Arh. farm. 2025; 75: 44 – 54 *Review article/Pregledni rad*

The role of oxidative stress in male infertility: connection to sperm telomere shortening and overall DNA damage

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Received: 9 January 2025; Revised in revised forme: 13 February 2025; Accepted: 16 February 2025

Abstract

Male infertility affects approximately 20% of men, with 30–40% of cases being linked to issues in both partners. While sperm production may be normal, DNA damage in spermatozoa can occur and become a primary cause of infertility. The exacerbation of oxidative stress leads to damage to various biomolecules, such as DNA fragmentation, lipid peroxidation, and protein oxidation, all of which can impair egg fertilization and embryo development. Elevated levels of reactive oxygen species (ROS) in semen are associated with poor sperm quality, reduced fertilization potential, and increased sperm DNA fragmentation. Additionally, shorter telomeres in semen correlate with reduced sperm vitality and function. Oxidative stress accelerates telomere attrition by inducing DNA damage, which leads to telomere shortening and potentially compromises sperm function and fertility. DNA damage can occur at different stages of spermatogenesis and fertilization. If the damage surpasses the oocyte's repair capacity, infertility may occur. Various tests are available to assess sperm DNA damage, with the sperm DNA fragmentation (SDF) test being one of the most promising. DNA damage is quantified as the DNA fragmentation index (DFI), which represents the percentage of spermatozoa with fragmented DNA. Although reference intervals for DFI may vary depending on the method used, DFI ≤ 15% is generally considered normal, 15–30% is considered average, and DFI ≥ 30% indicates poor DNA integrity, which may negatively impact pregnancy outcomes.

Key words: oxidative stress, telomere shortening, sperm DNA fragmentation, DNA fragmentation index

https://doi.org/10.5937/arhfarm75-55898

Introduction/Infertility

Infertility is defined as the inability to conceive within 12 months when the female partner is under 35, and within 6 months when she is over 35 (1). In about 20% of cases, male factors are solely responsible for infertility, while in 30–40% of cases both male and female factors contribute to the issue (1). Notably, about 15% of men who are unable to impregnate their partner have normal sperm analysis results (2). This can be explained by the fact that while sperm production may be adequate, DNA damage often occurs during sperm maturation and storage in the epididymis, impairing their ability to fertilize the egg and support embryo development (3).

In order to perform an adequate assessment of male fertility, it is necessary to perform a comprehensive examination of the patient, which includes male infertility, sexual, medical and surgical history, physical examination, genito-urinary and reproductive tract infections, and at least two semen analyses, hormonal and genetic evaluation (1, 4, 5). Semen analysis is the first step in the assessment of male infertility. The basic analysis includes a macroscopic examination of the ejaculate (volume, liquefaction, consistency, pH), determination of the number, mobility, vitality and morphology of spermatozoa, the number of leukocytes and other round cells, as well as the concentration of biochemical markers of the seminal plasma (fructose, zinc). Additional tests include microbiological examination of the semen, determination of antisperm antibodies, tests of hemizona and zona-pellucida binding, zona-free hamster egg penetration test, tests of sperm DNA damage and assessment of ROS (6, 7).

Treatment of male infertility depends on its cause and may include lifestyle changes (weight loss, quitting alcohol and cigarettes, etc.), surgical interventions (varicocelectomy, transurethral resection of the ejaculatory ducts (TURED)), hormonal therapy (aromatase inhibitors, clomiphene, and tamoxifen), gonadotropic therapy (human chorionic gonadotropin, LH, FSH, GnRH, human menopausal gonadotropin), selective oestrogen receptor modulators (SERMs), and antioxidant therapy. In patients with non-obstructive azoospermia and idiopathic infertility, some of the assisted reproductive techniques (ART) can be applied (intrauterine insemination, in vitro fertilization (IVF), intracytoplasmic sperm injection (ICSI)). In patients with elevated DFI, the use of testicular sperm using testicular sperm aspiration (TESA) or testicular sperm extraction (TESE) techniques is recommended (1, 5, 8).

