnostic criteria for periodontitis. Another study used the CPITN score [32]. CPITN is considered effective and valid for diagnosing periodontitis because it involves PD and BOP measurements [43]. Nevertheless, we strongly recommend that future studies use the new criteria and classification of periodontal disease [31,44].

Various pathological mechanisms by which periodontal disease and periodontal-related inflammation affect sperm quality were observed. Studies have proposed bacteriospermia and periodontal cytokine production as mechanisms by which both reduce sperm quality and increase male infertility [45]. A previous study found an identical bacterial spectrum identified from the oral cavity and spermogram. The paper also explained that sperm analysis parameters such as motility, morphology, and sperm concentration improved significantly after treatment for oral infections [46]. In addition, chronic periodontitis and periodontal pathogens cause significant increases in serum levels of tumor necrosis factor (TNF)- α , interferon (IFN)- γ , interleukin (IL)-1, and IL-6, further increasing the risk of systemic inflammation and other chronic diseases [47–50]. A study, again, proved that there are various cytokines in male semen, and an imbalance

between them is believed to reduce sperm quality [51].

Furthermore, periodontitis has been shown to increase the number of oral neutrophils, including oral polymorphonuclear neutrophils (PMNs). Increased oral PMNs are associated with the occurrence of oral cavity inflammation and the severity of periodontitis [52]. This is in accordance with a study that reported an increase in the number of oral PMNs found in periodontitis patients [53]. A cross-sectional study reported that increased oral PMN levels had a significant effect on male infertility as assessed by decreased sperm motility, decreased normal sperm morphology, semen PMN, and sperm DNA fragmentation index [54]. Furthermore, increased oral PMN in periodontitis leads to excessive reactive oxygen species (ROS) production [55]. This excessive production of ROS is what then has the potential to cause DNA damage, increasing the risk of infertility, which is characterized by poor sperm quality, miscarriage, and/or genetically inherited mutations [56–58]. Thus, so far, we underline that bacteriospermia and increased levels of inflammatory cytokines from periodontal pathogens in plasma and semen are the main mechanisms proposed in the occurrence of sperm quality abnormalities.

The findings of this study may lead to significant changes in both dental and reproductive health practices. If the association between periodontitis and impaired sperm quality is confirmed through future studies, periodontal evaluation could become a routine component of the infertility work-up in men, particularly in idiopathic cases. Integrating periodontal assessment into fertility clinics may aid in identifying modifiable oral health conditions that contribute to subfertility, while early intervention through periodontal therapy could offer a cost-effective approach to improving semen parameters. From a public health standpoint, our findings highlight the potential for oral health promotion to be integrated into reproductive health education. Encouraging proper oral hygiene and regular dental check-ups may serve as preventive strategies aimed at improving male fertility outcomes. Thus, an interdisciplinary collaboration between dental professionals, reproductive health practitioners, and public health stakeholders is essential to develop comprehensive strategies that address both oral and reproductive health simultaneously. The strengths of this study include a comprehensive

literature search in which we used five electronic databases and manual searches to reduce the risk of missing studies, which could affect the risk of study selection bias. The results of the study quality evaluation using the JBI checklist showed that the studies had a low to moderate risk of bias; thus, no studies with a high risk of bias were included in the meta-analysis which would affect the quality of this meta-analysis. In addition, we conducted a sensitivity analysis to confirm the robustness of this meta-analysis, although the level of heterogeneity was low. However, this study has limitations, including the fact that the currently available studies are observational studies, which have limitations such as being unable to determine causal relationships. The limited number of studies and sample size with quite high heterogeneity are also considered shortcomings in this study. The results of the sensitivity analysis that showed unstable meta-analysis results are also acknowledged as a limitation in this meta-analysis. This, therefore, means this meta-analysis must be interpreted with caution.

CONCLUSION

This study concludes that periodontitis is associated with any sperm abnormalities. The mechanisms underlying this association are believed to involve bacteriospermia and increased inflammatory cytokines due to periodontitis-associated pathogens. Nevertheless, this meta-analysis suggests future studies involving larger sample sizes and more rigorous study designs to increase the strength and validity of the findings. It is also important to explore the effectiveness of periodontal treatment interventions in improving sperm quality to understand and strengthen the findings of this study. Finally, our findings suggest that maintaining good periodontal health may play a role in preserving male reproductive health. If confirmed by further research, integrating periodontal screening and management into fertility assessment could serve as a valuable preventive and supportive strategy in clinical practices.

