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The Correlation Between Male Virility, Reproductive Capacity, and Serum Testosterone Levels: A Semen Morphology and Endocrine Study

Waleed Abd Ali Abbood Al-Khafaf

General Directorate of Education in Najaf Governorate, Iraq

Abstract

Male hypogonadism and semen abnormalities are two predominant parameters in male factor infertility. This retrospective cross-sectional study aimed at exploring the role of serum testosterone concentration (total and calculated free testosterone) in the establishment of a connection between sperm morphological integrity, evaluated by Kruger's strict criteria, and ability to fertilize, focusing on sperm head defects and related cell mechanisms. The electronic patient files of 436 men with infertility were used. In the period between 2019 and 2023, the patients enrolled in the assisted reproductive department of a tertiary hospital underwent examination for hormones and semen quality in accordance with the requirements set by the World Health Organization. Application of Kruger's strict criteria for morphological classification was undertaken. In the conditions of logistical regression analysis, potential confounding factors, including age, BMI, smoking, and varicocele were also co-evaluated. There was found positive correlation between serum testosterone concentrations, particularly calculated free testosterone, and the percentage of morphologically sound spermatozoa. It was noted that serum testosterone concentrations have a downward trend along with the raising age of men while jokey frequencies of teratozoospermia keep increasing (up to 68.1% in men aged ≥43 years). Sperm head malformation was found to be the main defect type.

Keywords

Testosterone,
Male Virility,
Sperm Morphology,
Kruger's Strict Criteria,
Teratozoospermia,
Sperm DNA Fragmentation,
ICSI.

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Faculty of Science, ATBU Bauchi

Corresponding Author: Waleed Abd Ali Abbood Al-Khafaf, General Directorate of Education in Najaf Governorate, Iraq

Email: alkhafafwlyd@gmail.com

1. Introduction

Redefining the Concept of Manhood in Today's Reproductive Endocrinology:

In the past, manhood (also referred to in medical jargon as potency) revolved only around men's sexual activity; more specifically, their skills regarding getting an erection, having sex, and feeling sexually attracted to someone. Nevertheless, modern reproductive endocrinology changed that. True manhood is a combination of biological factors that impact men's sexual performance and ability to reproduce, in a way that it is governed constantly by the Hypothalamic-Pituitary-Gonadal (HPG) axis.

Testosterone is the most important male hormone and one of the drivers of the HPG axis. It helps form the valves and nerves which are needed for men's ability to maintain an erection and to desire a sexual act; moreover, this hormone takes responsibility for the conditions required in the testicle tubule for the sperm production and formation. Thus, insufficient amounts of androgens on the one hand led to lower sexual performance and, on the other hand, to poorer quality of sperm. By studying various forms of testosterone, doctors will be able to understand that there are cases where there exist cases of impotence, despite having certain malfunctioning sperm.

The Changing Concept of Male-Related Infertility:

About 50% of involuntary infertility cases worldwide can be attributed to male infertility, either singly or in combination with female infertility. During past decades, diagnosis and treatment of male infertility have changed dramatically, including the shift from the simple assessment of the sperm count to the detailed evaluation of the sperm functions and morphology. The idea of male virility in a medical context is connected with the reproductive life span of the male which consists of the ability to produce satisfactory quantity of morphologically normal, progressively motile spermatozoa with preserved genetic information.

Testosterone is produced mainly by Leydig cells in the interstitial tissue of testis under the influence of the luteinizing hormone (LH). This process is controlled by the hormone produced by the hypothalamus, which is responsible for regulation of the hypothalamus-pituitary-gonadal (HPG) axis. Disturbances occurring at any level of this axis can lead to the development of primary or secondary gonadal insufficiency.

Semen Quality Assessment and Important Milestones:

The clinical examination of semen quality underwent development through significant milestones in history, starting from basic visual microscopy, passing through advanced counting chambers (e.g., Makler and Neubauer) and going to Computer-Assisted Sperm Analysis (CASA) systems. At the same time, the World Health Organization (WHO) updated its lab manuals by introducing its sixth edition in 2021 and determining lower reference limits on the basis of huge global datasets assembled together.

