Original Article

Root Cause Analysis of Diabetic Ketoacidosis Admissions at a Tertiary Referral Pediatric Emergency Department in North India

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Abstract

Objectives: To identify system-based factors contributing to Emergency Department (ED) admissions of children with diabetic ketoacidosis (DKA) and related complications with emphasis on parental and physician awareness and prereferral management. **Materials and Methods:** A prospective observational root cause analysis study of all consecutive admissions of children with DKA to pediatric ED of a tertiary care referral hospital in northern India over a period of 1 year (July 2010–June 2011). Prehospital, health-care system, referral, follow-up, and continuum of care related details were obtained through direct interview of parents and physicians and/or field observations for all enrolled children. **Results:** Of the 30 children enrolled, 26 (86.6%) were referrals; 16 (61.5%) from first, 7 (26.9%) from second, and 3 (11.5%) from third health-care facility. More than half (*n* [%], 18 [60%]) had new onset diabetes and belonged to lower socioeconomic strata. Twenty-two (73.3%) were complicated DKA; shock (*n* [%], 19 [63%]), hypokalemia (*n* [%], 11 [36%]), and CE (*n* [%], 3 [10%]) were the most common complications. Most parents were ignorant of diabetes, its symptoms or complicating DKA. Nearly, half of the cases remained undiagnosed ($n = 11$) at first contact health-care facility; more so for new onset as compared to known diabetes (9/18 vs. 2/8; $P = 0.022$). The referring hospitals had limited facilities for rapid blood glucose estimation (*n* [%], 12 [40%]), blood gas analysis (*n* [%], 6 [20%]) and insulin infusion. On univariate analysis, patients with missed/delayed diagnosis more often had severe and complicated DKA. **Conclusion:** Parental ignorance, lower socioeconomic status, lack of clinical experience, and limited primary health-care facilities were root causes for severe and complicated DKA.

Keywords: Complications, developing economy, diabetic ketoacidosis, root cause analysis

Introduction

Diabetic ketoacidosis (DKA) still remains the leading cause of death in children with type I diabetes mellitus (T1DM). Cerebral edema (CE) occurs in 0.3 to 1% of all episodes of DKA and accounts for 57%–87% of all DKA-related deaths.[1,2] Although mortality rates in the developed economies have decreased considerably from 10% in the 1980s to 0.21% in recent series,[3,4] the scenario in developing economies is far from reassuring. Delayed recognition of disease and presence of comorbidities such as infections and under-nutrition contribute to greater metabolic decompensation culminating into a hyperosmolar state, CE, and death.[5] We, therefore, decided to conduct a root cause analysis (RCA) for cases of DKA reporting to the pediatric Emergency Department (ED) of our hospital to evaluate the system-based factors leading to delayed diagnosis and increased rate of complications.

Materials and Methods

An observational RCA was conducted for all cases of DKA presenting to the Emergency Department (ED) of our center over a period of 1 year (July 2010–June 2011). Thirty children with DKA aged 1–12 years, were enrolled consecutively

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into the study after obtaining written informed consent from parent/guardian. No case was excluded. The study was approved by the Institute Ethics Committee. The management of these children was as per the unit's standard DKA protocol.[6]

Definitions used

DKA was defined as hyperglycemia (blood glucose >200 mg/dl) with acidosis (venous pH <7.3 or serum bicarbonate <15 mmol/L), and ketonuria (urine ketone ≥2 by dipstick).[7] CE was defined based on the clinical criteria laid by Muir *et al*.[8] Acute kidney injury (AKI) was defined based on pRIFLE classification.[9] The shock was defined based on the consensus criteria by Goldstein *et al*.[10] Socioeconomic strata were defined using the modified Kuppuswamy scale.[11]

Root cause analysis

The root causes for the development of DKA and its complications were obtained by direct interview and field observations. All the possible reasons under the above-mentioned categories were discussed *a priori* by the investigators using the RCA guidelines[12,13] following which multiple questionnaires were prepared for getting the requisite information. Since the root causes for DKA and its complications were different for known T1DM and new onset disease, separate questionnaires were prepared for both. Any new factors found during the RCA were added to the existing questionnaire.

