Original Article

The Impacts of Subclinical Varicoceles on Infertile Males

Ibrahim J. Hammadi* **MB ChB, MSc ART**
Ghassan Th. Saeed** **MB ChB, MSc PhD**
Read How. Abed Tawney*** **MB ChB, FICMs (Radiology)**

Abstract:

Background: it is well known that the varicocele affects male fertility and had adverse effects on the findings of the standard seminal analysis. According to size of that veins; the varicoceles are divided into clinical that are discovered in physical examination and their harmful effects are proved and subclinical varicoceles that are only discovered by Doppler examination. And till now, the indication of surgery in cases of subclinical varicocele is still controversial because of poor information about the impact of those non-clinically founded blood vessels on the testicular function.

Objective: To assess the seminal fluid, testicular volume, and hormone levels in infertile patients with subclinical varicoceles.

Patients and methods: two groups were studied; 79 infertile patients with subclinical varicoceles and 50 healthy males with normal scrotal ultrasound were included as control group. Semen samples were collected from all subjects after at least 48 hours of sexual abstinence in sterile wide containers by masturbation and analyzed for sperm concentration and percentage motility according to WHO criteria (2010). Serum FSH, LH, and Testosterone (T) levels were assessed using Radioimmunoassay. Ultrasound examination was done to evaluate the pampiniform plexus caliber and also measuring the testicular size.

Results: LH and Testosterone levels were not statistically different among the two groups. FSH levels were significantly higher in infertile men with subclinical varicoceles than in control group ($p<0.04$). The testicular size was significantly smaller in subclinical varicocele group. Regarding the sperm concentration and motility, there were also significant lower percentages in infertile men with subclinical varicoceles ($p<0.02$) and ($p<0.05$) respectively.

Conclusion: Infertile patients with subclinical varicoceles have higher levels of FSH, smaller testes, and lower percentages of sperm concentration and motility.

Key words: Subclinical varicoceles, Testicular volume, FSH.

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Introduction:

Varicocele is a state of dilated, elongated and tortuous veins of the pampiniform plexus of the spermatic cord. It typically develops during young age group and has been found in about 15٪ of the general healthy male populations (1).

Patients with varicoceles seek medical attention when they experience pain and or a dragging sensation in the scrotum and some studies found that up to 40٪ of men evaluated at infertility clinics have varicocele (2).

Clinical varicocele refers to those detectable by either visual inspection or palpation or after performing Valsalva maneuver (expiration against a closed glottis) which is an important part of the clinical examination as it causes distension of the pampiniform plexus and usually varicoceles greater than 3–4 mm in diameter are clinically apparent.

The most widely used classification is the Dubin grading system (1) that classified varicocele in 3 grades:

Grade 3: visible and palpable at rest.

Grade 2: palpable at rest.

Grade 1: palpable during Valsalva maneuver.

While subclinical varicocele is not palpable or visible at rest or under Valsalva maneuver but detected only by Doppler ultrasound (3).

Wide variety of explanations of the relation between varicocele and male infertility have been purposed including sperm damage from elevated temperature in the scrotum, retention of waste products and slowly flowing blood in the pampiniform plexus and high concentration of testosterone and other hormones in these vessels and also sperm DNA damage and high oxidative stress (4-6).

Varicocele treatment (varicocelectomy) is indicated in

1.Symptomatic, large varicocele causing testicular pain.

2.Palpable or visible varicocele with abnormal semen analysis in man desiring fertility.

3.Palpable varicocele with ipsilateral testicular atrophy defined as size less than 20% of the contralateral testicle.

4.Bilateral varicoceles with testicular atrophy.

