

Original article

Relationship of Adolescent Gynecomastia with Varicocele and Somatometric Parameters: A Cross-Sectional Study in 6200 Healthy Boys

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Abstract

Purpose: To evaluate the relationship of gynecomastia with varicocele and somatometric parameters in otherwise clinically healthy boys.

Methods: The relationship between gynecomastia and somatometric parameters was examined with 6200 clinically healthy boys aged 0–19 years of different socioeconomic backgrounds in various schools, kindergartens, and childcare centers. Multivariable logistic regression analysis was used to model the prevalence of gynecomastia (≥ 1 cm) in relation to height, weight, testicular volume, penile length and circumference, age, pubic hair Tanner stage, and residential status.

Results: Pubic hair Tanner stages 3 and 4 had the highest incidence of gynecomastia. Gynecomastia was found only in boys more than 10 years old and its prevalence in the age group of 10–19 years ($n = 3082$) was 3.93%. In boys 10–13 years old, gynecomastia was positively correlated with varicocele, the adjusted odds ratio (OR) was 2.1 (95% confidence interval [CI] = 1.1–4.1). For the age at which gynecomastia was most prevalent (group aged 12–14 years), the adjusted OR of gynecomastia occurring in boys with varicocele, using the Cochran-Mantel-Haenszel method of adjusting for age was 1.9 (95% CI = 1.1–3.4). Gynecomastia was negatively correlated with body mass index (BMI). In addition, it was weakly correlated with testicular volume, positively in age group 10–13 years and negatively in those 14–19 years. However no relationship was found between gynecomastia and penis size, urban/rural status, and sea level of residence.

Conclusions: Adolescent gynecomastia is a mid-puberty event. It is significantly associated with varicocele and somatometric parameters including BMI and testicular volume. © 2007 Society for Adolescent Medicine. All rights reserved.

Keywords: Adolescent; Gynecomastia; Varicocele; Somatometric parameters; Puberty; Anthropometric measurements; Socioeconomic status; Environmental factors

Gynecomastia is a benign proliferation of glandular tissue of the breast in males, resulting in a concentric enlargement of one or both breasts. It is a complex process resulting from many hormonal changes in the body. Estrogens strongly stimulate and androgens weakly inhibit mammary gland growth [1,2]. Various hypotheses have been put forth by a number of investigators explaining the etiology of gynecomastia, including elevated estrogen levels; lowered free testosterone; abnormal testosterone-to-estrogen ratio; in-

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creased peripheral conversion of testosterone to estrogens by higher aromatase activity; lower dehydroepiandrosterone sulphate (DHEA-S) to estrogen ratio and altered local action or breast tissue sensitivity [1,3,4]. However, the etiology still remains unclear. Gynecomastia is frequent during three phases in the age distribution curve: neonatal period, pubertal period, and senescence [1]. Pubertal gynecomastia is known to have a negative impact on the self-esteem of adolescent boys. It can lead to decreased participation in social activities and to depression in adolescents [5,6]. Therefore it is important to know the relationship between the occurrence of gynecomastia and various other physical and environmental changes occurring during the pubertal development of boys so as to explore its pathophysiology and predict its onset. However, conflicting study reports have created considerable controversy regarding the prevalence of gynecomastia and its association with weight, height, body mass index (BMI), testicular volumes, and penis size [7–12]. This prompted us to conduct a large population based study to evaluate the relationship of pubertal gynecomastia with various somatometric parameters.

It is known that varicocele is associated with a progressive decline in testicular function [13–15]. Because gynecomastia is related to either actual or relative decrease in testosterone-to-estrogen ratio [1,3,4], we tried to study the relationship between pubertal gynecomastia and adolescent varicocele. Furthermore, rural areas and those situated closer to sea level usually have agriculture as a predominant occupation. Therefore, to evaluate the effects of estrogenic or anti-estrogenic action of various pesticides and fertilizers used in agricultural farms on the development of gynecomastia, we also studied the relationship between gynecomastia and residential status of the study population.

The objective of our study was to investigate the relationship of gynecomastia with varicocele and various somatometric parameters and environmental factors in clinically healthy boys. In the present study we concentrated only on pubertal gynecomastia, which is classically described as a transient phenomenon by many investigators [7,9]. No hormonal evaluations were made. However, physical parameters dependent on hormonal actions such as height, weight, testicular volume, penile length and circumference, and Tanner stage according to pubic hair distribution were determined.

