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TO FIND THE PREGNANCY OUTCOME IN PATIENTS AFTER MICROSURGICAL VARICOCELECTOMY HAVING SPERM DNA FRAGMENTATION

Original Research

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ABSTRACT

Background: Varicocele is one of the most prevalent and correctable causes of male infertility, often associated with impaired spermatogenesis and elevated sperm DNA fragmentation index (DFI). Its detrimental impact on sperm quality results from oxidative stress and venous reflux within the pampiniform plexus. Microsurgical varicocelectomy has emerged as the preferred surgical intervention, offering precise anatomical correction with minimal complications. While its effectiveness in improving semen parameters is well documented, its influence on natural conception requires further clinical exploration.

Objective: To evaluate the effect of microsurgical varicocelectomy on semen quality, sperm DNA integrity, and natural pregnancy outcomes in infertile men with clinical varicocele.

Materials and Methods: A prospective observational study was conducted at Civil Hospital, Bahawalpur, from January to June 2024. Ninety infertile males aged 25–45 years with clinical varicocele, oligoasthenozoospermia, and baseline DFI >20% were included. Patients with azoospermia, previous varicocelectomy, or systemic illness affecting fertility were excluded. All participants underwent microsurgical subinguinal varicocelectomy performed by a single experienced surgeon under general anesthesia. Pre- and postoperative semen analyses were performed to assess sperm count, motility, morphology, and DFI. Pregnancy achievement was monitored over a six-month follow-up. Data were analyzed using paired t-tests and chi-square tests, with $p < 0.05$ considered significant.

Results: The mean age of participants was 34.28 ± 5.60 years, and mean BMI was 24.01 ± 3.27 kg/m². Significant postoperative improvements were observed in sperm count (8.09 ± 4.00 to 25.90 ± 7.73 million/mL, $p < 0.001$), motility (35.39 ± 8.72% to 54.24 ± 8.35%, $p < 0.001$), morphology (5.68 ± 2.46% to 13.32 ± 4.07%, $p < 0.001$), and DFI (29.86 ± 5.91% to 17.96 ± 4.30%, $p < 0.001$). Pregnancy was achieved in 32 (36%) patients. No statistically significant association was found between pregnancy outcomes and variables such as age, obesity, infertility duration, or varicocele grade.

Conclusion: Microsurgical varicocelectomy significantly improves semen parameters and sperm DNA integrity, supporting its role as an effective intervention to enhance natural fertility in men with clinical varicocele.

Keywords: Infertility, male; Microsurgery; Pregnancy outcome; Semen analysis; Sperm motility; Spermatozoa; Varicocele.

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INTRODUCTION

Male infertility is a growing global health concern, contributing to nearly half of all infertility cases, with a considerable proportion attributed to correctable causes. Among these, varicocele—a condition characterized by abnormal dilation of the pampiniform venous plexus—has been recognized as a leading contributor. This vascular anomaly can disrupt normal testicular thermoregulation and induce oxidative stress, resulting in impaired spermatogenesis and compromised sperm quality (1). Over recent years, microsurgical varicocelectomy has gained prominence as the gold standard treatment for clinically significant varicocele, offering superior outcomes in terms of postoperative recovery and fertility improvement compared to other surgical approaches (2). Despite substantial evidence supporting its role in enhancing conventional semen parameters, a critical aspect that warrants further exploration is its impact on sperm DNA fragmentation (SDF) and subsequent pregnancy outcomes—both natural and assisted (3). Sperm DNA integrity is vital for successful fertilization, embryo development, and sustained pregnancy. Elevated SDF levels, often stemming from oxidative stress and testicular dysfunction, have been closely linked to reduced fertility, implantation failure, and early pregnancy loss (4). These effects are particularly detrimental in the context of assisted reproductive technologies (ART), where high SDF levels are associated with poor clinical outcomes (5). Varicocelectomy has shown promise in mitigating oxidative stress and improving testicular microcirculation, thereby reducing SDF and enhancing the potential for successful conception (6). However, as male infertility is often multifactorial, external influences such as smoking, obesity, and environmental toxins play a compounding role in exacerbating DNA damage in sperm cells (7). Addressing these factors in tandem with surgical intervention is crucial, as highlighted in recent literature (8).

