

INVESTIGATING THE ESCALATING PREVALENCE OF PRECOCIOUS PUBERTY IN FEMALE CHILDREN: IMPLICATIONS FOR FUTURE SEXUAL IMBALANCES

ABSTRACT

Precocious puberty, the premature onset of secondary sexual characteristics before the age of 8 in girls, has emerged as a growing concern in pediatric endocrinology. The prevalence of precocious puberty has witnessed a noticeable rise in recent decades, attributed to various environmental, genetic, and lifestyle factors. This surge in early maturation poses significant challenges not only to affected individuals and their families but also to healthcare systems worldwide.

Moreover, beyond the immediate physical changes, there exists a complex interplay between precocious puberty and future sexual imbalances. Studies suggest that early puberty may predispose females to a myriad of health issues, including increased risk of metabolic disorders, psychological challenges, and reproductive complications later in life. Furthermore, the societal implications of this trend cannot be overlooked, as it may exacerbate existing gender disparities and contribute to broader socio-cultural issues.

Understanding the link between precocious puberty and future sexual imbalances is crucial for developing effective preventive strategies and providing comprehensive care to affected individuals. This necessitates interdisciplinary research efforts encompassing endocrinology, psychology, genetics, and public health.

In conclusion, this review shall highlight the urgent need for continued investigation into the escalating prevalence of precocious puberty in female children and its far-reaching implications

for sexual health and well-being across the lifespan. By elucidating the underlying mechanisms and risk factors, healthcare professionals can better address this growing public health concern and mitigate its long-term consequences on individuals and societies alike.

Keywords: precocious puberty, sexual health, reproductive health, young females, sexual imbalances.

INTRODUCTION

The term ‘precocious puberty’ (PP) refers to the emergence of secondary sexual characteristics before the age of eight in girls and nine in boys. (1)

Manifestations of puberty include the development of breasts (thelarche) in girls and enlargement of the testes, indicated by either volume (≥ 4 mL) or length (≥ 25 mm), in boys. PP comprises two main types: central PP (CPP) and peripheral PP (PPP). (2)

Gonadotropin-releasing hormone (GnRH)-independent PP (PPP) refers to early pubertal development unrelated to central activation of the hypothalamic-pituitary-gonadal (HPG) axis, categorized as either congenital/genetic or acquired. (3)

Common congenital/genetic causes include McCune-Albright syndrome (MAS), familial male-limited PP, and congenital adrenal hyperplasia, while acquired causes encompass exogenous androgen exposure, functioning tumors/cysts, and pseudo-PP secondary to severe primary hypothyroidism.(4)

Conversely, CPP represents the predominant gonadotropin-dependent form of PP, characterized by premature activation of the HPG axis. CPP may arise from genetic mutations affecting key regulators such as MKRN3, DLK1, or KISS1, alterations in epigenetic factors like Lin28b and let-7, or as a component of various syndromes or central lesions including hypothalamic hamartomas.

A comprehensive evaluation of patients with suspected PP entails a thorough medical history and meticulous physical examination.(5)

INVESTIGATIONS FOR PRECOCIOUS PUBERTY

The onset of puberty is marked by thelarche in girls and a testicular enlargement of 4 mL or more in boys, assessed using an orchidometer to differentiate between unilateral and bilateral enlargement and to detect any testicular masses. (6)

Careful physical examination is crucial to distinguish signs of precocious puberty (PP) from other conditions, such as lipomastia, particularly in overweight or obese girls. Additionally, the presence of café-au-lait spots on the skin may indicate a potential association with neurofibromatosis type 1 or McCune-Albright syndrome.(7)

Regular monitoring of height on growth charts is essential, with an increase of one full percentile space or more suggesting a diagnosis of PP. Height should also be compared to mid-parental height using specific formulas to assess growth patterns accurately.(8)

Moreover, differences in clinical presentation, sequence of pubertal changes, and rate of progression can distinguish between peripheral PP (PPP) and central PP (CPP). Features such as sudden versus gradual onset, intermittent changes, and specific hormonal involvement (estrogens, androgens, or both) may vary between the two types.(9)