Methods

The study was approved by the Institutional Review Board of our institute. In a population based cross-sectional study, we examined 6200 otherwise clinically healthy Caucasian boys, aged 0–19 years from different parts of the country. The number of study subjects was chosen according to the guidelines given by Lwanga et al, with assumed prevalence of 5% and 2% failure [16]. The towns and villages were chosen at random, representative of country's

population and structure. Informed consent was taken from the children and/or their parents. In each town, the investigator chose schools, kindergartens, and childcare centers randomly and examined children at random until he reached the required numbers. Approximately equal numbers of children were selected from urban and rural areas. Each of the 20 age groups (0–19 years) had equal numbers of children, and they were included in the respective age groups according to the completed age at the day of examination. All the boys were clinically healthy at the time of examination. Sea levels of respective towns and villages were also recorded. Clinical examination of all of the boys was conducted by a single investigator.

The presence of gynecomastia was defined as a palpable button of firm subareolar breast tissue at least 1 cm in diameter. The diagnostic criterion of 1 cm was chosen to avoid any doubt regarding its presence, although a few investigators [9,11] have used 0.5 cm and others [8] have used 2 cm diameter as a criteria to identify gynecomastia in the past. Presence of varicocele was determined by examining the boys in the standing position with the help of Valsalva maneuver when appropriate. The protocol of the remaining clinical examination included the following somatometric parameters: height (cm), weight (kg), testicular volume (ml), penile length (cm), penile circumference (cm), and Tanner stage according to pubic hair distribution [17]. A Prader orchidometer was used for the measurement of testicular volumes; data are given separately for the left and right testicles. We used a Prader orchidometer because its measurements have been shown to be highly correlated with ultrasonographic measurements, especially when used by experienced examiners [18,19]. The height of the children was measured with anthropometer (Siber Hegner). Weight was measured on a beam balance, with subjects wearing only pants and shirts. Body mass index (body weight in kilograms/height squared in meters) was calculated for all of the subjects. Stretched flaccid penile length was measured with a rigid tape from the pubo-penile skin junction to the top of the penis excluding the prepuce under maximal but not painful extension. Penile circumference was measured at the base of penis close to pubis with a measuring tape. In obese children the abdominal adipose tissue was shifted manually to one side to measure penile length and circumference.

Logistic regression analysis was used to assess the relationship between the presence of gynecomastia and somatometric parameters including age, pubic hair Tanner stage, BMI, testicular volume (both left and right), penile length and circumference, and patient residence location and sea level. Because the prevalence of gynecomastia peaks at age 13 years, the analysis was done separately for ages 10–13 and ages 14–19 to satisfy a linearity assumption. Variables in the final model were selected based on a reliability of 50% or more from 1000 bootstrap samples of equal observations drawn at random from the study population. Association of gynecomastia and varicocele was examined using

logistic regression analysis; and adjusted odds ratios (OR) of gynecomastia in the varicocele group was calculated adjusting for age and other influential factors. Odds ratios in the group having the highest prevalence of gynecomastia (ages 12–14) was also assessed using Cochran-Mantel-Hasenzel statistics. All results with p values less than 0.05 were considered significant. The statistical software package, SAS 9.1 (SAS Institute, Inc., Cary, NC) was used in the study.

Results

A total of 72 boys were excluded from the final analysis because of a missing testis. The overall prevalence of gynecomastia in clinically healthy population was 1.97% (121 of 6128). The gynecomastia was found only in boys 10–19 years old ($n = 3082$). Therefore, we decided to focus our study on these 10 age groups. The prevalence of gynecomastia among these boys was 3.93% (121 of 3082). Gynecomastia was unilateral in 43 subjects (35.5% of gynecomastia cases), with 25 boys having left-sided and 18 having right-sided gynecomastia. As expected the prevalence of bilateral gynecomastia was high, being present in 78 subjects (64.5% of gynecomastia cases). The incidence of gynecomastia was positively correlated with age in boys 10–13 years old (parameter estimate = 0.884, $p < 0.001$) and negatively correlated with age in the group 14–19 years age (parameter estimate = -0.591 , $p < 0.001$). The prevalence of gynecomastia in all the age groups is shown in Figure 1. The gynecomastia was more frequent in children with pubic hair Tanner stage 3 and stage 4 (Figure 2) and testicular volume between 5 and 10 ml (Figure 3).

