RESEARCH ARTICLE / *Araştırma Makalesi*

Evaluation of The Association Between Precocious Puberty and Obesity

Puberte Prekoks Ve Obezite Arasındaki Ilişkinin Değerlendirilmesi

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Abstract

Objective: The marked variation in the timing of puberty despite similar living conditions shows that many factors are effective in determining the onset of puberty. Many factors, such as genetic and environmental factors, stress, socioeconomic status, metabolic rate, and body fat ratio, affect the age of puberty onset. Recent studies have shown that the age of puberty onset has shifted to earlier ages. The increasing prevalence of childhood obesity is deemed to contribute this change. Therefore, we planned the present study to determine the rates of obesity and overweight, in patients followed for precocious puberty to evaluate the association between obesity, bone age, and height age, and to examine the association between obesity and hormone profile.

Materials and Methods: The medical records of 206 patients diagnosed with idiopathic precocious puberty who were being followed up at the Pediatric Endocrinology outpatient clinic of Sakarya Training and Research Hospital between October 2018 and October 2021 were retrospectively reviewed. Anthropometric data (age, gender, height, weight, body mass index, and puberty stage), bone age, height age, and weight age of the patients were recorded from the medical records. Patients were grouped as normal weight, overweight, and obese by body mass index (BMI).

Results: Of the included patients, 97,57% (201 patients) were female and 2,43% (5 patients) were male. One hundred and thirty-one patients (63,59%) had normal weight, 40 (19,41%) were overweight and 35 (17,00%) had obesity. Significant differences were found between the groups (normal weight, overweight and obese) in terms of weight age, BMI percentile, height age, bone age, and bone age standard deviation score (SDS) (p = <0,001; p = < 0,001; p = 0,015; p = 0,026; and p = 0,035; respectively). The current puberty stages of the patients were more correlated with bone age and weight age than with chronological age.

Conclusion: The overweight and obesity rates are increased in patients with precocious puberty. Obesity appears to be a facilitating factor for precocious puberty. Bone age and weight age are more determinants for the onset of puberty. Obesity should be considered when searching for etiological reason or deciding on treatment in girls with precocious puberty.

Keywords: Obesity; precocious puberty; early puberty; child.

Öz

Amaç: Benzer yaşam koşullarına rağmen ergenlik zamanlamasındaki belirgin değişiklik, ergenlik başlangıcında çok sayıda faktörün etkili olduğunu gösterir. Ergenlik başlama yaşını genetik ve çevresel faktörler, stres, sosyoekonomik durum, metabolik hız ve vücut yağ oranı gibi birçok faktör etkiler. Son çalışmalar, ergenlik yaşının daha erkene kaydığını göstermiştir. Çocukluk çağı obezitesinin artan prevalansı buna katkı sağladığı varsayılmaktadır. Bu nedenle puberte prekoks nedeni ile takip edilen hastalarda obezite ve fazla ağırlık sıklığını belirlemek, obezite kemik yaşı, boy yaşı ilişkisini değerlendirmek ve obezite ile hormon profili ilişkisini incelemek amacıyla bu çalışmayı planladık.

Gereç ve Yöntemler: Sakarya Eğitim ve Araştırma Hastanesi Çocuk Endokrinoloji polikliniğinde Ekim 2018 ile Ekim 2021 tarihleri arasında takip edilen idiopatik puberte prekoks tanılı 206 hastanın dosyaları retrospektif olarak tarandı. Hastaların dosyalarından antropometrik verileri (yaş, cins, boy, kilo, vücut kitle indeksi, puberte evresi), kemik yaşı, boy yaşı, kilo yaşı kaydedildi. Hastalar vücut kitle indeksine (VKİ) göre normal kilolu, fazla ağırlıklı ve obez olarak gruplandırıldı.

