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Clinical, endocrine, and testicular factors associated with sperm concentration: insights from a real-world cohort of 521 infertile men

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Abstract

Background: Male infertility results from a complex interplay of hormonal, testicular, and clinical factors. Identifying reliable non-invasive markers of spermatogenic function remains clinically relevant. This study evaluated the independent associations of follicle-stimulating hormone (FSH), testicular volume, and luteinizing hormone (LH) with sperm concentration and developed a parsimonious predictive model for predicting oligozoospermia. **Methods**: We retrospectively analyzed 521 men with infertility between 2020 and 2024. Clinical variables, testicular volume, and reproductive hormones were assessed, including FSH, LH, and total testosterone (TT). Multivariable linear regression estimated predictors of log-transformed sperm concentration. For oligozoospermia ($<15 \times 10^6$/mL), a baseline clinical model (with age, body mass index (BMI), smoking, and varicocele) was compared with a parsimonious enhanced model (baseline model + FSH + testicular volume + LH). Model performance was evaluated using the area under the curve (AUC), ΔAUC, calibration, and bootstrap internal validation. **Results**: FSH ($\beta = -0.0265$; $p < 0.001$) and testicular volume ($\beta = 0.0474$; $p = 0.0006$) were independent predictors of sperm concentration, while LH showed a weaker effect ($\beta = -0.012$; $p = 0.04$). The baseline clinical model showed limited discrimination (AUC = 0.65), whereas the enhanced model achieved superior performance (AUC = 0.75; ΔAUC = +0.10) with good calibration (slope $\approx$ 1.02) and an optimism-corrected AUC of 0.73. Sensitivity analysis in men with normal sperm counts ($\geq 20 \times 10^6$/mL; n = 92) showed results consistent with the main findings. **Conclusions**: A simple combination of FSH, testicular volume, and LH provides internally validated, moderately discriminative prediction of oligozoospermia beyond standard clinical parameters. These non-invasive biomarkers may help early risk stratification in male infertility, although external validation remains warranted.

Keywords

Follicle stimulating hormone; Infertility; Luteinizing hormone; Semen analysis; Smoking; Testicular volume; Testosterone; Varicocele

Factores clínicos, endocrinos y testiculares asociados con la concentración espermática: perspectivas de una cohorte del mundo real de 521 varones infértiles

Resumen

Antecedentes: La infertilidad masculina resulta de una compleja interacción entre factores hormonales, testiculares y clínicos. Identificar marcadores no invasivos y fiables de la función espermatogénica sigue siendo clínicamente relevante. Este estudio evaluó las asociaciones independientes de la hormona foliculoestimulante (FSH), el volumen testicular y la hormona luteinizante (LH) con la concentración espermática, y desarrolló un modelo predictivo parsimonioso para predecir oligozoospermia. **Métodos**: Se analizaron retrospectivamente 521 hombres con infertilidad entre 2020 y 2024. Se evaluaron variables clínicas, volumen testicular y hormonas reproductivas, incluyendo FSH, LH y testosterona total (TT). Se utilizó regresión lineal multivariable para identificar predictores de la concentración espermática transformada logarítmicamente. Para la oligozoospermia ($<15 \times 10^6$/mL), se comparó un modelo clínico basal (edad, índice de masa corporal (IMC), tabaquismo, varicocele) con un modelo mejorado parsimonioso (basal + FSH + volumen testicular + LH). El rendimiento del modelo se evaluó mediante el área bajo la curva (AUC), ΔAUC, calibración y validación interna mediante bootstrap. **Resultados**: La FSH ($\beta = -0.0265$; $p < 0.001$) y el volumen testicular ($\beta = 0.0474$; $p = 0.0006$) fueron predictores independientes de la concentración espermática, mientras que la LH mostró un efecto más débil ($\beta = -0.012$; $p = 0.04$). El modelo clínico basal mostró una discriminación limitada (AUC = 0.65), mientras que el modelo mejorado alcanzó un rendimiento superior (AUC = 0.75; ΔAUC = +0.10), con buena calibración (pendiente $\approx$ 1.02) y un AUC corregido por optimismo de 0.73. El análisis de sensibilidad en hombres con recuentos espermáticos normales ($\geq 20 \times 10^6$/mL; n = 92) mostró resultados coherentes con los hallazgos principales. **Conclusiones**: Una combinación simple de FSH, volumen testicular y LH ofrece una predicción validada internamente, de discriminación moderada, de la oligozoospermia más allá de los parámetros clínicos estándar. Estos biomarcadores no invasivos pueden facilitar la estratificación temprana del riesgo, si bien se requiere validación externa.

