Predictors of Diabetic Ketoacidosis among Patients with Type 1 Diabetes Mellitus Seen in the Emergency Unit

Abstract:

Aims: to identify the factors that can predict the development of diabetic ketoacidosis (DKA) among patients with type 1 diabetes mellitus (T1DM) in Basrah.

Materials and Methods:

Place and Duration of Study

The study was conducted at the emergency units of Al-Faiha General Hospital and Al-Basrah General Hospital for the period from June 2013 to June 2014.

Methodology

This study was cross-sectional enrolled four hundred patients with T1DM seen in the emergency unit were selected; patients and their families were subjected to specific questionnaires prepared for this study.

Results: In this study, 400 patients with T1DM enrolled, 160 patients were having DKA (40%), 240 (60%) were not. Factors that predict DKA include,age , gender, school level of both the patients and their parents , address of the patients, the early initiation of the proper insulin regimen after diagnosis of T1DM, presence of acute recent illness, missing insulin doses and frequency of the dose missing , number of previous DKA attacks, using of syringes or pens as a tool of insulin delivery, however, the most important two predictors are the source of insulin supply to patients , presence of glucometer at homes and frequency of its uses.

Conclusion: This result provided evidence that multiple factors interact together to play a vital role in the development of DKA among patients with T1DM in Basrah.

Keywords: Diabetes Mellitus, Type 1, Diabetic Ketoacidosis, Predictors.

INTRODUCTION

Diabetic ketoacidosis (DKA) is a serious acute complication of diabetes mellitus. According to American Diabetes Association, the mortality rate in patients with DKA is reported to be less than 5 % [1]. However, it is reported that there has been a 4.2% decrease in the death rate per year in the United States during 1985-2002 [2]. Mortality in patients developing DKA is predominantly due to the underlying morbidities such as sepsis or myocardial infarction [3].

The most common precipitating factor in the development of DKA is missed insulin doses [4]. Other factors that may precipitate the incidence of DKA are infections, cerebrovascular accident, alcohol abuse, pancreatitis, myocardial infarction, trauma and drugs such as corticosteroids, thiazides, and sympathomimetic agents.

In young patients with type 1 diabetes mellitus(T1DM), psychological problems with eating disorders may be a contributing factor for 20% of recurrent DKA [5].

The majority of DKA cases occurs in patients with previously diagnosed diabetes [5], and only a small proportion of patients accounts for the majority of hospitalizations [6]. Thus, it is estimated that 50% of hospital admissions could be prevented by improved outpatient treatment and better adherence to self-care [7].

Recent studies found higher glycosylated hemoglobin (HbA_1C), female sex, older age, family and school problems, higher insulin dose, underinsurance, and psychiatric disorders to be associated with an increase in DKA rate [5,8,9].

The early identification and treatment of patients at risk is essential to be targeted in intervention programs aimed at preventing DKA [10].

Despite major advances in the care of diabetes, DKA remains a leading cause of hospitalization and the leading cause of morbidity and death in children and adolescents with T1DM.

It is important to try to prevent DKA in order to reduce morbidity and mortality associated with severe metabolic decompensation [11]. This prevention can be accomplished through appropriate education, improved self-care and adherence, and consistent self-monitoring of blood glucose and ketones [12]. DKA as an initial manifestation of T1DM is less amenable to prevention [13], other than through surveillance in youth with a positive family history of diabetes, and increased public awareness of the symptoms of diabetes.

The study aimed to identify the factors that can predict the development of DKA among patients with T1DM in Basrah.

Materials and Methods
Design and data collection:
A cross-sectional case-control study was carried out to analyze the predictors of DKA among patients with type 1 diabetes mellitus seen in the emergency unit that involved four hundred patients with type1 diabetes mellitus seen in the emergency units of Al-Faiha and Al-Basrah General Hospitals in Basrah, Southern Iraq during a one-year period (June 2013-June 2014).
The ethical committee of the Basrah College of Medicine approved the study.
Measurements:
All patients are sometimes their relatives (parents , brothers, sisters) were subjected to specific questionnaires already prepared for this study. Written informed consent were taken from the patients or their relative if they age under19 years.
Patients were selected according to inclusion and exclusion criteria; the inclusion criteria for the patients were: patients who were 15 years (visiting adult emergency unit) and above and diagnosed with type 1 diabetes mellitus.
Patients who were not interested in questionnaires and those who's their first diagnosis of type 1 diabetes mellitus were as DKA during the carrying of the study in the emergency units were excluded.
T1DM was defined as insulin-dependent less than six months from diagnosis [14].
DKA was defined as a tetrad of blood glucose>200mg/dl (11mmol/L), ketonemia and ketonuria, venous PH<7.3 and or bicarbonate<15mmol/L [15], in addition to the clinical features of DKA in the patients. In this study arterial, blood gas analyzer {IRMA (TRU POINT)} was used to check the PH and bicarbonate level.

