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Paediatric endocrine disorders at a tertiary hospital in Lagos, Nigeria

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Abstract: *Background:* The global increase in paediatric endocrine disorders (PED) is thought to be a result of multiple factors including changing lifestyles, environmental pollution and increasing awareness and diagnostic capabilities. Studies on the prevalence of paediatric endocrine disorders in the developing world are few. A preliminary audit of PED at the Lagos State University Teaching Hospital two years ago revealed type 1 diabetes mellitus as the commonest diagnosis. Since then many more children with PED continue to be referred from various centres.

Objective: The aim of the present study was to describe the burden and pattern paediatric endocrine disorders over a three-year period. *Subjects and Methods:* Records of patients who presented in the paediatric endocrine unit between March 2017 and March 2020 were reviewed and relevant data on age at presentation, sex and diagnosis were extracted.

Results: A total of 172 patients representing 0.45% of the total paediatric patients seen within the period. There were more females 90(52.3%) than males 79(45.9%) and three patients (1.7%) presented with disorders of sexual differentiation. Age of presentation ranged between 11 days and 16 years with mean of 6.27 ± 4.5 years.

The commonest groups of endocrine disorders were disorders of pancreas/lipids-diabetes (n=33, 19.2%), pubertal disorders (n=25, 14.5%) and thyroid disorders (n=24, 14.0%).

Conclusion: Our unit witnessed a comparatively larger case-load of PEDs compared to earlier reports from other parts of Nigeria. Diabetes mellitus, pubertal and thyroid disorders constituted the commonest paediatric endocrine disorders encountered.

Key words: Diabetes, Goitre, Hypothyroidism, Precocious Puberty, Africa

Introduction

Globally, burden and pattern of paediatric endocrine disorders (PED) described as hormonal disorders of childhood and adolescence, are on the increase, attributable to changing lifestyles, environmental pollution and improving diagnostic capabilities.¹ PED comprise a wide range of conditions including diabetes, disorders of growth and puberty, disorders of thyroid function and sexual development, disorders of the adrenals, calcium and bone metabolism as well as obesity and its complications.¹ Most of these disorders manifest as a result of an under or over-activity of specific hormone(s) or reduced sensitivity of tissues to their effect.²

While developed countries have widely documented the population incidence and prevalence of PED such as congenital adrenal hyperplasia,^{3,4} congenital hypothy-

roidism^{5,6} and diabetes mellitus (DM),^{7,8} there are relatively fewer, mostly hospital-based, prevalence studies of the burden and pattern of PED in the developing world. However, following the development of the paediatric endocrinology sub-specialty and capacity-building programmes in Africa,⁹ more studies have emerged from sub-Saharan African countries like Nigeria, showing that the commonest PED are pubertal disorders,¹⁰ rickets,¹¹ and diabetes;¹² these studies however suggest that the pattern of PEDs may vary among different geographical regions of Nigeria.

In South Africa, the burden of disorders of sexual differentiation (DSD) has been well documented.¹³ A preliminary audit of the burden and pattern of paediatric endocrine disorders (PED) over an 18-month period in the paediatric endocrinology unit showed that the commonest PED was diabetes mellitus.¹⁴ The main objective of

the study was to describe the burden and pattern paediatric endocrine disorders over a three-year period. The study is expected to provide a more representative descriptive picture that will serve as baseline data and guide planning and allocation of scarce resources at institutional or national levels.

Subjects and Methods

The study was a retrospective study of all children seen and managed with suspected paediatric endocrine disorders (PED) at the paediatric endocrinology unit of the Lagos State University Teaching Hospital (LASUTH). The centre serves as a major referral centre for public and private hospitals within Lagos and adjoining states. Data including age at presentation, gender, clinical features, and diagnosis of children with PEDs between March 2017 and March 2020 were extracted from the clinic register and patients' case notes. Patients were referred, on suspicion of endocrine disorders to the unit from paediatric outpatient clinics and paediatric specialist units of our centre and from other public and private hospitals. Diagnoses were made using a combination of clinical features and laboratory investigations. Facilities for radiological and most chemical investigations were available at the hospital laboratory. Where the hospital did not have the facilities to carry out serological investigations, two private laboratories with international standard filled in the gap. In this study, diagnoses were further classified according to the International Classification of Pediatric Endocrine Diagnosis-ICPED.¹⁵ Ethical clearance for the study was obtained from the Health and Research Ethics Committee of the LASUTH. Data was analysed with Microsoft Excel 2013 version (Microsoft Inc., USA) and SPSS version 23 (IBM Inc., USA). Continuous variables were summarised with mean (with standard deviation, SD) or median (with interquartile range, IQR) if skewed. Categorical variables were expressed as frequencies and percentages.

