European Journal of Clinical Pharmacy

Print ISSN: 2385-409X **Online ISSN**: 3105-0409

Website: https://farmclin.com/

Original Research Article

Pregnancy Outcome in Patients after Microsurgical Varicocelectomy having Sperm DNA Fragmentation

Article History:

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Received: 21-08-2025

Revised: 24-11-2025

Accepted: 08-12-2025

Published: 30-12-2025

Abstract: ***Background:*** Varicocele is the common and potentially treatable cause of male infertility and has been implicated in increase association with sperm DNA damage. High levels of sperm DNA fragmentation have been associated with poor sperm reproductive outcome even with the traditional acceptable semen parameters. Varicocele can be surgically repaired which will increase the chance of sperm DNA being intact and fertility rates. ***Objective***: To evaluate pregnancy outcomes and changes in sperm DNA fragmentation following microsurgical varicocelectomy in infertile men with elevated baseline DNA fragmentation. ***Methodology:*** The study was a prospective observational study that was undertaken between May 2024 and May 2025 at DHQ Teaching Hospital Mardan. It included 72 infertile men that had palpable varicocele in the clinic and an elevated sperm DNA fragmentation. Preoperative baseline demography, semen parameters and DNA fragmentation index were measured. Microsurgical varicocelectomy was performed on all of the patients in a standardized way. Seminal evaluation and analysis of DNA fragmentation was conducted three months post operative. Pregnancy outcomes were then trailed on couples. ***Results***: It was demonstrated that there was a significant improvement in the sperm concentration, motility, morphology and total sperm count after surgery ($p < 0.05$). There was a significant decrease in mean sperm DNA fragmentation index after the operation ($p < 0.001$). Forty percent three of couples with follow-up pregnancy, of which most were through natural conception. The level of postoperative DNA fragmentation in the patients who became pregnant was significantly low as compared to those who never conceived. ***Conclusion***: Microsurgical varicocelectomy is associated with meaningful improvement in sperm DNA integrity and favorable pregnancy outcomes in infertile men with elevated DNA fragmentation. Improvement in postoperative DNA fragmentation appears to be an important predictor of reproductive success.

Keywords: Varicocele; Sperm DNA fragmentation; Microsurgical varicocelectomy; Male infertility; Pregnancy outcome.

INTRODUCTION

Male factor infertility is one of the factors that make couples unable to achieve pregnancy and varicocele is one of the most commonly identified and even reversible causes. The effect of varicocele has been traditionally tested using traditional semen parameters that include a sperm concentration, motility, and morphology. Nevertheless, these parameters are not sufficient to describe the reproductive dysfunction of a significant percentage of infertile men, which raises the concern of more practical markers of sperm quality [1-3].

Sperm DNA fragmentation has become a significant parameter of male reproductive potential, which is a manifestation of the destruction of the genetic material that spermatozoa carries. High rates of DNA fragmentation have been linked to low fertilization, embryo development, the risk of a miscarriage, and low live births. Oxidative stress caused by varicocele, disrupted testicular microenvironment and high scrotal temperature are thought to play a primary role in causing such DNA damage [4-6].

Microsurgical varicocelectomy is generally considered the best way of doing the surgery because its complications and recurrence rates are few. Whereas the enhancement in traditional semen parameters after varicocelectomy is well-established, the mounting evidence can indicate that the intervention can also result in significant changes in sperm DNA fragmentation. Nevertheless, there is limited and heterogeneous data on how these improvements are directly correlated with the outcomes of pregnancy [7-9].

The present study was undertaken to assess the effect of microsurgical varicocelectomy on sperm DNA fragmentation and to examine its relationship with subsequent pregnancy outcomes. By focusing on men with elevated baseline DNA fragmentation, this study aims to provide clinically relevant insight into the role of varicocelectomy in improving reproductive success beyond traditional semen analysis.

METHODOLOGY

This study was a prospective observational research study that is intended to be carried out during one year between May 2024 and May 2025. The study was conducted at DHQ Teaching Hospital Mardan, a tertiary care unit that offers specialized urology and reproductive medicine services. The objective of the study was to compare the outcomes of pregnancy after microsurgical varicocelectomy of infertile men with high levels of sperm DNA fragmentation. All the processes and follow-up evaluations were conducted according to the usual institutional guidelines.