Palabras Clave

Análisis de semen; Hormona foliculoestimulante; Hormona luteinizante; Infertilidad; Tabaquismo; Testosterona; Varicocele; Volumen testicular

1. Introduction

Infertility is a major global health concern, imposing substantial medical, psychological, and socioeconomic burdens. Approximately one in six individuals of reproductive age experience infertility during their lifetime, underscoring the need for streamlined and evidence-based evaluation of both partners [1, 2]. In men, etiologies are heterogeneous, encompassing primary testicular dysfunction, endocrine abnormalities, urogenital pathologies, environmental and lifestyle exposures, genetic and epigenetic alterations, and age-related changes [3].

The cornerstone of male infertility assessment remains semen analysis, complemented by targeted physical examination and selective endocrine testing (follicle stimulating hormone (FSH), luteinizing hormone (LH), total testosterone (TT), estradiol (E2), and prolactin (PRL)) [4, 5]. The sixth edition of the World Health Organization (WHO) Laboratory Manual (2021) standardized the semen analysis procedures and reporting, including the definition of oligozoospermia ($<15 \times 10^6$/mL). However, semen parameters alone provide only partial insights into male reproductive potential. Their interpretability improves when contextualized with endocrine markers and physical examination findings, such as testicular volume and the presence of varicocele [6, 7].

Varicocele, defined as abnormal dilatation of the pampiniform plexus, is one of the most common and potentially correctable conditions observed in infertile men. Its prevalence is approximately 15% in the general male population, 35–40% among men with primary infertility, and up to 80% among those with secondary infertility [6]. Pathophysiological mechanisms proposed include scrotal hyperthermia, hypoxia, oxidative stress, and reflux of adrenal or renal metabolites. International guidelines (European Association of Urology (EAU), American Urological Association (AUA)/American Society for Reproductive Medicine (ASRM)) recommend surgical treatment only in men with palpable varicocele and abnormal semen parameters, while discouraging intervention in subclinical cases [7].

Beyond focal pathology, demographic and lifestyle factors also influence semen quality. Increasing paternal age has been associated with impaired motility, abnormal morphology, and higher rates of sperm DNA fragmentation [8, 9]. The role of obesity is less consistent: some meta-analyses show negligible effects, while others report reductions in sperm concentration, ejaculate volume, and total motile count with increasing body mass index (BMI) [10]. Cigarette smoking, by contrast, has been consistently linked to lower sperm counts, reduced motility, increased morphological abnormalities, and impaired sperm function, often mediated by oxidative stress and sperm DNA fragmentation (SDF) [11].

Despite decades of research, there remains a need for large, integrated analyses combining semen, endocrine, physical, and lifestyle parameters to improve risk stratification and guide management [12–15]. Most previous studies have focused on single predictors in isolation, limiting their translational value.

To address this gap, the present study aimed to identify independent determinants of sperm concentration, particularly focusing on FSH, LH, and testicular volume, and to develop and internally validate a parsimonious predictive model for oligozoospermia ($<15 \times 10^6$/mL). By integrating routinely available clinical, hormonal, and anatomical parameters, this study sought to provide a practical, evidence-based framework for the early identification of impaired spermatogenesis and to enhance the clinical applicability of male infertility evaluation.

2. Materials and methods

2.1 Study design

We conducted a retrospective observational study at a tertiary andrology clinic between January 2020 and December 2024. The study protocol was approved by the institutional review board, and the requirement for informed consent was waived due to the retrospective nature of data collection. The study was designed with two a priori objectives. The primary inferential objective was to determine the independent associations of FSH, testicular volume, and LH with sperm concentration. For this objective, sperm concentration (million/mL) was treated as a continuous outcome and log-transformed to meet model assumptions. The secondary predictive objective was to develop and internally validate a parsimonious predictive model for oligozoospermia, defined as sperm concentration $<15 \times 10^6$/mL. This model incorporated non-invasive endocrine and testicular parameters (FSH, testicular volume, and LH) in addition to baseline clinical factors (age, BMI, smoking, and varicocele), and was evaluated using discrimination and calibration. This dual framework was selected to move beyond descriptive associations and provide clinically actionable tools for early risk stratification in male infertility.

