

Analysis of Outcomes of Surgical Treatment for Varicocele in Primary Infertility Based on Seminal Parameters and Pregnancy Rate

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Abstract

Introduction: Varicocele is the most commonly observed and correctable cause of male factor infertility. The exact pathophysiology of varicocele is not known for certain. The purpose of our study was to analyze the effect of varicocele on the semen composition characteristics by semen analysis before and after varicocele ligation and also to assess the improvement in fertility status after varicocele ligation.

Patients and Methods: A prospective, non-randomized study for a study period of 2½ years with a total number (*n*) of 51 cases was carried out. Screening, identification, evaluation, and treatment were given to the patients attending our infertility clinic over a period from August 2010 to January 2013. A detailed semen analysis was done after 3 days of sexual abstinence. The specimen was examined within 1 h of collection. The history and clinical data of the patients were analyzed using SPSS software and comparison done using paired Student's *t*-test.

Results: The median sperm concentration of 51 patients in baseline semen analysis was 8 million/ml, and the median total sperm count of 51 patients was 18 million. The median forward (A + B%) motility percentage of sperms in 51 cases was 20%. The median normal morphology of sperms in 51 patients was 8%. Except 4 patients (7.4%) who were smokers, others did not have any smoking history or exposure to tobacco in any form. On comparing the data, post-operative sperm count and motility improvement were slightly better in sub-inguinal varicocelectomy surgery as compared with other modalities such as inguinal surgery and laparoscopic surgery.

Conclusions: Varicocelectomy gives a statistically significant improvement in sperm concentration, motility, and overall morphology. All approaches to varicocelectomy (sub-inguinal, inguinal, or laparoscopic) have shown a significant improvement in seminal parameters, with sub-inguinal approach being good in improving motility parameter.

Key words: Male infertility, Oligospermia, Sperm motility, Varicocele, Varicocelectomy

INTRODUCTION

Varicocele is the most commonly observed and correctable cause of male factor infertility. Varicocele, defined as dilated and tortuous pampiniform plexus of veins, is caused mainly by retrograde blood flow through the

internal spermatic vein.¹ The percentage of clinically evidenced varicocele in young adult subjects varies from 9% to 23%, as reported by the most recent case studies.^{2,3} Furthermore, varicocele can be observed in over 40% of infertile males.^{4,5} The varicocele is a disease of puberty and is only rarely detected in boys <10 years of age.⁶ Many studies have been conducted to examine the etiology and pathophysiology of varicocele as well as the influence it can have on spermatogenesis. The exact pathophysiology of varicocele is not known for certain, but varicocele is thought to impair normal testicular function by elevating scrotal temperature via reflux of warm abdominal blood through incompetent valves of the spermatic veins.⁷⁻⁹ The veins that are most commonly involved are the internal

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spermatic veins, but the external spermatic veins and cremasteric veins have also been implicated.^{10,11} Varicoceles are currently the most common abnormality identified in men being evaluated for infertility.¹² Improvements in semen quality after varicocele repair were first suggested by Barwell, in 1885; Bennett, in 1889; Macomber and Sanders, in 1929.¹³⁻¹⁵ In spite of these reports, surgical repair of the varicocele as a treatment for infertility was virtually forgotten until 1952, when the Edinburgh surgeon Selby Tulloch demonstrated the restoration of fertility following excision of bilateral varicocele in an azoospermic patient.¹⁶ Since then, thousands of studies on the diagnosis and surgical correction of varicoceles have appeared in the literature. Unfortunately, this entire body of experimental evidence has not been able to either identify the mechanism of spermatogenesis impairment or explain why surgical correction improves semen parameters.

Varicocelelectomy, a commonly performed operation, is indicated in infertile males with varicocele who have oligospermia, asthenospermia, teratospermia, or a combination of these factors. It is not clear if varicocelelectomy is indicated if the patients have normal sperm density associated with asthenospermia or teratospermia. Ligation of varicocele is known to cause marked improvement in semen parameters and also improve the fertility and conception rate.

This study has been undertaken with an idea to analyze the effect of varicocelelectomy on semen parameters and fertility status. The purpose of our study was to analyze the effect of varicocele on the semen composition characteristics by semen analysis before and after varicocele ligation and also to assess the improvement in fertility status after varicocele ligation.

PATIENTS AND METHODS

A prospective, non-randomized study for a study period of 2-year and 6-month with a total number (*n*) of 51 cases was carried out. The screening, identification, evaluation, and treatment were given to the patients attending the infertility clinic of urology department over a period from August 2010 to January 2013. The following is the detailed description of the methodology adopted.

All those patients presenting with primary infertility with oligoasthenoteratospermia, with any grade of clinical varicocele, subclinical varicocele with oligoasthenoteratospermia diagnosed on Doppler study and in those men, who have a vein diameter >2.4 mm with reflux in Valsalva maneuver with no apparent female factor infertility were included in our study.

