Sperm DNA Fragmentation

Causes, DNA Fragmentation Index (DFI), Diagnosis, Fertility Impact, Miscarriage Risk, Treatment, IVF/ICSI and an Integrative Unani Approach

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Introduction: "Doctor, My Sperm Count Is Normal—Then Why Are We Still Not Getting Pregnant?"

One of the situations I increasingly encounter in male infertility is a couple who tell me:

"Doctor, the sperm count and motility are not very bad, the reports look almost normal, but pregnancy is still not happening."

Another couple may say:

"We became pregnant several times, but unfortunately the pregnancies ended in miscarriage."

And another may come after unsuccessful fertility treatment and ask:

"Could there be something wrong with the sperm that an ordinary semen analysis is not detecting?"

Sometimes, the answer may involve **sperm DNA fragmentation**.

A conventional semen analysis examines important external characteristics of sperm, particularly sperm concentration, total number, motility and morphology. These measurements remain the foundation of male-fertility assessment.

However, they do not directly tell us whether the **DNA carried inside the sperm head is intact**.

Sperm DNA fragmentation, abbreviated **SDF**, refers to breaks or damage within sperm DNA. When the proportion of sperm carrying significant DNA damage becomes elevated, it may be associated with reduced natural conception, poorer outcomes in some assisted-reproduction settings and an increased risk of pregnancy loss. Current European Association of Urology guidance recognizes elevated SDF as being associated with unexplained infertility, recurrent pregnancy loss and adverse reproductive outcomes, while also emphasizing that these tests do not perfectly predict whether an individual couple will or will not achieve pregnancy.

A major 2026 systematic review and meta-analysis involving **52 studies and 19,930 participants** reached an appropriately balanced conclusion: higher SDF was associated with poorer pregnancy outcomes across natural conception, IUI, IVF and ICSI, but the tests showed only **poor-to-moderate discrimination** and should not be treated as absolute fertility predictors.

This distinction is essential.

A high DNA-fragmentation result does not mean pregnancy is impossible.

And:

A low DNA-fragmentation result does not guarantee pregnancy.

The test is one piece of the couple's complete fertility assessment.

What Is Sperm DNA?

Every sperm cell carries the father's genetic information.

Inside the sperm head are **23 chromosomes**, containing the DNA that can combine with the 23 chromosomes contained in the egg.

The resulting embryo receives approximately half of its nuclear genetic material from the father and half from the mother.

For this reason, the sperm is not merely a cell that must swim toward an egg.

It is also a highly specialized **DNA-delivery cell**.

During sperm development, the DNA becomes packaged extremely tightly. Most of the ordinary histone proteins associated with DNA are replaced by proteins called **protamines**.

This intense packaging allows the genetic material to fit inside the very compact sperm head and helps protect it during transport.

If this packaging process is abnormal, or if DNA is damaged later through oxidative stress or other biological injury, breaks may develop within the DNA strands.

This is what we broadly describe as **sperm DNA fragmentation**.

What Does Sperm DNA Fragmentation Mean?

SDF refers primarily to **single-strand or double-strand breaks in the DNA carried by spermatozoa**.

A small amount of DNA damage can occur naturally.

The problem arises when an unusually high proportion of sperm carry fragmented DNA.

Current EAU guidance describes SDF as the accumulation of single- and double-strand DNA breaks and recognizes that elevated fragmentation is more common among infertile men.

The laboratory result is often reported as a percentage.

For example, a result may state that a certain percentage of analysed sperm demonstrate evidence of DNA fragmentation.

Depending on the test being used, this may be reported as a:

DNA Fragmentation Index — DFI

or another assay-specific measure of DNA damage.

Importantly, the number cannot be interpreted properly unless we know **which laboratory method produced it**.

Sperm DNA Fragmentation Is Not the Same as an Abnormal Chromosome Test

This is an important distinction.

DNA fragmentation means there are **breaks or damage within sperm DNA**.

It does not automatically mean the man has:

Klinefelter syndrome, a Y-chromosome deletion, a translocation or another inherited genetic disorder.

Those conditions require different genetic tests.

Similarly, sperm DNA fragmentation is not the same as sperm aneuploidy, in which a sperm carries an abnormal number of chromosomes.

A man can therefore have:

normal chromosomes but elevated SDF,

or a genetic disorder with a completely different DNA-fragmentation result.

The investigations answer different questions.

Sperm DNA Fragmentation Is Also Different From Sperm Morphology

Morphology evaluates how the sperm looks under the microscope.

A sperm may appear normally shaped yet contain DNA damage.

Conversely, a morphologically abnormal sperm is not automatically carrying fragmented DNA.

There can certainly be associations between poor semen quality and elevated SDF, but the two measurements are not interchangeable.

This helps explain why selected men with apparently satisfactory conventional semen parameters can still have abnormal sperm DNA integrity.

Why Can Sperm DNA Become Damaged?

There is no single cause.

The mechanisms are usually grouped into damage occurring **during sperm production** and damage developing **after the sperm has been produced**.

During sperm development inside the testes, DNA has to be packaged and condensed precisely.

Defective chromatin remodeling can leave the DNA more vulnerable.

Abnormal germ-cell development and incomplete elimination of defective sperm cells may also contribute.

After sperm leave the testes, they can be exposed to oxidative stress during transport through the male reproductive tract.

For many infertile men, these processes overlap.

Oxidative Stress: One of the Most Important Mechanisms

Oxidative stress is one of the major biological mechanisms associated with sperm DNA damage.

Our cells naturally produce substances known as **reactive oxygen species, or ROS**.

Small physiological amounts of ROS participate in normal sperm function.

The problem develops when oxidative production becomes excessive or antioxidant defenses are inadequate.

Excessive ROS can damage:

sperm-cell membranes, mitochondria, proteins and DNA.

Sperm cells are particularly vulnerable because their membranes contain large quantities of polyunsaturated fatty acids and mature sperm have limited cytoplasmic antioxidant and DNA-repair capacity.

The current EAU guideline considers oxidative stress an important mechanism in male infertility and specifically notes its relationship with sperm DNA damage. At the same time, routine laboratory measurement of seminal ROS remains insufficiently standardized and is still regarded as experimental rather than a routine diagnostic test.

