

Spermogram changes and pregnancy rate in Egyptian infertile males before and after varicocelectomy

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Abstract: Background: Varicoceles are abnormally dilated testicular veins in the scrotum, secondary to internal spermatic vein reflux. Varicocele is found in approximately 15% of the general population, 35% of men with primary infertility and in 75-81% of men with secondary infertility. Although there have been numerous theories regarding the pathophysiology of varicocele, some remains unknown about its role in management of male factor infertility. From clinical view, the main treatment options for infertile males with varicoceles have been varicocelectomy and assisted reproductive techniques (ART). **Aim of the study:** to assess the role of varicocelectomy in management of male infertility by observation of spermogram changes before and after varicocelectomy. **Patients and methods:** This study was carried out on 20 male patients attending General Surgery and Dermatology outpatient clinics at Al-Zahraa University Hospital with a history of primary and secondary infertility after taking informed consent. This study was conducted over a period of 2 years, from August 2010 to August 2012. All patients were subjected to complete history and thorough clinical examinations as well as laboratory investigations including complete blood count (CBC), hormonal profile and multiple semen analysis were done for all patients. Semen analysis for each patient was repeated after varicocelectomy for 3, 6, 9 and 12 months. Also, scrotal color Doppler ultrasound was done for all attendants for confirmation of the diagnosis. **Results:** Out of 20 patients with primary varicocele, 16 (86.6%) had corrected abnormal semen parameters and their wives get pregnant. 60% of those patients were complaining of primary infertility while the remaining (40%) patients were complaining of secondary infertility. **Conclusion:** varicocele repair for infertile men with clinically palpable varicocele and at least one or more abnormal semen parameters is recommended as easy and simple treatment of primary or secondary male infertility, and improving fertility rate.

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Keywords: (ART): assisted reproductive techniques, (CBC): complete blood count, (ROS): reactive oxygen species, (4-HNE): 4-hydroxy-2-nonenal modified proteins, (WHO): world health organization, (GFR- α 1): glial cell derived neurotrophic factor specific receptor, (8-OHdG): 8-hydroxy-2-deoxy-guanosine, (FSH): follicular stimulating hormone, (LH): luteinizing hormone.

1. Introduction

Varicocele is an abnormal enlargement, dilatation and torsion of the vein in the scrotum draining the testicles. The testicular blood vessels originate in the abdomen and course down through the inguinal canal as part of the spermatic cord on their way to the testis. Upward flow of blood in the veins is ensured by small one-way valves that prevent backflow. Defective valves, or compression of the vein by a nearby structure, can cause dilatation of the veins near the testis, leading to the formation of varicocele (*Chen et al., 2008*).

Although most men with varicoceles are able to father children, there is abundant evidence that varicoceles are detrimental to male fertility. A study by (WHO) on over 9,000 men showed that varicoceles are commonly accompanied by decreased testicular volume, impaired sperm quality, and a decline in Leydig cell function. Another report showed that 70% of healthy, asymptomatic persons

with palpable varicoceles had an abnormality on semen analysis (*Agarwal et al., 2007*).

There are various etiologies of varicocele-induced infertility. Among these etiologies, impairment of testicular microcirculation. Elevated reactive oxygen species (ROS) levels and decreased total antioxidant capacity. Also, elevated levels of malondialdehyde, which is a marker of lipid peroxidation and 4-hydroxy-2-nonenal (4-HNE) modified proteins, are another marker of oxidative stress found in human testes with varicocele (*Shiraishi and Naito, 2007*).

Also, among the theories that there was high levels of DNA damage have also been associated with elevated ROS levels in patients with varicoceles. Varicoceles are also associated with an increase in apoptosis within testicular tissue. Various apoptotic factors in patients with varicocele include cadmium, androgen deprivation, heat stress, IL-6, and gonadotropin-releasing hormone, like gonadal peptide (*Benoff et al., 2009*).

In addition, Aquaporins are a family of transcellular membrane proteins that mediate water transport across the cell membrane.

Another studies postulated other causes of infertility associated with varicocele including abnormal expression of leptin receptors, glial cell derived neurotrophic factor specific receptor GFR- α 1 on germ cells, and increased expression of heme oxygenase on Leyding cells (*Zini et al., 2008*).

