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Pediatric Hyperprolactinemia: Clinical Features, Diagnostic Groups, and Treatment Approaches

Author(s)

Emel Hatun Aytaç Kaplan[1], Zümrüt Kocabey Sütçü[1], Hasan Önal[2]

Affiliation(s)

[1]University of Health Sciences Türkiye, Başakşehir Çam and Sakura City Hospital, Clinic of Pediatric Endocrinology, İstanbul, Türkiye

[2]University of Health Sciences Türkiye, Başakşehir Çam and Sakura City Hospital, Clinic of Pediatric Metabolism, İstanbul, Türkiye

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Abstract

Hyperprolactinemia (HPRL) is a rare endocrinopathy in childhood caused by tumors, pituitary stalk interruption, and systemic diseases. In this retrospective study, we examined the clinical characteristics of pediatric patients with prolactin (PRL) elevation. The study examined 70 pediatric and adolescent patients with elevated PRL. The patients (52 female, 18 male; age range, 0.03-18) were divided into two groups: Physiological (n=46, 65.7%) and pathological (iatrogenic+sellar mass) (n=24, 34.3%) HPRL. Six patients (8.6%) were included in the pathological group due to iatrogenic causes and 18 patients (25.7%) due to a sellar mass. Subdiagnostic groups were found in the pathological group: 14 patients with prolactinoma (10 microadenomas; 4 macroadenomas), 6 patients with drug-induced HPRL, 2 patients with craniopharyngioma, 1 patient with dysgerminoma, and 1 patient with tuberculoma. Symptoms such as headache (p=0.004), galactorrhea (p=0.000), amenorrhea (p=0.037), and menstrual irregularity (p=0.037) were more common in the pathological group. Short stature and early thelarche complaints were more common in the physiological group (p=0.004, p=0.045, respectively). The presence of galactorrhea was significant in predicting pathological PRL elevation (p=0.002) (odds ratio=56.1%, 95% confidence interval=4.33-728.1). Twenty-seven point one percent (n=19) received cabergoline treatment, and 8.5% (n=6) received levothyroxine treatment. Three patients underwent surgical treatment for dysgerminoma and craniopharyngioma, respectively. The probability of detecting HPRL is high in the presence of galactorrhea. In prolactinoma, if there are significant pituitary compression symptoms, the disease can be controlled with medical treatment.

Keywords: Childhood, galactorrhea, hyperprolactinemia, prolactinoma

Introduction

Prolactin (PRL) is a hormone primarily secreted by lactotroph cells in the anterior pituitary, playing a crucial role in reproductive function. Factors such as disruption of dopamine inhibition due to pituitary stalk interruption, stress, estrogen, and oxytocin stimulate PRL release[1]. Hyperprolactinemia (HPRL) is a rare endocrinopathy in childhood, which can be physiological, pathological, or iatrogenic, with a prevalence ranging from 0.4% to 5%[2]. Physiologically, PRL levels may rise during stress, REM sleep, pregnancy, or a high-protein diet. Pathological

Correspondence: Emel Hatun Aytaç Kaplan, University of Health Sciences Türkiye, Başakşehir Çam and Sakura City Hospital, Clinic of Pediatric Endocrinology, İstanbul, Türkiye
E-mail: emel_ctf@hotmail.com **ORCID:** 0000-0002-8385-4049

causes include tumors, pituitary stalk interruption, and systemic diseases, with chronic kidney failure, hypothyroidism, and polycystic ovary syndrome being significant systemic conditions. Iatrogenic elevation of PRL levels can occur due to the use of antihypertensive drugs, oral contraceptives, antiepileptic drugs, and antipsychotic medications[3].

Childhood HPRL is most commonly attributed to medications and adenomas[3,4]. Prolactinomas are the most frequent type of pituitary adenoma[5].

