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Review article

Puberty

### Precocious puberty- A review and update

Jeeva James<sup>1\*</sup> Shyni J.R<sup>1</sup>, Dr. Lal Prasanth M.L<sup>2</sup>, Dr. Anson S Maroky<sup>3</sup>

<sup>\*1</sup>Associate Professor, Dr. Moopen's College of Pharmacy, Meppadi, Wayanad, Kerala, India, Pin-673577.

<sup>1</sup>Assistant Professor, Dr. Moopen's College of Nursing, Meppadi, Wayanad, Kerala, India, Pin-673577.

<sup>2</sup>Principal, Dr. Moopen's College of Pharmacy, Meppadi, Wayanad, Kerala, India, Pin-673577.

<sup>3</sup>Professor, Sree Dattha Institute of Pharmacy, Sheriguda, Ranga reddy, India.

\*Corresponding Author: Jeeva James

#### ABSTRACT

The sensitive time of life known as puberty is marked by the emergence of secondary sex traits that result in full sexual development. For girls, it begins biologically between the ages of 8 and 13 and for boys, between the ages of 9 and 14. Numerous studies conducted over the past 20 years have revealed that the onset of puberty has advanced by 12 to 18 months in younger ages. Various hypotheses have been put forth to explain this change, including the contribution of obesity and nutritional status as well as the impact of extrinsic factors like exposure to endocrine-disrupting chemicals (EDCs). Except for a brief period of activation after birth, the hypothalamic-hypophysis-gonadal axis develops during embryogenesis and is inhibited until the start of pubertal development. The pulse generator is likely engaged again towards the start of puberty as a result of glial signals and neurotransmitters gradually stimulating GnRH neurons. In this stage, kisspeptin and its receptor are crucial. Precocious pubertal development in the forms of premature pubarche/adrenarche, premature thelarche, and premature menarche is incomplete and is caused by endocrine systems that are only now beginning to be understood. In order to reassure patients and parents about the non-evolution of pubertal progression and prevent ineffective therapies with similar LHRH, it is crucial to identify these forms from the complete ones.

**Keywords:** Precocious puberty, Endocrine-disrupting chemicals, Pubarche, Thelarche, Menarche.

#### INTRODUCTION

Precocious puberty (PP) is the development of secondary sexual traits in boys before the age of nine, in African American and Hispanic girls before the age of seven and a half, and in Caucasian girls before the age of eight (1). The hypothalamic-pituitary-gonadal (HPG) axis's activation causes changes in behaviour, sexual development, and growth acceleration (2). Within the first few months of life, the human infant experiences a transient activation of the hypothalamus-pituitary-gonadal axis, a process that has been referred to as "mini-puberty," which is the culmination of a series of maturational steps starting in the uterus and proceeding during the neonatal period (3-5). The hypothalamus-pituitary-gonadal axis thereafter becomes inactive until the start of pubertal development (6). For girls, it begins biologically between the ages of 8 and 13 and for

boys, between the ages of 9 and 14 (7). The three main subtypes of PP are benign variations, peripheral PP, and central PP. This review will only address central precocious puberty (CPP), which is brought on by early development of the hypothalamic-pituitary-gonadal (HPG) axis. The pattern and timing of pubertal events remain the same as in typically timed puberty, notwithstanding the earlier onset. Breast growth is the first clinical symptom of CPP in girls. The first menstrual period often starts at Tanner stage 4, after the growth surge typically happens during Tanner stages 2-3 of the breast. Testicular enlargement in males is the first clinical symptom of CPP. Compared to girls, the growth spurt occurs later (8,9). In addition to having advanced bone ages, pubertal levels of luteinizing hormone (LH) and follicle stimulating hormone, both boys and girls with CPP show fast linear growth for their age (FSH). CPP can be idiopathic, caused by

genetic changes, or linked to anomalies in or injuries to the central nervous system (CNS). Regardless of the underlying cause, gonadotropin-releasing hormone analogues (GnRHAs) are a safe and effective therapy option with the primary objective of preventing short ultimate adult height.

### **ADVANCEMENT OF NORMAL PUBERTY**

The Sexual Maturity Rating, often known as the Tanner scale (SMR) is an impartial grading system used to record and follow the emergence of secondary sexual traits in kids going through puberty. The typical age of female puberty onset ranges from 8 to 13 years old, and it is distinguished by the emergence of breast buds. The step under the areola, commonly known as thelarche, stands for the Stage B2 of Tanner. The thelarche is first in the series of occurrences followed by pubarche, or the growth of pubic and axillary hair. As this is happening, growth velocity begins to rise between stage 2 and stage 3, peaking in stage 4 during menarche may show up. Males reach puberty between the ages of 9 and 14 and are identified by a testicular volume of at least 4 ml or Tanner Stage G2. Boys' development is defined by the growth of pubic hair and the penis, which occur after the enlargement of the testis, and they reach their peak growth velocity during Tanner stage 3, typically two years later than females (10,11).

