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Original Article

Challenges, Clinical and Laboratory Profile of Children Referred for Micropenis at a Nigerian Tertiary Hospital

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Abstract

Background: Micropenis in a child may not only be related to cosmesis but raise the suspicion of a disorder of sex development or endocrine conditions requiring urgent attention. The study aims to describe the clinical and laboratory profile of children referred for micropenis over a six-year period at the Lagos University Teaching Hospital (LUTH) and highlight challenges encountered in management of these children.

Methodology: This was a retrospective study. Case records of patients who were referred with complaints or diagnoses of "micropenis" from March 2018 to March 2024 were analysed. The Health Research and Ethics Committee of LUTH approved the study.

Results: Eighty-three children were referred for micropenis. On review, the stretched penile length (SPL) in 16 children (mean [SD]age of 8.9± 3.42 years) was within reference ranges and they were excluded from further evaluations. The remaining 67 children with confirmed micropenis constituted 12.4% of 541 new paediatric endocrine cases. The median age (range) at presentation was 9(0.7-16) years. Boys within the peripubertal age group constituted the majority of the patients. Co-morbidities included obesity, Down Syndrome, sickle cell anaemia, and growth hormone deficiency. Challenges in management included unaffordability of laboratory tests as only 21 children (31.3%) performed the human chorionic gonadotrophin (hCG) stimulation, our local testing, more than half (68.6%) could not carry out any investigations and age-appropriate/ preparations of testosterone were unavailable for treatment.

Conclusion: Micropenis constituted a sizeable proportion of the paediatric endocrine consultations in our setting. Accurate measurements are important to exclude unaffected children and prevent unnecessary expensive investigations. The National Health Insurance Services (NHIS) should be strengthened to enable patients to access necessary investigations and treatment related to micropenis. Licensing of age-appropriate drugs for treatment by relevant authorities is advocated.

Keywords: Micropenis; Children; Stretched Penile Length; Testosterone.

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Introduction

Micropenis is defined as a stretched penile length (SPL) less than 2.5 standard deviations (SD) below the mean without any other penile anomalies. [1-3] It should be differentiated from a buried or hidden penis. [4] Accurate measurements are important to prevent misdiagnosis, considerable parental/child anxiety, and unnecessary investigations and treatment. [2,5] Micropenis may occur as an independent abnormality or as a clinical finding of many syndromes. A study in the United States of America over a three-year period documented the incidence of micropenis as 1.5 in 10,000 male newborns.[2]

Aetiology of micropenis can be broadly classified into pituitary/hypothalamic, primary testicular insufficiency, partial androgen insensitivity syndrome, and idiopathic. [1,2,4] Associated anterior pituitary hormone deficiencies such as growth hormone (GH) deficiency and/or adrenocorticotropic hormone (ACTH) deficiency may put the infant with micropenis at high risk for death due to hypoglycaemia or cortisol deficiency.[3] Micropenis may also raise the possibility of a disorder of sex development in a child. [1,3] Therefore, attention to micropenis is beyond cosmesis and may require urgency.

Endocrine evaluation of the hypothalamic-pituitary-testicular axis is helpful in the determination of the aetiology of micropenis. Serum levels of the anterior pituitary hormones are helpful. Testicular functions are also evaluated using the chorionic gonadotropin (hCG) stimulation tests as well as serum Antimüllerian substance (AMH) and inhibin B produced by the Sertoli cells of the testis. Magnetic resonance imaging (MRI) may be indicated if midline structural defects like pituitary stalk dysplasia syndrome are suspected. [1-3]

The primary treatment for micropenis involves administration of exogenous testosterone (topical or intramuscular) to increase the penile length. [1-3] Most Nigerian and West African studies have focused on measurements of penile lengths in newborns [5-12] with very few studies on penile length abnormalities beyond the neonatal period. [13,14] Therefore this study sought to describe the clinical and laboratory profile of all children referred for micropenis in the paediatric endocrinology clinic over a 6-year period.