The clinical presentation of HPRL varies depending on the etiology, ranging from asymptomatic cases to complaints such as delayed puberty, amenorrhea, menstrual irregularities, galactorrhea, headaches, and vision problems[6]. HPRL can also occur in children with short stature and obesity[7]. PRL is known to play a role in breast development in girls and gynecomastia in boys[8,9].

Highlights

- The etiology of hyperprolactinemia is known.
- Medical therapy is the first choice of treatment for prolactin-secreting pituitary adenomas, including macroadenomas.
- Physiological prolactin elevation is a common condition in childhood.
- We believe that our study will guide clinicians in the diagnosis and treatment of hyperprolactinemia.
- Measuring prolactin levels is important in the etiology of short stature in childhood.
- Galactorrhea is almost always a sign of pathological hyperprolactinemia.

Since PRL is released in a pulsatile manner, a single measurement may not be reliable. PRL levels above 100 ng/mL do not require confirmation, but levels between 20-100 ng/mL necessitate at least two measurements. Values exceeding 500 ng/mL are indicative of macroprolactinomas[10]. In patients with HPRL, pituitary magnetic resonance imaging (MRI) and visual field examination are crucial for diagnosis and follow-up[11]. Treatment involves etiology-specific interventions and the use of dopamine agonist drugs such as cabergoline and bromocriptine. Cabergoline is better tolerated and more effective in pediatric cases[12,13]. Surgical treatment is necessary for patients who do not respond to medical treatment and experience vision problems. Caution is required postoperatively due to the risk of pituitary insufficiency. In this retrospective study, we examined the clinical, etiological, and treatment characteristics of pediatric patients with elevated PRL levels.

Material and Method

This study is a single-center retrospective analysis conducted with the approval of the local ethics committee (protocol code: 2023-240, date 07/06/2023). Seventy children and adolescents who presented to the pediatric endocrinology clinic between 2021 and 2023 with elevated PRL levels were screened. Age, sex, presenting symptoms, comorbidities, medications used, and physical examination findings were recorded. Pubertal signs were classified according to Tanner's staging[14,15]. Patients were categorized into two groups: Physiological and pathological (iatrogenic+sellar mass) HPRL. Patients whose PRL levels spontaneously returned to normal were considered physiologically elevated PRL (within 1 week-3 months period). PRL, adrenocorticotropic hormone, cortisol, thyroid-stimulating hormone (TSH), and free thyroxine levels were analyzed in venous blood taken in the morning after overnight fasting. PRL levels between 4.79 and 23.3 ng/mL were considered normal. Patients with at least two measurements showing elevated levels, taken at least one week apart, were regarded as having HPRL. The measurement was repeated to exclude elevation due to stress, infection, and other similar factors. PRL measurement intervals of patients under treatment after diagnosis varied among patients.

Those not considered physiological underwent pituitary MRI. Some of the physiological group also underwent MRI before the diagnosis was clear. MRI was performed on patients with at least two PRL measurements over 45 ng/mL. MRI was not performed during temporary mild elevations. The study states that patients diagnosed with adenomas with a diameter of 1 cm or less were defined as having microadenomas, while those larger than 1 cm were defined as macroadenomas. Patients diagnosed with prolactinoma underwent visual field examination. Dopamine agonist treatment was applied to all patients diagnosed with macroadenomas and symptomatic microadenomas (galactorrhea, amenorrhea). The dose and duration of treatment for those who received treatment were recorded. PRL levels were checked after treatment (at least two weeks later). Patients requiring brain surgery underwent a control pituitary MRI and regression was assessed. An echocardiogram was taken during the follow-up of patients, who had been using cabergoline for a long period.

Statistical Analysis

The study data were analyzed using Statistical Package for the Social Sciences 24.0 (SPSS Inc., Chicago, Illinois). Descriptive statistics were presented as mean ± standard deviation (SD) and frequency (%). The Kolmogorov-Smirnov test assessed the normal distribution of continuous variables between groups. Parameters that fit the normal distribution were compared using Student's t-test, and those that did not follow a normal distribution were compared using the Mann-Whitney U test. Categorical variables were compared between groups using the chi-square test. A p-value <0.05 was considered statistically significant. Logistic regression analysis was used to determine predictive factors for pathological findings.