We found 252 cases of left-sided varicocele in the entire study population, of which 245 were in subjects in the age

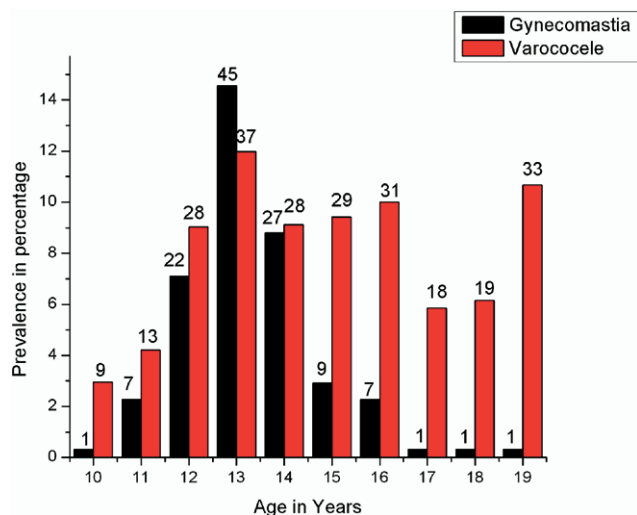


Figure 1. Prevalence of gynecomastia ($n = 121$) and varicocele ($n = 245$) in boys of age 10–19 years ($n = 3082$). Data are expressed as percentages. Raw numbers of cases in each age group are given on top of each bar.

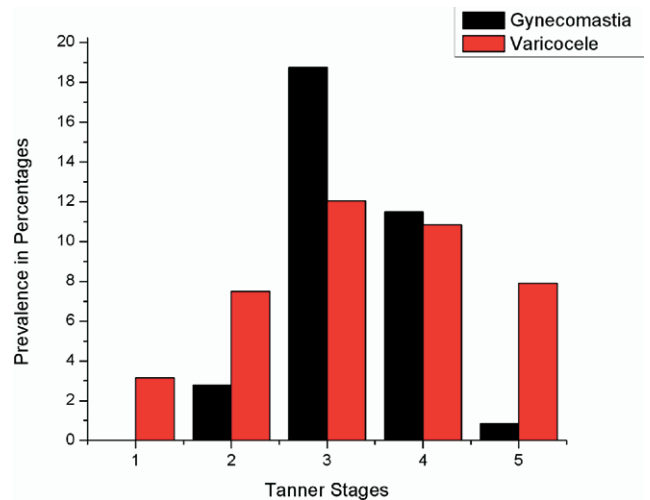


Figure 2. Prevalence of gynecomastia ($n = 121$) and varicocele ($n = 245$) according to pubic hair Tanner stages in boys of age 10–19 years ($n = 3082$). Data are expressed as percentages.

group 10–19 years (Figure 1). In the group 10–13 years of age, gynecomastia was positively correlated with varicocele ($p = 0.03$) adjusted for age and other influential parameters such as BMI and testicular volume (adjusted OR = 2.1, 95% confidence interval [CI] = 1.1–4.1). For the age at which gynecomastia was most prevalent (age 12–14 years), the adjusted OR of gynecomastia occurring in boys with varicocele ($p = 0.02$), using the Cochran-Mantel-Hasenzel method of adjusting for age was 1.9 (95% CI = 1.1–3.4). Figures 1–3 show the prevalence of varicocele along with gynecomastia according to age, pubic hair Tanner stage, and left and right testicular volumes.

Gynecomastia was negatively correlated with BMI (parameter estimate = -0.089 , $p = 0.04$ for ages 10–13 years; parameter estimate = -0.131 , $p = 0.035$ for ages 14–19). In addition, it was weakly correlated with combined testicular volume of left and right testis (parameter estimate = 0.047, $p = 0.004$), positively in the group 10–13 years of age and negatively in the group 14–19 years (parameter estimate = -0.063 , $p = 0.009$). However no relationship was found between gynecomastia and penis size, urban/rural status, and sea level of residence.