Oxidative stress

Oxidative stress is a physiological condition where there is an imbalance between ROS and the body’s antioxidant defenses. Free radicals are generated in our cells that operate in an oxygen-rich environment. This imbalance can lead to cellular damage, including DNA fragmentation, lipid peroxidation, and protein oxidation. In the context of male fertility, oxidative stress is implicated in various aspects of sperm function, including motility, morphology, and DNA integrity (9, 10). Kaltsas et al. demonstrated the beneficial effects of several antioxidants in reducing sperm oxidative stress (11).

While antioxidant supplementation in male infertility is beneficial, excessive use may result in reductive stress, which can impair sperm motility and interfere with ART (12).

Based on previous studies (2, 13–15), there is a growing need for novel diagnostic methods to assess male reproductive disorders. Evaluating oxidative stress in seminal fluid offers a promising and non-invasive approach to estimating sperm quality and fertilization potential. Such an approach could lead to new therapeutic strategies focused on proper antioxidant supplementation, reducing systemic oxidative stress in infertile men, and improving the diagnosis and management of male infertility by targeting oxidative stress, one of its key underlying mechanisms (16).

Agarwal and colleagues developed a system to estimate the global prevalence of male infertility, confirming that at least 30 million men are affected, particularly in Africa and Eastern Europe (9). This highlights the need for further research into its causes and treatments, as well as the importance of reducing stigma and cultural barriers, and establishing more accurate methods for assessing infertility rates (17).

DNA damage

Semen plasma, which surrounds sperm cells, contains various antioxidants that neutralize ROS, but excessive oxidative stress can overwhelm these defenses, leading to negative effects on sperm function. Elevated ROS levels in semen are linked to poor sperm quality, reduced fertilization potential, and increased sperm DNA fragmentation (18).

Furthermore, oxidative stress contributes to the shortening of telomeres, the protective caps at the ends of chromosomes, which are essential for maintaining genomic stability during cell division (19–21). There is a well-documented link between chronic stress and various health issues, including cardiovascular disease and weakened immune function. Stress may influence health by accelerating cellular aging, which could explain the impact of sperm telomere shortening on reproductive health (20, 22, 23). Telomeres naturally shorten with cell division, but in sperm this process is particularly significant because telomere length influences the health and longevity of the resulting embryo. Shorter telomeres in semen are associated with reduced sperm vitality and function (19, 22). Oxidative stress accelerates telomere attrition by inducing DNA damage, leading to telomere shortening and potentially compromising sperm function and fertility (24, 25). The relationship between oxidative stress, telomeres, sperm, cell damage and infertility is shown in Figure 1. Coluzzi et al. found a direct correlation between oxidative stress-induced telomere attrition and chromosome instability (24). Telomere length is also associated with metabolic risk factors, suggesting that other risk factors may influence telomere length and male infertility. Disturbances in redox balance during fertilization can also affect infertility, given that ROS play a key role in the fertilization process (26).

Several studies have shown that oxidative stress correlates inversely with telomere length in semen (18). Sperm exposed to high ROS levels often exhibits significantly shorter telomeres, suggesting that oxidative damage is a key factor in telomere attrition. Moreover, telomere shortening in sperm has been linked to lower fertilization rates and poorer embryo development (27–31).