Results

A total of 70 patients with a mean age of 11.35±4.73 years (range=0.03-18 years) were evaluated in our study, including 52 females (74.3%) and 18 males (25.7%). The patients' anthropometric measurements are presented in

the table (**Table 1**). Patients were divided into two groups: Physiological (n=46, 65.7%) and pathological (n=24, 34.3%) (iatrogenic+sellar mass). Six patients (8.6%) were included in the iatrogenic group (drug-related, four patients on risperidone, one on sertraline and fluoxetine, and one on levodopa), and 18 patients (25.7%) were included in the pathological group due to sellar masses. Among the pathological group, subdiagnostic groups were identified: 14 patients with prolactinoma, six with drug-induced HPRL, two with craniopharyngioma, one with dysgerminoma, and one with tuberculoma. In the physiological group, six patients had transient HPRL due to TSH elevation, and one patient had elevated PRL due to mini puberty. Normalization of PRL levels was observed with hypothyroidism treatment. In cases of elevated PRL levels without an identified etiology, levels often returned to normal upon repeated measurements. The mean age was lower in the physiological group. Height, body weight, and body mass index (BMI) SD score were significantly higher in the pathological group (**Table 1**).

The presenting complaints are shown in **Table 2**. Headaches, galactorrhea, amenorrhea, and menstrual irregularities were more frequent in the pathological group, with p-values of p=0.004 for headaches, p<0.001 for galactorrhea, and p=0.037 for amenorrhea and menstrual irregularities. Short stature and early telarche complaints were more frequent in the physiological group (p=0.004, p=0.045). Among the additional diseases, 14 patients (20%) had hypothyroidism, five (7.1%) had adrenal insufficiency, five (7.1%) had growth hormone deficiency, and four (5.7%) had hypogonadism.

Patients were at the following pubertal stages: 35.1% at stage 1, 15.7% at stage 2, 4.3% at stage 3, 2.9% at stage 4, and 41.4% at stage 5. The physiological group was more often at stage 1 (41.3%), but this was not statistically significant (p=0.17). The pathological group was more frequently at stage 5 (62.5%), significantly higher than the other group (p=0.01). Three patients (4.3%) had visual field problems and were diagnosed with craniopharyngioma and dysgerminoma. PRL levels were significantly higher in the pathological group (**Table 1**). PRL levels in the drug-induced group were 77.9±51.01 ng/mL (minimum=42, maximum=188). Laboratory findings of patients with primary hypothyroidism are presented in **Table 3**.

Among the 36 patients evaluated with contrast-enhanced pituitary MRI, ten patients (14.3%) had microadenomas, four (5.7%) had macroadenomas, two (2.9%) had craniopharyngioma, one (1.4%) had dysgerminoma, one (1.4%) had tuberculoma, one (1.4%) had hydrocephalus, one (1.4%) had an arachnoid cyst, and one (1.4%) had pituitary hypoplasia. Fifteen patients (21.4%) had a normal MRI.

In the etiological investigation, 38 patients (54.2%) had no underlying pathology; 14 patients (20%) had prolactinoma (10 microadenomas and four macroadenomas); six (8.5%) had drug-induced HPRL (four risperidone, one levodopa, and one fluoxetine); six (8.5%) had HPRL secondary to TSH elevation due to primary hypothyroidism; two (2.8%) had craniopharyngioma; one (1.4%) had dysgerminoma; one (1.4%) had tuberculoma; one (1.4%) had hydrocephalus; and one (1.4%) had HPRL due to mini puberty. Fifty percent of macroadenoma cases and all microadenoma cases were female. The mean age of patients with microadenomas was 14.29±4.34 years (range=3.3-17.5), and for those with macroadenomas, it was 14.42±2.59 years (range=11.2-17.4).