Bulgular: Hastaların %97,57'si (201 hasta) kız, %2,43'ü (5 hasta) erkekti. Hastaların 131'i (%63,59) normal kiloda, 40'ı (%19,41) fazla ağırlıklı, 35'i (%17,00) obezdi. Gruplar arasında (normal kilo, fazla ağırlıklı ve obez), kilo yaşı, VKİ persentili, boy yaşı, kemik yaşı ve kemik yaşı standart deviasyon skoru (SDS) değerleri arasında anlamlı fark saptandı (sırasıyla p=<0,001; p=< 0,001; p=0,015; p =0,026; p=0,035). Hastaların mevcut puberte evresi hastaların takvim yaşından ziyade kemik yaşı ve kilo yaşı ile daha korele idi.

Sonuç: Puberte prekoks hastalarında fazla ağırlık ve obezite sıklığı artmıştır. Obezite puberte prekoks için kolaylaştırıcı bir risk faktörü gibi görünmektedir. Puberte başlangıcında kemik yaşı ve kilo yaşı daha belirleyicidir. Erken ergenliği olan kızlarda etiyolojik neden ararken ya da tedaviye karar verirken obezite dikkate alınmalıdır.

Anahtar Kelimeler: Obezite; Puberte prekoks; Erken puberte; Çocuk.

INTRODUCTION

Precocious puberty is defined as the development of secondary sex characteristics before the age of 8 years in girls and 9 years in boys or the onset of puberty >2.5 standard deviations earlier than the expected normal age range in both female and male children.[1] The marked variation in the timing of puberty despite similar living conditions shows that many factors are effective in the onset of puberty. The age of puberty onset is affected by many factors, such as genetic and environmental factors, stress, socioeconomic status, metabolic rate, maturation of bones, and body fat ratio[2-4] Recent studies have shown that the age of puberty onset has shifted to earlier ages.[5,6] The increasing prevalence of childhood obesity is deemed to contribute to this change.[7,8] Overnutrition and the resulting obesity pandemic in childhood have recently become an important public health problem. High leptin levels in obese patients may lead to premature puberty by acting on GnRH neurons and the pituitary gland. However, there is not enough evidence to establish a cause and effect relationship between obesity and precocious puberty. Increased leptin levels in obese patients lead to an increase in growth rate by acting on the epiphyseal growth plates, resulting in advanced bone age.[9,10] It was reported that bone age, rather than chronological age, determines the onset of puberty.[11] We planned this study to determine the prevalence of obesity and overweight, to evaluate the association between obesity and bone age, and to investigate the relationship between obesity and hormone profile in patients followed up for precocious puberty.

MATERIALS and METHODS

Medical records of 227 patients receiving gonadotropin-releasing hormone (GnRH) analog treatment for precocious puberty followed up at the pediatric endocrinology outpatient clinic for the past 3 years (from 10.30.2018 to 10.30.202) were collected upon receiving approval from the Ethics Committee of Faculty of Medicine. After excluding 21 patients with missing data and underlying organic pathologies, the remaining 206 patients with idiopathic precocious puberty were included in the study (Figure 1).