Definition of Variables: In our conducted study the following variables are defined as:

- The address of the patients: all the centered areas in Basrah are considered as urban while all the peripheral areas are considered as rural.
- In regard to the insulin starting after diagnosis of T1DM: patients who started prescribing insulin therapy on the same day of T1DM diagnosis by the doctor are considered as immediate insulin users otherwise they are considered non-immediate insulin users.

- In regard to the regimen of insulin: in the study any patient used prandial regular human insulin three times daily with additional doses of basal insulin (including NPH insulin) at bed time is considered as basal-bolus insulin user otherwise they are considered non basal bolus insulin users.
- In the study, patients who use syringes for insulin delivery are considered as insulin syringe users otherwise they are considered non-insulin syringes users including those using insulin pens or using both syringes and insulin pens for insulin delivery.
- What is considered as "recent acute illness" in this study is that any patient who had an illness of belong to or occurring at a time immediately before the present, and his disease is of rapid onset and or a short course.
- In regard to missed insulin dose: in this study any patient who intentionally or unintentionally missed what prescribed insulin regimen dose is considered as missing an insulin dose.
- What is considered as "previous DKA" in this study is that any patient who had DKA diagnosis documentation by a doctor with hospital admission and discharging card.

Statistical analysis:

Data obtained from the questionnaires was analyzed using the Statistical Package for Social Sciences (SPSS) software version 15.0. Data are presented as a mean± standard deviation in case of continuous variables and as absolute numbers (percentage) in case of dichotomous variables with statistical analysis was carried out using Student's t test for continuous variables and Chi-square test for dichotomous variables.

The (p-value) less than 0.05 was considered significant. Univariate analysis was performed to determine each variable's association with diabetic ketoacidosis. In 400 patients, univariate analysis was performed for each of the factors in the presence or absence of diabetic ketoacidosis after the presence of diabetic ketoacidosis was used as the dependent variable. Variables found to be associated with diabetic ketoacidosis in univariate analysis were then entered into a multivariable model using logistic regression to determine the power of each variable for associated with diabetic ketoacidosis.

Results

The baseline characteristics of all patients are given in (Table 1) including: age, gender, duration of T1DM, school level of the patients and their parents, address, insulin started after the diagnosis, a regimen of insulin, tool for insulin delivery, recent acute illness, missed insulin dose, previous DKA, previous hospitalization, availability of glucometer at home and the frequency of its use, and finally the source of insulin supply.

Out of 400 patients included in this study 149 (37.2%) were females, and 251 (62.8%) were males. Studied all the patients had T1DM and were on insulin therapy. Their age was 15 years and above with the oldest patient was aged 45 years and with a mean age of 27.5 ±6. 2 years.

Patients were subdivided into 2 subgroups according to their duration of T1DM, group1<3 year and group2 ≥ 3years, whose number of patients and their percentages were 162 (40.5), 238 (59.5) respectively.

School level of participating patients was categorized into those who have ≤ 6 years of school achievement209 (52.3) and those who have>6 years school achievement 191 (47.7). The school level of the patients' parents participating in the study categorized into: those parents who have ≤6 year's school achievement 257 (64.3%) and those parents who have>6years school achievement 143 (35.7%).

Regarding the address of the patients included in this study, patients were divided into those living in rural areas 183 (45.8%) and those who live in urban areas 217 (54.2%).

According to starting on insulin therapy after diagnosis of T1DM, patients subdivided into 2 groups: group1 those who start insulin immediately after diagnosis and group2 included patients who not start insulin immediately and were found that their number and percentage 213 (53.3), 187 (46.7) respectively.

The regimen of the used insulin subdivided the studied patients into 2 groups: group1 those who used the regimen of basal-bolus insulin186 (46.5 %), group2 those who used non basal-bolus insulin regimen (Premix insulin 70:30 twice daily or modified basal-bolus) were 214 patients (53.5 %).

There were 214 (53.5%) of the studied patients were having a recent acute illness, whereas 186 (46.5%) did not have.