Nevertheless, the traditional indicators (sperm concentration and motility) remain insufficient to explain a lot of cases of unexplained infertility as well as poor results of Assisted Reproductive Technologies (ART). Morphology which is defined by Kruger's criteria has appeared to be an important index for assessing the fertilization ability of sperm, integrity of acrosome, and embryonic development after fertilization.

Problem Statement

Although there is ample evidence regarding testosterone's role in conventional semen parameters, there exists limited literature that explicitly addresses testosterone levels (both total and calculated free) in relation to specific sperm morphology defects based on Kruger's strict criteria. Additionally, re-definition of male virility to include both sexual power and healthy reproductive sperm makes for an intricate diagnostic dilemma since vascular, hormonal, and molecular factors intertwine with each other.

Therefore, there exists a need for a comprehensive study to examine the effects of testosterone shortage on identified morphological sperm abnormalities, oxidative stress indices, and outcomes of pregnancies achieved via natural conception versus ICSI.

The goals of this study are

1. To establish the statistical relationship between both total and calculated testosterone levels on free testosterone levels as well as Kruger's strict criteria-based percentage of normal spermatozoa.
2. To assess how testosterone deficiency affects specific defect morphology (head, midpiece, and tail defect) and the resulting effect on conception rate and ICSI success rate.
3. To identify the biological mechanisms through which androgen deficiency leads to teratozoospermia with an emphasis on seminal oxidative stress and DNA fragmentation (DFI).
4. To present findings from the study that can help build the basis for evidence-based clinical linkage of assessment of male virility with optimized diagnostic protocols in reproductive medicine.

2. Literature Review

Researchers have devoted considerable effort in the last 10 years to comprehending the relationship between male endocrine status and sperm quality. Studies have differed greatly in research designs as well as study groups. Below is a nice overview of the most significant findings on this topic:

1. Al-Ghamdi et al. (2021): The authors performed a cross-sectional study, which involved a sample of 312 men aged 24 to 52 years, who came to the assisted reproductive center in Saudi Arabia for primary or secondary infertility that persisted for at least one year. The level of total testosterone, free testosterone, LH, and FSH was measured, as well as comprehensive analysis of semen, which included a thorough morphological study according to Kruger's criteria. The researchers have discovered a statistically significant positive correlation between free testosterone and the percentage of morphologically normal spermatozoa. The relationship was less apparent in the case of total testosterone that did not hold any significance after taking into consideration BMI. The authors criticized total testosterone and regarded free testosterone as a more reliable physiological marker.

2. Rastrelli et al. (2019): performed a detailed retrospective study where they enrolled 4,173 adult males in Italy who had been referred for sexual dysfunction and fertility assessment. The authors used multiple logistic regression modeling to analyze both the endocrine and seminal parameters. The study results demonstrated that the risk of severe teratozoospermia was 2.7 times greater among men with total testosterone levels <8 nmol/L compared to eugonadal subjects despite adjusting for age, smoking, and varicocele status.

3. Al Masri and Al Hussaini (2022): A study conducted in Egypt measured a cohort of 185 men with isolated teratozoospermia (without significant abnormalities in count or motility) against a reference fertile control group of 90 men. Analysis revealed that the average total testosterone levels in men with teratozoospermia were significantly lower than in men in the control group (3.8 ng/mL vs. 5.2 ng/mL, $p<0.001$). It was also found that only head defects were found to have a statistically significant correlation with lower testosterone

levels, while no such correlation was found for midpiece and tail defects.

4. Balasubramanian et al. (2020): Balasubramanian and coworkers implemented a cohort study in India with the participation of 220 couples that received ICSI treatment with the goal of establishing how male testosterone levels impact ICSI success independently of semen characteristics. The study indicated that when total testosterone surpassed 120 nmol/L, the fertilization rate per egg injected was 71%. However, when testosterone values fell below the threshold, fertilization fell to 54% (p=0.003). However, the noted difference became non-significant after accounting for the percentage of normal forms of sperm, indicating that morphology has a mediating effect in the relationship between testosterone level and ICSI success.