Those patients with secondary infertility, varicocele with normal semen parameters, secondary varicocele, recurrent varicocele, and those males with associated female factor infertility were excluded from our study.

All the patients selected for the study were evaluated by a detailed history exploring all aspects related to fertility. This was necessary to exclude other factors which could affect the fertility. Only patients with demonstrable varicocele (clinically or by investigations) and with no other causes of infertility were taken up for the study.

A detailed semen analysis was done after 3 days of sexual abstinence. The specimen was examined within 1 h of collection. Three specimens from each patient were examined over a period of 2-month to give an assessment of baseline spermatogenesis. All the patients in the study were subject to repair of varicocele by sub-inguinal approach, inguinal approach, or laparoscopic approach. In cases of bilateral varicoceles, both the sides were operated at the same sitting. Meticulous follow-up of all the patients was done. The following parameters were assessed: History and clinical examination at every 3 months' interval, semen analysis at every 3 months' interval, and pregnancy rate.

The history and clinical data of the patients were analyzed using SPSS software and comparison done using paired Student's *t*-test.

RESULTS

During the study period from August 2010 to January 2013, a total (*n*) of 51 varicocele patients, who fulfilled our inclusion criteria were included in the study. The age of the patients ranged from 21 years to 40 years, majority of patients, and the median age was 30 years. About 33 patients (64.7%) belonged to 20-30 years age group. The median duration of infertility was 2.5 years with a range from 1 to 4 years. 29 patients (56.8%) had varicocele on the left side and 4 patients (7.8%) had varicocele on the right side. 18 patients (35.3%) had bilateral varicocele. Figure 1 demonstrates the pre-operative clinical and sonological findings of varicocele. Figure 1a depicts the Grade III varicoceles encountered in our study, which typically is described as a "Bag of Worms." Figure 1b shows the intraoperative findings of dilated pampiniform plexus. Figure 1c and d depict the Doppler findings of Grade III varicocele.

Even though, the clinical guidelines do not advice varicocelelectomy for sub-clinical varicoceles as a treatment for infertility, the palpatory method of examination and diagnosing varicocele is subjective, and accuracy may vary

by 50% in low-grade varicocele. We considered patients with Doppler diagnosed varicocele to be included in the study if the physical examination is not satisfactory in view of body habitus of the patient.

The median sperm concentration of 51 patients in baseline semen analysis was 8 million/ml, and the median total sperm count of 51 patients was 18 million. The median forward (A + B%) motility percentage of sperms in 51 cases was 20%. The median normal morphology of sperms in 51 patients was 8%. Except 4 patients (7.4%)

who were smokers, others did not have any smoking history or exposure to tobacco in any form. 29 patients (69.1%) underwent inguinal varicocele ligation, 13 patients (30.9%) underwent sub-inguinal varicocele ligation, and 9 patients (17.6%) underwent laparoscopic varicocele repair. In inguinal varicocele repair, 9 cases were bilateral and 20 were unilateral. In sub-inguinal varicocele repair, 7 cases were unilateral varicocele and 8 cases were bilateral. In laparoscopic varicocele repair, 2 cases were bilateral and 7 were unilateral.

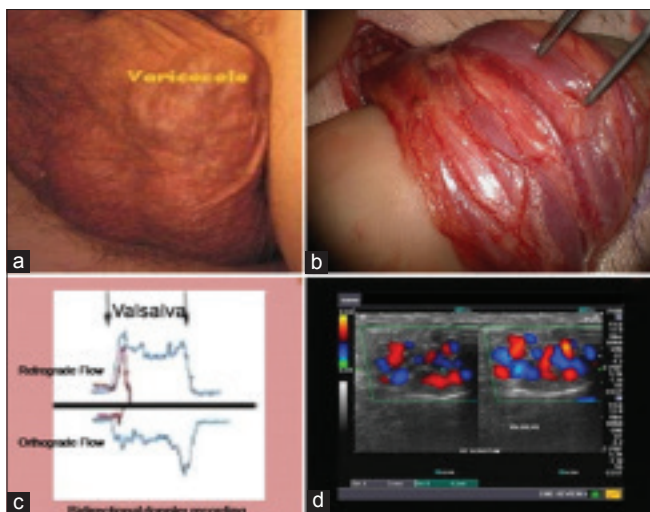


Figure 1: (a-d) Pre-operative clinical and sonological findings of varicocele

Figure 2 describes, in detail, the impact of the type of surgery on the ultimate outcome. In sub-inguinal varicocele repair ($n = 13$), the average pre-operative concentration of sperm is 11.22 million/ml, and post-operative average sperm concentration is 14.26 million/ml; this is statistically significant with $P < 0.001$. The average motility (A + B) in operative is 21.56% and that of in post-operative 38.27%, this is also statistically significant of $P < 0.001$. The average normal morphology of sperm in pre-operative is 8.65% and that of post-operative is 18.91%.