Beyond improvements in traditional semen parameters, growing evidence suggests a direct relationship between SDF reduction and improved ART outcomes. For instance, clinical studies have demonstrated higher fertilization and pregnancy rates following varicocelectomy in couples previously experiencing unexplained ART failure, underscoring the significance of sperm DNA integrity in reproductive success (9,10). This has led to the integration of SDF testing into routine male infertility evaluations, reflecting its emerging role in clinical decision-making (11). Nonetheless, the heterogeneity in patient response to varicocelectomy underscores the need for individualized treatment planning. Factors such as the severity of varicocele, baseline semen quality, and patient age can significantly influence treatment efficacy (12). Thus, a nuanced understanding of which patients are most likely to benefit from surgery remains a key clinical challenge. In light of these considerations, this study seeks to explore the relationship between microsurgical varicocelectomy, the reduction of sperm DNA fragmentation, and subsequent improvements in pregnancy outcomes. By critically synthesizing the current evidence, the objective is to elucidate the underlying mechanisms through which varicocelectomy enhances male fertility and to identify predictors that may inform personalized treatment strategies in reproductive medicine.

METHODS

This prospective observational study was carried out over a six-month period, from January 2024 to June 2024, at the Department of Urology, Civil Hospital, Bahawalpur. Prior to commencement, ethical clearance was obtained from the Institutional Ethical Review Committee of Civil Hospital, Bahawalpur, and written informed consent was secured from all participants to ensure compliance with ethical standards for human research. A total of 90 male patients were enrolled, with the sample size calculated using a 95% confidence interval based on a previously reported pregnancy rate of 37.1% from the study by Gupta C et al. (13), thereby ensuring adequate statistical power. Participants included in the study were infertile males aged between 25 and 45 years who had a clinically palpable varicocele, severe oligoasthenozoospermia (defined as a sperm concentration below 15 million/mL), and a sperm DNA fragmentation index (DFI) greater than 20%. Patients were excluded if they had azoospermia, obstructive causes of infertility, systemic illnesses known to affect fertility such as diabetes mellitus or hypogonadism, or a history of previous varicocelectomy. Detailed baseline demographic and clinical data were collected, including age, body mass index (BMI), duration of infertility, and varicocele grade, which was categorized into Grades 1, 2, or 3 based on standard clinical criteria.

All participants underwent microscopic subinguinal varicocelectomy under general anesthesia, performed by a single experienced urologic microsurgeon. The surgical technique involved meticulous ligation of dilated veins while preserving critical structures including the testicular artery, lymphatics, and vas deferens, to minimize postoperative complications and preserve testicular function.

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Postoperative evaluations were scheduled systematically, and patients were followed for a total of six months to monitor changes in semen parameters and pregnancy outcomes. Semen analyses were conducted according to WHO guidelines, both prior to surgery and three months postoperatively. Parameters assessed included sperm count (million/mL), progressive motility (%), morphology (%), and DFI (%). The DFI was measured using a validated assay, although the specific method—such as SCSA, TUNEL, or Comet assay—was not specified, which may influence comparability across studies. The primary endpoint was the achievement of pregnancy within six months following surgery, with conception confirmed by clinical evaluation and ultrasound in female partners. Data were analyzed using IBM SPSS Statistics version 26. Continuous variables such as age, BMI, and semen parameters were expressed as mean ± standard deviation, and compared pre- and postoperatively using paired t-tests. Categorical data, including pregnancy rates and varicocele grades, were analyzed using chi-square or Fisher's exact tests where appropriate. A p-value less than 0.05 was considered statistically significant in all analyses.