Discussion

We examined 6200 children aged 0–19 years for gynecomastia, varicocele, and various somatometric parameters in what is, to the best of our knowledge, the largest cross-sectional study done on gynecomastia so far. We found that pubertal gynecomastia appears only after the age of 10, therefore we limit our discussion to the age group 10–19 years. The prevalence of gynecomastia in this age group in our study population was 3.9%, which is low compared with other studies in the past [7,9,11]. This could

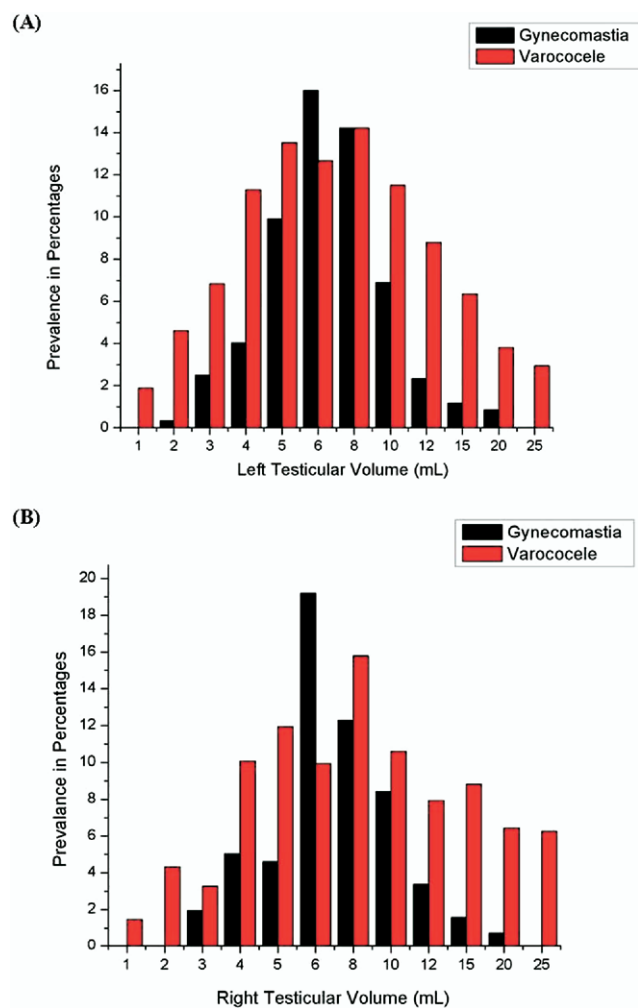


Figure 3. (A) Prevalence of gynecomastia ($n = 121$) and varicocele ($n = 245$) according to left testicular volume in boys aged 10–19 years ($n = 3082$). Data are expressed as percentages. (B) Prevalence of gynecomastia ($n = 121$) and varicocele ($n = 245$) according to right testicular volume in boys age 10–19 years ($n = 3082$). Data are expressed as percentages.

be caused by a number of factors: greater size of breast tissue set as a diagnostic criteria for gynecomastia as compared with other studies; a larger study population; more random selection of subjects than in other studies; and ethnic differences. However, in accordance with previous studies [7–9], the frequency of bilateral gynecomastia was greater than for unilateral gynecomastia.

We found that gynecomastia is more frequent in boys with pubic hair Tanner stage 3 and 4, which has led us to suggest that gynecomastia is a mid-puberty event. This is not in accordance with the idea of Ismail and Barth, who proposed that prevalence of physiologic gynecomastia increases with the stage of puberty [12]. However Guvenc et al found results similar to ours. In their study on 646 Turkish boys, the prevalence of gynecomastia was highest in pubertal stage 3 and 4 and the incidence dropped after stage 4 [11]. We believe that pubic hair Tanner stage is a

better indicator than age groups for determining the incidence of pubertal gynecomastia.