### **ETIOLOGY**

Girl's experience CPP much more frequently than boys do (12, 13). In 80 to 90 percent of instances in girls, it is idiopathic. Although traditionally more than half of cases involving boys involved cerebral lesions (14,15), there are just a few recent articles demonstrating a decreasing tendency in males (16,17). Congenital or acquired Neurological diseases and overseas adoption are risk factors for CPP. Moreover, a number of hereditary disorders are linked to CPP (8). Patients who initially exhibit peripheral PP may develop secondary CPP, especially if the bone age is greatly advanced. Moreover, familial cases have been documented (18,19).

### **PUBERTY DISORDERS**

Normal puberty's timing has changed over the centuries, as seen by the sharp reduction in menarche age from 17 years in the early 19th century to 13 years in the middle of the 20th century (20). Also, it appears that the age at which breast development first begins is getting younger over the past 20 years, with the average age of breast development flipping from 11 years old before the 1980s to 10 years old between 1988 and 1994 (21). With a prevalence of 0.2% in girls and 0.05% in boys in Denmark, it suggests that girls are around 10 times more likely than boys to have precocious puberty (PP) (22). There have been some questions about the validity of prior standards with the discovery that American girls may have developed breasts before the age of 8; nonetheless, the age at which menarche occurs hasn't changed significantly over time. While there is some evidence that early puberty may be linked to hyperinsulinemia and insulin resistance, the relationship between early puberty and obesity is still debatable (23).

### **PRECOCIOUS CENTRAL PUBERTY**

Precocious puberty is thought to occur in between 1/5,000 and 1/10,000 people (24). Precocious puberty (PP) is the development of secondary sexual traits before the age of eight in females. Puberty that begins before this age is regarded as abnormal. Researchers have proposed using the age of 7 for girls as a criterion for the classification of precocious puberty due to the clear anticipation in the age of commencement of puberty in several studies (25). The suitable threshold for assessment has returned to the previously advised criteria as other researchers have since decided that symptoms of puberty in girls aged 6–8 years cannot be regarded normal or benign as this could result in under diagnosed endocrine abnormalities (26).

### **FORMS OF PRECIOUS PUBERTY THAT ARE NOT COMPLETE**

Precocious puberty is a condition in which puberty starts too early, before the age of 8 years in girls and 9 years in boys. While complete precocious puberty involves the full range of physical and hormonal changes associated with puberty, there are also forms of precocious puberty that may not be complete.

**Isolated premature thelarche:** This is a condition in which a girl experiences breast development before the age of 8, without other signs of puberty, such as pubic hair growth or menarche. According to a review article published in the Journal of Clinical Research in Paediatric Endocrinology, isolated premature thelarche is the most common form of precocious puberty, accounting for 80-90% of cases. It typically does not progress to complete puberty and is not usually associated with any serious health issues. However, the condition should be monitored by a healthcare provider to ensure that it does not progress.

**Isolated premature adrenarche:** This is a condition in which a child experiences the early onset of pubic hair growth or body odor, without other signs of puberty. According to an article published in Paediatric Endocrinology Reviews, isolated premature adrenarche typically occurs in children between the ages of 6 and 8 years and is more common in girls than in boys. The condition does not usually progress to complete puberty and is not associated with any serious health issues (27).

**Incomplete precocious puberty:** This is a condition in which a child experiences some but not all of the signs of puberty. For example, a girl may experience breast development and pubic hair growth, but not menstruation. According to a review article published in the Journal of Paediatric Endocrinology and Metabolism, incomplete precocious puberty is less common than complete precocious puberty and can be caused by a variety of factors, including hormonal imbalances, genetic factors, and brain tumors. The condition should be evaluated and managed by a healthcare provider to prevent potential health complications (28).

Overall, while these forms of precocious puberty may not progress to complete puberty, it is important to monitor them and seek medical evaluation and management to ensure the best possible outcomes for the child.

