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Sperm DNA Fragmentation and Male Infertility: A Comprehensive Review

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Abstract

Male infertility remains a critical concern in reproductive medicine, with sperm DNA fragmentation (SDF) emerging as a key factor in impaired fertility potential. This review compiles and critically examines current literature on the biological mechanisms, diagnostic approaches, and clinical significance of SDF. The paper explores how oxidative stress, apoptosis, and defective chromatin packaging contribute to DNA damage in sperm cells. Various diagnostic tools such as TUNEL, SCSA, Comet assay, and SCD test are reviewed in terms of reliability and clinical relevance. The role of SDF in natural conception, intrauterine insemination (IUI), in vitro fertilization (IVF), and intracytoplasmic sperm injection (ICSI) is also discussed. Furthermore, the review addresses therapeutic interventions ranging from lifestyle modifications and antioxidant therapy to the application of advanced sperm selection techniques. It was observed that high levels of SDF are associated with lower fertilization rates, poor embryo quality, increased miscarriage risk, and reduced pregnancy outcomes. Recognizing and managing SDF could significantly enhance reproductive success and guide patient-specific fertility treatment.

Keywords; Sperm DNA fragmentation, male infertility, oxidative stress, assisted reproduction, embryo quality.

INTRODUCTION

Male infertility is a growing concern worldwide, contributing to nearly half of all infertility cases among couples. While various factors such as hormonal imbalances, anatomical issues, infections, and lifestyle habits play a role, increasing attention has been given to the quality of sperm at the genetic level [1]. Traditional semen analysis, which assesses count, motility, and morphology, often fails to detect hidden defects in sperm DNA. In many cases, men with normal semen parameters still face difficulty in achieving pregnancy. This has led researchers to explore deeper into sperm DNA integrity as a potential cause of unexplained infertility. Sperm DNA fragmentation, caused by oxidative stress, environmental toxins, and other cellular mechanisms, is now being recognized as a key factor affecting fertilization, embryo development, and even the success of assisted reproductive technologies. Understanding this aspect of male fertility is essential for improving diagnosis and designing targeted treatment strategies.

Emergence of Sperm DNA Fragmentation (SDF) as a Critical Factor

Over the past two decades, sperm DNA fragmentation has emerged as a significant marker for male infertility, particularly in cases where standard semen analysis fails to explain reproductive failure. Traditionally, fertility assessments focused mainly on parameters like sperm count, motility, and morphology [2]. However, it has been increasingly observed that men with normal semen profiles may still experience low fertilization rates, recurrent miscarriages, or failed assisted reproductive techniques [3]. Oxidative stress, infections, advanced age, environmental pollutants, and lifestyle habits such as smoking and alcohol consumption are among the leading causes of DNA damage. Clinical studies now associate high levels of DNA fragmentation with poor reproductive outcomes, making it a crucial diagnostic marker in male fertility assessments and treatment planning.

Table 1 Factors Contributing to Sperm DNA Fragmentation and Clinical Implications

Cause of DNA Fragmentation	Examples	Clinical Implication
Oxidative Stress	Smoking, radiation, pollution	Impaired fertilization and embryo development
Apoptosis (programmed cell death)	Abnormal spermatogenesis	Increased DNA strand breaks
Age-related changes	Male age above 40	Reduced sperm quality and increased DNA damage
Environmental exposure	Pesticides, industrial chemicals	Poor sperm DNA integrity
Lifestyle factors	Alcohol, poor diet, stress	Lower pregnancy rates in ART cycles

