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Retrospective Survey of Pediatric Diabetics at a Tertiary Healthcare Center in Uyo, South-South Nigeria

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Abstract: *Purpose*: Despite the high prevalence of diabetes mellitus (DM) reported among adult Uyo inhabitants in south-south Nigeria, no data exist on pediatric DM (PDM) to date. Hence, the current study aimed to evaluate pediatric subjects diagnosed with DM in Uyo, South-south Nigeria. *Methods*: This was a retrospective survey of incident/newly diagnosed PDM subjects diagnosed/managed over 15 years (2003-2018) at the University of Uyo Teaching Hospital (UUTH), South-south Nigeria. Patients' demographic, clinical, and laboratory variables at PDM diagnosis were retrieved from medical records and analyzed using descriptive statistics. *Results*: 45,551 pediatric cases were managed during the studied period among them 9 PDM cases, all of type 1 DM, giving PDM prevalence of 0.20/1000. Age at diagnosis was 7.00±4.82 years (range 2-16) with a predominance of ≤5-year-olds (44.4%) and females (66.6%). Most (77.8%) presented via the pediatric outpatient clinic, during the rainy season (55.6%), were urban-dwellers (55.6%), of Ibibio ethnicity (55.6%), and lower socioeconomic status (44.4%). Three (33.3%) had DM family history, mostly in first-degree (n=2) relatives. Predominant symptoms were polyuria (100%), polydipsia (100%), weight loss (88.9%), and weakness (77.8%); polyuria being the most prolonged symptom. Three (33.3%) were underweight/stunted, and 2 (22.2%) were overweight. DKA complicated with AKI and dehydration-induced AKI was recorded in 2 respective cases. The default rate to follow-up was discouragingly high following diagnosis. *Conclusion*: The prevalence rate of PDM was relatively low, occurred mostly among the ≤5-year-olds, with a high rate of default to follow-up. These findings could serve as health policy targets by various stakeholders within the studied region.

Keywords: Diabetes, Pediatric Diabetes, Pediatric Type 1 Diabetes

1. Introduction

In parallel to the increasing global burden of diabetes mellitus (DM) among the adult populations in recent times, the burden of the disease among the pediatric populations has also posed a major public health concern. [1] Consequently, recent epidemiologic evidence has documented an increasing burden of the metabolic disorder among the pediatric age-group with regards to the disease incidence, prevalence, morbidity, and overall mortality. [1-3]

Historically, type 1 DM (T1DM) was adjudged as the predominant pediatric age-group DM type, however, recent findings also indicate an increasing trend of type 2 DM (T2DM) among the pediatric populations. [3, 4] Etiologically, while TIDM undoubtedly has genetic attributes in association with some environmental triggers, the global overweight and obesity epidemic has been linked with the rising T2DM burden among the pediatric age-group populations. [1]

In Nigeria, a similar trend of worsening DM epidemiologic indices, especially of the T1DM variant, among the pediatric populations has also been reported from different regions of

the country in few published data. [5-13]

Uyo, the capital city of Akwa Ibom State in the Southern part of Nigeria, has been reported to have one of the highest adult DM prevalence rates in the country. [14, 15] However, no published data to date has been documented on DM among the pediatric populations in Uyo, South-south Nigeria. Hence, the current study aimed to evaluate subjects diagnosed with pediatric DM (PDM) in the University of Uyo Teaching Hospital, South-south Nigeria.

2. Materials and Methods

2.1. Design and Site

This study is a retrospective, descriptive, and cross-sectional hospital-based review of records of pediatric subjects diagnosed with DM over 15 years (2003-2018) at the University of Uyo Teaching Hospital (UUTH). UUTH is a tertiary medical facility located in Uyo, Akwa Ibom State, South-south Nigeria. The hospital is a major referral center for the primary, secondary, and other privately-owned healthcare facilities in Akwa Ibom State and its neighboring states. The hospital is well-equipped and adequately-staffed with various specialized Departments (outpatient, family medicine, internal medicine, obstetrics/gynecology, chemical pathology, pediatrics, health information management, etc).