On comparing the above data, the post-operative sperm count and motility improvement is slightly better in sub-inguinal varicocele surgery as compared with other modalities such as inguinal surgery and laparoscopic surgery, but it is statistically insignificant with $P < 0.568$.

Table 1 describes the percentage of improvement with the type of surgery. The percentage of improvement

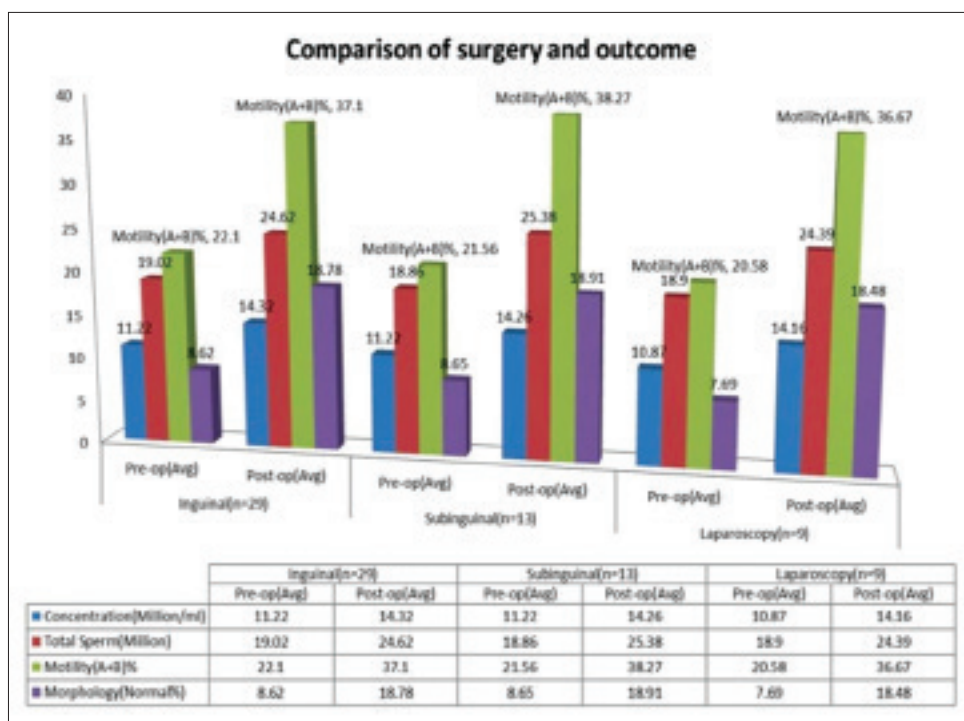


Figure 2: Comparison of surgery and outcome

in inguinal, sub-inguinal, and laparoscopy in seminal parameters such as concentration, total sperm count, motility of sperms, and morphology of normal sperms was higher in sub-inguinal surgery with 78.2%, 74.3%, 63.4%, and 49.4%, respectively. The improvement in motility and morphology is evidently higher when compared with other types of surgeries.

Complications

All were discharged after 48 h if they had no complications. The following were the complications noted. Post-operative fever on the 1st day was noted in 4 patients in laparoscopic repair. The fever subsided by oral antipyretics. Wound infection was noted on the 7th post-operative day in three patients in inguinal repair. This subsided by oral antibiotic and daily dressings as op basis.

Follow-up

All the patients were asked to come for follow-up investigations at 3, 6, 9, and 12 months after surgery. During the follow-up, the following parameters were assessed: A detailed history including the history of conception or pregnancy, a thorough clinical examination, investigations

including semen analysis, and Doppler study at 6 months postoperatively.

The findings of the follow-up study are presented below.

Pregnancy Rate

Of the 51 patients in our study, only 6 patients (11.8%) could successfully make his partner pregnant in the follow-up period. There were 3 patients of Grade II, 2 patients of sub-clinical, 1 patient of Grade 1 in the pregnancy.

Tables 2 and 3 illustrate the comparison of the percentage of improvement in successful pregnancy. On comparing the improvement of seminal parameters of successful pregnancy patients with the non-pregnant patients, there is statistically significant improvement in sperm concentration, total sperm count, motility, and morphology. On comparing the baseline values of the successful pregnant group with that of non-pregnant patients, the baseline values of pregnant were higher than as compared with baseline of non-pregnant.