Table 1.
Relationship between patients' anthropometric measurements and PRL levels

	Physiological; 35/52 girl, 11/18 boy		Pathological (iatrogenic+sellar mass); 17/52 girl, 7/18 boy		95% CI lower	p-value
	Mean ± SD	Minimum-maximum	Mean ± SD	Minimum-maximum		
Age	10.3±4.9	0.03-18	13.3±3.7	3.3-17.5	0.89-5.08	0.006
Weight SDS	-0.4±1.8	-4.1-3.3	0.4±1.8	-2.80-4.2	-0.15-1.85	0.054
Height SDS	-1.05±1.8	-6.3-4.0	-0.6±1.6	-5.4-1.56	-0.48-1.21	0.398
BMI SDS	0.07±1.4	-2.6-2.9	0.9±1.4	-2.07-3.5	0.12-1.57	0.023
Prolactin levels (ng/mL)	46.2±23.4	24-154	163.3±270.2	27.2-1.356	2.79-231-402	0.045

SD; Standard deviation, CI; Confidence interval, SDS; Standard deviation score, BMI; Body mass index

Table 2.
Patients' complaints

Complaint (n,%)	Physiological group (percentage %)	Pathological group (percentage %)	p-value
Short stature (25, 35.7%)	45.7%	16.7%	0.004
Galactorrhea (10, 14.3%)	2.2%	37.5%	<0.001
Menstrual irregularities (9, 12.9%)	6.5%	25%	0.037
Early breast development (7.10%)	15.2%	0	0.045
Increased body hair (6, 8.6%)	10.9%	4.2%	
Headaches (5, 7.1%)	0	20.8%	0.004
Vision problems (4, 5.7%)	2.2%	12.5%	
Amenorrhea (3, 4.3%)	0	12.5%	0.037

Sixty-four point three percent (n=45) of patients did not require treatment. Twenty-seven point one percent (n=19) received cabergoline treatment, and 8.5% (n=6) received levothyroxine treatment. Surgical treatment was applied to three patients with dysgerminoma and craniopharyngioma cabergoline treatment was discontinued for nine patients as it was no longer needed. The average duration of cabergoline treatment was 8.57±8.76 months (range=1-24). The treatment period for microadenomas was 7±7.9 months and for macroadenomas it was 13.5±9.6 months. The cabergoline dose was adjusted between 0.5 mg/week and 2 mg/week. No drug side effects were observed. Nine patients were still on cabergoline when the study was completed. The adenomas of the patients still on treatment had not completely regressed and their PRL levels were increasing without medication. Three patients with iatrogenic elevated PRL were treated with cabergoline, because they were symptomatic. The treatment duration was 2-3 months. Treatment durations were short for patients whose PRL levels improved quickly, whose adenomas regressed, or whose iatrogenic causes were eliminated. The duration of treatment was longer in patients with macroadenoma. The adenoma sizes on MRIs, control MRI durations, and adenoma sizes after regression, are shown in **Table 4** for the ten patients diagnosed with adenoma. An echocardiogram was taken during the follow-up of patients using cabergoline for for more than 6 months. Tricuspid regurgitation or aortic valve calcification was not observed in the patients. In regression analysis, galactorrhea complaints significantly predicted pathological HPRL (p=0.002) (odds ratio=56.1, 95% confidence interval=4.33-728.1). Logistic regression analysis was performed on variables that were found to be significant with the chi-square test (headache, galactorrhea, amenorrhea, menstrual irregularity, short stature, and premature telarche). Galactorrhea was found to be significant. The large range of odds ratio was attributed to the small proportions. Short stature, delayed puberty, amenorrhea, and menstrual irregularities were not significant in predicting pathology.