Biological Basis of Sperm DNA Fragmentation

Sperm DNA fragmentation refers to the presence of single- or double-strand breaks in the genetic material of spermatozoa. This condition arises during spermatogenesis or after ejaculation, often due to internal cellular events or external environmental stressors. During sperm maturation in the testes, chromatin is tightly compacted with the help of protamines, replacing histones to protect the genetic code. In cases where this packaging is incomplete or defective, the DNA becomes vulnerable to damage. Oxidative stress is considered the primary cause of sperm DNA fragmentation, where an imbalance between reactive oxygen species (ROS) and antioxidants leads to cellular injury. Other biological processes such as defective apoptosis (programmed cell death), improper chromatin remodelling, and inflammation in the male reproductive tract further contribute to DNA fragmentation. This damage can interfere with sperm function, impair embryo quality, and negatively affect implantation and pregnancy outcomes, even in assisted reproduction procedures. [4]

Table 2 Biological Mechanisms Leading to Sperm DNA Fragmentation

Mechanism	Description	Impact on Fertility
Oxidative Stress	Excess ROS due to smoking, pollution, varicocele, etc.	DNA damage, reduced fertilization potential
Abnormal Chromatin Packaging	Improper protamination leaves DNA unprotected	Susceptibility to DNA breaks
Apoptosis Dysfunction	Incomplete or failed cell death process during spermatogenesis	Retention of defective sperm
Inflammation/Infection	Leukocytospermia and genital tract infections elevate oxidative load	DNA integrity compromised
Environmental and Lifestyle	Radiation, chemicals, poor diet, alcohol, obesity	Long-term DNA damage, reduced ART success

Diagnostic Techniques for SDF Assessment

As awareness of sperm DNA fragmentation (SDF) grows, its accurate diagnosis has become essential in evaluating male fertility, especially in cases of unexplained infertility, recurrent implantation failure, or repeated miscarriages. Several diagnostic methods have been developed to assess the extent of DNA damage in spermatozoa. These tests differ in principle, sensitivity, complexity, and clinical applicability. Among the commonly used methods are the Sperm Chromatin Structure Assay (SCSA), TUNEL assay (Terminal deoxynucleotidyl transferase dUTP Nick-End Labelling), Comet assay (Single-cell gel electrophoresis), and the Sperm Chromatin Dispersion (SCD) test, also known as the Halo test. Each technique provides unique insights into the type and severity of DNA damage. Selection of the appropriate test often depends on the clinical scenario, laboratory setup, and required accuracy.

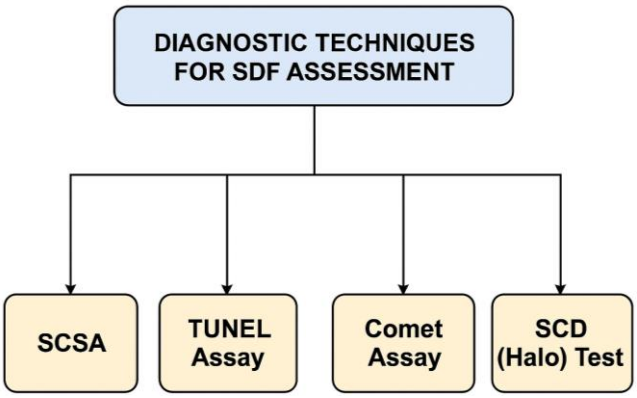

Figure 1 Diagnostic Techniques for SDF Assessment

Table 3 Common Diagnostic Tests for Sperm DNA Fragmentation

Test Name	Principle	Advantages	Limitations
SCSA	Uses flow cytometry to detect DNA denaturation in sperm heads	High reproducibility, fast, quantitative	Requires expensive equipment and expertise
TUNEL Assay	Labels DNA strand breaks using fluorescent markers	Detects both single and double strand breaks	Time-consuming, may overestimate damage
Comet Assay	Electrophoresis-based detection of fragmented DNA in sperm cells	Sensitive to low-level DNA damage	Complex protocol, limited standardization
SCD (Halo) Test	Identifies DNA fragmentation by halo formation under microscope	Simple, cost-effective, good for clinical use	Less precise quantification

Clinical Relevance of Sperm DNA Fragmentation (SDF)

Sperm DNA Fragmentation (SDF) plays a vital role in male fertility evaluation, especially when standard semen analysis fails to explain infertility. Its growing clinical importance lies in its association with fertilization potential, embryo development, and overall pregnancy success, both in natural and assisted conception.

