Journal Homepage: -www.journalijar.com

INTERNATIONAL JOURNAL OF ADVANCED RESEARCH (IJAR)

Article DOI:10.21474/IJAR01/18683
DOI URL: http://dx.doi.org/10.21474/IJAR01/18683

RESEARCH ARTICLE

PRECOCIOUS PUBERTY: EPIDEMIOLOGY, CLINICAL PRESENTATION, DIAGNOSIS, AND ETIOLOGIES

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Manuscript Info

Manuscript History
Received: 05 March 2024
Final Accepted: 09 April 2024
Published: May 2024

Key words:-
Precocious Puberty, Hypothalamic-Pituitary Axis, Gonad, Adrenal Gland

Abstract

Precocious puberty, defined as the onset of sexual characteristics before the age of 8 in girls and 9 in boys, can arise from various causes, including central and peripheral mechanisms. While central precocious puberty (CPP) originates from premature activation of the hypothalamic-pituitary axis, peripheral precocious puberty (PPP) results from gonadal or adrenal hormone secretion independent of hypothalamic control. We conducted a retrospective study spanning eight years, from 2015 to 2023, at the Mohamed 6 University Hospital in Marrakech, Morocco, to investigate the epidemiological, clinical findings, laboratory, and etiological aspects of precociuos puberty in 12 children. We found a predominance of CPP, particularly in girls, with breast development being the most common clinical sign. In boys, early puberty typically presented with pubic hair development and increased penile size. Diagnostic evaluation included hormonal assays and imaging studies, with elevated levels of gonadal hormones confirming the diagnosis. CPP was predominantly idiopathic in girls, while traumatic brain injury and CNS lesions were common causes in boys. Adrenal disorders, including congenital adrenal hyperplasia, accounted for PPP cases. Brain imaging was crucial for identifying central lesions, while adrenal imaging aided in diagnosing adrenal pathologies. Despite limitations such as retrospective design and incomplete data, our study emphasizes the importance of early recognition and appropriate diagnostic procedures for children showing signs of early puberty to optimize management and outcomes.

Introduction:-

Precocious puberty is defined as the development of sexual characteristics before the age of 8 or the occurrence of menarche before the age of 9 in girls. In boys, the appearance of secondary sexual characteristics before the age of 9 defines precocious puberty [1]. This development may correspond to a variant of normal puberty or to pathological precocious puberty [2]. The latter can be of central hypothalamic-pituitary origin (true precocious puberty or GnRH-dependent puberty) or of peripheral origin (pseudo precocious puberty or independent GnRH puberty): testicular, ovarian, or adrenal [3]. Precocious puberty is most often of central origin. In girls, central precocious puberty is idiopathic in more than 80% of cases. In boys, it is due to damage to the central nervous system (CNS) in 70% of cases [2]. Precocious puberty is a subject little studied in Africa, which justifies our retrospective review covering

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12children followed in the endocrinology department in Marrakech, Morocco, aimed at describing the epidemiological, clinical presentation, and etiological aspects of precocious puberty.

Methods:-

Context: This study is a retrospective, cross-sectional descriptive analysis. We enrolled children who were treated for precocious puberty in the endocrinology department of the Mohamed 6 University Hospital in Marrakech between January 2015 and October 2023. Data collection wasconductedretrospectively.

Participants:
The inclusion criteria comprised children who had sought medical consultation for the onset of puberty before the age of 8 for girls and before 9 years for boys. Children with advanced puberty were excluded from the study, as were those whose medical records lacked sufficient information.

Variables:
The parameters collected included age, sex, history of head trauma, brain radiotherapy, meningitis, steroid use, or pesticide contamination, as well as the presence of similar cases in the family. Diagnostic information comprised the stages of pubertal development according to the Tanner and Marshall classification, stature growth in standard deviations, and additional examinations (hormonal assays conducted by immunometric method: testosterone, estradiol, FSH, LH, SDHEA, 17 OH progesterone, left wrist x-ray, pelvic and testicular ultrasound, brain MRI, and adrenal scan).

