

## THE CLINICAL PROFILE AND THE ETIOLOGICAL CLASSIFICATION OF PRECOCIOUS PUBERTY AMONG CHILDREN PRESENTED TO AL KHANSA'A ENDOCRINE CENTER IN MOSUL CITY

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### ABSTRACT

**Background:** Precocious puberty is characterized by early secondary sexual characteristics appearance, which are an early sign of pubertal development. Precocious puberty has two main underlying mechanisms: The first mechanism is gonadotropin dependent (central or true) precocious puberty, which occurs when there is early activation of the hypothalamic-pituitary-gonadal (HPG) axis. and the second method involves increased synthesis of sex hormones, without the need for hypothalamic-pituitary axis activation. **Objectives:** To determine the clinical spectrum and underlying aetiologies of children presented with precocious puberty at Al Khansa'a endocrine center in Mosul. **Methods:** An observational, descriptive, cross-sectional study. All patients with precocious puberty who attend endocrine consultation unit of Al-Khansa'a Teaching Hospital between 10th of May 2019 to the end of June 2024 had been included. The Questionnaire was composed of two parts, the first included demographic information of the patients and the second the patient investigations, the third part include the final diagnosis. **Results:** The study includes 65 subjects with precocious puberty, 56 (86.2%) are females while 9 (13.8%) are males. With female to male ratio is 6.2:1. The mean age of the study population is 5.76 years, moreover; the mean age of females is 5.50 years and the mean age for males is 7.24 years. Idiopathic central precocious puberty is prevalent among 31 patients (30 females and 1 male) while neuropathic central precocious puberty is prevalent among 7 patients (6 females and 1 male). Moreover; with regards to peripheral precocious puberty; congenital adrenal hyperplasia (CAH) is prevalent among 19 patients (12 females and 7 males), Dehydroepiandrosterone increase, ovarian cyst and adrenal tumour are prevalent among 6, 1 and 1 female respectively. females are having more central causes of precocious puberty, normal height, weight, less tanner stage and more normal bone age at time of presentation versus male are showed more peripheral causes of precocious puberty, taller, thicker, more tanner stage and more advanced bone age at time of presentation. **Conclusion:** Precocious puberty affects females more than males, the commonest cause of central precocious puberty is idiopathic, while congenital adrenal hyperplasia is the commonest cause of peripheral precocious puberty. Precocious puberty is linked mostly with advanced bone age.

**KEYWORDS:** Precocious puberty, clinical presentation, etiology, Mosul city.

### 1- INTRODUCTION

Precocious puberty is characterized by early secondary sexual characteristics appearance, which are an early sign of pubertal development.<sup>[1]</sup> Precocious puberty is generally considered to occur before the ages of eight for girls and nine for boys.<sup>[2]</sup> Finding the underlying reason of precocious puberty is the primary challenge because it might be a clinical symptom of a significant underlying aetiologies such as a brain, adrenal or gonadal tumour, etc., which requires immediate assessment and

treatment.<sup>[3-5]</sup> The secondary challenge, which results in a short final height due to quick bone maturation resulted in early epiphysis closure.<sup>[6]</sup>

Precocious puberty has two main underlying mechanisms: The first mechanism is gonadotropin dependent (central or true) precocious puberty, which occurs when there is early activation of the hypothalamic-pituitary-gonadal (HPG) axis.<sup>[7-8]</sup> Early puberty appears to be gender dimorphic, with girls

having it at a rate higher than males.<sup>[9]</sup> The second method involves increased synthesis of sex hormones, without the need for hypothalamic-pituitary axis activation.<sup>[10]</sup> These sex steroids come from the adrenal glands, the gonads, external administration, or ectopic tumour formation.<sup>[11]</sup> This type of early puberty is known as "gonadotropin independent" (peripheral or pseudo) precocious puberty.<sup>[12]</sup> The causes of peripheral precocious puberty (PPP) range from congenital adrenal hyperplasia to gonadal tumours, hypothyroidism, Macune-Albright syndrome, virilizing adrenal tumours and testotoxicosis.<sup>[13-15]</sup>

Precocious puberty is a neglected condition in Iraq, and no much studies has been done to determine its cause in Iraqi people. A large number of children with pubertal problems are referred to Al Khansa'a a tertiary care hospital. Assessing the clinical profile and underlying aetiologies of premature puberty is the aim of this study.