Discussion

HPRL is rare in childhood, and physiological elevations are sometimes encountered[2]. HPRL is caused by excessive secretion from pituitary lactotroph cells or by the removal of dopamine inhibition on PRL (such as pituitary stalk incision, stress, oxytocin, and oestrogen effects). Drug-induced HPRL can also be seen in a considerable number of cases in childhood[3,4]. Pathological HPRL is often due to pituitary adenomas[3]. In a study by Kontbay et al.[16], 40.7% of 27 children with HPRL were found to have prolactinoma (6 macroadenomas and 5 microadenomas). In our study,

Table 3.
Thyroid hormone and prolactin levels in primary hypothyroid patients

	TSH (uIU/mL)	ft4 (ng/dL)	PRL before treatment (ng/mL)	PRL after treatment (ng/mL)
n	6	6	6	6
Mean	235.5	0.63	46.25	22.6
Median	185	0.65	35	22.5
Standard deviation	258.26	0.39	20.5	3.85
Minimum	7	0.05	30	17
Maximum	772	1.20	85	29

TSH; Thyroid-stimulating hormone, ft4; Free thyroxine, PRL; Prolactin

Table 4.
Pituitary adenoma sizes

Adenoma size (mm)	Prolactin levels (ng/mL) (before-after treatment)	MRI check-up time (month)	Adenoma size (mm) after treatment
38	204-28	3-6-12-24	30-21-12-6
30	unfollowed	unfollowed	
16	365-10	3-8	0
10	351-4.9	3	3
9	34-25 (amenorrhea)	3	7.9
9	75-11 (galactorrhea)	7	0
6.6	91-12 (galactorrhea)	4	0
6	155-3	4	1
5.6	180-25	11	1
4.5	156-19 (amenorrhea)	3	0
4	95-37 (amenorrhea)	8	1
3.5	68-7 (short stature)	4	0
2	42-0.4 (galactorrhea)	3	0
1	95-37 (amenorrhea)	3	0

MRI; Magnetic resonance imaging

34.3% of the cases had pathological HPRL, and there was a 25.7% prevalence of sellar masses.

The prevalence of macroadenomas is higher in affected males[17]. In a study by Eren et al.[18], 93.4% of microadenoma cases were female patients, and 77.7% of macroadenoma cases were female patients. In our study, the prevalence of macroadenomas was equal in both females and males, while microadenomas were more frequent in females, consistent with the literature.

The presenting complaints of HPRL vary according to etiology. Delayed puberty, amenorrhea, menstrual irregularities, galactorrhea, headaches, and visual problems are common reasons for consultation, though these conditions can sometimes be asymptomatic at first[6]. In a study by Breil et al.[13], the most common symptoms in 12 children with prolactinomas, who account for 21 HPRL cases, were headaches and delayed puberty, emphasizing the need to investigate HPRL in the presence of these symptoms. In a study of 39 patients, aged 9-20, with prolactinomas (30 macroadenomas, 9 microadenomas), 23 cases (all females) had galactorrhea[19]. In another study, 89% of those diagnosed with prolactinoma were symptomatic, with the most common symptom being headaches (54.5%)[16]. In our study, symptoms such as headaches, galactorrhea, amenorrhea, and menstrual irregularities were significantly more prevalent in pathological HPRL. Although the headache rate in the pathological group was lower than in previous studies, headaches were still more common in the pathological group than in the physiological group. In pediatric patients, symptoms such as short stature, amenorrhea, menstrual irregularity, early thelarche, narrowing of the visual field, and headache require measurement of routine PRL levels. Galactorrhea was particularly predictive of pathological PRL elevation. The presence of galactorrhea is an important finding that requires investigation for elevated PRL levels, as emphasized in the Pituitary Society International Consensus Statement[20].