In this work we tried to assess the role of varicocelectomy as easy, cheap and simple method for management of male infertility regardless to its cause.

2. Patients and Methods:

This study was carried out on 20 married males with palpable varicoceles and history of primary and secondary infertility for more than 1 year of unprotected sexual intercourse. This study was conducted over a period of 2 years, from August 2010 to August 2012.

Those patients attending General Surgery, Dermatology and Venereology outpatient clinics in Al-Zahraa University Hospital. Histories of infertility, general and local examination were done for the patients. Manifestations of secondary sexual characters were examined.

Patients were examined in standing position and Valsalva maneuver was done for all attendants in a warm room, also patients were examined in supine position to examine other pathological conditions associated with varicocele.

Varicocele was graded according to clinical examination into (*Lyon et al., 1982*):

Grade I: palpable varicocele with Valsalva maneuver.

Grade II: palpable varicocele without Valsalva maneuver.

Grade III: visible varicocele. Diagnosis of varicocele and its grade was confirmed by scrotal color Doppler ultrasound for grading of varicocele according to internal spermatic vein diameter and to find any associated testicular and extratesticular pathology.

Accordingly, by scrotal color Doppler ultrasound varicocele was graded into;

Grade I (small): internal spermatic vein diameter less than 1mm.

Grade II (medium): internal spermatic vein diameter greater than 1mm.

Grade III (large): internal spermatic vein diameter greater than 1mm and can be seen easily through the scrotal skin (*Cvitanić et al., 1993*).

Laboratory tests as CBC, and free testosterone, FSH, LH, and prolactin hormonal profile were done for the patients.

Semen analysis for every patient was done before operation. At least one abnormal semen parameter (decreased sperm count (oligozoospermia) below 20 million /ml, decreased sperm motility (asthenozoospermia) below 50% of forward progressive motility, and increased abnormal forms (teratozoospermia) above 75% were included in this study.

Exclusion criteria:

Sub clinical varicocele, normal semen parameters, azospermia, abnormal hormonal profiles, smoking, debilitating or chronic diseases (diabetes, hypertension and liver diseases) and female partners' medical problems were excluded from this study.

Varicocelectomy operation was done for included patients in this research.

Also, semen analysis was repeated for each patient after varicocelectomy after 3months, 6months and 9 months after operation.

Statistical analysis:

Data was analyzed by Microsoft Office 2003 (Excel) and Statistical Package for Social Science (SPSS) version 16. *P* value >0.05 is considered non-significant, <0.05 is considered significant and <0.01 is considered highly significant.

3. Results:

Table (1): Grade of Varicocele

| Grade | Frequency | Percent |
|-------|-----------|---------|
| 1 | 3 | 15% |
| 2 | 9 | 45% |
| 3 | 8 | 40% |
| Total | 20 | 100% |

This table revealed 3 patients (15%) with first grade varicocele, 9 patients (45%) with second grade varicocele and 8 patients (40%) with third grade varicocele.

Table (2): Side of Varicocele

| Side | Frequency | Percent |
|------------|-----------|---------|
| Unilateral | 6 | 30% |
| Bilateral | 14 | 70% |
| Total | 20 | 100% |

This table revealed the majority of the patients 14 patients (70%) with bilateral varicocele, while the minority 6 cases (30%) with left sided varicocele.

Table (3): Recurrence of Varicocele

| Recurrence | Frequency | Percent |
|------------|-----------|---------|
| Negative | 16 | 80% |
| Positive | 4 | 20% |
| Total | 20 | 100% |

This table revealed the great majority of the patients 16 patients (80%) with primary varicocele, while the minority 4 cases (20%) with recurrent varicocele.

Table (4): history of infertility:

| | Frequency | Percent |
|-----------|-----------|---------|
| Primary | 12 | 60% |
| Secondary | 8 | 40% |
| Total | 20 | 100% |

This table revealed the great majority of the patients 12 patients (60%) with primary infertility, while the minority 8 cases (40%) with secondary infertility.

Table (5): Associated problems with varicocele

| | Frequency | Percent |
|------------|-----------|---------|
| No | 14 | 70% |
| Hernia | 1 | 5% |
| Hydrocele | 4 | 20% |
| Hematocele | 1 | 5% |
| Total | 20 | 100% |

This table revealed (70%) without associated clinical problems, while (5%) associated with hernia, (5%) associated with hematocele and (20%) associated with hydrocele.

