

EFFECT OF VARICOCELE ON SPERMATOGENESIS

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Abstract:

Objective: To evaluate the effects of varicocele on spermatogenesis and determine its association with oligospermia or azoospermia.

Methods: This observational study was conducted from January 2010 to December 2011, in the Department of urology & surgery of DMCH on 100 adolescents & adults with unilateral or bilateral varicocele of grade I to III. Patients with cryptorchidism, testicular trauma, surgery of the urogenital tract and secondary varicoceles were excluded. Detailed history was taken and physical examination was done to diagnose varicocele with its grading and was reconfirmed by ultrasonogram with Color Doppler. Semen was collected accordingly and was examined within 90 minutes of collection. Chi-square (χ^2) Test and unpaired t-Test was used for qualitative for quantitative variables respectively and $p < 0.05$ was considered significant.

Results: Mean patients age 22.45 ± 4.3 years. Most of them have (94%) had inguino-scrotal swelling. Four (4.3%) had grade-I swelling, 27.6% grade-II and 68.1% grade-III swelling. Seventy eight percent was left-sided and 22% was bilateral varicocele, A may item 34% cases were infertile. Abnormal sperm morphology was present 18% cases. Oligospermia was present in 28% cases and 6% had azoospermia. No significant association was observed between age of the patients and sperm count ($p=0.437$) and also between oligospermia or azoospermia with side of varicocele ($p=0.076$). Long-standing varicocele (> 10 yrs.) patients were 2.7 times more likely to be oligospermic or azoospermic than those with shorter duration ($p=0.020$). Over 80% of the oligo or azoospermic patients belonged to grade III varicocele compared to 53.1% with normal sperm count ($p=0.006$).

Conclusion: Men with varicocele tend to be infertile and there is an increasing chance of being infertile with longer duration and higher grade (grade-III) of the disease. The age of the patients or side of varicocele were not found to be associated with oligo or azoospermia.

Key words: Varicocele, Azoospermia, Oligospermia, Infertility.

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Introduction:

A varicocele is an abnormally dilated, tortuous spermatic vein. It has long been associated with oligospermia and azoospermia and is the most common and correctable cause of male infertility. [1] Its incidence is 4.4–22.6% in the general population and 21–41% in men with primary infertility and 75–81% in men with secondary infertility.[2]

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Varicocele is associated with progressive decline in testicular function. [3] It occurs mainly in the left side (85–90%) than bilateral (10%), and a right sided varicocele is found mostly in bilateral cases, but rarely alone. [4] These findings raise two major questions; why does left varicocele also affect spermatogenesis on the right? Why do men with unilateral varicocele fail to produce adequate sperm from the other testis, considering that men with a single testis are known to be fertile? Recently, a few articles have suggested that

the incidence of bilateral varicocele can be underestimated. Besides physical examination, several diagnostic modalities are available today to detect varicocele, including thermography, Color Doppler sonography and venography. [5] Scrotal ultrasonography being the most used methods. The condition is graded at the time of the initial physical examination from I-III (Dubin grading system), with grade-III being visible while the patient is standing, grade-II is palpable without valsalva maneuver and grade-I is not visualized but only palpable with valsalva maneuver. The term clinical varicocele refers to those detectable by physical examination, either by palpation or visual inspection. [2]

Varicocele is associated with progressive and duration dependent decline in testicular function. A number of theories have been proposed. These include disordered testicular thermoregulation, hypoxia resulting from blood "stagnation" in the spermatic veins, reflux of adrenal metabolites, dilution of intra-testicular substrates and elevated levels of sperm-derived reactive oxygen species. Although the pathogenesis of varicocele still remains unclear, its effects on the testis are well-documented. These include reduced testicular volume, impaired sperm quality and reduced Leyding cell functions and ultimately to infertility. [3]

MacLeod first reported that majority of semen samples obtained from infertile men with varicocele presents a lower sperm count with decreased motility, and more frequently has abnormal morphologies compared to sperm from fertile men. World Health Organization (WHO) reported a prevalence of varicocele 25.4% in infertile men with abnormal semen; accompanied by decreased testicular volume, lower total sperm count, and a decline in Leydig cell function. [6,7]

Varicocele causes a progressive deterioration in testicular function and semen quality, ranging from oligospermia to complete azoospermia. Recent improvements in the diagnosis of varicocele with color doppler ultrasonography, thermography and internal spermatic vein venography have increased the detection rate of varicocele 20-40% in men with primary infertility and up to 80% with secondary infertility. Therefore it is quite logical to assume that varicocele may cause oligospermia or azoospermia. So, knowing the prevalence of oligospermia and azoospermia, especially in longstanding cases will be important to have clear idea about what proportion male infertility is attributed to varicocele.

