

Knowledge and Awareness of Mothers about Diabetic Ketoacidosis among Type-1 Diabetic Children and Their Action and Response in Emergency Conditions in Aseer Region of Saudi Arabia

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Abstract

Diabetic ketoacidosis is a common acute complication of children with type-1 diabetes. However, it can be easily dealt at home by the patient himself, their parents or families if they have been provided good diabetes self-management education by health educator. We conducted this study to know the mothers' knowledge, their perception, knowledge about symptoms of DKA in children, and their response in emergency conditions, which was not studied previously in our region. 142 patients and their mothers were selected for this study for the duration of one year. Data for collected from diabetes center and diabetes clinics in different hospitals. Regarding education level of mothers, our data has demonstrated that 3.5% were illiterate, while 38% completed university level education. 67% of them know that what is DKS, while 33% of all mothers were unaware of it. 48.6% received information from diabetes health educator, 41% from physicians and 15% from the internet or media. 68% of the patients had episodes of DKA previously; for this, mother's response or action was recorded. It was found that 67% went directly to hospital, 27% went to emergency only when the condition worsened, while 20% increased the insulin dose. We discovered also that no one knew about sick day management. We concluded and recommended that diabetes education is essential part of diabetes management and health education department should focus on all aspects of diabetes self-management education in multiple group sessions to prevent DKA and its complications.

Keywords: Blood ketones; Diabetes self-management education; Diabetic Ketoacidosis; Insulin; Mothers' knowledge; Sick day management; Urine ketones

Introduction

Diabetes mellitus is characterized by chronic hyperglycemia resulting from defects in insulin secretion, insulin action, or both. Insulin is the major anabolic hormone storing all fuels during the meals and in postprandial states. Metabolic abnormalities in carbohydrates, lipids, and proteins result from Imbalance of insulin action. The acuteness of symptoms is due to the type and duration of diabetes. Some of the diabetes patients are asymptomatic especially those with type-2 diabetes during the early years of the disease. However, children with marked hyperglycemia with absolute insulin deficiency may suffer from polyuria, polydipsia, polyphagia, weight loss, and blurred vision. Uncontrolled diabetes may lead to stupor, coma and if not treated death due to ketoacidosis or rarely from non-ketotic hyperosmolar syndrome [1-6]. Long-term complications affecting the eyes, the kidneys, and the cardiovascular system are the principal cause of morbidity and mortality among diabetic subjects, and significant health problem [7-12]. Hence, complications can be prevented by better diabetes control [13-16].

However, normalization of glycemic control is not an easy task and requires a team work and good education [17]. Type-1 diabetes is an autoimmune disease; diabetic ketoacidosis (DKA) is an acute metabolic disorder of type-1 diabetes, which is primarily characterized by an increased presence of circulating ketone bodies, and the development of severe ketoacidosis in the presence of prolonged uncontrolled hyperglycemia, usually due to insulin deficiency. DKA is more commonly seen between children and young adults with type-1 DM; especially those that are noncompliant with insulin therapy or who present severe infection or other complications [18-20]. The symptoms of uncontrolled diabetes that may lead to development of DKA are typically of short duration and include polyuria, polydipsia, polyphagia, weight loss, vomiting, abdominal pain and ultimately acidotic coma; rare complications of severe DKA includes cerebral edema [21-25]

Diabetes self-management education (DSME) is an important aspect of diabetes management. It has been shown that education and diabetes self-awareness improves the glycemic control and quality of life, especially in type-1 children [26-28]. Furthermore, mothers' knowledge is also important for the pediatric diabetes management. Well educated mothers can manage their children well as compared to non-educated one [29]. Sick day management is also part of diabetes education. There is research evidence that poorly controlled diabetic subjects may have impaired leukocyte function, and resulting in

impaired immunity and increased susceptibility to infection. Under any metabolically stressed conditions, or insulin resistance, insulin dose should be increased with hydration as well. Most of the patients ignore this issue and may go in impending DKA, and thereafter full clinical DKA.