2.2. Ethical Considerations

The study protocols conformed to the ethical guidelines of the 1975 Declaration of Helsinki and ethical approval was obtained from the Research Ethical Committee of UUTH. Written informed consent was waived owing to the solely data-based design of the study. All data was anonymized and treated with the utmost confidentiality. Permission was also obtained from the heads of relevant departments before commencement.

2.3. Study Instruments

The study instruments consisted of updated hospital data of each case in the Department of Health Information Management of UUTH of all eligible PDM patients within the study period.

2.4. Eligibility Criteria

The criteria for inclusion included records of pediatric diabetic patients aged ≤18 years of age who were diagnosed and managed, including those referred and later confirmed, in UUTH between the 1st of January 2003 and 31st December 2018. The criteria for exclusion included records of those with incomplete data and records of DM cases who are older than 18 years, pregnant patients, and those diagnosed outside the study period.

2.5. Data Acquisition

Relevant data were acquired from medical records from the Department of Health Information Management using the trained resident doctors from the Department of Chemical Pathology as research assistants.

The variables which data was collected at DM diagnosis included the followings: the number of all pediatric cases seen within the study period, number of PDM cases, DM type, age, sex, place of residence, tribe, educational/occupation of patients if any, occupation of parents/guardians, social class of parents/guardians, family history of diabetes, month diagnosed, year diagnosed, mode of presentations, weight at diagnosis, height at diagnosis, calculated height for age (HA), weight for age (WA), weight for height (WH) and body mass index (BMI) Z scores, clinical features (symptoms/signs), duration of clinical features, vital signs (temperature, heart and respiratory rates), co-morbid conditions, glycemic status, and urinalysis (glucose, proteins, ketones, blood, PH, specific gravity) findings. Survey pro forma with columns under the earlier mentioned major variable headings was utilized for the data acquisition from all the identified eligible PDM cases.

2.6. Specimen Collection/Biochemical Determinations

During the study period, all specimen collection and biochemical analysis had been done based on standard protocols and guidelines. Plasma glucose and the urine biochemical parameters were determined using the glucose oxidase/peroxidase principle and dipsticks, respectively.

2.7. Data Definitions and Stratifications

In the study center, the diagnosis of PDM is made by the specialist pediatricians based on the International Society for Pediatric and Adolescent Diabetes (ISPAD) consensus guidelines. [1]

In the current study, identification of TIDM cases was based on a detailed review of medical history, patient characteristics, classics clinical features (polyuria, polydipsia, polyphagia, weight loss, etc), laboratory findings, persistent usage of, and response to, insulin therapy for at least a year following diagnosis.

Diabetic ketoacidosis (DKA) was diagnosed in the presence of hyperglycemia of >11.1mmol/l, plasma bicarbonate level of <15mmol/l with ketonuria based on the ISPAD guidelines. [16]

Acute kidney injury (AKI) was defined by the Kidney Disease/Improving Global Outcomes (KDIGO) serum creatinine criteria. [17] The baseline creatinine was determined following the steps detailed by Hursch et al. [18]

Anthropometric Z scores were determined using the World Health Organization (WHO) recommended computer software [19, 20] The WHO Anthro for personal computer software version 3.22 was used for age-group 0-5 years. [19] While the WHO AnthroPlus for personal computer software version 1.04 was used for the age-group 5-18 years. [20] The Z scores were stratified based on the WHO guidelines. [19, 20]

HA Z score was stratified as normal (> -2), moderately stunted (-3 to ≤ -2), and severely stunted (≤ -3.0) among the age-groups 0-5 and 5-18 years. WA Z score was stratified as normal (> -2), moderately underweight (-3 to ≤ -2), severely underweight (≤ -3.0) among the age-group 0-10 years. WH Z

score was stratified as normal (> -2 to ≤ +1), moderately wasted (-3 to ≤ -2), severely wasted (≤ -3), overweight (+1 to ≤ +2), and obese (≥ +2) among the age-group 0-5 years. BMI Z score was stratified as eutrophic (> -1 to ≤ +1), moderately wasted (-3 to ≤ -2), severely wasted (≤ -3.0), overweight (+1 to ≤ +2), and obese (≥ +2) among the age-group 5-18 years.