So the objective of the present study was to see the effect of varicocele on spermatogenesis and to determine its association with oligospermia or azoospermia. The study finding may be of clinical significance in treatment planning in reducing the incidence of male infertility in the community.

Methods:

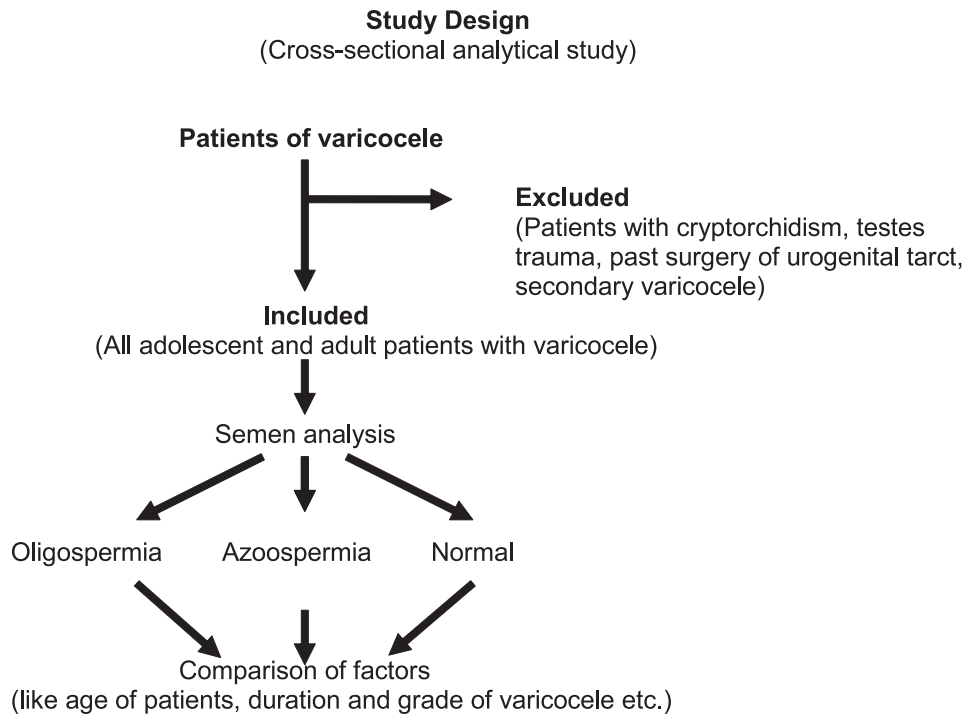
This observational analytical study was conducted in the department of Urology & surgery of Dhaka Medical College Hospital (DMCH), over a period of 2 year from January 2010 to December 2011. Adolescents and adult male subjects with varicocele attending at the Department of Urology of DMCH were considered as cases and were approached for the study. Patient with unilateral or bilateral varicocele of grade I, II & III, and those who gave voluntary informed consent were enrolled. Patients with cryptorchidism, history of testicular trauma, history of past surgery of the urogenital tract and patient with secondary varicocele were excluded. Calculated sample size was 163, but due to time and financial constraint total 100 cases has been enrolled by applying purposive sampling technique.

After enrollment, detailed history was taken from the subjects regarding age, socio-demographic status, duration of the testicular swelling, side of involvement, reproductive status, duration and type of infertility. Subjects were then examined physically of the inguino-scrotal swelling, presence of cough impulse, get above the swelling, feeling like bag of worms to diagnose and determine the grade of varicocele which were further confirmed by ultrasonography with color Doppler of the inguino-scrotal content. Semen specimens were obtained by masturbation after 2 to 3 days of sexual abstinence and analyzed within 90 minutes of collection. Semen parameters including volume, sperm concentration, percent motility and sperm morphology were assessed according to World Health Organization (WHO) and Kruger's strict criteria. [7,8] All the obtained information was recorded in a pre designed questionnaire.

This study has been approved by the Ethical Committee of Dhaka Medical College Hospital, Dhaka.

Data were processed and analyzed using the software SPSS (Statistical Package for Social Sciences) version 16. For qualitative variables Chi-square (χ^2) and for quantitative variables unpaired t-Test were used. P value of < 0.05 was considered as statistically significant.