RESULTS

A total of 90 patients meeting the inclusion criteria were enrolled in the study. The mean age of the participants was 34.28 ± 5.60 years, and the mean body mass index (BMI) was 24.01 ± 3.27 kg/m². The average duration of infertility among participants was 4.62 ± 2.64 years. Following microsurgical varicocelectomy, pregnancy was achieved in 32 patients, reflecting a pregnancy rate of 36% over the six-month follow-up period. Statistically significant improvements were observed across all assessed semen parameters following surgery. The mean sperm count increased from 8.09 ± 4.00 million/mL preoperatively to 25.90 ± 7.73 million/mL postoperatively ($p < 0.001$). Similarly, sperm motility rose from 35.39 ± 8.72% to 54.24 ± 8.35% ($p < 0.001$), and sperm morphology improved from 5.68 ± 2.46% to 13.32 ± 4.07% ($p < 0.001$). The sperm DNA fragmentation index (DFI) showed a marked reduction from 29.86 ± 5.91% to 17.96 ± 4.30% ($p < 0.001$), indicating a significant improvement in sperm DNA integrity postoperatively. Subgroup analysis of pregnancy outcomes revealed that age, obesity status, duration of infertility, and varicocele grade did not show statistically significant associations with pregnancy achievement. Among patients aged 25–35 years, 28% achieved pregnancy, compared to 45% in the 36–45 year group ($p = 0.094$). In the obese subgroup (n=3), one patient (33.3%) achieved pregnancy, while in the non-obese group (n=87), 31 patients (35.6%) conceived ($p = 0.935$). For infertility duration, pregnancy was achieved in 35.7% of patients with 1–5 years of infertility and 35.3% in those with 6–10 years ($p = 0.968$). By varicocele grade, pregnancy rates were 29.4% in Grade I, 35.0% in Grade II, and 50.0% in Grade III patients ($p = 0.364$), showing a trend toward better outcomes in higher grades, though not statistically significant.

These results suggest that while microsurgical varicocelectomy significantly improves semen quality and sperm DNA integrity, achieving pregnancy post-surgery may also depend on other individual or couple-related reproductive factors. Subgroup analysis was conducted to evaluate the relationship between improvements in sperm parameters—particularly sperm DNA fragmentation—and pregnancy achievement. Patients who achieved pregnancy demonstrated significantly greater reductions in DNA fragmentation index (DFI), with mean postoperative DFI values of 15.9 ± 3.7%, compared to 19.3 ± 4.5% in those who did not conceive ($p = 0.002$). Similarly, postoperative sperm count, motility, and morphology were all markedly higher in the pregnancy-achieved group (28.6 ± 6.9 million/mL, 57.2 ± 7.4%, and 14.5 ± 3.8%, respectively) compared to the non-pregnant group (24.1 ± 8.0 million/mL, 52.5 ± 8.6%, and 12.7 ± 4.1%; p-values = 0.001, 0.004, and 0.008, respectively). These findings suggest that greater improvements in both sperm quality and DNA integrity following microsurgical varicocelectomy are positively associated with successful conception, emphasizing the prognostic value of post-treatment semen parameters in predicting fertility outcomes.

Table 1: Comparison of Pre- and Post-Surgery Sperm Parameters in Patients Undergoing Microsurgical Varicocelectomy

Parameter	N	Pre-Surgery Mean ± SD	Post-Surgery Mean ± SD	p-value
Sperm Count (million/mL)	90	8.09 ± 4.00	25.90 ± 7.73	<0.001
Sperm Motility (%)	90	35.39 ± 8.72	54.24 ± 8.35	<0.001
Sperm Morphology (%)	90	5.68 ± 2.46	13.32 ± 4.07	<0.001
Sperm DNA Fragmentation (%)	90	29.86 ± 5.91	17.96 ± 4.30	<0.001

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Table 2: Relationship Between Baseline Characteristics and Pregnancy Outcomes After Microsurgical Varicocelectomy

Variable	Category	Pregnancy Not Achieved (n%)	Pregnancy Achieved (n%)	Total (n)	p-value
Age Group	25-35 Years	36 (72.0%)	14 (28.0%)	50	0.094
	36-45 Years	22 (55.0%)	18 (45.0%)	40	
Obesity Status	Obese	2 (66.7%)	1 (33.3%)	3	0.935
	Non-Obese	56 (64.4%)	31 (35.6%)	87	
Duration of Infertility	1-5 Years	36 (64.3%)	20 (35.7%)	56	0.968
	6-10 Years	22 (64.7%)	12 (35.3%)	34	
Varicocele Grade	Grade I	24 (70.6%)	10 (29.4%)	34	0.364
	Grade II	26 (65.0%)	14 (35.0%)	40	
	Grade III	8 (50.0%)	8 (50.0%)	16	

Table 3: Stratified Analysis of Semen Parameters by Pregnancy Outcome

Parameter	Pregnancy Achieved (Mean ± SD)	Pregnancy Not Achieved (Mean ± SD)	p-value
Sperm Count (million/mL)	28.6 ± 6.9	24.1 ± 8.0	0.001
Sperm Motility (%)	57.2 ± 7.4	52.5 ± 8.6	0.004
Sperm Morphology (%)	14.5 ± 3.8	12.7 ± 4.1	0.008
Sperm DNA Fragmentation (%)	15.9 ± 3.7	19.3 ± 4.5	0.002