This is an important distinction:

oxidative stress is biologically important, but commercial oxidative-stress testing is not automatically necessary for every infertile man.

Varicocele and Sperm DNA Fragmentation

A **varicocele** is an abnormal enlargement of veins surrounding the testicle.

It is one of the most clinically relevant potentially modifiable conditions associated with elevated SDF.

Varicocele may increase:

testicular temperature, oxidative stress, venous pressure and local metabolic disturbance.

All of these can potentially damage spermatogenesis and sperm DNA.

Current EAU guidance recognizes varicocele as an important association with elevated SDF.

A systematic review and meta-analysis cited by the EAU found that varicocele repair was associated with an average reduction in SDF of around **7 percentage points**, independent of the particular SDF assay used.

A larger 2025 meta-analysis examining more than 8,000 patients similarly found progressive reductions in SDF following varicocelectomy, with the largest pooled reduction seen around six months after treatment.

A dedicated 2026 meta-analysis has also reinforced the relationship between clinical varicocele and sperm DNA fragmentation.

However, this does **not** mean every man with an elevated DFI needs varicocele surgery.

There must actually be a clinically meaningful varicocele and an appropriate fertility indication.

Smoking

Smoking is one of the lifestyle factors most consistently associated with impaired sperm quality and increased DNA damage.

Tobacco smoke contains oxidants and toxic compounds capable of increasing oxidative stress throughout the reproductive tract.

A large systematic review and meta-analysis examining lifestyle, environmental and health factors found smoking among the strongest lifestyle associations with elevated sperm DNA fragmentation.

For a smoker with infertility and high SDF, stopping tobacco is therefore not merely generic healthy-living advice.

It addresses a potentially relevant reproductive exposure.

Age and Sperm DNA Fragmentation

Male fertility does not end suddenly at a specific age, but sperm biology changes with ageing.

DNA-repair mechanisms, chromatin packaging and oxidative balance may become less efficient.

Current EAU guidance reports increased SDF in older men and cites a cohort of approximately 10,000 semen samples showing higher fragmentation in older age groups.

A systematic review including more than 40,000 men likewise found that the majority of included studies showed increasing paternal age associated with higher DNA fragmentation.

Age is obviously not something we can "treat," but knowing its relevance helps us interpret the full reproductive picture.

Obesity, Diabetes and Metabolic Health

Metabolic health may influence sperm DNA integrity.

Obesity, insulin resistance, diabetes and metabolic syndrome can promote:

systemic inflammation, oxidative stress, hormonal changes and increased scrotal temperature.

A systematic review of metabolic health and male fertility found adverse associations between obesity, diabetes, metabolic syndrome and several aspects of semen quality, including sperm DNA integrity.

A 2026 study of more than 1,000 men further found that obese men with elevated fasting glucose had a greater prevalence of high DFI than metabolically healthier obese men, although the observational nature of the data means it cannot establish that glucose elevation itself directly caused the fragmentation.

For me, the practical message is straightforward:

when an infertile man has obesity, diabetes or metabolic dysfunction, these problems deserve treatment for his general health and may also matter for reproductive health.

Heat and Hyperthermia

Sperm production is highly temperature-sensitive.

Potential excessive heat exposure can include occupational heat, frequent intense scrotal heating and febrile illness.

A recent expert review of sperm DNA damage recognizes **hyperthermia** among factors associated with increased fragmentation.

This does not mean ordinary daily warmth causes infertility.

The significance depends on the duration and intensity of exposure.

Infection and Inflammation

Inflammation in the male reproductive tract can produce reactive oxygen species and expose sperm to oxidative injury.

Possible conditions include:

prostatitis, epididymal/reproductive-tract inflammation and certain genitourinary infections.

Current EAU guidance includes chronic infection among factors associated with increased SDF and recommends correcting accessory-gland infections before considering more invasive measures such as testicular sperm retrieval for high fragmentation.

However, an abnormal DFI alone does **not** prove infection.

Antibiotics should not be prescribed simply because sperm DNA fragmentation is high.

Documented infection should be evaluated and treated appropriately.

Hormonal Disorders

Abnormal reproductive hormones can interfere with normal sperm development.

The EAU includes hormonal abnormalities among factors associated with increased SDF.

Depending on the patient's clinical picture, assessment may therefore include testosterone, FSH and LH and, when indicated, prolactin or other endocrine investigations.

Again, high SDF does not mean that every patient requires a large hormone panel.

Testing should follow the medical history, semen findings and physical examination.

Cancer and Gonadotoxic Exposure

Testicular cancer and certain cancer treatments can affect sperm DNA integrity.

Chemotherapy and radiotherapy can impair rapidly dividing germ cells.

Environmental and occupational gonadotoxins can also contribute in selected cases.

A large meta-analysis of health and environmental exposures found increased SDF associated with testicular tumors and pollution among several studied factors.

Men facing potentially gonadotoxic cancer treatment should ideally receive fertility-preservation counselling before treatment whenever circumstances allow.

Medications

Some medications may affect sperm production or DNA integrity.

The relationship varies greatly between medicines, dosage and individual patients.

A recent review of sperm DNA damage includes medication exposure among the potential contributing factors that should be reviewed in selected patients.

Patients should therefore bring a complete medication history—including non-prescription supplements and anabolic hormones—to fertility consultations.

But an important caution applies:

do not stop an essential prescription medicine simply because a DFI report is high.

The relationship needs professional assessment.

Anabolic Steroids and Testosterone

Exogenous testosterone and anabolic steroids can suppress LH and FSH and dramatically impair sperm production.

Their primary reproductive effect is suppression of spermatogenesis rather than DNA fragmentation alone.

A patient being evaluated for fertility should therefore disclose:

testosterone injections, gels, bodybuilding hormones and anabolic steroids.

The current EAU male-infertility guideline advises against testosterone therapy in men trying to preserve fertility.

Can Normal Semen Analysis Exist With High DNA Fragmentation?

Yes.

This is one of the major reasons SDF testing became clinically interesting.

Conventional semen analysis evaluates sperm from one perspective.

SDF evaluates another.

A man can have sperm concentration, motility and morphology within accepted reference ranges yet still have impaired DNA integrity.

Current EAU guidance therefore recommends SDF testing particularly in selected situations such as **unexplained infertility**, where standard evaluation may be normal despite failure to conceive.