5. Al-Bardisi and colleagues (2018): Al-Bardisi and his colleagues conducted a study on the data from 5000 males visiting Hamad Medical Corporation Infertility Clinic in Qatar with the aim of studying the relationship between oxidative stress in semen (as defined by the degree of lipid peroxidation in seminal plasma), testosterone values and sperm morphology. Their multivariate analysis indicated a significant inverse relationship between oxidative stress and normal sperm morphology ($r=-0.41$, $p<0.001$) and oxidative stress and testosterone levels ($r=-0.28$, $p<0.001$). They proposed a causal model which states that if one has a low concentration of testosterone, intratesticular antioxidant defenses are compromised and oxidative stress gets higher, leading to the detrimental impact of ROS on developing sperm membranes and nuclear DNA thus resulting in the production of spermatozoids that are abnormal in their structure and performance.

Critical and Integrative Physiological Appraisal of Prior Literature

Synthesizing these empirical findings reveals several pivotal takeaways:

1. **Agreement Reached in Connection between Endocrine-Morphological Aspects:** There is a general agreement among specialists about the positive link existing between testosterone levels and the number of normal-looking spermatozoa produced, but this relation varies in terms of strength based on what testosterone value is measured (total or free) and on what extraneous factors have been taken into account.

2. **Structural Fragility of the Sperm Head:** Studies show that head deformities are particularly vulnerable to testosterone changes because of its distinct effect. This is probably due to the unusually high levels of testosterone in the testes, which are far greater than testosterone levels circulating in the bloodstream and are required for the functioning of acrosome and histone-to-protamine chromatin exchange.

3. **Oxidative Stress as an Important Mediator:** It appears that seminal oxidative stress acts as a major mechanism connecting hypogonadism and morphological changes. This opens up new possibilities for developing treatments based on testosterone replenishment or antioxidant supplementation. However, there is still a gap in knowledge concerning the role of randomized interventional

studies in determining whether raising testosterone levels can indeed save sperm morphology and enhance pregnancy results.

3. Materials and Methods

1. Study Design: This particular study was based on a cross-sectional retrospective design, using the data extracted from the electronic medical records (EMRs) recorded by an assisted reproduction facility that is affiliated with a university. This kind of design makes it possible to evaluate the relationship between the indicators of hormonal function and properties of semen in a relatively large study sample without the need for prospective follow-up.

2. The Target Audience and Sample: The target audience for this study was all male patients visiting the Andrology and Male Infertility unit of the institution from January 2019 to December 2023 who had undergone complete semen and serum testosterone analysis in one visit (or within a maximum leave of two weeks). The total sample finally included in the study consisted of 436 males after applying inclusion and exclusion criteria.

3. The inclusion criteria will be:

- Male candidates from 20 to 55 years old.
- History of either primary or secondary infertility for at least one year with no protected sexual intercourse.
- The availability of sperm analysis report with regards to sperm morphology assessment according to Kruger's strict criteria performed by certified lab technician.
- Signed permission to use clinical data for research purposes.

4. **Exclusion Criteria:** Patients who met the following criteria were disqualified from the study: Confirmed Obstructive Azoospermia: Diagnosis was performed using radiologic study or via surgical operation. Exogenous Hormonal Manipulation: Involvement of exogenous hormones into the body, e.g. testosterone, clomiphene citrate, gonadotropin or any other hormone capable of the alteration of testosterone dynamics during three-month period prior to the collection of blood and sperm samples.

   Recent Testicular Interventions: History of testis biopsy, epididymal sperm extraction or surgical operation on scrotum within the prior 6 months. Documented Genetic Aberrations: Chromosomal anomalies or genetic alterations, e.g. the presence of Klinefelter syndrome or AZF regions deleted from Y chromosome. Severe Unstable Systemic Pathology: Systemic diseases that can cause violation of the spermatogenesis process on their own as well as to impede the operation of the HPG axis, e.g. severe liver pathology, kidney failure or some malignancies.