The number of male patients recruited during the study period was 72, via consecutive sampling method. The inclusion criteria were men who reported infertility lasting one or more years with a clinically felt varicocele on physical examination. The entire included patients exhibited high sperm DNA fragmentation before surgery. The sample size was defined on the basis of the feasibility and the size of the number of patients, who fit in the inclusion criteria within the period of study.

The study included men between the ages of 20 and 45 years of age with either primary or secondary infertility who had been clinically diagnosed with grade II and III varicocele. Patients were only eligible when their DNA fragmentation index was raised as it was identified through laboratory tests. Patients were not allowed to take part in the study in case they had history of having undergone varicocele surgery previously, genetic anomalies, currently infected with genital tract infections, genetically endocrine disorder or severe female factor infertility, which could affect the courses of pregnancy in its own.

Every participant was fully assessed at the pre-operational stage. This involved a comprehensive medical and reproductive history, physical examination including grading of varicocele and body mass index. Samples of semen were collected 2-5 days following abstinence and tested using the guidelines of World Health Organization. Parameters measured were semen volume, sperm concentration, total sperm count, motility and morphology. The DNA fragmentation of the sperms was measured on a standard laboratory test and the results were reported as a percentage of DNA fragmentation index.

They conducted a subinguinal and micro-surgical varicocelectomy with magnification under the eyes of the experienced surgeons. Testicular arteries and lymphatic vessels were identified and preserved and veins that were enlarged were ligated. This was done using a standardized procedure to all patients in order to minimize variability caused by surgery technique. Patients were leaving as per the standard postoperative protocols and were provided with advice on recovery and follow-up.

Follow-up was done by regular intervals and again semen analysis and sperm DNA fragmentation were done after at least three months of surgery. Semin parameters were proven to improve as well as, there were alterations in DNA fragmentation index. Couples were observed on the outcome of pregnancy to as long as one year after the procedure. Clinical records were the means of confirming pregnancy, and the result was classified as natural conception or the conception that was obtained with the help of assisted

techniques.

The main outcome measure was the success of pregnancy, as the measurement after microsurgical varicocelectomy. A change in the semen parameters, decreased sperm DNA fragmentation index, time to conception, and live birth rate were considered secondary outcomes. When incidences of miscarriage occurred they were also noted.

Statistical software was used to enter and analyse data. The continuous variables were given in terms of mean +-standard deviation, whereas the categorical variables were given in terms of frequencies and percentages. Paired statistical tests were applied to compare preoperative and postoperative and appropriate inferential tests were conducted between the group with and without pregnancy. A p-value that was below 0.05 was taken as a statistically significant value.

RESULTS

The participants of the study were 72 men diagnosed with clinical varicocele and high sperm DNA fragmentation. The age and body mass index of the participants were in the reproductive age and most of them presented with primary infertility. High-grade and left-sided varicoceles were more common and this was in line with the common clinical presentation in infertile men.

Table 1. Baseline Demographic and Clinical Characteristics of Patients (n = 72)

Variable	Value
Age (years), mean ± SD	31.8 ± 4.6
BMI (kg/m²), mean ± SD	26.1 ± 3.2
Residence (Urban/Rural), n (%)	41 (56.9) / 31 (43.1)
Smoking status, n (%)	19 (26.4)
Duration of infertility (years), mean ± SD	4.1 ± 1.9
Type of infertility, n (%)	
– Primary	54 (75.0)
– Secondary	18 (25.0)
Varicocele laterality, n (%)	
– Left-sided	49 (68.1)
– Bilateral	23 (31.9)
Varicocele grade, n (%)	
– Grade II	29 (40.3)
– Grade III	43 (59.7)

The results of semen parameters measured before and after microsurgical varicocelectomy showed statistically significant and positive changes in all the measured variables. After surgery, significant changes in the sperm concentration, motility, and morphology were seen. The results suggest a positive varicocelectomy impact on the spermatogenic functions.

