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ORIGINAL ARTICLE

To Find the Effect of Microsurgical Varicocelectomy on Serum Testosterone and FSH Hormones in Infertile Men

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ABSTRACT

Background: A common and perhaps treatable cause of male infertility, varicocele is frequently linked to altered testicular hormone activity and decreased spermatogenesis. Because to impaired Leydig cell activity, it is known to alter blood testosterone levels adversely and is especially common in men with primary infertility. Although microsurgical varicocelectomy is regarded as the gold standard of care, further research is needed to determine its effects on hormonal profiles, particularly those of testosterone and follicle-stimulating hormone (FSH).

Objective: To evaluate the effect of microsurgical varicocelectomy on serum testosterone and FSH levels in infertile men with clinical varicocele.

Methodology: The Institute of Kidney Disease (IKD), Medical Teaching Institution (MTI), Hayatabad Medical Complex (HMC), Peshawar, carried out this prospective observational study between 1st May 2023 to 30th Oct 2023. Using non-probability successive sampling, 100 infertile males with clinical Grade II or III varicocele were included in the study. Preoperative baseline levels of FSH and testosterone were measured, and three months after microsurgical subinguinal varicocelectomy, follow-up levels were evaluated. Pairwise t-tests were used to examine hormonal changes, with a significance level of $p<0.05$.

Results: A statistically significant increase in mean serum testosterone was observed postoperatively, with a greater rise noted in hypogonadal men. Serum FSH levels showed a modest but significant decrease following surgery. Patients with Grade III varicocele experienced a more pronounced hormonal response.

Conclusion: Microsurgical varicocelectomy significantly improves testosterone levels and moderately reduces FSH levels in infertile men, particularly in those with baseline hypogonadism and higher-grade varicoceles.

Keywords: FSH, Hormonal Profile, Infertility, Microsurgical Varicocelectomy, Testosterone, Varicocele

INTRODUCTION

A global health concern, infertility affects 15% of couples globally, with male factors responsible for about 50% of instances[1] One of the most common and treatable causes of male infertility is varicocele, a pathological dilatation of the spermatic cord's pampiniform venous plexus[2] Varicoceles are a major cause of subfertility and reduced testicular function, occurring in up to 40% of infertile men and in roughly 15% to 20% of the overall male population[3]

Varicocele has been linked to the disturbance of the typical testicular microenvironment by means of oxidative stress, elevated scrotal temperature, and toxic metabolite reflux[4] These alterations can negatively impact both spermatogenesis and Leydig cell function, which will likely establish changes in reproductive hormone levels, including serum testosterone and follicle-stimulating hormone (FSH)[5] Leydig cells produce testosterone in response to luteinising hormone (LH), which is critical for spermatogenesis and male sexual function[6] The anterior pituitary secretes FSH, regulating Sertoli cell function, and is important for the maturation of spermatozoa. Changes in the levels of these hormones may represent biochemical signs of testicular dysfunction[5]

Although microsurgical varicocelectomy is considered to be the best standard for varicocele repair and provides a superior view with high accuracy, allowing ligation of dilated veins while preserving testicular arteries and lymphatics, the hormonal response to varicocelectomy and the effects on serum testosterone and serum FSH are being studied[7-9] Following varicocelectomy, there are numerous reports of serum testosterone levels that have risen, especially in hypogonadal men, suggesting improved Leydig cell function, while the results are less clear with regard to serum FSH than perhaps due to feedback regulation from the hypothalamic-pituitary-gonadal (HPG) axis or differences in Sertoli cell activity[10,11]

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In developing nations, especially Pakistan, the limited opportunities for assisted reproductive technologies (ART) and social pressures related to family building make an exploration of low-cost, reversible interventions like varicocelectomy critical. By understanding the hormonal impact of this procedure, practitioners will be able to develop better prognostic value and subsequently guide counseling and management of this population.

Though varicocele and infertility are associated, there is debate, particularly in low-resource settings, on the hormonal effects of microsurgical varicocelectomy and the relevant case studies are scarce. This study investigates the limited data on the effect of microsurgical varicocelectomy on salivary testosterone and FSH reproductive hormones in infertile men. Evidence of the relevance of varicocelectomy in improving fertility outcomes, restoring hormonal balance, and benefiting overall male reproductive health may come from the discovery of hormonal changes that result from surgical correction. The present study aimed to investigate the effects of microsurgical varicocelectomy on the serum levels of follicle-stimulating hormone (FSH), testosterone in infertile men with clinical varicocele.

METHODOLOGY

The Institute of Kidney Disease (IKD) of the Medical Teaching Institution (MTI) at Hayatabad Medical Complex (HMC), Peshawar, conducted this prospective observational study. The study ran for 06 months, starting from 1st May 2023 to 30th Oct 2023. Ethical approval was obtained from the Institutional Review Board (IRB) of HMC-MTI before commencing the study. After fully explaining the objectives and methods of the study, each participant gave informed consent in writing.