DISCUSSION

Varicocele and its association with infertility have been recognized for many centuries. In *De Medicina*, written during the first century A.D., Celsus credits the Greeks with the first description of a varicocele and then remarks on veins that are swollen and twisted over the testicle, which becomes smaller than its fellow, in as much as its nutrition has become defective.¹⁷

It is generally accepted that treatment of varicocele improves semen parameters, with improvement rates ranging between 60% and 80%. The WHO study has clearly identified varicocele as an important detectable cause of male infertility.¹⁶ Improvement in seminal parameters following correction of varicocele has been variably reported in the literature ranging from 8% to 55%. Schlesinger *et al.* reviewed 16 studies that assessed the effect of varicocelelectomy on sperm density and reported that post-operative significant improvements were demonstrated in 12 studies and that sperm motility was noted in 5 of these studies.¹

Table 1: Percentage of improvement in type of surgeries

Percentage of improvement	Inguinal (%)	Sub-inguinal (%)	Laparoscopy (%)
Concentration (million/ml)	78.3	78.2	74.7
Total sperm (million)	73.2	74.3	71.5
Motility (A+B)%	60.6	63.4	56.2
Morphology (normal %)	45.6	49.4	41.6

Table 2: Percentage of improvement in pregnant patients

Parameters	Pre-operative (Avg)	Post-operative (Avg)	Percentage of improvement in pregnant (%)
Concentration (million/ml)	8.83	11.1	79.50
Total sperm (million)	18.5	24.5	75.50
Motility (A+B)%	38.3	48.25	79.40
Morphology (normal %)	15.33	23.16	66.20

Table 3: Analysis of successful pregnant post-varicocelelectomy patients with non-pregnant

Parameters	Non-pregnant			Percentage of improvement in pregnant (%)
	Pre-operative (Avg)	Post-operative (Avg)	Percentage of improvement (%)	
Concentration (million/ml)	10.49	14.57	72.50	79.50
Total sperm (million)	16.4	21.3	73.50	75.50
Motility (A+B)%	22.6	35.56	67.50	79.40
Morphology (normal %)	8.77	18.1	49.50	66.20

Table 4: Grades of varicocele and percentage of improvement in semen parameters

Parameters	Percentage of improvement sub-clinical (%)	Percentage of improvement Grade I and II (%)	Percentage of improvement Grade III (%)
Concentration (million/ml)	70.80	72.70	46.70
Total sperm (million)	69.80	88.80	75.00
Motility (A+B)%	52.00	60.00	39.00
Morphology (normal %)	39.20	56.60	23.20

The total number of cases in our study was 51 patients, 33 patients (64.2%) had a unilateral varicocele, and 18 patients (35.3%) had a bilateral varicocele.

Table 4 illustrates the percentage of improvement in varicocele grades. On comparing the percentage of improvement in different grades of varicocele, the highest improvements in seminal parameters such as sperm concentration, total sperm count, motility, and morphology is seen in Grade I and II varicocele. The percentage of improvement in sub-clinical varicocele and Grade III varicocele is low as compared with that of Grade I and II. This implies that good improvement can be expected in Grade I and II varicocele after surgery.

Moazzam *et al.* have reported seminal improvement of sperm density, sperm motility, and sperm morphology in 60-80%.¹⁸ 43 of the 51 patients (84.1%) in our study showed improvement of seminal parameters in the post-operative follow-up period. The two most widely quoted, prospective randomized controlled trials by Madgar *et al.* and Nieschlag *et al.* revealed a statistically significant improvement in sperm density after varicocele repair.^{17,19}

Madgar *et al.* demonstrated a statistically significant improvement in pregnancy rate with 60% and Nieschlag *et al.* have shown a pregnancy rate of 29%. In our study, of the 51 patients, only 6 patients (11.8%) could have successful pregnancy in the follow-up period.

Matthews and coworkers found that 55% of men with azoospermia and 69% of men with zero motile sperm before surgery had motile sperm in their ejaculate after varicocele surgery.¹¹

Sperm motility is another important factor that is taken into account for describing the fertilizing potential of the semen sample. Studies by Tinga *et al.*, Okuyama *et al.*, and Goldstein demonstrated an increased motility as well as increased sperm concentrations after varicocelelectomy.⁷⁻⁹ Similar results were seen in our study.

CONCLUSIONS

Varicocelelectomy gives a statistically significant improvement in sperm concentration, motility, and overall morphology. The improvement in semen parameters did not have any significance in fertility potential. All approaches to varicocelelectomies (sub-inguinal, inguinal, or laparoscopic) have shown a significant improvement in seminal parameters, with sub-inguinal approach being good in improving motility parameter. 6 patients (11.8%) post-varicocelelectomy were able to successfully impregnate their partners. Even though there is an improvement in seminal parameters in 84.1% patients postoperatively, only 11.8% were only fertile. The rest of the patients cannot achieve successful improvement in fertility potential. On analyzing the patients with successful pregnancy showed that motility is probably the most crucial factor followed by morphology in achieving fertility. We need further studies to identify the reliable parameters based on which varicocelelectomy as a treatment modality can be suggested.

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