According to the tool used for insulin delivery, the studied patients were subdivided into: those who used syringes only to deliver insulin 186 (46.5 %), those who not used syringes only (using pens or both pens and syringes) 214 (60.3 %).

According to the presence of insulin missing doses; the studied patients were subdivided into two groups: group1 those who had missed insulin dose 166 (41.5%), and group2 were those who not missed insulin dose 234 (58.5%), and according to the frequency of missed insulin doses; patients were subdivided into 2 groups also: group1 those who had one missed insulin dose 101 (60.8 %) and group2 were those who had multiple missed insulin doses 65 (39.2 %).

According to the availability of glucometer at home and frequency of its use for monitoring blood sugar, we subdivided the participated patients into 2 groups: group1those who had glucometer 131(32.8 %) and group2 were those who not had glucometer at home 265(67.2%); and according to the frequency of glucometer using at home the studied patients subdivided into two groups: those who use glucometer < 4 times daily to check blood sugar 52(39.7%) and those who use glucometer ≥ 4 times daily 79(60.3%).

According to the presence of previous DKA attack; patients were categorized into two groups: group1 those who had previous DKA 223(55.8%) and group2 included those who did not have previous DKA attack 177(44.2%); and according to the frequency of previous DKA; patients participating in this study were subdivided into: those who had <2 attacks of previous DKA 106(47.5%) and those who had≥2 attacks of previous DKA 117(52.5%).

Finally, according to the source of insulin supply, patients participating in this study were subdivided into two groups: group1 those who depend on Al-Faiha Specialized Diabetes, Endocrine, and Metabolism Center (FDEMC) as a source of insulin supply 203 (50.8 %) and group2 were those who depend on the public clinic as an insulin source supply 197 (49.2 %).

It was found that there was a significant relationship between the gender of the patients with T1DM and DKA development; *p*-value was 0.001 and the female patients mainly affected; from a total of

149 female patients with T1DM enrolled in this study; 77 developed DKA compared to 83 DKA male patients from a total of 251 male patients with T1DM involved in this study (Table 2).

Age also had a significant association with DKA development; p-value was 0.003, and young age is associated with DKA occurrence; 92 patients out a total of 193 patients aged ≤ 20 year compared to 68 patients for a total of 207 at age group> 20 year .

There is a strong relationship between duration of T1DM and DKA development; p-value=0.025.

A high effect of the educational level of both the patients and their parents on DKA developments with p-value=0.001 for both .

There was a significant effect of the patients' address on DKA developments; 105patients out of 183 of those with TIDM living in the rural areas developed DKA, while only 55 out of 207 of those with T1DM living in urban areas developed DKA;p-value=0.001.

It was also found that there is a significant effect of the time of starting insulin therapy in patients with T1DM on DKA development, and a delay in initiation of insulin therapy after diagnosis of T1DM increase the risk of DKA development among those patients; p-value=0.001 .

The initiation of a proper regimen of insulin in patients with T1DM strongly influence DKA development, with the lowest risk of DKA among those used basal-bolus regimen in which 62 patients, developed DKA from a total of 186 patients used that regimen; and the highest risk was among those who not used the regimen of basal-bolus insulin (using twice daily premix 70:30 insulin or modified basal-bolus) from a total of 214 used that regimen, 98 patients developed DKA, p-value=0. 011.

The tool of insulin delivery used by patients with T1DM strongly affect the DKA development, with the highest number among those used insulin pens only (non -syringes) while the lowest number of those used syringes, p-value=0. 001.

One hundred and nine(50.9%) from a total of 214 patients had acute recent illness developed DKA while only 51(27.4) patients developed DKA from a total of 186 patients who did not have acute recent illness, p-value=0.001;so there is a significant correlation between DKA development among patients with T1DM and presence of recent acute illness among them .

This study also reveals a significant relationship between DKA development and missing an insulin dose, *p*-value=0. 001 .

The importance of the frequency of the missed insulin dose also highlighted in our study and our results revealed a strong association between increased the frequency of the missed insulin doses and DKA development, *p*-value=0.001.

The presence of glucometer at home and the frequency of its used for checking blood sugar has a strong effect on DKA development, with only 7 patients from a total of 79 patients who had glucometer and using it frequently developed DKA,sixteen patients developed DKA from a total of 52 patients who had a glucometer at home but used it infrequently while 137 patients from a total of 256 did not have a glucometer developed DKA, *p*-value=0.01 .