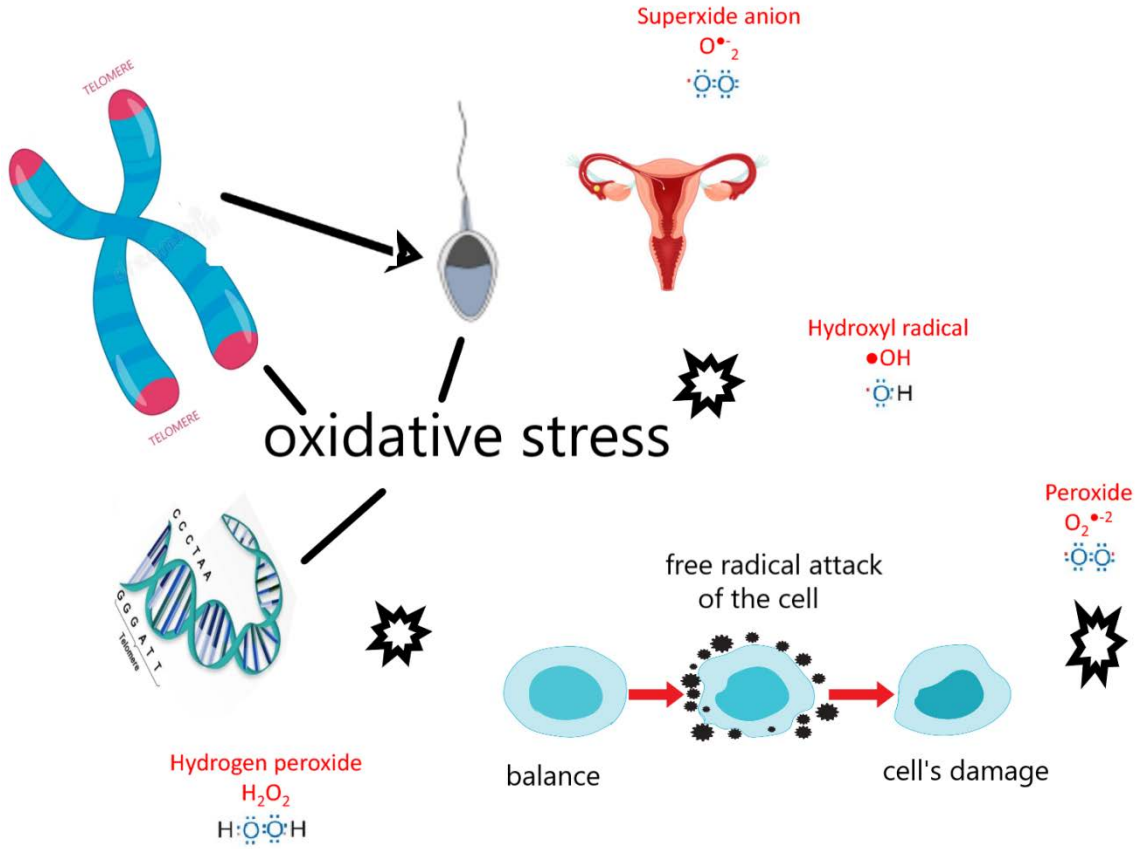

Figure 1. Oxidative stress, telomere, spermatozoa, cell damage, infertility
Slika 1. Oksidativni stres, telomere, spermatozoidi, oštećenje ćelije, neplodnost

Sperm DNA is bound to protamine and packaged into stable structures that allow intact genetic material to be transferred to the fertilized egg (32). DNA damage can occur during spermatogenesis, the transport of sperm through the male and female reproductive tracts, fertilization, and the transfer of genetic material to the oocyte. Some of these damages may be repaired within the oocyte cytoplasm (33), but if damage exceeds the repair capacity of the oocyte, this can result in infertility. DNA damage can manifest in several ways (34, 35): a. breaks in one or both DNA strands, b. deletions or modifications of bases, c. cross-linking of DNA strands, or d. protamine deficiency and/or e. improper DNA packaging (32). These damages can be caused by diseases (e.g., infections, varicocele), oxidative stress, drug use, elevated temperatures, environmental pollutants, occupational toxins, smoking, and aging (2, 3, 34).

Methods of determining DNA damage

Sperm DNA damage is still a subject of scientific debate due to a lack of standardization. Several tests are available to assess sperm DNA damage, which can be categorized into three groups: 1) tests using enzymatic reactions to mark DNA break sites

(TUNEL – terminal deoxynucleotidyl transferase-mediated deoxyuridine triphosphate-nick end labeling and ISNT – in situ nick translation assay), 2) tests based on controlled DNA denaturation and protein removal to detect breakpoints (SCSA – sperm chromatin structure assay, Comet assay, SCD – sperm chromatin dispersion test), and 3) tests using dyes that detect chromatin packaging abnormalities by binding to the G/C rich regions (aniline blue, toluidine blue, chromomycin A3, acridine orange). These tests detect different DNA disorders resulting from various mechanisms. For instance, inadequate chromatin packing is related to a lack of protamine or its mispackaging, while DNA fragmentation is linked to oxidative stress (32). Therefore, in 2021 Estevez et al. proposed a new nomenclature of tests: 1) SDF tests (which include TUNEL, ISNT, SCSA, SCD, and Comet tests) and 2) sperm chromatin compaction tests (SND – sperm nucleus decondensation) including aniline blue, toluidine blue, chromomycin A3, and acridine orange staining (32). The most commonly used tests in clinical practice are TUNEL, SCD and SCSA (33).