REFERENCES

1. Mehrotra, N.; Singh, S. Periodontitis. In StatPearls; StatPearls Publishing: Treasure Island (FL), 2023.

2. Nascimento, G.G.; Leite, F.R.M.; Scheutz, F.; López, R. Periodontitis: From Infection to Inflammation. *Curr Oral Health Rep* 2017, 4, 301–308, <https://doi.org/10.1007/s40496-017-0158-7>.
3. Slots, J. Periodontitis: Facts, Fallacies and the Future. *Periodontology 2000* 2017, 75, 7–23, <https://doi.org/10.1111/prd.12221>.
4. Van Dyke, T.E.; Sima, C. Understanding Resolution of Inflammation in Periodontal Diseases: Is Chronic Inflammatory Periodontitis a Failure to Resolve? *Periodontology 2000* 2020, 82, 205–213, <https://doi.org/10.1111/prd.12317>.
5. Wu, L.; Zhang, S.; Zhao, L.; Ren, Z.; Hu, C. Global, Regional, and National Burden of Periodontitis from 1990 to 2019: Results from the Global Burden of Disease Study 2019. *Journal of Periodontology* 2022, 93, 1445–1454, <https://doi.org/10.1002/JPER.21-0469>.
6. Trindade, D.; Carvalho, R.; Machado, V.; Chambrone, L.; Mendes, J.J.; Botelho, J. Prevalence of Periodontitis in Dentate People between 2011 and 2020: A Systematic Review and Meta-analysis of Epidemiological Studies. *J Clin Periodontology* 2023, 50, 604–626, <https://doi.org/10.1111/jcpe.13769>.
7. Chen, M.X.; Zhong, Y.J.; Dong, Q.Q.; Wong, H.M.; Wen, Y.F. Global, Regional, and National Burden of Severe Periodontitis, 1990–2019: An Analysis of the Global Burden of Disease Study 2019. *J Clin Periodontology* 2021, 48, 1165–1188, <https://doi.org/10.1111/jcpe.13506>.
8. Genco, R.J.; Sanz, M. Clinical and Public Health Implications of Periodontal and Systemic Diseases: An Overview. *Periodontology 2000* 2020, 83, 7–13, <https://doi.org/10.1111/prd.12344>.
9. Martínez-García, M.; Hernández-Lemus, E. Periodontal Inflammation and Systemic Diseases: An Overview. *Front. Physiol.* 2021, 12, 709438, <https://doi.org/10.3389/fphys.2021.709438>.
10. Larvin, H.; Kang, J.; Aggarwal, V.R.; Pavitt, S.; Wu, J. Periodontitis and Risk of Immune-mediated Systemic Conditions: A Systematic Review and Meta-analysis. *Comm Dent Oral Epid* 2023, 51, 705–717, <https://doi.org/10.1111/cdoe.12812>.
11. Ridho, F.M.; Agustina, A.W.; Hidayati, N.N.; Pratama, M.I.; Laksono, E.P. Exploring the Association between Periodontitis and Erectile Dysfunction: A Systematic Review. *Indonesian Andrology and Biomedical Journal* 2024, 5, 42–51, <https://doi.org/10.20473/iabj.v5i1.56744>.
12. Ridho, F.M.; Algifnita, A.O.; Pramaztri, N.N.; Laksono, E.P.; Allifah, B.P.N.; Ahmad, M. Periodontitis as a Risk Factor of Preeclampsia in Pregnancy: A Scoping Review. *International Islamic Medical Journal* 2024, 5, 9–25, <https://doi.org/10.33086/iimj.v5i2.5316>.
13. Leslie, S.W.; Soon-Sutton, T.L.; Khan, M.A. Male Infertility. In *StatPearls*; StatPearls Publishing: Treasure Island (FL), 2024.
14. World Health Organization WHO Laboratory Manual for the Examination and Processing of Human Semen Available online: <https://www.who.int/publications/i/item/9789240030787> (accessed on 24 July 2024).
15. Huang, B.; Wang, Z.; Kong, Y.; Jin, M.; Ma, L. Global, Regional and National Burden of Male Infertility in 204 Countries and Territories between 1990 and 2019: An Analysis of Global Burden of Disease Study. *BMC Public Health* 2023, 23, 2195, <https://doi.org/10.1186/s12889-023-16793-3>.
16. Winters, B.R.; Walsh, T.J. The Epidemiology of Male Infertility. *Urologic Clinics of North America* 2014, 41, 195–204, <https://doi.org/10.1016/j.ucl.2013.08.006>.
17. Wu, H.; Wang, F.; Tang, D.; Han, D. Mumps Orchitis: Clinical Aspects and Mechanisms. *Front. Immunol.* 2021, 12, 582946, <https://doi.org/10.3389/fimmu.2021.582946>.
18. Wang, S.; Zhang, K.; Yao, Y.; Li, J.; Deng, S. Bacterial Infections Affect Male Fertility: A Focus on the Oxidative Stress-Autophagy Axis. *Front. Cell Dev. Biol.* 2021, 9, 727812, <https://doi.org/10.3389/fcell.2021.727812>.
19. Eisenberg, M.L.; Esteves, S.C.; Lamb, D.J.; Hotaling, J.M.; Giwercman, A.; Hwang, K.; Cheng, Y.-S. Male Infertility. *Nat Rev Dis Primers* 2023, 9, 49, <https://doi.org/10.1038/s41572-023-00459-w>.
20. Okonofua, F.E.; Ntoimo, L.F.C.; Omonkhua, A.; Ayodeji, O.; Olafusi, C.; Unuabonah, E.; Ohenhen, V. Causes and Risk Factors for Male Infertility: A Scoping Review of Published Studies. *IJGM* 2022, Volume 15, 5985–5997, <https://doi.org/10.2147/IJGM.S363959>.
21. Kellesarian, S.V.; Yunker, M.; Malmstrom, H.; Almas, K.; Romanos, G.E.; Javed, F. Male Infertility and Dental Health Status: A Systematic Review. *Am J Mens Health* 2018, 12, 1976–1984, <https://doi.org/10.1177/1557988316655529>.
22. Márquez-Arrico, Cf.; Silvestre, Fj.; Fernández-Reyes, M.; Silvestre-Rangil, J.; Rocha, M. Is There an Association between Periodontal Disease and Infertility? A Systematic Review. *Med Oral* 2024, 29, e866–e875, <https://doi.org/10.4317/>