Participants were informed of their right to withdraw from the research at any time without any adverse consequences to their care, and the confidentiality of participants was respected throughout all stages of the study. The sample size of 100 patients was calculated using OpenEpi version 3.01, to attain a 95% confidence level, 80% power, and a mean predicted increase in serum testosterone following varicocelectomy based on meta-analyses with the usual reported increases between 90 to 110

ng/dL.[12] The calculator suggested enlisting roughly 100 patients in order to have sufficient statistical power and identify a hormonal shift that is clinically significant, based on these effect size estimations and a 5% margin of error.

A non-probability consecutive sampling technique was employed to recruit participants who fulfilled the eligibility criteria during the study period. Inclusion criteria consisted of men aged 20 to 45 years with clinical varicocele (Grade II or III confirmed on physical examination and Doppler ultrasound), a history of infertility for at least one year, and abnormal semen parameters documented on two separate occasions at least four weeks apart. Only patients willing to undergo microsurgical varicocelectomy and follow-up hormonal assessments were included. Exclusion criteria involved men with subclinical varicocele, prior scrotal or varicocele surgery, other known causes of infertility such as obstructive azoospermia or hypogonadotropic hypogonadism, endocrine disorders (e.g., thyroid or pituitary abnormalities), use of hormonal therapy or anabolic steroids, and those with severe comorbidities preventing surgery or proper follow-up.

At baseline, each participant underwent a detailed clinical evaluation, and data were recorded using a structured proforma. Blood samples were collected under aseptic conditions between 8:00 and 10:00 AM after overnight fasting to measure serum testosterone and FSH levels, using chemiluminescent immunoassay (CLIA). A standard semen analysis was also conducted according to the World Health Organization (WHO) 2021 guidelines. All enrolled patients underwent microsurgical subinguinal varicocelectomy, performed by a single experienced urologist using an operating microscope to enhance precision and reduce complication rates. At 3 months postoperatively, repeat blood samples were drawn using the same protocol to reassess serum testosterone and FSH levels.

All acquired data were analyzed using Statistical Package for the Social Sciences (SPSS) version 26. Means and standard deviations (mean ± SD) were used to report quantitative variables such as serum testosterone and FSH. Hormonal levels within patients were compared before and after surgery using the paired t-test. P-values below 0.05 were regarded as statistically significant. Additionally, subgroup analyses were performed to assess the results for patients whose baseline testosterone levels were low.

RESULTS

A total of 100 infertile men with clinical varicocele were included in the study. The mean age of the participants was in the early 30s, with the average duration of infertility slightly exceeding three years. Most cases involved left-sided varicoceles, and the majority presented with Grade II varicocele on clinical examination. Approximately 42% of the patients had baseline serum testosterone levels below 300 ng/dL, qualifying them as hypogonadal. A notable proportion of participants were current smokers, which was documented as a potential contributing factor to reproductive hormone imbalance. (Table 1)

Table 1: Baseline Demographic and Clinical Characteristics of Study Participants (n = 100)

Variable	Mean ± SD / n (%)
Age (years)	32.6 ± 5.8
Duration of Infertility (years)	3.1 ± 1.7
Grade II Varicocele	64 (64%)
Grade III Varicocele	36 (36%)
Laterality of Varicocele	
Left-sided	88 (88%)
Bilateral	12 (12%)
Baseline Low Testosterone (<300 ng/dL)	42 (42%)
Smoking Status (Current Smoker)	30 (30%)

Following microsurgical varicocelectomy, there was a statistically significant improvement in serum testosterone levels across the entire cohort. The mean post-operative testosterone showed a marked increase when compared to baseline values. In contrast, serum FSH levels demonstrated a modest but statistically significant decrease after surgery, indicating improved Sertoli cell function or reduced compensatory pituitary stimulation. (Table 2)

Table 2: Comparison of Serum Testosterone and FSH Levels Before and After Microsurgical Varicocelectomy (n = 100)

Hormonal Marker	Pre-Operative (Mean ± SD)	Post-Operative (Mean ± SD)	Mean Difference	p-value
Serum Testosterone (ng/dL)	310.2 ± 78.5	389.6 ± 86.3	+79.4	<0.001 **
Serum FSH (mIU/mL)	8.1 ± 3.4	6.9 ± 3.1	–1.2	0.004 **
Note: Paired t-test applied; p < 0.05 considered statistically significant.				