Methodology:

This was a retrospective study in which data was extracted from the case records of all the patients aged from 0 to 18 years who were referred with complaints of "micropenis" to the paediatric endocrinology clinic of the Lagos University Teaching Hospital in March 2018 to March 2024. Demographic information and other information such as age at presentation, presenting complaints, duration of symptoms before presentation, investigation results, endocrine, and any treatment and management were extracted.

***Measurement of the penis*:** The stretched penile length had been determined by the glans of the penis being held between the thumb and forefinger and stretched perpendicular to the pubis. The distance from the pubic ramus to the tip of the penis was then marked off on a disposable wooden spatula. The shaft of the penis was stretched to the point of resistance and the suprapubic fat pad was compressed as completely as possible. The tip of the glans was marked on the spatula by a pen. A measuring tape was used to determine this distance from the marked point to the spatula's tip. [12]

The widely used age-appropriate penile length chart developed by Schonfeld and Beebe [15] was used.

Human chorionic gonadotropin (hCG) stimulation test for those who could afford it was performed by using the single dose protocol of intramuscular 5000IU/$m^{2,}$ after collection of baseline samples for testosterone (T) and dihydrotestosterone (DHT). Repeat blood samples were drawn 72 hours after the injection. [16,17]

The Health Research Ethics Committee of the Lagos University Teaching Hospital approved the study and waived the requirement for informed consent (ADM/DSCST/HREC/APP/6598). Data retrieved were collated and analysed with Microsoft Excel 2016 and presented as counts, frequencies, and percentages while continuous data were expressed as means ± standard deviation or median(range) as appropriate.

Results

Eighty-three children were referred for micropenis. Measurements revealed SPL within reference ranges in 16 children (19.2% of referred cases) with a mean (SD) age of 8.9± 3.42 years at presentation. Two of them were obese while one had associated gynaecomastia. One child had orchidopexy previously and parents were anxious about penile length. They were reassured and excluded from further evaluations.

The remaining 67 children with micropenis constituted 12.4% of 541 new paediatric endocrine cases seen over the period. There were no interventions in all the cases before referral to our centre. The median age (range) at presentation was 9(0.7-16) years.

Table 1 shows the summary of the age group at presentation of children with micropenis.

Age Group	Number	Percentage (%)
0-1month	1	1.5
>1month -1year	11	16.4
2years- 5years	9	13.4
6years-10years	24	35.8
>11years	22	32.8
Total	**67**	**100**

Boys within the peripubertal age group constituted the majority of the patients followed by the pubertal age group. The associated co-morbidities are depicted in Figure 1. Almost a fifth of the children with micropenis were obese. Other co-morbidities included Down Syndrome, sickle cell anaemia, and growth hormone deficiency.

