Frequency and Pattern of Serum Sodium and Potassium Abnormalities at Point of Hospitalization of Type 1 Diabetic Children with Ketoacidosis: A Retrospective Review from a North-western Nigerian Teaching Hospital

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Abstract

Background: Electrolyte abnormalities are often encountered in various illnesses and may be associated with poor prognosis. This study described the frequency and pattern of abnormalities of serum sodium and potassium concentrations in type 1 diabetic (T1D) children with ketoacidosis (DKA) at point of hospitalization in the Emergency Paediatric Unit (EPU) of Usmanu Danfodiyo University Teaching Hospital (UDUTH), Sokoto.

Materials and Methods: A retrospective medical records’ review was performed on all children diagnosed with type 1 diabetes complicated by DKA in UDUTH, Sokoto over a 15-year period from 1st June 2007 to 31st May 2022. The obtained Information included the age, gender, presenting complaints, and treatment outcome (dead or alive). Data on serum electrolyte concentration (sodium, potassium, chloride, bicarbonate) as well as blood glucose before initiation of treatment were extracted. The anion gap and effective osmolality were calculated.

Results: Overall, 14 (70.0%) of 20 DKA patients had abnormalities of serum sodium, potassium or a combination of both. Sodium abnormalities occurred in 11(55.0%) patients; Isolated in 5(25.0%) [Hyponatraemia- 4(20.0%), hypernatraemia- 1(5.0%)] and combined [Hyponatraemia with hyperkalaemia] in 6(30.0%) cases. Potassium abnormality occurred in 9(45.0%) patients; isolated hyperkalaemia- 3(15.0%) and combined [hyperkalaemia with hyponatraemia] - 6(30.0%). The mean ± SD and ranges of blood glucose, anion gap and resolution time of ketoacidosis were 25.31 ± 6.95; 12.3-33.3 mmol/L; 21.60 ± 12.8; 14.50-57.50mmol/L and 1.5 ± 0.6; 1.2-1.8 days. Eleven (55.0%) children were newly diagnosed T1D while 9 (45.0%) were already established diabetics with repeated ketoacidosis. Majority (70%) of the study population were >10 years old. They were managed according to standard protocols. There was no mortality.

Conclusion: There is a high frequency of sodium and potassium abnormalities at point of hospitalization in T1D children with DKA; commonest being a combination of hyponatraemia and hyperkalaemia.

Keywords: Electrolyte abnormality, ketoacidosis, Type1 diabetes, children, frequency

Introduction

Type 1 diabetes mellitus (T1D) is a heterogeneous disorder characterized by autoimmune-mediated pancreatic beta cell destruction that culminates in absolute insulin deficiency (1). It is most commonly diagnosed in children and adolescents, and usually presents with symptomatic hyperglycaemia, and imparts the immediate need for exogenous insulin replacement (1).

Diabetic ketoacidosis (DKA) has been recognised as the main complication and potentially fatal emergency in children and adolescents with type 1 diabetes mellitus (T1D) (2). Ketoacidosis results from decrease in effective circulating insulin, associated with increases in Insulin counter regulatory hormones including glucagon, catecholamine, cortisol, and growth hormone. These increases in counter regulatory hormone leads to increased glucose production by the liver and kidney, and impaired peripheral glucose utilisation, causing hyperglycaemia, and resultant hyperosmolality. In addition, increased lipolysis, ketonaemia, and metabolic acidosis occur. Hyperglycaemia and acidosis leads to osmotic diuresis, dehydration, and obligate loss of electrolytes, which then upsets the body’s balance of electrolytes, particularly serum sodium and potassium (3).

Diabetic ketoacidosis is associated with major abnormalities in plasma electrolytes; the most characteristic abnormality is total body potassium loss. This loss is not mirrored in serum potassium levels, which may be low, within the reference range, or even high. This is simply a reflection of how long the DKA process has been ongoing before treatment is commenced (4).