Table 3: Subgroup Analysis of Testosterone Change in Hypogonadal vs. Eugonadal Patients

Group	n	Pre-op Testosterone (ng/dL)	Post-op Testosterone (ng/dL)	Mean Change	p-value
Hypogonadal (<300 ng/dL)	42	245.6 ± 32.3	352.8 ± 55.6	+107.2	<0.001 **
Eugonadal (≥300 ng/dL)	58	357.8 ± 41.9	412.1 ± 46.3	+54.3	0.002 **

Table 4: Postoperative Hormonal Improvement by Varicocele Grade

Grade of Varicocele	n	Testosterone Change (ng/dL)	FSH Change (mIU/mL)	p-value (T)	p-value (FSH)
Grade II	64	+74.6 ± 28.2	–1.0 ± 0.8	<0.001	0.012
Grade III	36	+86.1 ± 30.7	–1.4 ± 1.1	<0.001	0.009

Subgroup analysis revealed that the increase in testosterone was more pronounced among men who were hypogonadal before surgery. While eugonadal men also experienced significant hormonal improvement, the magnitude of change was comparatively lower. These findings suggest that men with lower baseline testosterone levels may benefit more substantially from varicocelectomy in terms of endocrine recovery. (Table 3)

When stratified by varicocele grade, both Grade II and Grade III patients showed significant hormonal improvements postoperatively. However, those with higher-grade varicoceles exhibited slightly greater hormonal gains, reinforcing the potential role of disease severity in predicting the degree of response to surgical intervention. (Table 4)

DISCUSSION

We found that, three months after microsurgical varicocelectomy, the mean serum testosterone levels of 100 infertile men significantly increased, while the FSH levels decreased somewhat but statistically significantly. The testosterone improvement was significantly larger in individuals with higher-grade varicocele and most noticeable in hypogonadal patients.

Our findings are consistent with several contemporary studies. For instance, in a cohort of 202 hypogonadal men (baseline testosterone <3.5 ng/mL), microsurgical repair resulted in a substantial rise in mean testosterone from approximately 2.55 ± 0.66 ng/mL to 3.72 ± 1.34 ng/mL ($p < 0.001$), with over half achieving normalization, a pattern similar to our more pronounced hormonal response in hypogonadal patients[13,14] Likewise, a study of 100 patients stratified into hypogonadal and eugonadal groups showed significant testosterone increases postoperatively among hypogonadal men, with no significant change in the eugonadal subgroup, mirroring our subgroup analyses and supporting the concept that baseline level predicts degree of hormonal recovery[15]

By contrast, a prospective study from 2021–2024 involving 115 patients found no statistically significant increase in age-adjusted testosterone levels following varicocelectomy, despite improvements in semen parameters[16] This underscores variability among populations and measurement methodologies, reinforcing that not all men derive endocrine benefit from surgery, especially those with baseline eugonadal status.

Regarding FSH, our observed postoperative decline aligns closely with results of a systematic review and meta-analysis, which reported a pooled mean decrease in serum FSH of about 0.48 ng/mL (95% CI 0.19–0.77; p = 0.001), and also a small but significant drop in LH. Several investigations have also highlighted the predictive role of preoperative FSH and testosterone. In the Asian Journal of Andrology, lower baseline FSH and testosterone were independently correlated with improved sperm concentration post-repair[17] Similarly, our subgroup findings echo that hormonal improvement is greatest in those with initially low testosterone and higher-grade varicocele.

Some studies emphasize heterogeneity in response based on pathology. One report focused on patients with sickle cell disease (SCD) demonstrated high rates of primary hypogonadism (≈66.7%), with poorer outcomes in those with elevated FSH and low testosterone[13] While a different patient population, this reinforces that underlying testicular health modulates hormonal recovery post-varicocelectomy, a concept corroborated in our cohort where grade III varicocele and baseline hypogonadism predicted greater gains.

Finally, a meta-analysis of varicocelectomy in azoospermic men found no significant change in gonadotropins or LH levels post-repair, despite improvements in sperm retrieval metrics[18] This suggests that in severe infertility settings, endocrine markers may not shift, although fertility endpoints might improve, pointing to a dissociation between hormonal and spermatogenic outcomes in selected populations.

Strengths of our study include a prospective design, standardized timing for blood sampling, and a uniform surgical technique. Limitations include modest follow-up duration (3 months), absence of long-term follow-up data, and lack of measurement for other hormonal markers such as LH or inhibin-B. Future studies should aim for longer-term follow-up, include hormone panels as well as semen parameter correlation, and consider randomized or controlled comparisons. The present study is in broad agreement with several contemporary studies demonstrating significant testosterone improvements and modest reductions in FSH following microsurgical varicocelectomy, particularly in hypogonadal men. Nonetheless, variability exists across studies, highlighting the importance of patient selection based on baseline hormonal status and varicocele grade when counseling about expected endocrine outcomes.

CONCLUSION

This study demonstrates that microsurgical varicocelectomy leads to a significant improvement in serum testosterone levels and a modest reduction in FSH among infertile men, particularly in those with baseline hypogonadism and higher-grade varicocele. These hormonal changes suggest a restoration of testicular endocrine function following surgical intervention. The findings support the role of varicocelectomy not only in enhancing fertility potential but also in improving overall hormonal balance in selected patients. Careful preoperative assessment, including hormonal profiling, can help identify individuals most likely to benefit from the procedure, thereby guiding personalized management strategies in male infertility.

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