Tropical Health and Medical Research
Vol.3, No.1, March 2021, pp.36-43
ISSN (Online) : 2684-740X
Journal homepage: http://tropicalhealthandmedicalresearch.com

Prevalence and Pattern of Diabetic Ketoacidosis among Children an Enugu, Southeast Nigeria: a 10 Year Retrospective Study

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Abstract: Diabetic ketoacidosis (DKA) is the most severe complication in pediatric cases of type 1 diabetes and also the leading cause of death in these children. There is a broad geographic variation in the frequency of DKA at the onset of diabetes. This study sought to determine DKA's prevalence and pattern in Enugu and review the treatment and outcome over ten years. This retrospective study conduct in the Children Emergency Rooms (CHER) of the two tertiary institutions in Enugu State, southeast Nigeria: Enugu State University Teaching Hospital (ESUTH) and the University of Nigeria Teaching Hospital (UNTH). The biochemical criteria for the diagnosis of diabetic ketoacidosis (DKA) base on the presence of hyperglycemia (blood glucose > 11 mmol/L), acidosis (serum bicarbonate < 15 mmol/L), and ketonuria (urine ketone ≥1+). A total of 16,488 children were admitted during the ten years, of which 21 children presented with DKA, representing a prevalence of 0.13%. Six (28.6%) of the patients were newly diagnosed diabetics, while fifteen (71.4%) known diabetics, of which 9 (60%) were presenting with DKA for the first time. A total of two patients died, giving a mortality rate of 9.5%. The rest treated and discharged. The total hospitalization duration ranged from 1–31 days, with a mean duration of 13.3 ± 7.5 days. This study has revealed some of the challenges with the management of children with DKA and the unacceptably high mortality rate.
Keywords: Diabetic ketoacidosis; children; Nigeria; prevalence

INTRODUCTION

Diabetic ketoacidosis (DKA) is the most serious complication in pediatric cases of type 1 diabetes and also the leading cause of death in these children[1,2]. There is a broad geographic variation in the frequency of DKA at the onset of diabetes ranging from 13 to 70% in Europe and North America and up to 80% in the United Arab Emirates, while African studies have documented rates of DKA at initial diagnosis in type 1 diabetes between 33%, and 88%[1,3-14].

Cerebral injury is the primary cause of morbidity and mortality in children, and cerebral edema accounts for 60–90% of all DKA deaths.[1] Other complications include hypercoagulability, leading to stroke and deep vein thrombosis, rhabdomyolysis, pulmonary and gastrointestinal complications, and long-term memory dysfunction.[1]

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DKA management protocols for pediatric patients differs from adult protocols. Therefore, it is essential to have clear written guidelines and ensure that in-patient care occur in centers with experience in pediatric DKA management[2]. The subspecialty of pediatric endocrinology is developing in Africa by creating the African Paediatric Endocrinology Training Centres, first in Nairobi, Kenya (2008), and later in Lagos, Nigeria (2012). This result has heightened awareness of the importance of early detection of pediatric endocrine disease symptoms, especially diabetes[15]. These advances in endocrinology training are expected to impact the quality of care for these patients positively. Most studies in the literature focused on diabetic children in general. This study sought to determine the prevalence and pattern of DKA in Enugu and review the treatment and outcome over ten years.

MATERIALS AND METHODS

This retrospective study was conducted in the Children Emergency Rooms (CHER) of the two tertiary institutions in Enugu State, Southeast Nigeria: Enugu State University Teaching Hospital (ESUTH) and the University of Nigeria Teaching Hospital (UNTH). Both hospitals receive most referral cases from within and around Enugu state and operate 24-hour pediatric emergency services. Ethical approval was obtained from hospital research and the ethic committee of UNTH (NHREC/05/01/200BB-FWA00002453-1RB00002323).

The admission records of all the children aged 17 years and below admitted into CHER of ESUTH and UNTH over ten years from January 2009 to December 2018 were reviewed. Those with a diagnosis of DKA were identified and their case records retrieved for data extraction. Data collected with questionnaires designed for the study. Data obtained included demographic information. Other information obtained were presenting symptoms, laboratory features, treatment protocol, and outcome.

The biochemical criteria for the diagnosis of diabetic ketoacidosis (DKA) was based on the presence of hyperglycemia (blood glucose > 11 mmol/L), acidosis (serum bicarbonate < 15 mmol/L), and ketonuria (urine ketone ≥1+). The severity of DKA was categorize as mild (pH 7.21 to 7.3, HCO3 10 mmol/L to 15 mmol/L), moderate (pH 7.11 to 7.2, HCO3 5 mmol/L to 10 mmol/L), or severe (pH of less than 7.1, HCO3 level of less than five mmol/L)[2].

