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Effect of Body Mass Index on Severity and Prevalence of Varicocele

[1]Kamaleddin Hassanzadeh, [2]Parisa Yavari-kia, [3]Hassan Soleymanpour,
[4]Nasser Ebrahimpour-tolouei and [5]Hossein Alikhah
[1]Department of Urology, Imam Reza Hospital, Tabriz University of Medical Sciences, Tabriz, Iran
[2]Faculty of Nursing and Midwifery, Tabriz University of Medical Sciences, Tabriz Iran
[3]Department of Emergency Medicine, Imam Reza Hospital,
Tabriz University of Medical Sciences, Tabriz, Iran
[4]Tabriz University of Medical Sciences, Tabriz, Iran
[5]Journal of Medicine, Tabriz University of Medical Sciences, Tabriz, Iran

Abstract: Varicocele is classified as grade I-III regarding its severity. This study was aimed to determine the correlation between height and weight with varicocele grade in 18-30 years age group. We enrolled 400 persons aged 18-30 years referred to the specialist's clinics of Tabriz Medical Sciences University or Medical Commission Since Sep. 2004 to Mar. 2005. First we divided the volunteers in two groups including Varicocele Group and Non-varicocele Group, then varicocele patients were classified to three grades considering the severity of the disease: severe (Grade III), moderate (Grade II) and mild (Grade I). Finally, the correlation between height, weight and Body Mass Index (BMI) was evaluated. There was a significant relation between height and grades of left-side varicocele; in other words the severity of disease was increased with height ($p = 0.004$). Also, height increased the prevalence of varicocele ($p = 0.011$). On the other hand, low weight and BMI increased the prevalence of varicocele ($p = 0.000$, $p = 0.004$) but did not affect the severity of disease ($p = 0.364$, $p = 0.172$). In conclusion, the height of patients directly affected the prevalence and severity of left-side varicocele which probably is related to length of left internal spermatic veins in these patients and increased hydrostatic pressure in taller patients. Also, the weight and BMI is effective on the prevalence of varicocele. It seems that slim and tall persons will benefit from evaluation while puberty.

Key words: Pampiniform plexus, spermatic vein, infertility, anthropometric parameters, hyperthermia

INTRODUCTION

Varicocele is characterized by abnormal dilatation and tortuosity of the veins of the pampiniform plexus within the spermatic cord and represents the most common identifiable cause of male infertility (Robinson *et al*., 2010; Chen and Huang, 2010; Tarhan *et al*., 2010; Kumanov *et al*., 2008; Saalu *et al*., 2008). It is found in approximately 15% of the general population but in at least 35% of infertile men (Tarhan *et al*., 2010; Paduch and Skoog, 2001; Fode and Sonksen, 2009; Dohle, 2006).

In spite of substantial research, uncertainty remains about etiology, pathophysiology and treatment modalities (Fode and Sonksen, 2009; Lim, 2006; Silber, 2001). Many theories have been proposed to explain the mechanism by which the disease disrupts normal testicular function and causes infertility; however, none has been proved and the exact cause remains an enigma (Kumanov *et al*., 2008). The pathophysiology seems to be multifactorial including hyperthermia, hypoxia, adrenal reflux and endocrinological disorders (Fode and Sonksen, 2009; Lim, 2006; Silber, 2001).

Interest has focused on varicocele because of the significant improvement of the sperm concentration and motility after varicocele treatment (Cayan *et al*., 2002). Studies have shown relationships between some anthropometric parameters and the incidence of Varicocele (Delaney *et al*., 2004; Nielsen *et al*., 2006; Handel *et al*., 2006). Several studies suggest that some physical characteristics of the adolescent could influence the development of varicocele (Kumanov *et al*., 2008; Prabakaran *et al*., 2006). It can develop during puberty and thus affect the testicular growth and function (Kumanov *et al*., 2008). Recent studies indicate the protective role of higher Body Mass Index (BMI) and/or weight on the development of Varicocele (Nielsen *et al*., 2006; Handel *et al*., 2006; Prabakaran *et al*., 2006) as well as the negative influence of height (Kumanov *et al*., 2008; Delaney *et al*., 2004; May *et al*., 2006).

