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ORIGINAL ARTICLE

THE IMPACT OF MICROSURGICAL VARICOCELECTOMY ON SERUM TESTOSTERONE LEVEL AND SEMEN PARAMETERS IN SUBFERTILE MEN WITH CLINICALLY EVIDENT TESTICULAR VARICOCELE

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ABSTRACT

Background: Testicular varicocele is a prevalent condition contributing to male infertility by disrupting spermatogenesis and reducing testosterone production. This study aimed to evaluate the impact of sub-inguinal microscopic varicocelectomy on serum testosterone levels and seminal fluid parameters in subfertile men.

Materials & Methods: This prospective study was conducted in the Azadi Teaching Hospital in Kirkuk between January 2023 and February 2024. Fifty men, aged 19-45, diagnosed with unilateral or bilateral varicocele and abnormal semen parameters (oligo-, astheno-, or oligoasthenoteratospermia) were recruited. Infertility duration exceeded three years in all cases. Exclusion criteria included azoospermia or normal semen profiles. Varicocele was confirmed via physical examination and scrotal ultrasound. Preoperative and six-month postoperative serum testosterone levels and seminal parameters were compared. Data collection involved standardized hormonal assays and semen analyses, with statistical analysis conducted to determine significance.

Results: Of the participants, 76% had left-sided varicocele, and 24% had bilateral involvement. Postoperative serum testosterone levels significantly increased from 3.18 ±0.88 to 4.07 ±0.70 ng/ml ($p < 0.001$). Sperm motility also improved significantly from 17.2% ±7.43% to 27.4% ±8.22% ($p < 0.001$). However, sperm count and morphology showed no statistically significant changes after surgery ($p > 0.05$).

Conclusion: Sub-inguinal microscopic varicocelectomy is effective in improving testosterone levels and sperm motility in men with varicocele. Despite these benefits, no significant enhancements were observed in sperm count or morphology, suggesting a partial therapeutic impact on seminal parameters.

KEY WORDS: Varicocele; Male Infertility; Microsurgical Varicocelectomy; Testosterone; Semen Analysis.

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INTRODUCTION

Testicular varicocele, characterized by the pathological dilation of the pampiniform venous plexus, is a leading cause of male infertility, disrupting spermatogenesis and overall testicular function.[1] Clinically evident varicocele is strongly associated with subfertility, with negative effects on seminal parameters and testosterone production well-documented.[2] Historical observations, starting with Bennet in 1889, revealed improved semen quality following surgical correction.[3] Modern research confirms that varicocelectomy enhances sperm parameters and natural conception rates, yet the precise mechanisms underlying varicocele-induced subfertility and the full impact of surgical correction remain poorly understood.[4]

Varicocele affects about 15% of the general male population but is more common among infertile men, found in 20-40% of primary infertility cases and up to 80% of secondary infertility cases.[5] The condition predominantly occurs on the left side due to anatomical differences in venous drainage, valve absence in the left spermatic vein, and the nutcracker phenomenon.[6] Despite these insights, the exact pathophysiology remains unclear. Hypotheses include increased scrotal temperature, hypoxia, oxidative stress, and toxic effects of adrenal metabolites, with

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scrotal hyperthermia widely considered the primary mechanism disrupting spermatogenesis.[7]

Beyond its effects on sperm production, varicocele impacts Leydig cell function, leading to reduced testosterone levels.[8] This hormonal deficiency affects not only reproduction but also muscle mass, bone density, libido, energy, and psychological well-being.[9] Histological studies reveal Leydig cell abnormalities and compensatory hyperplasia in varicocele patients. While some evidence suggests testosterone levels improve after varicocelectomy, findings are inconsistent, necessitating further investigation.[10]

Diagnosis relies on clinical examination, often supplemented by Doppler ultrasonography for subclinical cases.[11] Varicocele severity is graded using the Dubin classification, from Grade 0 (subclinical) to Grade 3 (visible and palpable at rest).[12] Treatment typically involves surgical varicocelectomy, the most effective option for clinically significant cases.[13] Observation or embolization may be considered for asymptomatic individuals or those not seeking fertility improvement.[14] Advances in microsurgical techniques have reduced complications and recurrence rates, underscoring the importance of precision in surgery.[15]

Despite the demonstrated benefits of varicocelectomy in improving seminal parameters, its broader effects on testosterone levels and overall reproductive health are underexplored.[16] Current studies often focus on isolated outcomes, overlooking the interplay of hormonal, thermal, and vascular factors.[17] By addressing the reproductive and endocrine consequences of varicocele surgery and gaining information in this area, especially in microsurgical surgery, appropriate measures can be taken to improve clinical guidelines and optimize the care of affected individuals, improve understanding of the pathophysiology of varicocele and its treatment.[18] This research aimed to evaluate the impact of microsurgical varicocelectomy on serum testosterone levels and semen parameters in subfertile men with clinically evident varicocele.