But this does not justify performing DFI testing on every man before ordinary semen analysis.

Should Every Infertile Man Have a DNA Fragmentation Test?

No.

This is one of the clearest areas in which current guidelines need to be understood carefully.

The **AUA/ASRM male-infertility guideline, amended in 2024, specifically states that sperm DNA fragmentation testing should not be performed routinely during the initial evaluation of every infertile couple** because evidence has not shown that routine testing improves fertility outcomes.

The EAU takes a more targeted approach and strongly recommends SDF testing in men or couples with:

unexplained infertility, recurrent pregnancy loss from natural conception, or failure of assisted reproductive treatment.

The newest 2026 ASRM recurrent-pregnancy-loss guidance is somewhat more cautious, saying SDF testing **may be considered** when otherwise unexplained recurrent miscarriage/RPL coexists with infertility and emphasizing that evidence is still insufficient to know whether treating an abnormal test necessarily improves pregnancy outcomes.

Therefore, the modern interpretation is:

SDF is a selected advanced male-fertility test—not a universal first-line screening test.

When I Consider SDF Testing Most Useful

In clinical practice, I consider the test most meaningful when there is a specific question it may help answer.

For example, the couple has otherwise unexplained infertility.

Or they have experienced repeated miscarriages.

Or fertility treatment has repeatedly failed despite apparently adequate sperm concentration and motility.

Or the male partner has a clinical varicocele and additional information could influence treatment planning.

Or the patient has major lifestyle or medical factors strongly associated with oxidative sperm damage.

The test should change counselling or management.

Otherwise, simply adding another expensive number to the laboratory file does not help the patient.

Sperm DNA Fragmentation and Recurrent Miscarriage

This is one of the most important clinical applications of SDF testing.

Embryonic development depends upon both maternal and paternal genetic material.

A sperm with significant DNA damage may still fertilize an egg, particularly through ICSI, but DNA integrity can influence subsequent embryo development.

Current EAU evidence recognizes an association between elevated SDF and recurrent pregnancy loss, supported by meta-analyses using SCSA, SCD and TUNEL testing.

The 2026 ASRM recurrent-pregnancy-loss committee opinion now states that SDF testing **may be considered in otherwise unexplained recurrent miscarriage or RPL with concomitant infertility**, while making clear that evidence that treating the test improves outcomes remains incomplete.

This nuance matters.

A high DFI may identify a potentially relevant paternal factor.

It does not prove that sperm DNA fragmentation caused every miscarriage.

SDF and Recurrent Implantation Failure

Recurrent implantation failure is different from recurrent miscarriage.

The 2026 ASRM committee opinion on recurrent implantation failure specifically states that there is currently insufficient evidence to recommend sperm DNA fragmentation testing routinely in the RIF population because evidence linking testing and treatment to improved live-birth outcomes remains inadequate.

This is a good example of why the same test can be reasonable in one clinical situation but not established in another.

Sperm DNA Fragmentation and Natural Pregnancy

Higher SDF has been associated with lower natural-conception rates.

The EAU cites an SCSA DFI around **25% or higher** as being associated with reduced chances of natural conception and IUI.

However, that number applies specifically to the **SCSA method** and should not be used as a universal cutoff for every test.

The 2026 meta-analysis of nearly 20,000 subjects confirms that elevated SDF has some ability to identify men at higher risk of adverse reproductive outcomes but also shows that its predictive ability is far from perfect.

A couple should therefore never be told:

"Your DFI is above this number, so natural pregnancy cannot occur."

That is not scientifically correct.

SDF and IUI

IUI depends upon an adequate population of motile, functionally competent sperm.

Higher SDF has been associated with lower IUI pregnancy rates in several studies.

The EAU considers an SCSA DFI above roughly 25% associated with reduced natural-conception and IUI success.

Again, the result should be interpreted with sperm number, motility, female age and other fertility factors.

SDF and IVF

In conventional IVF, sperm must still interact with and penetrate the oocyte.

Very high levels of sperm DNA damage have been associated with poorer reproductive outcomes in some IVF studies.

EAU guidance notes poorer IVF outcomes particularly at very high SCSA DFI levels, while acknowledging substantial controversy and assay variability.

Does ICSI Solve DNA Fragmentation?

No.

This is an important misconception.

ICSI solves the problem of getting one sperm into an egg.

It does **not repair the DNA inside that sperm**.

An embryologist can select a sperm based mainly on viability and microscopic appearance, but ordinary ICSI microscopy cannot show whether that individual sperm carries DNA strand breaks.

The oocyte has some ability to repair sperm DNA damage after fertilization, but that capacity is not unlimited and is influenced by several factors.

This is why elevated SDF may remain relevant even when ICSI is being used.

The 2026 meta-analysis found associations between elevated SDF and adverse reproductive outcomes even after IVF/ICSI, although the predictive strength remained only modest.

The Four Major SDF Testing Methods

Several laboratory techniques are used worldwide.

The important point is that they do **not measure exactly the same biological phenomenon in exactly the same way**.

TUNEL Test

TUNEL — Terminal deoxynucleotidyl transferase-mediated dUTP nick end labeling detects DNA strand breaks by labeling exposed DNA ends.

The EAU classifies TUNEL as a test that directly assesses DNA damage.

Results are generally reported as the percentage of sperm demonstrating fragmentation.

COMET Assay

In the **COMET assay**, sperm DNA is released and subjected to electrophoresis.

Damaged DNA moves farther away from the sperm nucleus, producing an appearance resembling a comet with a head and tail.

The greater the DNA migration, the greater the damage.

The EAU classifies alkaline COMET as a direct method of assessing sperm DNA damage and notes that COMET measures can provide information associated with reproductive outcomes.

SCSA – Sperm Chromatin Structure Assay

The **Sperm Chromatin Structure Assay** is one of the most extensively studied methods.

Rather than directly counting DNA strand breaks in exactly the same way as TUNEL, it evaluates how susceptible sperm DNA is to acid-induced denaturation and uses fluorescent staining and flow cytometry.

The result is commonly expressed as:

DNA Fragmentation Index — DFI

The EAU identifies SCSA as one of the most widely studied SDF methods.