The socio-economic status (SES) of parents and/or their guardians was determined using the highest educational attainment and occupation of both parents/guardians based on the protocols detailed by Oyedeji et al. [21] SES 1 and 2 were considered high, SES 3 as middle, and SES 4 and 5 as low.

Season of diagnosis was defined as rainy (April to September) or dry (October to March) seasons based on southern Nigerian climate season expression as recently described by Tamunopriye et al. [10]

Dehydration was categorized as mild, moderate, and severe grades based on the guidelines recommended by the American Academy of Pediatrics. [22]

Age was arbitrarily stratified into four age-groups (≤5 years, 6-10 years, 11-15 years, and ≥16 years).

Default to follow-up was defined as permanently missing clinic appointments following discharge from the hospital or following the last clinic visit exclusive of death or referral to other clinics within/outside of the hospital.

2.8. Data Handling and Analysis

Data was initially inputted into Statistical Package for Social Science software version 21 (IBM Corp., Armonk, NY, USA). Thereafter, the inputted data was reviewed, properly validated, coded, transformed into a specially designed template to be ideal for the computer input process, and subsequently analyzed using simple descriptive statistics.

3. Results

During the studied period (2003-2018), 45,533 pediatric cases were managed through various units in the study center with nine (9) cases of PDM diagnosed, giving an overall PDM prevalence of 0.20/1000. All nine (100%) identified PDM cases were of TIDM type.

The mean (±SD) age and random plasma glucose (RPG) at presentation were 7.00±4.82 (range 2-16 years) and 17.82±4.37 (range 13.3-23.40 mmol/l), respectively (Table 1). Results of the descriptive statistics of the other metric variables (heart rate, respiratory rate, and temperature) are depicted in Table 1.

Depicted in Table 2, the majority of the diagnosed TIDM cases were females (n=6; 66.7%), presented mostly through the clinic unit (n=7; 77.8%) and diagnosed during the rainy season (n=5; 55.6%) of the southern Nigerian climate expression (Table 2). The majority of the cases were ≤5 years (n=4; 44.4%) of age, dwelt in the urban center (n=5; 55.6%), and of Ibibio ethnic group (n=5; 55.6%) (Table 2). DM history in a family relative was reported by 33.3% (n=3) of the cases of which 66.7% (n=2) and 33.3% (n=1) were of first-degree and second-degree relatives, respectively (Table 2).

Most (n=4; 44.4%) of the parents/guardians of the nine (9) cases were of lower SES at diagnosis (Table 2). Dehydration was recorded among 8 (88.8) of the cases with 4 (44.4%) each of moderate and severe grades, respectively (Table 2). UTI (n=2; 22.2%) was the most pronounced co-morbid condition reported. Of the 2 (22.2%) cases presenting at the emergency unit, one was diagnosed with DKA complicated by AKI, while the other had dehydration-associated AKI (Table 2).

Of the seven (7) who presented/diagnosed in the clinic, 6 (66.7%) defaulted from clinic appointments following DM diagnosis (Table 2). Of the two (2) who presented through the emergency unit, one (1) who presented in DKA complicated with AKI was lost to follow-up following discharge to the endocrine clinic, while the other with dehydration-associated AKI opted for discharge against medical advice (DAMA) and was also lost follow-up (Table 2).

Depicted in Table 3, 100% (n=9) of the cases presented with polyuria/polydipsia, seconded by generalized body weakness (n=8; 88.9%), and weight loss (n=7; 77.8%) (Table 3). The duration of polyuria (mean: 43.78±8.58; range: 7-84 days) was the highest and most prolonged compared to other reported symptoms at diagnosis (Table 3).

In Table 4, 5 (55.6%) of the diagnosed cases had various abnormal anthropometric parameters at diagnosis. One (1) was moderately wasted and severely underweight/stunted, one (1) was moderately underweight/stunted, one (1) was severely stunted, while two (2) were overweight for age/sex (Table 4). Hence, three (33.3%) were concurrently underweight/stunted while the other two (22.2%) were both overweight.