Direct interview

Parents/guardian were interviewed for their knowledge and awareness about diabetes and DKA within the first 7 days of enrolment using the preformed questionnaire as a base after seeking informed consent.

Field observations

Over the next 45 days, the investigators made field visits to the referring hospitals, clinics, and nursing homes for direct assessment of the diagnostic and treatment facilities available. Treating physicians were interviewed and details regarding the diagnosis, investigation, treatment, and referral facilities were collected. Any missing information was collected telephonically from the concerned physicians at a later time. The identity of the physician and health-care facility was kept strictly confidential.

Identification of contributory/root causes

Using the information collected, a detailed time frame depicting the exact sequence of events was made for each patient, and a causal factor diagram was designed using RCA techniques to identify the contributing factors for DKA and its complications in each case [Figure 1].

Statistical analysis

Descriptive statistics were used. For RCA, the cohort was divided into two groups, namely, those referred with a diagnosis of DKA versus those without. Similarly, known TIDM versus new-onset diabetes were compared for possible factors predisposing to complications. Intergroup comparisons were done with Student's *t*-test for numerical variables and Chi-square for proportions, $P < 0.05$ was considered statistically significant. IBM SPSS Statistics for Windows, Version 19.0 (Armonk, NY: IBM Corp) was used for analysis.

Results

A total of 30 patients with DKA were enrolled during the study. The baseline characteristics of the study subjects are as shown in Table 1. More than half of our patients (*n* - 18, 60%) belonged to lower socioeconomic strata. Twenty-two (73.3%) children had some complication of DKA at the time of presentation. All children belonging to lower socioeconomic strata had complications though the difference in the incidence of complications was insignificant between socioeconomic strata ($P = 0.36$).

Root cause analysis

Of the 30 enrolled patients, 26 (87%) children including all the new-onset T1DM patients (*n* = 18, 69%) were referred from other health-care facilities. A total of 16 (61.5%), 7 (26.9%), and 3 (11.5%) were referred from the first, second, and third contact health-care facility, respectively.

Prereferral factors

Parental factors

The majority of the parents interviewed were ignorant of diabetes, its symptoms or complications. Only one-third (*n* = 9; 30%) were aware that diabetes can occur in children, most of them 7 (78%) being parents of children with diagnosed TIDM. In children with recurrent episodes of DKA, the majority of parents were unaware of the nature of the illness, the etiology or the preventive measures to be taken. Only half of the parents of known TIDM were aware that insulin omission can cause DKA. There were issues regarding the usage of insulin, technique, storage, compliance, monitoring, and adherence to insulin regimen. The median (interquartile

Table 1: Baseline characteristics of study patients (*n*=30)

Parameters	
Demographic variables	
Age in years, mean (SD)	8.0 (3.5)
Number of children aged >5 years, *n* (%)	24 (80)
Boys:Girls ratio	0.4:1
Known TIDM, *n* (%)	12 (40)
New onset T1DM, *n* (%)	18 (60)
Duration of polyuria/polydipsia in days, median (IQR)	10 (5.5-20)
Biochemical parameters*	
Blood pH	7.1 (0.14)
Serum bicarbonate (mmol/L)	7.3 (4.8)
Base deficit (mmol/L)	20.6 (7.6)
Serum potassium (mmol/L)	4.1 (1.0)
Blood glucose (mmol/L)	24.8 (7.2)
Serum sodium (mmol/L)	135 (6)
Calculated serum osmolality (mmol/kg)	303 (17)
Blood urea nitrogen (mmol/L)	7.68 (6)
Serum creatinine (μmol/L)	78.7 (61.9)

*Values are mean (SD). SD: Standard deviation, T1DM: Type I diabetes mellitus, IQR: Interquartile range

