UNREVEALING THE ASSOCIATION BETWEEN SPERM DNA FRAGMENTATION AND LIFESTYLE FACTORS

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Unrevealing The Association Between Sperm DNA Fragmentation and Lifestyle Factors

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ABSTRACT

Male infertility makes up almost half of all cases of infertility globally, and its etiology involves a complicated interaction between behavioral, environmental, and genetic factors. Sperm DNA fragmentation (SDF) has emerged as a significant biomarker of male reproductive potential, with increasing attention given to its role in infertility and assisted reproductive technology (ART) outcomes. While traditional semen analysis focuses on parameters such as concentration, motility, and morphology, SDF provides insight into the genetic and structural integrity of spermatozoa. Numerous studies have investigated the relationship between lifestyle factors and SDF; however, findings remain inconsistent. This review synthesizes the current scientific literature on key lifestyle factors, such as age, smoking, alcohol, body mass index (BMI), nutrition, physical activity, and environmental exposures, and their association with SDF, highlighting both the established correlations and areas of uncertainty.

Keywords: *Male Infertility, Sperm, DNA Fragmentation, Lifestyle*

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Introduction

Male infertility accounts for nearly 50% of infertility cases worldwide, with its etiology encompassing a complex interplay of genetic, environmental, and lifestyle-related factors. Among the emerging biomarkers of male reproductive health, *sperm DNA fragmentation* (SDF) has garnered significant attention due to its critical role in fertilization, embryo development, and pregnancy outcomes (Tang et al., 2018). Unlike conventional semen parameters, such as sperm count, motility, and morphology, SDF provides direct insight into the structural integrity of the paternal genome. Elevated levels of DNA fragmentation in sperm have been associated with increased risks of implantation failure, miscarriage, and poor outcomes in assisted reproductive technologies (ART), including in vitro fertilization (IVF) and intracytoplasmic sperm injection (ICSI) (Lyons et al., 2024).

Given its clinical significance, there is growing interest in identifying modifiable lifestyle factors that may influence SDF levels. A wide array of studies has investigated the impact of age, smoking, alcohol consumption, diet, body mass index (BMI), physical activity, and environmental exposures on sperm DNA integrity. However, the results remain heterogeneous, with some studies demonstrating strong correlations and others reporting negligible associations. This variability underscores the need for a critical synthesis of current evidence to better understand the extent to which lifestyle factors modulate SDF and, by extension, male fertility potential (Lyons et al., 2024). This review explores the current scientific literature on the relationship between lifestyle determinants and SDF, examining both well-established and emerging factors. By elucidating these associations, the aim is to inform clinical practice and guide future research on non-invasive strategies for improving male reproductive health.

Age and SDF

Age is one of the most determining factors of increased SDF. Multiple studies (Al Omrani et al., 2018; Kaur Arora et al., 2023; Khosravi et al., 2023; Szabó et al., 2023) demonstrate a positive correlation between advancing male age and elevated DNA fragmentation in sperm. The underlying mechanisms may involve cumulative oxidative stress, telomere shortening, reduced DNA repair efficiency, and epigenetic alterations. Notably, SDF levels are observed to rise significantly after the fifth decade of life (Szabó et al., 2023),

coinciding with declining reproductive potential and increased risk of adverse outcomes in ART and natural conception.

Tobacco Use and Alcohol Consumption

Cigarette smoking is widely regarded as a major modifiable risk factor for elevated SDF. Tobacco smoke introduces a high burden of reactive oxygen species (ROS), which induce oxidative damage to sperm chromatin. Several investigations confirm a statistically significant increase in DNA fragmentation among smokers, with evidence suggesting a dose-response relationship and interaction with genetic polymorphisms in oxidative stress pathways (Du & Tuo, 2023; Fatool & Harlev, 2018; Szabó et al., 2023).

In contrast, the effects of alcohol consumption on SDF remain equivocal. Some studies report increased SDF associated with regular or heavy alcohol intake, while others detect no significant impact (Broussard et al., 2023; Khosravi et al., 2023). These discrepancies may stem from differences in alcohol type, intake frequency, genetic metabolism such as ADH/ALDH polymorphisms, and confounding lifestyle variables.

BMI and Nutritional Status

Obesity and elevated BMI are hypothesized to influence SDF through hormonal dysregulation, chronic inflammation, and increased systemic oxidative stress. However, empirical findings are mixed. While several studies support a positive association between increased BMI and SDF, others report no statistically significant relationship, suggesting heterogeneity in population characteristics or assessment methods (Al Omrani et al., 2018; Du & Tuo, 2023)

Nutritional quality exerts a more consistent impact on sperm genomic stability. Diets rich in saturated fats and low in antioxidants have been linked to elevated SDF. In contrast, consumption of antioxidant-rich diets, particularly those containing vitamins C, E, folate, zinc, selenium, and omega-3 fatty acids, has been associated with improved sperm DNA integrity (Fatool & Harlev, 2018). These micronutrients may mitigate oxidative damage through enhanced scavenging of free radicals and upregulation of DNA repair mechanisms.

Physical Activity and Systemic Health

Physical activity presents a dualistic influence on SDF. Moderate-intensity exercise appears to improve overall sperm parameters and reduce oxidative stress. However, excessive physical exertion, particularly in endurance athletes or those using anabolic steroids, has been associated with increased SDF, potentially due to elevated ROS production, testicular heat

stress, and hormonal disruption. General health metrics such as blood pressure, insulin sensitivity, and psychological well-being have also been investigated. A recent study by Lyons et al. (2024) found weak to moderate correlations between systemic health indicators and SDF, suggesting that metabolic and cardiovascular health may play contributory roles in maintaining sperm DNA integrity (Lyons et al., 2024).

Environmental Exposures

Exposure to environmental toxins, such as air pollutants, heavy metals like lead and cadmium, ionizing radiation, and endocrine-disrupting chemicals (EDCs), has been implicated in increased SDF. These agents can cause direct genotoxicity, interfere with spermatogenesis, and disrupt hormonal homeostasis (Fatool & Harlev, 2018; Szabó et al., 2023). Epidemiological studies indicate that men residing in industrial regions or working in occupations with high toxicant exposure have elevated SDF and reduced fertility outcomes.

Clinical Relevance and Implications for ART

Elevated SDF has been correlated with poorer outcomes in ART, including lower fertilization rates, impaired embryo development, increased miscarriage risk, and reduced live birth rates (Al Omrani et al., 2018; Du & Tuo, 2023; Ebrahimi et al., 2024). These findings support the integration of SDF testing in the diagnostic workup of unexplained male infertility, recurrent pregnancy loss, and failed ART cycles.

Although not all lifestyle factors exhibit strong or consistent correlations with SDF, the available evidence suggests that certain modifiable behaviors, such as smoking cessation, dietary improvement, weight management, and avoidance of environmental toxins, may serve as non-invasive interventions to optimize male reproductive health.

Conclusion and Future Directions

The current body of evidence underscores a complex, multifactorial relationship between lifestyle factors and sperm DNA fragmentation. While variables such as age, tobacco exposure, and environmental pollutants show strong associations with increased SDF, other factors, such as BMI and alcohol, yield mixed results. These inconsistencies may reflect differences in study design, genetic background, environmental exposure, and interaction effects.

Further research is warranted to elucidate causal pathways, establish standardized SDF testing protocols, and identify effective lifestyle interventions. Longitudinal and interventional studies, particularly those incorporating genomic and metabolomic profiling, will be critical in advancing our understanding of SDF and its role in male fertility.

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