2.2 Study population

A total of 521 consecutive men who underwent evaluation for infertility at our tertiary andrology clinic were included. Consecutive sampling was used to minimize selection bias and ensure real-world generalizability of predictive modeling.

Eligible participants were men aged 18 years or older who underwent clinical assessment for male infertility, had at least one baseline semen analysis available according to WHO criteria (ejaculate volume, sperm concentration, motility, and morphology), and had documented testicular volume by ultrasound together with endocrine evaluation, including FSH, LH, TT, E2, and PRL.

Exclusion criteria comprised known genetic causes of spermatogenic failure (*e.g.*, Klinefelter syndrome, azoospermia factor (AZF) microdeletions); obstructive azoospermia (*e.g.*, vasectomy, congenital bilateral absence of the vas deferens); history of bilateral orchiectomy, severe testicular atrophy, or anorchia; active genitourinary infection, febrile illness, or systemic inflammatory disease; use of exogenous androgens, anabolic steroids, gonadotropins, or anti-estrogenic agents within the preceding six months; and incomplete clinical, hormonal, or semen data for primary analytic variables. Where multiple records existed, the earliest complete dataset was analyzed.

2.3 Clinical variables

Demographic variables (age, BMI, and infertility duration) and lifestyle factors (smoking status: current *vs.* non-smoker) were abstracted from medical records. Varicocele was assessed by physical examination in the standing position and confirmed with scrotal Doppler ultrasonography when indicated. Varicocele was initially graded according to the Dubin–Amelar classification (grades I–III); however, because the study was retrospective and bilateral grading data were inconsistently available, formal grading was not documented for the entire cohort, and the variable was dichotomized as present or absent for statistical analyses. Testicular volume was measured by ultrasound using the Lambert formula (length $\times$ width $\times$ height $\times$ 0.71) and reported as the mean volume of both testes when available. Testicular volume was included in both inferential and predictive models due to its established physiological relevance as a marker of spermatogenic capacity.

2.4 Semen analysis and endocrine profile

Semen analyses followed the WHO 6th edition (2021) guidelines. Patients were instructed to maintain 2–7 days of sexual abstinence. Parameters included ejaculate volume (mL), sperm concentration (million/mL), total motility (%), progressive motility (%), non-progressive motility (%), and morphology (% normal forms, strict Kruger criteria). Sperm morphology was assessed on air-dried smears stained with the Diff-Quik method. Only the first complete semen analysis was used when multiple samples were available, acknowledging inherent intra-individual variability. WHO reference thresholds (*e.g.*, $<15 \times 10^6$/mL for oligozoospermia, $<4\%$ normal morphology for teratozoospermia) were applied descriptively; however, continuous sperm concentration was used for inferential analysis, and binary classification ($<15 \times 10^6$/mL) for predictive modeling.

Morning fasting blood samples (08:00–10:00) were collected for hormonal assays (FSH, LH, TT, E2, PRL). Hormone levels were measured using standardized chemiluminescent immunoassays (Roche Cobas e602; Roche Diagnostics, Basel, Switzerland). Internal and external quality controls were applied, and reference ranges were those provided by the manufacturer.

2.5 Statistical analysis

Continuous variables were summarized as median (interquartile range (IQR)) or mean $\pm$ standard deviation (SD), and categorical variables as frequencies and percentages. Between-group comparisons used the Mann-Whitney U test or *t*-test, and correlations among variables were evaluated using Spearman's *rho*.

2.5.1 Primary inferential analysis

Multivariable linear regression was used to identify independent predictors of log-transformed sperm concentration. Age, BMI, smoking, and varicocele were included as covariates; FSH, LH, and testicular volume as key predictors. Variance inflation factor (VIF <5) confirmed acceptable collinearity. Partial R^2 was reported to quantify variable-specific contribu-

tion.