SCD – Sperm Chromatin Dispersion Test

The **Sperm Chromatin Dispersion test**, sometimes called a halo test, evaluates the pattern produced by sperm chromatin after controlled processing.

Sperm with intact DNA generally produce a characteristic halo pattern, while damaged sperm produce reduced or absent halos depending upon the method.

The EAU considers SCD an indirect test of SDF.

Which SDF Test Is Best?

There is currently no single universally accepted “perfect” SDF test.

TUNEL, COMET, SCSA and SCD each have strengths and limitations.

Current EAU guidance explicitly states that controversy remains over routine clinical use and that available methods do not reliably predict all ART outcomes.

ASRM's 2026 implantation-failure guidance similarly notes that several methods exist and it remains unclear which test is best.

For this reason, I advise patients not to compare:

a 22% result from one assay with a 22% result from another assay as though they were identical.

They may not be.

What Is a "Normal" DFI?

There is no single universal cutoff that applies across every assay and laboratory.

For SCSA specifically, EAU guidance cites approximately **25% DFI** as a level associated with lower natural-conception and IUI pregnancy rates and notes poorer IVF outcomes at particularly high values above 50%.

But TUNEL, COMET and SCD have their own validated thresholds.

Laboratories may also use somewhat different reference categories.

Therefore:

the correct threshold is assay-specific.

The result should be interpreted using the laboratory's validated method and clinical context.

Why I Prefer Repeat Testing in the Same Laboratory

If SDF testing is being used to monitor treatment, using the same validated technique and preferably the same experienced laboratory improves comparability.

Changing from SCSA to TUNEL, for example, can make the percentages difficult to compare directly.

The semen sample itself is also biologically variable.

A result should therefore never be interpreted in isolation from:

abstinence period, recent illness, semen parameters, laboratory methodology and clinical history.

Does the Abstinence Period Affect DNA Fragmentation?

It can.

Sperm stored for longer periods within the male reproductive tract may be exposed to additional oxidative stress.

The current EAU guideline cites evidence that **repeated ejaculation separated by approximately three hours can reduce measured SDF** in some men.

For selected patients undergoing ART, a fertility specialist may therefore consider shorter abstinence or a second ejaculate.

However, this does not mean every man should repeatedly ejaculate without a structured plan.

The effect can differ between patients, and semen volume and total sperm number can also change.

Should the Test Be Repeated?

Sometimes.

A repeat test can be reasonable when the result is unexpected, when sample conditions were suboptimal or after treatment of a potentially reversible factor.

Sperm development takes roughly several months from early germ-cell development to a mature ejaculated sperm.

Therefore, when lifestyle or medical treatment is introduced, reassessment is often performed after an interval rather than after only a few days.

The exact timing should depend on the cause being treated.

How I Evaluate a Patient With High SDF

When a patient presents with an elevated DFI, I do not immediately prescribe antioxidants.

My first question is:

Why is the DNA fragmentation elevated?

I review the semen analysis and reproductive history.

I examine for clinical varicocele where appropriate.

I ask about smoking, obesity, diabetes, fever and heat exposure.

I review medicines, anabolic steroids and occupational exposures.

I consider infection or inflammation when the history and semen findings justify it.

I assess reproductive hormones when indicated.

And just as importantly, I review the **female partner's fertility**.

The SDF result belongs to the couple's reproductive story, not only to the man's laboratory report.

Can High SDF Be Reduced?

In some men, yes.

The probability depends on what is causing it.

A man with a clinically significant varicocele may improve after appropriate varicocele treatment.

A smoker may reduce an avoidable oxidative exposure by stopping smoking.

A man with uncontrolled diabetes may benefit from improved metabolic control.

An active reproductive-tract infection can be treated.

Excessive heat or gonadotoxic exposures may be reduced.

The abstinence interval may sometimes be modified.

But a high DFI is not always completely reversible.

And reducing the laboratory percentage does not automatically guarantee pregnancy.

Lifestyle Treatment

Lifestyle management is one of the most reasonable first steps when obvious modifiable risks are present.

For an infertile man, I pay particular attention to:

healthy body weight, regular physical activity, smoking cessation, avoiding anabolic steroids, sensible alcohol intake, adequate sleep, healthy diet, diabetes control and avoiding unnecessary excessive scrotal heat.

A 2025 systematic review and meta-analysis found that lifestyle interventions were associated with a modest average reduction in SDF, although the authors emphasized that stronger standardized studies are still needed.

So lifestyle treatment is sensible—but it should not be advertised as a guaranteed DFI cure.

Treatment of Varicocele

When an infertile man has a **clinical varicocele** and appropriate fertility indications, repair can be considered.

Evidence suggests varicocelectomy can reduce sperm DNA fragmentation.

WHO's first global infertility guideline, published in 2025, also suggests surgical or radiological treatment over expectant management for infertile men with a clinical varicocele, particularly when semen parameters are abnormal, although the certainty of evidence is limited.

This does not mean DFI alone is an automatic indication for surgery.

The varicocele itself, semen profile, duration of infertility and female partner's reproductive condition must all be considered.

Treatment of Infection

If a clinically meaningful genitourinary infection is documented, treating it may reduce inflammatory and oxidative injury.

However:

high SDF by itself does not justify antibiotics.

The diagnosis of infection requires appropriate evidence.

Unnecessary antibiotics expose patients to side effects and antimicrobial resistance without addressing the true cause.

Antioxidant Treatment

This is probably one of the most heavily marketed areas in male infertility.

Antioxidants commonly promoted include vitamin C, vitamin E, coenzyme Q10, carnitine, zinc, selenium, N-acetylcysteine and numerous combinations.

Biologically, the idea is reasonable: oxidative stress contributes to sperm damage, so reducing oxidative injury might improve sperm DNA integrity.

Some studies show reductions in DFI.

For example, the 2025 systematic review found a small average reduction in SDF following antioxidant interventions.

But this is not the same as proving improved **live-birth rates**.

That distinction is very important.

What Does WHO Say About Antioxidants?

The **2025 WHO infertility guideline** reviewed randomized-trial evidence for antioxidant supplements in men with abnormal semen parameters.

Its conclusion was that the evidence was too heterogeneous to make a recommendation either **for or against** routine antioxidant supplementation.