Results

A total of 172 patients with PED presented and were seen over the three-year period. This represents 0.45% of the total number of new cases registered in the paediatric outpatient clinics in the time period [38,031(20,484 - male, and 17,547 - female)]. Of the study subjects, there were more females (n=90, 52.3%) than males (n=79, 45.9%) whilst three (1.7%) could not be gender-assigned at the time of presentation. The ages ranged from 11 days and 16 years, with a mean of 6.27 ± 4.5 years. There was a slight reduction in the number of cases in the second year and the highest number of cases was seen in the third year of review (Figure 1). As shown in Table 1, the commonest groups of PED were disorders of pancreas/lipids (33/172, 19.2%), and pubertal disorders (25/172, 14.5%) and thyroid disorders (24/172, 14%). They also presented mostly in the age group of 6 to 11 years (Table 2).

The endocrine disorders affecting the youngest age groups in this cohort were ovarian/female tract disorders, sex development and gender disorders and disorders of puberty while those with pancreas/lipid disorders, on average, affected pre-adolescents and adolescents. There were at least five times as more females with thyroid and pubertal disorders than there were males, and there were twice as more males than females with disorders of energy balance (obesity) (Table 1).

Of those diagnosed with diabetes, the commonest was Type 1 diabetes mellitus (T1DM) constituting 72.7%. Overall, T1DM was also the commonest specific diagnosis constituting 14.0% of PED. Simple/multinodular goiter, eight (33.3%) and congenital hypothyroidism, seven (29.2%) were the commonest diagnoses of the thyroid disorders. Down syndrome represented about two thirds (62.5%) of syndromes with endocrine features of congenital hypothyroidism.

Table 1: Distribution of Paediatric endocrine disorders

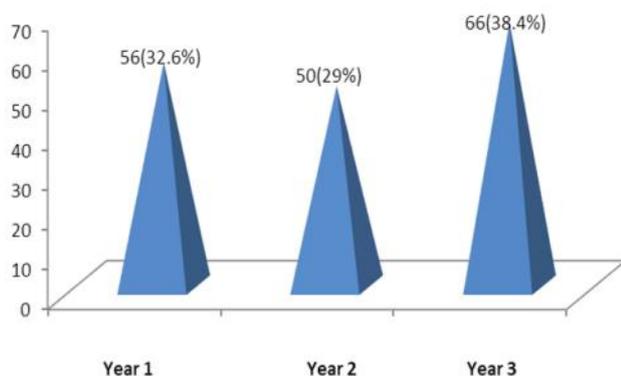
| ICPED Class/Specific diagnosis | N (%) | Sex (F:M) | Age range (Years) | Mean age at presentation SD(Years) |
|--|-----------|-----------|-------------------|------------------------------------|
| Disorders of Pancreas/Lipids | 33 (19.2) | 1.5:1 | 2.0-16.0 | 9.8 ± 3.5 |
| T1DM | 24 | | | |
| T2DM | 6 | | | |
| Steroid-induced diabetes | 3 | | | |
| Thyroid disorders | 24 (14.0) | 5:1 | 0.08-12.0 | 6.3 ± 4.5 |
| Simple/multinodular goitre | 8 | | | |
| Hypothyroidism | 7 | | | |
| Grave's disease | 3 | | | |
| Thyroiditis | 3 | | | |
| Hyperthyroidism | 2 | | | |
| Thyroglossal cyst | 1 | | | |
| Puberty disorders | 25 (14.5) | 3:1 | 0.6-12.0 | 2.41±2.79 |
| Precocious puberty | 16 | | | |
| Precocious thelarche | 4 | | | |
| Delayed puberty | 1 | | | |
| Non-pathologic | 4 | | | |
| Adrenal disorders | 15 (8.7) | 2:1 | 0.03- 12.0 | 5.62 ± 3.87 |
| Premature adrenarche | 13 | | | |
| Congenital adrenal hyperplasia | 1 | | | |
| Virilizing Adrenal tumor | 1 | | | |
| Syndromes with endocrine disorders | 16 (9.3) | 1:1.5 | 0.1- 11.0 | 6.03±3.55 |
| Down syndrome | 10 | | | |
| Multiple congenital anomalies | 3 | | | |
| Turner syndrome | 1 | | | |
| Russel-Silverman syndrome | 1 | | | |
| Kallman syndrome | 1 | | | |
| Testicular/male reproductive tract disorders | 17 (9.8) | 0: 17 | 0.2- 11.0 | 7.26±4.23 |
| Micropenis | 10 | | | |
| Absent/atrophic testes | 7 | | | |
| Disorders of energy balance | 13 (7.6) | 1:2 | 0.7-12.0 | 8.11±4.20 |
| Obesity | 13 | | | |
| Sex development/Gender disorders | 9 (5.2) | 1:1.3 | 0.1- 7.0 | 2.08±3.26 |
| DSD | 8 | | | |
| Hypospadias | 1 | | | |
| Growth disorders | 6 (3.5) | 1:2 | 1.4-12.0 | 5.36±3.94 |
| Achondroplasia | 3 | | | |
| Short stature | 3 | | | |
| Pituitary/Hypothalamic disorders | 3 (1.7) | 2:1 | 8.0- 12.0 | 10.66±2.30 |
| MPHD | 2 | | | |
| Cushings disease | 1 | | | |
| Ovarian/female tract disorders | 2 (1.2) | 2:0 | 1.6-2.0 | 1.79±0.29 |
| Absent vagina/Vaginal atresia | 2 | | | |
| Calcium, phosphate metabolism and bone disorders | 1 (0.6) | 1:0 | 4 | 4 |
| Blount disease | 1 | | | |
| Others (non-classified) | 8 (4.7) | 1:3 | 0.04- 15.0 | 5.24±5.88 |
| Infants of mothers with endocrine disorders | 5 | | | |
| Hypoglycaemia | 3 | | | |
| Total | 172 | | | |