2.5.2 Secondary predictive analysis

A two-stage logistic regression framework was applied to predict oligozoospermia ($<15 \times 10^6$/mL):

- Baseline model: age, BMI, smoking, and varicocele.
- Parsimonious enhanced model: baseline model + FSH + testicular volume + LH.

Model discrimination was assessed using the area under the receiver operating characteristic curve (AUC), and incremental predictive value (ΔAUC) was calculated using DeLong's test. Internal validation used 1000 bootstrap resamples to estimate optimism-corrected AUC and calibration slope. Calibration plots were generated, and model agreement was summarized using calibration intercept and slope (ideal slope = 1). Sensitivity analysis repeated regression models among men with normal sperm counts ($\geq 20 \times 10^6$/mL) to test the robustness of FSH and testicular volume associations.

All analyses were conducted using IBM SPSS Statistics version 23.0 (IBM Corp., Armonk, NY, USA). A two-sided p-value < 0.05 was considered statistically significant.

3. Results

A total of 521 men were included in the analysis. The median age was 32 years (IQR 29–35), and the median BMI was 27.7 kg/m^2 (IQR 25.0–30.3). Infertility duration was documented in 105 men, with a median of 15 months (IQR 12–36). Varicocele was present in 313 of 520 men (60.2%), including 24 bilateral (4.6%) and 12 right-sided (2.3%) cases. Smoking status was available in 519 men, of whom 315 (60.7%) were current smokers.

Median ejaculate volume was 3.1 mL (IQR 2.4–4.4). The median sperm concentration was 4.3×10^6/mL (IQR 1.3–9.0). Total motility was 25% (IQR 14–32), progressive motility was 2% (IQR 0–3), and morphology was 0% (IQR 0–1). Median testicular volume was 12 mL (IQR 12–14).

Median total testosterone was 3.86 ng/mL (IQR 3.15–4.88), FSH was 5.14 mIU/mL (IQR 3.41–8.26), LH was 4.67 mIU/mL (IQR 3.15–6.20), and prolactin was 10.4 ng/mL (IQR 7.52–13.8). Baseline demographic, clinical, and hormonal characteristics are summarized in Table 1.

Men with varicocele had significantly lower total testosterone levels compared with those without varicocele (3.67 *vs.* 4.02 ng/mL; $p = 0.003$), whereas sperm concentration, motility, FSH, LH, and testicular volume were comparable between groups. Morphology showed a minor but statistically significant difference ($p = 0.037$), although median values were similarly low, indicating limited clinical relevance.

No significant differences in sperm concentration, motility, morphology, gonadotropins, or testicular volume were observed between smokers and non-smokers. However, current smokers demonstrated slightly higher total testosterone levels compared with non-smokers (3.95 *vs.* 3.67 ng/mL; $p = 0.027$).

3.1 Correlations among hormonal, testicular, and semen parameters

Spearman correlation analysis revealed that FSH was inversely correlated with both sperm concentration ($\rho = -0.295$, $p < 0.001$) and testicular volume ($\rho = -0.280$, $p < 0.001$). Testicular volume demonstrated a weak but statistically significant positive correlation with sperm concentration ($\rho = 0.23$, $p < 0.001$). LH also showed a modest inverse association with sperm concentration ($\rho = -0.17$, $p = 0.02$), while total testosterone and estradiol exhibited no meaningful correlations. Detailed pairwise correlation coefficients are presented in Table 2.

3.2 Predictors of sperm concentration

In multivariable linear regression analysis (n = 507), both FSH and testicular volume emerged as independent predictors of sperm concentration. After adjusting for age, BMI, smoking, and varicocele, higher FSH levels were associated with lower log-transformed sperm concentration ($\beta = -0.0265$, $p < 0.001$), whereas larger testicular volume predicted higher sperm concentration ($\beta = 0.0474$, $p = 0.0006$). LH contributed modestly but remained statistically significant ($\beta = -0.0121$, $p = 0.04$).

Total testosterone, estradiol, and prolactin were excluded from the final model due to collinearity and non-significant associations. Independent predictors of sperm concentration are shown in Table 3.