Table 1. *Baseline clinical/laboratory variables at diagnosis.*

Variables	n (%)	M±SD	Range
Age, years	9 (100)	7.00±4.82	2-16
Temperature,°C	9 (100)	37.48±0.99	36.4-37.48
Heart/pulse rate, bpm	8 (88.9)	89.56±5.90	79.0-138.0
Respiratory rate, cpm	9 (100)	23.22±6.49	14.00-37.00
RPG, mmol/l	9 (100)	16.72±3.83	13.30-23.40

SD: standard deviation; RPG: random plasma glucose; bpm: beats per minute; cpm: cycles per minute; mmol/l: milimole per liter.

Table 2. *Distributions of the clinical/demographic stratifications at diagnosis.*

Variables	Stratifications	N	%
Mode of presentation	Via emergency unit	2	22.2
	Via clinic unit	7	77.8
Season of DM diagnosis	Dry	4	44.4
	Rainy	5	56.6
Gender	Male	3	33.3
	Female	6	66.7

Variables	Stratifications	N	%
Age-groups, years	≤5	4	44.4
	6-10	3	33.3
	11-15	1	11.1
	≥16	1	11.1
Place of residence	Rural	4	44.4
	Urban	5	55.6
Ethnic groups	Ibibio	5	55.6
	Annang	2	22.6
	Efik	1	11.1
	Igbo	1	11.1
DM family history	Negative family history	6	66.7
	Positive family history	3	33.3
Degree of positive DM family history	First-degree relative	2	66.7
	Second-degree relative	1	33.3
Parents'/guardians' SES	Higher	2	22.2
	Middle	3	33.3
	Lower	4	44.4
Dehydration status	None	1	11.1
	Moderate	4	44.4
	Severe	4	44.4
Co-morbid conditions	Pneumonia	1	11.1
	UTI	2	22.2
	Malaria	1	11.1
	Gastroenteritis	1	11.1
Complications	DKA complicated with AKI	1	11.1
	Dehydration-induced AKI	1	11.1
Outcome	Default to clinic follow-ups	6	66.7
	DAMA	1	11.1
	Discharged, thereafter lost to follow-up	1	11.1

DM: diabetes mellitus; SES: socioeconomic status; UTI: Urinary tract infection.
DKA: Diabetic ketoacidosis: AKI: Acute kidney injury; DAMA: Discharged against medical advice.

Table 3. *Presenting symptoms at diagnosis.*

Symptoms	n	%	Duration of symptoms, day Mean±SD	Range, duration of symptoms, days
Polyuria	9	100	43.78±8.58	7-84
Polydipsia	9	100	27.11±3.79	5-56
Weakness	8	88.9	13.78±3.80	3-21
Weight loss	7	77.8	30.29±4.74	14-56
Vomiting±nausea	5	55.6	4.70±2.1	1-7
Abdominal pain	5	55.6	5.20±1.66	2-10
Polyphagia	4	44.4	35.50±7.84	14-56
Fever	4	44.4	4.50±1.90	3-7
Breathlessness	2	22.2	2.00±1.40	1-3
Altered sensorium	2	22.2	5.00±2.20	3-7
Enuresis	2	22.2	17.50±4.84	7-28

SD: standard deviation.

Table 4. *Anthropometric parameters at diagnosis.*

S/N	Gender	Age, yrs	Wt, kg	Ht, cm	HAZ	WAZ	WHZ	BMIZ
1	F	2	6.6	60	-5.39	-4.70	-2.44	-1.59
2	F	2	11.0	85	-1.03	-0.69	-0.22	-0.11
3	F	3	13.0	92	-1.73	-0.84	+0.31	-0.31
4	F	4	12.0	90	-2.80	-2.42	-1.04	-0.80
5	M	8	27.0	130	+0.16	+0.18	-	+0.09
6	M	7	20.0	116	-1.38	-1.25	-	-0.51
7	M	9	36	135	+0.35	+1.46	-	+1.75
8	F	12	50.0	146	-1.04	-	-	+1.60
9	F	16	37	136	-3.91	-	-	-0.26

yrs: years; Wt: weight; Ht: height; HAZ: height for age Z score; WAZ: weight for age Z score.
WHZ: weight for height Z score; BMIZ: body mass index Z score; kg: kilogram; cm: centimeter.