1. Detection of Hidden Infertility

SDF testing helps identify DNA damage in sperm even when semen count, motility, and morphology appear normal.

2. Reduced Natural Conception Rates

High SDF is linked to lower chances of natural conception due to impaired sperm function and fertilization capability.

3. Poor ART Outcomes (IVF/ICSI)

Elevated DNA fragmentation correlates with lower fertilization, implantation, and pregnancy rates in assisted reproductive technologies.

4. Higher Risk of Miscarriage

Men with increased SDF have been associated with a greater incidence of early pregnancy loss and recurrent miscarriage.

5. Link with Oxidative Stress and Lifestyle

Oxidative stress—caused by smoking, pollution, infections, or poor diet—is a major contributor to DNA fragmentation.

6. Clinical Guidance for Treatment

High SDF levels guide clinicians in recommending antioxidant therapies, lifestyle changes, or advanced sperm selection methods like PICSI or MACS.

7. Improved Patient Management

SDF analysis enables more personalized treatment strategies, improving the likelihood of successful pregnancy in infertile couples.

REVIEW OF LITERATURE

Agarwal et al., (2024) investigate the worldwide use of SDF assays and the challenges that medical professionals have when incorporating these tests into their practice. 436 reproductive clinicians participated in a survey. The TUNEL assay was the most commonly used, with a preference rate of 28.5 percent. “The sperm chromatin structure assay” ranked second with a preference rate of 24.1 percent, sperm chromatin dispersion assay, which had a 19.1% preference rate, came next. Seventy percent of the participants indicated that the accessibility of the test largely determined their selection. Approximately 33.7 percent of doctors commonly use a threshold of 30 percent for increased SDF. Furthermore, a majority of 53.6 percent of participants suggested conducting SDF testing during a period of 3 to 5 days without any substance use. 75.3 percent of people think that SDF testing can help explain some cases of infertility that can't be explained by other factors. The main problems they mentioned were the lack of guidelines from professional groups (62.7 percent) and widely accepted sources for interpreting SDF results (50.3%). The largest study ever done on the technical aspects of SDF testing was conducted in this study. It draws attention to the problems that clinicians face and stresses the need for internationally agreed-upon guidelines for using and interpreting SDF tests in clinical settings [5].

Busnelli et al., (2023) investigated the “relationship between sperm Deoxyribonucleic acid fragmentation” and idiopathic recurrent gestation loss, controlling for confounding factors. The study comprised a total of 174 participants, divided into two groups. Team A consisted of 37 men with verified fertility, while Team B consisted of 100 men from infertile couples. The median sperm Deoxyribonucleic acid fragmentation index in control team A was 17%, which was lower than that in both the case group (24.5 percent, which was lower than the interquartile range of 17 percent to 32 percent; p less than 0.0001) and control group B (24 percent, which was lower than the interquartile range of 18.9 percent to 30 percent; p = 0.001). Also, the amount of people in the

event team and the regulator group B who had a sperm Deoxyribonucleic acid fragmentation index higher than 30% was considerably greater than in the control cohort A. It was found that there was a statistically considerable link between the “sperm DNA fragmentation index” or losing multiple pregnancies. However, the study found no considerable link between the sperm DNA fragmentation index and infertility. The study found that men in couples who experienced repeated gestation loss or infertility had a considerably greater rate of sperm Deoxyribonucleic acid fragmentation compared to fertile individuals. However, accounting for other variables revealed a sole association between the sperm Deoxyribonucleic acid fragmentation index and recurrent pregnancy loss [6].