The data was entered and analyzed with Statistical Package for Social Sciences (SPSS) version 19 (Chicago IL). Chi-square statistics test for significance in the presentation time between newly diagnosed and previously diagnosed children for categorical variables. A p-value of ≤ 0.05 at a 95% confidence interval was deemed significant. Results were presented as tables and prose.

RESULTS AND DISCUSSION

A total of 16,488 children were admitted during the ten years, of which 21 children presented with DKA. This result represents a prevalence of 0.13%. Their ages ranged from 3 years to 16 years, with a mean age of 11.7 ± 3.6. There were nine males with an M: F ratio of 1: 1.3. All but one (95.2%) were of Igbo extraction, and all of the children were Christians.

Nine (42.9%) of the children studied belonged to the upper socioeconomic class (SEC), while 57.1% belonged to the lower SEC. In terms of family structure, 9 (42.9%)

had both parents alive, whereas 12 (57.1%) had only one parent live. There was no orphan among the studied group.

Six (28.6%) of the patients were newly diagnosed diabetics, while fifteen (71.4%) known diabetics, of which 9 (60%) were presenting with DKA for the first time. The remaining six subjects of the known diabetics had previous DKA once (83.3%) and twice (16.7%).

Table 1 shows the presenting symptoms. Common symptoms include: polyuria (66.7%), dyspnoea (57.1%), fever (52.4%), and alteration of consciousness (52.4%). The duration of symptoms before presentation to the hospital ranged from 0.25 days (6 hours) to 14 days (mean: 6.0±4.1 days). For the newly diagnosed cases, the presentation time ranged from 4 days to 2 weeks with a mean of 7±3.5 days, whereas for the known diabetics, the presentation time ranged from 6 hours to 2 weeks (mean: 5.5±4.4 days). There is no significant difference in early presentation (within 24 hours) between the two groups ($\chi 2=2.63$, $P=0.11$). The blood glucose levels at presentation ranged from 312mg/dl–600mg/dl (17.3-33.3mmol/l) with a mean of 481.6±98.0mg/dl (26.7± 5.4mmol/l)

The serum potassium level (in the 13 patients done) ranged from 1.8 to 8.4mmols/l with a mean value of 4.7 ± 1.6 mmol/l. Eight (61.5%) patients had normal potassium levels at presentation, 2 (15.4%) had hypokalaemia, whereas 3 (23.1%) had hyperkalemia. The serum bicarbonate level done in 10 patients ranged from 4.0 to 31mmols/l, with a mean value of 16.3±8.2 mmol/l. Half (50%) had normal bicarbonate levels, 30% had mild acidosis, whereas 20% had severe acidosis.

Five out of 11 (45.5%) had leukocytosis, of which 4 (80%) had neutrophilia. The remaining 6 had normal total white blood cell count. Glycosylated hemoglobin (HbA1C) and blood/ urine cultures do not do for any patient. The identified precipitating factors and urinalysis results highlight in table 2.

Table 1: Presenting Features in the 21 Children

Symptoms	Frequency	Percentage (%)
Polyuria	14	66.7
Dyspnoea	12	57.1
Fever	11	52.4
Altered Consciousness	11	52.4
Weight loss	10	47.6
Vomiting	7	33.3
Polyphagia	6	28.6
Acetone breath	4	19.0
Polydypsia	4	19.0
Diarrhoea	3	14.3
Abdominal pain	2	9.5
Painful micturition	1	4.8
Shock	4	19.0
Raised ICP	4	19.0
Hypothermia	2	9.5

Table 2: Factors that Precipited DKA in the Children

Condition	Frequency (n=21)	Percentage %
Urinary Tract Infection	11	52.4
Inadequate insulin use	6	28.6
Acute gastroenteritis	2	9.5
Malaria	2	9.5
Sepsis	1	4.8
Tonsilitis	1	4.8
Pyomyosisitis	1	4.8

Table 3: Results of Urinalysis Done in the Children

Parameter	1+	2+	3+	4+	Total (n=21)
	Frequency (%)	Frequency (%)	Frequency (%)	Frequency (%)	Frequency (%)
Glucose	2 (9.5)	5 (23.8)	8 (38.1)	6 (28.6)	21 (100.0)
Ketones	4 (19.1)	7 (33.3)	10 (47.6)	-	21 (100.0)
Leucocyte	9 (42.9)	2 (9.5)	-	-	11 (52.4)

Nineteen (90.5%) of the children were treated with intravenous insulin, whereas two (9.5%) received subcutaneous insulin. Most (85.7%) were resuscitated with normal saline according to standard protocols, while one patient (4.8%) received Ringer's lactate. Subsequently, all the children resuscitated with normal saline or Ringer's lactate received dextrose saline. Only one patient (4.8%) had correction with bicarbonate because of severe acidosis. All received potassium correction except four (19.0%) with documented hyperkalemia. Almost all (90.5%) the children received antibiotics therapy.

