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ORIGINAL ARTICLE

Evaluation of the COVID-19 pandemic process effect on the increase of Precocious Puberty and Premature Thelarche

Santral Puberte Prekoks ve Prematur Telarş Sıklığının Artmasında COVID-19 Pandemi Sürecinin Etkisinin Değerlendirilmesi

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ABSTRACT

Objective: To determinate COVID-19 pandemic process effect on the increase of Precocious Puberty and Premature Thelarche
Materials and Methods: Total 60 girls, younger than 8 years old, who complaint with breast development. Medical history and physical examination findings, bone age, free T4, TSH, FSH, LH, estradiol levels of patients were recorded in their first visits. According to LHRH test results patients were divided to subgroups such as PT and CPP. Differences in the use of technological tools were recorded before and during the pandemic
Results: Higher Body Mass Index (BMI) (P=0.033), bone age (P<0.001) basal LH (P<0.001), basal FSH (P<0.001), basal estradiol (P<0.001) in cases with central puberty precocious level was detected. There was no difference between the two groups in terms of age and weight. Compared to the pre-pandemic period, there was a significant increase in the use of technological tools (smartphone, computer, television) in both groups. In cases with PT, it was 2.54 ±0.65 hours/day before the pandemic and 6.22±1.25 hours/day during the pandemic (p<0.001), in cases with Spp it was 2.7 ±0.46 hours/day before the pandemic, 7.36±1.36 hours/day during the pandemic (p<0.001). The main reason for using technological tools was school lessons (4.6 ± 1.2 hours/day in cases with Pt, 5±1.2 hours/day in cases with Spp p =0.393).
Conclusion: In our study, it was observed that there was a significant increase in the use of technological devices and puberty symptoms started at a younger age in both groups after the pandemic. It was thought that environmental factors such as weight and increased use of electronic devices triggered the onset of puberty and the rate of progression.
Keywords: Precocious Puberty, Coronavirus, Pandemics

ÖZ

Amaç: Bu çalışmada amaç; COVID-19 pandemi sürecinin santralpuberte prekoks (SPP) ve prematur telarş (PT) sıklığının artış ve ilişkisini araştırmaktır.
Gereç ve Yöntem: Çocuk Endokrinoloji polikliniğine başvuran 60 kız hasta çalışmaya dahil edildi. Hastalarınilk başvuruanamnez ve fizik muayene bulguları, kemik yaşı, serbest T4, TSH, folikülstimüle edici hormon (FSH), lüteinize edici hormon (LH), estradiol (E2), düzeyleri kaydedildi. Gerekli olgularda yapılmış olan luteinize edici hormon releasing hormon (LH-RH) testi sonucuna göre PT ve SPP olarak ayrıldı.Pandemi öncesi ve sırasında teknolojik araçların kullanımındaki farklılıklar kayıt edildi.
Bulgular: Santral puberte prekokslu olgularda daha yüksek vücut kitle indeksi (VKİ)(P=0.034), kemik yaşı (p<0.001), bazal LH (P<0.001), bazal FSH(P<0.001), bazal estradiol (P<0.001) düzeyi tespit edildi. Yaş ve kilo bakımından her iki grup arasında farklılık yoktu. Her iki grupta da pandemi öncesine göre kıyaslandığındateknolojik araçların (akıllı telefon, bilgisayar, televizyon)kullanımında belirgin artış vardı. Prematur telarşı olan olgularda pandemi öncesinde 2,54 ±0,65 saat/gün pandemi sırasında 6,22±1,25 saat/ gün idi (p<0,001).SPP'li olgularda pandemi öncesinde 2,7 ±0,46 saat/gün pandemi sırasında 7,36±1,36 saat/gün idi (p<0,001). Teknolojik araçların kullanımının ana sebebi okul dersleri idi (PT olan olgularda 4,6 ± 1,2 saat/gün, SPP' li olgularda 5±1,2 saat/gün p=0,393).
Sonuç: Çalışmamızda her iki grubumuzda da pandemi sonrasında teknolojik alet kullanımında belirgin artış olduğu görüldü.Ayrıca santral puberte prekoks başlangıç yaşının erkene kaydığını saptandı.Kilo,elekronik aletlerin kullanımın artışı gibi çevresel faktörlerin ergenlik başlangıcını ve ilerleyiş hızını tetiklediğini düşünüldü.
Anahtar Sözcükler: Puberte Prekoks, Koronavirüs,Pandemik

Introduction

Puberty is the period in which reproductive functions and sexual maturity are acquired in the transition from childhood to adulthood (1). The first sign of puberty is often breast development in girls. Acceleration in somatic growth, development in internal and external genital organs, formation of secondary sex characteristics, and acquisition of reproductive capacity occur during this period (2). Breast development in girls at 8 years, pubic hair at 8.5 years, menarche at 9 years, and pubic hair growth at 9 years in boys is defined as precocious puberty.

