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Clinical Profile of Pediatric Diabetic Ketoacidosis in Karbala City, IRAQ

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Abstract
BACKGROUND Diabetic ketoacidosis (DKA) is the most severe diabetic emergency and is still associated with a significant mortality (~1–2% in western countries, but particularly in developing countries where mortality is substantially higher). It is a state of severe uncontrolled diabetes caused by insulin deficiency and requires urgent treatment with insulin and fluids to prevent death. DKA occurs more commonly in younger people, but the mortality is higher in the elderly. Approximately 25% of new patients with diabetes will present with DKA. In children with established diabetes the risk of DKA is increased in those with poor metabolic control and previous episodes of DKA, adolescent girls, children with psychiatric disorders including eating disorders and those with psychosocial difficulties. The majority of the remainder are due to inadequate insulin during intercurrent illness. **THE AIM OF STUDY:** To evaluate the clinical profile of pediatric DKA in Karbala city /Iraq. **PATIENTS AND METHODS:** This is a retrospective study involved diabetic patients admitted to Karbala paediatric teaching hospital and al Hindyia general hospital from the 1st of January to the 31th of December 2014 who had been admitted as a case of diabetic ketoacidosis. A total no. of 68 patients included in this study, they are classified according to the age, gender, severity of DKA, the precipitating factor of DKA and according to the residency. **RESULTS:** From the 68 patients whom included in this study, there were 16 males and 52 females with male: female ratio of 0.3: 1. The patients divided according to the age into 3 groups (1-5, 6-10 & 11-15 years). The factors which precipitate DKA were: 18 patients presented in state of DKA as first presentation of IDDM, infections were the precipitating factor in 31 patients and the other 24 patients were due to omission of insulin. The patients classified according to the severity of DKA in regard to the age groups and gender and the results show as that 18 patients were presented in mild DKA, 24 patients in state of moderate DKA and the other 26 patients were presented in state of severe DKA. **CONCLUSION:** DKA is an acute metabolic complication of IDDM that can be life-threatening**.** Although the incidence of DKA is more common in girls, the severity of the condition is more in boys.
Keywords: pediatric, DKA, IDDM, Karbala.

INTRODUCTION

Diabetic ketoacidosis is the most severe diabetic emergency and is still associated with a significant mortality (~1–2% in western countries, but particularly in developing countries where mortality is substantially higher). It is a state of severe uncontrolled diabetes caused by insulin deficiency and requires urgent treatment with insulin and fluids to prevent death. DKA occurs more commonly in younger people, but the mortality is higher in the elderly. It is estimated that 2–8% of hospital admissions in children occur because of DKA and there are ~5–8 episodes per year per 1000 people with type 1 diabetes. (1) . Approximately 25% of new patients with diabetes will present with DKA. In children with established diabetes the risk of DKA is increased in those with poor metabolic control and previous episodes of DKA, adolescent girls, children with psychiatric disorders including eating disorders and those with psychosocial difficulties. Inappropriate interruption of insulin pump therapy may also lead to DKA. Seventy-five per cent of DKA episodes are associated with insulin omission or treatment error. The majority of the remainder are due to inadequate insulin during intercurrent illness[2].

DKA is characterized by hyperglycemia (>200 mg/dL), acidosis (serum pH< 7.35, bicarbonate < 20 mmol/L), along with evidence of an accumulation of ketoacids in the blood (3).

DKA results from absolute or relative deficiency of circulating insulin and the combined effects of increased levels of the counterregulatory hormones: catecholamines, glucagon, cortisol and growth hormone (4). Absolute insulin deficiency occurs in the following conditions:

1- undiagnosed type 1 diabetes mellitus (T1DM); DKA reported to be the first presentation in about 25% of the cases especially in those less than 5 years old (5).

2- Patients on treatment who miss their insulin doses, especially the long-acting component of a basal-bolus regimen. It is estimated that 75% of DKA episodes are associated with insulin omission or treatment errors (6). patients who use insulin pump if insulin delivery fail (7).