Due to the distinct characteristics of these tests, results from one method may not correlate with those from another, especially when comparing SDF and SND methods (36). However, there is a good correlation among commonly used SDF tests (37). Results are expressed as DFI, representing the percentage of spermatozoa with fragmented DNA. Although reference intervals for DFI may vary depending on the method used, DFI ≤ 15% is considered normal, DFI 15–30% is average, and DFI ≥ 30% indicates poor DNA integrity that may affect pregnancy outcomes (38).

Diagnostic challenges

Agarwal et al. presented several clinical scenarios where DFI testing has clinical significance: varicocele, unexplained infertility / repeated miscarriages / ART failure, IVF and/or ICSI failure, and borderline abnormal (or normal) semen analysis with risk factors (39). After each case presented, they performed an evidence-based analysis of the clinical utility of SDF and provided recommendations for the use of SDF. SDF may have clinical significance in the following situations: DFI allows better selection of candidates for varicocelectomy in men with clinical varicocele and normal to borderline parameters of semen analysis, 2) in patients with recurrent ART failure, DFI may provide useful prognostic information about subsequent cycles of ART and possible use of testicular sperm instead of ejaculated sperm in men with oligozoospermia (it has been shown that the DFI value in testicular sperm is lower than in ejaculated sperm) (40), and 3) DFI can help to increase the importance of lifestyle changes (e.g., smoking cessation, antioxidant therapy), predict fertility and monitor the patient’s response to therapy (39).

In 2024, the AUA/ASRM (American Urological Association / American Society for Reproductive Medicine) published guidelines for diagnosing and treating male infertility. These guidelines recommend against using SDF in the initial infertility evaluation, but suggest considering it for couples with recurrent pregnancy loss and for patients with elevated DFI in ART procedures (1).

Despite increasing interest in SDF testing, several challenges remain: there are no standardized criteria for selecting the appropriate SDF test, the tests are not standardized, and they lack clear cut-off values. Current recommendations for SDF application are classified as level C, and further research is needed to identify the types of DNA defects affecting fertility and isolate sperm with intact DNA for use in artificial insemination (2, 41).

Pańczyszyn et al. evaluated the role of new biomarkers in predicting reproductive success, with SIRT1 emerging as a promising candidate. This protein plays a key role in protecting against oxidative stress and telomere shortening, thereby enhancing genomic stability and improving the success of assisted reproduction (42).

Antioxidant therapy

To mitigate oxidative stress and preserve telomere length and DNA integrity, antioxidants such as vitamin E, carnitines, vitamin C, Coenzyme Q10, N-acetyl cysteine, zinc, folic acid, selenium and lycopene have been explored (43). These antioxidants help neutralize ROS, potentially preserving sperm DNA integrity and telomere length (44, 45). However, the relationship between oxidative stress, telomere shortening, overall DNA damage and male fertility remains complex, and further research is needed to understand how these factors interact and identify effective therapeutic strategies to improve semen quality.

It is well-documented that antioxidant supplementation can improve sperm quality, DNA integrity, and fertility outcomes, though results can vary (2, 21, 22, 46–49). Factors such as individual differences, the underlying cause of infertility, supplementation dosage and duration, and lifestyle habits all play a role. Therefore, lifestyle modifications – such as a healthy diet, regular exercise, and quitting smoking and alcohol – are crucial for reducing oxidative stress and optimizing male reproductive health (10).

Although several studies and meta-analyses (46, 47) showed that antioxidant therapy had a positive impact on live-birth and pregnancy rates in sub-fertile couples and on the improvement of sperm parameters, a study by Steiner et al. (48) showed no differences between the groups that used antioxidant therapy and the placebo group. Based on the aforementioned studies, the European Association of Urologists (EAU) considers the use of antioxidants in the treatment of male infertility to be inconclusive (5). AUA/ASRM state that the available studies do not provide adequate data to recommend the routine use of antioxidants. However, Leslie et al. believe that the use of antioxidant therapy should be considered in every male infertility patient because of its low cost and absence of side effects (8).