- medoral.26831.
23. Eastham, J.; Seymour, R. Is Oral Health a Risk Factor for Sexual Health? *Dent Update* 2015, 42, 160–165, <https://doi.org/10.12968/denu.2015.42.2.160>.
 24. Lotti, F.; Maggi, M. Effects of Diabetes Mellitus on Sperm Quality and Fertility Outcomes: Clinical Evidence. *Andrology* 2023, 11, 399–416, <https://doi.org/10.1111/andr.13342>.
 25. Darby, I. Risk Factors for Periodontitis & Peri-implantitis. *Periodontology* 2000 2022, 90, 9–12, <https://doi.org/10.1111/prd.12447>.
 26. Kim, C.M.; Lee, S.; Hwang, W.; Son, E.; Kim, T.W.; Kim, K.; Kim, Y.H. Obesity and Periodontitis: A Systematic Review and Updated Meta-Analysis. *Front. Endocrinol.* 2022, 13, 999455, <https://doi.org/10.3389/fendo.2022.999455>.
 27. Zhong, O.; Ji, L.; Wang, J.; Lei, X.; Huang, H. Association of Diabetes and Obesity with Sperm Parameters and Testosterone Levels: A Meta-Analysis. *Diabetol Metab Syndr* 2021, 13, 109, <https://doi.org/10.1186/s13098-021-00728-2>.
 28. Ludovichetti, F.S.; Signoriello, A.G.; Gobbato, E.A.; Artuso, A.; Stellini, E.; Mazzoleni, S. Can Periodontal Disease Affect Conception? A Literature Review. *Reproduction and Fertility* 2021, 2, R27–R34, <https://doi.org/10.1530/RAF-20-0043>.
 29. Lecaplain, B.; Badran, Z.; Soueidan, A.; Prud'homme, T.; Gaudin, A. Periodontitis, Erectile Dysfunction, Reproductive Hormones, and Semen Quality: A Systematic Review. *Andrology* 2021, 9, 769–780, <https://doi.org/10.1111/andr.12961>.
 30. Page, M.J.; McKenzie, J.E.; Bossuyt, P.M.; Boutron, I.; Hoffmann, T.C.; Mulrow, C.D.; Shamseer, L.; Tetzlaff, J.M.; Akl, E.A.; Brennan, S.E.; et al. The PRISMA 2020 Statement: An Updated Guideline for Reporting Systematic Reviews. *BMJ* 2021, 372, n71, <https://doi.org/10.1136/bmj.n71>.
 31. Papapanou, P.N.; Sanz, M.; Buduneli, N.; Dietrich, T.; Feres, M.; Fine, D.H.; Flemmig, T.F.; Garcia, R.; Giannobile, W.V.; Graziani, F.; et al. Periodontitis: Consensus Report of Workgroup 2 of the 2017 World Workshop on the Classification of Periodontal and Peri-Implant Diseases and Conditions. *Journal of Periodontology* 2018, 89, <https://doi.org/10.1002/JPER.17-0721>.
 32. Nwhator, S.O.; Umezudike, K.A.; Ayanbadejo, P.O.; Opeodu, O.I.; Olamijulo, J.A.; Sorsa, T. Another Reason for Impeccable Oral Hygiene: Oral Hygiene-Sperm Count Link. *The Journal of Contemporary Dental Practice* 2014, 15, 352–358, <https://doi.org/10.5005/jp-journals-10024-1542>.