Early puberty is examined in 3 groups as central,

peripheral precocious puberty, and benign variant puberty. Central precocious puberty occurs as a result of early maturation of the Hypothalomo-Pituitary-Gonadal (HPG) axis.

The mechanism of action of the neuroendocrine and genetic factors providing pubertal development is still not known. Previous epidemiological studies showed that stress, metabolic rate, bone maturation, and environmental factors are effective in pubertal development as well as ethnic and genetic factors. Nutrition, chronic diseases, frequent infections, migration, environmental pollution, insecticides, antiandrogens, and exposure to estrogen-like endocrine disruptors can be counted among the environmental factors that affect puberty (3). It was shown in most previous studies that the timing of puberty is affected largely by genetic factors, and it is considered that the timing of puberty is determined by genes at a rate of 50-80% (4).

Other signs of sexual maturation in premature Thelarche girls are growth spurt and isolated breast development without acceleration in bone age.

The Coronavirus Disease, named "COVID-19", which emerged in December 2019 in the city of Wuhan, China, was reported to the World Health Organization on December 31, 2019. The Coronavirus is considered to be the most important healthcare issue of the 21st Century because it has had serious effects on almost every age group. Based on the understanding that the Coronavirus is contagious, social isolation and quarantine measures increased gradually (5). Social isolation paved the way for the emergence of various psychological disorders in individuals (6). It is already known that children spend more time with digital media and technological tools than previous generations today (7). The fact that children have to spend most of their time at home causes them to spend more time with technological tools. The use of the internet, technology, and playing digital games rates increased in individuals who stayed at home for a long time with social isolation and quarantine measures (8). The purpose of the present study was to investigate the increase and relationship of the frequency of SPP and PT in the COVID-19 pandemic process.

Materials and Methods

The findings of the 60 female patients between the ages of 2 and 8 who applied to the Pediatric Endocrinology Clinic with the complaint of the onset of puberty findings were evaluated. The study was approved by Başkent University, Medical and Health Sciences Research Board (Project No: E-94603339-604.01.02-69825) and was supported by Başkent University Research Fund.

The study was conducted by examining the file records of the patients who applied between November 2020 and June 2021 retrospectively. The duration of the children's use of technological tools in the pre- and post-pandemic periods was recorded. Anthropometric measurements were made in the morning on an empty stomach and with shoes and top clothes of the child were on. Bodyweight was recorded as "kg" and height as "cm". Bodyweight and height Standard Deviation Score (SDS) values were calculated (9, 10). Body Mass Index (BMI) was calculated with the formula BMI=Body Weight (kg) / Height (m)2 (11). The pubertal staging was performed according to Marshall and Tanner Method (12). The levels of follicle-stimulating hormone, LH, and E2 were recorded. LH-RH stimulation test results were used to differentiate between central prepubertal precocious and PT. Bone age was evaluated according to the Greulich-Pyle Method (13). Pituitary Magnetic Resonance (MR) imaging data of the patients with central precocious puberty were used.

Precocious Puberty: Breast development that initiated before the age of 8 accompanied by one or more of the symptoms (menstruation, pubic hair, bone age more than 2SDS ahead of the calendar age), increased gonadotropin (LH, FSH), and/or sex steroid (estradiol in females) levels was defined as the LH-dominant response to the LH-RH test.

Premature Thelarche: It was defined as the development of the breast with pubic hair and axillary hair without acceleration in bone age or growth, and FSH dominant response in the LH-RH test.

Statistical Evaluation

The SPSS 25.0 program was used for statistical analyses. A descriptive analysis was made for the parameters in the study. The categorical variables were shown as frequency and percentage, and the continuous variables were expressed as mean ± standard deviation. Whether the data showed normal distribution or not was evaluated with the Kolmogorov-Smirnov Test. The T-Test was used for the group comparisons of the normally distributed continuous variables, the Mann-Whitney Test was used for group comparisons of the non-normally distributed variables, and the Pearson Correlation Test was used to calculate the correlation coefficients. Statistical significance level was taken as $p < 0.05$.

Results

The characteristics of the cases are presented in Table 1. PT was detected in 76.6% (n=46) and SPP in 23.4% (n=14) of the Study Group. In the pituitary MRI examination of the 14 cases that had early puberty, a Pineal cyst was detected in 1 patient, 1 had Rathke-cleft cyst, and microadenoma was detected in 1 patient. Two of the 23 patients who underwent the LH-RH test were diagnosed as SPP.

Elevated BMI (P=0.034), bone age (p<0.001), height SDS (p=0.050), basal LH (P<0.001), basal FSH(P<0.001),

and basal estradiol (P<0.001) levels were found in the study. No differences were detected between the two groups in terms of age and weight.