But not indicated for patient of subclinical varicocele as state by the Practice Committee of the American Society for Reproductive Medicine reports on optimal evaluation of the infertile male (7). But still some authors have suggested improvement in sperm parameters after varicocelectomy in

* *Corresponding toibrahimhamadi988@yahoo.com AL-Yarmouk Teaching Hospital/Infertility Center*
** *Baghdad Medical College/Department of physiology*
*** *Acting Chairman of Iraqi Board of Radiology*

men having subclinical Varicoceles (8-10).
Cina et al found no significant associations between Doppler ultrasound parameters (venous diameter and retrograde flow) and standard semen analysis parameters among healthy men with normal semen analyses (11) while Caşkurlu et al who examined 100 infertile patients with subclinical varicocele, 100 infertile patients with clinical varicocele, and 50 fertile men without clinical varicocele, concluded that venous diameters should not be used as diagnostic criteria for subclinical varicocele because the highest mean diameters of the veins did not differ significantly across the groups and the impact of varicocele on the seminal fluid finding was similar in both cases (12).
In infertility clinics, the infertile males without palpable scrotal lesion are usually not referred for ultrasound studies (13). Hence, this study was performed to find out the significance of subclinical varicocele in male infertility.

Patients and Methods:
This study was carried out at AL-Yarmouk Teaching Hospital in the period between January 2013 and November 2014. 79 patients with subclinical varicocele (mean age: 26 years; range: 17–40 years) diagnosed previously by Doppler examination (53 unilateral and 22 bilateral subclinical varicocele). The second group was of 50 fertile men without varicoceles that were included in this study as a control group. All patients were assessed via physical examination and scrotal color Doppler imaging for classification purposes and with ultrasound scan in B-mode to obtain testicular volume, which was calculated using the ellipsoid formula (volume 54/3 *a*b*c) where a, b, and c are the semi axes of the ellipsoid (14). Scrotal ultrasonic examination using (ALOKA SS 08 (TOKYO, JAPAN)) was performed to the patient in the supine position and the scrotum supported by a towel placed between the thighs. Optimal results are obtained with a 7–10-MHz high-frequency linear array transducer. Scanning is performed most often with the transducer in direct contact with the skin, but if necessary a stand-off pad can be used for evaluation of superficial lesions. The testes are examined in at least two planes, long and transverse axes. Color Doppler is optimized to measure the diameter of testicular veins using cut-point values of >2.45 mm in rest or >2.95 mm during Valsalva maneuver in the supine position to be diagnosed as subclinical varicocele (4).
Semen samples were collected from all included subjects after at least 48 hours of sexual abstinence in sterile wide containers by masturbation in near private room and allowed to liquefy at 37°C for about 60 minutes and analyzed for sperm concentration (million/ml), percentage motility and percent of sperms with normal morphology according to WHO criteria (15). Serum follicle stimulating hormone (FSH), luteinizing hormone (LH) and testosterone (T) levels were also assessed using Radioimmunoassay.
All patients' information remained confidential.
Statistical analysis: Values are presented as mean ±SD all statistical analyses were performed with Statistical Package for the Social Sciences (SPSS), and version 17. Multivariate analysis was performed using, seminal fluid parameters, Testicular volume and hormonal assay of both groups. P<0.5 was considered statistically significant.

Results:
TABLE 1: Hormonal assay, ultrasound findings, and spermogram results of men with subclinical varicoceles and fertile men. (Control group).

Parameters	Patients with subclinical varicocele group	Control group	P values
FSH (IU/L)	7.8 ±7.6	3.4 ±1.7	0.04
LH (IU/L)	4.3 ±1.9	4.7 ±2.1	0.451
Testosterone (IU/L)	540.36 ±94.5	590.72 ±112.6	0.673
Right testicle (cm^3)	17.6 ±8.9	22.4 ±9.3	0.03
Left testicle (cm^3)	19.7 ±7.3	23.9 ±9.7	0.03
Sperm concentration (*10^6/ml)	31.7 ±22.5	100.8 ±71.2	0.02
Sperm motility (%)	35.2 ±22.9	60.9 ±14.8	0.05

Both right and left testicle were smaller in subclinical varicocele (P<0.05).
LH and total Testosterone levels were not statistically different across the two groups (P>.05). FSH levels were significantly higher in infertile patients with subclinical varicoceles (P<0.05).
Regarding the sperm concentration and sperm motility, both were lower in than the control group (P<0.05).