MATERIALS AND METHODS

Study Design and Setting: This prospective observational study was conducted in the Azadi Teaching Hospital in Kirkuk between January 2023 and February 2024. The study aimed to evaluate the impact of microscopic varicocelectomy on serum testosterone levels (TST) and seminal fluid analysis (SFA) parameters in men with clinically palpable varicocele presenting with subfertility.

Study Population: A total of 50 male patients aged 19-45 years with clinically palpable varicocele referred for subfertility evaluation were enrolled. The study utilized convenience sampling, enrolling consecutive eligible patients who met the inclusion criteria. Inclusion criteria included a history of primary or secondary subfertility of at least three years, and evidence of abnormal SFA parameters, including oligospermia, asthenospermia, or oligoasthenoteratospermia (OAT syndrome). Patients with azoospermia or unexplained infertility (normal SFA) were excluded, along with those referred for varicocele pain, adolescent patients, or men aged over 50 years. Additionally, patients with less than three years of subfertility or subclinical varicoceles (as determined by physical examination and ultrasound) were excluded.

Clinical and Diagnostic Assessment: All patients underwent comprehensive clinical evaluation, including physical examination and scrotal Doppler ultrasonography to confirm the presence and severity of varicoceles. Varicocele grading was performed based on physical examination findings and categorized as grade 1 (mild), grade 2 (moderate), or grade 3 (severe). Only varicoceles with a vein diameter of $\geq$3 mm on Doppler ultrasound were included, while subclinical varicoceles were excluded.

Preoperative TST levels were measured using venous blood samples collected in the early morning after fasting. Seminal fluid analysis was performed on at least two separate occasions, one week apart, using standardized World Health Organization (WHO) protocols. Parameters assessed included semen volume, sperm concentration, motility, and morphology.

Intervention: Microscopic varicocelectomy was performed under general anesthesia by a single experienced surgeon using a sub-inguinal approach. Standard preoperative preparation included blood grouping, hematological tests, renal function tests, random blood glucose, and virology screening. Patients received prophylactic antibiotics (cefuroxime 750 mg IV or amoxiclav 1.2 g IV) during induction of anesthesia.

The surgical procedure involved ligation of the dilated veins under an operative microscope to preserve arterial and lymphatic structures. Patients were discharged on the same day and advised on postoperative care, including abstinence from strenuous activities for six weeks.

Postoperative Follow-Up and Data Collection: Patients were followed up at six months postoperatively to evaluate changes in TST levels and SFA parameters. Venous blood samples were drawn for TST measurement, and SFA was repeated under the same laboratory conditions as preoperative assessments.

Data collected included demographic information, varicocele grade, laterality, fertility history, and laboratory parameters (pre- and post-operative TST and SFA results). Data were documented using structured physician-completed questionnaires.

Instruments and Validity: All laboratory analyses

were performed using validated equipment calibrated according to manufacturer specifications. SFA procedures adhered to WHO guidelines to ensure consistency and reliability. TST levels were measured using chemiluminescent immunoassay techniques, with quality control procedures implemented for accuracy. The validity of the clinical grading of varicoceles was corroborated by Doppler ultrasound findings.

Statistical Analysis: Data were analyzed using SPSS software (version 25.0). Continuous variables were summarized as means ±standard deviations, and categorical variables were expressed as frequencies and percentages. The Student's t-test was employed to compare pre and post-operative continuous variables, while the chi-square test was used for categorical variables. A p-value of <0.05 was considered statistically significant.

Ethical Considerations: The study adhered to the principles outlined in the Declaration of Helsinki. Written informed consent was obtained from all participants, emphasizing voluntary participation, confidentiality, and the right to withdraw at any stage without consequence. Data were anonymized and securely stored to maintain participant privacy. Ethical approval was obtained from the ethical committee of Kirkuk University (Code number: 386).