**2- PATIENT AND METHODS**

The study is confidential and did not include any information that might be used to identify a specific individual. Ethical approval was given by Nineveh Health Directorate. It is a an observational, descriptive, case series study. All patients with precious puberty who attend endocrine consultation unit of Al-Khansa'a Teaching Hospital between 10<sup>th</sup> of May 2019 to the end of June 2024 had been included. The patients case sheets were reviewed to acquire the mandatory information. This information was used to fill the checklists that been made especially for this purpose. Age and gender of

patients is documented, anthropometric information of each patient is fixed, detailed information about each patient sexual maturity rating, bone age, hormonal assessment: FSH, LH, Estradiol, testosterone, TSH, ACTH, Cortisol, 17- Hydroxyprogesterone level. Ultrasound, MRI and the final diagnosis.

Version 26 of the SPSS (Statistical Package for Social Sciences) program was used to analyze the data (IBM Corporation, USA).

**3-RESULTS**

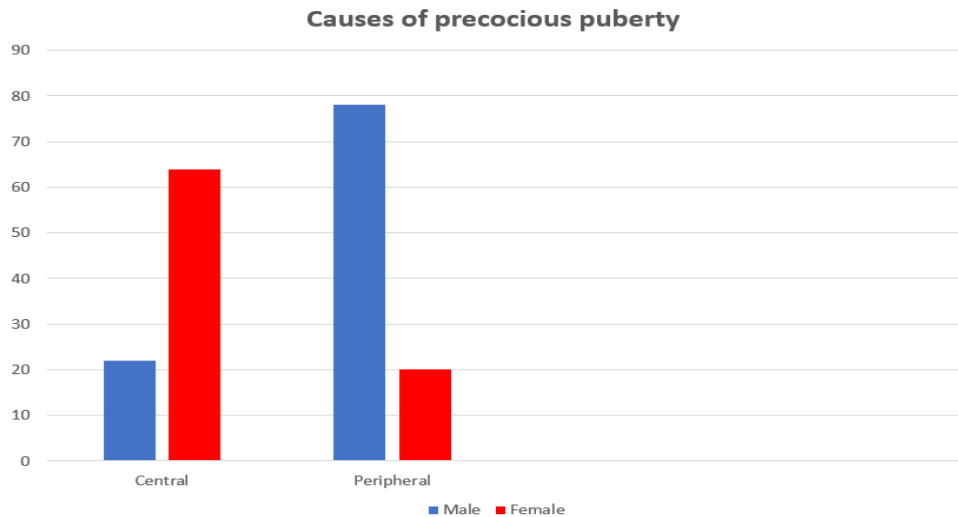
The study includes 65 subjects with precocious puberty, 56 (86.2%) are females while 9 (13.8%) are males. With female to male ratio is 6.2:1. The mean age of the study population is 5.76 years, moreover; the mean age of females is 5.50 years and the mean age for males is 7.24 years.

Table 1 shows distribution of study population according to different causes of precocious puberty. Regarding central precocious puberty, it's evident that idiopathic central precocious puberty is prevalent among 31 patients (30 females and 1 male) while neuropathic central precocious puberty is prevalent among 7 patients (6 females and 1 male). Moreover; with regards to peripheral precocious puberty; congenital adrenal hyperplasia (CAH) is prevalent among 19 patients (12 females and 7 males), Dehydroepiandrosterone increase, ovarian cyst and adrenal tumor are prevalent among 6, 1 and 1 female respectively.

**Table 1: Distribution of study population according to different causes of precocious puberty.**

Variables		Male		Female		Total	
		No.	%	No.	%	No.	%
Central Precocious Puberty	Idiopathic Central Precocious Puberty	1	3.2	30	96.8	31	100
	Neuropathic Central Precocious Puberty	1	16.6	6	83.4	7	100
Peripheral Precocious Puberty	CAH	7	36.8	12	63.2	19	100
	DHEA	0	0	6	100	6	100
	Ovarian Cyst	0	0	1	100	1	100
	Adrenal tumor	0	0	1	100	1	100