ICPED: International Classification of Pediatric Endocrine Disorders; N: number of cases under each class; SD: standard deviation; F: M- female/male ratio; N: number of cases; T1DM: Type 1 diabetes mellitus; T2DM: Type 2 diabetes mellitus; DSD: disorders of sex differentiation; MPH: multiple pituitary hormone deficiency

Table 2: Frequency of disorders according to age groups

| | <2years | 2-5years | 6-11years | 12years | Total n (%) |
|--|----------|----------|-----------|----------|-------------|
| Disorders of Pancreas/Lipids | 0(0.0) | 4(12.1) | 17(51.5) | 12(36.4) | 33(100) |
| Thyroid disorders | 5(20.9) | 2(8.3) | 11(45.8) | 6(25.0) | 24(100) |
| Puberty disorders | 2(8.0) | 6(24.0) | 14(56.0) | 3(12.0) | 25(100) |
| Adrenal disorders | 2(13.3) | 4(26.7) | 8(53.3) | 1(6.7) | 15(100) |
| Syndromes with endocrine disorders | 12(75.5) | 2(12.5) | 2(12.5) | 0(0.0) | 16(100) |
| Testicular/male reproductive tract disorders | 3(17.6) | 4(23.5) | 10(58.9) | 0(0.0) | 17(100) |
| Disorders of energy balance | 2(15.4) | 1(7.7) | 8(61.5) | 2(15.4) | 13(100) |
| Sex development/Gender disorders | 5(55.6) | 2(22.2) | 2(22.0) | 0(0.0) | 9(100) |
| Growth disorders | 2(33.3) | 1(16.7) | 2(33.3) | 1(6.7) | 6(100) |
| Pituitary/Hypothalamic disorders | 0(0.0) | 0(0.0) | 1((33.3) | 2(66.7) | 3(100) |
| Ovarian/female tract disorders | 1(50.0) | 1(50.0) | 0(0.0) | 0(0.0) | 2(100) |
| Calcium, phosphate metabolism and bone disorders | 0(0.0) | 1(100.0) | 0(0.0) | 0(0.0) | 1(100) |
| Others | 5(62.5) | 2(25) | 1(12.5) | (0.00) | 8(100) |

Fig 1: Yearly distribution of Paediatric endocrine cases



Discussion

In this retrospective review, 172 cases of PED were seen, with the commonest being diabetes mellitus, thyroid disorders and pubertal disorders. The study embodies the experience of a tertiary specialist referral centre located in a megacity, and is useful in planning and advocating for local paediatric endocrinology services including the allocation of limited resources.