In this study, it was found that the source of insulin supply strongly affects the DKA development in patients with T1DM with 91 patients developed DKA from a total 197 type 1 diabetic patients took their insulin supply from public clinics while only 69 patients developed DKA from a total number of 203 took their insulin supply from FDEMC, *p*-value=0.013 .

With a *p*-value=0.001 indicating that there is a strong relationship between presence of previous DKA attack and DKA development in patients with T1DM, from a total of 223 patients had a previous DKA attack, 114 were developed DKA at the time of the study while only 46 patients were found with DKA from a total of 136 patients with T1DM and did not have a previous DKA attack.

Finally, our study revealed that increased the number of previous DKA attacks, increase the risk of future DKA development in patients with T1DM, with a strong relationship was found in this study between number of previous DKA attacks and DKA development, from a total of 117 patients who had ≥2 previous DKA attack, 75patients developed DKA, while among those patients who had just < 2 previous DKA attack, which were 106 patients, only 39 patients developed DKD, *p*-value=0. 001.

So variables associated with DKA with statistical significance were all the studied variables. Predictors of DKA identified by multivariate analysis are shown in table 3.

Variables that remain statistically significantly associated with diabetic ketoacidosis were: age, gender, duration of type1 diabetes mellitus, the address of the patients, insulin regimen, tool of insulin administration, presence of acute recent illness and previous diabetic ketoacidosis attacks and its number, missing of insulin and its frequency, frequency of glucometer usage at home to check blood sugar and the source of insulin supply to the patients with type1 diabetes mellitus.

Discussion

The prevalence of T1DM is increasing worldwide [16]. DKA was universally fatal, especially before the days of insulin in the 1920s, after that, the overall mortality decreased to relatively low figures, but there is still the potential of case fatality from DKA either from acidosis or as a complication of therapy [17,18]. There was a predominance of females with DKA in our study that is similar to the universal findings [19-20]. This could be attributed to the fact that insulin purging is frequent to control weight in young women with diabetes[21,22]. Furthermore, adolescent girls with diabetes are at greater risk of developing disordered eating patterns[23]. Adolescent girls and young women are also the group at highest risk to suffer from 'brittle' diabetes, a form of severe unstable diabetes with increased metabolic complications, especially recurrent DKA [24].

In accordance with previous studies [17,20], teenage at diabetes onset was related to elevated incidence of DKA. On one hand, greater personal responsibility diabetes management and less parental monitoring adolescents may lead to a deterioration of metabolic control in this group. On the other hand, endocrine changes associated with puberty lead to greater insulin resistance [24]. Comparable reasons may account for the trend toward a higher incidence of DKA in patients with longer duration of diabetes.

The Low educational level of the patients and their parents had significantly associated with the development of DKA in our study, and these results were also demonstrated in other universal similar studies [20,25].

As expected and supported by similar studies in neighboring countries [26,27,28], the patient address significantly associated with DKA occurrence and this is clearly related to the educational level of the patients and their families, their economic status and their access to the medication supply and specialized diabetic centers.

Delayed initiation of prompt insulin therapy following a diagnosis of T1DM has been associated with increased risk of DKA development among patients with T1DM [29]; the same result was found in this study also.

It is found that the initiation of the suitable and the effective insulin regime was associated with reduced DKA rate [29,30] , as found in this study that the lowest DKA was among those patients using the prandial regular human insulin before each of the three-day major meals with further dose of basal insulin at bedtime (basal-bolus insulin regimen).

To our knowledge, the effect of how insulin delivered on DKA rate has not been investigated before. In our study, it has been found that using of insulin pens had been associated with increased rate of DKA when compared with the using of the insulin syringes; this is perhaps related to the ignorance of the proper technique for the use of these pens especially among those patients with low educational levels, also in Iraq we use vial and syringes for all, except few used reusable pen ,and with unavailability of insulin cartridge make patients refill them by syringes that definitely end with dosing errors because manufacturer recommendation was against the rifling of insulin cartridge.

The recent acute illness and mainly infections are important DKA precipitators in 109 patients.Most patients presented with nausea, vomiting and abdominal pain, which was interpreted as an indication to reduce or stop their insulin.This is a deep-rooted belief shared by some doctors and diabetic educators. The situation is made worse when such patients consume large amounts of sugar-rich fluid to counteract presumed hypoglycemia[31] .

Insulin omission intentionally and unintentionally was found in patients with DKAin the present study. Among patients with poor compliance with insulin therapy, patients stopped insulin therapy either because they are away from insulin supply (lost, broken,

etc.), not gave clear reason for stopping insulin or did not know how to handle insulin on sick day. Insulin discontinuation has long been recognized as an important precipitating cause of DKA in retrospective studies[32] .