Varicocele has been described to occur in 2–20.5% of adolescents by various studies in the past [20–22]. In our study, the prevalence of palpable left-sided varicocele in the entire study population was 4.11% and in the age group 10–19 years was 7.95%. We found that in boys 10–14 years old, the incidence of gynecomastia is positively correlated with varicocele, suggesting that adolescent boys with left-sided varicocele are more likely to have gynecomastia. Very few investigators in the past have studied the association between gynecomastia and varicocele. In six boys aged 15–19 years with combined occurrence of varicocele and gynecomastia, Castro-Magna et al found that hCG-stimulated levels of estradiol were significantly lower and levels of testosterone were significantly higher after varicocelectomy. Increased levels of estradiol after hCG administration and its normalization after varicocelectomy suggested a pathogenetic role of varicocele in the development of gynecomastia [23]. Our results support the preliminary finding of this small hormonal study in a much larger clinical setting. Although Goblyos et al found some association between gynecomastia and left-sided varicocele in a small number of boys aged 14–18 years [24], we did not find any significant correlation between gynecomastia and varicocele in this age group.

Our study suggests that adolescent boys with low BMI are more likely to develop gynecomastia. There has been a number of conflicting study reports regarding this in the past. Sher et al demonstrated that boys with gynecomastia tend to be taller and heavier than those without [10], whereas Georgiadis et al found them to be heavier only [8], and in concordance with Nydick et al could not find any significant difference in their height compared with that of their peers [9]. Only one study, by Biro et al, found that boys with pubertal gynecomastia are shorter, leaner, and have a lower Quetlet index [7]. We consider BMI as a better index than evaluating weight and height separately, as both are correlated with each other. The results of our cross-sectional study are in accordance with what Biro et al achieved in a longitudinal study. Therefore the idea that adipose tissue, being the site of peripheral conversion of androgens to estrogens, is positively correlated with the development of breast tissue in adolescent boys [10,25] may not be true. The fact that it is easier to detect gynecomastia in lean boys may also be the cause of the above finding. However, the reason for lean boys being more likely to develop gynecomastia is not completely understood.

We found that gynecomastia was most prevalent in boys with right and left testicular volumes in the range of 5–10 ml. Another significant finding in our study is that in boys 10–13 years of age, gynecomastia is positively correlated with testicular size, whereas among boys 14–19 years, individuals with smaller testicles are more likely to develop

gynecomastia. Although this correlation was weak, it needs clinical explanation. Nydick et al found a positive correlation between testicular size and male breast development in boys 10–16 years of age; however they also could not give a satisfactory explanation for their findings [9].

We could not find any significant correlation between incidence of gynecomastia and penis size. A possible explanation could be that, although there exists a relative deficiency of free testosterone in pubertal males with gynecomastia [4], dihydrotestosterone and not testosterone is primarily responsible for the growth of the external genitalia [26,27]. In contrast to our results, Nydick et al demonstrated a positive correlation between gynecomastia and penis size ($r = 0.22$) in their study in 1890 normal boys in a scout camp [9]. However the results achieved by these investigators might not have any clinical significance, as the investigation did not consider age while conducting statistical analysis even though both penile size and gynecomastia are significantly dependent on age.

We did not find any significant difference between the prevalence of gynecomastia in boys from urban versus rural areas, of different socioeconomic backgrounds, and of residences at different sea levels. Thus we believe that these environmental factors may not play a significant role in the development of this condition. In a study on 1530 school boys in Istanbul, Neyzi et al achieved results similar to ours and did not find any differences in the incidence of gynecomastia between different socioeconomic groups [28].

Our study is unique in multiple ways. It is the largest cross-sectional study done on gynecomastia so far, and the entire physical examination of all the boys was done by only one investigator, thus reducing the possibility of interobserver bias. We measured the size of left and right testes separately and evaluated obese adolescents, whereas some previous investigators excluded them [9]. Moreover, unlike us, most of the earlier investigators did not adjust their data for age even though all somatometric parameters are age dependent; and hence their results might be biased. However, our study also had limitations too. Gynecomastia was diagnosed only visually and by palpation, and was not confirmed by ultrasonography or by X-ray mammography. Because ours is a large population-based study, use of ultrasonography to measure testicular volumes was not practical. Although we did not study hormonal levels in boys, the differences we found between boys with versus without gynecomastia suggest that hormonal alterations are involved in development and/or support of the developed gynecomastia. Estimation of the hormonal changes leading to breast development proves to be a challenge, given the transient nature of the change. Although some of our findings support the preliminary results of a few investigators, others are not in accordance with previous studies. Nevertheless our study has revealed significant findings that pave the way for future research in this area.

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