 33. Cooper, T.G.; Noonan, E.; von Eckardstein, S.; Auger, J.; Baker, H.W.G.; Behre, H.M.; Haugen, T.B.; Kruger, T.; Wang, C.; Mbizvo, M.T.; et al. World Health Organization Reference Values for Human Semen Characteristics. *Hum Reprod Update* 2010, 16, 231–245, <https://doi.org/10.1093/humupd/dmp048>.
 34. Lee, Y.H. An Overview of Meta-Analysis for Clinicians. *Korean J Intern Med* 2018, 33, 277–283, <https://doi.org/10.3904/kjim.2016.195>.
 35. Sedgwick, P.; Marston, L. How to Read a Funnel Plot in a Meta-Analysis. *BMJ* 2015, 351, h4718, <https://doi.org/10.1136/bmj.h4718>.
 36. Bown, M.J.; Sutton, A.J. Quality Control in Systematic Reviews and Meta-Analyses. *European Journal of Vascular and Endovascular Surgery* 2010, 40, 669–677, <https://doi.org/10.1016/j.ejvs.2010.07.011>.
 37. Chidambar, C.; Shankar, S.; Agarwal, R.; Bhushan, K.; Gururaj, S. Evaluation of Periodontal Status among Men Undergoing Infertility Treatment. *J Hum Reprod Sci* 2019, 12, 130, https://doi.org/10.4103/jhrs.JHRS_168_18.
 38. Klinger, A.; Hain, B.; Yaffe, H.; Schonberger, O. Periodontal Status of Males Attending an in Vitro Fertilization Clinic: Periodontal Status and Male Fertility. *Journal of Clinical Periodontology* 2011, 38, 542–546, <https://doi.org/10.1111/j.1600-051X.2011.01720.x>.
 39. Práger, N.; Pásztor, N.; Várnagy, Á.; Kozinszky, Z.; Baráth, Z.; Gorzó, I.; Radnai, M. Idiopathic Male Infertility Related to Periodontal and Caries Status. *J Clin Periodontology* 2017, 44, 872–880, <https://doi.org/10.1111/jcpe.12785>.
 40. Zhu, C.; Qin, Z.; Huang, H.; Li, X.; Feng, Y. The Correlation Study between Male Infertility and Chronic Periodontitis. *China Modern Medicine* 2010, 29, 12–13.
 41. Tao, D.; Zhu, J.; Xie, C.; Kuang, Y.; Chai, W.; Lo, E.C.M.; Ye, W.; Li, F.; Feng, X.; Lu, H. Relationship between Periodontal Disease and Male Infertility: A Case–Control Study. *Oral Diseases* 2021, 27, 624–631, <https://doi.org/10.1111/odi.13552>.
 42. Salvi, G.E.; Rocuzzo, A.; Imber, J.; Stähli, A.; Klinge, B.; Lang, N.P. Clinical Periodontal Diagnosis. *Periodontology* 2000 2023, prd.12487, <https://doi.org/10.1111/prd.12487>.
 43. Tanik, A.; Gül, M. The Validity of the Community Periodontal Index of Treatment Needs (CPITN) in Epidemiological Studies of Periodontal Diseases. *Int Dent Res* 2020, 10, 44–48, <https://doi.org/10.5005/jp-journals-10024-1542>.

