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Etiopathological Factors Associated with Gynecomastia Patients Seeking Surgical Correction in the South Indian Population

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Abstract

Background Although several medical conditions are associated with gynecomastia, around 60% of cases are idiopathic. The role of endocrine testing in idiopathic gynecomastia is controversial. This study was done to determine the etiological and lifestyle factors associated with different grades of gynecomastia.

Patients and Methods This was a descriptive study conducted at the department of plastic surgery in a tertiary care hospital in South India between January 2014 and December 2016, among the patients seeking corrective surgery for gynecomastia.

Results A total of 73 patients were included in the study with a mean age of 22.56 years. The majority of the patients displayed Simon's Grade IIa gynecomastia (56.2%). The etiological factors identified in this study were hormonal abnormalities (47.95%), hypogonadism (2.7%), and drug intake (1.4%). The most common hormonal abnormality discovered was high estradiol values (15.1%) followed by decreased testosterone levels (13.7%). The chi-squared test revealed no statistically significant relationship between the hormonal values, type of food, body mass index (BMI), or physical activity and the grades of gynecomastia.

Conclusion Most of the patients (50.68%) in our study had idiopathic gynecomastia. The most common hormonal abnormality detected was high estradiol values. No correlation was found between the hormonal values, type of food, BMI, or physical activity and the grades of gynecomastia.

Keywords
- gynecomastia
- etiology
- lifestyle factors
- hormone assay

Introduction

Gynecomastia is defined as benign proliferation of the glandular tissue in the male breast under the subareolar region. The overall prevalence of gynecomastia in hospitalized male patients was 65% as per the observation of Niewoehner and Nuttal.[1] Apart from the cosmetic reasons, the psychological impact imparted by this disease also plays an important role in the management of this disease. The pathophysiology of gynecomastia is felt to be an imbalance of estrogens and androgens, with a decreased testosterone-to-estradiol ratio.[2] Although several medical conditions are associated with gynecomastia such as primary or secondary gonadal failure, androgen resistance syndromes, hyperthyroidism, chronic liver disease, the use of some medications such as spironolactone, digoxin, bicalutamide, cimetidine, anabolic

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steroids, and drugs of abuse such as alcohol and marijuana, around 60% of cases are idiopathic.[3]

Frequently, the causes of gynecomastia can be found when a thorough history and physical examination are performed. Anthropometric measurements like body mass index (BMI) may be helpful because obesity can be associated with the increased peripheral conversion of androgens to estrogens and is associated with a higher prevalence of gynecomastia.[4] There is a strong association between the presence of varicoceles and gynecomastia.[5] About 58% of patients with persistent pubertal gynecomastia were found to have a family history of gynecomastia.[6]

When the cause is not apparent by physical examination, then a series of laboratory tests may be performed to rule out the underlying pathophysiology. Liver, kidney, and thyroid function tests can be done to exclude the respective diseases. The role of endocrine hormone assay in idiopathic gynecomastia is controversial. Hormonal assay of testosterone, estradiol, prolactin, luteinizing hormone (LH), follicle-stimulating hormone (FSH), and human chorionic gonadotropin, and its findings can direct toward pituitary, gonadal, and extragonadal endocrinopathies and neoplasms.[3] Hormonal studies and detailed clinical examination may reveal the etiology in most of the cases.

Only a few studies within the literature investigate the etiology of gynecomastia in patients undergoing corrective surgeries for gynecomastia.[7,8] The association of gynecomastia in South Indian patients seeking surgical treatment with some of the lifestyle, clinical, and laboratory factors is evaluated in this study. The relationship between the various etiological factors with the different grades of gynecomastia has not been studied previously. In this study, we are trying to find out this association as well.

Patients and Methods

This was a descriptive study conducted at the department of plastic surgery in a tertiary care institution in Southern India. All patients who underwent surgical correction of gynecomastia between January 2014 and December 2016 were included in this study. Patients below 10 years and above 50 years of age were excluded from the study. At the time of admission, all these patients were interviewed and examined. Data were collected from the hospital records and patient questionnaires as well. Data collected included the duration and family history of gynecomastia, their lifestyle factors like types of food consumed, physical activity, BMI, various medical etiological factors, physical examination findings, routine laboratory values, and hormonal profile (estradiol, testosterone, FSH, LH, prolactin, and thyroid-stimulating hormone [TSH]). The collected data were statistically analyzed using SPSS software version 26.0.