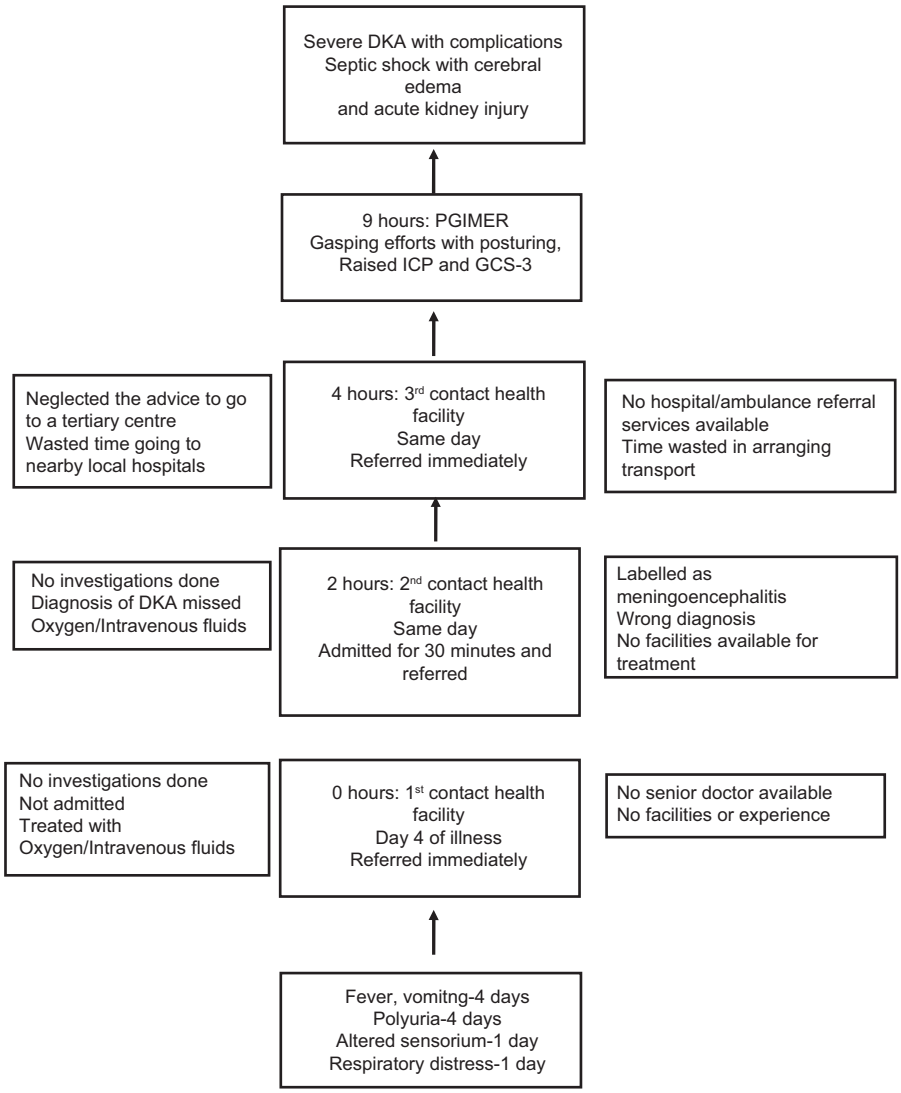

Figure 1: Causal factor diagram

range [IQR]) duration of symptoms (polyuria and polydipsia) before seeking medical care was 10 (5.5–20) days.

Out of 12 children with known T1DM, only 4 (33%) patients adhered strictly to insulin doses and schedule. Nearly, half (n = 5; 41.7%) were on inappropriate treatment; 2 not on any insulin therapy, 3 on inappropriate dosage, and scheduling of insulin. In the rest (n = 3, 25%), the frequency of missing insulin varied from once a month to once in 2 weeks. The most cited reasons for noncompliance were carelessness, lack of proper supervision and low blood glucose records. None of the patients were following any exercise program or dietary modifications. Regular home-based blood glucose monitoring was carried out only by three patients.