Table (6): Pregnancy after varicocele repair:

| | Frequency | Percent |
|-------|-----------|---------|
| Yes | 16 | 80% |
| No | 4 | 20% |
| Total | 20 | 100% |

This table revealed the great majority of the patients' 16 patients (80%) became fertile, while the minority 4 cases (20%) did not become fertile.

Also, there was significant correlation between varicocele and oligozoospermia, asthenospermia and teratozoospermia, (stress parameters). Mean and SD were for oligozoospermia (13.10±3.94), for asthenospermia (14.75±6.38) and for teratozoospermia (71.25±7.23) respectively.

While, no significant association with other parameters as viscous semen or leucospermia.

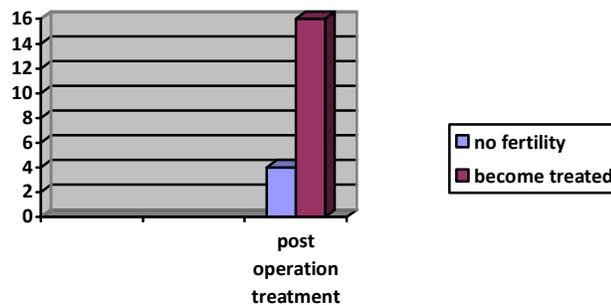


Fig (1): Frequency of cases become fertile post varicocelelectomy

In this study 16 of total 20 patients were treated and show improved abnormal semen parameters.

As regarding duration, 8 patients show improvement after 3 m, 6 cases improved after 6 m while other 6 cases show improvement after 9 m.

The improvement of abnormal parameters shows inverse proportional relationship with age of the patients. (Patients with younger ages show more and rapid improvement).mean ±SD (35.55±5.27) respectively.

4. Discussion:

Varicocele is a common finding among men with infertility and its repair has been a mainstay of surgical therapy in these men. Although each year multiple discoveries are made concerning the

mechanism of varicocele-induced infertility, the exact pathophysiologic mechanism remains unknown.

So, we aimed in this research to assess the role of varicocelelectomy as simple, more economic and effective method for management of male infertility.

In the current study, we observed that (80%) of the cases were treated, (Their wives get pregnant and the cases show improved semen parameters which were abnormal prior to varicocelelectomy.

This was in contrast to *Evers et al., 2008* who concluded that varicocele repair do not improve sub-fertility, and hence recommended against varicocele repair for unexplained infertility.

But (*Agarwal et al., 2007; Marmar et al., 2007*) agreed with our results. They concluded that surgical varicocelelectomy in selected patients demonstrated a beneficial effect on fertility status. Also, they added that varicocelelectomy significantly

improves semen parameters in infertile men with palpable varicocele and abnormal semen parameters. In addition they observed that the couples, who fail to achieve a natural pregnancy after varicocele repair, may achieve better results with assisted reproductive techniques because of improvement in semen quality after varicocelectomy.

The real mechanism by which varicocelectomy improves fertility remains unknown. But many researchers observed that oxidative stress and DNA damage improved after varicocele repair (*Khera et al., 2008*).

Other study explained how varicocelectomy improve the outcome of fertility by observing a significant decrease in the levels of 8-hydroxy-2-deoxy-guanosine (8-OHdG), another marker of oxidative stress in all post-varicocele repair patients. Also they demonstrated a significant decline in the incidence of mitochondrial DNA deletion, a marker of oxidant mediated DNA damage after varicocele repair (*Chen et al., 2008*).

In the current study, we observed significant association of bilateral varicocele with infertility which was agreed with (*Richardson et al., 2008*).

Also, young patients show better improvement than older individuals after varicocele repair. This was also agreed with (*Marmar et al., 2001*).

Conclusion and recommendation:

- Varicocelectomy is a cost effective and simple treatment modality for infertility.
- Increased incidence of bilateral varicocele associated with infertility more than left sided varicocele.
- Improvement of semen parameters and fertility rate with younger than older patients.
- Association of varicocele with stress parameters of semen analysis more than other parameters.
- Other researches are needed on large numbers to explain the mechanism of fertility improvement by varicocelectomy.

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