### **PREMATURE PUBARCHE/ADRENARCHE**

Pubarche refers to the onset of pubic hair growth, while adrenarche refers to the activation of the adrenal glands that

occurs before puberty, leading to the production of androgens (male sex hormones) like DHEA-S (dehydroepiandrosterone sulfate). Premature pubarche (PP) and premature adrenarche (PA) are two conditions in which these processes begin earlier than normal (29). PP is defined as the onset of pubic hair before the age of 8 years in girls and before the age of 9 years in boys. It is the most common cause of genital ambiguity (unclear or ambiguous genitalia) in females. Causes of PP can be divided into central (involving the hypothalamic-pituitary-gonadal axis) and peripheral (involving the adrenal glands). Central causes include premature activation of the hypothalamic-pituitary-gonadal axis, such as in idiopathic (unknown cause) or congenital (present at birth) causes. Peripheral causes include adrenal hyperplasia (a group of genetic disorders affecting the adrenal glands) and tumors that produce androgens (30). PA, on the other hand, refers to the early activation of the adrenal glands before the age of 8 years in girls and before the age of 9 years in boys. It is associated with an increase in androgen levels, which can cause early appearance of pubic and axillary hair, acne, and body odor. PA is usually benign and does not require treatment. However, it can be a sign of underlying disorders such as congenital adrenal hyperplasia, McCune-Albright syndrome (a genetic disorder affecting bones and endocrine glands), and adrenal tumors (31). The diagnosis of PP and PA involves a thorough medical history and physical examination, including assessment of growth velocity and bone age. Blood tests may be ordered to measure hormone levels and rule out underlying disorders. Treatment depends on the underlying cause and may involve observation, hormonal therapy, or surgery in some cases (32). It is important to note that premature pubarche and premature adrenarche are two different conditions, but they may share similar causes and have overlapping symptoms. A proper diagnosis is essential for effective management and prevention of long-term complications.

### **PREMATURE THELARCHE**

Premature thelarche is a medical condition in which a young girl, typically under the age of 8, develops breast tissue and/or pubic hair before the onset of normal puberty. It is considered to be a benign condition that is not associated with any other underlying medical problems (33).

The exact cause of premature thelarche is not fully understood, but it is believed to be related to the early activation of the hypothalamic-pituitary-gonadal axis, which is the hormonal system that regulates puberty. Some factors that may contribute to the development of premature thelarche include genetics, obesity, and exposure to endocrine-disrupting chemicals (34). Most cases of premature thelarche do not require treatment, as the condition typically resolves on its own within a few years (35). However, in some cases, further testing may be necessary to rule out underlying medical conditions, such as adrenal or ovarian tumors, that may cause early puberty (36). If you are concerned that your child may be experiencing premature thelarche, it is important to speak with a paediatrician or

endocrinologist, who can evaluate your child and provide appropriate guidance and management (37, 38).

### **PREMATURE MENARCHE**

Premature menarche is a term used to describe the onset of menstruation at an earlier age than what is considered normal. The average age of menarche is around 12 years old, but it can occur as early as 8 years old in some girls. Menarche before the age of 8 is generally considered to be premature and may be associated with certain medical conditions. Premature menarche can be caused by a variety of factors, including genetics, obesity, hormonal imbalances, and certain medical conditions such as thyroid problems, pituitary tumors, and ovarian tumors. In some cases, there may not be an underlying medical condition that can be identified. Early onset of menstruation can have a significant impact on a girl's physical and emotional development. It may lead to shorter stature, increased risk of breast cancer, and psychological difficulties related to early sexualization. Therefore, it is important to identify and treat the underlying cause of premature menarche, if possible. If a girl experiences premature menarche, it is recommended that she undergo a thorough medical evaluation to determine the underlying cause. Treatment will depend on the underlying cause, but may include hormonal therapy, surgery, or lifestyle changes such as weight loss and exercise (39).

### **EARLY PUBERTY**

When clinical and auxological symptoms of pubertal development appear between the ages of 8 and 10 years (40), or between the ages of 7.5 and 8.5 years (41) or between the ages of 8 and 9 years it is said to be early puberty (42). Several writers discovered that a longer pubertal development period may make up for a relatively early onset to puberty (43). Although the exact mechanism underlying early pubertal development is still unknown (44), some research has indicated a link between limited prenatal growth and early puberty as a result of an endocrine axis permanently reset (45). Moreover, the secular trend in pubertal time anticipation may be connected to this illness (46).

### **CONCLUSION**

Even while the age of menarche has not altered, in recent decades we have seen a stable anticipation of the initial stages of pubertal development. Consequently, it's crucial to carefully distinguish between individuals who have full-blown pubertal precocity symptoms that call for proper hormone therapy and patients who just have partial or slowly increasing symptoms that can be managed with careful monitoring. Because the existing studies are still preliminary and do not draw a clear conclusion, it is impossible to pinpoint the precise involvement of endocrine disruptors in the development of sexual precociousness, which poses a constraint to our review. Further extensive research is required to definitively determine which genes may be involved in the various forms of pubertal development while also verifying the existence of inheritance in pubertal development.

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