5. **Data Collection:** The following data were obtained from the EHR database at the center:

Demographic and Clinical Variables: Age (years) BODY MASS INDEX (BMI, "kg/m" ^2), smoking status (active smoker/former smoker/nonsmoker), duration of infertility (years), type of infertility (primary vs secondary), and the presence/grade of varicocele.

- **Endocrine Profile:** Total testosterone (ng/dL), calculated free testosterone

(pg/mL), luteinizing hormone (LH, mIU/mL), follicle stimulating hormone (FSH, mIU/mL), and sex hormone binding globulin (SHBG, nmol/L).

- **Semen Parameters:** Volume of ejaculate (mL), sperm count (×10^6/mL), total motile sperm count (×10^6), progressive motility (%), percentage of normal spermatozoa (%), and main cause of defective spermatozoa (head, midpiece, tail, or mixed defects).

- **Fertilization Outcomes:** Natural pregnancy achieved within six months after the first appointment or successful ICSI cycles (fertilization rate, cleavage rate, clinical pregnancy rate).

6. Evaluation of Sperm Characteristics and Structure: First, semen samples were taken using the masturbation technique and delivered to the laboratory within half an hour. Samples were then liquefied at 37 °C in the incubator for less than 60 minutes. Macroscopic observation (color, volume, viscosity, and pH measurements) was done first, followed by the microscopic analysis using light microscopic observation and computerized sperm analysis for sperm count and their motility.

For morphological assessment of the smear, both dry air-dried smear preparation and staining technique employing modified Papanicolaou or Diff-Quik stain technique, and use of oil immersion lens at 1000× magnification was used. More than 200 spermatozoa were used for assessment while following Kruger's classification of sperm morphology. The percentage of observed normal forms of sperm morphology and the most commonly occurring abnormality were assessed. The assessment was carried out independently by two professional medical personnel ensuring accurate results.

7. Statistical Analysis: Data entry and analysis were done using SPSS (Version 28). Descriptive statistics were reported as mean ± standard deviation (SD) for continuous variables and in terms of frequency and percentage for categorical variables. Correlations were evaluated using either Pearson's correlation coefficient or Spearman's rank correlation coefficient depending on the normality of the data. Group means were compared using either independent samples t-test or analysis of variance (ANOVA). Multivariable logisitic regression models were formulated to find independent predictors of teratozoospermia and fertilization success. A p-value of <0.05 was regarded as statistically significant.

8. Ethical Considerations: The study design received approval from the Ethics Committee for Scientific Research at the center. The confidentiality of the patients was preserved by anonymizing their medical records. Since the study was retrospective and carried out on already existing medical data, there were no further interventions or risk.

4. Results

Demographic Characteristics and Their Association with Teratozoospermia

A total of 436 men aged between 22 and 54 years, averaging at 34.7±7.2 years were included in the study. The men were divided into 4 different age groups, and for each group, the ratio of men with the required

criterion of ≥4% normal spermatozoa as compared to the ones having less than 4% normal spermatozoa was computed as well as the average serum total testosterone. It is noted that there is a tendency for teratozoospermia to increase and the serum testosterone to decrease with age, especially in men above 40 years of age.

Table (1)
Demographic distribution, age of patients, and their association with teratozoospermia rate and testosterone levels.

Age Group (Years)	Patient Count (n)	Percentage (%)	Mean Normal Morphology (%±SD)	Teratozoospermia Prevalence (<4%)	Mean Total Testosterone (ng/dL±SD)	p-value*
22–29	87	20.0	5.8±1.4	28.7% (25/87)	542±98	Reference
30–35	148	33.9	4.9±1.2	39.2% (58/148)	485±82	0.031
36–42	132	30.3	3.6±1.1	52.3% (69/132)	412±75	0.002
43–54	69	15.8	2.4±0.9	68.1% (47/69)	325±64	<0.001
Total / Overall	436	100.0	4.3±1.5	44.7% (195/436)	458±95	—

* p-value calculated via One-Way Analysis of Variance (ANOVA) compared to the reference age group (22–29 years).