WHO specifically noted that studies used very different antioxidants, combinations, doses and patient populations and often measured semen parameters rather than pregnancy or live birth.

Therefore, I do not consider it scientifically appropriate to say:

“Every high-DFI patient needs this antioxidant combination.”

Antioxidants may be considered selectively, but they should not replace identification of a varicocele, infection, metabolic disease, tobacco exposure or another treatable cause.

More Antioxidants Are Not Necessarily Better

Another common mistake is using ten or fifteen antioxidant ingredients simultaneously in very high doses.

Antioxidants participate in a balance.

Excessive supplementation can theoretically disturb normal redox signalling, and high doses of supplements may produce adverse effects or interactions.

The goal should therefore be **appropriate treatment**, not the largest supplement list.

FSH Treatment

Some studies have examined FSH therapy for selected infertile men and reported reductions in SDF.

A 2025 meta-analysis found a pooled decrease in SDF following FSH treatment in included studies.

However, this does not establish FSH as standard treatment for every man with high DFI.

FSH is a hormone with specific reproductive indications.

The decision should depend on the patient's endocrine profile and infertility diagnosis rather than the DFI number alone.

Shorter Abstinence and Second-Ejaculate Strategies

For selected men, reducing ejaculatory abstinence may decrease the time sperm spend exposed to oxidative conditions within the reproductive tract.

Current EAU guidance cites evidence that a second ejaculation after a short interval can reduce SDF.

In ART, some centres therefore use a shorter abstinence period or consider a second sample in selected high-DFI patients.

This strategy is simple and low risk but should still be coordinated with the fertility laboratory because very short abstinence can also reduce semen volume and total sperm count.

Sperm Selection Techniques

IVF laboratories use several approaches to identify viable or apparently high-quality sperm for ICSI.

However, no routine laboratory selection technique can guarantee that a sperm has perfectly intact DNA.

Various advanced methods have been studied, but evidence that they consistently improve live birth specifically in high-SDF couples remains incomplete.

Patients should be cautious about laboratory add-ons promoted as guaranteed solutions to DNA fragmentation.

Testicular Sperm for High DNA Fragmentation

This is an important but controversial area.

Sperm recovered directly from the testis may have **lower DNA fragmentation than ejaculated sperm** because they have not spent as much time passing through the epididymis and distal reproductive tract, where additional oxidative injury can occur.

The EAU acknowledges evidence showing lower SDF in testicular sperm and reports observational studies suggesting potentially improved ICSI outcomes in selected men with very high ejaculated SDF.

However, the evidence is not strong enough to make this routine treatment.

Is TESE Recommended Simply Because DFI Is High?

No.

This point deserves emphasis.

The EAU classifies the use of testicular sperm for ICSI in men with high ejaculated SDF as **experimental/weakly supported**, because large randomized trials have not confirmed a clear benefit.

Its practical guidance is that potentially correctable factors should first be addressed, including:

varicocele, lifestyle factors, accessory-gland infection and abstinence interval.

Only afterward, particularly following unsuccessful ART and after discussion with the couple and reproductive specialists, may testicular sperm be considered on a case-by-case basis.

This approach avoids exposing a man with otherwise available ejaculated sperm to unnecessary surgery.

Why Testicular Sperm Retrieval Has Risks

TESE is an invasive procedure.

Potential risks include:

pain, bleeding, hematoma, infection, scarring and testicular injury.

When testicular sperm retrieval is medically necessary because sperm cannot otherwise be obtained, these risks may be justified.

But when millions of sperm are already present in the ejaculate and surgery is being considered solely because DFI is high, the benefit must be much more carefully weighed.

What Does the Newest Evidence Say About SDF Overall?

The 2026 systematic review and meta-analysis of nearly 20,000 subjects provides one of the most useful modern perspectives.

It found that elevated SDF was associated with poorer pregnancy outcomes and miscarriage across natural conception, IUI, IVF and ICSI.

But the tests had **low sensitivity, higher specificity and only modest overall discriminatory performance**.

In simpler language:

High SDF identifies an increased-risk group.

But the test cannot accurately tell us:

“This couple will conceive” or **“this couple will not conceive.”**

That is why SDF should inform clinical reasoning rather than dominate it.

Sperm DNA Fragmentation and the Female Partner

One of the most important concepts in fertility care is that sperm DNA does not operate in isolation.

After fertilization, the oocyte has molecular machinery capable of repairing some sperm DNA damage.

The capacity and success of this repair depend on many biological factors.

Therefore, the same male DFI result may have different reproductive consequences in different couples.

Female age, ovarian reserve, egg quality and reproductive diagnosis remain important.

This is why I never interpret SDF without understanding the female partner's reproductive condition.

SDF Is a Couple-Level Fertility Issue

Suppose a 28-year-old woman with excellent ovarian reserve has a partner with moderately elevated SDF and a correctable clinical varicocele.

There may be reasonable time to treat the male factor.

Now imagine a similar male result in a couple where the female partner has substantially diminished ovarian reserve.

Spending many months attempting to perfect the DFI number may not serve that couple's reproductive goals.

WHO's 2025 infertility guideline emphasizes person-centred fertility care and evaluation of relevant factors in both partners.

The best laboratory number is not necessarily the best reproductive strategy.

Can Sperm DNA Fragmentation Cause Infertility?

Elevated SDF can **contribute** to infertility.

But it should usually not be presented as the sole proven cause simply because one test is high.

A couple may simultaneously have:

female age-related fertility decline, reduced ovarian reserve, ovulatory dysfunction, tubal disease, endometriosis, abnormal sperm concentration, varicocele and high SDF.

Our job is to determine which factors are likely to be clinically important and which can realistically be treated.

Does High SDF Cause Miscarriage?

Elevated SDF is **associated with increased miscarriage risk**, particularly in recurrent pregnancy-loss populations.

That association is now recognized by EAU, AUA/ASRM and the 2026 ASRM RPL guidance, although these organizations differ somewhat in how strongly they recommend testing.

But association is not certainty.

Most miscarriages, particularly sporadic early miscarriages, have many possible causes, and maternal age-related embryo chromosome abnormalities remain especially important.

A couple with recurrent miscarriage therefore needs a proper RPL evaluation rather than focusing exclusively on the man's DFI.