Discussion:
In this study, LH and T levels were statistically indifferent between the two studied groups. However, FSH levels were significantly higher in the infertile patients with subclinical varicoceles. The high levels of FSH seen in those patients might be due to subclinical varicoceles and their effects on the testicular function and spermatogenesis as it is well known that levels of FSH is an indicator of the testicular function and high

FSH levels is usually associated with low sperm concentration and poor sperm motility (16).

The present results were in harmony with Cantoro and his co-workers' study that showed that subclinical varicocele cause higher reduction on semen parameters and pregnancy rates (17) and authors proved that surgical treatment of subclinical varicocele was effective even when compared with clinical varicocele. Another study performed by Mcclure and coworkers (18) suggested that the detection of subclinical varicocele might be warranted in infertile males with abnormal seminal parameter and there was an improvement in sperm motility seen in both clinical and subclinical varicocele after the surgical treatment being slightly higher in the subclinical cases. In contrast, there was a disagreement with the findings of Jarow and coworkers who found that the seminal parameters abnormalities were statistically insignificant of subclinical varicocele patients when compared with that of clinical varicocele (19).

A study done by Gonda et al showed that surgery cause improvement in the seminal fluid parameters (count and motility) in infertile patients with subclinical varicocele and patients became fertile. The accepted pregnancy rates that were achieved in those patients who were treated emphasize the importance of making the diagnosis of subclinical patients (20).

Our study supports the findings of Zini et al (21) who demonstrated that testicular volume in men with subclinical varicocele was significantly decreased compared to controls without varicocele. But in disharmony with the results of Muley and his team (22) that found no significant difference in the testicular size among subclinical varicocele patients. However, these finding alone does not appear to be predictive of fertility potential in men with subclinical varicoceles as it was still within the accepted values.

It is well known that varicocele might lead to testicular atrophy and damage to the testicular tissue thus the decision for performing a varicocelectomy must be suggested to fertile man with clinical varicoceles to avoid testicular atrophy (23).

Saleh and coworkers and Talebi and coworkers reported that surgical treatment of varicocele decrease the percentage of sperm DNA fragmentation (SDF) (24, 25). This test has been experienced as a growing interest in recent years as a new method to assess not only sperm quality and function but also the pregnancy outcome and some genetic abnormalities (26).

García-Peiró and coworkers had used sperm DNA fragmentation test and found that clinical and subclinical varicoceles have a similar negative effect on sperm DNA integrity in infertile patients and that varicocelectomy improves sperm DNA quality in clinical but not in subclinical varicocele patients (27).

Zampieri and Dall'Agnola (28) found that Subclinical varicocele might be considered as the first stage of varicocele development and the rate of their progression to a clinically palpable varicocele was found to be significantly greater in the athletes.

In clinical practice, the subclinical varicocele is sometimes the only founded abnormality in couples suffering from infertility of unknown cause in which despite technological advances, the cause of male infertility is unknown and their incidence is about 10% of total infertility cases. These cases categorized as "infertility of unknown origin" that is classified into idiopathic male infertility (an unexplained reduction of semen quality) and unexplained male infertility (normospermic infertility) (29). Thus, the surgical treatment of the ultrasonic founded varicocele might be suggested if the methods of assisted reproductive techniques were not available.

According to the results of the present study, subclinical varicoceles associated with abnormal seminal fluid parameters and FSH that affect the spermatogenesis process and also showed also some adverse effects on the testicular size that might lead to testicular atrophy in the future.

Further studies are suggested to find the improvement of the seminal fluid quality after surgical treatment of subclinical varicocele.

Authors contributions:

Ibrahim Jasim Hammadi: Work designer.

Ghassan Thabet: Final approval of the work to be published.

Read H. Abed Taweny: Data analyzer.

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