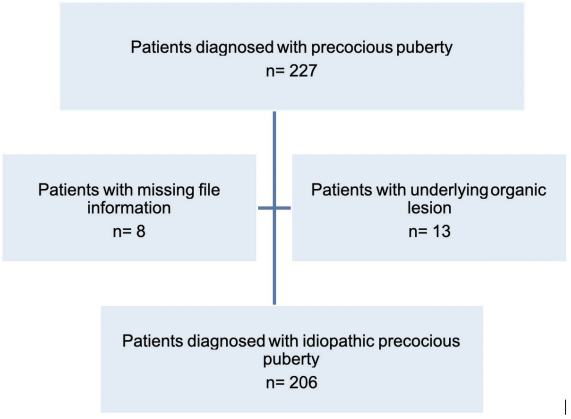

Figure 1: Flow chart of the study population

Anthropometric data (age, gender, height, weight, body mass index, and puberty stage) were recorded from the medical records of the patients. Puberty staging was done as per the method of Marshall and Tanner (stages 1-5).[12] In addition, the results of luteinizing hormone-releasing hormone (LHRH) stimulation tests, if performed, were also recorded from the medical records. Precocious puberty diagnosis was made with an LHRH stimulation test in 66,51% of the patients and with basal luteinizing hormone (LH) values in 33,49% of the patients without an LHRH stimulation test. Bone age at the time of precocious puberty diagnosis was evaluated and recorded by the same radiologist based on the Greulich-Pyle method using the PACS radiology system of the hospital. Bone age standard deviation score (SDS) was calculated by using the BoneXpert Adult Height Predictor V3.1 software.[13] BMI percentiles of the patients with precocious puberty were calculated using the data from the study by Olcay Neyzi et. al.[14] standardized for the Turkish population. The patients were categorized by BMI percentile as normal (BMI percentile <85), overweight (BMI percentile ≥85-95) and obese (BMI percentile ≥95). Weight age (age corresponding to 50th percentile at the same weight) and height age (age corresponding to 50th percentile at the same height) of the patients at the time of diagnosis were determined.

Statistical analysis of the data was performed using SPSS Version 26 software. Data distribution was assessed using Kolmogorov-Smirnov and Shapiro-Wilk tests. Variables with normal distribution were compared using a one-way analysis of variance (ANOVA) test. Variables with abnormal distribution were compared using the Kruskal-Wallis H test. The results were presented as mean (SD) or median (min-max). The overweight and obesity rates were determined in patients with precocious puberty. Bone age, (and bone age SDS), height age, weight age, basal luteinizing hormone (LH) levels, follicle-stimulating hormone (FSH) levels, peak LH levels, peak FSH levels, and peak LH/FSH ratios were compared by BMI percentile. P<0.05 was considered statistically significant.

RESULTS

Of the included patients, 97,57% (201 patients) were female and 2,43% (5 patients) were male. Of the patients, 92,23% presented with breast enlargement, 4,37% with pubic or axillary pilosity, and 3,40% with obesity. The median age was 8,00 (2.50-10,25) years, the median height age was 9,00 (3,50-12,00) years, the median weight age was 9,50 (4,50-15,50) years and the median bone age was 9,00 (3,25-13,00) years at presentation. At presentation, Tanner's breast stage was 2 in 24,76% of the patients, 3 in 59,71%, and 4 in 15,53%. The median basal LH concentration was 0,76 mlU/ml (0,01-11.30) and the median basal FSH level was 2,92 mlU/ml (0,34-26,00) at presentation. One hundred and thirty-one patients (63,59%) had normal weight, 40 (19,41%) were overweight and 35 (17,00%) had obesity. The age at presentation, basal LH, basal FSH, peak LH, and peak FSH values were similar between normal weight, obese and overweight groups (p=0,203; p=0,090; p=0,061; p=0,381; and p =0,842; respectively) (Table 1). However, significant differences were found between the groups in terms of weight age, BMI percentile, height age, bone age, and bone age SDS (p=<0,001; p=< 0,001, p=0,015; p =0,026; and p=0,035; respectively) (Table 2). Of the obese patients, 5,71% were Tanner breast stage 2, 60,00% were stage 3 and 34,29% were stage 4 and they showed a statistically significant difference compared to non-obese subjects (p=0,032).

Table 1. Comparison of the laboratory findings of the patients

	Normal weight group (n = 131) Median (25%-75% range)	Overweight group (n = 40) Median (25%-75% range)	Obese group (n = 35) Median (25%-75% range)	p values
Basal LH	0,69 (0,16-1,70)	0,29 (0,13-1,52)	1,13 (0,24-2,39)	0,090
Basal FSH	2,96 (2,00-4,44)	2,31 (1,50-4,09)	3,52 (2,00-5,00)	0,061
	(n = 90) Median (25%-75%range)	(n = 28) Median (25%-75% range)	(n = 19) Median (25%-75% range)	
Peak LH	6,49 (4,83-13,65)	6,41 (4,07-8,62)	8,26 (4,73-17,00)	0,381
Peak FSH	9,28 (7,37-13,07)	9,65 (7,95-12,32)	11,00 (8,21-12,50)	0,842