Can High SDF Affect Embryo Quality?

Research suggests an association between elevated SDF and impaired embryo development in some populations.

Current EAU guidance lists impaired embryo development among reported adverse ART associations.

However, embryo development is influenced by both gametes and by laboratory conditions.

A poor embryo cannot automatically be attributed to the sperm DNA-fragmentation result.

Can High SDF Be Completely "Cured"?

Sometimes a reversible cause can be substantially improved.

But there is no universal treatment that guarantees a normal DFI.

One patient may respond to varicocele repair.

Another may improve after stopping smoking and improving metabolic health.

Another may have an inflammatory condition requiring specific treatment.

Another may remain high despite all reasonable interventions.

I therefore prefer the phrase:

reduce modifiable sperm DNA damage

rather than promising a permanent cure.

Sperm DNA Fragmentation and the Unani System of Medicine

As a physician trained in the **Unani System of Medicine**, I find sperm DNA fragmentation particularly relevant to the traditional principle of:

Izala-i-Sabab — identifying and addressing the causative factor

Official CCRUM material describes removal or correction of causative factors as a fundamental therapeutic principle in Unani medicine. It also recognizes **Ilaj-bil-Ghiza, Ilaj-bil-Tadbir, Ilaj-bil-Dawa and Ilaj-bil-Yad** as major therapeutic approaches.

For me, this principle can be applied responsibly to SDF.

If the patient smokes, smoking needs attention.

If a clinical varicocele is contributing, it needs proper assessment.

If diabetes is uncontrolled, metabolic health matters.

If there is infection or inflammation, that should be addressed.

If the patient uses testosterone or anabolic steroids, the reproductive effects need specialist management.

This is much more rational than simply giving every high-DFI patient the same "sperm medicine."

Ilaj-bil-Ghiza — Dietotherapy

Nutrition is important for general and reproductive health.

An individualized dietary approach can support:

healthy body weight, metabolic control, adequate protein and micronutrient intake, cardiovascular health and general antioxidant balance.

This becomes particularly relevant in patients with obesity, diabetes or poor dietary habits.

However, I explain clearly that:

there is no specific Unani food proven to normalize sperm DNA fragmentation in every patient.

Diet can support the biological environment in which sperm develop.

It cannot guarantee repair of already fragmented DNA.

Ilaj-bil-Tadbir — Regimental and Lifestyle Care

This is perhaps where the Unani whole-person approach can contribute most naturally.

CCRUM describes regimental and lifestyle-oriented treatment as one of the main Unani modalities.

For the infertile male, a responsible contemporary approach may emphasize:

healthy physical activity, adequate sleep, weight optimization, tobacco avoidance, stress management and correction of unhealthy daily habits.

These measures also overlap substantially with modern male-fertility recommendations.

I consider this an area of genuine integration rather than simply placing two treatment systems side by side.

Ilaj-bil-Dawa — Unani Pharmacotherapy

Unani medicine contains many single and compound preparations historically used for male reproductive complaints.

However, SDF is a modern molecular laboratory concept, and high-quality clinical evidence specifically showing that a particular Unani formulation reliably reduces sperm DNA fragmentation and improves live-birth rates is currently lacking.

Therefore, I would describe Unani pharmacotherapy as **individualized supportive care where clinically appropriate**, not as a proven molecular cure for high DFI.

This distinction is especially important when patients see advertisements claiming:

“DNA fragmentation 100% cured.”

No responsible fertility treatment should make such a guarantee.

Herbal Medicines Are Not Automatically Antioxidant Fertility Treatments

The word “natural” should not be confused with “clinically proven.”

A plant may contain antioxidant compounds in laboratory experiments, but this does not automatically establish that a commercial herbal product improves live-birth rates in infertile couples.

WHO's 2025 antioxidant recommendation did not include herbal preparations and concluded that evidence was insufficient even to recommend for or against conventional antioxidant supplements.

This makes it even more important not to overstate evidence for herbal treatment of sperm DNA fragmentation.

Why Quality Control Matters in Unani Treatment

When Unani medicines are used, the product should have appropriate manufacturing quality and should be selected after proper diagnosis.

The patient should disclose all conventional medicines and supplements because interactions are possible.

The Ministry of AYUSH and CCRUM maintain systems intended to support research, pharmacopoeial standards and quality control for Unani medicine.

In fertility treatment, quality and traceability matter because patients are often taking multiple products for months.

The Specialized Saira Health Care Approach to Sperm DNA Fragmentation

At **Saira Health Care**, my approach to sperm DNA fragmentation is not to treat the DFI percentage alone.

My first objective is to determine whether SDF testing was actually indicated and whether the test was performed by a reliable laboratory.

Then I interpret the result alongside:

the conventional semen analysis, reproductive history, physical examination, possible varicocele, lifestyle, metabolic health, hormonal status, medications, previous fertility treatment and the female partner's reproductive assessment.

Saira Health Care's current published physician profile describes my focused clinical practice in sexual disorders and infertility and lists my professional education and additional training in infertility, urological subjects, male infertility and integrated sexual and reproductive health.

My Clinical Framework for High DFI

First: Confirm That the Test Means What We Think It Means

Which assay was performed?

Was it SCSA, TUNEL, SCD or COMET?

What cutoff does that laboratory use?

Was the semen sample collected under appropriate conditions?

An isolated percentage without the assay name is incomplete information.

Second: Review the Ordinary Semen Analysis

SDF does not replace semen analysis.

I still need to know:

sperm concentration, total sperm number, progressive motility, morphology and semen volume.

A man with normal semen plus elevated SDF is different from a man with severe oligoasthenoteratozoospermia plus high SDF.

Third: Look for a Treatable Cause

This is where I pay special attention to:

clinical varicocele, tobacco, metabolic disease, significant heat exposure, reproductive-tract inflammation, medications and other relevant medical factors.

The objective is not simply:

“lower the number.”

The objective is:

“understand what may be injuring the sperm.”

Fourth: Understand the Couple's Reproductive History

Has pregnancy ever occurred?

Have there been miscarriages?

How long has infertility continued?

Has IUI failed?

Has IVF or ICSI failed?

What was embryo development like?

These questions help determine whether an SDF result is clinically meaningful.