Data Source:
The collection was sourced from comprehensive and usable medical records.

Bias:
Two individuals collected data independently to mitigate the risk of information and recording bias, and they merged their lists to create the final dataset.

The size of the study population:
We determined the sample size based on the number of patients who met the inclusion criteria and had no elements of the exclusion criteria.

Results:-

We initially collected data from 21 patients, out of which 9 were excluded due to incomplete files. Consequently, only 12 children who met our criteria were included in the study. The average age among the girls was 5.16 ± 3.25 years, and among the boys, the average age was 5.33 years ± 2. We observed a clear female predominance in 75% of cases (9 girls, 3 boys).

Regarding background information, one girl diagnosed with central precocious puberty had a history of head trauma. Additionally, one girl had a history of neonatal distress, while another girl had a history of psychomotor delay, hydrocephalus, epilepsy, and enuresis. No cases of medication taken during pregnancy were documented. We noted a similar case in the family of a boy and a family history of polycystic kidney disease in another boy.

In girls, the predominant signs indicating early puberty were primarily breast development in 33.33% (3 girls), followed by pubic hair in 22.22% (2 girls). Advanced stature was the presentingfeature in one girl. Various combinations of symptoms were observed: the combination of pubic hair with breast development in one girl, pubic hair with leucorrhea in another girl, pubic hair with tall stature in a third girl, and pubic hair with both breast development and tall stature in a fourth girl. Among the boys, the most common clinical presentation was pubic hair associated with increased penis size and testicular volume in 66.67% (2 boys). The average advancement in stature was +2.5 ± 1 SD.

There was an acceleration of bone maturation with a mean bone age of 15 ± 2 years. Additional examinations revealed the following: In the central precocious puberty group, pelvic ultrasound revealed a uterine size > 35 mm in all girls. Biochemically, the average baseline level of LH was increased to 2.33 ± 4.75 IU/L, while estradiol levels were measured in 7 girls with an average level of 36.78 pg/ml. In boys, the average testosterone level was increased

to5.28 ± 3.42 ng/ml. DHEA-S assay was conducted in 3 patients, with only one showing a high result (1584 ng/ml), in whom the adrenal scan showed congenital adrenal hypertrophy. The dosage of 17 OH-progesterones was carried out in 8 patients, with only one showing a high level of 562 ng/ml, and in whom the adrenal scan revealed a left adrenal nodule. It is noteworthy that this patient has a family history of polycystic kidney disease.

In our series, central precocious puberty, the most common etiological group (66.67%), was observed in 8 patients, including 1 boy in whom the cause was idiopathic, as well as in 3 out of 7 girls. Among the remaining 4 girls, four causes were identified: pituitary stalk cyst, pituitary microadenoma, hydrocephalus, and head trauma.

Pseudo-precocious puberty, the second most common etiological group (33.33%), was observed in 2 girls, with etiologies identified as congenital adrenal hypertrophy, as well as in one boy. In another case, it was attributed to an adrenal tumor.

Etiologies	Boys	girls
Idiopathic	**1**	**3**
Head trauma	**0**	**1**
Stem cyst	**0**	**1**
microadenoma	**0**	**1**
Hydrocephalus	**0**	**1**

Table 1:-Etiologies of central precocious puberty.

Etiologies	Boys	Girls
HCS	**1**	**2**
Adrenaltumor	**1**	

Table 2:-Etiologies of pseudo- precocious puberty.

Discussion:-

Our study revealed a significant female predominance, with central precocious puberty being the primary etiology. Among cases of central precocious puberty, the idiopathic form was predominant in girls. Conversely, in boys, pseudo-precocious puberty, often associated with an adrenal lesion, was the predominant form observed. Precocious puberty is a common reason for consultation in pediatric endocrinology. According to a Danish study conducted by Teilmann between 1993 and 2001, among 670 children, the prevalence of precocious puberty was estimated at 0.2% in girls and <0.05% in boys [4]. However, our hospital prevalence was notably low (1,125, cases per year), possibly due to the fact that patients often first consult pediatricians. In Africa, population-based studies are scarce. Nonetheless, in a cross-sectional study by Abodo et al. [5], approximately 8 cases of precocious puberty were reported, showing a similar female predominance as observed in our study, consistent with literature findings. This trend was also observed in another study conducted by Kaoutar Rifai et al. [11], where 90% of cases were girls, aligning with our findings of female predominance.