Observational studies in urban African Americans have reported that more than one-half of DKA cases in patients with diabetes were caused by noncompliance with insulin therapy[32,33] . Likewise, a retrospective study in a multiethnic population in Texas listed noncompliance with insulin injections as their most common precipitating cause of DKA [34] .

Higher insulin doses were observed in the DKAgroup, which corresponds to the results of Rewerset al [35] . They hypothesized that a higher reported insulin dose may represent lower endogenous insulin secretion because of longer duration of diabetes because of puberty, but it could be that in patients who miss insulin injections, a higher prescribed insulin dose may not be consistent with the actual applied insulin dose, and that what is found in this study with high number of DKA among patients with multiple missed insulin doses than those who missed a single dose.

Previous DKA and increase number of previous DKA were associated with increased DKA rate [36] , and this, what is found in our study.

The goal of glucose monitoring in diabetes is to obtain useful information about the patient's overall glucose status to normalize glucose and prevent hypoglycemia and minimize hyperglycemia through meaningful and timely interventions. As glucose control is the foundation of diabetic care, self-monitoring of blood glucose (SMBG) is the foundation of glucose monitoring. Studies have shown a direct correlation between SMBG and improve HbA1C levels and reduce DKA rate[37-39], the American Diabetes Association recommends that patient with T1DM should self-test at least three times daily. This is identical to what is found in our study of reducing the number of DKA among those who frequently used SMBG (7 patients with DKA out of a total of 72) compared with (16 patient without DKA out of 36)of those who used SMBG infrequently or not used it respectively.

Finally, to our knowledge, the effect of source of insulin supply on DKA rate has not been investigated before. In our study, we found

that the source of insulin was significantly associated with the development of DKA, and patients who depend on FDEMC as source of insulin supply were significantly had lower DKA compared with those who took insulin from the public clinic. This is may be related to the advantage of more experienced staff and multidisciplinary treatment as well as the availability of follow-up investigations and better communication with patients and the dealing with all their aspects.

Study limitations: It was a cross-sectional study; so no data available on mortality. The age of onset of T1DM was not studied because ,but its play a role in DKA development. The incomes of the family also play a role and was not assessed in our study. The puberty stage was not assessed in the studied patients since puberty plays an important role in the loss of control of diabetes during the transition period [40] .

Conclusion
The results of this study provided evidence that multiple factors interact together to play a vital role in the development of DKA among patients with T1DM in Basrah.

Data sharing statement

No additional data available

References

1-KitabchiAE, Umpierrez GE, Miles JM, and Fisher JN.Hyperglycemic Crises in Adult Patients with Diabetes. Diabetes Care . 2009 Jul;32(7):1335-43.

2-Wang J, Williams DE, Narayan Kev, Geiss LS. Declining Death Rates from Hyperglycemic Crisis Among Adults with Diabetes, U.S., 1985-2002. Diabetes Care. 2006; 29: 2018- 22.

3-Basu A, Close CF, Jenkins D, Nattrass, Wright AD. Persisting Mortality in Diabetic Ketoacidosis. Diabet Med. 1993; 10: 282-4.

4-QARI FA. Precipitating Factors for Diabetic Ketoacidosis. Saudi Med J. 2002; 23:173-6.

5-Smith CP, Firth D, Bennett S, Howard C,Chisholm P. Ketoacidosis Occurring in Newly Diagnosed and Established Diabetic Children. Acta Paediatr. 1998:87 :537–41.

6-Kovacs M, ProchownikCD, Obrosky DS. A Longitudinal Study of Biomedical and Psychosocial Predictors of Multiple Hospitalizations among Young People with Insulin-Dependent Diabetes Mellitus. Diabet Med. 1995: 12: 142–8.

7-Kaufman FR, Halvorson M. The Treatment and Prevention of Diabetic Ketoacidosis in Children and Adolescents with Type I Diabetes Mellitus. Pediatr Ann.1999 :28 :576–82.

8-Levine BS, Anderson BJ, Butler DA, Antisdel JE,Brackett J, Laffel LM. Predictors of Glycemic Control and Short-Term Adverse Outcomes in Youth with Type 1 Diabetes. J Pediatr. 2001: 139: 197–203.

9-Rewers M, Chase HP, Mackenzie T. Predictors of Acute Complications in Children with Type 1 Diabetes. JAMA. 2002: 287: 2511- 18.