Relative insulin deficiency, on the other hand, occurs when the concentrations of counterregulatory hormones increase in response to stress in conditions such as: sepsis, trauma, or gastrointestinal illness with diarrhea and vomiting. Hyperglycemia and hyperketonemia cause osmotic diuresis, dehydration, and electrolyte loss. This stimulates stress hormone production, which induces insulin resistance and leads to a vicious circle,

worsening of the hyperglycemia and severe hyperketonemia. Fatal dehydration and metabolic acidosis will ensue if management is not initiated. Poor tissue perfusion or sepsis may lead to lactic acidosis which can aggravate the ketoacidosis [8].

Risk factors for DKA in children with newly diagnosed type 1 diabetes include: young age (<5 years), first degree relative with type 1 diabetes, lower socioeconomic status, medications (high dose glucocorticoids, antipsychotics, diazoxide and immunosuppressive). Risk factors for DKA in children with established type 1 diabetes include: poor metabolic control, previous episodes of DKA, female adolescents, psychiatric disorders (especially eating disorders) and lower socio-economic status [9].

The metabolic abnormalities associated with DKA develop rapidly, usually within 24 hours. However, signs and symptoms of poor diabetic control may precede DKA by several days. [8] [10]. Patients often present with polyuria, polydipsia, weakness, fatigue, and altered sensorium [2,4,5]. Abdominal pain, nausea, and vomiting are common features in DKA that usually resolve with correction of acidosis [8] [10] [11]. On physical examination, signs of hypovolemia are often present, including dry mucosal membranes, decreased skin turgor, tachycardia, and hypotension. Additionally, patients may have a fruity odor to their breath as a consequence of acetone release. Deep and labored breathing, or Kussmaul's respirations, may also be observed and are an attempt to correct the metabolic acidosis with a compensatory respiratory alkalosis; however, the excess acid cannot be expired. Mental status can range from an intact sensorium to diabetic coma [8] [10-13]. Blood samples should be obtained to check serum or plasma glucose, electrolytes, bicarbonate, blood urea nitrogen, creatinine, osmolality, venous (or arterial in critically ill patient) pH, partial pressure of Carbon dioxide(pCO2), calcium, phosphorus, and magnesium concentrations (if possible), Glycosylated Hemoglobin (HbA1c), hemoglobin and hematocrit or complete blood count. Increased serum urea nitrogen and hematocrit may be useful markers of the severity of extracellular fluid (ECF) contraction. [14] . It has to be noted that an elevated white blood cell count in response to stress is characteristic of DKA and is not necessarily indicative of infection [15]. Metabolic acidosis being an important landmark of DKA is also helpful to grade the severity of the condition and hence the prognosis by assessing its degree as follows ([16]: Mild DKA: venous pH <7.35, bicarbonate <20 mmol/L., Moderate DKA: pH <7.25, bicarbonate <15 mmol/L and Severe DKA: pH <7.15, bicarbonate <10 mmol/L. Other investigations include: urinalysis for ketones. , Measurement of blood ß-OHB concentration(if available, is useful to confirm ketoacidosis and may be used to monitor the response to treatment. Appropriate specimens for culture (blood, urine, throat), if there is evidence of infection. If laboratory measurement of serum potassium is delayed, an electrocardiogram (ECG) is performed for baseline evaluation of potassium status. [17] The aim of treatment is the slow, smooth restoration of clinical and biochemical normality while avoiding anticipatable complications. Usually the goal is a return to normal metabolic parameters within 48-72 hours. Safe treatment is dependent on careful observation of progress, biochemical monitoring and meticulous record keeping [18]. The management considerations for Paediatric DKA are broadly similar to those for adults, namely: exogenous insulin, IV fluid therapy and replacement of electrolytes. The management of DKA requires frequent monitoring of both the clinical status of the patient and physiochemical changes that occur during treatment. In addition to the routine observation chart documenting vital signs and neurological status hourly, it is helpful to have a flow chart to record all electrolyte and blood gas results over each 24 h period [19]. With prompt treatment, complications of diabetic ketoacidosis (DKA) are uncommon. However, when complications do occur they are usually serious. The complications of diabetic ketoacidosis include: Cerebral edema, acute kidney failure and adult respiratory distress syndrome [20].