LH :Luteinizing hormone, FSH: Follicle-stimulating hormone

Table 2. Comparison of the sociodemographic data of the patients

	Normal weight group (n = 131) Median (25%-75% range)	Overweight group (n = 40) Median (25%-75% range)	Obese group (n = 35) Median (25%-75% range)	p values
Age	8,00 (7,40-8,75)	7,82 (7,20-8,47)	8,20 (7,75-9,00)	0,203
Weight age	8,50 (7,50-9,50)	10,00 (9,50-10,50)	11,00 (10,50-12,00)	< 0,001[a,b,c]
BMI (%)	54,50 (31,50-71,00)	90,55 (88,92-92,95)	97,50 (96,40-98,70)	< 0,001[a,b,c]
Height age	8,50 (7,50-9,50)	8,50 (8,00-9,50)	9,50 (8,50-10,50)	0,015[b,c]
Bone age	9,00 (8,00-10,00)	9,00 (8,00-10,50)	9,50 (8,80-10,75)	0,026[b]
Bone age SDS	1,18 (0,53-1,86)	1,57 (0,62-2,30)	1,64 (0,91-2,33)	0,035[b]

a Normal weight-Overweight, b Normal weight-Obese, c Overweight-Obese, BMI: Body mass index

DISCUSSION

Obesity is an important environmental factor affecting the timing and rate of pubertal development. It was shown that childhood obesity may result in precocious puberty in addition to several negative physical and psychosocial disorders.[15,16] The link between obesity and puberty is thought to be due to the interaction of adipokine and leptin with kisspeptin that important regulator of puberty. However, increased aromatase activity in adipose tissue may contribute to changes in the onset of puberty.[17] A meta-analysis showed that obesity poses an increased risk for precocious puberty in girls (2.44-fold) but does not cause a change in age at menarche.2 Our study found significant differences in terms of weight age, BMI percentile, height age, bone age, and bone age SDS between the groups when the patients followed up for precocious puberty were grouped as normal weight, overweight and obese (p=<0,001; p=< 0,001; p=0,015; p =0,026; and p=0,035; respectively). Li et al.[18] have shown that obesity type (central obesity, general obesity) is also associated with precocious puberty. This study showed that for girls, general obesity contributes more to the risk of developing precocious puberty than central obesity. In the same study, for boys, central obesity (not a general obesity risk factor) was shown to be an independent risk factor for precocious puberty. Due to the small number of men in our study, a comparison could not be made. In a wide series of patients, a 1-point increase in BMI was shown to shift the mean age of puberty onset to 0,11 years earlier in patients of 2 to 8 years of age.[19] Although our patients had a mean age of 7,89 years at presentation, their mean weight age (9,21 years) and mean bone age (9,12 years) were more advanced and complied better with the normal age of pubertal development (9,65-10,16 years for breast stage 2).[20,21] These findings showed that pubertal development is more correlated with weight age and bone age.

In our study, we showed that overweight and obesity rates were higher than those found in a study conducted on a similar age group in our region[22] (overweight rates 19.4%, and 15.7%, respectively; obesity rates 17%, and 8.5%, respectively). The high rates of overweight and obesity in patients with precocious puberty support the thesis that obesity is a promoting factor for precocious puberty.

A large part of the patients was Tanner's breast stage 2 at presentation. Tanner's breast stage was higher among the obese patients (5,71% stage 2, 60,00% stage 3, and 34,29% stage 4) (p=0,032). It is possible that progression in the breast stage in obese patients may be considered increased fatty tissue (lipomastia) by the families. The presentation of obese patients with more advanced breast stages is deemed to be caused by misinterpreting breast enlargement as fatty tissue.

In conclusion, the rates of overweight and obesity are increased in patients with precocious puberty. Obesity appears to be a facilitating factor for precocious puberty. Bone age and weight age are more determinant for the onset of puberty. Obesity should be considered when searching for etiological reasons or deciding on treatment in girls with precocious puberty.

Declaration of Conflict of Interest

The authors declare that they have no conflict of interest.

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Ethical approval

Approval was obtained from the Sakarya University Faculty of Medicine Ethics Committee (Approval No: 71522473-050.01.04-64758-440)

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