4. Discussion

In the present study, we had retrospectively reviewed the demographic, clinical, and laboratory characteristics of nine (9) subjects with PDM who had presented at the University of Uyo Teaching Hospital, Akwa Ibom State, south-south Nigeria over 15 years.

The prevalence of PDM among our studied population was 0.2/1000, which is in accord with the rate recorded in a similar study reported from Abakaliki (0.1/1000), south-eastern Nigeria, and Sokoto (0.33/1000), north-eastern Nigeria. [7, 9] The low prevalence is in keeping with the pattern of PDM reported in Sub-Sahara Africa. [23, 24] However, our reported prevalence was lower than the rates, which ranges between 1.4/1000 to 10.1/1000, recorded in most other Nigerian studies. [5, 6, 10-13] This may be adduced to the high patronage for informal healthcare services among the inhabitants within the studied region [25] Furthermore, the entire nine (9) PDM cases were all of type 1 DM variant consistent with other reports within the studied region. [5-13]

Most of the PDM cases were females with is in tandem with most recent Nigerian reports and those documented in the western populations. [5-12] This has been attributed to the increased susceptibility to autoimmune disorders, which defines T1DM, in females. 26 Most of our studied population were ≤5 years at diagnosis which is at variance with most reports in the literature. [9-13, 24] These previous studies [9-13, 24] had documented a peak incidence of type 1 PDM within the 10-14 age-groups which coincides with the onset of puberty-induced hormonal impact on insulin sensitivity. [27, 28] The incidence of PDM in ≤5-year-olds is clinically significant because diabetes-related symptoms at this age are not usually classic which may further worsen symptoms and diabetic complications. [29]

The majority (n=7;77.8%) presented via the clinic unit compared to only 22.2% (n=2) subjects who presented via the emergency unit (one with DKA complicated by AKI and the other with dehydration-induced AKI). This finding is in contrast with most reports on PDM in Nigeria and most other parts of the developing countries. [5-13, 24] Presentation mostly in the emergency unit with DM complications (usually with DKA) has been the norm in most other reports in Nigeria and developing societies. [5-13] The basis for this unusual finding in the current study is unknown but remains an area to be explored in future research. However, being a tertiary hospital-based retrospective study, it likely that patients had sort alternative primary/secondary healthcare services, opted for non-orthodox therapies, died at home, or misdiagnosed in the hospital.

In parallel with a recent finding in a similar study documented by Tamunopriye et al, most were diagnosed during the rainy season which is the coldest season of the studied region. [10] Similar observation was recently documented in Poland. [30] It is believed that the rainy cold season increases the risk of viral infections and reduces sun-derived vitamin D acquisition; factors that are known to trigger islet autoimmunity with progression to overt PDM. [30] Most of our subjects dwelt in urban centers at diagnosis. This finding is concordant with similar observations documented by John et al from north-central Nigeria and Hayes et al from Western Australia. [8, 31] The dominance of urban residents in the current study may indicate enhanced exposures to other environmental toxins and pollutants known to trigger PDM in genetically susceptible children. [32]

Based on ethnicity, cases from the Ibibio ethnic group dominated among the PDM subjects. No comparable Nigerian-based pediatric study was found in the literature to evaluate this finding and no reason can be adduced to the dominance by the Ibibio ethnic from the current study due to its limited sample size. Nevertheless, the Ibibio ethnic group is the most populous in the studied region which may explain their dominance.