Health-care facility-related factors

First health-care contact

Twenty-six sought medical aid at a first contact health-care facility of which 12 were admitted, 10 were investigated and treated on an outpatient basis, and 4 were referred immediately without any treatment or investigations. Of all the children seen in the first health-care facility 15 (57.7%) were diagnosed as DKA of which 6 were known TIDM. The median (IQR) duration after admission for the establishment of diagnosis in the above cases was 3 (1–4) h. Eleven (42%) children remained undiagnosed at the first health-care facility; significantly higher proportion of new-onset T1DM remained undiagnosed (undiagnosed 2/8 for known TIDM vs. 9/18 for new onset T1DM; P = 0.02). Only 3 received insulin; 2 as subcutaneous bolus and 1 as an infusion. None of the patients received fluids or insulin as per standard recommendations.

Second health-care contact

Of the 10 patients who reported to the second health-care facility, 3 more were diagnosed to have DKA of whom only 1 received insulin, but not as per standard recommendation. The mean (SD) duration for the establishment of the diagnosis of DKA at the second health-care facility was 3 (2) hours. At the end of treatment at the second health-care facility, 7 (70%) continued to remain undiagnosed.

The 3 patients who visited a third contact facility were immediately referred to pediatric ED of tertiary center without any investigations or treatment. The type of health-care contacts visited, and their facilities are depicted in Table 2.

Referral factors

Eighteen children (69.2%) were referred to our center for lack of facilities, while 8 (30%) were referred for worsening clinical condition and complications. Financial constraints were cited as additional reasons for referral by two physicians. The median (IQR) duration of prereferral hospital stay was 3 (2.2-11) hours. The median (IQR) duration to reach the tertiary care after referral was 4.5 (3–7.2) hours. The common reasons for the delay in reaching tertiary center after the decision of referral was taken were financial issues, nonavailability of ambulance (50%), ignoring the advice of referring physician (28.5%), and seeking medical care in other hospitals before coming to the designated tertiary center (17.8%).

On univariate analysis, we found that those who remained undiagnosed presented more often as severe DKA and had significantly higher incidence of complications such as shock, CE, and renal failure [Table 3]. The only death that occurred in our cohort was in the undiagnosed group. Those with new onset T1DM also had a tendency to seek medical care from multiple health-care facilities before reaching tertiary care facility unlike the diagnosed cases (4/12 [33.3%] for known TIDM vs. 0/18 for new onset T1DM; $P = 0.003$).

Table 2: Prereferral health-care facility-related factors ($n=26$)

Prereferral factors	*n* (%)	
Type of health care		
Primary physician/private practitioner	5 (19)	
Small hospital (IPD*)	9 (35)	
Primary health center	4 (15)	
District hospital	3 (11.5)	
Multispecialty private hospital	3 (11.5)	
Government medical college	1 (4)	
Others (indigenous)	1 (4)	
Facilities	**Available, *n* (%)**	**Utilized for the patient, *n* (%)**
Laboratory blood glucose estimation	26 (100)	18 (69)
Glucometer	12 (46)	4 (15)
Urine ketones	22 (85)	11 (42)
Blood gas	6 (23)	1 (4)
Infusion pump	6 (23)	0
IPD* facilities	22 (85)	15 (58)

*IPD: In-Patient Department

Table 3: Comparison between diagnosed cases versus missed diagnosis patients

Parameters	Diagnosed cases ($n=18$)	Missed diagnosis ($n=8$)	*P*
New onset diabetes, *n* (%)	10 (55.5)	8 (100)	0.03*
Children with severe DKA, *n* (%)	6 (33)	8 (100)	0.007
Blood pH, mean (SD)	7.16 (0.13)	6.97 (0.07)	0.001#
Serum bicarbonate (mmol/L), mean (SD)	8.5 (5)	3.8 (1.3)	0.001#
Children with one or more complications, *n* (%)	11 (61)	8 (100)	0.039
Shock	9 (50)	8 (100)	0.013
Cerebral edema	0	3 (37.5)	0.006
AKI	5 (28)	7 (87.5)	0.005
Death	0	1	

#Students *t*-test, *Chi-square test. AKI: Acute kidney injury, SD: Standard deviation, DKA: Diabetic ketoacidosis

Discussion

We found that there are several factors operating at home/family, health-care facility level and at the time of referral that increased the incidence of severe DKA and its complications.