THE AIM OF STUDY

To evaluate the clinical profile of pediatric patients who admitted with the diagnosis of DKA in Karbala city/Iraq.

PATIENTS AND METHODS

This is a retrospective study done in Karbala city which is located in the middle of Iraq with a population of 1,100000. The study involved diabetic patients admitted to Karbala paediatric teaching hospital and al Hindyia general hospital from the 1st of January to the 31st of December 2014 who had been admitted as a case of DKA. The data collected from the medical files of these patients and by phone contact. The total number were 140. Fifty-nine patients were excluded because they don't apply to the definitive criteria of DKA while 13 patients excluded because of incomplete medical reports. The other 68 patients are studied for the following factors:
1-Age: the cases divided into 3 age groups (1-5), (6-10) and (11-15) years.
2-Gender:16 males and 52 females.
3-Severity of acidosis.: mild (PH <7.35, bicarb <20mmol /l), moderate (PH <7.25, bicarb <15 mmol /l) and severe acidosis (PH <7.15, serum bicarb <10 mmol/l).
4-Precipitating factor: classified into 3 categories:
DKA (as a first presentation of DM), Infection (manifested by fever and significant elevation of WBC count) and omission of insulin or non-compliance.

5-Residency: classified into urban (those who lived in the centre of the city), rural (those who lived outside the centre of the city) and visitors (those who live in other cities of Iraq and admitted during their visit to the holy shrines).

Other factors that had been intended to be included in this study such as HbA1c, other autoimmune diseases, family history of DM are excluded because of incomplete information from medical files. The statistical data of the study obtained by chi square method. P value of <0.05 is regarded as significant while p value of >0.05 is regarded as insignificant.

RESULTS

From the 68 patients whom included in this study, there were 16 (23,52 %) male and 52 (76.47 %) female with male: female ratio of 0.3: 1. The patients divided according to the age into 3 groups (1-5, 6-10 & 11-15 years) and the result was 12 patients (17.64%) from 1-5 years, 25 patients (36.76 %) from 6-10 years and 31 patients (45.58 %) from 11-15 years as shown in the table 1 which show also the distribution of cases according to the gender and age group.

TABLE [1] Distribution of cases according to the age groups and gender

Age group	Male	Female	Total	%
1-5 years	3	9	12	17.64
6-10 years	7	18	25	36.76
11-15 years	6	25	31	45.58
Total	16	52	68	100

The precipitating factors of DKA in our patients are shown in table 3 which show that 18 patients (26.74 %) presented in state of DKA as first presentation of diabetes mellitus, the infections were the precipitating factor of DKA in 31 patients (45.58 %) and the other 24 patients (35.29 %) were develop DKA because of omission of insulin.

Table [2]: Distribution of cases according to the precipitating factor and gender

Precipitating factor	Male	Female	Total	%
First presentation of DM	5	13	18	26.74
Infections	6	25	31	45.58
Omission of insulin	5	19	24	35.29

The patients classified according to the severity of DKA (table 3) which show us that 18 patients (26.47%) were presented in mild DKA, 24 patients (35.29 %) in state of moderate DKA and the other 26 patients (38.23 %) were presented in state of severe DKA. the severity of the DKA also classified according to the age groups and the results also shown in table 3.

Table [3]: Distribution of cases according to severity of DKA and age group

Age group/year	Mild DKA	Moderate DKA	Sever DKA	Total	%
1-5	6	2	4	12	17.64
6-10	6	11	8	25	36.76
11-15	6	11	14	31	45.58
Total	18	24	26	68	100

p= 0.1146(non-significant)

The severity of the DKA in our patients was compared according to the gender (table 4) which show that the male patients (1 in mild DKA, 5 in moderate DKA and 10 in severe DKA) while the female patients (17 in mild DKA, 19 in moderate DKA and 16 in severe DKA).

Table [4]: Distribution of cases according to the severity of DKA and gender

Severity of DKA	Male	Female	Total	%
mild	1	17	18	26.47
Moderate	5	19	24	35.29
Sever	10	16	26	38.23
Total	16	52	68	100

P= 0.0150 (significant)

The patients also divided according to residency as shown in table 5 and the result was 40 cases (58.82) from the center of the city (urban area), 24 cases (35.29%) from rural area and 4 visitors (5.88%).