The mean percentage of normal morphology showed a consistent decline from 5.8% in the youngest age group to 2.4% in the older group. The decline in normal morphology correlated with a decrease of mean total testosterone from '542 ng(dL)' to '325 ng(dL).' Moreover, the presence of teratozoospermia was 68.1% among men older than 43 years of age, which is approximately two times more than that of men in their twenties.

Correlation Between the Rate of Teratozoospermia and Success of Fertilization:

The subjects were divided into three different categories based on their percentage of normal sperm morphology: Normal Morphology (≥4%), Mild Teratozoospermia (2-3%), and Severe Teratozoospermia (0-1%). The natural conception/ICSI outcomes were monitored for 6 months after the evaluation.

Table (2)
Association between normal morphology percentage, natural conception, and ICSI success rates.

Morphology Group	Patient Count (n)	Mean Total Testosterone (ng/dL)	Spontaneous Pregnancy Rate within 6 Months (%)	ICSI Fertilization Rate per Injected Oocyte (%)	ICSI Clinical Pregnancy Rate (%)	p-value*
Normal Morphology (≥4%)	241 (55.3%)	512±88	24.5% (59/241)	68.3%±12.1	41.9% (101/241)	Reference
Mild Teratozoospermia (2%–3%)	118 (27.1%)	415±74	11.0% (13/118)	57.6%±14.3	32.2% (38/118)	0.008
Severe Teratozoospermia (<2%)	77 (17.6%)	310±59	3.9% (3/77)	43.1%±16.5	19.5% (15/77)	<0.001

* p-value calculated using Chi-square (χ^2) test for pregnancy rates and independent samples t-test for fertilization rates, relative to the reference group.

The information presented shows noteworthy variations in reproductive success rate, where spontaneous pregnancy percentages decreased from 24.5% in the standard morphology group to a mere 3.9% in the severe teratozoospermia group. In terms of ICSI results, the fertilization rate reduced from 68.3% to 43.1% and the clinical pregnancy rate reduced from 41.9% to 19.5%. These figures were parallel with a gradual reduction in serum testosterone values across the three categories of study group participants, lending support to the theory of a three-parameter link between testosterone, sperm morphology and fertilization capability.

Morphological Defect Patterns and Their Impact on Motility

Commonly observed defect patterns were assessed in 195 workers having been diagnosed with teratozoospermia (with normal forms being less than 4%). Each of the workers was assigned a type based on the primary structural defect of the sample. The measurement parameters every subgroup were total progressive mobility, serum testosterone, and DNA Fragmentation Index (DFI).

Table (3)
Most common morphological defect patterns and their impact on sperm motility, testosterone levels, and DNA fragmentation.

Predominant Defect Pattern	Patient Count (n)	Proportion of Teratozoospermic Cases (%)	Mean Progressive Motility (%±SD)	Mean Total Testosterone (ng/dL±SD)	Mean DFI (%±SD)
Head Defects (Macro, Pyriform, Vacuolated, Tapered)	112	57.4%	32.4±7.8	342±61	28.6±5.4
Midpiece Defects (Bent neck, Distended, Cytoplasmic droplets)	29	14.9%	28.1±6.2	428±71	21.2±4.1
Tail Defects (Short, Coiled, Duplicate, Absent)	22	11.3%	16.8±4.5	451±76	18.4±3.9
Mixed Defects (Multiple anatomical regions)	32	16.4%	21.5±5.3	318±58	31.2±6.1

According to Table 3, the main type of defect is head defect, which is involved in 57.4% of cases with teratozoospermia, and this defect type is characterized by the lowest value of total testosterone (342" ng/dL") and maximum level of DNA fragmentation (28.6%).

Tail defect has the strongest negative effect on motility (16.8%); however, a decline in testosterone is not high. This may indicate that tail deformation process could take place through different mechanism from those related to hormonal level. Defects mixed have the worst clinical situation

because of a decrease in testosterone level (318ng/dL) and high DFI score (31.2%).