10-Diabetes Control and Complication Trial Research Group. Effect of Intensive Diabetes Treatment and on the Development and Progression of Long-term Complications in Adolescents with Insulin-Dependent Diabetes Mellitus: Diabtetes Control and Complication Trial. J Pediatr .1994: 125: 177–88.

11-Basu A, Close CF, Jenkins D, Krentz AJ, Nattrass M, Wright AD. Persisting Mortality in Diabetic Ketoacidosis. Diabet Med. 1993: 10: 282– 4.

12-Dunger DB, Sperling MA, Acerini CL et al. European Society for Paediatric Endocrinology/Lawson Wilkins Pediatric Endocrine Society Consensus Statement onDiabetic Ketoacidosis in Children and Adolescents. Pediatrics. 2004: 113: 133–40.

13-Levy-Marchal C, Patterson CC, Green A. Geographical Variation of Presentation at Diagnosis of Type I Diabetes in Children: The EURODIAB Study. Europeanand Diabetes. Diabetologia. 2001: 44 (Suppl. 3): B75–B80.

14-Leslie RD, Kolb H, Schloot NC, Buzzetti R, Mauricio D, De Leiva A, et al. Diabetes Classification: Grey Zones, Sound andSmoke: Action LADA I.Diabetes Metab Research Rev. 2008 Oct; 24(7): 511-9.

15-Savage MW, Dhatariya KK, Kilvert A, Rayman G, Rees JA, Courtney CH et al. Joint British DiabetesSocieties Guideline for the Management of Diabetic Ketoacidosis. Diabetic Med. 2011; 28(5): 508-15.

16-Word Heath Organization (WHO). Prevention of Diabetes Mellitus. Report of aWHO Study Group. Tech Rep Ser No 144 : WHO Geneva; 1994.

17-Elleman K, Noverted SJ, Pederson L, Edsberg B, Ortved AO. Epidemiology and Treatment of Diabetic Acidosis. A Population Based Study. Am J Epidemiol. 1984; 7: 528-32.

18-Tunbrdige WM. Factors Contributing to Death of Diabetes less than Fifty Years of Age. Lancet. 1981; 11: 560-71.

19-Levine BS, Anderson BJ, Butler DA, Antisdel JE, Brackett J, Laffel LM. Predictors of Glycemic Control and Short-Term Adverse Outcomes in Youth with Type 1 Diabetes. J Pediatr. 2001: 139: 197–203.

20-Smaldone A, Honig J, Stone PW, Arons R,Weinger K. Characteristics of California Childrenwith Single versus Multiple Diabetic Ketoacidosis Hospitalizations (1998–2000). Diabet Care. 2005: 28:2082–4.

21-Stancin, DT, Link and JL, Reuter M. Binge Eating and Purging in Young Women with IDDM. Diabet Care.1989 :12 : 601–3.

22-Meltzer LJ, Johnson SB, Prine JM, Banks RA,DesrosiersPM, Silverstein JH. Disordered Eating, BodyMass, and Glycemic Control in Adolescents with Type 1 Diabetes. Diabet Care. 2001: 24: 678–82.

23-Kent L, Gill GV, Williams G. Mortality and Outcome of Patients with Brittle Diabetes and Recurrent Ketoacidosis. Lancet. 1994: 344: 778–81.

24-Amiel SA, Sherwin RS, Simonson DC, Luritano AA, Tamborlane W. Impaired Insulin Action in Puberty: A Contributing Factor to Poor Glycemic Control in Adolescents with Diabetes. N Engl J Med. 1986: 315:215–9.

25-Rewers M, Chase HP, Mackenzie T. Predictors of Acute Complications in Children with Type 1 Diabetes.JAMA. 2002: 287: 2511–8.

26-Shaltout A. Diabetic Ketoacidosis in Childhood. Kuwait Medical Journal. 1985; 19: 3-6.

27-Kadiki OA. Childhood Diabetes mellitus in Benghazi, Libya.Topical Pediatrics Journal. 1987; 33: 136-139 .

28-Ahmed IS, Kheir MM, Ahmed NH. Precipitating Factors for Ketoacidosis in Adult's Sudanese Patients.Diabetes International Journal. 2000; 3: 86-7.

29-Morris AD,Boyle DIR,McMahon AD,Greene SA,Macdonald TM,Newten RW. Adherence to Insulin Treatment, Glycemic Control and Ketoacidosis in Insulin Dependent Diabetes Mellitus.Lancet .1997;350; 1505-10.