Conclusion

In conclusion, oxidative stress plays a significant role in telomere shortening and DNA damage in sperm, which negatively affects sperm quality and male fertility. Maintaining a balance between ROS and antioxidants is essential for preserving telomere length and ensuring optimal sperm function. In the future we expect to resolve the

molecular mechanisms that link male infertility and oxidative stress and telomere attrition. Oxidative stress, caused by an imbalance between reactive oxygen species and antioxidants, is known to damage sperm DNA and disrupt spermatogenesis, while telomere attrition, a natural process associated with aging, may further damage sperm function. Advances in genomic and proteomic technologies will probably uncover how oxidative stress accelerates telomere shortening in male gametes, providing new therapeutic targets. Additionally, the potential of antioxidant therapies to mitigate oxidative damage and slow telomere attrition could be explored as a promising path for improving fertility outcomes in men.

Acknowledgements

This research was funded by the Ministry of Science, Technological Development and Innovation, Republic of Serbia through two Grant Agreements with University of Belgrade-Faculty of Pharmacy No 451-03-136/2025-03/ 200161 and No 451-03-137/2025-03/ 200161.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Author contributions

BG: Conceptualization, Writing - original draft. JKS: Conceptualization, Writing - review & editing

References

1. Brannigan RE, Hermanson L, Kaczmarek J, Kim SK, Kirkby E, Tanrikut C. Updates to male infertility: AUA/ASRM Guideline (2024). J Urol. 2024;212(6):789–799. doi: 10.1097/JU.0000000000004180.
2. Agarwal A, Allamaneni SS. Sperm DNA damage assessment: a test whose time has come. Fertil Steril. 2005;84(4):850–3. doi: 10.1016/j.fertnstert.2005.03.080.
3. Esteves SC, Roque M, Bradley CK, Garrido N. Reproductive outcomes of testicular versus ejaculated sperm for ICSI among men with high levels of DNA fragmentation in semen: systematic review and meta-analysis. Fertil Steril. 2017;108(3):456–467.e1. doi: 10.1016/j.fertnstert.2017.06.018.
4. Fraga LG, Gismondi JP, Sanvido LV, Lozano AFQ, Teixeira TA, Hallak J. Clinical and Laboratorial Evaluation of Male Infertility. A Detailed Practical Approach. Arch Med Res. 2024 Dec;55(8):103139. doi: 10.1016/j.arcmed.2024.103139.