When compared to the pre-pandemic period, significant increases were detected in the use of technological tools (smartphones, computers, televisions) in both groups. In cases with premature Thelarche, it was 2.54 ±0.65 hours/day before the pandemic and 6.22±1.25 hours/day during the pandemic (p<0.000). In cases with SPP, it was 2.7 ± 0.46 hours/day before the pandemic and 7.36±1.36 hours/day during the pandemic (p<0.000). The main reason for using technological tools was school lessons (4.6 ± 1.2 hours/day in cases with PT, 5±1.2 hours/day in cases with SPP, p=0.393).

A positive correlation was detected between the use of electronic devices, bone age, and body weight in the study group (Table 2).

Table 1: General characteristics of the study group

		Puberty	p
Age	6.52±0.83		0.246
Weight (kg)			0.499
Weight SDS	1.54±1.15	1.57±0.85	0.531
Height (cm)	127±8.5	131±11	0.202
Height SDS	1.21±1.1	1.44±1.64	0.050
Body Mass Index (kg/m^2)	18.72±3.4	19.4±1.02	0.034
BMI-SDS	1.1±1.07	1.4±0.4	0.080
Bone age (years)	8.02±1.24	9.7±1.4	<0.001
LH. IU/L	0.07± 0.05	1.5±1.4	<0.001
FSH. IU/L	1.4±0.88	4.4±2.2	<0.001
Estradiol (pmol/L)	11.45±7.2	22.6±17.9	<0.001
Post-pandemic exposure to technological devices (hours)	6.22±1.25	7.36±1.36	<0.001
Pre-pandemic exposure to technological devices (hours)	2.54 ±0.65	2.72±0.46	0.286

SDS: Standard Deviation Score, FSH: Follicle -Stimulating Hormone, LH: Luteinizing Hormone

Table 2: The correlation between electronic device use, body weight, and bone age

	p	r
Body weight	0.053	0.254
Bone age	0.001	0.495

Discussion

Puberty is a process representing the neuroendocrine changes occurring in the transition from childhood to adulthood and the accompanying changes in somatic and sexual functions. Although the onset of puberty is already well known, the timing of puberty varies. Genetic and environmental factors also play roles in its timing (14).

True puberty occurs with the activation of the HPG axis. Early activation of the axis is called SPP (15). All of our cases that were diagnosed with precocious puberty were SPP.

Advanced bone age and acceleration in growth are observed in the development of early puberty (16). In the present study, bone age, BMI, and height SDS were found to be higher in patients with SPP, similar to the literature data (16, 17).

The COVID-19 outbreak was classified by the World Health Organization as an "international public health emergency" on January 30, 2020, and was then declared a "global epidemic (i.e. pandemic)" on March 11, 2020. After the increasing number of cases in the entire world, the first COVID-19 case was detected in Turkey on March 11, 2020 (8). Social isolation and quarantine measures increased gradually with the understanding that the Coronavirus is infectious (5). The COVID-19 pandemic will inevitably have socioeconomic and psychological effects.

Recent studies examining various effects of the pandemic have gained momentum. It was found that 30.9% of adults and children were at high risk for Post-Traumatic Stress Disorders during the pandemic process (17). Again, a survey study that examined the prevalence of behavioral problems in school-age children during quarantine in the pandemic showed that children had positive social behaviors (10.3%), distress (8.2%), behavioral problems (7.0%), peer problems (6.6%), Attention Deficit - Hyperactivity Disorder (6.3%), and emotional problems (18). It is already known that children spend more time with digital media and technological tools than previous generations today. The fact that children have to spend most of their time at home causes them to spend more time with digital tools. The rates of using the internet, technology, and playing digital games increased in individuals who stayed at home for a long time because of social isolation and quarantine measures. In a recent study, the duration of students playing digital games was examined, and it was found that this time increased at significant levels during the pandemic when compared to the pre-pandemic period, and students played digital games on the phone the most (8).

In the present study, significant increases were detected in the use of technological tools (smartphone, computer, television) when compared to the pre-pandemic period. It was also remarkable that the mean age of our cases that had SPP was low and the cases were idiopathic. Stress, metabolic rate, bone maturation, and environmental factors play major roles in pubertal development as well as ethnic and genetic factors. Weight gain in the pandemic period

and increased exposure to digital tools may pose a risk factor for precocious puberty and premature Thelarche. A positive correlation was found in the study between the use of electronic devices and bone age and body weight.

As a conclusion, it was found in the present study that children spent more time with digital tools during the pandemic period when compared to the pre-pandemic period, and puberty symptoms started at a younger age. We think that long periods of inactivity in front of the screen may cause weight gain and early puberty. Opportunities must be initiated for children to spend sufficient time in the open air and meet their physical movement needs. Families, children, and teachers must be made aware of this issue. Attention must be drawn to activities that can keep children away from the screen, and they must not be allowed to be alone with the screen for a long time.

The present study is one of the rare studies that examine the relations between the COVID-19 pandemic process and SPP and PT in Turkish children. For this reason, studies that will address this issue with more cases and additional findings are still needed.

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