Fifth: Assess the Female Partner

Age, ovarian reserve, ovulation, tubal status, uterine factors and other female fertility conditions can alter the entire plan.

This prevents unnecessary delay.

Sixth: Correct Modifiable Factors

When appropriate, treatment may include:

lifestyle improvement, smoking cessation, metabolic management, treatment of documented infection, varicocele assessment and modification of ejaculation interval.

Unani supportive care may be integrated for nutrition, lifestyle, general health and appropriately selected individualized treatment.

Seventh: Reassess Objectively

If treatment has been undertaken specifically to improve sperm quality, I prefer objective follow-up rather than relying on how strong or energetic the patient feels.

The semen and, when clinically useful, SDF can be reassessed after an appropriate biological interval.

Eighth: Escalate Fertility Treatment When Appropriate

Some couples cannot afford to wait indefinitely for a perfect DFI result.

Depending on female age and the couple's overall reproductive condition, it may be appropriate to proceed with IUI, IVF or ICSI.

In highly selected men with persistent high SDF and unsuccessful ART despite correction of modifiable factors, testicular sperm for ICSI may be discussed with an experienced reproductive urologist—but current EAU guidance considers this approach experimental and supported by low-quality evidence.

Contribution of Saira Health Care in Sexual Disorders and Infertility

Sperm DNA fragmentation is a good example of why infertility treatment requires more than reading a sperm-count number.

At Saira Health Care, my focused approach to sexual disorders and infertility emphasizes separating several different questions.

Is sperm production adequate?

Are sperm moving properly?

Is morphology severely abnormal?

Is DNA integrity impaired?

Is there a varicocele?

Is ejaculation normal?

Are sexual difficulties reducing the frequency of intercourse?

Is fertility pressure causing erectile or relationship problems?

Does the female partner have a simultaneous reproductive factor?

These issues can coexist.

A comprehensive infertility plan should therefore treat the **couple and the cause**, rather than one isolated laboratory report.

SDF and Sexual Function

High sperm DNA fragmentation itself generally does not cause:

erectile dysfunction, premature ejaculation or low sexual desire.

A man can have completely normal erections and sexual performance while having elevated SDF.

However, infertility investigations can produce significant anxiety.

Once a man is told his “DNA is damaged,” he may become frightened and interpret the result as though something is genetically wrong with his entire body.

That interpretation is incorrect.

Sperm DNA fragmentation describes DNA damage within a proportion of sperm cells.

It does not mean the man's entire DNA is damaged.

It does not mean he is genetically defective.

And it does not measure masculinity.

Psychological Impact of the Term “DNA Damage”

The words themselves can be frightening.

I often explain the result in simpler language:

“Some of the sperm are carrying more DNA strand damage than we would like. Our job is to identify why and determine whether reducing that damage could improve your reproductive plan.”

That explanation is medically more useful than telling the patient:

“Your sperm DNA is bad.”

Infertility care should not create unnecessary fear.

Common Mistakes I Encourage Patients to Avoid

One major mistake is performing DFI testing before a basic fertility evaluation has even been completed.

Another is assuming that one elevated result proves the exact cause of infertility.

Patients also frequently buy multiple antioxidants without investigating varicocele, diabetes, smoking or other relevant factors.

Some repeat the test every few weeks, even though sperm biology changes over a much longer interval.

Another mistake is believing that ICSI automatically eliminates the impact of damaged sperm DNA.

And perhaps the most serious mistake is proceeding directly to testicular sperm extraction solely because the DFI is high, without first correcting simpler reversible factors or understanding the limited evidence supporting that surgery.

Frequently Asked Questions

What is sperm DNA fragmentation?

It refers to single- or double-strand breaks or related damage within DNA carried by sperm cells. Higher levels have been associated with male infertility, pregnancy loss and poorer reproductive outcomes in some populations.

What does DFI stand for?

DFI means **DNA Fragmentation Index**. It is particularly associated with the SCSA test and represents the proportion of sperm showing abnormal DNA/chromatin characteristics.

Is DFI part of a normal semen analysis?

No. Conventional semen analysis and sperm DNA fragmentation testing are separate investigations.

Can my sperm count be normal but DFI high?

Yes. Selected men with unexplained infertility can have relatively normal conventional semen parameters but increased sperm DNA damage.

Does every infertile man need SDF testing?

No. AUA/ASRM recommends against routine SDF testing during the initial male-infertility evaluation. It is more useful in selected situations.

When is the test most useful?

Current EAU guidance particularly supports testing in unexplained infertility, recurrent pregnancy loss and ART failure. The 2026 ASRM RPL guideline says it may be considered in otherwise unexplained recurrent miscarriage with concomitant infertility.

What is a normal DFI?

There is no single universal threshold for every method. For SCSA, the EAU cites approximately 25% as a level associated with poorer natural-conception and IUI outcomes, but TUNEL, COMET and SCD require their own assay-specific interpretation.

Is 30% DFI always severe infertility?

No. Interpretation depends on assay, laboratory standards and the complete fertility situation. DFI is not a yes-or-no fertility test.

Can high DFI cause miscarriage?

Higher SDF is associated with recurrent pregnancy loss at the population level, but it does not prove that the man's sperm caused an individual miscarriage.

Can varicocele increase DFI?

Yes. Varicocele is a recognized association with elevated SDF, and varicocele repair can reduce fragmentation in appropriately selected infertile men.

Can smoking increase DNA fragmentation?

Yes. Smoking is one of the lifestyle factors most consistently associated with elevated SDF.

Can diabetes and obesity contribute?

Metabolic dysfunction is associated with impaired sperm quality and DNA integrity, although individual causation varies.

Can antioxidants lower DFI?

Some studies report modest reductions, but evidence that routine antioxidant supplementation improves pregnancy or live-birth outcomes is uncertain. WHO made no recommendation for or against routine antioxidant supplements in infertile men with abnormal semen parameters.

Does IVF solve high DNA fragmentation?

Not necessarily. Elevated SDF can remain relevant to IVF outcomes.

Does ICSI solve DNA fragmentation?

ICSI helps a sperm fertilize an egg but does not repair the DNA inside the injected sperm.

Is testicular sperm better if DFI is high?

Testicular sperm often has lower fragmentation, and observational data suggest possible benefits in selected cases, but large randomized trials have not confirmed routine use. EAU therefore considers this strategy experimental and case-specific.