However, the literature regarding the constitutional results about influence of weight and height on prevalence and grade of the disease (Fode and Sonksen, 2009; Lim, 2006; Silber, 2001; May *et al*., 2006;

Corresponding Author: Hossein Alikhah, Journal of Medicine, Tabriz University of Medical Sciences, Tabriz, Iran

Stavropoulos *et al*., 2002). The aim of this investigation was to examine a possible influence of weight, height and BMI on the formation and grade of varicocele in young adults aged 18-30 years.

MATERIALS AND METHODS

This is a case-control, descriptive and cross sectional study performed on 400 persons presenting to Urology Clinics of Tabriz Medical Sciences University or Medical Commissions from September 2004 to March 2005. Inclusion criteria were having age of 18-30 years. Exclusion criteria were having mental or systemic disease, having inguinal herniation, hydrocele or any pathology within scrotum and not having tendency for enrollment.

A total of 400 patients were classified in two groups according to presence or absence of varicocele: (1) Case group and (2) Control group.

All patients underwent careful examination by two expert urologists separately. Varicocele was diagnosed by physical examination and confirmed by Doppler ultrasonography. The severity of varicocele was determined and classified as mild (Grade I), moderate (Grade II) and severe Grade III).

The study was approved by the Regional Ethics Committee. Patients signed informed consent before the operation.

The studied variables were age, side of involvement, grade of varicocele, duration of disease, background disease, familial history, weight, height and the most widely used anthropometric index, Body Mass Index (BMI) or weight-for-height (Gholamreza and Mohsen, 2007).

The collected data were analyzed by SPSS-13 statistical software. The data were expressed as percentage and mean±SD. Continuous (quantitative) variables were compared by Student t-test or One-way ANOVA (Independent samples). Categorical (qualitative) variables were compared by contingency tables and Chi-square test or Fisher's Exact Test. The p-value = 0.05 was considered statistically significant.

RESULTS

We studied 200 normal males (Controls) with 200 patients with varicocele (Cases). All 200 cases had left-sided varicocele and 9 of them had bilateral varicocele. The grade of varicocele was I in 21, II in 38 and III in 141 cases. Also the grade of right- sided varicocele was II in 7 and III in 2 cases. There was not any significant relation between grades of left- and right-sided varicoceles (p = 0.162).

The demographic characteristics of two studied groups are showed in Table 1.

Age: The mean age of all studied patients (case and control) in various grades of left-sided varicocele was not significantly different (p = 0.094). Also, the difference of mean age of all cases in various grades of left-sided varicocele was not significant (p = 0.094).

The mean age of all studied patients (case and control) in various grades of right-sided varicocele was not significantly different (p = 0.919). Also, the difference of mean age of all cases in various grades of right-sided varicocele was not significant (p = 0.619).

Height: As showed in Table 1, the control patients were taller than cases. The average height of all studied males was 175.61 cm. In patients with Grade II and III right varicocele, the average height was 179.29 and 176.5 cm, respectively. In patients with Grade I, II and III left varicocele, the average height was 173.24, 176.82 and 176.74 cm, respectively.

The mean height of all studied patients (case and control) in various grades of left-sided varicocele was significantly different. It was less in grade I and more in grade II than other grades (p = 0.005). There was significant difference between the mean height of cases in various grades of varicocele (p = 0.041) (Fig. 1).

The mean height of all studied patients (case and control) in various grades of right-sided varicocele was not significantly different (p = 0.267). Also, the difference of mean height of all cases in various grades of right- sided varicocele was not significant (p = 0.437).

