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Clinical spectrum of precocious puberty and its normal variants in children: insights from a seven-year review in a tertiary hospital, Calabar, Nigeria

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Abstract

Context: Precocious puberty, clinically defined as the development of secondary sexual characteristics before 8 years of age in girls and 9 years in boys, represents a clinical spectrum that encompasses both pathological and non-pathological variants of early pubertal onset. Given the paucity of data from African settings, there is a compelling need to characterize the local spectrum of precocious puberty and its normal variants.
Objective: To describe clinical patterns, demographics, aetiologies, diagnostic patterns, management, and outcomes of children presenting with precocious puberty (PP) and its normal variants at University of Calabar Teaching Hospital, Nigeria, over seven years.
Materials and Methods: This was a retrospective descriptive study carried out between January 2015 and December 2021 involving children aged 0-18 years who presented with signs of early pubertal development. Data collected included demographics, clinical presentation, diagnosis (CPP, PPP, normal variants), skeletal age (Greulich–Pyle), Tanner staging, radiology, and biochemistry. GnRH analogues were used for children confirmed to have idiopathic central precocious puberty, specific treatments were given to children for the cause of peripheral precocious puberty when identified and parents were reassured for patients identified with the normal variants. Descriptive statistics used to analyse data.
Results: 24 patients (12.3% of endocrine cases) had precocious puberty with a M: F ratio of 1:2.3 and median age of 5.5 years. CPP was diagnosed in 8 (33%) patients, all female and idiopathic precocious puberty including PPP: 4 (17%) with causes—virilizing adrenal tumour (1), CAH (1), McCune-Albright (1), exogenous hormone (1). Normal variants were seen in 12 (50%) children presenting as premature thelarche/adrenarche. Approximately 91.6% were from middle socioeconomic class. Most cases of normal variants required only monitoring, whereas true precocious puberty cases were managed with endocrine evaluation and treatment as indicated.
Conclusion: Benign variants and female predominance were noted among children presenting with precocious puberty. CPP was most common true form of precocious puberty. Awareness and accurate diagnosis are essential for targeted management. Regional data as presented in this study will enhance understanding of epidemiology of PP in sub-Saharan-Africa.

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Introduction

Precocious puberty, clinically defined as the development of secondary sexual characteristics before 8 years of age in girls and 9 years in boys, represents a clinical spectrum that encompasses both

pathological and non-pathological variants of early pubertal onset.[1] The condition is broadly classified into central precocious puberty (CPP), arising from the premature activation of the hypothalamic–pituitary–gonadal axis, and peripheral precocious puberty (PPP), which results from sex steroid production independent of gonadotropin stimulation.[2,3] In contrast, normal variants such as premature thelarche, premature menarche, and premature adrenarche are typically benign, non-progressive, and do not reflect true activation of the pubertal axis.[4] Early differentiation between true precocious puberty and its benign forms is crucial. Precocious puberty if not treated is associated with adverse effects such as short stature as well as psychosocial stress.[5] Also, early menarche following PP is associated with increased risk of metabolic syndrome,[6] cardiovascular diseases such as stroke and ischaemic heart disease,[7] and increased risk for breast cancer in adulthood.[8]

While CPP may require pharmacological intervention to preserve adult height and mitigate psychosocial consequences, normal variants generally follow a self-limited course and warrant only observation.[2,4] Misclassification can lead to overtreatment or missed opportunities for timely intervention, particularly in resource-constrained settings where access to hormonal assays and neuroimaging may be limited.

The overall incidence of PP is estimated to be 1:5,000 to 1:10,000 children[9]. The prevalence of PP was estimated as 0.2% of girls and 0.05% of boys in Denmark[10]. A School based study in China reported a prevalence of 11.47% in girls and 3.26% in boys.[11] Also, there is an increasing trend in prevalence and incidence of PP in children in Taiwan and South Korea.[12,13] In Africa and Nigeria, the prevalence of PP is unknown, with only few isolated case reports from few hospital centres.[14-17]

Epidemiologically, CPP is more prevalent in females, with reported female-to-male ratios as high as 10:1 in population-based studies.[1,9,10] However, existing literature predominantly reflects findings from high-income countries as stated above, and little is known about the clinical characteristics and presentations of children with early pubertal development in sub-Saharan Africa, which may be influenced by genetic, nutritional, and environmental factors.[10]

Given the paucity of data from African settings, there is a compelling need to characterize the local spectrum of precocious puberty and its normal variants. This retrospective study provides a seven-year review of children presenting with signs of early puberty at a tertiary care centre in Calabar, South-South geopolitical region of Nigeria. By delineating the clinical profiles, the aetiologies, diagnostic patterns and outcomes, we aim to contribute regionally relevant evidence that may inform best practices in paediatric endocrinology within low-resource environments.