Certain clinical features can help differentiate between PPP and CPP. For instance, PPP may present with a testicular volume of less than 4 mL alongside pubic hair development and penile growth, while CPP typically manifests with a testicular volume exceeding 4 mL along with other signs of puberty.(10) Exceptions include familial male-limited precocious puberty (FMPP) and hCG-secreting germ cell tumors, where mild testicular enlargement may be present. FMPP,

caused by an LH receptor mutation, leads to Leydig cell hyperactivity and increased testosterone secretion.(11)

Additionally, adrenal tumors may exhibit signs of virilization and excess glucocorticoid effects, such as rapid weight gain, facial plethora, moon face, striae, hirsutism, hypertension, and related systemic changes in affected girls.(12)

Specific presenting signs may indicate particular causes of PP. For instance, sudden vaginal bleeding with minimal breast development may suggest MAS, caused by a mutation in the α -subunit of the G-protein. In MAS, PPP results from excessive estrogen secretion by functioning ovarian cysts. (2)

Vaginal bleeding occurs due to estrogen withdrawal following cyst involution. Additional features suggestive of MAS include café-au-lait spots and polyostotic fibrous dysplasia of the bone, alongside precocious sexual maturation.(13)

THE INCREASING INCIDENCE OF PRECOCIOUS PUBERTY IN FEMALES

During the COVID-19 pandemic lockdown, there has been a notable surge in cases of central precocious puberty (CPP) and rapid progressive precocious puberty (RPEP), with incidence rates approximately three times higher than pre-pandemic levels.(14) Various reports from different centers have highlighted an increased occurrence of precocious puberty, early menarche, and RPEP among girls following the pandemic. The exact mechanisms underlying this rise in precocious puberty during the pandemic remain unclear, although several potential explanations have been proposed.(15)

One suggested mechanism for the heightened frequency of CPP and RPEP during the COVID-19 pandemic involves the angiotensin-converting enzyme-2 (ACE2) receptor, which serves as the binding site for the Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) virus.

(16) These receptors are abundant in the cranial nervous system, particularly around the olfactory bulb, where they coexist with gonadotropin-releasing hormone (GnRH) neurons and GABAergic neurons. Research has linked an increased olfactory bulb volume to precocious puberty, suggesting that SARS-CoV-2 might initiate puberty by disrupting the blood-brain barrier or directly interacting with neural pathways. Additionally, inflammatory cytokines stimulating N-methyl-D-aspartate (NMDA) receptors may elevate GnRH secretion.(17) Notably, our patients did not exhibit any signs or history of SARS-CoV-2 infection, considering that COVID-19 infection in children is often asymptomatic, making symptom recognition challenging.(18)

The prolonged stress induced by COVID-19 lockdown measures, stemming from fear of infection and extended home quarantine, could also contribute to increased GnRH release via certain neurotransmitters and neurons. (19)

Animal studies have demonstrated that chronic stress accelerates puberty through mechanisms involving NMDA, GRF1, CRF, and GABA A receptors in rats, as well as elevated cortisol and catecholamines in mice. However, while these mechanisms have been observed in animal models, their applicability to humans remains speculative.(20)

Furthermore, a separate study investigating the incidence of early puberty associated with methylphenidate use suggested that dopamine and norepinephrine might trigger puberty by blocking transporters, leading to increased synaptic concentrations of these neurotransmitters.(21)

THE IMPACT OF PRECOCIOUS PUBERTY IN FEMALES

As living standards improve, the issue of childhood precocious puberty is garnering increasing concern from both parents and healthcare professionals due to its potential detrimental effects.

Physiologically and pathologically, children experiencing precocious puberty exhibit rapid development in height, weight, and bone age. This early maturation can result in premature closure of epiphyses, leading to a shortened growth period and ultimately impacting adult height, with severe cases potentially resulting in dwarfism. (22)

Additionally, precocious puberty may manifest in secondary sexual characteristics, such as menstrual cramps, and heighten the risk of certain cancers, as foreign studies have indicated an increased risk of breast and uterine cancer in girls with precocious puberty.(23)

Beyond the physiological ramifications, the psychological impact of sexual development can impose a significant burden on children, potentially leading to social issues such as early sexual behavior or juvenile sexual offenses. (24)

Domestic research underscores a trend towards precocious puberty occurring at younger ages, with idiopathic central precocious puberty representing the most prevalent form, accounting for 92% of cases. Consequently, childhood precocious puberty has emerged as a significant concern affecting healthy growth.(25)