Flow diagram of the study protocol



Results:

Among the 100 enrolled subjects, 42% were d" 20 years of age, 24% were between 21-25 years and 34% were of > 25 years. Mean age of the enrolled subjects was 22.45± 4.3 years. Nearly one-quarter (22%) of them were businessmen, 24% farmers, 8% service-holders and 46% involved in other professions. Majority (86%) of them was of lower and middle income group and 14% were from affluent class. Over three-quarters (78%) had left-sided varicocele and the remaining 22% bilateral varicocele. Majority (94%) had inguino-scrotal swelling. Four (4.3%) of them had grade-I swelling, 26(27.6%) grade-II and 64(68.1%) grade-III swelling. Fifty percent of the cases complained of pain over the swelling. On examination, cough impulse was present in 60% of the cases and in 96% of the cases the swelling was felt 'like a bag of worm.' Only in 4% cases it was feasible to get above the swelling.

Semen analysis of the enrolled subjects revealed 66% fertile and 34% infertile with oligospermia and azoospermia. Eighteen percent showed abnormal morphology. (Table-I)

Table-II shows, there was no significant association between age of the varicocele patients and sperm count (p = 0.437). No association was found on side of varicocele with infertility (p = 0.076). Over 80% of the oligo or azoospermic patients fell in grade III varicocele

Table-I
Semen analysis of the patients

Semen Analysis:n-100	Case n(%)
Sperm volume (adequate)	100(100.0)
Sperm count (million/ml)	35.2 ± 7.3
Sperm motility (%)	45.6 ± 9.5
Sperm morphology (Abnormal)	18(18.0)
Classification of cases:n-100	
Oligospermia	28(28.0%)
Azoospermia	6(6.0%)
Normal	66(66.0%)
Reproductive status: n-100	
Fertile	66(66.0%)
Infertile	34(34.0%)

compared to 53.1% of varicocele patients with normal sperm count (p = 0.006).

Nearly 56% of the oligospermic or azoospermic patients Table-III had long-standing varicocele (> 10 yrs.) compared to 31.8% of those who had normal sperm count (p = 0.020). Patients with longer duration varicocele (> 10 yrs) were 2.7(95% CI = 1.1 – 6.3) times more likely to be infertile than the patients with shorter duration varicocele (d" 10 yrs). (Table-III)

Table-II
Comparison of different factors associated with fertility:

Age (yrs)	Sperm count		p-value
	Oligo/azoospermia (n-34)	Normal count (n-66)	
d" 20	14(41.2%)	11(16.7%)	0.437*
21 – 25	6(17.6%)	11(16.7%)	
> 25	14(41.2%)	44(66.6%)	
Laterality			
Left	30(88.2%)	48(72.7%)	0.076*
Bilateral	4(11.8%)	18(27.3%)	
Grade of swelling			
Grade-I	4(13.3%)	4(6.0%)	0.006*
Grade-II	2(6.6%)	27(41.0%)	
Grade-III	28(80.1%)	35(53.0%)	

* Chi-square (χ^2) Test

Discussion:

The findings of the present study revealed that the population was relatively younger (20 or <20 years). They also differ by occupation and middle class comprised the main bulk. Left-sided varicocele was predominant (78%) and the rest 22% were bilateral varicocele. Ugwuja et al. reported that the highest abnormalities (oligospermia and azoospermia) were found among the civil servants (75%-86%) and the least in the farmers (4%). Thirty one to 40 years had the highest abnormalities for oligospermia and azoospermia (68–72%) and the lowest abnormalities were found in older age groups (7-14%). However, no significant association between age and sperm count was observed.⁹ Similar findings were observed by Larsen et. al. who found 81% left sided varicocele and 19% bilateral varicocele. Varicoceles are found in 10-15 % of the male population and they occur predominantly on the left side. [10] Both the study did not enrolled adolescents which was enrolled in this study and was the predominant population.

In this study 66% subjects were fertile and 34% infertile. There was no significant association between age of the varicocele patients and sperm count. Although left-sided varicocele patients were more prone to develop oligospermia or azoospermia, the association was not statistically significant (p=0.076) in this study. Nearly 56% of the oligospermic or azoospermic patients had long-standing varicocele (>10yrs.) compared to 31.8% of those who had normal sperm count indicating that longer the duration of the disease, greater is the chance

of testicular damage resulting in oligospermia or azoospermia. This is supported by Cozzolino and Lipshultz, who reported a progressive decline in testicular function with duration and progression of varicocele. [11]

In the present study grade of varicocele was found to be associated with oligo or azoospermia which is consistent with findings of a study carried out by WHO in 1992.¹² The study enrolled 9038 men with infertility, 921 of them had varicoceles with inverse correlation between sperm count and grade of the varicocele. The finding is further strengthened by Steckel et al who reported that men with a larger varicocele present with lower sperm densities. [13]

Conclusion

The findings of the present study suggest that men with varicocele tend to be infertile and there is increasing chance of being infertile with increasing duration and progression of diseases. Age of the patients or side of varicocele were not found to be associated with oligo or azoospermia.

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