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Clinical Profile and Outcome of Pediatric Patients with Diabetic Ketoacidosis

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Abstract:
Objective: *This study was done to evaluate clinical profile, precipitating factors and outcome of Pediatric patients with diabetic ketoacidosis (DKA).*
Material and Methods: *This study was conducted at G. B. Pant Children hospital Srinagar between December 2012 to November 2014 which is tertiary care hospital and is associated hospital of government medical college Srinagar India. Children ≤ 15 years with DKA were included in this study. Severity of DKA was defined as mild (venous pH<7.30 or bicarbonate=15mEq/l), moderate (venous pH<7.2 or bicarbonate=10mEq/l) and severe (venous pH<7 or bicarbonate<5mEq/l). These classes correspond to first, second and third degree of DKA severity respectively. Cases in which diabetic ketoacidosis had occurred at the onset of diabetic diagnosis were not included in the study.*
Results: *Mean age was 7.5 ± 3.6 years; 31 (70%) patients were males and 13(29.5%) were girls. Fourteen patients had first degree DKA, 20 patients had second degree DKA while 10 had 3rd degree DKA at the time of presentation. Severity of DKA was significantly associated with presence of infection, history of omission of insulin, poor compliance, presence of shock at the time of presentation, length of stay in hospital, final outcome and Glasgow coma score. Mortality in this study was 2.2%.*
Conclusion: *Poor compliance was associated with the severity of diabetic ketoacidosis. Pediatric endocrinologists should ensure the patients and their parents should understand the importance of the need for regular insulin injection and regular monitoring of blood glucose.*
Keywords: *Diabetic ketoacidosis, clinical profile, outcome, insulin, compliance*

I. Introduction

Diabetic ketoacidosis (DKA) is a potentially life-threatening acute complication of type 1 diabetes mellitus (T1DM), characterized by a biochemical triad of hyperglycemia, ketonemia (ketonuria) and acidemia[1]. DKA is caused by a decrease in effective circulating insulin associated with elevation in counter-regulatory hormones[1,2]. The likelihood of ketoacidosis occurring at the onset of diabetes varies considerably (between 15% and 67%) from one country to another[3]. The reason for DKA occurring at the onset of newly-diagnosed diabetes is multifactorial[4]. DKA is the most frequent cause of diabetes-related death in children with the mortality rate ranging between 6% and 24% in developing countries[5,6].The mortality rate for DKA in children in the developed countries has declined to 0.15% to 0.31%[7,8]. Recent studies have documented a 21% to 24% mortality rate in patients who develop cerebral oedema with DKA, hence accounting for most of the DKA deaths and a high rate of permanent neurologic morbidity[9,10-12]. Other causes of morbidity and mortality in DKA include hypoglycemia, infections, pulmonary oedema, central nervous system haemorrhage or thrombosis, other large vessel thrombosis, cardiac arrhythmias caused by electrolyte disturbances, pancreatitis, renal failure and intestinal necrosis[9,10-12]. The cornerstones of the treatment of DKA are rehydration, insulin therapy and rectification of electrolyte disorders with particular attention to potassium, sodium and phosphate. Timely recognition of DKA and appropriate subsequent management to counter the metabolic derangements are important to minimize complications. In young children, it is often difficult to characterize the classical signs and symptoms of diabetes mellitus, such as polyuria, polydipsia and weight loss[8,9,13]. Many patients will have recurrence of their DKA[14]. The number of episodes of DKA is a significant outcome measure for diabetic care. The frequency of hospitalization for DKA has been reduced following diabetes education programs, improved follow up care and access to medical advice[15].

II. Methods

This study was conducted at G B Pant children hospital Srinagar between December 2012 to November 2014. Ethical committee of this children hospital approved the study protocol. The age group included in this study were ≤ 15 years of age. The diagnosis of DKA was based on finding with characteristic picture of

ketonuria, hyperglycemia (>200mg/dl or 11.1 mmol/l) and metabolic acidosis (venous pH <7.3 and/or serum bicarbonate < 15 mEq/l) in established cases of diabetes mellitus. Severity of DKA was defined as mild (venous pH<7.30 or bicarbonate=15mEq/l), moderate (venous pH<7.20 or bicarbonate=10mEq/l) and severe (venous pH<7 or bicarbonate=5mEq/l). These correspond to first, second and third degrees or grades of DKA of severity respectively. The detailed evaluation of all patients included the measurement of atleast the following parameters: random blood sugar, urine ketones, serum electrolytes, arterial blood gases and complete blood count.

These patients were managed in Pediatric intensive care unit (PICU) of our hospital once they were admitted and diagnosed. Hourly monitoring of vital signs and blood glucose levels was done in these patients. Intravenous rehydration and insulin infusion was initially given to all patients. Once their condition stabilized and their DKA resolved; they were shifted to subcutaneous insulin. The resolution of DKA in the patients was based on the consideration of multiple factors such as the resolution of acidosis noted on arterial blood gas analysis, normalization of blood sugar levels and stabilization of patient's clinical condition.