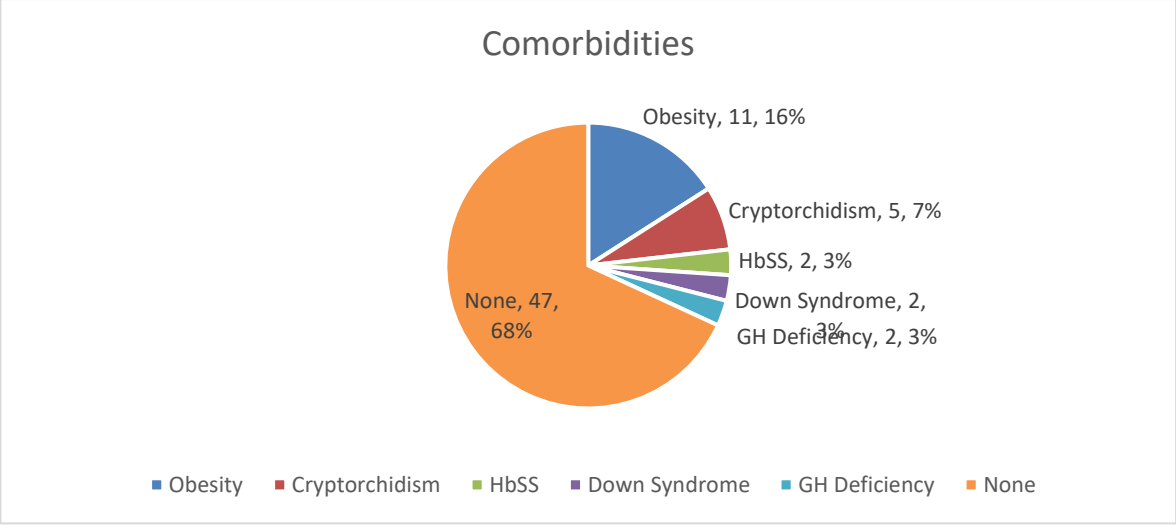

Fig 1: Comorbidities associated with micropenis

Only 21 children (31.3%) could afford the minimal necessary hCG stimulation testing. Fifteen (71.4%) boys showed a median increase of baseline serum testosterone nine times with a range of 4 to 26. These patients were reassured and are being followed up to monitor their penile growth until puberty is completed. There was no increase in serum testosterone in six patients with a median (range) age of 1.5 (0.75 -15) years. The testosterone/dihydrotestosterone (T/DHT) ratio in all 21 hCG-stimulated patients was normal with a median (range) value of 1.4 (0.27 to 5.33).

Table 2: Nigerian Studies of Stretched Penile Lengths (SPL) in the New-born

Authors/ Year of Publication	Sample size	Study location	Major Ethnicity	Mean ±(SD)SPL (cm)	-2.5SD (cm)	3rd centile (cm)	Recommendation of definition of micropenis by authors (cm)
Jarrett/ 2014 [6]	261	South-West	Yoruba	3.4 ±0.48	2.2	2.39	<2.39
Chikani/2014 [7]	811	South-East	Ibo	3.46±0.44	2.36	Not stated	<2.36
Elusiyan/2016 [5]	411	South-South	Not stated	3.17 ± 0.5	1.92	2.3	<2.3
Ogundoyin/2016 [8]	675	South-West	Yoruba	3.14±0.65	1.52	2.0	<2.0
Adekoya /2019 [9]	303	South-West	Not stated	3.94±0.42	2.89		Recommended a consensus on the definition
Kareem/2020 [10]	124	South-West	Not stated	3.2 ± 0.4	2.2	2.2	<2.2
Fagbuyi /2023 [11]	76	South-West	Yoruba	3.28±0.6	1.78	Not stated	<2.5

Two of the six patients with poor response to hCG testing responded positively (by an increase in penile length) to testosterone enanthate injections administered for 3 months and 9 months respectively. Two patients (who did not get testosterone injections or any other treatment) who have commenced puberty showed spontaneous penile length increase to the reference range for age. The remaining two are yet to attain puberty and are still being followed up.

Challenges of management of these patients included erratic availability of testosterone injections. Some of the available preparations in Nigeria are not licensed for younger children. Other challenges in management included the inability to afford the necessary laboratory tests by some patients as more than half (68.6%) could not carry out any investigations.

Discussion

Micropenis constituted a sizeable portion of the children referred for paediatric endocrine disorders. Two previous Nigerian studies [13,14] had reported on the epidemiology of micropenis. In Port Harcourt South-South Nigeria, Yarhere *et al,*[13] reported that micropenis constituted 2.2% (11males) of genital anomalies seenin 34 children over a five-year period. A cross-sectional study by Adekanye *et al,*[14] documented 27 cases (4.07%) of micropenis among 663 primary school male pupils in Bida, Noth-Central Nigeria. Micropenis constituted 11% out of the 240 children with abnormalities of the external genitalia and groin in the study. [14]

The age of presentation in the present study showed similarities with a previous Nigerian study [13] which reported a median age of 121months (10.1years) and a range of 9-168months. A Korean study [18] documented a similar mean age at first presentation of 9.8 years (5-12 years). This age group of 9 -10 years represents the peri-pubertal period when body image becomes important to many males.[19] They

are also likely to compare themselves with peers and get anxious. Likewise, some parents who had hoped that the length of the penis will improve with time from the neonatal period (when they first noticed the smallness in length) may get worried and seek medical attention for their children. Other parents have also volunteered that they became concerned about seeing that the younger brothers of the affected child have surpassed them in penile length.