Table 1: The demographic characteristics of two studied groups

Parameter	Case group	Control group	p-value
Age (y)	19.73	20.43	0.013
Height (cm)	176.39	174.83	0.011
Weight (kg)	65.74	68.72	0.000
BMI (kg m^{-2})	21.15	22.47	0.000

BMI: Body Mass Index

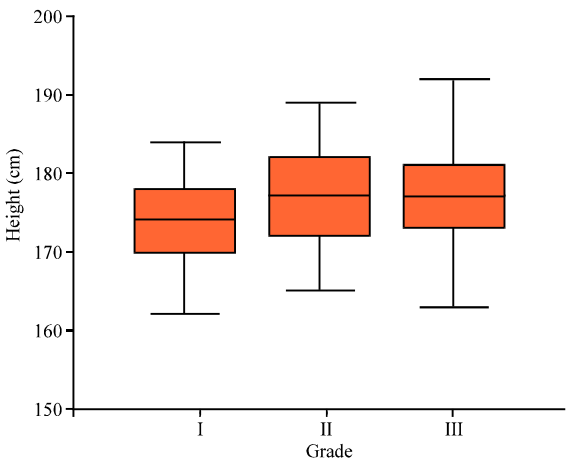

Fig. 1: The height ranges in various grades of varicocele

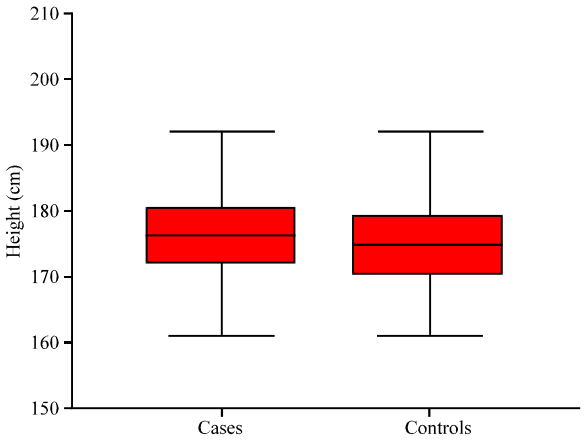

Fig. 2: The height in case and control groups

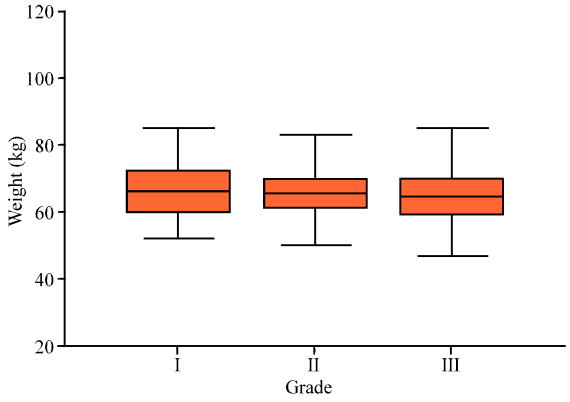

Fig. 3: The weight ranges in various grades of varicocele

The mean height of cases with higher grade of the disease (II or III) was significantly more than others (p = 0.009). Also, the cases were significantly taller than controls (P=0.011) (Fig. 2).

Weight: The average weight of all studied males was 67.23 kg. In patients with Grade II and III right varicocele, the average height was 68.57 and 75.50 kg, respectively. In patients with Grade I, II and III left varicocele, the average height was 65.90, 67.76 and 65.17 kg, respectively.

The average weight of all studied males was 21.81 kg m^{-2}. In patients with Grade II and III right varicocele, the average height was 21.36 kg m^{-2} and 24.27 kg m^{-2}, respectively. In patients with Grade I, II and III left varicocele, the average height was 22 kg m^{-2}, 21.66 kg m^{-2} and 20.88 kg m^{-2}, respectively.

The mean weight of all studied patients (case and control) in various grades of left-sided varicocele was significantly different. It was less in grade III than other grades (p = 0.004). There difference between the mean height of cases in various grades of varicocele was not significant (p = 0.364) (Fig. 3).