Logistic Regression Analysis Results:

A multivariable model was used in order to create the logistic regression to determine independent predictors of teratozoospermia (<4% normal forms) while taking into account the possible effects of age, BMI, smoking status and varicocele.

The model proved that measured free testosterone is an independent predictor with the values of ("OR"=0.87; 95% CI=0.81-0.93; p<0.001) proving that for each 1" pg/mL" unit increased in free testosterone, chances for teratozoospermia decrease by 13%. In addition, age over 40 is also an independent risk factor ("OR"=2.14; 95% CI=1.38-3.32; p=0.001) as well as active smoking ("OR"=1.78; 95% CI=1.19-2.67; p=0.005). Varicocele did not show independent statistical significance while controlling for free testosterone (p=0.072) indicating that the negative influence of it on sperm morphology might be mediated by the

decrease of testosterone levels because of the presence of varicocele.

5. Discussion

1. Age-Related Decline in Testicular Function, Sperm Morphology, and Systemic Virility:

According to the empirical data included in Table 1, there is a statistically significant correlation between paternal age and the two measured parameters: serum total testosterone and the percentage of morphologically normal spermatozoa ($p<0.001$).

Specifically, mean total testosterone levels in males aged 22–29 years were 542±98 ng/dL, and those in men aged 43–54 years are only 325±64 ng/dL. In parallel to the changes in testosterone levels, the mean percentage of morphologically normal sperm decreased from 5.8±1.4% to 2.4±0.9%, leading to the increases in the proportion of the teratozoospermia cases (<4% normal forms) from 28.7% in men aged 22–29 years to 68.1% in men aged 43 and older.

The phenomenon has a strong connection with the pathophysiology of Late-Onset Hypogonadism (LOH). Androgens circulating in the blood typically decline by 1 to 2% every year after the age of 30. This age-related decline influences not only the systemic virility of the organism, including energy levels and muscle balance, but also the litestical microenvironment.

The loss of Leydig cells with age, combined with their lower responsiveness to LH, results in testosterone levels dropping below the critical point needed to maintain the stages of spermiogenesis properly. Moreover, results obtained via multivariable binary logistic regression demonstrated that free testosterone is a predictor of teratozoospermia, even after age-related factors are taken into consideration, which indicates that androgen deficiency is an independent factor responsible for impaired sperm forming and not only serves as an epiphenomenon of aging.

2. Sperm Morphology as a Biomarker of Systemic Male Virility and Fertilizing Competence:

The information in Table 2 indicates the negative effect of sperm morphology deterioration on fertility in both natural conception and assisted reproductive processes. The spontaneous pregnancy rate within six months decreased substantially, from 24.5% in a normal morphology group down to 11.0% in mild teratozoospermia group and only 3.9% in a severe teratozoospermia group, ($p<0.001$). This exactly replicates the decline in serum testosterone levels (512±88" ng/dL", 415±74" ng/dL" and 310±59" ng/dL", correspondingly).

This negative impact was also manifested during ICSI cycles when the fertilization rate per every injected oocyte was observed. The fertilization rate dropped from 68.3±12.1% in normal group down to 43.1±16.5% in the case of severe teratozoospermia. Clinical pregnancy rates diminished from 41.9% down to 19.5%. Why does sperm morphology influence ICSI results when physical barriers of zona pellucida are avoided?

This answer confirms that sperm morphology anomalies are not just anatomic changes but also biological markers of men's fertility problems that stem from low male hormone levels. Insufficient testosterone reduces the

activity of crucial sperm elements needed for egg fertilization (for instance, it affects Phospholipase C zeta expression) and violates centriole organization necessary for spindle formation after fertilization. Thus, morphology is indicative of subcellular and genomic competence.

3. Predominance of Sperm Head Defects and Their Hormonal Dependence:

One of the most important pieces of evidence seen in Table 3 shows that the leading defect in teratozoospermic individuals was the defect of the head region because of head anomalies occurred in 57.4% of the surveyed group (n=112) and were linked to the lowest level of testosterone (342±61 ng/dL) as well as the highest DNA fragmentation index ("DFI"=28.6±5.4%).

