

Association of Varicocele and Secondary Infertility Improvement among Yemeni Patients in Aden

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Abstract:

Background: Varicocele is believed to be the most important factor in secondary male infertility.

Objective: The objective was to investigate the association of varicocele with improvement of semen parameters and pregnancy rate post- varicocele among Yemeni men with secondary infertility.

Materials and method: The study was a prospective non-controlled trial conducted on Yemeni men during the period of January 2012 to December 2014 who attended Algamhoria Teaching Hospital and Al-Saeedi hospital, in Aden for infertility treatment.

Results: The total study subjects was 100 men with varicocele, secondary infertility and reduced semen parameters. The mean age of the patients was 33.7 ± 7.7 years. Doppler Ultrasound categorized varicocele into Grade I (20%), Grade II (48%), and Grade III (32%). The majority (70%) of participants had varicocele on the left side. The preoperative semen results showed that the average of total sperm number and motility were $17.84 \pm 5.64 \times 10^6$ and 19.19 ± 6.17 %, respectively. Varicocele lead to 80%, and 78% improvements in semen total number and motility of the study men respectively, and they were collectively showed significant higher pregnancy rate. Pregnancy had occurred in 63 (78.8%) and 61 (78.2%) of women whom partners showed improvements in semen total number ($\Phi = 0.26$, $P = 0.022$) or semen total motility ($\Phi = 0.23$, $P = 0.042$), respectively.

Conclusion: The study confirmed the association of varicocele with secondary male infertility. However, more controlled randomized clinical trials and biomedical studies are necessary to establish the causal relationship between varicocele and male infertility.

Keywords: Varicocele, secondary infertility, varicocele, semen parameters, pregnancy rate, Aden.

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العلاقة بين رفع دوالي الخصية وتحسين العقم الثانوي لدى المرضى اليمنيين في عدن

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الخلفية: يعتقد أن دوالي الخصية هي العامل الأكثر أهمية لعقم الذكور الثانوي.

الهدف: كان الهدف هو التحقق من ارتباط دوالي الخصية مع تحسين بارامترات السائل المنوي ومعدل الحمل بعد عملية رفع الدوالي بين الرجال اليمنيين الذين يعانون من العقم الثانوي.

المنهجية: كانت الدراسة مستقبلية خلال الفترة من يناير 2012 إلى ديسمبر 2014 ، للمرضى الذين حضروا مستشفى الجمهورية التعليمي ومستشفى السعيد في عدن ويعانون من وجود دوالي في الخصية ويطلبون علاج للعقم.

النتائج: مجموع المبحوثين في الدراسة هو 100 رجل يعانون من دوالي الخصية والعقم الثانوي وانخفاض معايير السائل المنوي. كان متوسط عمر المرضى 33.7 ± 7.7 سنة. دوبلر الموجات فوق الصوتية صنفت دوالي الخصية درجة أولى (20%) ، ودرجة ثانية (48%) ، ودرجة ثالثة (32%). وكان الغالبية (70%) من المبحوثين لديهم دوالي الخصية في الجانب الأيسر. وأظهرت نتائج السائل المنوي قبل الجراحة أن المتوسطات من إجمالي عدد الحيوانات المنوية والحركة كانت $17.84 \pm 5.64 \times 10^6$ وكذا 19.19 ± 6.17 % على التوالي. رفع دوالي الخصية أدى إلى تحسن 80% في عدد السائل المنوي و 78% في حركة الحيوانات المنوية وقد أظهرت التحسن بشكل جماعي في ارتفاع معدلات الحمل. وقد حدث الحمل في 63 (78.8%) و 61 (78.2%) من الزوجات اللواتي ظهر التحسن لدى الأزواج في العدد الكلي للحيوانات المنوية ($\Phi = 0.26$ ، $P = 0.022$) أو مجموع حركة السائل المنوي ($\Phi = 0.23$ ، $P = 0.042$)، على التوالي.

الاستنتاج: أكدت الدراسة ارتباط دوالي الخصية مع عقم الذكور الثانوي. ومع ذلك ، فمن الضروري إجراء التجارب السريرية العشوائية والدراسات الطبية من أجل تحديد العلاقة السببية بين دوالي الخصية والعقم عند الذكور.

Introduction:

A varicocele is defined as dilated and tortuous veins within the pampiniform plexus of scrotal veins. It is the most surgically correctable cause of male secondary infertility. The varicocele is a disease of puberty and is only rarely detected in boys <10 years of age. A left-sided varicocele is found in 15% of healthy young men (1).