The Body Mass Index (BMI) was calculated by dividing the weight (in Kilograms) by the square of the height (in meters). Socio-economic status of the household of the children was calculated using set of variables that included area of residence and cumulative family income. It was divided into three categories including high, middle and low socioeconomic status. The diagnosis of cerebral oedema was suspected in the following two scenarios a) declining neurological status after initial improvement; b) persistently poor neurological status without any obvious cause. The early signs that were suspicious for this condition included headache, vomiting, lethargy and decreased arousal, relative bradycardia and hypertension while late signs included seisures, incontinence, pupillary changes, papilloedema, upgoing plantars and respiratory arrest. The diagnosis of cerebral oedema was verified by computed tomography (CT Scan) in all cases. Immediate management strategies employed to reduce cerebral oedema included elevation of head end of the bed, immediate reduction in rate of fluid therapy and use of intravenous mannitol. Shock in the patients was indicated by the presence of signs of systemic hypo perfusion accompanied by at least one these: tachycardia and/or hypotension. Signs of systemic hypoperfusion were assessed by measurement of pulse characteristics, cutaneous temperature, capillary refill time, neurological status and urine output.

HbA 1c, was measured via high performance liquid chromatography method. Presence of infection was indicated by positive radiological imaging or culture. This was supported by elevated white blood cell count and clinical examination by the Doctor. The measure of compliance with regards to insulin was based on the history given by the attendants of the patients. Poor compliance was defined as missing insulin injections on multiple days, especially before or during the period of illness.

III. Results

The results of this study showed total of 44 DKA patients. Among 44 patients, all 44 (100%) patients showed signs of dehydration and other signs and symptoms were polyuria 41 (93%), respiratory distress 40 (90%), polydipsia 32 (72%), weakness 28 (63), abdominal pain 23 (52%), impaired consciousness 20 (45%), weight loss 19 (43%), vomiting 15 (34%), Nocturnal enuresis 8 (18%), smell of ketones 4 (9%) and pyrexia 3 (6%).

Table-1 Frequency of signs and symptoms among 44 patients with DKA.

Clinical presentation	NO.	%
1. Dehydration	44	100
2. Polyuria	41	93
3. Respiratory distress	40	90
4. Polydipsia	32	72
5. Weakness	28	63
6. Abdominal pain	23	52
7. Impaired consciousness	20	45
8. Weight loss	19	43
9. Vomiting	15	34
10. Nocturnal enuresis	8	18
11. Smell of ketones	4	9
12. Pyrexia	3	6

The mean age of patients was 7.5±3.6 years. Thirty one of the patients in our study were boys (70%) and 13 patients were girls (29.5%). Fourteen patients had first degree DKA, 20 patients had second degree DKA while 10 had 3rd degree DKA at the time of presentation to emergency department. This grading was also reflected by the blood pH of the patients. Table-2 shows the distribution of the socio-demographic characteristic along with some other baseline variables at presentation of the study population in relation to severity of DKA.

Presence of infection, history of omission of insulin and poor compliance were factors that were associated significantly with the severity of DKA at presentation.

Table-2 Socio-demographic and baseline disease features of patients with DKA (n=44).

Socio-demographic and other base line variables	Grades of severity of diabetic ketoacidosis		
	Mild/ Grade 1	Moderate/ Grade 2	Severe/ Grade 3
Age			
< 6 months	1	0	0
< 6-12 months	0	0	0
> 1-5 years	4	5	4
> 5-10 years	6	9	4
> 10 years	3	6	2
Gender			
-Male	9	14	6
-Female	4	8	3
Socio-economic status			
-High	2	1	0
-Middle	9	13	7
-Low	2	7	3
Body Mass Index (kg/m^2)			
-<12	3	5	4
-27.1	5	9	3
-15.1 – 18	3	3	2
-18 – 21	2	3	2
Family history of diabetes	8	15	8
History of omission of Insulin	2	3	7
Poor compliance	2	1	4
Duration of symptoms in days			
-≤ 1 day	5	7	2
-2-4 days	4	11	4
-5-10 days	4	2	3
-> 10 days	1	1	0
Presence of infection	3	5	8

Shock was present in total of 9 (20.4%) patients at the time of presentation. Out of these 9 patients 7 (77.7%) had grade 3 DKA. Three patients (6.8%) had a Glasgow Coma Scale of 8 0r less. Blood cultures were positive in only 3 patients (6.8%). The mean values of various important serum parameters in patients included: 1) random blood sugar: 486 mg/dl ±128 mg/dl (26.6mmol/l±7.1mmol/l), 2) Sodium: 133±9.4mEq/l, 3) Potassium: 4.5±0.8mEq/l, 4) bicarbonate: 15±6 mEq/l, 5) HBA1c: 9%±2.5%.

The mean duration of stay in hospital was 6.4±2.9 days. The associations between biochemical and clinical parameters with the degree of severity of DKA are presented in table-3

Table-3 Association between different biochemical and clinical parameters and grade of severity of DKA.