Elevation of TSH can lead to HPRL due to subunit similarity. A study by Arslan et al.[21] compared non-prolactinoma HPRL, prolactinoma, and a healthy control group, showing that hyperprolactinemic patients had increased thyroid volume, thyroid nodules, and thyroid autoimmunity. The prevalence of HPRL in subclinical hypothyroidism in children is unknown. In a study evaluating hormonal data from 602 pediatric patients, overt primary hypothyroidism was more predictive of HPRL, and subclinical hypothyroidism predicted HPRL more frequently than in euthyroid patients[22]. In our study, HPRL due to TSH elevation was detected in 6 patients, and PRL levels returned to normal with levothyroxine treatment. Due to the small sample size, no statistical conclusions could be drawn regarding thyroid volume and autoimmunity.

Drug use is a significant cause of HPRL, especially since many antipsychotic drugs affect the dopaminergic system and increase PRL levels[23]. In a multicenter study, drug-induced HPRL was observed in 6% of cases[16]. In our study, drug-induced HPRL was found in 8.6% of cases. A meta-analysis of 32 studies involving 4,643 pediatric participants examined the effects of antipsychotics on PRL levels, reporting that risperidone, paliperidone, and olanzapine significantly increased PRL levels, while aripiprazole, decreased them[24]. In our study, four patients were using risperidone, one was using levodopa, and one was using sertraline and fluoxetine. Three of our patients were treated with short-term cabergoline because they were symptomatic as psychiatric medication could not be stopped. However, we did not have enough data for statistical analysis.

Disruption of normal dopaminergic inhibition of PRL occurs in pituitary stalk lesions, leading to HPRL. In a study of 55 pituitary stalk incisions, the frequency of HPRL was 36.4%[25]. In our study, three patients with sellar masses had HPRL. PRL levels above 100 ng/mL do not require further investigation, but values between 20-100 ng/mL warrant at least two measurements. Values above 500 ng/mL are diagnostic of macroadenomas[10]. In a study, the average PRL level in the prolactinoma group was 118 (range=34-4.340) ng/mL, while in the non-prolactinoma group, it was 38.7 (range=22.9-200) ng/mL[16]. In our study, PRL levels were significantly higher in the pathological group, consistent with the literature.

Children with short stature and obesity are at risk and should be investigated for HPRL[7]. In our study, short stature was more common in the physiological group, whereas BMI increased in the pathological group. In a study by Eren et al.[18], 22.6% of cases reported weight gain, and 30.9% were overweight or obese. In our clinic, PRL levels are routinely checked for short stature; this may explain the higher incidence observed in our study.

Repeated measurements are necessary when PRL levels are less than five times the upper limit of normal, as physiological increases occur in stress-related situations[20]. Temporary increases were also observed in our study. Unnecessary further examinations were avoided by repeating measurements. Dopamine agonist drugs, such as cabergoline and bromocriptine, are used to treat prolactinomas. Cabergoline is better tolerated and more effective in childhood compared to other similar medications[12,13]. In a study of 39 patients aged 9-20 with prolactinomas (30 macroadenomas, 9 microadenomas), only two patients underwent surgery and radiotherapy, while all others received medical treatment. The average follow-up period was 56 months, and medical treatment is concluded to be reliable and preserves pituitary functions[19]. In a study by Breil et al.[13], cabergoline reduced tumor sizes by 80% in 12 pediatric patients with prolactinomas over a treatment period of 12-89 months. Additionally, the study included 21 patients with HPRL.

Preserving vision is essential for patients with treatment-resistant vision problems, and surgical treatment is often performed using the transsphenoidal method in these cases[7]. Rarely, radiotherapy is recommended[13]. In a study of 11 pediatric patients with prolactinomas, surgical treatment was performed on three patients with vision problems[16]. In our study, none of the patients with prolactinomas required surgical treatment. Even patients with macroadenomas responded to medical treatment. Surgery was performed on only three patients diagnosed with dysgerminoma and craniopharyngioma.

Medical treatment reduced tumor size, with an average treatment duration of 8.57 months. The short duration was due to the presence of microadenomas in most of our cases. However, since the longest follow-up period was 24 months, our average duration of treatment appears short, and we still have patients undergoing treatment.