Braga et al., (2023) determined whether sperm DNA fragmentation had an impact on intracytoplasmic sperm injection results based on the occurrence of oocyte dimorphisms. The study found that cycles with less than 30% sperm DNA fragmentation had much higher rates of fertilisation, high-quality embryos, implantation, and pregnancy than cycles with 30% or more fragmentation. This was true even when the oocytes were different types. The presence of different forms of oocytes had a substantial impact on both laboratory and clinical results. To be more specific, we saw low rates of fertilisation and good embryos when things like dark cytoplasm, vacuoles, resistant membranes, and non-resistant membranes were linked to high levels of sperm Deoxyribonucleic acid fragmentation. Similarly, researchers reported the lowest rates of implantation and gestation when there was considerable sperm DNA fragmentation, vacuoles, deficient perivitelline space, and fractured polar bodies. Also, having cytoplasmic granulation in the middle, a flawed perivitelline gap, and membranes that aren't resistant to DNA fragmentation had a big effect on how likely it was that the pregnancy would end in a miscarriage. So, oocyte dimorphisms may make the effect of a higher sperm Deoxyribonucleic acid fragmentation index on miscarriage more severe in ICSI cycles [7].

Du et al., (2023) examined the relationship between routine semen evaluation parameters and sperm Deoxyribonucleic acid integrity in male infertile patients. The researchers also investigated the influence of the Deoxyribonucleic acid fragmentation index on the quality of embryos and the success of in vitro fertilization and embryo transfer procedures, as well as the factors that affect it. The team with high DFI had considerablely reduced rates of good-quality embryos, blastocyst development, and gestation in comparison to the other two team. They also had lower rates of concentration, spermatozoa that moved forward, and a normal morphology rate. Researchers found a positive correlation between Sperm DFI and the BMI, man's age, and bad habits like drinking and smoking, and a negative link with semen concentration, normal sperm morphology, and sperm motility. Furthermore, the quantity of fully developed eggs and the typical rate of fertilization showed no discernible variation between the groups. The parameters they used to test semen and sperm DFI were strongly linked. This suggests that bad habits like smoking and drinking raise DFI levels, which in turn lowers the rate of high-quality embryo and blastocyst growth, ultimately affecting the success of pregnancies [8].

Zhang et al., (2023) analysed the association between the age of males and the fragmentation index of sperm Deoxyribonucleic acid. They also investigated whether the number of eggs obtained from the female partner affected the influence of sperm DFI on clinical pregnancy rates. The study found no considerable decline in semen characteristics, such as movement and concentration, as the male partner's age increased ($P > 0.05$). DFI had a positive relationship with male age, specifically in cases where the age was 40 years or older ($P = 0.002$). They discovered that the rate of successful pregnancies decreased with a smaller egg collection (less than 4), mirroring the impact of a decrease in Deoxyribonucleic acid fragmentation index. Moreover, it was observed that when the male partner's age exceeded 40 years, both the Deoxyribonucleic acid fragmentation index and the quantity of eggs retrieved had a notable impact on the clinical pregnancy rate [9].

Pozzi et al., (2023) improved the model for diagnosis of altered sperm Deoxyribonucleic acid fragmentation in primary infertile men and assessed its predictive power in comparison to the most recent European Association of Urology Guidelines. 268 (51.9 percent) of the 515 individuals had SDF greater than 30 percent at the time of clinical manifestation. There was a considerable difference between these patients' testicular volumes 15 vs. 17.5, total motile sperm counts 1.80 vs. 11.82, and their ages, with a intermediate age of 39 year vs. 37 year. There were no additional clinical variations. The incidence of repeated miscarriages and infertility without a known cause was comparable in both groups. It was found that age over 38 years and a baseline total motile sperm count below 20 × 10^6 were both linked with SDF > 30%, even when Prader < 15 and a history of miscarriages and infertility that couldn't be explained were taken into account. A new model was better than the EAU Guidelines in terms of clinical net benefit and accuracy in finding SDF >30% at baseline. The

EAU Guidelines do not allow for reliable identification of primary infertile men with abnormal SDF. Therefore, we suggest a novel and more effective prognostic model for the initial clinical evaluation of infertile males with altered sperm Deoxyribonucleic acid fragmentation [10].

