# Relation between Varicocele and Erectile Dysfunction among Men in Egypt

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**ABSTRACT**

**Background:** Erectile Dysfunction (ED) and varicocele significantly affect men's health globally. This study investigates the link between varicocele severity, ED, and testosterone levels among Egyptian men.

**Methods:** This cross-sectional study involved 120 male participants, categorized into varicocele-diagnosed and control groups. Varicocele severity was identified clinically, followed by hormonal profiling and ED diagnosis using the International Index of Erectile Function-5 (IIEF-5) questionnaire.

**Results:** The study found no significant differences in age or hormone levels (testosterone, prolactin, LH, and FSH) between the varicocele and control groups, as confirmed by p-values (0.061, 0.574, 0.356, 0.121, and 0.293, respectively). Among participants with varicocele, 31.7% had a left-sided varicocele, while 68.3% were bilateral. Regarding severity, 46.7% had Grade I, 40.0% had Grade II, and 13.3% had Grade III varicocele. Testosterone levels dropped from 5.51±1.10 ng/ml (Grade I) to 4.27±1.32 ng/ml (Grade II) and 3.57±1.18 ng/ml (Grade III) varicocele ($p<0.001$). IIEF-5 scores declined from 22.52±1.11 (Grade I) to 20.27±2.68 (Grade II) and 16.50±5.47 (Grade III) ($p<0.001$). ED was diagnosed in 31.7% of varicocele participants. Higher bilateral varicocele prevalence was seen in Grades II and III (87.5% and 75.0%) than in Grade I (50.0%; $p=0.014$). ED prevalence surged from 10.7% (Grade I) to 41.7% (Grade II) and 75.0% (Grade III).

**Conclusion:** The study revealed that varicocele severity was associated with increased ED prevalence. Higher varicocele grades corresponded to decreased testosterone levels and IIEF-5 scores, indicating worsened erectile function.

**Keywords:** Varicocele, erectile dysfunction, men, Egypt.

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## Introduction

Erectile Dysfunction (ED) and varicocele represent two significant areas of concern within male sexual health, impacting not only the quality of life but also the overall health and well-being of men across the globe (Burnett et al., 2020). It is estimated that ED affects approximately 150 million men globally, with projections suggesting this number may rise to 322 million by 2025 (Patel et al., 2016). In Egypt, local studies indicate that ED is a growing health issue, with prevalence rates ranging from 10% to 52% among different age groups (El-Sakka, 2012; Seyam et al., 2003). ED significantly impacts men's self-esteem, relationships, and psychological health, enhancing its burden beyond physical symptoms (Althof et al., 2006; Yafi et al., 2016).

On the other hand, varicocele, characterized by abnormal dilation and tortuosity of the veins within the pampiniform plexus, is recognized as a prominent cause of male infertility (Leslie et al., 2023), affecting 15-20% of the general male population and up to 40% of men presenting with primary infertility (Valentino et al., 2014). The prevalence of varicocele in the Egyptian male population remains under-studied, emphasizing the necessity for targeted research in this geographical demographic (Alsaikhan et al., 2016).

Emerging research has indicated potential links between varicocele and ED (Ji & Jin, 2017; Keller et al., 2012). By nature of its pathophysiology, varicocele can decrease Leydig cell function, affecting testosterone levels, which play a vital role in erectile function (Luo et al., 2011; Vakalopoulos et al., 2017). The hypoxia, temperature increase, and venous pressure associated with varicocele may also have a negative impact on erectile function ,this demonstrated by Sathya and Belur (2011). Despite these observations, the relationship between the severity of varicocele and ED, particularly in the context of the Egyptian population, remains unclear.

This study aimed to discern the relationship between varicocele severity and ED among men in Egypt. Additionally, the association between varicocele and testosterone levels was investigated.

## Patients and Methods

### Study Design and Participants

This prospective comparative study recruited 120 male participants, aged between 25 and 45 years, from Helwan University Hospitals, Egypt. The study was conducted from June 2021 to March 2022. The participants were divided into two groups: 60 patients diagnosed with varicocele, and 60 patients free of varicocele. Participants with varicocele were further subdivided based on the grade of varicocele.