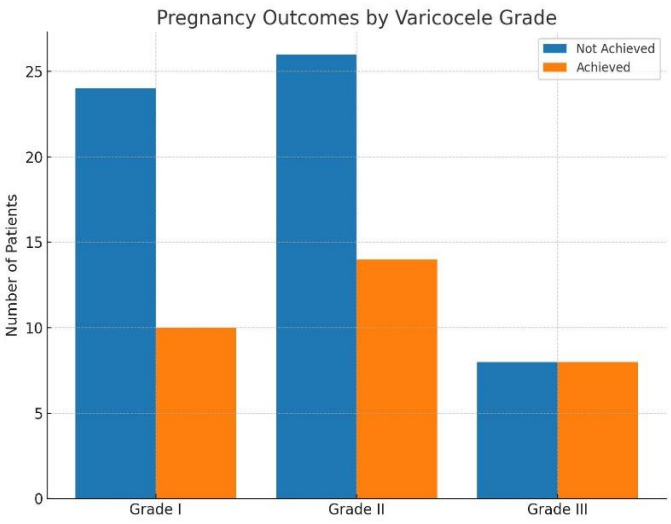

Figure 1 Pregnancy Outcomes by Varicocele Grade

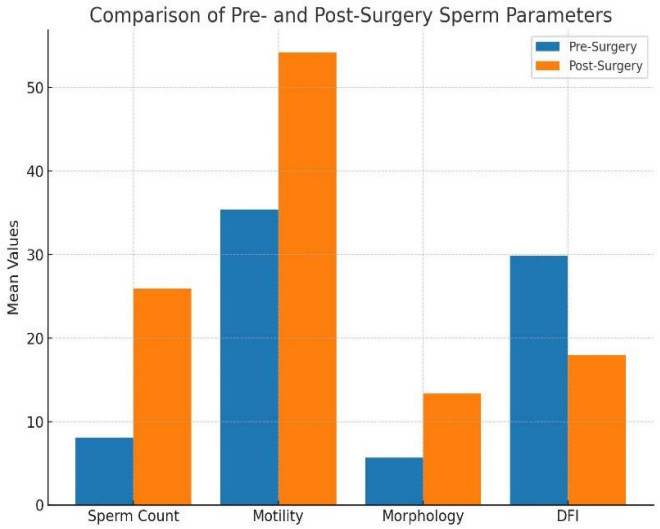

Figure 2 Comparison of Pre- and Post-Surgery Sperm Parameters

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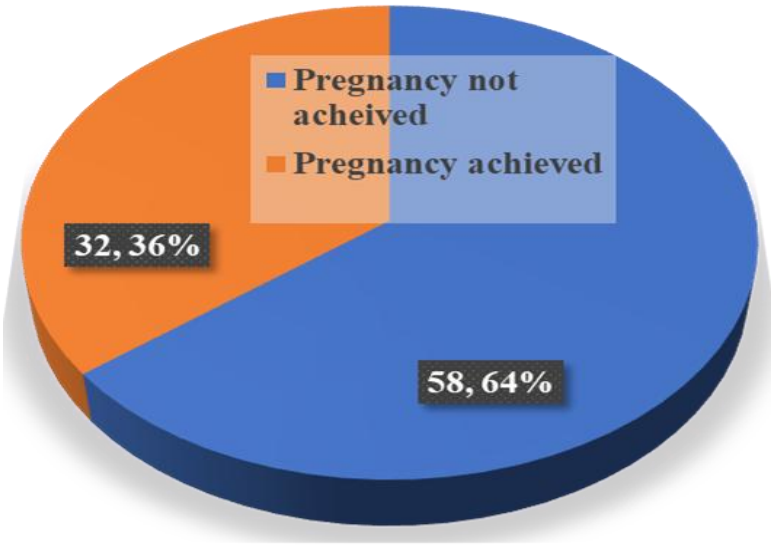