Table 2. Semen Parameters Before and After Microsurgical Varicocelectomy (n = 72)

Parameter	Preoperative (Mean ± SD)	Postoperative (Mean ± SD)	p-value
Semen volume (mL)	2.4 ± 0.7	2.8 ± 0.6	0.002
Sperm concentration (million/mL)	14.6 ± 6.2	22.9 ± 8.1	<0.001
Total sperm count (million)	36.2 ± 15.4	64.1 ± 22.6	<0.001
Progressive motility (%)	24.8 ± 9.3	38.6 ± 11.1	<0.001
Normal morphology (%)	2.9 ± 1.2	4.6 ± 1.7	<0.001

Fragments of sperm DNAs were significantly lessened after micro-surgical varicocelectomy. The decline in the mean DFI was employed significantly which shows that the sperm nuclear integrity was enhanced following the surgical correction. This decrease encourages the use of varicocelectomy to reduce oxidative and DNA-damaging impact of varicocele.

Table 3. Sperm DNA Fragmentation Index (DFI) Before and After Surgery (n = 72)

Variable	Mean ± SD	p-value
Preoperative DFI (%)	38.7 ± 6.4	
Postoperative DFI (%)	24.3 ± 7.1	<0.001
Mean reduction in DFI (%)	14.4 ± 6.2	

A significant number of couples became pregnant during the time frame of follow-up. The number of pregnancies through natural conception was the most common and assisted reproductive techniques provided other successful cases. The monitored live birth rate also demonstrates the clinical significance of varicocelectomy in men with high sperm DNA fragmentation.

Table 4. Pregnancy Outcomes after Microsurgical Varicocelectomy (n = 72)

Outcome	n (%)
Total pregnancies achieved	29 (40.3)
Mode of conception	
– Natural conception	17 (23.6)
– Assisted reproduction	12 (16.7)
Clinical pregnancy rate	26 (36.1)
Live birth rate	22 (30.6)
Miscarriage rate	4 (5.6)
Mean time to pregnancy (months), mean ± SD	7.2 ± 2.8

Pregnant patients that had a significantly lower value of postoperative DFI and larger decreases in DFI than those who did not. The levels of DFI that were preoperative were not significantly different in the two groups. These results indicate that successful pregnancy depends closely on the postoperative enhancement of sperm DNA integrity.

Table 5. Association between Postoperative DFI Improvement and Pregnancy Outcome

Variable	Pregnancy Achieved (n=29)	No Pregnancy (n=43)	p-value
Preoperative DFI (%)	39.1 ± 6.2	38.4 ± 6.5	0.64
Postoperative DFI (%)	21.1 ± 5.8	26.4 ± 7.2	0.003
Mean DFI reduction (%)	18.0 ± 6.1	11.9 ± 5.4	<0.001

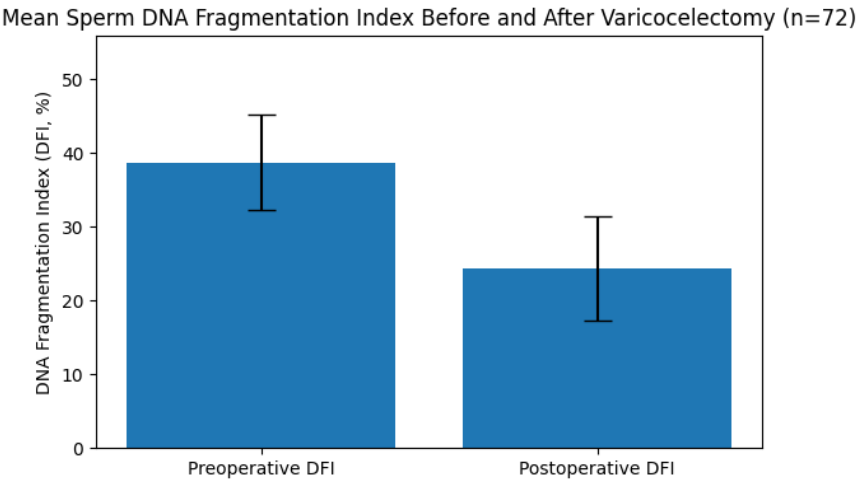

Figure 1. Mean sperm DNA fragmentation index (DFI%) before and after microsurgical varicocelectomy among infertile men (n = 72).