Our findings revealed that the parents and family were largely ignorant of the disease, its symptoms, and warning signs and many showed an indifference/neglect in seeking timely medical care. In addition, the lower socioeconomic status could have added to the problems, as the incidence of DKA and its complications was higher among lower socioeconomic class, although this difference was not statistically significant. Similar findings were reported by Booth and Hux who showed that the incidence of adverse events and recurrent admissions among diabetics was much higher among the lower socioeconomic strata.[14] Mallare *et al.* also reported an association between income level and incidence of DKA, wherein they found higher incidence in families with lower income.[15] Ting *et al.* reported in a study from Finland that children from families in which at least one parent had an academic degree had a lower incidence of DKA at presentation than those without.[16]

A more disturbing concern identified was the inappropriate treatment among known T1DM patients, which was seen in about 40% of these children. Noncompliance to insulin was seen in more than half of the patients that remained the commonest precipitant for ketoacidosis. Lack of supervision by a senior family member in cases where insulin was self-administered was seen in more than half of the children and was one of the reasons for insulin omission. Our findings compare favorably with that of Morris *et al.* who also reported poor adherence to insulin therapy among young adolescents in about 28% which was associated with poor long-term glycemic control and episodes of DKA.[17] The episodes of DKA among known T1DM children imply missed opportunities for health education and counseling of caregivers.

Equally concerning observation revealed by our analysis was that a diagnosis of DKA was missed in nearly half of the patients ($n = 11$; 43%) at the time of first contact with a health-care facility; most of them (8 out of 11) continued to remain undiagnosed despite multiple health-care facility visits

before reaching tertiary center. There are many factors that could have contributed to this missed diagnosis. First, nearly, two-thirds had new onset diabetes presenting as DKA for the first time, and children and parents disregarded polydipsia and polyuria as worrisome symptoms. Second, the majority of physicians attending to these children lacked the clinical experience for diagnosing DKA. Lack of facilities for prompt diagnosis and therapy added to the problems; more so for known TIDM where there was a delay of about 4–5 h in establishing the diagnosis of ketoacidosis. None of the patients irrespective of whether diagnosed or missed/undiagnosed, received appropriate fluids or insulin as recommended. Similar findings were reported by Pawlowicz *et al.* in a study from Poland, where the wrong interpretation of diabetic symptoms leads to delayed diagnosis of TIDM.[18] Several logistic reasons operating at the time of referral like distance from the tertiary care center, nonavailability of ambulance, financial constraints, ignored or neglected medical advice further compounded the delay. The above factors put together resulted in nearly three-quarter of the patients presenting as complicated DKA to our center.

The incidence of severe DKA and complications of shock, renal failure, and CE were particularly higher in patients with missed diagnosis. We believe that the prolonged uncorrected hypovolemia in our cohort resulted in hypotension and the ensuing complications. Furthermore, all 3 patients with CE were also hypotensive, underscoring the importance of uncorrected hypovolemia in the aggravation of cerebral hypoperfusion and hypoxia.[19,20]

Conclusion

The severity, complications, morbidity, and mortality associated with DKA in developing economies is far higher than that reported from the west. The root causes for the above are parental ignorance, lower socioeconomic status, missed or delayed diagnosis due to lack of clinical experience and facilities for managing DKA in the peripheral health-care facilities. This is compounded by logistic problems associated with referral services and lack of follow-up and continuum of care among known diabetics.

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Conflicts of interest

There are no conflicts of interest.

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