We included the patients who were married males diagnosed with varicocele, with normal levels of serum testosterone, Follicle-Stimulating Hormone (FSH), Luteinizing Hormone (LH), and prolactin levels. The exclusion criteria were the presence of diabetes mellitus, neurological and cardiovascular diseases, endocrinal abnormalities such as hypo or hyperthyroidism, congenital anomalies like hypospadias, use of drugs known to cause or predispose to ED such as antihypertensive beta blockers, and psychological causes of ED.

### Procedures

The initial diagnosis of varicocele was made through detailed history taking and clinical examination. A hormonal

profile was drawn for each participant, including Serum testosterone, LH, FSH, and prolactin levels. The International Index of Erectile Function-5 (IIEF-5) questionnaire was utilized to diagnose Erectile Dysfunction.

Patients with varicocele were subdivided according to the degree of varicocele into three groups (Grade I, Grade II, and Grade III). The correlation between ED and the grade of varicocele was assessed. The control group was clinically assessed to confirm the absence of varicocele.

**Statistical Analysis**

The sample size was justified according to the rule of thumb. Data were collected from history taking, clinical examination, laboratory investigations, and outcome measures. Data were coded and entered using Microsoft Excel software, then imported into the Statistical Package for the Social Sciences (SPSS version 20.0) software for analysis. Qualitative data were represented as numbers and percentages. Quantitative continuous data were expressed as mean ± standard deviation (SD). Statistical tests employed include the Chi-square test for qualitative variables, independent t-test for quantitative differences between two groups, and Analysis of Variance (ANOVA) for differences between multiple quantitative groups. Significance was set at a p-value of <0.05, while high significance was defined as a p-value of <0.001.

**Results**

**Demographic and clinical characteristics**

The mean age of the varicocele group was 29.85±5.14 years, which was not significantly different from the control group's mean age of 31.33±6.24 years (p=0.061). The mean testosterone levels in the varicocele group (4.75±1.34 ng/ml) did not differ significantly from the control group (4.89±1.04 ng/ml; p=0.574). Similarly, the mean prolactin levels in the varicocele and control groups were 6.21±1.21ng/ml and 6.39±0.84ng/ml, respectively, and this difference was not statistically significant (p=0.356). The varicocele group showed a mean luteinizing hormone (LH) level of 4.54±0.82 mIU/ml, which was not significantly different from the control group's level of 4.76±0.71 mIU/ml (p=0.121). Finally, the mean follicle-stimulating hormone (FSH) level was 5.49±0.79 mIU/ml in the varicocele group and 5.32±0.95 mIU/ml in the control group, with no significant difference observed (p=0.293), as shown in Table 1.

**Table 1:** Hormones distribution between groups A and B

| Variables | Varicocele | Control | P-value |
|---|---|---|---|
| **Age** | 29.85±5.14 | 31.33±6.24 | 0.061 |
| **Testosterone (ng/ml)** | 4.75±1.34 | 4.89±1.04 | 0.574 |
| **Prolactin (ng/ml)** | 6.21±1.21 | 6.39±0.84 | 0.356 |
| **LH (mIU/ml)** | 4.54±0.82 | 4.76±0.71 | 0.121 |
| **FSH (mIU/ml)** | 5.49±0.79 | 5.32±0.95 | 0.293 |

**Erectile Function and Varicocele Characteristics**

Among participants with varicocele, 31.7% had a left-sided varicocele, while 68.3% were bilateral. In terms of severity, 46.7% had Grade I, 40.0% had Grade II, and 13.3% had Grade III varicocele, as shown in **Table 2**.

**Table 2:** Varicocele characteristics

| Characteristics | | N | % |
|---|---|---|---|
| **Side** | **Left** | 19 | 31.7 |
| | **Bilateral** | 41 | 68.3 |
| **Grade** | **I** | 28 | 46.7 |
| | **II** | 24 | 40.0 |
| | **III** | 8 | 13.3 |
| | **Total** | 60 | 100.0 |

Regarding the International Index of Erectile Function-5 (IIEF-5) scores, patients with varicocele had a significantly ($p<0.001$) lower mean score (20.78±3.42) than control group (23.54±1.0). Furthermore, according to the IIEF-5 scores, 68.3% had no ED, and 31.7% had confirmed diagnoses of ED. The severity of ED was distributed as the following: 20% were mild, 8.4% were mild to moderate, and 3.3% were moderate, as shown in **Table 3**.