Given these challenges, the prevention and treatment of childhood precocious puberty have become focal points of clinical research. Analyzing the factors influencing its occurrence is imperative for developing effective prevention strategies.(26)

Recent research has highlighted significant disparities between girls and boys in terms of endocrine function and growth and development, with studies consistently demonstrating a notably higher incidence of precocious puberty in girls compared to boys. (26)

Bone age assessment, a common diagnostic measure in skeletal examination, evaluates the relationship between skeletal bone nucleus appearance and healing time in relation to chronological age.(27)

Furthermore, reduced daily exercise duration has been linked to increased fat accumulation in the body, which can stimulate hormone secretion and contribute to the onset of sexual precocity. Estradiol (E2), primarily produced by the placenta, corpus luteum, and ovarian follicles in pregnant women, serves as a crucial indicator of normal sexual hormone function and levels.(8) Additionally, follicle-stimulating hormone (FSH) and luteinizing hormone (LH) play complementary roles in regulating the menstrual cycle. LH acts on the ovary to stimulate estrogen synthesis, which in turn impacts the growth plate, accelerating growth, advancing bone maturity, and consequently influencing bone age progression.(16)

It is important that clinicians carefully consider various factors such as the child's gender, bone age, exercise habits, levels of E2, FSH, LH, leptin, maternal menarche timing, living environment, eating habits, and sleep duration to monitor for signs of precocious puberty. Regular assessments of bone age, E2, FSH, LH, and leptin levels in children are crucial for early detection.(2)

Parents play a pivotal role in promoting healthy eating and exercise habits in children, thereby mitigating the risk of excessive fat accumulation. Creating a conducive living environment can also aid in preventing premature puberty.(28) However, it is important to acknowledge some limitations in this study. Firstly, its retrospective nature and small sample size may limit the generalizability of the findings. Secondly, the extended duration of certain characteristic data could introduce inaccuracies and potential bias. Thirdly, subtle symptoms of precocious puberty may go unnoticed, leading to selection bias. Future studies should aim to address these limitations by conducting prospective studies with larger sample sizes to further explore this important topic.(5)

The notion that earlier puberty is linked to heightened psycho-sexuality in both genders aligns more closely with life history theory and the hypothesis initially proposed by Sisk and colleagues.

According to this hypothesis, earlier puberty is correlated with increased phenotypic masculinization (DSH). In line with the decreasing sensitivity hypothesis, it is suggested that the brain becomes less responsive to the organizational effects of pubertal hormones over the course of puberty, with individuals experiencing puberty earlier exhibiting the highest levels of masculinity in brain morphology, psychology, and behavior.(18)

The predictions derived from life history theory suggest that individuals undergoing earlier pubertal development may allocate more resources towards mating efforts. This may be facilitated by the development of psychological and behavioral traits that promote mating behaviors.(25)

The study provides evidence supporting the relationship between earlier puberty and heightened psychosexuality in adult men and women. Additionally, it suggests variations in this relationship based on factors such as group (e.g., typically developing individuals and those with Internet Gaming Disorder) and the type of psychosexuality being examined. (28)These findings offer insights into the organization of the brain and behavior during the peripubertal period and carry clinical implications for physicians treating conditions where pubertal timing is medically altered. Notably, the study indicates that associations with psychosexuality were more apparent when hormone replacement therapy (HRT) timing was documented compared to the recalled timing of pubertal events.(23)

CONCLUSION

The escalating prevalence of precocious puberty in female children demands urgent attention due to its profound implications for future sexual imbalances. Factors such as changes in environmental exposures, lifestyle habits, and societal influences may play pivotal roles in the observed rise in precocious puberty among girls.

Understanding the mechanisms behind precocious puberty is crucial not only for early detection and intervention but also for mitigating its long-term consequences on physical and psychological health. Moreover, the potential implications of precocious puberty on future sexual imbalances necessitate proactive measures to address this issue comprehensively.

Efforts should focus on implementing strategies aimed at promoting healthy lifestyles, reducing environmental exposures to endocrine-disrupting chemicals, and enhancing awareness among parents, healthcare providers, and policymakers. Furthermore, continued research into the interplay between genetics, hormonal factors, and environmental influences is essential for developing targeted interventions and preventive measures.

By addressing the escalating prevalence of precocious puberty in female children today, we can strive towards a future where sexual imbalances are minimized, and all individuals can attain optimal health and well-being.

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