Methodology

Study design

This was a retrospective descriptive cross-sectional study. The study population included all children (0-18 years) seen and managed for signs and symptoms of early puberty at the Paediatric Endocrinology Clinic of the University of Calabar Teaching Hospital, over a seven year period, from January 1, 2015, to December 31, 2021.

Study Setting

The study was conducted in the Paediatric Endocrinology Unit, Department of Paediatrics, University of Calabar Teaching Hospital (UCTH), Calabar, Cross River State, South-South Nigeria. This is the only tertiary hospital in the state and serves as a referral centre to the General Hospitals, Primary Health Care facilities and Private Hospitals across the state and beyond. It is a 550-bed facility located in Calabar, the capital city of the state with the inhabitants mainly Efiks, Ibibios, Ejaghams and other ethnic groups. The common occupation of the dwellers includes civil service, farming, fishing, trading, and artisans.

Children who presented with signs of early pubertal development were included. These signs included breast development, pubic or axillary hair, testicular enlargement, menstruation, or accelerated linear growth occurring earlier than the standard age thresholds (before age 8 in girls and age 9 in boys). Information was extracted from patient case files using a structured data extraction form. Variables collected included: Demographic data (age, sex), social class as described by Ibadin et al, 18 age at onset of symptoms, clinical features at presentation, skeletal (or Bone) age at presentation using the Greulich and Pyle Atlas, pubertal staging for breast development and pubic hair as described by Marshall and Tanner (Tanner staging), testicular volume in boys measured by using the Prader orchidometer, type of precocious puberty (central or peripheral), diagnosis of normal variants (e.g., premature

thelarche, adrenarche), laboratory and imaging findings, treatment modalities and outcomes.

The data was entered into Microsoft Excel and analysed using SPSS version 20. Descriptive statistics (means, frequencies, percentages) were used to summarize findings.

Results

A total of 194 subjects were seen in the Paediatric Endocrinology Clinic of the University of Calabar Teaching Hospital, Calabar within the review period. Twenty-four (24) of these patients had Precocious Puberty giving a total prevalence of 12.3%. There were 23 females and one male giving an F:M ratio of 23:1. The age ranged from 0.6 years to 7.6 years with a median age of 5.5 years. Two (96.6%) of subjects were in the middle social class (Table 1).

Table I. Socio-demographic characteristics of patients with precocious puberty in the review period

Variable	Frequency	Percentages
Sex		
Male	1	4.2%
Female	23	95.8%
Total	24	100%
Age		
1-3	8	33.3%s
4-6	12	50%
7-9	4	6%
Total	24	100%
Social class		
Upper	1	4.2%s
Middle	22	91.6%
Lower	1	4.2%

Precocious puberty and the variants of puberty

Eight (33%) of the patients had Central Precocious Puberty (CPP), 4 (6.7%) had Peripheral Precocious Puberty (PPP) and 12 (50%) had normal variant of puberty respectively. The mean age ± standard deviation (SD) of patients with Central Precocious Puberty was 5.6 ± 1.9 SD, and all were females with all of them having idiopathic CPP. Mean age of patients with PPP was 3.7 ± 3.2 SD years and they were all females. Mean age of patients with normal variant of puberty was 3.34 ± 2.1 SD years.

The four patients with Peripheral Precocious puberty had varying aetiologies of metastatic virilizing adrenal tumour (1), Congenital Adrenal hyperplasia (1), Mc Cune Albright (1), and one suspected exogenous exposure to sex steroid (Implanon) implanted 2 weeks after delivery in the mother for contraception. Of the 12 patients with Normal variant of puberty, 6 (25%) had Premature thelarche, 6 (25%) had Premature adrenarche and none (0%) had Premature menarche; 11 were female and only one was a male (Tables II and III respectively)

The radiological and laboratory findings and clinical outcome of the patients with CPP and PPP are shown in table IV. All the patients that had bone age assessment showed advancement by more than two years at presentation. Pelvic ultrasound findings indicated pubertal uterine size, and baseline levels of LH, FSH and oestradiol were suggestive of either Central or Peripheral Precocious Puberty. The GnRH stimulation test was not performed due to unavailability and high cost of the drug. The clinical outcome was favourable: breast development either regressed or stabilized, and height velocity normalized for the age (Table IV).