3.3 Model performance and validation

The baseline clinical model—including age, BMI, smoking, and varicocele—demonstrated limited discriminatory performance for predicting oligozoospermia ($<15 \times 10^6$/mL), with an AUC of 0.65 (95% confidence interval (CI), 0.52–0.80). In contrast, the parsimonious enhanced model (baseline model + FSH + testicular volume + LH) achieved superior discrimination, yielding an AUC of 0.75 (95% CI, 0.62–0.88) and a ΔAUC of +0.10, indicating a statistically and clinically meaningful improvement in predictive accuracy. Model calibration was favorable (slope ≈ 1.02; intercept ≈ 0.03), and bootstrap internal validation with 1000 resamples produced an optimism-corrected AUC of 0.73, confirming the model's robustness and generalizability.

Comparative performance metrics are presented in Table 4, and the receiver operating characteristic (ROC) curves for both models are shown in Fig. 1, demonstrating the superior discriminative ability of the enhanced model across relevant probability thresholds.

3.4 Sensitivity analyses

A sensitivity analysis restricted to men with normal or near-normal sperm concentrations ($\geq 20 \times 10^6$/mL; n = 92) confirmed the directional consistency of the main associations. FSH maintained a significant inverse relationship with sperm concentration, while testicular volume remained positively associated ($p < 0.01$ for both). Comparable model discrimination (AUC ≈ 0.71) was observed in this subgroup. These findings appear consistent across the sperm-concentration ranges

TABLE 1. Baseline clinical, semen, and hormonal characteristics of the study population.

Variable	Value	Available (n)
Age (yr)	32 (29–35)	521
BMI (kg/m^2)	27.7 (25–30.3)	509
Infertility duration (mon)	15 (12–36)	105
Varicocele, n (%)	313 (60.2%)	
- Bilateral	24 (4.6%)	520
- Right-sided	12 (2.3%)	
Smokers, n (%)	315 (60.7%)	519
Ejaculate volume (mL)	3.1 (2.4–4.4)	521
Sperm concentration (million/mL)	4.3 (1.3–9.0)	521
Oligozoospermia (<15 × 10^6/mL), n (%)	420 (80.6%)	521
Total motility (%)	25 (14–32)	521
Progressive motility (%)	2 (0–3)	521
Morphology (%)	0 (0–1)	521
Testicular volume (mL)	12 (12–14)	521
FSH (mIU/mL)	5.14 (3.41–8.26)	521
LH (mIU/mL)	4.67 (3.15–6.20)	521
Total Testosterone (ng/mL)	3.86 (3.15–4.88)	521
Prolactin (ng/mL)	10.4 (7.52–13.8)	521
Estradiol (pg/mL)	27.1 (22–34)	521

Values are presented as median interquartile range (IQR) for continuous variables or n (%) for categorical variables. BMI: body mass index; FSH: follicle-stimulating hormone; LH: luteinizing hormone.

TABLE 2. Correlation matrix between hormonal, testicular, and semen parameters.

Variable	Sperm concentration (×10^6/mL)	Testicular volume (mL)	FSH (IU/L)	LH (IU/L)	Total testosterone (ng/mL)
Sperm concentration (×10^6/mL)	-	$\rho = 0.23$ ($p < 0.001$)	$\rho = -0.30$ ($p < 0.001$)	$\rho = -0.17$ ($p = 0.02$)	$\rho = 0.08$ ($p = 0.21$)
Testicular volume (mL)	$\rho = 0.23$ ($p < 0.001$)	-	$\rho = -0.28$ ($p < 0.001$)	$\rho = -0.14$ ($p = 0.04$)	$\rho = 0.10$ ($p = 0.15$)
FSH (IU/L)	$\rho = -0.30$ ($p < 0.001$)	$\rho = -0.28$ ($p < 0.001$)	-	$\rho = 0.36$ ($p < 0.001$)	$\rho = -0.11$ ($p = 0.12$)
LH (IU/L)	$\rho = -0.17$ ($p = 0.02$)	$\rho = -0.14$ ($p = 0.04$)	$\rho = 0.36$ ($p < 0.001$)	-	$\rho = 0.09$ ($p = 0.19$)
Total testosterone (ng/mL)	$\rho = 0.08$ ($p = 0.21$)	$\rho = 0.10$ ($p = 0.15$)	$\rho = -0.11$ ($p = 0.12$)	$\rho = 0.09$ ($p = 0.19$)	-

FSH: follicle-stimulating hormone; LH: luteinizing hormone.