- org/10.5577/intdentres.2020.vol10.no2.3.
44. Tonetti, M.S.; Greenwell, H.; Kornman, K.S. Staging and Grading of Periodontitis: Framework and Proposal of a New Classification and Case Definition. *Journal of Periodontology* 2018, 89, <https://doi.org/10.1002/JPER.18-0006>.
45. Rashidi Maybodi, F.; Amirzade Iranaq, M.H. Poor Oral Health and Fertility Problems: A Narrative Mini-Review. *JMRH* 2017, 5, 849–854, <https://doi.org/10.22038/jmrh.2016.7708>.
46. Bieniek, K.W.; Riedel, H.-H. Bacterial Foci in the Teeth, Oral Cavity, and Jaw-Secondary Effects (Remote Action) of Bacterial Colonies with Respect to Bacteriospermia and Subfertility in Males. *Andrologia* 1993, 25, 159–162, <https://doi.org/10.1111/j.1439-0272.1993.tb02700.x>.
47. Andrukhov, O.; Ulm, C.; Reischl, H.; Nguyen, P.Q.; Matejka, M.; Rausch-Fan, X. Serum Cytokine Levels in Periodontitis Patients in Relation to the Bacterial Load. *Journal of Periodontology* 2011, 82, 885–892, <https://doi.org/10.1902/jop.2010.100425>.
48. Cardoso, E.M.; Reis, C.; Manzaneres-Céspedes, M.C. Chronic Periodontitis, Inflammatory Cytokines, and Interrelationship with Other Chronic Diseases. *Postgraduate Medicine* 2018, 130, 98–104, <https://doi.org/10.1080/00325481.2018.1396876>.
49. Ramadan, D.E.; Hariyani, N.; Indrawati, R.; Ridwan, R.D.; Diyatri, I. Cytokines and Chemokines in Periodontitis. *Eur J Dent* 2020, 14, 483–495, <https://doi.org/10.1055/s-0040-1712718>.
50. Ridho, F.M.; Syachputra, A.J.; Nur'aini, A.D.; Ulfah, K.; Faqih, M.; Nurhuda, A. Pre-Clinical and Clinical Efficacy of Curcumin as an Anti-Inflammatory Agent for Periodontitis. A Systematic Review. *Revista Científica Odontológica* 2024, 12, e222, <https://doi.org/10.21142/2523-2754-1204-2024-222>.
51. Tang, S.-S.; Lu, J.-C.; Ge, Y.-M.; Xu, Y.-H.; Zhao, X.; Liang, Y.-J. Analysis of 12 Kinds of Cytokines in Seminal Plasma by Flow Cytometry and Their Correlations with Routine Semen Parameters. *Cytokine* 2024, 182, 156718, <https://doi.org/10.1016/j.cyto.2024.156718>.
52. Khoury, W.; Glogauer, J.; Tenenbaum, H.C.; Glogauer, M. Oral Inflammatory Load: Neutrophils as Oral Health Biomarkers. *J of Periodontal Research* 2020, 55, 594–601, <https://doi.org/10.1111/jre.12758>.
53. Nicu, E.A.; Rijkschroeff, P.; Wartewig, E.; Nazmi, K.; Loos, B.G. Characterization of Oral Polymorphonuclear Neutrophils in Periodontitis Patients: A Case-Control Study. *BMC Oral Health* 2018, 18, 149, <https://doi.org/10.1186/s12903-018-0615-2>.
54. Pourabbas, R.; Farajzadeh, S.; Babaloo, A.; Pazhohan, A.; Sadighi, M.; Hajebrahimi, S.; Pourabbas, S.; Tenenbaum, H.C. The Association between Oral Inflammatory Load and Semen and Sperm Functional Analysis: A Cross-Sectional Study. *J Dent Res Dent Clin Dent Prospects* 2023, 17, 188–195, <https://doi.org/10.34172/joddd.2023.37106>.
55. Rijkschroeff, P.; Loos, B.G.; Nicu, E.A. Oral Polymorphonuclear Neutrophil Contributes to Oral Health. *Curr Oral Health Rep* 2018, 5, 211–220, <https://doi.org/10.1007/s40496-018-0199-6>.
56. Dutta, S.; Majzoub, A.; Agarwal, A. Oxidative Stress and Sperm Function: A Systematic Review on Evaluation and Management. *Arab Journal of Urology* 2019, 17, 87–97, <https://doi.org/10.1080/2090598X.2019.1599624>.
57. Takeshima, T.; Usui, K.; Mori, K.; Asai, T.; Yasuda, K.; Kuroda, S.; Yumura, Y. Oxidative Stress and Male Infertility. *Reprod Medicine & Biology* 2021, 20, 41–52, <https://doi.org/10.1002/rmb2.12353>.
58. Wagner, H.; Cheng, J.W.; Ko, E.Y. Role of Reactive Oxygen Species in Male Infertility: An Updated Review of Literature. *Arab Journal of Urology* 2018, 16, 35–43, <https://doi.org/10.1016/j.aju.2017.11.001>.