In tandem with local reports documented by Anochie et al (south-south Nigeria), Adeleke et al (north-west Nigeria), John et al (north-central Nigeria), Tamunopriye et al (South-south Nigeria), and Idris et al (North-west Nigeria), most of the studied subjects were of lower SES at diagnosis. [5, 6, 8, 10, 12] In contrast, a higher SES was associated with PDM incidence among Australian children [31] Lower SES may adversely impact the capacity to financially cope with PDM care, thereby worsening the disease burden, as recently documented. [33]

DM family history rate, a major risk factor for PDM, ranging from 11.1% to 70% had been reported in various Nigerian studies [5, 8, 12], which agrees with our 33.3% rate. However, these previous studies [5, 8, 12] did not define the degree of family relationships with their PDM subjects. In the current study, we recorded 66.7% rate of DM family history in first-degree relatives which is higher than the rates reported in sub-Sahara Africa and the western populations [24, 34].

The higher rate may be because subjects with family history survive more often than those with no family history, due to greater awareness in families where the disease already exist. [24]

The predominant symptoms at presentation were polyuria (100%), polydipsia (100%), weight loss (88.9%), and generalized body weakness (77.8%) which are classic DM symptoms previously reported by Tamunopriye et al and Umar et al and other Nigerian studies among children presenting with PDM [5-13] In terms of the symptoms and their durations, polyuria remains the most prolonged which reflects the duration of DM evolution before presentation since polyuria is one of the earliest clinical manifestations of DM in children. [1, 35]

In line with a previous local report documented by Adeleke et al, infection was the most co-morbid condition recorded among the studied subjects with UTI predominating (22.2%). [6] Though our reported UTI rate (22.2%) was lower than the rate documented by Adeleke et al (36.4%). [6] Infection is a common finding among newly

diagnosed PDM subjects which is reportedly related to the persistent glycosuria and aberrations of immune responses in DM. [36] UTI may act as a stressor, via increased stressed-induced secretion of the counter-regulatory hormones resulting in relative insulin deficiency, which could ultimately trigger DM in these subjects with already depleted beta cells.

The incidence of PDM in children, especially in resource-poor settings such as sub-Sahara Africa, can be influenced by malnutrition particularly undernutrition [37, 38] However, only three (33.3%) of our subjects were concurrently underweight/stunted while only two (22.2%) were solely overweight at diagnosis. The rates of nutritional disorders observed in the current study are lower than the rates recently documented by Tamunopriye et al and indicate that malnutrition might not have played a major role in DM incidence among our studied subjects [10] Similar conclusion had been documented by John et al from North-central Nigeria. [8]

The outcome of our studied subjects was very discouraging with very high rates of defaults to clinic follow-ups. This finding is consistent with previous reports, documented by Ibekwe et al, Ugege et al, and Idris et al, in similar Nigerian studies [7, 9] This trend also mirrors the findings in many other parts of the developing societies [33, 39] The reason for this discouraging finding in the current study could be adduced to the low SES of the studied subjects. However, Ugege et al had generally attributed this to frustration, financial constraints, inadequate parent/patient education, underlying poverty, and poor standard of care. [9]

The study was limited by some factors that warrant mentioning and hence, must be interpreted in that context. First, the study was limited by its small sample size. Secondly, due to a lack of relevant data, subjects were diagnosed based on history, clinical findings, and glycemic status without the standard autoimmune and genetic markers for T1DM, which could have led to misclassification/misdiagnosis. Thirdly, since the data were retrospectively acquired, there is also a likelihood of missing data. Finally, the study was solely hospital-based, therefore, its findings might not reflect the general population in the studied region.

5. Conclusion

The prevalence of PDM was relatively low among the studied population in the current study with the ≤5-year-olds, females, urban-dwellers, and children of lower socio-economic backgrounds predominating. Most of the PDM subjects surprisingly presenting through the clinic unit with prolonged classic DM clinical features. Under-nutrition was documented among a few of the PDM subjects. The rate of default to follow-up following PDM diagnosis was discouragingly very high. Hence, the study findings could serve as health policy targets by various concerned stakeholders within the studied region.

Ethical Statement

The study protocol was approved by the Institutional (UUTH) Research Ethics Committee (2019-330).

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Conflict of Interest

There are no conflicts of interest to declare regarding this study.

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