Peng et al., (2023) investigated the relatively unknown combined impact of regular semen characteristics and the sperm DNA fragmentation index. Out of 1258 couples, 549 "live births took place during the follow-up period." We observed a" linear exposure-response connotation between sperm motility, sperm DNA fragmentation index," and IVF results. Higher sperm DNA fragmentation index values, worse sperm motility, and lower levels of semen concentration were all associated with a lower likelihood of successful IVF treatments after multivariable correction. The researchers identified four distinct co-exposure patterns by analyzing the sperm DNA fragmentation index and semen characteristics. Cluster 1 exhibits a low sperm DNA fragmentation index, high motility, and high concentration. Cluster 2 displays a low sperm DNA fragmentation index, moderate motility, and moderate concentration. Cluster 3 demonstrates a low sperm DNA fragmentation index, low movement, and low concentration. Lastly, Cluster 4 showcases a high sperm DNA fragmentation index, low motility, and low concentration. Participants in Cluster 3 and 4 had decreased odds ratios for live births compared to those in Cluster 1. Poor IVF outcomes were observed when sperm parameters were low, even with low values of DNA fragmentation index. Excellent IVF results were related with high to moderate levels of sperm concentration and motility, when combined with low values of sperm DNA fragmentation index. Participants with high sperm DNA fragmentation index values and low levels of motility and concentration achieved the worst results. These results offer fresh perspectives on the interactions between routine semen characteristics and sperm DNA fragmentation index [11].

Liang et al., (2023) examined the effect of sperm Deoxyribonucleic acid disintegration on the outcomes of aided reproduction technologies, with a specific emphasis on the cumulative live birth rate as a novel measure of pregnancy success. Scientists have shown growing interest in understanding the impact of sperm Deoxyribonucleic acid fragmentation on clinical gravidity rates. The objective of this study was to examine if the number of viable embryos may be used as an indicator of the impact of Sperm DAF on the overall success rate of live births in IVF cycles. The study looked at information from 1,347 couples who had in vitro fertilization cycles and used the "sperm chromatin structure assay" to measure the amount of Deoxyribonucleic acid fragmentation in their sperm. We compared the cumulative live birth rate and available embryos on Day 3 between two groups: one with sperm Deoxyribonucleic acid fragmentation values less than or equal to thirty percent, and the other with Sperm Deoxyribonucleic acid fragmentation values greater than thirty percent. The correlation analysis revealed a strong correlation between cumulative live birth rate and available embryos, indicating the potential use of available embryos as a predictor for cumulative live birth rate. Cumulative live birth rate and available embryos were considerably different between the two groups, which shows that "sperm Deoxyribonucleic acid fragmentation has an effect" on both parameters. Covariance analysis revealed that the sperm Deoxyribonucleic acid fragmentation $\leq 30\%$ team had a higher rate of available embryos per mature egg. On Day 3, the rate of available embryo formation varied considerably, "but there were no considerable changes in fertilization or cleavage rates." Higher SDF levels have the effect of decreasing embryo quality, resulting in decreased available embryos and increasing live birth frequency in IVF cycles [12].

Okubo et al., (2023) compared the two tests utilizing semen variables and examined the sperm DNA fragmentation index and general semen parameters according to World Health Organization guidelines. Additionally, they examined the validity of DFI as a predictor of in vitro fertilization results. The average sperm DFI of the study participants was 15.3 percent ± 12.6 percent, and DFI increased with age. On the other hand, as DFI increased, motility and normal morphology diminished. In comparison to patients who did not fulfill the WHO standards for concentration, total sperm count, and motility, those who did had a considerably reduced DFI. The WHO recommends viewing general semen testing as a qualitative assessment of all variables, apart from semen volume and normal morphology. We found a link between a lower blastocyst development rate after intracytoplasmic sperm injection and a high DFI of approximately 30 percent. The WHO guidelines recommend considering male infertility due to increased DFI when "in vitro fertilization results are poor despite normal semen parameters." The study's findings highlight the importance of focusing on DFI measurements by indicating that the SCD test may more precisely indicate the association between IVF clinical outcomes and male infertility [13].