5. Salonia A, Bettocchi C, Capogrosso P, Carvalho J, Corona G, Dinkelman-Smith M, et al. EAU Guidelines on Sexual and Reproductive Health. Presented at the EAU Annual Congress, Paris; 2024.
6. Sikka SC, Hellstrom WJ. Current updates on laboratory techniques for the diagnosis of male reproductive failure. Asian J Androl. 2016 May–Jun;18(3):392–401. doi: 10.4103/1008-682X.179161.
7. WHO laboratory manual for the examination and processing of human semen, sixth edition. Geneva: World Health Organization; 2021. Licence: CC BY-NC-SA 3.0 IGO.
8. Leslie SW, Soon-Sutton TL, Khan MAB. Male Infertility. StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2025 Jan– [cited 2024 Feb 25]. Available from: https://www.ncbi.nlm.nih.gov/books/NBK562258/.
9. Agarwal A, Virk G, Ong C, du Plessis SS. Effect of oxidative stress on male reproduction. World J Mens Health. 2014;32(1):1–17. doi: 10.5534/wjmh.2014.32.1.1.
10. Sikka SC. Oxidative stress and role of antioxidants in normal and abnormal sperm function. Front Biosci. 1996;1:e78–86. doi: 10.2741/a146.
11. Kaltsas A. Oxidative stress and male infertility: The protective role of antioxidants. Medicina (Kaunas). 2023;59(10):1769. doi: 10.3390/medicina59101769.
12. Moustakli E, Zikopoulos A, Skentou C, Katopodis P, Domali E, Potiris A, et al. Impact of reductive stress on human infertility: underlying mechanisms and perspectives. Int J Mol Sci. 2024;25(21):11802. doi: 10.3390/ijms252111802.
13. Yang H, Li G, Jin H, Guo Y, Sun Y. The effect of sperm DNA fragmentation index on assisted reproductive technology outcomes and its relationship with semen parameters and lifestyle. Transl Androl Urol. 2019 Aug;8(4):356–365. doi: 10.21037/tau.2019.06.22.
14. Agarwal A, Cho CL, Majzoub A, Esteves SC. The Society for Translational Medicine: clinical practice guidelines for sperm DNA fragmentation testing in male infertility. Transl Androl Urol. 2017 Sep;6(Suppl 4):S720–S733. doi: 10.21037/tau.2017.08.06.
15. Robert KA, Sharma R, Henkel R, Agarwal A. An update on the techniques used to measure oxidative stress in seminal plasma. Andrologia. 2021 Mar;53(2):e13726. doi: 10.1111/and.13726.
16. Mannucci A, Argento FR, Fini E, Coccia ME, Taddei N, Becatti M, Fiorillo C. The Impact of Oxidative Stress in Male Infertility. Front Mol Biosci. 2022;8:799294. doi: 10.3389/fmolb.2021.799294.
17. Agarwal A, Mulgund A, Hamada A, Chyatte MR. A unique view on male infertility around the globe. Reprod Biol Endocrinol. 2015;13:37. doi: 10.1186/s12958-015-0032-1.
18. Walke G, Gaurkar SS, Prasad R, Lohakare T, Wanjari M. The impact of oxidative stress on male reproductive function: exploring the role of antioxidant supplementation. Cureus. 2023;15(7):e42583. doi: 10.7759/cureus.42583.
19. Fernández de la Puente M, Valle-Hita C, Salas-Huetos A, Martínez MÁ, Sánchez-Resino E, Canudas S, et al. Sperm and leukocyte telomere length are related to sperm quality parameters in healthy men from the Led-Fertyl study. Hum Reprod Open. 2024;2024(4):hoae062. doi: 10.1093/hropen/hoae062.
20. Epel ES, Blackburn EH, Lin J, Dhabhar FS, Adler NE, Morrow JD, Cawthon RM. Accelerated telomere shortening in response to life stress. Proc Natl Acad Sci USA. 2004;101(49):17312–5. doi: 10.1073/pnas.0407162101.