Biochemical and clinical parameters in DKA	Grade of severity of Diabetic ketoacidosis (n=44)		
	Mild/Grade 1	Moderate/Grade 2	Severe/ Grade 3
Presence of shock at presentation	0	2	7
Glasgow coma scale at presentation		1	2
-≤8	0	2	1
-> 8-11	0	19	6
-≥ 12	13		
Random blood sugar at admission			
-250-350 (mg/dl).	4	4	2
-350.1-450 (mg/dl).	2	6	3
-450.1-550 (mg/dl).	2	4	0
->550(mg/dl)	5	8	4
Serum sodium (mEq/l).			
-≤ 120	1	1	3
-120.1-130	4	8	8
-130.1-140	7	4	4
->140	0	2	2
Serum potassium (mEq/l).			
-≤2.5	0	1	0
-2.6-3.5	4	3	2
-3.6-5	7	14	7
->5	2	4	0
Blood urea nitrogen (mg/dl)			

-12 -11-20 ->20	 6 5 2	 6 10 5	 3 2 5
Length of stay in hospital in days -2-5 -6-10 ->10	 5 7 1	 11 10 1	 1 1 7
Final outcome: successful resolution of DKA -Death.	 13 0	 22 0	 8 1

Mean duration of the insulin infusion was 29.2 ± 22.2 hours. The mean duration of acidosis was 19.1 ± 19.5 hours. A total of 2 (4.5%) patients developed cerebral oedema. There were one death only, therefore the mortality rate was 2.2%. This patient had severe DKA, sepsis and cerebral oedema. Presence of cerebral oedema, need for mechanical ventilation, low socio-economic status, low serum sodium and potassium levels, low arterial pH and sepsis were factors that impacted the outcome of patient. Review at the time of last follow-up, of these patients in the out-patient clinic after discharge showed that 37 (84%) patients were taking insulin therapy at home. Thirty (68%) patients were compliant in the receipt of insulin therapy. Reasons of non-compliance were not documented.

IV. Discussion

Our study has revealed that there is no association between the age and severity of DKA. This finding is consistent with results of a study in which although age was found to be significantly associated with incidence of DKA, but not with its severity[16]. Our data also showed no significant correlation between severity of DKA and other demographic factors like gender, body mass index and family history of diabetes and this is supported by other reports in literature[17]. In our study, the severity of acidosis as a reflection of the severity of DKA, appeared to have a clinically significant association with the GCS at the time of presentation. Acidosis has been reported as an independent predictor of the level of consciousness in DKA as it affects the GCS even without the development of cerebral oedema[18].

We found that presence of infection, poor compliance and omission of insulin had a positive correlation with degree of severity of DKA in our study. In a study done in Egypt, infection was found to precede the diagnosis of DKA in 21.9% cases[19]. This association is clearer in the context of extreme metabolic disturbances as shown in our study, where infections have been found to significantly affect the severity of DKA. A study from Manchester[20] based on a 6-year retrospective review of 135 diabetic children found that abnormal insulin treatment behavior was an important factor in the development of DKA episodes in established diabetic children. This is in agreement with a study conducted in Dundee where adherence to insulin treatment protocols was found inversely related to hospital admission for DKA suggesting that poor adherence to insulin treatment was a major factor in DKA hospitalization[8]. This notion is confirmed by our results where history of insulin omission had a direct correlation with DKA severity.

Our study revealed significant association between PICU stay and a worse patient outcome, which can be explained by the fact that all the mentioned indications for PICU admission adversely affect the outcome in these patients. This is consistent with our study that showed DKA, represents a decompensated phase of diabetes mellitus, which may require PICU admission, especially in the presence of cardiovascular instability, inability to protect the airways, altered state of consciousness, the presence of acute abdominal signs or symptoms suggestive of acute gastric dilatation[21]. The results of our study suggest that most of our patients developed DKA because they had omitted insulin doses; also poor compliance was associated with severity of DKA in the study population. This is similar to study which showed that insulin omission precipitated DKA in upto 38% pediatric patients with established diabetes[22]. We had total of 2 (4.5%) cases of cerebral oedema, one died and one recovered completely. Our figure is slightly higher than reports from UK and USA where less than 1% of cases developed cerebral oedema[23]. The mortality rate from DKA in developed counties is from 0.15% to 0.31%, with higher rate (13%) being reported from developing countries[24,25]. Boys were more affected than girls in our study with a ratio of 2.3:1. This is similar to study in which boys were more involved than girls[26]. The most common signs and symptoms of DKA were dehydration, polyuria, polydipsia, respiratory distress, weakness and abdominal pain. This is consistent with some literature[27].

V. Conclusion

Poor compliance is an important modifiable precipitating factor for diabetic ketoacidosis in children in our setup. Education of patients and their parents/guardians with regards to the importance of regular blood sugar

monitoring and insulin dosing should be considered an important long-term management strategy. Further studies are needed to improve the data about DKA in the pediatric population in Kashmir India.

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