Study Limitations

This study has several limitations, including its retrospective design, potential selection bias, and the relatively small sample size. While the findings may be generalizable to certain populations, larger and more extensive prospective studies are needed to validate the results. Additionally, the study did not assess long-term outcomes or potential complications associated with different treatment modalities. The maximum duration of treatment is 24 months, and long-term studies are needed. Future research should address these limitations and provide more comprehensive insights into the management and outcomes of HPRL in children and adolescents.

Conclusion

Our study aimed to highlight both the physiological and pathological causes of HPRL by presenting cases with elevated PRL levels. Although most of our patients with short stature were in the physiological group, a significant proportion were also in the pathological group. Measurement of PRL levels should be among the first investigations in cases of short stature. The likelihood of detecting HPRL is high in the presence of galactorrhea, as it is almost always considered a pathological finding. In cases of prolactinoma, where there are no visual field defects or significant signs of pituitary compression, the disease can typically be effectively controlled with medical treatment.

Ethics

Ethical Approval: This study is a single-center retrospective analysis conducted with the approval of the local ethics committee (protocol code: 2023-240, date 07/06/2023).

Informed Consent: Because the study was designed retrospectively no written informed consent form was obtained from the patients.

Footnotes

Author Contributions: Aytaç Kaplan EH, Kocabey Sütçü Z, Önal H: Surgical and Medical Practices; Aytaç Kaplan EH: Consept; Aytaç Kaplan EH: Design; Aytaç Kaplan EH, Kocabey Sütçü Z, Önal H: Data Collection or Processing; Aytaç Kaplan EH, Önal H: Analysis or Interpretation; Aytaç Kaplan EH, Kocabey Sütçü Z: Literature Search; Aytaç Kaplan EH, Önal H: Writing.