Zhu et al., (2022) evaluated the effects of a higher sperm Deoxyribonucleic acid fragmentation index on transfer cycles involving both fresh and frozen embryos. The delivery amount in the normal sperm Deoxyribonucleic acid fragmentation index team was substantially greater than that

in the abnormal sperm Deoxyribonucleic acid fragmentation index team, according to their statistical analysis of 549 "fresh embryo transfer cycles." The biochemical pregnancy rate, miscarriage rate, clinical gestation rate did not differ considerably between the two teams, though. If you look at the study of 1340 frozen embryo transfer cycles, the normal sperm DFI group had much higher biochemical pregnancy rates 57.9 percent vs. 45.6 percent, P = 0.006 and clinical gestation rates than the abnormal sperm Deoxyribonucleic acid fragmentation index group. The study found no considerable difference in the delivery rate 40.9 percent vs. 33.3 percent, P = 0.074 or miscarriage rate 18.6 percent vs. 18.0 percent, P = 0.919 between the two teams. The study found that an elevated sperm Deoxyribonucleic acid fragmentation index considerablely lowered both the biochemical and clinical pregnancy rates in frozen embryo transfer cycles and the delivery rate in fresh embryo transfer cycles [14].

Wang et al., (2022) examined polycystic ovarian syndrome, a prevalent hormonal condition in women of childbearing age associated with adverse pregnancy results. In modern society, there has been a predominant emphasis on female factors. However, it was still uncertain whether the quality of sperm also affected the pregnancy outcomes of individuals with polycystic ovary syndrome. Their investigation revealed no notable disparities in the fundamental clinical characteristics between couples with a sperm Deoxyribonucleic acid fragmentation index of 15 percent or less and those with a DFI exceeding fifteen percent. Similarly, the control group exhibited no considerable changes in IVF outcomes. There were no considerable differences in fertilization rates, rates of high-quality embryos, rates of clinical gestation, and rates of termination between the two groups of individuals with polycystic ovary syndrome. In spite of this, couples whose sperm DNA fragmentation index was higher than 15 percent had a much lesser rate of high-quality blastocyst development than couples whose sperm Deoxyribonucleic acid fragmentation index was lower than 15 percent. Therefore, in the case of PCOS patients undergoing IVF, the use of sperm with a greater Deoxyribonucleic acid fragmentation index led to a decrease in the rate of high-quality blastocyst formation. However, it did not have an impact on fertilization, high-quality embryo development, clinical pregnancy, or loss rates [15].

Repalle et al., (2022) examined the influence of sperm Deoxyribonucleic acid fragmentation on the "cumulative live birth rate in intracytoplasmic sperm injection cycles for couples with unexplained infertility." The findings indicated that the group with high sperm Deoxyribonucleic acid fragmentation (SDF >30 percent) had a considerably lower cumulative live birth rate and a markedly greater rate of miscarriage compared to the group with low sperm Deoxyribonucleic acid fragmentation (SDF ≤ 30 percent). However, no substantial changes were seen in the cumulative pregnancy frequencies or implantation rates among both groups of sperm deoxyribonucleic acid fragmentation. Additional examination classified the overall quantity of embryo transfers into two categories: "fresh and frozen embryo transfers. In fresh embryo transfers, there were big differences ($p<0.05$)" between the groups that had low sperm Deoxyribonucleic acid fragmentation and those that had high SDF in the rates of implantation, clinical pregnancy, and live birth However, there were no notable variation in clinical outcomes between the two teams in frozen embryo transfers. Furthermore, a multivariable logistic regression study showed that Sperm Deoxyribonucleic acid fragmentation was a considerable predictor of CLBR after accounting for other factors that could influence the results. In summary, high sperm Deoxyribonucleic acid fragmentation was found to be associated with a lower cumulative live birth rate and a higher rate of miscarriage in in vitro fertilization cycles for couples with unexplained infertility [16].