**Table 3:** ED distribution among patients with varicocele

| ED severity | Score | N | % |
|---|---|---|---|
| **No ED** | **22-25** | **41** | **68.3** |
| **Mild** | **17-21** | **12** | **20.0** |
| **Mild to Mod** | **12-16** | **5** | **8.3** |
| **Moderate** | **8-11** | **2** | **3.3** |
| **Total** | | **60** | **100.0** |

Significant differences were observed in testosterone, FSH, LH, and IIEF-5 scores across different grades of varicocele. Grade I participants had the highest mean testosterone level (5.51±1.10 ng/ml), which decreased significantly with the severity of the varicocele to 4.27±1.32 ng/ml in Grade II and 3.57±1.18 ng/ml in Grade III ($p<0.001$). No significant difference was found in prolactin levels across the grades ($p=0.335$). FSH and LH levels were higher in Grade III participants (6.67±0.82 mIU/ml and 5.36±0.98 mIU/ml, respectively) compared to those in Grade I (5.40±0.52 mIU/ml and 4.43±0.88 mIU/ml, respectively) and Grade II (5.20±0.72 mIU/ml and 4.39±0.51 mIU/ml, respectively) (FSH: $p<0.001$; LH: $p=0.008$).

IIEF-5 scores also significantly differed among grades ($p<0.001$), with the highest mean score in Grade I (22.52±1.11), decreasing to 20.27±2.68 in Grade II and 16.50±5.47 in Grade III. In terms of varicocele location, bilateral cases were more common in Grades II and III (87.5% and 75.0%, respectively) compared to Grade I (50.0%; $p=0.014$). ED prevalence also differed significantly across the grades ($p<0.001$). In Grade I, 89.3% had no ED, whereas this proportion decreased to 58.3% in Grade II and 25.0% in Grade III. Mild to moderate ED and moderate ED were only present in Grades II and III, as shown in **Table 4**.

**Table 4:** Comparison between grades of Varicocele

| Variables | | Grade I | Grade II | Grade III | P-value |
|---|---|---|---|---|---|
| **Testosterone (ng/ml)** | | 5.51±1.10 | 4.27±1.32 | 3.57±1.18 | 0.001 |
| **Prolactin (ng/ml)** | | 6.41±±1.0 | 5.92±1.43 | 6.35±1.11 | 0.335 |
| **FSH (mIU/ml)** | | 5.40±0.52 | 5.20±0.72 | 6.67±0.82 | 0.001 |
| **LH (mIU/ml)** | | 4.43±0.88 | 4.39±0.51 | 5.36±0.98 | 0.008 |
| **IIEF_5** | | 22.52±1.11 | 20.27±2.68 | 16.50±5.47 | 0.001 |
| **Side** | **Left** | 14 (50.0%) | 3 (12.5%) | 2 (25.0%) | 0.014 |
| | **Bilateral** | 14 (50.0%) | 21 (87.5%) | 6 (75.0%) | |
| **ED** | **No ED score (22-25)** | 25 (89.3%) | 14 (58.3%) | 2 (25.0%) | 0.001 |
| | **Mild score (17-21)** | 3 (10.7%) | 7 (29.2%) | 2 (25.0%) | |
| | **Mild to Mod score (12-16)** | 0 (0.0%) | 3 (12.5%) | 2 (25.0%) | |
| | **Moderate score (8-11)** | 0 (0.0%) | 0 (0.0%) | 2 (25.0%) | |
| **Total** | | 28 (100.0%) | 24 (100.0%) | 8 (100.0%) | - |