30-Walker M, Marshall SM, Alberti KG. Clinical Aspects of Diabetic Ketoacidosis. Diabetes Metabolism Review. 1989; 5:651-63.

31-Barrett EJ, DeFronzo RA. Diabetic Ketoacidosis: Diagnosis and Treatment. Hosp Pract. 1984; 19: 89-93.

32-36-Umpierrez GE, Kelly JP, Navarrete JE, Casals MM, Kitabchi AE. Hyperglycemic Crises in Urban Blacks. Arch Intern Med. 1997;157:669–75.

33-Musey VC, Lee JK, Crawford R, Klatka MA, McAdams D, Phillips LS. Diabetes in Urban African-Americans: I. Cessation of Insulin Therapy is the Major Precipitating Cause of Diabetic Ketoacidosis. Diabetes Care. 1995;18:483–9.

34-Maldonado MR, Chong ER, Oehl MA,Balasubramanyam A. Economic Impact of Diabetic Ketoacidosis in a Multiethnic Indigent Population: Analysis of Costs Based on the Precipitating Cause. Diabetes Care. 2003;26:1265–9.

35-Rewers M, Chase HP, Mackenzie T. Predictors of Acute Complications in Children with Type 1 Diabetes. JAMA 2002: 287: 2511–8.

36-Tattersal R, Gregory R, Selby C, Heller S, Kerr D. Course of Brittle Diabetes: a twelve year follow up. BMJ. 1991; 302: 1240-3.

37-Norris SL, Lau J, Smith SJ. Self-Management Education for Adults with Type I Diabetes: A Meta-Analysis of the Effect on Glycemic Control. Diabetes Care. 2002;25:1159-71.

38-Polonsky WH, Earles J, Smith S. Integrating Medical Management with Diabetes Self-Management Training: A Randomized Control Trial of the Diabetes Outpatient Intensive Treatment program. Diabetes Care. 2003;26:3048-53.

39-Sheppard P, Bending JJ, Huber JW. Pre- and Post-prandial Capillary Glucose Self-Monitoring Achieves Better Glycaemic Control than Pre-prandial only Monitoring. A Study in Insulin Treated Diabetic Patients. Practical Diabetes Int.2005; 22:15-22.

40-Trast J. CE. Diabetes and Puberty: A Glycemic Challenge.Am J Nurs. 2014 Jun 10; 129-33.

Table 1:Study Characteristics of Patients

Variables		No.(%)
Gender	Male	251(62.8)
	Female	149(37.2)
Age(Years) Mean ± SD 27.5±6.2	≤ 20	193(48.3)
	>20	207(51.7)
Duration of Diabetes Mellitus(Years)	<3	162(40.5)
	≥3	238(59.5)
School Level of Patients(Years)	≤ 6	209(52.3)
	>6	191(47.7)
School Level of Parents(Years)	≤ 6	257(64.3)
	>6	143(35.7)
Address of Patients	Rural	183(45.8)
	Urban	217(54.2)
Insulin Starting after Diagnosis	Immediately	213(53.3)
	Non Immediately	187(46.7)
Regimen of Insulin	Basal Bolus	186(46.5)
	Non Basal Bolus	214(53.5)
Recent Acute Illness	Yes	214(53.5)
	No	186(46.5)
Tool of Insulin Administration	Syringes	186(46.5)
	Non Syringes	241(60.3)
Missed Insulin Dose	Yes	166(41.5)
	No	234(58.5)
Frequency of Missed Insulin Dose	One Dose	101(60.8)
	Multiple Doses	65(39.2)
Self-monitoring of Blood Glucose (SMBG)	Present	131(32.8)
	Not Present	265(67.2)
Frequency of Self-Monitoring of Blood Glucose Usage(Number/Day)	<4	52(39.7)
	≥ 4	79(60.3)
Source of Insulin	Al-Faiha Specialized Diabetes, Endocrine, and Metabolism Center (FDEMC)	203(50.8)
	Public Clinic	197(49.2)
Previous Diabetic Ketoacidosis	Yes	223(55.8)
	No	177 (44.2)
Number of Previous Diabetic Ketoacidosis	<2	106(47.5)
	≥ 2	117(52.5)
DKA	Yes	**160(40)**
	No	**240(60)**

Table-2- Univariate Association of Potential Confounding Variables with DKA (No.=400).