Table 4 Key Findings from Recent Studies on Sperm DNA Fragmentation (SDF)

Author (Year)	Study Focus	Key Findings	Implications
Agarwal et al., 2024	Global use and challenges of SDF assays	TUNEL (28.5%) most used; 70% influenced by accessibility; 75.3% believe SDF explains unexplained infertility; lack of standard guidelines a concern	Need for international consensus on testing and interpretation
Busnelli et al., 2023	SDF and recurrent pregnancy loss	SDF >30% significantly higher in men with recurrent pregnancy loss; not linked with general infertility	SDF strongly linked to miscarriage but not infertility
Braga et al., 2023	Impact of SDF on ICSI with oocyte dimorphisms	High SDF (>30%) leads to lower fertilization, embryo quality, implantation; oocyte anomalies worsen effect	Combined impact of SDF and oocyte quality critical in ART outcomes
Du et al., 2023	SDF vs semen parameters, embryo quality & lifestyle	High SDF linked to poor embryo/blastocyst quality; correlated with BMI, smoking, age; negatively with motility and morphology	SDF affected by lifestyle; lower success in ART

Zhang et al., 2023	Male age, egg count, and SDF impact on pregnancy	Age >40 linked to higher SDF; fewer eggs + higher SDF = lower pregnancy rate	Age and egg count modulate SDF's effect on pregnancy
Pozzi et al., 2023	Predictive model for SDF in primary infertile men	Age >38 & low motile sperm count predict SDF >30%; proposed model better than EAU guidelines	New model enhances early detection of high SDF
Peng et al., 2023	SDF and semen parameters combined effect on IVF	Cluster with high SDF + poor motility = worst IVF outcome; low SDF + good semen = best outcome	Co-exposure profiles improve IVF prediction
Liang et al., 2023	SDF's effect on cumulative live birth rates in IVF	SDF >30% leads to fewer viable embryos and lower cumulative live births	Available embryos can predict live birth success
Okubo et al., 2023	WHO semen parameters vs SDF and IVF outcomes	High DFI (~30%) linked to lower blastocyst development despite normal WHO semen criteria	Recommends including DFI testing for unexplained IVF failures
Zhu et al., 2022	SDF impact on fresh vs frozen embryo transfer	High SDF lowers clinical and biochemical pregnancy in frozen cycles; fresh cycles show lower delivery rate	SDF affects outcomes differently in fresh and frozen transfers
Wang et al., 2022	SDF's impact in PCOS patients undergoing IVF	High SDF lowers blastocyst quality but not fertilization or pregnancy rates	SDF matters more for embryo development than pregnancy in PCOS cases
Repalle et al., 2022	SDF & cumulative live birth in unexplained infertility	SDF >30% leads to lower live birth, higher miscarriage in ICSI; no difference in frozen transfers	SDF significant predictor of miscarriage and live birth rate

CONCLUSION

This review highlights how sperm DNA fragmentation (SDF) is becoming an important factor in understanding male fertility. Even when semen appears normal in routine tests, high levels of DNA damage in sperm can affect fertilization, reduce embryo quality, and increase the chances of miscarriage. Studies have shown that age, poor lifestyle habits like smoking and drinking, and other health issues can raise the SDF level. While some findings differ depending on the condition—such as in cases of PCOS or frozen embryo transfers—the overall pattern shows that SDF plays a role in many fertility problems. However, there's still a lack of clear guidelines for how to use and interpret SDF tests in daily clinical practice. More agreement is needed among doctors and researchers to make these tests more useful. Including SDF testing in fertility assessments, especially when no other cause is found, may help improve treatment decisions and outcomes.

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