Results

A total of 73 patients were included in the study, with ages ranging from 13 to 45 years. Their distribution among various age groups is given in ►**Table 1**. The bulk of the patients ($n = 41$) belonged to the 20 to 29 years age group. The mean age of the patients was 22.56 years (standard deviation = 6.51). The mean duration of gynecomastia was 5.89 years. Only 15.1% of the patients had a positive family history of gynecomastia. The distribution of the patients according to the various grades of gynecomastia according to Simon's classification[9] is given in ►**Table 2**. The majority of the patients belonged to Grade IIa (56.2%). Six patients had unilateral gynecomastia.

Table 1 Distribution of gynecomastia patients among different age groups

Age group (y)	10–19	20–29	30–39	40–50	Total
No. of patients	24	41	6	2	73
Percentage	32.9	56.2	8.2	2.7	100

Table 2 Distribution of patients among various grades of gynecomastia

Simon's grade	I	IIa	IIb	III	Total
No. of patients	11	41	12	9	73
Percentage	15.1	56.2	16.4	12.3	100

Lifestyle Factors That May Affect the Incidence of Gynecomastia

The data regarding BMI, alcohol intake, diet, food habits, and physical activity were collected. The majority of the patients were having BMI less than 25 (61.6%). About 11% of patients had the habit of alcohol intake. Almost 97.3% of the patients were nonvegetarian. More than one-third (35.6%) of the patients used to have chicken meat once every week. Only 4.1% of patients used to have beef at least once a week. The majority of the patients used to have moderate physical activity on a routine basis (54.8%). About one-third (35.6%) of the patients were having a sedentary lifestyle. None of the patients had chronic medical conditions that may predispose them to the development of gynecomastia.

When considering chronic drug intake, only one patient was taking spironolactone that can be mentioned as an etiology of gynecomastia. Two patients (2.7%) had hypogonadism—one had Klinefelter's syndrome and the other primary hypogonadism.

Examination Findings and Hormonal Profile of the Patients

Secondary sexual characters were present in 91.8% of patients. Of the six patients having an absence of secondary sexual characteristics, two were suffering from Klinefelter's syndrome and primary hypogonadism, two had increased estrogen levels, and two had normal hormonal levels. About 97.3% of patients had normal scrotal size. Nobody had a breast mass or scrotal mass.

The hormonal profile of the patients is given in ►**Table 3**. The majority (52.05%, $n = 38$) of the patients were having normal values for all the six assayed hormones. The most

Table 3 Hormonal profile of the patients with gynecomastia

Hormone	Testosterone	Estradiol	LH	FSH	Prolactin	TSH
Patients with normal levels (in %)	83.6	83.6	87.7	90.4	86.3	93.2
Patients with increased levels (in %)	2.7	15.1	8.2	4.1	12.3	5.5
Patients with decreased levels (in %)	13.7	1.4	4.1	5.5	1.4	1.4

Abbreviations: FSH, follicle-stimulating hormone; LH, luteinizing hormone; TSH, thyroid-stimulating hormone.

common hormonal abnormality discovered was high estradiol values that were seen in 15.1% of patients. The next most common abnormality observed was decreased testosterone levels that were seen in 13.7% of patients.

Relationship between the Grades of Gynecomastia and Various Lifestyle and Hormonal Factors

A chi-squared test was done to find out the relationship between the grade of gynecomastia and the frequency of chicken meat intake in a week. There was no statistically significant relationship between them (p-value = 0.480). There was no statistically significant relationship between the grade of gynecomastia and the frequency of beef intake (p-value = 0.074). BMI and physical activity also had no significant relation with the grade of the gynecomastia (p-values = 0.018 and 0.377, respectively). The chi-squared test results to find out the relationship between the hormonal values and the grades of gynecomastia are given in ►**Table 4**. None of them were statistically significant.

Discussion

The number of gynecomastia patients attending plastic surgery clinics is on the rise in our institution. The incidence of gynecomastia is increasing in various other parts of the world as well.[10] Idiopathic gynecomastia in young males can cause a psychological threat to their self-esteem and normal sexual identity.[11] Although many etiological factors are attributed to the development of gynecomastia, idiopathic remains the most common.[12] But possible etiopathological factors should be evaluated. This study was performed to find out the association between the various proposed etiological factors and grades of gynecomastia in a group of patients attending the plastic surgery clinic for the surgical treatment of the gynecomastia.