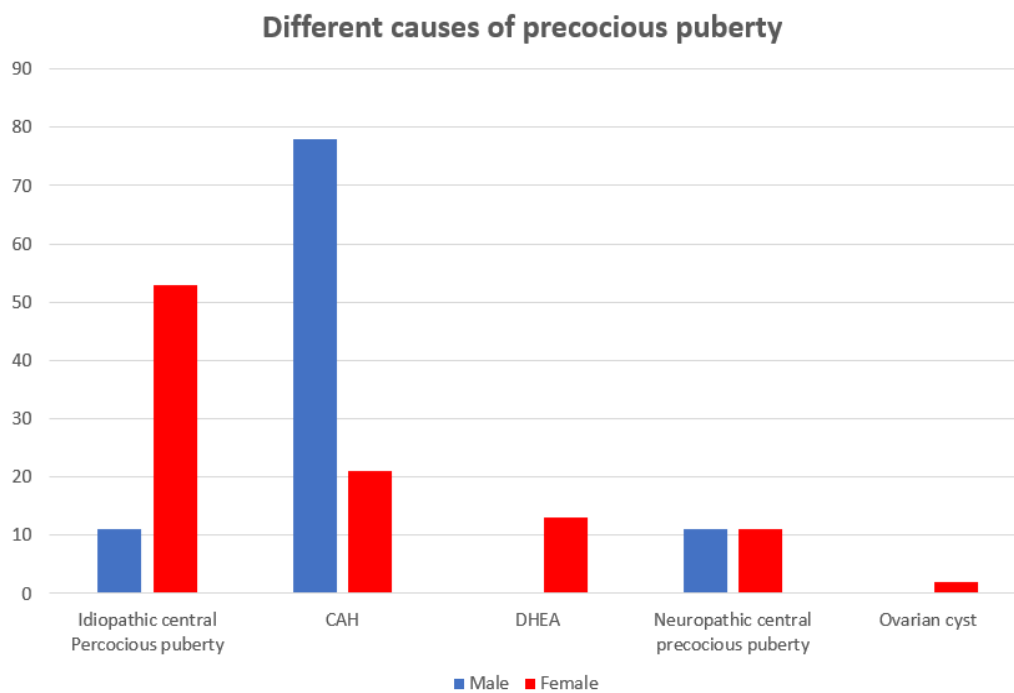
Figure 1 shows comparison between the study population regarding central and peripheral cause of precocious puberty (in percent). It's evident that females are having more central causes of precocious puberty versus male are showed more peripheral causes of precocious puberty.



**Figure 1: Comparison of females and males regarding main causes of precocious puberty.**

Figure 2 explains different causes of precocious puberty among both genders (in percent). Females are showed more Idiopathic central precocious puberty and DHEA

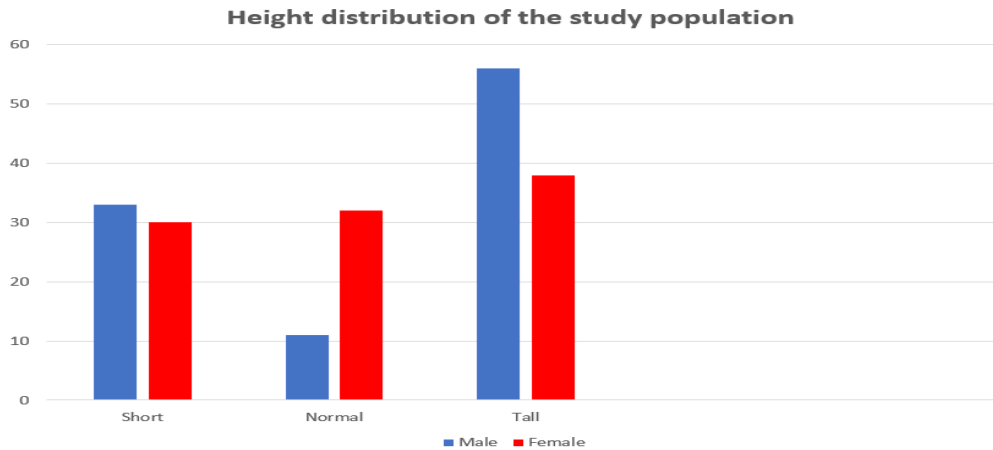
increase, while males are having more congenital adrenal hyperplasia. Furthermore; equal percent of neuropathic precocious puberty are shown in both groups.