Table [5]: Distribution of cases according to the residency

Residency	No. Of cases	%
Centre of city (urban)	40	58.82
Rural	24	35.29
Visitors	4	5.88
Total	68	100

DISCUSSION

This study gives the basic profile of DKA in this area of Iraq where studies about DKA are few. There were many limitations in our study like small sample size, retrospective analysis and difficulties in following the patients.

The study shows that the frequency of DKA was higher among girls than among boys with female to male ratio 1:0.3 and this is consistent with the results of a study done in Indonesia by Nur Fochmah (boys comprised only 31% of cases) [21] and also consistent with a study done by Neu et al who report statistically significant increase in the frequency of DKA in girls [22]. By the distribution of the cases according to the age group , our study show that the incidence of DKA increases with increasing age with peak incidence among those of 10-15 years old which is consistent with the results of the study which is done by Mohammed A. Naeem in Saudi Arabia who found that the incidence of DKA increases with age and the peak incidence was among those patients more than 10 years old [23] .This is may be explained by the fact that the incidence of IDDM increase with increasing age with a peak incidence in the preadolescent patients .

There are many factors which may precipitate the occurrence of DKA , our study shows that the infections were the main factor which contribute to the occurrence of DKA (45.58 %) followed by omission of insulin (35.29 %) and first presentation of IDDM as DKA (26.74 %) and this is similar to a lesser extent to the results of a study done in Saudi Arabia by Satti Abdulrahim who found that the infections were the main precipitating factor for the occurrence of DKA (82.1 %) while poor compliance with omission of insulin was the second factor (17.9 %) (24) , this results also consistent with the results of a study done in south India by Basavanthappa(25) but it was in the opposite of the results of Mohammed A. Naeem who found that noncompliance to the insulin as the cause of precipitating DKA found in 67% of the cases (23) .We noted that infections were the main factor which precipitate DKA , therefore preventive measures to decrease and early treatment of childhood infections may reduce the incidence of DKA . The exact reason for the omission of insulin in our patients is not known but it may be related to under education and general reluctance to accept insulin as a long-life therapy but using remedy and herbal mixtures in the treatment of IDDM rather than insulin. Our study shows that 26.74% of cases were presented as a first diagnosis of IDDM which may be attributed to the delay in the diagnosis of IDDM, therefore increase awareness of signs and symptoms of IDDM among general population and primary health care givers may reducing the incidence of DKA.

Our study shows that there is no difference in the severity of DKA regarding age group with P value=0.1146 which is similar to the results done in India by Shabir ahmed [26] which revealed no association between the age and severity of DKA and it is also consistent with another study done in India by Sudhir Mehta showing no correlation between age and severity of DKA [27].

Although the incidence of DKA was more among girls than boys , our study show that the severity of DKA was significantly more in boys than girls (P value = 0.015) and this similar to a study done by Ramaswany et al from India [28] and this is also seen in most earlier studies except in the study by Neu et al [22] which show higher frequency of severe DKA in girls but the results of the study of Shabir ahmed [26] show no significant correlation between the severity of DKA and gender .There is another study done in Pakistan by Madiha Syed show no significant correlation between the severity of DKA and gender [27] .The distribution of our patients regarding residency show that 58.82% of the patients from urban area while 35.29% of them from rural area which is not consistent with the results of the study by Basavanthappa [25] which show that 78% were from rural area , this may be explained by increase the incidence of IDDM in urban area due to increment in the stressful factors, complexity of life and sources of pollution in urban area .

CONCLUSION

DKA is an acute metabolic complication of IDDM that can be life-threatening. It's may be the first presentation of IDDM in children, so increase awareness of signs and symptoms of IDDM among general population and primary health care givers may reducing the incidence of DKA. The important precipitating factor was infections which can be decreased by preventive measures to decrease the incidence of DKA. Omission of insulin was the other important precipitating factor for DKA which mandates the education of the patients and their parents about the importance of the competent to long term insulin therapy. Although the incidence of DKA is more common among girls, the severity of the condition is more among boys necessitating more attention during the management.

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