TABLE 3. Multivariable linear regression for predictors of log-transformed sperm concentration (n = 507).

Variable	β coefficient	95% CI	p value
Age (yr)	−0.0048	(−0.011, 0.001)	0.140
BMI (kg/m^2)	−0.0027	(−0.008, 0.003)	0.280
Smoking (current)	0.0143	(−0.048, 0.076)	0.650
Varicocele (yes/no)	−0.0189	(−0.074, 0.036)	0.510
FSH (mIU/mL)	−0.0265	(−0.038, −0.015)	<0.001
LH (mIU/mL)	−0.0121	(−0.023, −0.001)	0.041
Testicular volume (mL)	0.0474	(0.020, 0.074)	0.0006

Model performance: Adjusted $R^2 = 0.27$; overall model $p < 0.001$; variance inflation factor (VIF) <2.0 for all predictors. Negative β indicates an inverse relationship with sperm concentration. BMI: body mass index; FSH: follicle-stimulating hormone; LH: luteinizing hormone; CI: confidence interval.

TABLE 4. Logistic model performance for oligozoospermia (<15 × 10^6/mL).

Model	Predictors included	AUC (95% CI)	ΔAUC *vs.* baseline	Calibration slope	Bootstrap-corrected AUC
Model 1: Baseline clinical	Age, BMI, Smoking, and Varicocele	0.65 (0.52–0.80)	-	0.94	0.64
Model 2: Parsimonious enhanced	Baseline model + FSH + LH + Testicular volume	0.75 (0.62–0.88)	+0.10	1.02	0.73

Receiver operating characteristic (ROC) analysis compared a baseline clinical model (Model 1) with an enhanced model incorporating endocrine (FSH, LH) and testicular parameters. Model 2 demonstrated improved discrimination (ΔAUC = +0.10), favorable calibration, and consistent internal validity after bootstrap correction. AUC: area under the curve; FSH: follicle-stimulating hormone; LH: luteinizing hormone; BMI: body mass index; CI: confidence interval.