**Figure 2: Comparisons of females and males regarding different causes of precocious puberty.**

Figure 3 illustrates comparison between females and males (in percent) regarding height. Females are more likely to have normal height, while males are more likely

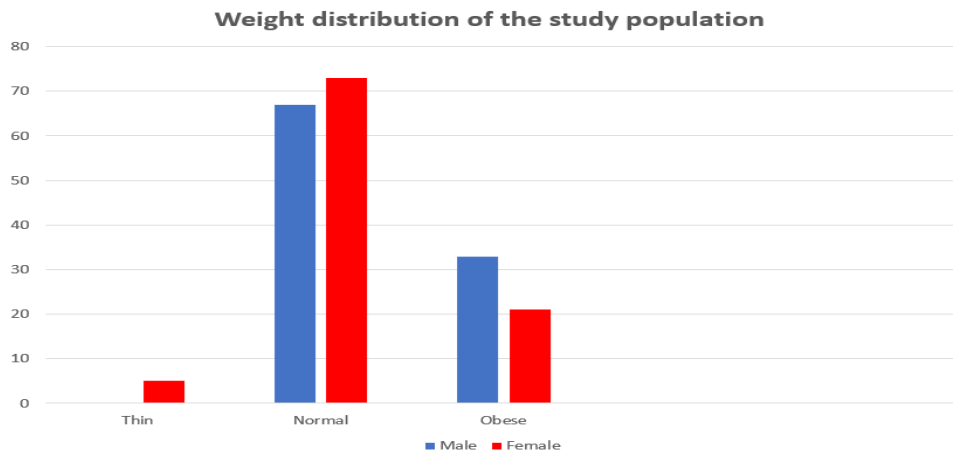
to have tall stature. Comparable results are shown regarding short stature with little more males having it.



**Figure 3: Comparison of females and males regarding height (percent).**

Figure 4 illustrates comparison between females and males (in percent) regarding weight. Females are more likely to be thin, while males are more likely to be obese.

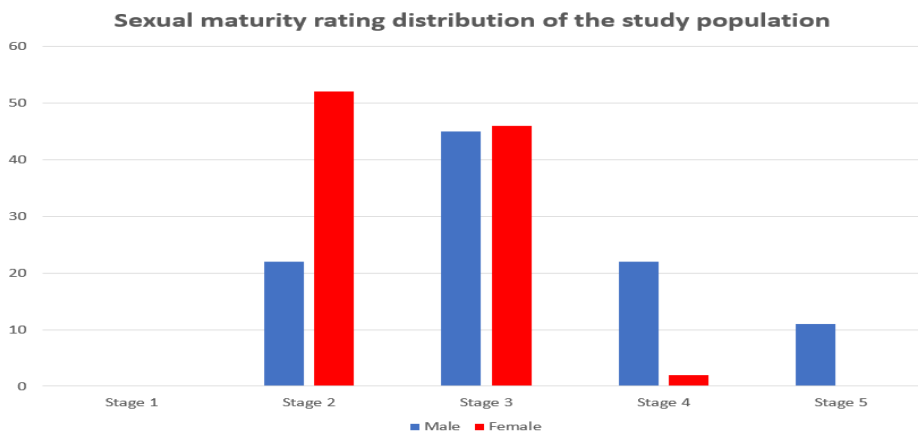
Comparable results are shown regarding normal weight with little more females having it.



**Figure 4: Comparison of females and males regarding weight (percent).**

Figure 5 explains comparison of the study population regarding sexual maturity rating (in percent). Females are more likely to present at stage 2 and stage 3, while

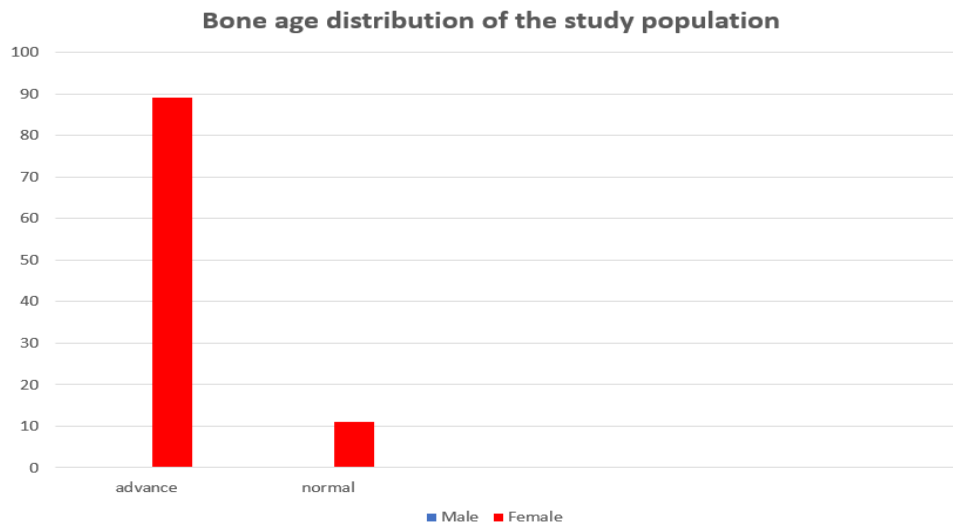
male are more likely to present at stage 4 and stage 5. Of note no patient is present at stage 1.