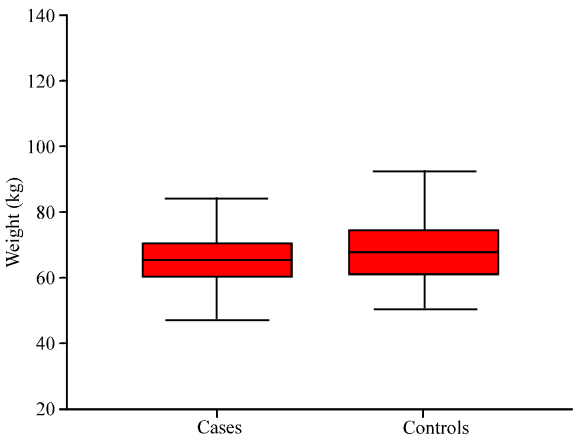

Fig. 4: The weight in case and control groups

Table 2: The comparison of testes size in studied groups

Testis size	Case group	Control group	All
Right	19.73 (c c)	19.13 (c c)	19.43(cc)
Left	19.10 (c c)	18.99 (c c)	19.05(cc)

The mean weight of all studied patients (case and control) in various grades of right- sided varicocele was not significantly different (p = 0.497).

The mean weight of cases with higher grade of the disease (II or III) was significantly less than others (p = 0.007). Also, the controls were significantly heavier than cases (p = 0.004) (Fig. 4).

BMI: BMI was significantly more in controls than cases (p = 0.000). The mean BMI of all studied patients (case and control) in various grades of left-sided varicocele was significantly different. It was less in grade III than other grades (p = 0.000). There difference between the mean BMI of cases in various grades of varicocele was not significant (p = 0.172).

The mean BMI of all studied patients (case and control) in various grades of right- sided varicocele was not significantly different (p = 0.588).

The mean BMI of cases with higher grade of the disease (II or III) was significantly less than others (p = 0.000).

Testis size: The comparison of testis size in both groups is shown in Table 2.

Testes sizes were not significantly different in patients with any grade of left-sided varicocele (right, p = 0.522; left, p = 0.134). Also, this difference was not significant within patients with varicocele (right, p = 0.383; left, p = 0.289).

The size of right testis was significantly more in cases than controls ($p = 0.046$) but this difference was not significant for left testis ($p = 0.739$).

DISCUSSION

There is probably no subject that is more controversial in the area of male infertility than varicocele (Silber, 2001). Varicocele could be defined as an abnormal dilation and tortuosity of the veins of the pampiniform plexus (Kumanov *et al*., 2008; Paduch and Skoog, 2001). It can be found in boys as young as 5 years (Greenfield *et al*., 2002). The prevalence of varicoceles markedly increases with pubertal development. It is a progressive lesion that may hinder testicular growth and function over time and is the most common and correctable cause of male infertility (Robinson *et al*., 2010; D'Agostino *et al*., 1996). Approximately 40% of men with primary infertility have a varicocele and more than half of them experience improvements in semen parameters after varicocelectomy (Robinson *et al*., 2010; D'Agostino *et al*., 1996).

The epidemiologic studies revealed a gradually increasing incidence of varicocele in patients 10 to 18 years old, as height at the end of puberty as that of the adult male population (D'Agostino *et al*., 1996). Grade III varicoceles and grade II associated with testicular hypotrophy must be early operated on. This provides a higher fertility rate and can prevent the reduced fertility associated with delayed varicocelectomy (D'Agostino *et al*., 1996; Giagulli and Carbone, 2010).

The developmental changes that occur as a result of puberty have been hypothesized to be important causes of varicocele. Various somatometric parameters were known to affect the occurrence of varicocele during the growth period (Prabakaran *et al*., 2006). Wishahi (1992) reexamined venous anatomy of the testis by retrograde spermatic venography during surgery in 17 men with and in 11 without a varicocele. In men with a varicocele the spermatic venous plexus was formed of numerous venous sinuses and large dilated veins (Wishahi, 1992). The predominance of left-sided varicocele and the unique anatomy of left testicular vein are the base for several theories explaining the cause of the disease. The nutcracker effect is thought to occur when the left renal vein is compressed between the superior mesenteric artery and aorta, proximal of the point where the left testicular vein runs in it. The subsequent increase of the hydrostatic pressure could result in varicocele formation (Kumanov *et al*., 2008).

