

# Varicocele in Brothers of Patients With Varicocele

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**Introduction:** The aim of this study was to evaluate varicocele patients' brothers to determine whether they are at a higher risk of varicocele than the general population of men.

**Materials and Methods:** A total of 56 patients with varicocele and their 131 brothers (> 16 years old) were evaluated. The brothers had no complaints of infertility, pain, or cosmetic problems. They were all examined for varicocele. One hundred and fifty men who referred for employment medical examinations were considered as the control group.

**Results:** Of the subjects, 39 (69.6%) had grade III varicocele. Sixty (45.8%) of the brothers had varicocele. The grade of varicocele was III in 16 (26.7%) brothers. In the control group, varicocele was present in 15 (10%) which was grade III in 5 (33.3%). The frequency of varicocele was 4.5-fold greater in the brothers of the patients than the controls ( $P < .001$ ). Also, the frequency of grade III varicocele was significantly more than grades I and II in the patients in comparison with their brothers and controls with varicocele ( $P < .001$ ). There was no significant difference in the grades between the controls and the patients' brothers ( $P = .31$ ). The frequency of bilateral varicocele was not statistically different between the three groups ( $P = .14$ ).

**Conclusion:** Our findings showed that a significant increase is seen in the prevalence of varicocele in the patients' brothers compared to men in the general population, warranting evaluation of the first-degree relatives of men who present with varicocele.

Keywords: varicocele, inheritance patterns, infertility

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## INTRODUCTION

Varicocele is the most common surgically correctable disorder in infertile men and may result in impaired sperm motility, sperm morphology, and sperm count.<sup>(1)</sup> Upward drainage of the gonadal veins into the renal vein that has a horizontal position, pressure of the superior mesenteric artery on the renal vein, and insufficiency of the venous valves have been proposed as the causes of varicocele; but, there is no documented hereditary pattern for the disease.<sup>(2)</sup> Findings such as damage to the DNA in the

sperm of patients with varicocele and genetic causes of infertility, warrants the evaluation of the disease inheritance pattern.<sup>(3-5)</sup> The prevalence of varicocele has been reported to be 15% in the adolescence and 20% to 40% in infertile men.<sup>(6,7)</sup> Infertility results from the harmful effects of varicocele on spermatogenesis and growth of testes.<sup>(8)</sup> Surgical repair of varicocele can improve the impairment of sperm parameters in about 70% and infertility in 40% to 50% of patients.<sup>(9)</sup> Early diagnosis of varicocele is very important for preventing the progression of testis atrophy.<sup>(7)</sup> Varicocele can be easily

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diagnosed and its consequences can be prevented; however, no precise information is available about its risk factors and inheritance pattern to determine the high risk men or asymptomatic cases. In this study, we examined brothers of patients with varicocele.

## MATERIALS AND METHODS

In a case-control study between September 2003 and September 2004, patients who presented with varicocele to the clinic of Kashani Hospital in Shahr-e-Kord, Iran, were recruited into the study. Their chief complaints were infertility, testis pain, and cosmetic problems.

The patients were instructed and asked to refer their brothers to be examined. Of 95 consecutive patients, 56 could refer with their 131 brothers. Inform consent was obtained from all of the patients and their brothers. The exclusion criteria for the brothers were age of less than 16 years, infertility, testis pain, anatomic disorders in the genitalia, history of trauma to the testes, and history of diagnosed varicocele in their family members. Physical examinations were preformed by a single physician and the grade of varicocele and presence of bilateral varicoceles were determined. Meanwhile, 150 consecutive healthy people referred for employment medical examinations without a history of subfertility were considered as the control group and were examined for varicocele.

Varicocele was graded according to the standard classification: grade I, palpable only with the Valsalva maneuver; grade II, palpable without the Valsalva maneuver in the standing position; and grade III, easily visualized without the Valsalva maneuver. Statistical analyses were done using the chi-square test by the SPSS software (Statistical Package for the Social Sciences, version 11.5, SPSS Inc, Chicago, Ill, USA).