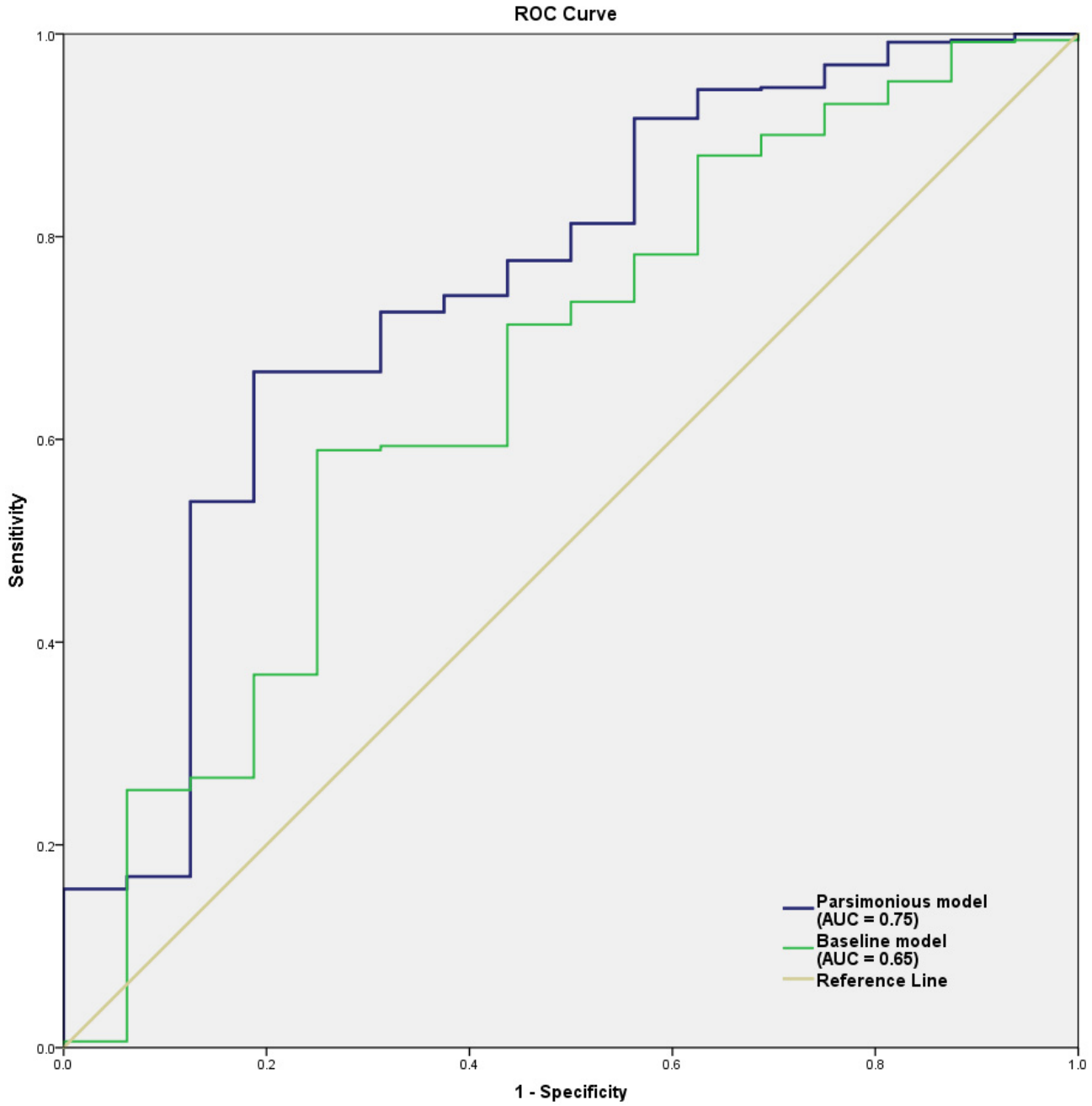

FIGURE 1. Receiver operating characteristic (ROC) curves for the baseline clinical model (green, AUC = 0.65) and the enhanced model (blue, AUC = 0.75) predicting oligozoospermia (<15 × 10^6/mL). The enhanced model, including FSH, LH, and testicular volume, showed better discrimination than the baseline model. AUC: area under the curve.

and should be regarded as supportive rather than confirmatory.

4. Discussion

This study analyzed a large, real-world cohort of 521 infertile men and provides new insights into the diagnostic value of hormonal and testicular parameters. Beyond descriptive correlations, our work advances the field by developing and internally validating a parsimonious predictive model incorporating FSH, LH, and testicular volume to identify oligozoospermia. The model demonstrated good discrimination (AUC = 0.75) and maintained consistent performance after bootstrap internal validation (optimism-corrected AUC = 0.73), suggesting that these routinely available markers may offer practical, non-invasive support for individualized risk assessment in male infertility.

Serum FSH emerged as the most consistent hormonal correlate of sperm concentration, maintaining a significant inverse association after multivariable adjustment. This finding aligns with established physiology, as elevated FSH reflects Sertoli cell dysfunction and reduced inhibin B feedback, both characteristic of impaired spermatogenesis [13]. LH also showed a modest but independent negative association with sperm concentration, consistent with its complementary role within the hypothalamic–pituitary–gonadal axis and possible subtle Leydig cell dysfunction [14]. In contrast, total testosterone, estradiol, and prolactin were not independently associated with sperm concentration, consistent with previous evidence indicating limited diagnostic value of these hormones in the absence of overt endocrine abnormalities [15].

Testicular volume demonstrated a modest yet statistically significant positive relationship with sperm concentration, supporting its physiological relevance as a surrogate of seminiferous mass and spermatogenic capacity [16–18]. This association remained independent of gonadotropin levels and contributed meaningfully to model performance, with the inclusion of testicular volume improving discrimination from AUC 0.65 to 0.75. Although the effect size was moderate, testicular ultrasonography remains a simple, low-cost, and non-invasive adjunct that can provide supportive diagnostic information, particularly when semen testing is inconclusive or unavailable [19].

Varicocele was identified in approximately 60% of participants. Although semen parameters did not differ significantly between groups, men with varicocele exhibited lower total testosterone levels, indicating possible Leydig cell dysfunction. This observation is consistent with previous studies showing that varicocele may impair androgen synthesis and that surgical correction can partially restore testosterone production [20, 21]. These findings highlight the relevance of monitoring endocrine function in men with varicocele, even when semen parameters appear normal.