RESULTS

A total of 50 patients who underwent varicocelectomy for the treatment of sub-fertility were analyzed. The patients' ages ranged from 19 to 42 years, with a mean age of 30.92 ±6.60 years. The duration of infertility varied between 3 and 12 years, with an average of 7.6 ±2.64 years. Among patients with primary infertility, the mean duration of infertility was 8.5 years, whereas it was 4.5 years for those with secondary infertility, as shown in Table 1.

Regarding fertility status, 64% of patients had secondary infertility, while 36% had primary infertility, as depicted in Figure 1. In terms of varicocele laterality, 76% of patients presented with left-sided varicocele, and 24% had bilateral varicocele, as shown in Figure 2. Of the 50 cases, the grading of varicocele revealed grade 1 in 6 cases (9.7%), grade 2 in 32 cases (51.6%), and grade 3 in 24 cases (38.7%), as shown in Figure 3. It should be noted that 12 patients exhibited bilateral varicocele.

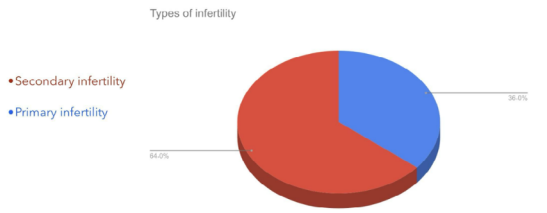

Figure 1: Types of infertility in study individuals.

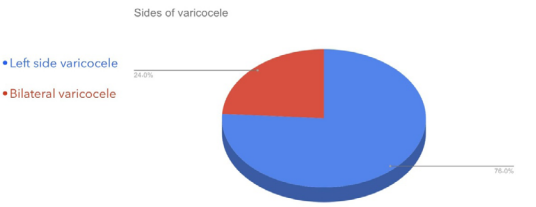

Figure 2: Sides (laterality) of varicocele.

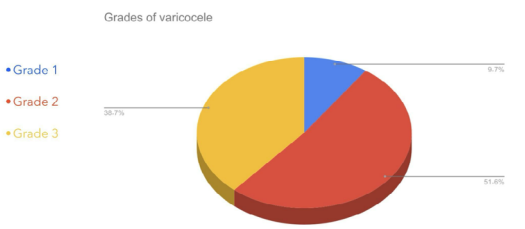

Figure 3: Grades of varicocele.

All patients underwent open varicocelectomy using a sub-inguinal approach under microscopy. Postoperatively, most patients exhibited elevated total serum testosterone levels. Comparing preoperative and postoperative values, the mean total serum testosterone increased significantly from 3.18 ±0.88 ng/ml to 4.068 ±0.77 ng/ml ($p < 0.001$), as shown in Table 2.

Regarding seminal fluid analysis (SFA) parameters, no significant change was observed in semen volume at six months postoperatively (2.5 ± 0.8 ml vs. 2.6 ±0.7 ml, $p > 0.05$). However, sperm motility showed a statistically significant improvement, with mean values increasing from 17.2% ±7.43% preoperatively to 27.4% ±8.22% postoperatively ($p < 0.001$). On the other hand, sperm concentration and morphology did not exhibit significant changes. The mean sperm concentration decreased slightly from 26.78 ±12.57 million/ml to 25.68 ± 14.42 million/ml ($p = 0.71$), and normal sperm morphology remained largely unchanged at 44.5% ±10.51% versus 45.4%

Table 1: Age and duration of infertility.

Variable	Number	Minimum	Maximum	Mean	Standard Deviation
Age (years)	50	19	42	30.92	6.60
Duration of infertility (years)	50	3	12	7.60	2.64

Table 2: Comparison of Pre-Operative and Post-Operative Measurements (Microscopic Varicocelectomy)

	Preoperative (N=50)		Postoperative(N=50)		
Variable	Mean	SD			P-value
TST (ng/ml)	3.18	0.88	4.068	0.77	<0.001
Total Motility (%)	17.2	7.43	27.4	8.22	<0.001
Normal Morphology (%)	44.5	10.51	45.4	10.70	0.59
Sperm Count (million/ml)	26.78	12.57	25.68	14.42	0.71
TST: Total Serum Testosterone, ng/ml: nanogram/milliliter					

±10.7% (p=0.59). These findings are summarized in Table 2.