The tail deformation caused 11.3% (n=22) along with the maximum effect on progressive motility (16.8±4.5%) and still had the best level of testosterone (451±76 ng/dL).

In the case of the head defects, the hormones play a very important role in the formation of heads. The changes in the levels of testosterone will violations in the process of the replacement of somatic histones with protamines (shown as P1 and P2), which takes place during the process of chromosome condensation and needs to be held under the influence of the elevated level of testosterone.

The low level of testosterone will lead to the failure of this process and is linked with the presence of histone nucleosomes. At the same time, the tail deformation is thought to be more genetic than hormonal.

4. Molecular Mechanisms: Oxidative Stress and Sperm DNA Damage:

Testosterone acts directly to protect against the occurrence of oxidative stress in the testes by increasing the activity of the antioxidant enzymes (SOD, catalase, and GST) in Sertoli cells and germ cells, while at the same time it helps to keep the Blood-Testis Barrier (BTB) intact.

When the available testosterone is reduced, an increase in reactive oxygen species (ROS) decapitates the process of lipid peroxidation in the sperm membrane full of polyunsaturated fatty acids making it impossible for the membrane to become fluid and perform acrosomal reaction. In addition, ROS penetrate through the nuclear membrane making breaks in the DNA with the help of ROS.

The above-mentioned molecular mechanism is confirmed by our data presented in the Table 3 showing the greatest percentages of DFI in the groups of head (28.6%) and mixed defect (31.2%) whereas these groups have the lowest testosterone levels among other groups (342" ng/dL and 318" ng/dL respectively).

6. Conclusions and Recommendations

1. Conclusions

Based on the empirical data and integrated physiological examination, it is concluded in this study that:

- Androgen-Morphology Association: A decrease in testosterone levels in serum (in the first place calculated free testosterone) is independently connected with drastic deterioration of sperm morphology according to strict Kruger's criteria.

- Decline With Age: Increase in age of father brings about simultaneous decline in testosterone in the blood and sperm morphology, attaining maximum occurrence of teratozoospermia in men aged 43 years and older (68.1%).
- Head Defect Susceptibility: An abnormality of sperm head shape is the most widespread defect (57.4%) caused by a lack of androgens, increased oxidative stress in sperm, and fragmentation of chromatin ("DFI"=28.6%).
- Effect on Male Fertility and ART: Structural teratozoospermia indicates serious subcellular impairments leading to reduction of natural fertility (3.9%) and significant decrease of ICSI fertilization rates (43.1%).

2. Recommendations

A. Clinical Recommendations

1. **Routine Hormonal Evaluation:** Include the determination of total and free testosterone levels in the course of examination of all male patients with infertility due to teratozoospermia.
2. **Targeted Hormonal Therapy:** For patients with predominating sperm head typing defects start with the therapy enhancing natural production of androgens (such as SERMs, aromatase inhibitors, or gonadotropins) prior any expensive ART procedures. Avoid using testosterone from outside organism because it prevents the process of spermatogenesis.
3. **Sperm DNA Fragmentation Index:** Use the evaluation of DNA fragmentation tests together with strict morphology assessment. In case of advanced chromatin damage of spermatozoa, it is reasonable to consider TESE for ICSI instead of bypassing oxidative damage in ductus deferens.
4. **Lifestyle Modifications:** Explain to patients the basics of body mass management, smoking cessation, resistance training, and vitamins C and E, zinc, selenium, and coenzyme Q10 intake for HPG axis better functioning and reducing oxidation stress.

B. Academic & Research Recommendations

1. Randomized Controlled Trials: Carry out several clinical trials to assess if hormonal optimization prior to ART increases the chances of live births in teratozoospermic males.

2. Measurement of testicular testosterone: Include measurement of intratesticular and serum androgen in future studies to determine spoilers of spermiogenesis accurately.

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