## RESULTS

The mean age of the subjects was  $21.8 \pm 8.1$  years (range, 16 to 48 years). Varicocele was grade III in 39 (69.6%). The brothers included 131 men with a mean age of  $20.0 \pm 8.9$  years (range, 16 to 46 years). Sixty (45.8%) of these men had varicocele. The grade of varicocele was III in 16 (26.7%) brothers. The control group included 150 healthy people with a mean age of  $19.2 \pm 5.6$  years (range, 17 to 42 years). Varicocele

Varicocele Characteristics in Patients, Their Brothers, and Controls\*

Characteristics	Patients	Brothers	Controls
Number	56	131	150
Varicocele	56 (100.0)	60 (45.8)	15 (10.0)
Bilateral varicocele	10 (17.9)	20 (33.3)	5 (33.3)
Varicocele grades			
I	8 (14.3)	20 (33.3)	2 (13.3)
II	9 (16.1)	24 (40.0)	8 (53.3)
III	39 (69.6)	16 (26.7)	5 (33.3)

\*Values in parentheses are percents.

was present in 15 (10%) and was grade III in 5 (33.3%). Table shows the frequencies of varicocele and its clinical characteristics in the three groups.

The frequency of varicocele was 4.5-fold greater in the brothers of the patients than the controls ( $P < .001$ ). Also, the frequency of grade III varicocele was significantly more than grades I and II in the patients in comparison with their brothers and controls with varicocele ( $P < .001$ ); however, there was no difference in the grades between the controls and the patients' brothers ( $P = .31$ ). The frequency of bilateral varicocele was not statistically different between the three groups ( $P = .14$ ).

## DISCUSSION

Given the results of the previous studies on the etiology and incidence of varicocele in general population, our findings indicated that the frequency of varicocele increases significantly in the first-degree relatives of the patients especially in their brothers.

The literature lacks ample investigation to conclude a hereditary basis for varicocele. Although several genetic roles have been identified in the infertility of the men, varicocele has not been separately studied.<sup>(10)</sup> Ziv and colleagues found no relation between HLA and the varicocele; however, other genetic and environmental factors could not be excluded.<sup>(11)</sup> There are limited information about the high frequency of Y chromosome microdeletion in infertile men with varicocele, but their association is still controversial.<sup>(4,12)</sup>

In a similar case-control study to ours, performed by Raman and associates, a total of 44 patients with 62 available male first-degree family members were compared with 263 men who had referred for vasectomy reversal. It was shown that 56.6% of the first-degree family members (especially their brothers

[74%]) had varicocele in the clinical examinations which showed a significant difference with the control group (6.8%;  $P < .001$ ).<sup>(13)</sup> In their study, no association of varicocele grade or its bilaterality was found with the possibility of varicocele occurrence in the family members of the patients. The control group in the study of Raman and colleagues included fertile people who might be different from the general population. This explains the greater difference between the first-degree relatives and controls in their study compared to ours (8-fold versus 4.5-fold). In our study, the prevalence of varicocele was reported to be 45.8% and 10% in the patients' brothers and the controls which showed a familial background in the occurrence of the disease ( $P < .001$ ). Our findings suggest that evaluation of the genetic factors and the people with more than one patient in their families can be helpful.

The frequency of grade III varicocele was significantly higher than grades I and II in the patients compared with their brothers and controls with varicocele ( $P < .001$ ); however, there was no difference in the grades between the controls and the patients' brothers ( $P = .31$ ), which showed no relationship between the severity of the disease and the possibility of its detection in the patients' brothers. The frequency of bilateral varicocele was not statistically different between the three groups ( $P = .14$ ). Also, no clinically significant difference was found between the brothers and controls regarding the bilaterality which was in accordance with the study of Raman and colleagues that failed to show a relationship between the bilaterality and the chance of varicocele in the first-degree relatives of the patients.

In our study, only the patients' brothers were evaluated and therefore, no genetic relation could be considered in the occurrence of varicocele. Evaluation of other male relatives and genetic and environmental factors are needed. Also, studies on larger samples of varicocele patients and their family members are needed to evaluate the relation between the grade of varicocele and the possibility of its detection in other people of the family and determining the clinical importance of the disease in family members.

## CONCLUSION

Due to the importance of varicocele in the men's

infertility and its easy diagnosis and treatment subject to on-time diagnosis, evaluation of the patients' brothers is recommended.

## CONFLICT OF INTEREST

None declared.

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