Variables		Diabetic Ketoacidosis	Non Diabetic Ketoacidosis	Total (%)	p value	Odds Ratio (95% Confidence Interval)
Age Years (Mean±SD)	≤ 20	92	101	193(48.3)	0.003	1.862 (1.242-2.791)
	>20	68	139	207(51.7)		
Sex	Male N (%)	83	168	251(62.8)	0.001	2.165 (1.429-3.279)
	Female N (%)	77	72	149(37.2)		
Duration of Type 1 DM (Year) No(%)	< 3	54	108	162(40.5)	0.025	1.606 (1.061-2.432)
	≥ 3	106	132	238(59.5)		
School Level of Patients(Years) No(%)	≤ 6	102	107	209(52.3)	0.001	2.186 (1.450-3.296)
	> 6	58	133	191(47.7)		
School Level of Parents (Year) No (%)	≤ 6	121	136	257(64.3)	0.001	2.373 (1.525-3.692)
	> 6	39	104	143(35.7)		
Address No(%)	Rural	105	78	183(45.8)	0.001	3.965 (2.596-6.056)
	Urban	55	162	217(54.2)		
Insulin Started after Diagnosis No(%)	Immediately	46	167	213(53.3)	0.001	0.176 (0.144-0.274)
	Non Iimmediately	114	73	187(46.7)		
Regimen of insulin No(%)	Basal bolus	62	124	186(46.5)	0.011	1.690 (1.125-2.537)
	Non basal bolus	98	116	214(53.5)		
Tool of Insulin Administration No(%)	Syringes	52	107	159(39.7)	0.017	1.671 (1.101-2.536)
	Non syringes	108	133	241(60.3)		
Recent Acute Illness No(%)	YES	109	105	214(53.5)	0.001	2.748 (1.807-4.178)
	No	51	135	186(46.5)		
Missed Insulin Dose(s) No(%)	YES	81	85	166(41.5)	0.001	1.870 (1.244-2.810)
	NO	79	155	234(58.5)		
Number of Insulin Missed Doses N(%)	Single	32	69	101(60.8)	0.001	6.604 (3.269-13.338)
	Multiple	49	16	65(39.2)		
Previous Diabetic Ketoacidosis No(%)	Yes	114	109	223(55.8)	0.001	2.978 (1.945-4.562)
	No	46	131	177 (44.2)		
Number of Previous Diabetic Ketoacidosis No(%)	< 2	39	67	106(47.5)	0.001	3.068 (1.778-5.298)
	≥ 2	75	42	117(52.5)		
Presence of Self-Monitoring Blood Glucose Device No(%)	Yes	23	108	131(32.8)	0.001	0.205 (0.123-0.342)
	No	137	132	265(67.2)		
Frequency of Self-Monitoring Blood Glucose Device Usage(Number/Day) No(%)	< 4	16	36	52(39.7)	0.01	4.571 (1.726-12.109)
	≥ 4	7	72	79(60.3)		
Source of Insulin Supply No (%)	Al-Faiha Diabetic Endocrine and Metabolic Center	69	134	203(50.8)	0.013	1.667 (1.114-2.496)
	Public Clinic	91	106	197(49.2)		

Table-3- Predictors of Diabetic Ketoacidosis Identified by Multivariate Analysis(No=400).

Variable	Standard Error	Significance Probability	Odd Ratio (95%confidence interval)
Age	0.207	0.003	1.212 (1.042-2.371)
Sex	0.220	0.001	2.121 (1.217-3.149)
Duration of Type1 Diabetes Mellitus	0.212	0.025	1.106 (1.011-2.231)
School Level of Patients	0.245	0.001	1.186 (1.430-2.286)
School Level of Parents	0.229	0.002	2.353 (1.317-3.432)
Address	0.372	0.001	2.762 (2.566-4.053)
Regimen of Insulin	0.207	0.013	1.690 (1.125-2.537)
Tool of Insulin Administration	0.513	0.012	1.221 (1.101-2.122)
Recent Acute Illness	0.214	0.001	2.748 (1.807-4.178)
Missed Insulin Dose	0.208	0.003	1.870 (1.244-2.810)
Number of Missed Insulin Dose(S)	0.359	0.001	4.612 (3.266-8.298)
Previous Diabetic Ketoacidosis	0.218	0.001	2.978 (1.945-4.562)
Number Of Previous Diabetic Ketoacidosis	0.279	0.001	3.068 (1.776-5.298)
Frequency of Self-Monitoring Blood Glucose Device Usage	0.497	0.002	3.531 (1.524-8.104)
Source of Insulin Supply	0.206	0.012	1.347 (1.104-2.146)