21. Cawthon RM. Telomere length measurement by a novel monochrome multiplex quantitative PCR method. Nucleic Acids Res. 2009;37(3):e21. doi: 10.1093/nar/gkn1027.
22. Darmishonnejad Z, Zarei-Kheirabadi F, Tavalaee M, Zarei-Kheirabadi M, Zohrabi D, Nasr-Esfahani MH. Relationship between sperm telomere length and sperm quality in infertile men. Andrologia. 2020;52(5):e13546. doi: 10.1111/and.13546.
23. Guzonjić A, Sopić M, Ostanek B, Kotur-Stevuljević J. Telomere length as a biomarker of aging and diseases. Arch Pharm. 2022;72:105–26.
24. Coluzzi E, Colamartino M, Cozzi R, Leone S, Meneghini C, O'Callaghan N, Sgura A. Oxidative stress induces persistent telomeric DNA damage responsible for nuclear morphology change in mammalian cells. PLoS One. 2014;29;9(10):e110963. doi: 10.1371/journal.pone.0110963.
25. Garfein J, Flannagan KS, Rittman D, Ramirez-Zea M, Villamor E; Nine Mesoamerican Countries Metabolic Syndrome Study (NiMeCoMeS) Group. Leukocyte telomere length is inversely associated with a metabolic risk score in Mesoamerican children. Am J Hum Biol. 2022;34(1):e23596. doi: 10.1002/ajhb.23596.
26. Opuwari CS, Henkel RR. An update on oxidative damage to spermatozoa and oocytes. Biomed Res Int. 2016;2016:9540142. doi: 10.1155/2016/9540142.
27. Mishra S, Kumar R, Malhotra N, Singh N, Dada R. Mild oxidative stress is beneficial for sperm telomere length maintenance. World J Methodol. 2016;6(2):163–70. doi: 10.5662/wjm.v6.i2.163.
28. Berby B, Bichara C, Rives-Feraille A, Jumeau F, Pizio PD, Sétif V, et al. Oxidative stress is associated with telomere interaction impairment and chromatin condensation defects in spermatozoa of infertile males. Antioxidants (Basel). 2021;10(4):593. doi: 10.3390/antiox10040593.
29. Rocca MS, Speltra E, Menegazzo M, Garolla A, Foresta C, Ferlin A. Sperm telomere length as a parameter of sperm quality in normozoospermic men. Hum Reprod. 2016;31(6):1158–63. doi: 10.1093/humrep/dew061.
30. Randell Z, Dehghanbanadaki H, Fendereski K, Jimbo M, Aston K, Hotaling J. Sperm telomere length in male-factor infertility and reproduction. Fertil Steril. 2024;121(1):12–25. doi: 10.1016/j.fertnstert.2023.11.001.
31. Alahmar AT. Role of oxidative stress in male infertility: an updated review. J Hum Reprod Sci. 2019;12(1):4–18. doi: 10.4103/jhrs.JHRS_150_18.
32. Esteves SC, Zini A, Coward RM, Evenson DP, Gosálvez J, Lewis SEM, et al. Sperm DNA fragmentation testing: Summary evidence and clinical practice recommendations. Andrologia. 2021;53(2):e13874. doi: 10.1111/and.13874.
33. Majzoub A, Esteves SC, Gosálvez J, Agarwal A. Specialized sperm function tests in varicocele and the future of andrology laboratory. Asian J Androl. 2016;18(2):205–12. doi: 10.4103/1008-682X.172642.
34. Sakkas D, Alvarez JG. Sperm DNA fragmentation: mechanisms of origin, impact on reproductive outcome, and analysis. Fertil Steril. 2010;93(4):1027–36. doi: 10.1016/j.fertnstert.2009.10.046.
35. Martin JH, Aitken RJ, Bromfield EG, Nixon B. DNA damage and repair in the female germline: contributions to ART. Hum Reprod Update. 2019;25(2):180–201. doi: 10.1093/humupd/dmy040.
36. Esteves SC, Sharma RK, Gosálvez J, Agarwal A. A translational medicine appraisal of specialized andrology testing in unexplained male infertility. Int Urol Nephrol. 2014;46(6):1037–52. doi: 10.1007/s11255-014-0715-0.