## DISCUSSION

This cross-sectional study provided valuable insights into the specific relationship between varicocele and impaired erectile function. Focusing on patients presenting normal hormonal profiles, particularly testosterone levels, we assessed the impact of varicocele on erectile function, measured by the IIEF-5. We selected patients diagnosed with varicocele and those without, excluding participants presenting any organic or psychological cause of ED. Hormonal profiles were evaluated, and the IIEF-5 was applied. Age distribution showed no significant difference between the two groups (29.85±5.14 years for varicocele group vs. 31.33±6.24 years for control group). Importantly, testosterone levels in both groups remained within the normal range (4.75±1.34 ng/ml for varicocele group and 4.89±1.04 ng/ml for control group). Interestingly, despite normal testosterone levels, varicocele group displayed significantly lower IIEF-5 scores, suggesting impaired erectile function. Approximately 31.7% of cases in this group had ED, with the majority classified as mild. Further analysis revealed a clear correlation between varicocele severity and hormonal profiles. Testosterone levels were significantly lower, while FSH and LH levels were higher in participants with more severe varicocele. The IIEF-5 scores were also significantly lower with higher varicocele grades, with ED being significantly associated with higher grades. Our findings align with a study by **Zohdy et al., (2011)** which reported lower IIEF-5 scores and testosterone levels in varicocele patients with hypogonadism. Despite our limited understanding of the exact mechanisms through which varicocele leads to reduced testosterone production and impaired sexual function, existing reports suggest a negative feedback effect of varicocele on Leydig cell function and serum testosterone levels this demonstrated by Ji and Jin (2017). Several hypotheses attempt to explain the influence of varicocele on Leydig cell function and testosterone levels, including testicular hyperthermia (Goldstein et al., 1989), increased oxidative stress within the testicular environment (Ishikawa et al., 2007), hormonal dysfunction (Diemer

et al., 2003), and hypoxia in the seminiferous tubules (Gat et al., 2010). While previous research on the impact of varicocele on erectile function is limited, one older study (Comhaire et al., 1975) reported that varicocelectomy normalized low testosterone levels and sexual inadequacy in ten patients. Similarly, systematic reviews have recognized the correlation between varicocele and decreased testosterone production (Fisch et al., 2012). Notably, a study focusing on grade II and III varicocele reported these grades were more predictive of hypogonadism and its association with ED ,this demonstrated by Ji and Jin (2017). Our study adds to this literature by suggesting that even within a normal hormonal profile, cases of high-grade, bilateral varicocele with the lowest limit of testosterone can be diagnosed with ED. Contrarily, another study reported higher serum testosterone levels in grade III varicocele compared to grade II and I (Al-Ali et al., 2010), a result inconsistent with our findings. However, the reported testosterone levels in this study were below 3 ng/ml, which calls for further investigation into the impact of varicocele grade on testosterone levels (Al-Ali et al., 2010).

Our study has some limitations; for example, some participants may have felt uncomfortable answering IIEF-5 questions related to ED truthfully. Furthermore, given that testosterone levels peak between 7 and 10 AM this explained by Swerdloff and Wang (2020), future studies should consider this when scheduling testing to ensure optimal accuracy. Despite these potential constraints, this study provides a critical look into the nuanced relationships between varicocele, hormonal profiles, and erectile function.

## CONCLUSION

In conclusion, our study reveals significant associations between the severity of varicocele and the prevalence of erectile dysfunction. More specifically, higher varicocele grades were linked to lower testosterone levels and IIEF-5 scores, indicating impaired erectile function. Additionally, the presence of bilateral varicocele was observed to exacerbate these effects, further underscoring the complex interplay between varicocele grade, hormonal profiles, and sexual function. Future research is necessary to further elucidate these relationships and their potential implications for treatment strategies.

## References

1. Burnett AL, Edwards NC, Barrett TM, Nitschelm KD, Bhattacharyya SK. Addressing Health-Care System Inequities in the Management of Erectile Dysfunction: A Call to Action. Am J Mens Health [Internet]. 2020 Sep 1;14(5):1557988320965078. Available from: https://doi.org/10.1177/1557988320965078
2. Patel CK, Bennett N. Advances in the treatment of erectile dysfunction: what's new and upcoming? F1000Research. 2016;5.
3. Seyam RM, Albakry A, Ghobish A, Arif H, Dandash K, Rashwan H. Prevalence of erectile dysfunction and its correlates in Egypt: a community-based study. Int J Impot Res. 2003 Aug;15(4):237–45.
4. El-Sakka AI. Erectile dysfunction in Arab countries. Part I: Prevalence and correlates. Arab J Urol. 2012 Jun;10(2):97–103.
5. Yafi FA, Jenkins L, Albersen M, Corona G, Isidori AM, Goldfarb S, et al. Erectile dysfunction. Nat Rev Dis Prim. 2016 Feb;2:16003.
6. Althof SE, O'Leary MP, Cappelleri JC, Crowley AR, Tseng L-J, Collins S. Impact of erectile dysfunction on

confidence, self-esteem and relationship satisfaction after 9 months of sildenafil citrate treatment. J Urol. 2006 Nov;176(5):2132–7.