Several anatomic features contribute to the predominance of left-sided varicoceles. The left internal spermatic vein is longer than the right; in addition, it usually joins the left renal vein at right angle. The right internal spermatic vein has a more oblique insertion into the inferior vena cava. This particular anatomy in the standing man may cause higher venous pressures to be transmitted to the left scrotal veins and result in retrograde reflux of blood into the pampiniform plexus (2).

Approximately 8% of males experience infertility-related problems during their reproductive age (3). Varicocele is reported as one of the most important causes of male infertility in particular secondary infertility (4). It is estimated that varicocele has an incidence of 75%–81% among men with secondary infertility compared to 4%–23% in the general population and 21%–41% with primary infertility (5,6,7).

Accordingly, varicocele treatment is found to improve 45% of reduced semen parameters in patients with secondary infertility. As well, spontaneous pregnancy is achieved in 32.9% of patients' partners subjected to varicocele treatment compared to 13.9% of untreated group (8).

Despite the above mentioned, the causal relationship between varicocele and infertility is still confounded in reading that woman conception caused by either or both of male and female associated infertility factors. Generally, the contributory effects of varicocele on male infertility can be justified by increase of male infertility incidence in varicocele clinical cases as well as improvements achieved in semen parameters and pregnancy following varicocele treatment (4).

The objective of this study is to investigate the association of varicocele with improvement of semen parameters and pregnancy rate post- varicocele treatment among Yemeni men with secondary infertility.

Patients and Method:

This study was a prospective non-controlled trial carried out among Yemeni patients attending Algamhoria Teaching Hospital in Khormaksar district and

Al-Saeedi Hospital in Sheikh Othman district in Aden for infertility treatment during the period between January 2012 and December 2014.

The inclusion criteria involved entailed patients with varicocele suffering from secondary infertility and reduced semen parameters. World Health Organization (WHO) criteria regarding lower reference limits of total sperm number [39×10^6 ($33-46 \times 10^6$)] and motility [40% (38–42%)] were followed in this study [9].

The exclusion criteria entailed patients with primary infertility, azoospermia or if cause of infertility is established in the woman.

A total of 100 patients aged 20 – 52 years with female partners of 18 – 37 years successfully participated in this study.

Varicocele grade was assessed by Doppler Ultrasound. At least two semen specimens were collected from each patient and examined before varicocele treatment surgery. Follow-up of the studied patients was performed about three months intervals post-varicocele treatment or until pregnancy was achieved. For statistical analysis, pregnancy rate was examined as the dependent variable, while improvements in total sperm number and total sperm motility post-varicocele treatment as the explanatory variables.

Data were analyzed using SPSS statistical software (version 17). We used Phi or Cramer's tests to measure the strength of the association between the variables. Results with a P value < 0.05 were considered significant.

Results:

The general characteristics of the 100 patients participated in this study are shown in Table 1. The mean age of patients was 33.7 ± 7.7 years.

Majority (84%) of the participants aged 20 – 41 years and only 16% were 42 – 52 years. Doppler Ultrasound categorized varicocele into Grade I (20%), Grade II (48%), and Grade III (32%).

The majority (70%) of the participants had varicocele on the left side, 24% bilateral and 6% on the right side. Similarly, the preoperative semen results showed that the averages (mean) of total sperm number and motility were $17.84 \pm 5.64 \times 10^6$ and $19.19 \pm 6.17\%$, respectively.

Table 1: General characteristics of the 100 patients participated in this study

Characteristic	Percentage
Age (years):	
20 – 30	37
31 – 41	47
42 – 52	16
Mean age (years):	33.7 ± 7.7
Degree of varicocele:	
Grade I	20
Grade II	48
Grade III	32
Location of varicocele:	
Right	6
Left	70
Bilateral	24
Seminal parameters (mean ± SD)	
Total sperm number	17.84 ± 5.64 × 10 ⁶
Total sperm motility	19.19 ± 6.17 %

As shown in Table 2, majority of the participants showed improvements in semen total number (80 improved versus 20 not improved) and semen total motility (78 improved versus 22 not improved). Similarly, pregnancy had occurred in 75 of patients' wives.