Major loss of potassium is from the intracellular pool. Potassium loss is caused by
transcellular shift of potassium from the intracellular to the extracellular space in an exchange with hydrogen ions that accumulate extracellularly in acidosis. Much of the shifted extracellular potassium is lost in urine because of osmotic diuresis and vomiting. Patients with initial hypokalemia are considered to have severe and serious total body potassium depletion (3, 4). The other reasons for potassium loss include insulin deficiency; insulin promotes potassium entry into cells thus when circulating insulin is lacking, as in DKA, potassium moves out of cells as a result of hypertonicity and solvent drag of water and potassium, thus raising plasma potassium levels even in the presence of total body potassium deficiency. Hypokalaemia is further aggravated by vomiting, and secondary hyperaldosteronism from volume depletion (5-7).

High serum osmolarity drives water from intracellular to extracellular space, causing dilutional hyponatraemia. Sodium is also lost in the urine during the osmotic diuresis (4). Hypernatraemia, though rare, has been reported in DKA and in situations where both DKA and HHS (Hyperglycaemic Hyperosmolar State) coexist (8, 9). This has been attributed to water losses in excess of sodium, ingestion of large volumes of high calorie carbohydrate drinks prior to admission to quench thirst in new onset type-1 diabetics and ingestion of herbal mixtures (8, 9).

There is a dearth of published studies on the profile of serum electrolytes (sodium and potassium), in type 1 diabetic children with ketoacidosis. This study was therefore necessary to add to existing knowledge as it aimed to determine the frequency and pattern of sodium and potassium abnormalities in both the new onset and already established type 1 diabetic children with recurrence of ketoacidosis.

**Methodology**

This was a 15-year retrospective study. The case folders of all children and adolescents with type 1 diabetes complicated by Ketoacidosis (DKA) in the Paediatric department of UDUTH, Sokoto from 1st June 2007 to 31st May 2022 were retrieved and audited. Diabetic ketoacidosis was diagnosed based on the presence of hyperglycaemia (blood glucose > 11.1 mmol/L or 200 mg/dL), ketonuria and metabolic acidosis (serum bicarbonate < 15 mmol/L or Venous PH < 7.3) (6). These patients were initially admitted to the Emergency Paediatric Unit (EPU) for stabilization and subsequently transferred to the Paediatric medical ward for continuation of management. At the point of hospitalization, each patient had the following biochemical parameters measured: blood glucose, serum electrolytes, urea, creatinine, full blood count, and urine ketones.

Serum sodium and potassium concentrations were estimated by flame photometer in the chemical pathology department of UDUTH, Sokoto. In children with established diabetes who has had two or more DKA episodes since diagnosis, the serum electrolyte and other biochemical parameters of the last episode of DKA prior to audit was utilized. Hourly monitoring of vital signs, neurologic status and blood glucose were performed and recorded. The ketoacidosis was considered to have resolved if serum bicarbonate rose above 15 mmol/L or venous PH > 7.3, with a normal anion gap and stabilization of the patient’s clinical condition judged by regain of full consciousness, presence of normal vital signs and absence of symptoms of DKA such as vomiting, and abdominal pain. Additional information obtained from the case files included the age, gender, time of resolution of DKA and final outcome (dead or alive). Effective osmolality was calculated, using the formula: Effective osmolality = \[2 \times \text{serum sodium} + \text{blood glucose} \text{ mmol/L}\]. Anion gap was calculated using the formula: Anion gap = \[\text{serum sodium} - (\text{serum chloride} + \text{serum bicarbonate})\] (6).

**Definition of terms:**

Hypernatraemia: serum sodium < 135 mmol/L; Hypokalaemia: serum sodium > 149 mmol/L; Hypokalaemia: serum potassium < 3.5 mmol/L; Hyperkalaemia: serum potassium > 5.2 mmol/L. These were defined according to the reference values provided by the Chemical pathology department of UDUTH where the tests were done. Severe hypernatraemia: serum sodium < 120 mmol/L (15) and Severe hypokalaemia: serum potassium < 2.5 mmol/L (16).