7. Leslie SW, Sajjad H, Siref LE. Varicocele. In Treasure Island (FL); 2023.
8. Valentino M, Bertolotto M, Derchi L, Pavlica P. Children and adults varicocele: diagnostic issues and therapeutical strategies. J Ultrasound. 2014 Sep;17(3):185–93.
9. Alsaikhan B, Alrabeeah K, Delouya G, Zini A. Epidemiology of varicocele. Asian J Androl. 2016;18(2):179–81.
10. Ji B, Jin X -b. Varicocele is associated with hypogonadism and impaired erectile function: a prospective comparative study. Andrologia [Internet]. 2017 Aug 1;49(6):e12683. Available from: https://doi.org/10.1111/and.12683
11. Keller JJ, Chen Y, Lin H. Varicocele Is Associated with Erectile Dysfunction: A Population-Based Case-Control Study. J Sex Med [Internet]. 2012;9(7):1745–52. Available from: https://www.sciencedirect.com/science/article/pii/S1743609515340182
12. Vakalopoulos I, Kampantais S, Lymperi S, Grivas N, Ioannidis A, Mykoniatis I, et al. Should we expand the indications for varicocele treatment? Transl Androl Urol. 2017 Oct;6(5):931–42.
13. Luo D-Y, Yang G, Liu J-J, Yang Y-R, Dong Q. Effects of varicocele on testosterone, apoptosis and expression of StAR mRNA in rat Leydig cells. Asian J Androl. 2011 Mar;13(2):287–91.
14. Sathya Srini V, Belur Veerachari S. Does varicocelectomy improve gonadal function in men with hypogonadism and infertility? Analysis of a prospective study. Int J Endocrinol. 2011;2011:916380.
15. Zohdy W, Ghazi S, Arafa M. Impact of varicocelectomy on gonadal and erectile functions in men with hypogonadism and infertility. J Sex Med. 2011 Mar;8(3):885–93.
16. Goldstein M, Eid JF. Elevation of intratesticular and scrotal skin surface temperature in men with varicocele. J Urol. 1989 Sep;142(3):743–5.
17. Ishikawa T, Fujioka H, Ishimura T, Takenaka A, Fujisawa M. Increased testicular 8-hydroxy-2'-deoxyguanosine in patients with varicocele. BJU Int. 2007 Oct;100(4):863–6.
18. Diemer T, Allen JA, Hales KH, Hales DB. Reactive oxygen disrupts mitochondria in MA-10 tumor Leydig cells and inhibits steroidogenic acute regulatory (StAR) protein and steroidogenesis. Endocrinology. 2003 Jul;144(7):2882–91.
19. Gat Y, Gornish M, Perlow A, Chakraborty J, Levinger U, Ben-Shlomo I, et al. Azoospermia and Sertoli-cell-only syndrome: hypoxia in the sperm production site due to impairment in venous drainage of male reproductive system. Andrologia. 2010 Oct;42(5):314–21.
20. Comhaire F, Vermeulen A. Plasma testosterone in patients with varicocele and sexual inadequacy. J Clin Endocrinol Metab. 1975 May;40(5):824–9.
21. Fisch H, Hyun G. Varicocele repair for low testosterone. Curr Opin Urol. 2012 Nov;22(6):495–8.
22. Al-Ali BM, Marszalek M, Shamloul R, Pummer K, Trummer H. Clinical parameters and semen analysis in 716 Austrian patients with varicocele. Urology. 2010 May;75(5):1069–73.
23. Swerdloff RS, Wang C. The Testis and Male Hypogonadism, Infertility, and Sexual Dysfunction. In: Goldman-Cecil Medicine [Internet]. Twenty Six. 2020. p. 1537-1547.e2. Available from: https://www.clinicalkey.com/#!/content/book/3-s2.0-B9780323532662002216?scrollTo=%23hl0001280