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References

1. Saranac L, Zivanovic S, Radovanovic Z, et al. Hyperprolactinemia: different clinical expression in childhood. *Horm Res Paediatr.* 2010;73:187-192. *[CrossRef]*
2. Mancini T, Casanueva FF, Giustina A. Hyperprolactinemia and prolactinomas. *Endocrinol Metab Clin North Am.* 2008;37:67-99. *[CrossRef]*
3. Catli G, Abaci A, Altincik A, et al. Hyperprolactinemia in children: clinical features and long-term results. *J Pediatr Endocrinol Metab.* 2012;25:1123-1128. *[CrossRef]*
4. Saito E, Correll CU, Gallelli K, et al. A prospective study of hyperprolactinemia in children and adolescents treated with atypical antipsychotic agents. *J Child Adolesc Psychopharmacol.* 2004;14:350-358. *[CrossRef]*
5. Palubska S, Adamiak-Godlewska A, Winkler I, et al. Hyperprolactinaemia - a problem in patients from the reproductive period to the menopause. *Prz Menopauzalny.* 2017;16:1-7. *[CrossRef]*
6. Fideleff HL, Boquete HR, Suárez MG, Azaretzky M. Prolactinoma in children and adolescents. *Horm Res.* 2009;72:197-205. *[CrossRef]*
7. Eren E, Yapıcı Ş, Çakır ED, et al. Clinical course of hyperprolactinemia in children and adolescents: a review of 21 cases. *J Clin Res Pediatr Endocrinol.* 2011;3:65-69. *[CrossRef]*
8. Frantz AG. The breasts. In : Textbook of Endocrinology 1981, edited by R.H. Williams, W.B. Saunders, Philadelphia, pp. 400-411. *[CrossRef]*
9. Kaplan SL, Grumbach MM, Friesen HG, Costom BH. Thyrotropin releasing factor (TRF) effect on secretion of human pituitary prolactin and thyrotropin in children and in idiopathic hypopituitary dwarfism: further evidence for hypophysiotropic hormone deficiencies. *J Clin Endocrinol Metab.* 1972;35:825-830. *[CrossRef]*
10. Karavitaki N, Thanabalasingham G, Shore HC, et al. Do the limits of serum prolactin in disconnection hyperprolactinaemia need re-definition? A study of 226 patients with histologically verified non-functioning pituitary macroadenoma. *Clin Endocrinol (Oxf).* 2006;65:524-529. *[CrossRef]*
11. Özçetin M, Karacı M, Toroslu E, Edebali N. A pediatric case of pituitary macroadenoma presenting with pituitary apoplexy and cranial nerve involvement: case report. *Turk Pediatri Ars.* 2016;51:162-165. *[CrossRef]*
12. Webster J, Piscitelli G, Polli A, Ferrari CI, Ismail I, Scanlon MF. A comparison of cabergoline and bromocriptine in the treatment of hyperprolactinemic amenorrhea. Cabergoline Comparative Study Group. *N Engl J Med.* 1994;331:904-909. *[CrossRef]*
13. Breil T, Lorz C, Choukair D, et al. Clinical features and re-sponse to treatment of prolactinomas in children and ado-lescents: a retrospective single-centre analysis and review of the literature. *Horm Res Paediatr.* 2018;89:157-165. *[CrossRef]*
14. Marshall WAT, Tanner JM. Variations in the pattern of pubertal changes in boys. *Arch Dis Child.* 1970;45:13-23. *[CrossRef]*
15. Marshall WAT, Tanner JM. Variations in pattern of pubertal changes in girls. *Arch Dis Child.* 1969;44:291-303. *[CrossRef]*
16. Kontbay T, Şıklar Z, Özsu E, et al. Hyperprolactinemia in children and adolescents and longterm follow-up results of prolactinoma cases: a single-centre experience. *Turk J Pediatr.* 2022;64:892-899. *[CrossRef]*
17. Hoffmann A, Adelmann S, Lohle K, Claviez A, Müller HL. Pediatric prolactinoma: initial presentation, treatment, and long-term prognosis. *Eur J Pediatr.* 2018;177:125-132. *[CrossRef]*
18. Eren E, Törel Ergür A, İşgüven ŞP, et al. Clinical and laboratory characteristics of hyperprolactinemia in children and adolescents: national survey. *J Clin Resp Pediatr Endocrinol.* 2019;11:149-156. *[CrossRef]*
19. Acharya SV, Gopal RA, Bandgar TR, et al. Clinical profile and long term follow up of children and adolescents with prolactinomas. *Pituitary.* 2009;12:186-189. *[CrossRef]*
20. Petersenn S, Fleseriu M, Casanueva FF, et al. Diagnosis and management of prolactin-secreting pituitary adenomas: a Pituitary Society International Consensus Statement. *Nat Rev Endocrinol.* 2023;19:722-740. *[CrossRef]*

21. Arslan MS, Sahin M, Topaloğlu O, et al. Hyperprolactinaemia associated with increased thyroid volume and autoimmune thyroiditis in patients with prolactinoma. *Clin Endocrinol (Oxf).* 2013;79:882-886. *[CrossRef]*

22. Sharma N, Dutta D, Sharma LK. Hyperprolactinemia in children with subclinical hypothyroidism. *J Clin Resp Pediatr Endocrinol.* 2017;9:350-354. *[CrossRef]*

23. Ajmal A, Joffe H, Nachtigall LB. Psychotropic-induced hyperprolactinemia: a clinical review. *Psychosomatics.* 2014;55:29-36. *[CrossRef]*

24. Kroigaard SM, Clemmmensen L, Tarp S, Pagsberg AK. A meta-analysis of antipsychotic-induced hypo- and hyperprolactinemia in children and adolescents. *J Child Adolesc Psychopharmacol.* 2022;32:374-389. *[CrossRef]*

25. Guo Q, Yang Y, Mu Y, et al. Pituitary stalk interruption syndrome in Chinese people: clinical characteristic analysis of 55 cases. *PLoS One.* 2013;8:e53579. *[CrossRef]*