Our data showed that our unit managed a comparatively larger number of PED compared with previous reports from other parts of Nigeria. About two to five times more cases presented to the paediatric endocrine unit within the three-year study period than the total cases of PED that presented in other units within Nigeria with a longer study period of between eight and ten years.^{11,12,16}

While we managed a total of 172 PED in three years, Oluwayemi over an 8-year period in Ekiti,¹¹ Onyiriuka *et al* over 10 years in Benin¹² and Jarrett *et al* over eight years in Ibadan,¹⁶ managed 110, 99, and 52 children with PED respectively. The relatively higher case-load in our facility possibly reflects the fact that Lagos is a highly populous megacity compared to the aforementioned cities. This may be buttressed by a similarly comparatively large case-load of PEDs at a sister tertiary

paediatric endocrinology clinic in Lagos where Oyenusi *et al* reported that 546 children with PED were seen over 10 years.¹⁷ The decrease observed in the number of patients who presented in the second year under review may have been due to industrial action by health care workers. We cannot exclude the possibility of a true increase in the incidence and prevalence of PEDs in our setting as there were no previous studies carried over a similar or longer period of time for comparison. Increase in PEDs has been attributed to true increase in the incidence due to changing genetic and environmental factors like pollution. Also, increased referral of cases of PEDs to tertiary units like ours may arise from increasing awareness and availability of paediatric endocrinology expertise (which had lagged profoundly behind adult endocrinology services until in the last decade when local sub-specialist trainings were commenced).¹⁸ It is probable that higher levels of education in care givers in the cosmopolitan city of Lagos led to improved health-seeking behaviour to appropriate health care facilities.

Similar to a report from Benin City by Onyiriuka *et al*,¹² T1DM was the commonest PED in our clinic. This contrasted with reports of rickets and metabolic disorders as the commonest PED in the studies by Jarrett *et al* in Ibadan¹⁶ and Oluwayemi *et al* in Ekiti.¹¹ This disparity is most likely due to the alluded fact that in some centres including ours children with rickets are seen at the Paediatric Gastroenterology unit being partly a nutritional disorder and also at orthopaedic clinics. A similar observation may hold for obesity. Disorders of pancreas and lipids were the most frequently encountered group with the majority being due to T1DM. Children with T2DM constituted about one fifth of those with DM in the current study. Compared to earlier reports from Nigeria in which cases of T2DM were either absent¹⁶ or fewer,¹² this may suggest a possible new trend in PED in Nigeria in view of the rising global diabetes epidemic which involves adult and children.¹⁹ Clinicians need to be aware of this trend so that they can evaluate children with diabetes more thoroughly rather than assume that T2DM only occurs in adults. Steroid-induced diabetes was also observed as a cause of diabetes in the current

study. Since it is an established fact that this complication may arise from prolonged steroid use,²⁰ children who are placed on steroids for long periods should be screened periodically for hyperglycaemia, rather than wait for overt symptoms of diabetes to occur.

There were slightly more females compared with males in the current review. This is similar to the pattern reported in Ekiti,¹¹ Port Harcourt¹⁰ and Benin¹², but differed in the review from Ibadan.¹⁶ The higher number of females in our study may be explained in part by the fact that thyroid disorders (which constitute the third largest group in our study) occur more commonly in females. Thyroid problems are common PED.²¹ Congenital hypothyroidism constituted a significant proportion of the diagnosis in this group, in a setting where newborn screening is not routinely carried out. There is a high probability that the introduction of newborn screening programme for congenital hypothyroidism will result in diagnosis of more babies with this condition as is the case in many parts of the world including Saudi Arabia.²² The group of pubertal disorders was one of the commonest groups of PED in our study. This is not surprising because puberty is a major developmental stage²³ and a main cause for concern by parents when it occurs early or late. Our report reflects that early puberty is one of the main causes of referrals to paediatric endocrinolo-

gists.²⁴ Gender disorders presented at a lower mean age than diabetes and thyroid disorders. This is not surprising as disorders of congenital origin are known to present earlier than acquired disorders.

Conclusion

In conclusion, our study has reported higher numbers of PEDs than other previous Nigerian studies with T1DM as the leading diagnosis, along with pubertal and thyroid disorders. Although the retrospective nature of our report is a limitation due to relatively poorer data quality of retrospective reviews compared to prospective studies, the baseline data is useful for planning PED care at institutional and national level and also for advocacy for resource allocation for PED. The absence of data on mode of presentation and outcomes such as death and loss-to-follow-up also warrant the need for future prospectively designed study. Even more importantly, there is need for multi-centre prospective studies and population-based studies including registries which will provide better epidemiologic profiles of PED in Nigeria.

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