**Data Analysis**

The data obtained were analysed with the Statistical Package for Social Sciences (version 23.0, IBM Corp, USA). Descriptive statistics such as frequencies, mean, median, standard deviation were used in describing all the variables. Continuous variables were presented as...
mean ± SD, while categorical variables were presented as frequency and percentages. Student’s t -test was used in ascertaining the significance of difference between two means with p-value set at <0.05.

Ethical Approval
Approval for the study was obtained from the Research and Ethics Committee of the Usmanu Danfodiyo University Teaching Hospital, Sokoto (UDUTH/HREC/2018/No 667).

Results
General characteristics of study Population
Twenty T1D children were admitted for DKA over the period of review and these constituted the study subjects. Nine (45.0%) had already established diabetes with recurrence of DKA while 11(55.0%) were new onset diabetics presenting for the first time with ketoacidosis. The mean age was 11.7(± 3.1) (range 6-15) years. The mean duration of living with diabetes was 2.1 (± 2.5) years, (median age: 2 years; range 0.06-7years). The median duration of symptoms before presentation in hospital was 9.5 days (range 3-42days). The mean time for resolution of DKA was 1.5 ± 0.6days (range 1.2 - 1.8 days), whilst the mean anion gap and effective osmolality were 21.6 (±12.8) mmol/L and 294.3 (±23.9) mmol/Kg respectively (range -14.5-57.5mmol/L and 248.4-323.4 mmol/Kg respectively).

Distribution of gender, age and presenting complaints of subjects
Eighteen (90%) of the subjects were male; the male to female ratio was 9:1. Fourteen (70%) subjects were above 10 years old. The most frequent presenting complaints were polyuria and abdominal pain and the least frequent were polyphagia and weight loss as depicted in table 1.

Mean admission serum sodium and potassium by age, gender and blood glucose levels
The lowest mean serum sodium (117.1 ± 5.5mmol/L) was observed in females followed by subjects aged ten years and below (125.8 ± 7.8 mmol/L), and those with blood glucose between 20-30mmol/L (130.0 ± 11.9 mmol/L). The highest mean serum potassium (5.5 ± 2.1mmol/L) was observed in subjects with blood glucose greater than 30mmol/L, followed by those with blood glucose between 20-30mmol/L (5.3 ± 0.9mmol/L) as shown in Table 2.

<table>
<thead>
<tr>
<th>Parameter mmol/L</th>
<th>Serum Na⁺</th>
<th>95% CI</th>
<th>range</th>
<th>Serum K⁺</th>
<th>95% CI</th>
<th>range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age in years (n = 20)</td>
<td>Mean±SD</td>
<td>Min – Max</td>
<td>Mean±SD</td>
<td>Min – Max</td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤ 10 (n=10)</td>
<td>123.8 ± 7.6</td>
<td>117.9-144.0</td>
<td>116.0-154.0</td>
<td>3.2 ± 1.6</td>
<td>2.4-4.7</td>
<td>2.5-6.8</td>
</tr>
<tr>
<td>&gt; 10 (n=10)</td>
<td>130.4 ± 11.3</td>
<td>121.5-144.0</td>
<td>113.2-153.2</td>
<td>5.2 ± 1.2</td>
<td>3.9-7.6</td>
<td>3.9-7.6</td>
</tr>
<tr>
<td>Gender (n=20)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male (n=18)</td>
<td>106.6 ± 10.5</td>
<td>93.0-120.1</td>
<td>110.6-116.2</td>
<td>5.2 ± 1.3</td>
<td>4.5-8.8</td>
<td>4.5-8.8</td>
</tr>
<tr>
<td>Female (n=2)</td>
<td>117.7 ± 5.5</td>
<td>75.1-160.7</td>
<td>113.2-121.0</td>
<td>5.1 ± 0.8</td>
<td>1.9-12.0</td>
<td>4.5-12.0</td>
</tr>
<tr>
<td>Blood glucose (mmol/L)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤ 20 (n=6)</td>
<td>144.6 ± 10.7</td>
<td>127.6-161.5</td>
<td>129.0-155.2</td>
<td>4.3 ± 0.6</td>
<td>2.2-6.3</td>
<td>3.0-6.2</td>
</tr>
<tr>
<td>20-30 (n=11)</td>
<td>100.0 ± 11.9</td>
<td>92.1-137.9</td>
<td>110.2-146.0</td>
<td>3.5 ± 0.9</td>
<td>4.7-5.9</td>
<td>4.4-6.8</td>
</tr>
<tr>
<td>&gt;30 (n=3)</td>
<td>136.6 ± 7.7</td>
<td>127.3-148.3</td>
<td>130.0-145.0</td>
<td>5.5 ± 2.1</td>
<td>2.9-8.1</td>
<td>3.5-7.6</td>
</tr>
</tbody>
</table>