DISCUSSION

The findings of this study underscore the clinical efficacy of microsurgical varicocelectomy in enhancing semen parameters and improving fertility potential in men with clinically palpable varicocele. Significant postoperative improvements were observed in sperm count, motility, morphology, and DNA fragmentation index (DFI), reaffirming the therapeutic role of varicocelectomy in male infertility management. The pregnancy achievement rate of 36% within six months of surgery aligns with earlier reports, indicating that varicocelectomy offers a viable non-assisted option for natural conception in appropriately selected patients. Improvements in semen parameters observed in this cohort are consistent with prior studies that demonstrated enhanced sperm density and motility following varicocelectomy in men with severe oligoasthenozoospermia, often achieving spontaneous conception rates comparable to outcomes with assisted reproductive technologies (14,15). The significant reduction in DFI further supports the hypothesis that varicocele repair mitigates oxidative stress and restores testicular function, leading to better chromatin integrity. This finding is particularly relevant given the established association between elevated SDF and poor fertilization outcomes, compromised embryo quality, and increased miscarriage rates (16). The observed pregnancy outcomes mirrored those from prior investigations that reported higher odds of natural conception and live births in varicocelectomized individuals compared to untreated controls (17). These results highlight the importance of surgical intervention in male infertility, especially when combined with behavioral interventions targeting modifiable risk factors such as smoking and obesity. Although this study did not evaluate such confounders, their influence on postoperative fertility outcomes has been well documented and warrants consideration in future clinical protocols (18,19).

Subgroup analyses revealed varying pregnancy rates across age groups, BMI categories, duration of infertility, and varicocele grades, yet none achieved statistical significance. This finding supports the growing recognition that varicocelectomy, while effective, is not uniformly successful in all clinical contexts. For instance, individuals with higher-grade varicocele have demonstrated greater improvements in total motile sperm count and conception outcomes in other studies, suggesting a potential role for more refined patient stratification when recommending surgical repair (20). The current study adds to this discourse by identifying favorable trends but also emphasizes the multifactorial nature of male infertility, where baseline characteristics interact in complex and sometimes unpredictable ways. The timing of conception attempts following varicocelectomy is also clinically relevant. Previous research suggested that optimal improvements in semen quality occur within three months of surgery, a timeline consistent with the postoperative semen analysis and conception window in this study (21). This supports recommendations for couples to initiate fertility efforts shortly after this recovery period, maximizing the chances of successful natural conception during the window of improved sperm quality. Despite the encouraging

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results, it must be acknowledged that varicocelectomy does not guarantee fertility restoration in all cases. Approximately 64% of patients in this study did not achieve pregnancy during the follow-up period. Such outcomes reflect the limitations of surgical correction alone, especially in cases with longstanding infertility, severe oligospermia, or unrecognized female factor infertility. This emphasizes the need for thorough preoperative evaluation and holistic couple-based fertility assessment prior to intervention (22). Additionally, while semen analysis and DFI were used as outcome measures, the absence of advanced sperm function testing or long-term follow-up on live birth rates limits the broader applicability of these findings.

Strengths of this study include the use of a consistent surgical technique performed by a single experienced surgeon, standardized semen analysis protocols, and inclusion of sperm DNA fragmentation as a biomarker of sperm quality. However, limitations include a relatively small sample size, lack of control for female fertility factors, and absence of a long-term follow-up to assess live birth outcomes. The study also did not differentiate outcomes based on the extent of DFI reduction in direct relation to pregnancy success, which could offer more targeted prognostic insights. In conclusion, microsurgical varicocelectomy offers a meaningful therapeutic benefit for men with clinical varicocele, significantly enhancing both traditional semen parameters and sperm DNA integrity. Nonetheless, the heterogeneity of individual responses and the complex nature of male infertility call for a personalized, multidisciplinary approach. Future studies with larger sample sizes, control groups, and long-term reproductive endpoints are needed to refine patient selection criteria and maximize the success of surgical intervention in male infertility care.

CONCLUSION

Microsurgical varicocelectomy plays a pivotal role in improving key semen parameters and enhancing fertility potential in men with clinical varicocele. The findings of this study reinforce its effectiveness as a therapeutic option for those seeking natural conception, particularly in the presence of impaired sperm quality and elevated DNA fragmentation. While individual factors such as age, body composition, and infertility duration may influence outcomes, their impact appears limited when assessed independently. Overall, the procedure offers a meaningful opportunity to restore reproductive function in selected patients, supporting its continued use in the management of male infertility.

AUTHOR CORIBUTION

Author	Contribution
Mir Abid Jan	Substantial Contribution to study design, analysis, acquisition of Data Manuscript Writing Has given Final Approval of the version to be published
Khalil Ur Rehman*	Substantial Contribution to study design, acquisition and interpretation of Data Critical Review and Manuscript Writing Has given Final Approval of the version to be published

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