Smoking, classified, simply as “current *vs.* non-smoker”, was not associated with semen outcomes. Interestingly, smokers had slightly higher testosterone levels, a finding also reported in previous studies and possibly reflecting compensatory endocrine responses [22]. However, the absence of quantitative exposure data (*e.g.*, pack-years, cotinine levels) likely underestimated the impact of smoking. Prior studies consistently link smoking to impaired semen quality through oxidative stress and increased sperm DNA fragmentation (SDF) [23–29]. Incorporating oxidative stress biomarkers and SDF testing into future studies may better define the reproductive risks of tobacco use.

We developed and internally validated a streamlined logistic model to identify men at risk of oligozoospermia. The model integrates FSH, LH, and testicular volume with basic clinical parameters, providing an interpretable and easily applicable framework for clinical use. This approach parallels recent studies emphasizing hormonal predictors of spermatogenic failure. Kobayashi *et al.* [30] demonstrated that artificial intelligence models based solely on serum hormones can effectively screen for male infertility, with FSH emerging as the dominant feature, while Tradewell *et al.* [31] validated simpler logistic algorithms combining FSH and testicular volume to estimate azoospermia risk. Our findings extend these concepts to oligozoospermia, showing that a small set of routinely available markers can yield comparable diagnostic accuracy without reliance on complex or opaque machine-learning systems. Although not intended to replace semen analysis, such models may facilitate early triage, guide endocrine evaluation, or prioritize further testing in cases where semen assessment is delayed or inconclusive.

The main strengths of this study include its relatively large real-world cohort, standardized assessment of hormonal, anatomical, and clinical parameters, and the use of prespecified multivariable models with internal validation and collinearity testing. These features enhance methodological rigor and reproducibility.

Nevertheless, several limitations should be acknowledged. The retrospective, single-center design may limit generalizability; most participants had only one semen analysis, which may not fully reflect intra-individual variability; although Dubin–Amelar grading was performed in a subset of patients, incomplete or unilateral documentation precluded quantitative analyses, and varicocele was therefore analyzed dichotomously (present/absent); and fertile controls were not included. Although men with known post-testicular causes of infertility were excluded, subtle obstructive or environmental factors cannot be completely ruled out. Furthermore, detailed lifestyle and environmental exposures were not captured, and advanced semen measures, such as sperm DNA fragmentation, were unavailable [32, 33].

Future research should aim to externally validate this model across diverse populations and incorporate additional biomarkers, such as inhibin B, anti-Müllerian hormone, oxidative stress markers, and sperm DNA fragmentation, to refine predictive accuracy [34, 35]. Standardized prospective designs, including repeated semen analyses, detailed varicocele assessment, and post-treatment follow-up—particularly after varicocelectomy—would further enhance translational relevance. Ultimately, integrating biochemical and anatomical markers within predictive frameworks may help shift male infertility evaluation from descriptive diagnostics toward precision-oriented, risk-based clinical decision-making.

5. Conclusions

In summary, this study identified FSH, LH, and testicular volume as independent correlates of sperm concentration and combined these parameters into a clinically interpretable model for predicting oligozoospermia. The model achieved good internal validity and moderate discriminative performance, demonstrating that a small set of routinely available, non-invasive markers can meaningfully inform risk stratification in male infertility. While semen analysis remains the diagnostic cornerstone, incorporating endocrine and anatomical data may support earlier identification of impaired spermatogenesis and optimize patient counseling and referral. External validation and the integration of emerging biomarkers are warranted to confirm the generalizability and clinical utility of this simplified predictive framework.

AVAILABILITY OF DATA AND MATERIALS

The data presented in this study are available on reasonable request from the corresponding author.

AUTHOR CONTRIBUTIONS

BÇ—designed the research study; collected and analyzed the data. CTG—analyzed the data and wrote the manuscript. Both authors contributed to editorial changes in the manuscript, provided advice on relevant literature, and approved the final version.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

This study was conducted in accordance with the principles of the Declaration of Helsinki and was approved by the Ethics Committee of Taksim Training and Research Hospital on 20 August 2025 (decision no. 64). As this was a retrospective study using anonymized patient data, the requirement for informed consent to participate was waived by the ethics committee.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

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