Frequency and pattern of serum sodium and potassium abnormalities in 20 T1D children with DKA at point of hospitalization.
The frequency of serum sodium and potassium abnormality was 70.0 %. Overall, sodium abnormalities was observed in 11 (55.0%) subjects, made up of 10 (50.0%) hyponatraemia [4(20%) isolated; 6(30%) in combinations with hyperkalaemia], and 1(5.0%) hypernatraemia. Potassium abnormality occurred in 9(45%) subjects, all were hyperkalaemia [3(15%) Isolated; 6(30%) in combinations with hyponatraemia]. The most frequent pattern of electrolyte abnormality was a combination of hyponatraemia and hyperkalaemia- 6(30.0%) as depicted in table 3.

Comparing the mean serum sodium and potassium of the new onset diabetic and established diabetic children with DKA
The mean serum sodium of children with established T1D with recurring DKA was 129.1 ± 12.0 while their mean potassium was 5.9± 1.3mmol/L. For the new onset T1D children presenting for the first time with DKA, the mean sodium and potassium levels were 139.1 ± 10.0mmol/L and 4.5± 0.7mmol/L respectively. This observation was statistically significant for
potassium $p=0.01$ but not for sodium $p=0.06$. This is depicted in table 4.

Table 3: Frequency of serum sodium and potassium abnormalities amongst Subjects at point of hospitalization

<table>
<thead>
<tr>
<th>Type of Electrolyte disturbance</th>
<th>number</th>
<th>percent (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sodium abnormalities</td>
<td>11</td>
<td>55.0</td>
</tr>
<tr>
<td>Potassium abnormalities (All hypokalemia)</td>
<td>9</td>
<td>45.0</td>
</tr>
<tr>
<td>Hyperkalemia</td>
<td>4</td>
<td>20.0</td>
</tr>
<tr>
<td>Hyponatremia</td>
<td>2</td>
<td>10.0</td>
</tr>
<tr>
<td>Hypokalemia</td>
<td>3</td>
<td>15.0</td>
</tr>
<tr>
<td>Total</td>
<td>14</td>
<td>70%</td>
</tr>
</tbody>
</table>

Management and Outcome

All the patients were managed according to the International Society for Paediatric and Adolescent Diabetes- ISPAD 2018 consensus guidelines (6). All the patients recovered and were discharged to endocrine/diabetes clinic for follow up.

Table 4: Comparing the mean serum sodium and potassium in the new onset diabetics with established diabetic children with DKA

<table>
<thead>
<tr>
<th>Diabetes status</th>
<th>Newly diagnosed</th>
<th>Established Diabetics</th>
<th>t</th>
<th>df</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean sodium (SD)</td>
<td>139.1 ± 10.0</td>
<td>129.1 ± 12.0</td>
<td>2.04</td>
<td>18</td>
<td>0.06</td>
</tr>
<tr>
<td>Mean potassium (SD)</td>
<td>4.5 ± 0.7</td>
<td>4.5 ± 1.3</td>
<td>-3.19</td>
<td>12</td>
<td>0.01</td>
</tr>
</tbody>
</table>

*All the established diabetics with DKA and five of the new onset diabetic patients had Na+ and K+ abnormalities whilst others had normal Na+ and K+ values.