Table II: Precocious puberty and variants of puberty

Variables	Frequency	Percentage
Central precocious puberty	8	33.3%
Peripheral precocious puberty	4	16.7%
Premature thelarche	6	25%
Premarure adrenarche	6	25%
Premature menarche	0	0%
Total	**24**	**100%**

Table III: Aetiology of precocious puberty

CENTRAL PP	MALE	FEMALE
Idiopathic	Nil	8 (100%)
PERIPHERAL PRECOCIOUS PUBERTY		
Adrenal tumour (Virilizing adrenal tumour)	Nil	1(25%)
Congenital adrenal hyperplasia		1(25%)
Mc Cune Albright syndrome	Nil	1(25%)
Suspected exposure to exogenous sex steroid	Nil	1(25%)

Table IV: Radiologic and laboratory findings and outcome of treatment of children with CPP and PPP

Serial no	Chronological Age	sex	Bone age in years/ months	Abdomino-pelvic ultrasound Scan	CT Scan	LH (0.0-0.5 µIU/ml)	FSH (0.4-3.0 u I./ml)	Estradiol (<15 pg/ml)	GnRH stimulation test	Outcome	
		Central precocious puberty								Clinical signs	height velocity
1	6	F	8 [illegible]	Pubertal uterus	Normal study	0.3	20	20	Not done	Regressed	Stabilized
2	6	F	8	Pubertal uterus	Normal study	1.0	7.4	24	Not done	Regressed	Stabilized
3	6.5	F	9	Pubertal uterus	Normal study	6.8	7.9	15	Not done	Regressed	Stabilized
4	7.5	F	13	Pubertal uterus	Normal study	3.4	12.2	43.4	Not done	Did not treat	Progressed
5	6	F	8	Not done	-	1.25	13	25	Not done		
6	5	F	9	Pubertal uterus	Normal study	1.0	10	25	Not done	Regressed	Stabilized
7	4.5	F	11	Pubertal uterus	Normal study	1.7	7.8	19	Not done	Regressed	Stabilized
8	6	F	7 [illegible]	Pubertal uterus	Not done	0.88	3.9	13.39	Not done	Regressed	Stabilized
		Peripheral precocious puberty									
1	1.5	F	6	Not done	Not done	3.8	9.4	99	Not done	Regressed	Stabilized
2	7	F	9	Pubertal uterus	Not done	Not done	Not done	Not done	Not done	Regressed	stabilized
3	5.5	F	Not done	Pubertal uterus, supra-renal mass	Not done	Not done	Not done	Not done	Not done	Referred out	Referred out on request
4	1.5	F	Lost to follow up						Not done	Lost to follow up	Lost to follow up

Discussion

Precocious puberty (PP) accounted for 12.3% of paediatric endocrine consultations in this seven-year retrospective review in a tertiary hospital in South-South geo-political area of Nigeria. This finding, while clinic-based and not necessarily reflective of community prevalence, underscores the clinical relevance of early pubertal development in paediatric endocrine practice in sub-Saharan Africa. There are no previous records of prevalence of PP in this region to compare with this review. However, there are reported increasing trend and prevalence of Precocious Puberty worldwide,[11,19,23] and therefore, the prevalence in this review is not very surprising.

The female predominance observed is consistent with global trends, where girls are significantly more likely to be diagnosed with precocious puberty than boys[1,10]. This sex disparity is well documented and is thought to reflect both biological and behavioural factors, including differences in pubertal timing, hormonal sensitivity, and parental awareness[20]. Of the 24 diagnosed cases of PP, one-third (33%) had Central Precocious Puberty (CPP), 16.7% had Peripheral Precocious Puberty (PPP), while half (50%) had normal variants of puberty. The predominance of Central Precocious Puberty (CPP) in this cohort over PPP is consistent with global literature, where CPP represents the most frequent pathological cause of early pubertal onset, especially in females.[1,21] Notably, all CPP cases in this study were idiopathic and occurred exclusively in girls with a mean age of 5.6 years. This mirrors established data showing that idiopathic CPP is overwhelmingly more common in females, whereas in boys it often warrants evaluation for underlying CNS pathology.[21] The absence of identified neurogenic causes on CT scans in these patients may therefore reflect the true idiopathic nature of CPP in females.