In our study, the most prevalent clinical indicators of precocious puberty were breast development in girls and pubic hair growth accompanied by penis enlargement in boys. Therefore, when faced with any suspicion of precocious puberty, clinical examination should include an assessment of pubertal signs using the Tanner and Marshall classification [6]. Establishing a growth curve is essential to identify any acceleration in stature. In our study, we observed an average stature of +2.5 ± 1 SD.

Clinical presentation, supported by supplementary examinations, confirms the diagnosis of precocious puberty by revealing pubertal-type gonadal secretions. In boys, testosterone acts as a dependable marker of testicular maturation, with a level >0.3 ng/ml indicating the onset of puberty [7]. In our series, the mean testosterone level was notably elevated at 5.28 ± 3.42 ng/ml, consistent with literature findings.

However, in girls, determining estradiol levels using radioimmunoassay does not reliably evaluate the onset of puberty due to its low specificity and fluctuations [7]. Hence, it is essential to systematically complement this with pelvic ultrasound. The onset of puberty in girls is characterized by an increase in ovarian volume >1.5 ml [7] and, particularly, by uterine development, where a length exceeding 3.7 cm demonstrates estrogen impregnation with

asensitivity of 88% and specificity of 95% [8]. In our study, all girls exhibited a uterine length >35 mm, consistent with literature data.

Etiologically, precocious puberty is predominantly of central origin, stemming from premature activation of the hypothalamic-pituitary-gonadal axis. The baseline LH level can be indicative for diagnosing central precocious puberty, where a level >0.6 IU/L (IFMA) or >0.3 IU/L (ICMA) signals the onset of puberty [8, 9]. In our series, the mean baseline LH level in girls with central precocious puberty was elevated to 2.33 IU/L, consistent with literature findings.

According to primary literature data, the proportions of organic and idiopathic forms of central precocious puberty vary by sex. Idiopathic central precocious puberty is rare in boys (20-30%) but prevalent in girls (90%) [2]. This differentiation aids in selecting neuroradiological examinations. Therefore, magnetic resonance imaging (MRI) should be the first-line investigation when an organic cause is suspected, particularly in boys. For girls under 6 years old with elevated estradiol levels or presenting neurological signs suggestive of CNS pathology, MRI is also recommended [7]. In cases of isolated precocious puberty in girls over 6 years old, brain scanning serves as a sufficient exploratory tool [7].

Our study highlights a notable characteristic: the predominance of central precocious puberty. This could potentially be attributed to a high incidence of CNS anomalies, as well as genetic or environmental factors that warrant further investigation.

In cases of peripheral precocious puberty, premature secretion of sex steroids may originate from the adrenal or gonadal glands, with congenital adrenal hyperplasia being the most common cause, consistent with our findings.

As with any study, there are limitations to consider. Firstly, our study is retrospective, which may lead to some missing data. Secondly, we did not conduct genetic studies in cases of idiopathic precocious puberty, which could be associated with genetic mutations. Lastly, the number of files collected was limited, reflecting the challenge of pediatric populations rarely presenting to endocrinologists. However, these limitations do not diminish the standard of the information provided by our study.

Conclusion:-

Our study confirms that precocious puberty can manifest as either a variant of normal puberty or as pathological precocious puberty. In cases of pathological precocious puberty, it can originate centrally or peripherally, from the adrenal or gonadal glands. Based on literature data and our study results, when central precocious puberty occurs in girls, brain imaging should be systematically requested to rule out a CNS lesion. Additionally, in children presenting with pseudo-precocious puberty, a thorough evaluation for congenital adrenal hyperplasia should be prioritized.

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