37. Javed A, Talkad MS, Ramaiah MK. Evaluation of sperm DNA fragmentation using multiple methods: a comparison of their predictive power for male infertility. Clin Exp Reprod Med. 2019;46(1):14–21. doi: 10.5653/cerm.2019.46.1.14. Erratum in: Clin Exp Reprod Med. 2019 Dec;46(4):211. doi: 10.5653/cerm.2019.46.1.14.e1.
38. Yifu P, Lei Y, Shaoming L, Yujin G, Xingwang Z. Sperm DNA fragmentation index with unexplained recurrent spontaneous abortion: A systematic review and meta-analysis. J Gynecol Obstet Hum Reprod. 2020:101740. doi: 10.1016/j.jogoh.2020.101740.
39. Agarwal A, Majzoub A, Esteves SC, Ko E, Ramasamy R, Zini A. Clinical utility of sperm DNA fragmentation testing: practice recommendations based on clinical scenarios. Transl Androl Urol. 2016;5(6):935–950. doi: 10.21037/tau.2016.10.03.
40. Zhao G, Jiang X, Zheng Y, Bai H, Jiang Z, Cheng S, Li D. Outcomes comparison of testicular versus ejaculated sperm for intracytoplasmic sperm injection in infertile men with high DNA fragmentation: updated systematic review and meta-analysis. Transl Androl Urol. 2023;12(12):1785–802. doi: 10.21037/tau-23-415.
41. Esteves SC, Agarwal A, Cho CL, Majzoub A. A strengths-weaknesses-opportunities-threats (SWOT) analysis on the clinical utility of sperm DNA fragmentation testing in specific male infertility scenarios. Transl Androl Urol. 2017;6(4):S734–S760. doi: 10.21037/tau.2017.08.20.
42. Pańczyszyn A, Boniewska-Bernacka E, Wertel I, Sadakierska-Chudy A, Goc A. Telomeres and SIRT1 as biomarkers of gamete oxidative stress, fertility, and potential IVF outcome. Int J Mol Sci. 2024; 25(16):8652. doi: 10.3390/ijms25168652.
43. Dimitriadis F, Borgmann H, Struck JP, Salem J, Kuru TH. Antioxidant Supplementation on Male Fertility-A Systematic Review. Antioxidants (Basel). 2023 Mar 30;12(4):836. doi: 10.3390/antiox12040836.
44. Qamar AY, Naveed MI, Raza S, Fang X, Roy PK, Bang S, et al. Role of antioxidants in fertility preservation of sperm – A narrative review. Anim Biosci. 2023;36(3):385–403. doi: 10.5713/ab.22.0325.
45. Pavuluri H, Bakhtiary Z, Panner Selvam MK, Hellstrom WJG. Oxidative stress-associated male infertility: current diagnostic and therapeutic approaches. Medicina. 2024;60(6):1008. doi: 10.3390/medicina60061008.
46. Showell MG, Mackenzie-Proctor R, Brown J, Yazdani A, Stankiewicz MT, Hart RJ. Antioxidants for male subfertility. Cochrane Database Syst Rev. 2014;(12):CD007411.
47. Smits RM, Mackenzie-Proctor R, Yazdani A, Stankiewicz MT, Jordan V, Showell MG. Antioxidants for male subfertility. Cochrane Database Syst Rev. 2019;3:CD007411.
48. Steiner AZ, Hansen KR, Barnhart KT, Cedars MI, Legro RS, Diamond MP, et al. The effect of antioxidants on male factor infertility: the Males, Antioxidants, and Infertility (MOXI) randomized clinical trial. Fertil Steril. 2020;113:552.
49. Micic S, Lalic N, Djordjevic D, Bojanic N, Bogavac-Stanojevic N, Busetto GM, et al. Double-blind, randomised, placebo-controlled trial on the effect of L-carnitine and L-acetylcarnitine on sperm parameters in men with idiopathic oligoasthenozoospermia. Andrologia. 2019 Jul;51(6):e13267. doi: 10.1111/and.13267.

Uloga oksidativnog stresa u muškoj neplodnosti: veza sa skraćivanjem telomera spermatozoida i generalnim oštećenjem DNK

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Kratak sadržaj

Muška neplodnost pogađa oko 20% muškaraca, pri čemu je 30–40% slučajeva povezano sa problemima kod oba partnera. Iako spermatogeneza može biti normalna, određeni faktori mogu da dovedu do oštećenja DNK u spermatozoidima i uslove pojavu neplodnosti. Oksidativni stres dovodi do oštećenja različitih biomolekula, kao što su fragmentacija DNK, peroksidacija lipida i oksidacija proteina, što sve može narušiti fertilizaciju jajne ćelije i razvoj embriona. Povišeni nivoi reaktivnih kiseonikovih jedinjenja (ROS) u semenoj tečnosti su povezani sa lošim kvalitetom spermatozoida, smanjenim potencijalom oplodnje i povećanom fragmentacijom DNK. Pored toga, kraće telomere u semenoj tečnosti koreliraju sa smanjenom vitalnošću i funkcijom spermatozoida. Oksidativni stres ubrzava skraćivanje telomera spermatozoida izazivanjem oštećenja DNK, što ugrožava sposobnost oplodnje. Oštećenje DNK može nastati u različitim fazama spermatogeneze i oplodnje. Ako oštećenje premašuje sposobnost popravke oocita, može doći do neplodnosti. Dostupni su različiti testovi za procenu oštećenja DNK spermatozoida, pri čemu je test fragmentacije DNK spermatozoida (SDF) jedan od najperspektivnijih. Oštećenje DNK se kvantifikuje kao indeks fragmentacije DNK (DFI), koji predstavlja procenat spermatozoida sa fragmentovanom DNK. Iako referentni intervali za DFI mogu da variraju u zavisnosti od korišćene metode, DFI ≤ 15% se generalno smatra normalnim, 15–30% se smatra prosečnim, a DFI ≥ 30% ukazuje na loš integritet DNK, što može negativno uticati na ishod trudnoće.

Ključne reči: oksidativni stres, skraćivanje telomera, fragmentacija DNK sperme, indeks fragmentacije DNK