Varicocele, presents in 15 to 20% of men, is the most common abnormal finding among men presenting with infertility, yet controversy exists regarding their etiology. The researches suggest that varicocele is more prevalent in lean men, supporting the utcracker effect of the superior mesenteric artery compressing the left renal vein over the aorta (Nielsen *et al*., 2006). Varicocele is less likely to be diagnosed among obese men. This suggests that the nutcracker phenomenon or other biophysical effects of increased adiposity may play a role in the pathogenesis (Nielsen *et al*., 2006). We examined this hypothesis in a young adult population in our region, northern-east of Iran.

Other potential causes for the development of varicocele in the adolescent are the incompetent venous valve system, the increased arterial blood flow to the testis at puberty exceeding the venous capacity and the elevated levels of nitric oxide in plexus pampiniformis (Kumanov *et al*., 2008; Paduch and Skoog, 2001). The genetic susceptibility is also important, considering that 50% of first-degree relatives and >70% of brothers of men with varicocele also had a palpable varicocele (Kumanov *et al*., 2008; Raman *et al*., 2005; Gokce *et al*., 2010). In a retrospective study, 12.2% of all brothers of the patients had varicocele (May *et al*., 2006).

Stavropoulos *et al*. (2002) conducted a study to examine the effect of height and weight on the incidence of varicocele in 3047 schoolboys aged 5-16 years and the impact of varicocele on testicular size. Left varicocele was detected in 98 of the boys who were all aged 9-16 years. The mean weight of boys with and without varicocele was 42 and 47 kg, respectively (Stavropoulos *et al*., 2002). This is compatible with our study in which the controls were significantly heavier than cases, although our study performed on 18- 30 years patients.

In a retrospective study, 193 patients aged 9-19 years with left-sided varicocele grade 2-3 were studied. The mean weight and height were significantly above and the mean and BMI was significantly below than those of normal population. Patients with varicocele were heavier and taller than an age-correlated normal population but had a distinctly lower BMI (May *et al*., 2006). Stavropoulos *et al*. (2002) found no difference in mean height between the two groups or in left and right testicular volume. Boys with varicocele weighed significantly less but there were no significant differences in height or left versus right testicular volumes. They suggested that the use of left testicular hypotrophy ($\geq$2 mL compared with the right testicle) should be reconsidered as an indicator for varicocele-induced damage of the testicle in this age group (Stavropoulos *et al*., 2002). Also, the study of 43 consecutive males under long-term follow-up for varicocele indicated that patients with varicocele are

significantly taller and heavier than age-matched controls (Delaney *et al*., 2004).

In contrast with these findings, our study suggested that height, weight and BMI, all are effective on varicocele occurrence. Also, the right testis was significantly smaller in controls than cases but this difference was not significant for left testis. This difference is probably due the fact that their study was performed in schoolboys aged 5-16 years but we studied the patients aged 18 to 30 years.

Lemcke *et al*. (1996) revealed a significantly higher prevalence of varicoceles in the testosterone-treated tall men compared with the controls. Semen analysis revealed significantly lower progressive motility, lower sperm concentration, lower total sperm count and reduced normal sperm morphology in the testosterone-treated tall men. Although there was no difference in testicular volume between the groups, testosterone was lower in the testosterone-treated tall men. The small difference in semen variables may be explained by a higher prevalence of varicocele in the testosterone-treated tall men (Lemcke *et al*.,1996). Varicocele was present in 42% of the adult tall men. High-dose testosterone treatment is applied during puberty to reduce the predicted adult height in excessively tall boys (Lemcke *et al*., 1996; De Waal *et al*., 1995).

Prevalence of varicocele decreases with increasing BMI. One explanation is increased adipose tissue preventing compression of the left renal vein. Another explanation is decreased detection due to adipose tissue in the spermatic cord. The decrease in varicocele prevalence as a function of BMI regardless of varicocele grade suggests this explanation is less likely (Handel *et al*., 2006). Changes in BMI affect the prevalence of varicoceles during adolescence (Shin and Lee, 2007). Tsao *et al*. (2009) investigated 1050 young males to determine the relationship between obesity and varicocele occurrence. A total of 490 (46.67%) subjects had varicoceles. The means of BMI, waist circumference (WC) and waist-to-hip ratio (WHR) of those without varicoceles were greater than those with varicoceles. BMI, WC and WHR all had a significantly negative correlation with severity of varicocele (Tsao *et al*., 2009).