DISCUSSION

The detrimental impact of clinically evident testicular varicocele on spermatogenesis has been well-documented, but its connection to reduced testosterone production and the efficacy of varicocelectomy in enhancing Leydig cell activity remain less understood. The current study provides evidence supporting the role of varicocelectomy in improving testosterone production. This finding aligns with previous studies that demonstrated a positive effect of surgical repair on total serum testosterone (TST) levels, suggesting a possible restoration of Leydig cell function post-surgery.[19-22] Conversely, a few studies reported no significant improvement in TST following varicocele repair, highlighting the variability in response, which may depend on factors such as the baseline testosterone levels and individual patient characteristics.[23,24]

The literature also supports the hypothesis of diffuse Leydig cell dysfunction in individuals with varicocele, as evidenced by the prevalence of testosterone deficiency in this population and its subsequent correction postoperatively.[25] These findings underline the therapeutic potential of varicocelectomy in addressing hormonal deficiencies beyond its established role in enhancing spermatogenesis.

Regarding semen parameters, our findings reveal a lack of significant improvement in semen volume after surgery, which aligns with studies by Srini and Veerachari and Jangkhah et al., both of which reported similar outcomes.[20,26] However, contradictory findings exist, such as those of Kamar et al., who noted a marked improvement in semen volume at early postoperative intervals.[27] These discrepancies could stem from differences in study designs, patient selection criteria, and timing of postoperative assessments.

Sperm motility emerged as a parameter that significantly improved following varicocele repair. This observation is consistent with multiple studies, including those by Srini and Veerachari (2011)[20] and Choi et al.[28], which reported notable enhancements in sperm motility and its association with improved spontaneous pregnancy rates. Interestingly, some researchers identified that pretreatment motility levels and patient age influenced the degree of postoperative improvement.[28] However, these encouraging results are not universally accepted, as certain studies, such as those by Jangkhah et al. and Okeke et al. failed to demonstrate significant improvements in motility post-surgery.[26,29]

Contrary to expectations, sperm morphology did not exhibit significant changes in our study. This finding is consistent with previous investigations by Srini and Veerachari and Choe et al., which suggested that teratozoospermia might be influenced by factors unrelated to varicocele.[20,30] However, other studies, such as those by Marinaro et al. and Choi et al., reported progressive improvements in morphology after surgery, emphasizing the multifactorial nature of this parameter and the possible influence of comorbidities and patient characteristics.[28,31]

Sperm density or concentration similarly showed no significant changes postoperatively in our cohort, which aligns with findings from Okeke et al. and Choe et al.[29,30] Conversely, other studies have reported significant improvements, particularly in older patients or those with initially low preoperative sperm counts.[20,32] This variability may reflect differences in baseline characteristics, sample sizes, and surgical techniques employed across studies.

Microsurgical varicocelectomy has increasingly become the gold standard for managing clinically detectable varicocele. Despite occasional disagreements in the literature, the overall evidence strongly supports its efficacy in improving seminal fluid parameters and spontaneous pregnancy rates, as confirmed by systematic reviews and meta-analyses.[33] However, further high-quality randomized controlled trials are needed to address lingering uncertainties and optimize patient selection criteria for this intervention.

This study contributes valuable insights into the nuanced role of varicocelectomy in male infertility

management. While it reinforces its benefits for hormonal and some seminal parameters, it also highlights the variability in outcomes and the need for individualized treatment approaches based on patient characteristics.

This study was limited by its relatively small sample size and the lack of long-term follow-up to assess sustained improvements in testosterone levels and seminal parameters.

CONCLUSION

This study demonstrates that varicocelectomy improves testosterone production and sperm motility in men with clinically detectable varicocele, addressing key aspects of male infertility. While benefits to other seminal parameters, such as sperm density and morphology, were less consistent, the findings confirm varicocelectomy's role in enhancing hormonal and reproductive health.

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CONFLICT OF INTEREST
Authors declare no conflict of interest.
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AUTHORS' CONTRIBUTION

The following authors have made substantial contributions to the manuscript as under:

Conception or Design:	AMH, AAIS
Acquisition, Analysis or Interpretation of Data:	AMH, AAIS, AAS
Manuscript Writing & Approval:	AMH, AAIS, AAS

All the authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.