Can shorter abstinence reduce SDF?

It may in selected men. Current EAU guidance cites evidence that a repeat ejaculation after a short interval can reduce SDF.

Can Unani medicine help?

An individualized Unani approach may be useful in addressing **modifiable supporting factors** such as diet, weight, metabolic health, sleep, stress and lifestyle through the cause-oriented principle of Izala-i-Sabab. However, no high-quality evidence currently proves that a specific Unani formulation universally normalizes sperm DNA fragmentation or guarantees pregnancy.

A Message to My Patients

When a man says to me:

“Doctor, my DFI is 35%. Does this mean I cannot have a healthy child?”

I explain that a DFI result is not a final verdict.

We need to know:

which test was used,

why the DNA fragmentation may be elevated,

whether a varicocele is present,

whether he smokes,

whether diabetes or obesity is contributing,

whether infection is present,

whether fertility treatment has failed previously,

and what the female partner's reproductive condition is.

Then we can decide whether treatment is likely to help.

Another patient may ask:

“My sperm count is normal, so why should DNA matter?”

I explain that quantity and genetic integrity are different properties.

And another patient asks:

“Can you guarantee my DFI will become normal?”

My answer is that responsible fertility medicine should never make such a guarantee.

Some causes are modifiable.

Some improve substantially.

Others remain persistent.

The purpose of treatment is to improve every realistic reproductive factor while protecting the couple's time and avoiding unnecessary interventions.

About Dr. Nizamuddin Qasmi

Dr. Nizamuddin Qasmi
Founder & Chief Physician, Saira Health Care
Focused Practice in Sexual Disorders & Infertility

Professional Education & Additional Training

BUMS – Hamdard University, Delhi
MD
CGO
Certificate in Infertility – MGBIMS, Delhi
Certificate in Urology – London, UK
Masters in Male Infertility – MasterHealthPro (HealthPro)
Integrated Sexual and Reproductive Health – ISRH, UNFPA

Saira Health Care's current published professional profile lists this education and additional training and describes Dr. Nizamuddin Qasmi's focused clinical practice in sexual disorders and infertility, including male infertility and sperm-related disorders.

At **Saira Health Care**, the specialized approach to sperm DNA fragmentation is therefore intended to combine contemporary male-infertility assessment with individualized Unani supportive care.

The objective is not to advertise one tablet as a “DNA repair medicine.”

The objective is to determine whether the high SDF reflects a **modifiable biological problem**, treat the factors we can reasonably change and guide the couple toward the most appropriate reproductive option.

When advanced reproductive urology, varicocele surgery, IVF/ICSI, testicular sperm retrieval, genetics or another specialist service is required, appropriate collaboration and referral should form part of comprehensive care.

Conclusion

Sperm DNA Fragmentation is an advanced measure of sperm quality that evaluates damage to the genetic material carried inside sperm cells.

It is different from sperm count, motility and morphology and may sometimes reveal a male reproductive factor that is not obvious on conventional semen analysis.

Current evidence associates elevated SDF with reduced chances of natural conception, recurrent pregnancy loss and less favorable outcomes in some IUI, IVF and ICSI populations. However, the newest 2026 meta-analysis involving nearly 20,000 subjects also shows that SDF tests have only limited-to-moderate ability to predict an individual couple's reproductive outcome.

Therefore, SDF is best understood as:

a useful advanced biomarker in selected infertility cases—not a universal fertility score.

Testing should not ordinarily replace the initial male-fertility evaluation. AUA/ASRM recommends against routine first-line testing, while current EAU guidance recommends it particularly in unexplained infertility, recurrent pregnancy loss and ART failure. The 2026 ASRM recurrent-pregnancy-loss guidance also allows consideration of SDF testing in otherwise unexplained RPL with concomitant infertility.

When SDF is high, treatment should be **cause-oriented**.

Clinical varicocele, smoking, metabolic dysfunction, infection, lifestyle, environmental exposures and abstinence interval are among factors worth assessing. Varicocele treatment can reduce SDF in properly selected men.

Antioxidants deserve more cautious interpretation. Some studies show reductions in laboratory-measured fragmentation, but WHO's 2025 infertility guideline concluded that current evidence was insufficient to recommend either for or against routine antioxidant supplementation because clinically meaningful outcomes such as live birth remain uncertain.

Testicular sperm may show less fragmentation than ejaculated sperm, but using TESE solely for high SDF remains an experimental, case-by-case strategy rather than routine first-line treatment.

From the **Unani perspective**, the traditional principle of **Izala-i-Sabab—identifying and addressing causative factors—** is highly relevant. CCRUM officially describes cause-oriented treatment along with **Ilaj-bil-Ghiza, Ilaj-bil-Tadbir, Ilaj-bil-Dawa and Ilaj-bil-Yad** as established elements of the Unani therapeutic framework.

The strongest responsible role for Unani care in SDF is therefore to support the patient's **whole reproductive health**—diet, metabolic health, lifestyle, sleep, stress and other modifiable factors—while modern investigation identifies varicocele, infection, hormonal abnormalities, ART-related issues and other causes requiring specific treatment.

At **Saira Health Care**, my preferred principle is simple:

Do not treat the DFI number alone. Treat the man, identify the cause, understand the couple's reproductive situation and use the sperm DNA result only where it helps us make a better clinical decision.

A high sperm DNA fragmentation result should not create hopelessness.

It should create a more focused question:

"What is damaging these sperm—and which of those factors can we realistically change?"

That is where meaningful treatment begins.

Saira Health Care official website
Book an appointment with Saira Health Care
Saira Health Care Pharmacy

Medical Disclaimer: This article is intended for medical education and patient awareness. Sperm DNA fragmentation testing should be interpreted in the context of complete male and female fertility evaluation. A high DFI does not prove infertility or predict an individual pregnancy outcome with certainty. Patients should not start or stop antioxidants, antibiotics, hormones, testosterone, supplements, herbal products or Unani medicines solely on the basis of a DNA-fragmentation report. Varicocele surgery, IVF/ICSI and testicular sperm retrieval require individualized specialist assessment, and no medical, surgical, Unani or assisted-reproductive treatment can guarantee pregnancy or live birth.