Complications of therapy observe in 2 patients (9.5%). Both had clinical features of raised intracranial pressure, whereas one of them had convulsions. Glucose monitoring does hourly in all patients that received intravenous insulin. The blood glucose level at the transition to subcutaneous insulin ranged from 76mg/dl to 310mg/dl with a mean of 189.5±66.9mg/dl. Serum electrolyte was done once in ten patients (47.6%) and twice in only one patient, while in the remaining 10 (47.6%), it does not do at all. Blood gases do not do in any of the patients. A total of two patients died, giving a mortality rate of 9.5%. The rest treated and discharged. The total hospitalization duration ranged from 1–31 days, with a mean duration of 13.3 ± 7.5 days.

Diabetic ketoacidosis is a common presentation of type 1 diabetes mellitus (T1DM) amongst children in our environment[4-10]. The prevalence of DKA in our study was 1.3 per 1000 emergency room admissions. This result is similar to Ibekwe and Ibekwe in Abakiliki and Adeleke et al. in Kano,[5,7] both in Nigeria. However, incidence studies in lower-income countries in Africa and other regions may underestimate true incidence as new cases are frequently missed and die undiagnosed[16].

The children's mean age in this study is consistent with the mean age of children with T1DM in studies done in other parts of Nigeria, Africa, and the rest of the world[7,10,15,17-19]. There was a greater female preponderance in our study, similar to other studies among children in Abakiliki and Benin.7,10 The female prevalence among DKA patients may be explained by the hormonal changes which accompany puberty, notably the elevation in the serum levels of some counterregulatory hormones, such as growth hormone and estrogen, which counter the effect of insulin on glucose[20].

A higher proportion of the children belonged to the lower socioeconomic class. Another Nigerian study reported a similar pattern[15]. However, there seems to be no agreement on the SEC's effect on DKA in European and North American studies presentation[21-23]. Although a more significant number of the children in our study had only one parent alive, studies have shown that living in a single-parent family has no significant association with diabetic ketoacidosis[24-26].

The most familiar symptoms in our study were polyuria, dyspnea, fever, alteration of consciousness, and weight loss, which are all consistent with features of DKA. Polyuria and dyspnea were the most frequent symptoms observed in the children at the time of diagnosis. Similar findings have been reported by other researchers[8,27-30].

Before diagnosis, the mean duration of symptoms was 6.0 ± 4.1 days; shorter than reports from Lagos, Benin, and other countries[10,15,27,29]. This is probably because our study focused on children who presented with DKA, unlike most other courses that studied the general population of diabetic children with or without DKA.

Less than 30% of the children in our study presented with DKA at time of diagnosis of diabetes. Onyiriuka and Ifebi in Benin[10] Ugege et al[8] in Sokoto and Xin et al[27] in China reported higher frequencies of DKA at time of diagnosis. However, the frequency of DKA at the onset of diabetes in children varies considerably within and between countries[27].

Half of the children had metabolic acidosis, and the mean random blood sugar (RBS) was 26.7±5.4mmol/l), similar to values reported in Sokoto[8], Benin[10], and Ethiopia[17]. However, the mortality in patients with DKA rarely caused by metabolic complications of hyperglycemia or metabolic acidosis and is usually related to underlying medical illnesses that precipitate the metabolic decompensation[31].

Urinary Tract Infection was the most common precipitating factor in our study, and similar patterns reported in other studies[17,30-33]. A history of prior infection is a known factor associated with an increased risk of diabetic ketoacidosis[3]. This is as a consequence of inflammation from the disease with pro-inflammatory cytokine release and a counter-regulatory response that collectively lead to insulin resistance and metabolic decompensation[34].

Treatment protocols mostly followed the recommended guidelines. However, investigations for monitoring such as serum electrolytes, glycosylated hemoglobin (HbA1C), blood gas analysis, and blood and urine cultures did not follow the guidelines. The probable reason for this lapse is inadequate finance as these investigations are expensive, and the patients pay from their pockets. This is a recurrent challenge in low to medium-income countries, such as Nigeria.

Most of the children were treated and discharged. Our mortality rate was similar to 11.1% reported by Umar in Kano. These figures are much higher than the global mortality rate, which is 0.3–1% of the patients, and it’s been suggested that the rates may be much

higher because of limited published data[14,16]. Delayed diagnosis and presentation have been adduced as reasons for this high mortality rate in developing countries[17].

A major limitation of this study is its retrospective nature, which is prone to recall bias, misclassification bias, and incomplete data.

CONCLUSION

This study has revealed some of the challenges with managing children with DKA and the unacceptably high mortality rate in our environment.

ACKNOWLEDGEMENT

We wish to acknowledge the medical records clerk who assisted in the retrieval of the case records of the children.

CONFLICT OF INTEREST

The authors wish to declare that they have no conflict of interest and did not receive any funding for this study.

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