Peripheral precocious puberty was less common in this cohort (16.7%) but presented with diverse and clinically significant aetiologies. The identification of rare causes such as metastatic virilizing adrenal tumour, congenital adrenal hyperplasia (CAH), McCune-Albright syndrome (MAS), and exogenous hormone exposure (Implanon) highlights the diagnostic complexity and importance of thorough endocrine evaluation. These conditions, though uncommon, can have serious long-term health consequences if not promptly recognized and managed. The child with metastatic virilizing adrenal tumour (an echogenic irregular shaped mass arising from right supra renal area extending to paravertebral region on ultrasound scan) presented late when the tumour had spread to vital organs (liver and lungs) with altered liver enzymes and pleural effusion. She eventually died from the disease. This was an avoidable death, due to lack of suspicion and late referral of the index child by a peripheral health facility to the Endocrinologist. A cultural and religious connotation was also given for the child with suspected McCune-Albright syndrome who presented at the age of 18 months with breasts development, café-au-lait pigmentation and monthly spotting of blood. The parents had blamed it on witchcraft and had therefore gone to different churches for deliverance from the witchcraft. Cultural and religious beliefs are known to be a challenge to early presentation of endocrine conditions, and this may affect the outcome of treatment.[22] This underscores the need for public health enlightenment in the general population. The case of Implanon insertion in the patient's mother post-partum was the only incriminating history to explain the development of breasts in one infant in the cohort who presented with Tanner stage 3 breasts, pubic hair and spotting for three days. Unfortunately, the patient was lost to follow up, and we did not have even baseline hormone profile and radiological investigations to explain the cause of precocity or proceed further with treatment. The loss to follow-up is a common occurrence in our clinic and has been reported in literature,[22] because of poverty, cost of investigations and lack of health insurance coverage for most Nigerians. We cannot in all certainty say if the implant was associated with precocity since we did not investigate further and the implant is a progestogen, not known to cause PP in a breastfeeding child.

The mean age of patients with PPP (3.7 ± 3.2 years) and normal variants (3.34 ± 2.1 years) was notably lower than in CPP, reinforcing the diagnostic challenge clinicians face in evaluating pubertal signs in toddlers and preschool-aged children. This age pattern is consistent with other studies indicating that normal variants, particularly premature thelarche and adrenarche, often emerge in early childhood and may mimic true puberty.[10,23] In this review, premature thelarche and adrenarche were equally represented (each accounting for 25% of all precocious puberty cases), while no cases of premature menarche were recorded. The strong female predominance among those with normal variants further supports the established gender differences in pubertal

development and parental concern thresholds for evaluation.[20] The relatively high proportion (50%) of children presenting with benign pubertal variants emphasizes the need for a clinically discerning and judicious approach to the evaluation of early puberty. Over-investigation of such variants can strain already limited diagnostic resources and subject children to unnecessary procedures or interventions, whereas under-diagnosis risks delaying appropriate management in cases of true pathology. This diagnostic equilibrium is particularly crucial in sub-Saharan Africa, where access to paediatric endocrine expertise and advanced diagnostic infrastructure is often limited or unaffordable. The absence of GnRH stimulation testing highlights the challenges faced in resource-limited settings, where the cost and availability of essential diagnostic tools may affect precise classification.[22] Nonetheless, the integration of clinical, radiological, and baseline hormonal data provided a reasonable working diagnosis, guiding effective follow-up and supportive intervention. Despite the diagnostic limitations, clinical follow-up revealed encouraging outcomes. Most patients experienced stabilization or regression of breast development and normalization of height velocity for age. More so, most of the children had gone on to have normal pubertal development after the drugs were stopped and the final adult height within the target height according to their genetic potentials.

It was interesting to see that 96.6% of patients with PP were from the middle socioeconomic class. Previous studies have suggested socioeconomic status may influence the timing of puberty, possibly through factors such as nutrition, exposure to endocrine-disrupting chemicals, or psychosocial stress.[24] This high percentage may reflect both improved health-seeking behaviour and increased awareness among caregivers in this social class as well as easy access to specialist endocrinology services rather than a causal relationship of PP with socioeconomic class.

Conclusion

This study reveals that, while Central Precocious Puberty is the most common form encountered, a substantial proportion of children present with benign variants or rare but serious forms of peripheral precocity. The predominance of idiopathic CPP among females and the varied causes of PPP underscore the need for a structured diagnostic approach, tailored to the resource availability in African settings. Prospective multicentre studies, coupled with capacity-building initiatives in Paediatric Endocrinology and public education, are crucial to improving early diagnosis and management outcomes in the region.

Limitations of the study

While this study provides valuable insight, some limitations must be acknowledged. As a retrospective, hospital-based review, the findings cannot be extrapolated to the general paediatric population in terms of prevalence. A longitudinal study may therefore be necessary in the population and is recommended. Nevertheless, the predominance of female cases, the clustering in mid-childhood, and the high proportion from the middle class all align with patterns observed in similar populations and reinforce the need for continued clinician vigilance and public education. Another major limitation of this study was the inability to perform GnRH stimulation testing, which remains the gold standard for diagnosing Central Precocious Puberty. However, the clinical implication of this study is the fact that in resource-constrained environments, a combination of clinical evaluation, bone age assessment, pelvic ultrasound, and baseline hormonal profiling may offer a pragmatic alternative to full diagnostic workup.

Conflicts of interest

None declared

Ethical approval

Not applicable

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