In Tsao *et al*. (2009) study, the prevalence of grade II and III varicoceles showed a statistically inverse association with all three anthropometric indexes. The prevalence and severity of varicoceles inversely correlated with obesity. These findings are compatible with study of Hsieh study (Hsieh, 2010) and support the explanation that obesity may result in a decreased nutcracker effect which accounts for prevention of the renal vein compression by the adipose tissue (Tsao *et al*., 2009). In our study, weight and BMI were effective on varicocele occurrence although they had not effect on the grade of disease. However, the height was significantly related not only to varicocele occurrence but also to its grade.

Chen and Huang (2010) compared 102 varicocele patients with 95 age-matched healthy males. The range of ages was between 18 and 50 years old. Of the 102 varicocele patients, 20 were grade I, 55 were grade II and 27 were grade III. The BMI of patients with varicocele was significantly lower than that of controls. Patients with grade 3 varicocele had a lower BMI than patients with grades I and II varicocele but this was not significant. In addition, the prevalence of varicocele was higher in patients with a lower BMI. The findings suggest that patients with a greater BMI may have advantages in relieving the nutcracker phenomenon which causes significant varicoceles (Chen and Huang, 2010).

Celiktas *et al*. (2009) evaluated a possible effect of the amount of retroperitoneal fat tissue (RPFT) on testicular venous drainage. Left and right testicular vein maximum diameters measured by ultrasonography were significantly larger in obese patients. Also, the left and right pampiniform plexus diameters were larger in the obese group than in the normal and overweight groups. There was significant correlation between the right testicular vein maximum diameter and mean RPFT. The relationship between bilateral pampiniform plexus diameters and RPFT was significant. Also, there was a significant relationship between BMI and retroperitoneal fat distribution which could be a contributing factor in the etiology of right varicocele (Celiktas *et al*., 2009).

Varicocele is more prevalent in tall boys with a lower BMI (Prabakaran *et al*., 2006). In a prospective study, 6200 boys aged 0 to 19 years were evaluated for varicocele. Varicocele was found in 4.1% of all investigated boys, whereas in the age group 10 to 19 years, it was 7.9%. After adjustment for age, the negative factors associated with the development of the disorder were height, penile length and penile circumference, whereas the weight and BMI had a protective role (Kumanov *et al*., 2008). In another study on adolescents, varicocele was found in 5.6% of the participants. The 13- to 19-year age-group had the highest incidence of varicocele (10.5%). Analysis showed that the incidence was positively correlated with age, height and penile length and negatively correlated with left testicular volume, BMI and pubic hair distribution (Prabakaran *et al*., 2006).

Handel *et al*. (2006) examined the records of 3,213 males presenting with infertility. A total of 1,093 (34%) patients had varicoceles. The mean BMI of those without

varicoceles was greater than the BMI of those with varicoceles. The prevalence of varicocele was 43% in normal weight group (BMI<25), 35% in overweight group (BMI 25 to less than 30) and 22% in obese group (BMI≥30). Prevalence of varicocele decreased with increasing BMI for all varicocele grades (Handel *et al*., 2006). In one study, a total of 2106 men were evaluated for infertility. The mean age was 47 years (range 18 to 85) and the median BMI was 26.4 kg m^{-2}. A varicocele was present in 18.9%. Stratified by grade, 14.8% were grade III, 38.9% were grade II and 46.2% were grade I. analysis revealed a statistically significant inverse relationship between BMI and the presence of varicocele (Nielsen *et al*., 2006).

In our study, weight and BMI was significantly more in controls than cases. However, the height was significantly related not only to varicocele occurrence but also to its grade and the control patients were taller than cases.

CONCLUSIONS

In conclusion, the height of patients directly affected the prevalence and severity of left-side varicocele which probably is related to length of left internal spermatic veins in these patients and increased hydrostatic pressure in taller patients. Also the weight and body mass index is effective on the prevalence of varicocele. It seems that slim and tall persons will benefit from evaluation while puberty.

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