Table 2: Results of semen parameters and pregnancy improvements post-varicocelectomy

Variable	Improved	Not improved
Semen total number	80	20
Semen total motility	78	22
Pregnancy rate	75	25

Association of improvements in semen parameters and degree of varicocele with pregnancy rate is shown in Table 3. Improvements in semen total number and motility were collectively showed significant higher pregnancy rate. Pregnancy had occurred in 63 (78.8%) and 61 (78.2%) of women whom partners showed improvements in semen total number ($\Phi = 0.26$, $P = 0.022$) or semen total motility ($\Phi = 0.23$, $P = 0.042$), respectively, compared to those with no improvements in either total semen number (60%) or motility (63.6%). In contrast, the results revealed a gradual decrease in the pregnancy rate significantly associated ($\Phi = 0.56$, $P = 0.001$) with varicocele's degree (Grade I = 100%, Grade II = 87.5% and Grade III = 40.6%). Accordingly, the highest improvement

in pregnancy rate was reported among patients with varicocele located on the right side (100%) followed by bilateral (79.2%) and left (71.4%) sides. However, this distribution was not significantly associated with pregnancy rates ($\Phi = 0.16$, $P = 0.259$).

Table 3: Association of semen parameters' improvement and varicocele's degree and location with pregnancy rate post-varicocelectomy

Improvements	Pregnancy						Phi/C V	P
	Occurred		Not occurred		Total			
	No	(%)	No	(%)	No	(%)		
Semen total number*:								
Improved	63	(78.8)	17	(21.2)	80	(100)	0.26	0.022
No improvement	12	(60.0)	8	(40.0)	20	(100)		
Semen total motility**:								
Improved motility	61	(78.2)	17	(21.8)	78	(100)	0.23	0.042
No improvement	14	(63.6)	8	(36.4)	22	(100)		
Degree of varicocele:								
Grade I	20	(100)	0	(0.0)	20	(100)	0.56	<0.001
Grade II	42	(87.5)	6	(12.5)	48	(100)		
Grade III	13	(40.6)	19	(59.4)	32	(100)		
Location of varicocele:								
Right	6	(100)	0	(0.0)	6	(100)	0.16	0.259
Left	50	(71.4)	20	(28.6)	70	(100)		
Bilateral	19	(79.2)	5	(20.8)	24	(100)		

* Total semen number was examined against pregnancy rate layered by total semen motility ** Total semen motility was examined against pregnancy rate layered by total semen number

Discussion:

The association between the presence of a varicocele and poorer semen quality is well documented in men presenting to fertility clinics (10) and in small-scale studies of patients not selected on fertility criteria (11,12).

In the present study the mean age of the patients was 33.7 ± 7.7 years and the majority of the patients (84%) aged 20 – 41 years and only 16% were 42 – 52 years. Our patients were older than findings reported by Shabana et al (13) from Egypt which was 28.3 ± 7.4 years and the finding by Tulit et al (14) from India 28.34 ± 5.72 years. The enrolled patients were younger than mean age reported by Sampalski et al (15) which was 35.8 years.

In our current study, the results revealed that 78 – 80% of semen total number and motility was improved post-varicocelectomy. As well, these improvements were significantly (< 0.05) associated with pregnancy rate of 75% among the study couples. These findings were in agreement with previous uncontrolled studies reporting significant association between varicocele and improvement of sperm number and motility (13,16,17). Varicocelectomy had

been reported to significantly improve 65% of one or more semen parameters and pregnancy rates of 40% in couples (17).

This study also showed that varicocele degree has a negative significant ($P < 0.001$) association with pregnancy rate indicating that higher improvement in pregnancy rate could be expected in Grade I varicocele. These findings were in disagreement with Steckel et al (18) study indicated a greater relative improvement was achieved after varicocelectomy in semen quality among patients with Grade 3 varicocele compared to those of Grade I or II varicoceles. However, our study findings were in harmony with a study carried out by Kumar et al (19) which revealed that improvements in semen parameters were higher among patients with Grade I or II varicocele.

In the current study we found that the majority of patients (70%) had varicocele on the left side. Saypol et al (16) mentioned that it was important to note that in 78% - 93% of cases varicocele is located on the left side. The present study, however, was relatively in agreement with Kumar et al (19) who reported varicocele located on the left, right and bilateral sides in 56.8%, 7.8% and 35.3% of all investigated patients, respectively.

Although this rudimentary study showed significant association with semen parameters and pregnancy rate, the surgical repair of varicocele remains one of the most controversial issues. Many researchers consider that the surgical intervention should be performed with restricted inclusion criteria for selection of infertile men (20).

Conclusion:

The present study, however, further confirms that varicocele is significantly associated with decreased pregnancy rate among Yemeni patients with secondary infertility in Aden city. Further well-designed studies including controlled randomized clinical trials and biomedical investigations are highly recommended in order to ascertain the causal effect of varicocele on male infertility.

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