Discussion

The findings of this study show that seven in ten T1D children with ketoacidosis had abnormalities of serum sodium and potassium at the point of hospitalization in the EPU of UDUTH, Sokoto. This proportion is higher than the 53.2%, reported by a previous Nigerian study, conducted in two Nigerian Teaching hospitals (14). A likely reason for the wide disparity in frequency reported between the current and previous study could be related to the differences in study population utilized. Even though both studies were retrospective in design, the previous study utilized the new onset diabetics with DKA while the current study included both new onset and established diabetic patients with recurrence of ketoacidosis. Another reason could be related to the differences in climatic conditions like environmental temperatures and humidity of the study locations. Current study was conducted in Sokoto which has a higher ambient temperature and lower humidity on an average than Lagos and Benin, where the earlier study was conducted. It is possible that the dehydrating effects of hyperglycaemia induced osmotic diuresis and vomiting, as occurs in ketoacidosis, may be worsened by the hot and dry climate of the study location via increased insensible water losses thus predisposing to more severe dehydration, and consequently more electrolyte abnormalities. Lone et al (17), in Karachi, Pakistan, reported that 14.5% of DKA patients had abnormalities in serum sodium and potassium in the course of treatment. Their study population included both patients with newly diagnosed and established diabetes similar to our study, however, the low figure reported in contrast to ours may be because the frequency of sodium and potassium abnormalities reported were those observed during treatment; after initiation of fluid resuscitation and intravenous Insulin, in contrast to current study which studied the abnormalities of the said electrolytes at point of admission; before fluid therapy and intravenous insulin was initiated.

Possibly, commencement of treatment may have normalized some of the initial electrolyte derangement hence the lower figure. It is expected that administration of insulin which ultimately results in correction of acidosis would alter the electrolyte pattern, notable, is the driving of potassium ion into cells potentiating hypokalaemia, and a gradual rise in sodium levels to normal. Insulin also has an aldosterone-like effect leading to increased urinary potassium excretion (6). The finding by Lone et al (17) of predominantly hypokalaemia -6.0% and rarely hyperkalaemia-0.9% complicating DKA in their patients on treatment seem to buttress this explanation.

Our finding of sodium abnormality being more frequent than potassium abnormality is consistent with previous reports (14, 17-19). We observed isolated hyponatraemia in 20% of patients, closer to the findings of Onyiriuka and Oyenusi(14) in Lagos and Benin, Nigeria - 25.5%, but much lower than was reported by, Rochmah et al (19) in Indonesia -32.8%, and Bhardwaj et al (20) in Himalayan, India - 44.8%. Also higher than those of Onyiriuka and Ifebi (18) in Nigeria- 8.1%, and Lone et al (17) in Karachi, Pakistan-7.7%. The differences in frequencies reported could be due to varying methodology employed. It was not stated in some of these studies whether severe hyponatraemia and co-existing hyponatraemia with
potassium abnormalities were inclusive or exclusive in the figure reported for hyponatraemia (19–21), moreover some researchers (14, 18) studied only new onset diabetics with DKA in contrast to current study that studied both new onset and established diabetics with DKA.