Gynecomastia is more common in pubertal males with a high BMI.[13] In our study, most of the patients had BMI less than 25 (61.6%). In another study, Costanzo et al found out that 62.7% of the patients were overweight or obese.[14] Most of the circulating estradiol in man is derived from the aromatization of testosterone in adipose tissue. Chronic renal or hepatic diseases were not there in any of the patients included in the study. In the study by Costanzo et al, the cause of gynecomastia was drug intake in 7.8% of patients, renal failure in 2.1%, and chronic liver disease in 1.2% of patients.[14]

In our study, etiological factors could be discovered in 36 (49.32%) patients. They include hormonal abnormalities (47.95%), hypogonadism (2.7%), and drug intake (1.4%). About 50.68% ($n = 37$) of patients fall into the category of idiopathic gynecomastia. In a multicentric study by Costanzo et al, of patients presenting with gynecomastia, etiologies of gynecomastia were found in 54.9% of cases.[14] He also noticed that among the young population, the use of anabolic steroids and persistent pubertal gynecomastia were the most common cause of gynecomastia. However, hypogonadism and the use of drugs were the most common causes in elderly patients. A decreased androgen to estrogen ratio exists in boys with pubertal gynecomastia when compared with boys who do not develop gynecomastia.[15] The skin fibroblasts of boys with gynecomastia showed increased aromatase activity.[16]

Currently, hormonal assay plays an important role in the workup of gynecomastia. In this series, 47.95% ($n = 35$) of patients showed some deranged hormonal values. The most common hormonal abnormality discovered was high estradiol values (15.1%) followed by decreased testosterone levels (13.7%). In a study by Emin Sir et al,[17] free T4, TSH, prolactin, and the other sex hormones of the patients and controls were similar. They arrived at an inference that there may be no relationship between hormones (especially sex steroids) and idiopathic gynecomastia in young adults. Al-Alwan et al found that testosterone and estradiol levels were significantly higher in individuals diagnosed with gynecomastia. They found no significant difference in FSH and LH hormone levels between the two groups.[18] The study by Yazici et al[19] revealed significantly higher LH, FSH, and total testosterone levels of the patients ($n = 31$) aged between 20 and 30 years with idiopathic gynecomastia than the healthy controls. So, the association between the hormonal levels and the gynecomastia is inconsistent in various studies. Ersöz et al[4] noticed significantly lower LH and total testosterone levels in patients with gynecomastia than in the controls but the estradiol levels were similar between them.

In the current study, two patients (2.7%) had a combination of the absence of sexual characteristics and abnormal hormonal levels (increased estrogen level). Since no consistent association

Table 4 The chi-squared test results of hormonal values and the grades of gynecomastia

Hormone	Testosterone	Estradiol	LH	FSH	Prolactin	TSH
p-Value	0.399	0.879	0.219	0.063	0.578	0.651

Abbreviations: FSH, follicle-stimulating hormone; LH, luteinizing hormone; TSH, thyroid-stimulating hormone.

is present between a particular hormonal value and gynecomastia, the practice of performing hormonal assay is not compulsory, especially in patients who are presenting for cosmetic surgery. Nuttall states that hormonal evaluation in gynecomastia is unnecessary unless the observed breast enlargement is clearly of recent origin or is increasing in size.[20] These investigations are not cost-effective and drain the resources, especially when more and more patients are seeking surgical correction nowadays, especially for cosmetic reasons. So, hormonal assay can be limited to those patients who are having clinical features of hormonal abnormalities rather than doing it on a routine basis.

In our study, no statistically significant relationship was found between the hormonal values and the grades of gynecomastia. So, it is inferred that the difference in the hormonal values does not influence the grades of gynecomastia. Costanzo et al observed that there was no difference in the plasma levels of estradiol or testosterone in patients with unilateral or bilateral gynecomastia.[14] In recent years, there has been a gradual shift toward increased meat consumption in our study population. About 97.3% of our patients were nonvegetarian. So, the relationship between meat consumption and gynecomastia was studied in this series. The meat consumption, BMI, or physical activity had no statistically significant relationship with grades of gynecomastia. The size of the gynecomastia does not depend upon the variation in the so-called etiological factors. There is a paucity of studies in the literature examining lifestyle factors and the relationship with gynecomastia, especially among cosmetic surgery patients. The relationship between various etiological factors and the grades of gynecomastia has not been studied before. The current level of evidence on this subject is very low and future studies examining the impact of etiological factors on the grades of gynecomastia are greatly needed.

In this study, the gynecomastia was evaluated clinically and ultrasonography or other imaging modalities were not used. The sample size of this study is small and an objective evaluation of many factors was not done. More molecular studies may reveal the exact etiological factors of this common condition in the future.

Conclusion

Most of the patients seeking surgical management of gynecomastia in our study had idiopathic gynecomastia. The commonest hormonal abnormality detected was high estradiol values. No correlation was found between the hormonal values, chicken meat and beef consumption, BMI, or physical activity and the grades of gynecomastia.

Conflict of Interest
None declared.

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