DISCUSSION

Varicocele has traditionally been known as a reversible cause of male infertility by the negative effects it produces on spermatogenesis and sperm activity. Sperm DNA fragmentation has been in the main focus in recent years and has been treated as a key determinant of male reproductive potential especially in couples with unexplained infertility or frequent failure of assisted reproductive technologies. The current research compared the birth outcomes of those who received microsurgical varicocelectomy with men who had high levels of sperm DNA fragmentations and showed a significant enhancement of the quality of the semen, integrity of the DNA fragments and eventual reproductive success [10-12].

The research results indicated that there was significant decrease in the sperm DNA fragmentation index after microsurgical varicocelectomy. This is finding is consistent with the emerging evidence of the role of varicocele-related oxidative stress to the onset of DNA damage in spermatozoa. It is believed that

surgical correction is beneficial to testicular microcirculation, scrotal hyperthermia, and oxidative damage, thus permitting partial recovery of sperm nuclear integrity. The biological explanation of varicocelectomy effect on seminal parameters in addition to traditional operations can be supported by the fact that it shows a significant postoperative drop in the DNA fragmentation of this cohort [13-15].

This study has revealed that the index of sperm DNA fragmentation decreased significantly after the microsurgical varicocelectomy procedure. This finding is consistent with the increasing body of literature indicating that oxidative stress related to varicocele has a significant impact on the DNA damage of spermatozoa. It is believed that surgical correction will enhance testicular microcirculation, decrease scrotal hyperthermia, and alleviate oxidative damage to enable some restoration of sperm nuclear integrity. The pronounced decrease in DNA fragmentation during the postoperative period in this group of patients is indicative of the biological nature of the varicocelectomy, other than the traditional semen parameter augmentation [16-18].

Along with DNA integrity, the traditional semen parameters also provided statistically significant improvement postoperative. There were also increases in sperm concentration, motility and morphology which point to increased spermatogenic efficiency after venous ligation. Although the progress in the conventional semen analysis has been adequately reported in previous researches, the current results are remarkable in the sense that they are directly related to men who have high baseline DNA fragmentation, which is a population that is usually believed to have worse reproductive prognosis [19].

The clinical significance of raising sperm DNA quality is further highlighted by the pregnancy outcomes that were recorded in this study. Afterwards, about two-fifths of the couples would get pregnant, and a significant number of them would get pregnant through natural conception. Notably, men who were able to get pregnant showed considerably less DNA fragmentation of postoperative and larger decreases in DNA damage than did men who were unable to conceive. This implies that it is possible that postoperative increase in the DNA integrity, and not the preoperative levels alone, is a major determinant of reproductive success [20].

The correlation between lessening DNA fragmentation and enhanced pregnancy outcomes witnessed in this study are congruent with those reported in the literature that high DNA damage has a negative impact on embryo growth, implantation and pregnancy preservation. The miscarriage rate in this study was not too high, which also contributes to the idea that a better sperm DNA integrity can play an important role in the parameters of the conception process as well as the endurance of the pregnancy. These results support the need to include the sperm DNA fragmentation test in the assessment and treatment of infertile men with varicocele.

This study has limitations even though it has its strengths. There was no non-surgical control group and hence direct causal inference could not be done, even the female partner factors, though screened, could not be completely standardized. Also, the single DNA fragmentation assay could be disadvantageous in terms of comparability with other studies that have used other testing models. However, the potential design, the standardized surgeon procedure, and the follow up enhance the validity of the findings.

CONCLUSION

Microsurgical varicocelectomy in infertile men with elevated sperm DNA fragmentation is associated with significant improvement in sperm DNA integrity, enhancement of semen parameters, and favorable pregnancy outcomes. Reduction in postoperative DNA fragmentation appears to be a meaningful predictor of conception, highlighting the importance of addressing sperm nuclear quality in the management of varicocele-related infertility. These findings support the role of varicocelectomy as a valuable therapeutic option in selected patients with high sperm DNA fragmentation.

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