Our finding of hyponatraemia (isolated, severe or in combination with hyperkalaemia) being the commonest sodium abnormality encountered is not unusual. As we know, hyperglycaemia results in fluid movement from the extra vascular to the intravascular space and a decrease in the serum sodium concentration. This decrease can be calculated as a 1.6 meq/L decrease in sodium concentration for every 5.5mmol/dL increase in serum glucose more than 5.5mmol/dL (21). Hyperlipidemia caused by lipolysis may also affect serum sodium measurements and result in a decrease in measured serum sodium concentrations (21). This is in addition to sodium loss through osmotic diuresis caused by uncontrolled hyperglycaemia; worsened by ketosis. Contrary to our finding, Razavi et al in Hamadan, Iran (22) and Kanwal et al in Delhi, India (23) reported hypokalaemia-34.7% and hypernatraemia-20% respectively as the commonest electrolyte complications of DKA. A possible reason for these varying reports may be a function of when the assays were done, whether before treatment or during treatment as mentioned earlier, as this was not specified in these studies. Ishikawa et al, in Japan (24), highlight from their study of 19–79 year old patients with diabetic coma, reported alterations in serum Na+ and K+ levels which are in opposite directions to each other. They found two groups of patients with diabetic coma; those who had hyponatraemia and hyperkalaemia in DKA coexisting with Non-ketotic Hyperosmolar Coma (NKHC) and those who had hypernatraemia with hypokalaemia in NKHC. They concluded that the disorder may be based on the altered distribution of electrolytes between intra- and extracellular spaces, but the exact mechanism for the disorder has not been determined. No such study has been reported in children. Our finding of Hyperkalaemia (Isolated and combined) being the only potassium abnormality encountered in current study is contrary to the findings of Onyiriuka and Oyenusi et al (14) who reported prevalence’s of 10.6% and 8.5% for hyperkalaemia and hypokalaemia respectively. Figures of 32.5% and 7.5% were reported by Su et al (25) in Japan, whilst Pulungan et al (26) in Jakarta reported equal prevalence’s of hyperkalaemia and hypokalaemia-31.3% each. Initially, DKA patients experience hyperkalaemia which swiftly changes to hypokalaemia with insulin treatment. Studies have shown that patients with DKA tend to have elevated serum potassium (K+) concentration despite decreased body potassium content (27). This is due to decreased potassium ion excretion by the kidney once volume depletion reduces glomerular filtration rate, also due to the corresponding acidosis and insulin deficiency resulting in shift of potassium ion from intracellular to extracellular compartment. It has been demonstrated that serum potassium correlates independently with both blood pH and renal function (27).

Hypokalaemia at presentation is said to be related to prolonged disease whereas hyperkalaemia primarily results from reduced renal function (3). It is however, not clear, why hypokalaemia was not seen in any of our patients at point of hospitalization in spite of a relatively long median duration of symptoms (9.5days) prior to presentation. It has been shown that children with DKA have total body potassium deficits of the order of 3–6 mmol/Kg (6). The major loss of potassium is from the intracellular pool as a result of hyper tonicity, insulin deficiency, and buffering of hydrogen ions within the cell. Serum potassium levels at the time of presentation therefore may be normal, increased or decreased. Administration of insulin and the correction of acidosis will drive potassium back into the cells, decreasing serum levels (3).

Our finding of mean serum sodium and potassium levels of the newly diagnosed diabetic children with DKA in the normal range and those with established diabetes; deranged (low sodium and high potassium) was statistically significant for potassium (p= 0.01) but not so for sodium p= (0.06). The small study size however does not allow for strong inferences, hence, there is need for future robust collaborative studies to explore the differences in electrolyte patterns of these two populations of diabetics. There was no mortality. All the patients were discharged for follow up in the endocrine clinic.

Limitation of study

The major limitation of this study is the small sample size, in spite of this; it has described the pattern and frequency of serum sodium and potassium abnormalities at point of hospitalization in T1D children with DKA over the review period. In conclusion, abnormalities of sodium and potassium were common in both paediatric new onset and established diabetics with DKA, sodium abnormalities...
were slightly more frequent than potassium abnormalities; a combination of hyponatraemia and hyperkalaemia was the most frequent pattern of abnormality observed in T1D children with DKA in UDUTH, Sokoto. We recommend a robust multicentre collaborative study, be undertaken, particularly in Nigeria, where data on the subject is scarce, to compare the electrolyte changes in the new onset and already established diabetics with ketoacidosis, and to determine their relationship with clinical outcome.

Acknowledgment
We acknowledge all the doctors and nurses in the pediatric department who were involved in the management and care of these children.

Conflict of interest
None

References