**Figure 5: Comparison of females and males regarding Sexual maturity rating (percent).**

Figure 6 expresses the comparison between the study population with regards to have advanced or normal bone age. It's evidence that all males having advanced

bone age, while females have advanced bone age among 49 (87.5%) but normal bone age was present among 7 (12.5%).



**Figure 6: Comparison of females and males regarding bone age (percent).**

#### 4- DISCUSSION

Under conventional definitions, precocious puberty occurs when secondary sexual characteristics begin to emerge two to two and half standard deviations (SD) earlier than the average age at which sex-related puberty begins.<sup>[16]</sup> If secondary sexual characteristics begin to emerge before the ages of eight for girls and nine for boys, there is a consensus that premature puberty will result.<sup>[17]</sup> Younger ages at presentation are more alarming and require careful investigation to determine the underlying reason.<sup>[18]</sup> There may be early signs of typical precocious puberty due to a number of variables, including obesity, a family history of precocious puberty.<sup>[19]</sup>

Precocious puberty shown in this study to be predominant among females. With female to male ratio is 6.2:1. The mean age of the study population is 5.76 years, moreover; the mean age of females is younger than that of males, in other word, 5.50 years for females versus 7.24 years for males respectively. About three fifths of the study population had central precocious puberty versus two fifths had peripheral puberty. Moreover; females have more central precocious puberty (36/56) while males have more peripheral precocious puberty (7/9). Comparable results were obtained by Sommayya Aftab *et al.*<sup>[20]</sup> Among central precocious puberty; the study shows that the most common cause is idiopathic central precocious puberty followed by neurogenic causes, this is runs with Ana Pinheiro Machado Canton *et al.*<sup>[21]</sup> From the other hand; the study illustrates that congenital adrenal hyperplasia is the commonest cause of peripheral precocious puberty which is consistent with Sommayya Aftab *et al* study findings.<sup>[20]</sup> The current study shows females are presented with normal height more than males who presented with taller stature more than females.

Moreover; females are more likely to be thinner, while males are more likely to be thicker than females. Unlike Yawen Zhang *et al.*, who discovered that there is a sex difference in this impact that is more pronounced in girls, also he founded that the prevalence of precocious puberty in overweight and obese children is higher than that in children of normal weight.<sup>[22]</sup> However; more prospective studies are need for confirmation of the exact relationship. Additionally; the study shows that females are more likely to present at stage 2 and stage 3, while male are more likely to present at stage 4 and stage 5. As this is depend on parents educational and awareness levels, however; Paul Kaplowitz *et al* found that most of girls seen for early puberty will be at the breast bud (Tanner 2) stage, while boys, voice change, acne, or facial hair are the presenting signs (Tanner 4-5).<sup>[23]</sup> Lastly; the study shows only 7 patients (females) having normal bone age, which is parallel to Yue-Qin Xu *et al* who claimed that advanced bone age as an indicator facilitates the diagnosis of precocious puberty.<sup>[24]</sup>

The limitations of study are depended on retrospective data and it have small sample size, moreover; the study is depended on Nineveh government population so that more generalize studies are needed to assess the clinical profile and etiological factors of precocious puberty in Iraq.

#### 5- CONCLUSIONS AND RECOMMENDATIONS

Precocious puberty affects females more than males, female have more central precocious puberty while male have more peripheral precocious puberty, the commonest cause of central precocious puberty is idiopathic, while congenital adrenal hyperplasia is the commonest cause of peripheral precocious puberty, most of females having normal height and weight, while most of males are tall and obese. Precocious puberty is linked mostly with

advanced bone age. More prospective studies are needed for this topic in future.

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#### Conflict of interest

About this study, the authors disclose no conflicts of interest.

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