Obesity was a co-morbidity observed in some of the children with micropenis in our study. Likewise, a large Italian cohort study by Marcini *et al* [20] involving 1130 participants monitored from birth to age 20 years reported that growth of the penis was significantly reduced by a tenth in obese boys relative to boys who had normal weight. The study also noted decreased testosterone levels across the different stages of puberty. [20]

Another co-morbidity noticed in the patients was cryptorchidism. Ryu et al [21] documented significantly shorter SPL in children with cryptorchidism compared to a cohort of healthy Korean boys aged 6–24 months. Trisomy 21 was noted in two of our patients as has been described in patients with autosomal or sex chromosomal aneuploidies and other genetic syndromes.[3]

A retrospective South-Korean study of 27 boys with micropenis noted that there was no statistical significance between the mean increment of SPL in the group who received hormonal therapy and those who did not. [18] Our study also noted that two boys who never got any hormonal treatment had achieved an increase in penile length to the reference range as they commenced puberty. This may raise the question regarding ensuring hormonal intervention since some children will achieve normal penile length at puberty. However, most authors [3,18] still advocate for short-term hormonal therapy for micropenis since this has not shown any adverse effects in adolescence and adulthood but rather improved psychosocial outcomes in some patients. [3] Almost a fifth of the children who were referred for micropenis to our centre were found to have SPL within reference ranges. This raises discussions about what is termed normal penile length by different clinicians and in different ethnicities.

In our setting, Nigeria where a lot of studies [5-11] had been done on SPL in newborns, there are marked differences even within the same ethnic groups as shown in Table 2. The majority (5 out of 7) of these studies [6,8-11] were carried out in South- West Nigeria involving majorly children from the Yoruba ethnic group (even where not stated, many of the inhabitants of these locations belong to the Yoruba ethnic group) reported varying mean SPL of 3.14 to 3.94cm. The reasons for the differences are not obvious but may be related to techniques of measurements, or the peculiarity of the sample population.

Other country-specific studies have shown some variations in penile lengths even within the same country, which results in different values of SPL being regarded as -2.5SD.[22-25] Additionally, within commonly used charts, mean penile lengths have not shown a natural geometric progression which is likely due to the cross-sectional nature of each study and /or population.[15,22] Adequately powered longitudinal studies in different ethnicities will help in establishing reference penile lengths which may be more representative, especially beyond the neonatal period.

Limitations:

The study is limited by its retrospective nature, poor availability and inability of clients to pay for comprehensive hormonal investigations (AMH, inhibin among others). The use of imaging modalities like MRI and genetic testing which would have aided the determination of specific aetiology of micropenis in some of the patients was also limited.

Conclusion

Micropenis constituted a sizeable proportion of the paediatric endocrine consultations in our setting. Accurate measurements are important to exclude unaffected children and prevent misdiagnosis, undue anxiety for both children and parents, and unnecessary expenses on investigations. Efforts should be made to establish normative values of SPL across all ages in childhood in various ethnicities in Nigeria using longitudinal studies. Obesity and cryptorchidism were associated with co-morbidities. Delayed diagnosis and treatment may have dire medical and psychological consequences. National Health Insurance Services (NHIS) should be strengthened to enable patients to access necessary investigations and treatment related to micropenis. The licensing of age-appropriate drugs for treatment by relevant authorities is advocated.

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