If pediatric mothers are well educated for diabetes, they can manage stress conditions at home by the rule of sick day management, recognizing signs and symptoms of DKA, increasing insulin dose and hydration, before reaching to emergency department; this has been shown to reduce DKA complications.

Hence, we conducted this research to study the mothers' knowledge, their perception, knowledge about symptoms of DKA in children, and their response in emergency conditions, which was not studied previously in our region.

Methods

The study was conducted in Diabetic Center at Aseer hospital, diabetic clinics in Abha maternity hospital, and diabetic clinics in khamis mushayt maternity hospital. These are largest tertiary care centers for diabetes in Ministry of Health and receiving patients from whole Aseer Region. Study duration was one year, commencing from April 2017 until May 2017.

This is cross-sectional study, was on Mothers of children with type-1 diabetes. We included all pediatric type-1 DM patients who were in follow up in respective clinics and their mothers. Adult diabetic patients were excluded from this study.

Overall, 142 pediatric diabetic patients and their mothers were selected for this study. Questionnaire was developed in Arabic Language and was then translated in English for further study and statistical analysis.

Statistical package for social sciences (SPSS) was used for data entry and analysis. Data were summarized as frequencies and percentages.

Results

Table 1 demonstrates mother's age, ranging from 20 and up to more than 40 years. The results of the table indicate that most of age group was between 36-40 years (31%), and the lowest age group was between 20-25 years (5%)

Age in years	Numbers (%)
20-25	7 (5)
26-30	23 (16)
31-35	37 (26)
36-40	44 (31)
>40	31 (22)

Table 1: Mothers' age.

Table 2 demonstrates education level of mother. 3.5 % were illiterate, while 38% completed university level education. Table 3 categorizes the age of pediatric diabetic patients. 2 % were between one to two years of age. Maximum numbers were observed between 7 to 12 years of age (55%).

Educational level	Number (%)
Illiterate	5 (3.5)
Primary School	27 (19)
Middle School	22 (15.5)
Secondary School	34 (24)
University level	54 (38)

Table 2: Education level of mother.

Age in years	Numbers (%)
<1 years-2 years	3 (2)
2 years-6 years	34 (24)
7 years-12 years	78 (55)
13 years-15 years	27 (19)

Table 3: Age of pediatric diabetic patient.

Table 4 demonstrates answer for the question regarding DKA; while Table 5 demonstrates mother's knowledge and perception regarding DKA. 67% responded that they know about DKA. However, 33 % responded that they do not know about DKA.

Answer	Numbers (%)
Yes	96 (67)
No	46 (33)

Table 4: Do you know what DKA is?

What is DKA?	Numbers (%)
High levels of acid in blood and urine	28 (19.7)
One of the complications of diabetes due to high blood sugar	41 (28.8)
High sugar with dryness, abdominal and exhaustion	30 (21)
Blood acidity	14 (10)
High blood sugar	10 (7)
I do not know	12 (8.5)
Acidity in the blood due high blood sugar	7 (5)

Table 5: If Answer is yes (for Table 4), then knowledge and perception of mothers about DKA.

Similarly, Tables 6-9 demonstrates answers to the questions regarding previous history source of information, hospitalization with DKA, signs with symptoms observed before the emergency hospitalization, and mothers' response or action while they observed the emergence DKA condition. Maximum number of mothers got the knowledge from diabetes health educators and physicians (48.6% and 41%, respectively). Only 10.4 % receive this knowledge from internet or media (news from television). 68% of the patients experience DKA

with hospital admissions previously, with frequent symptoms of abdominal pain and vomiting (42% and 21%, respectively). 14% developed rapid breathing and 2% experienced coma (Table 8). Table 9 demonstrates mothers' action or response of DKA as emergency condition. 67% went to emergency directly, 19% delayed until the condition worsen, and only 14% increased the dose.

Source of information of DKA	Numbers (%)
Diabetes health Educator	69 (48.6)
Physician (Diabetologist /Endocrinologist)	58 (41)
Electronic Media/Internet	15 (10.4)

Table 6: Source of information for DKA.

Answer	Numbers (%)
Yes	97 (68)
No	45 (32)

Table 7: Previous history of DKA with hospitalization?

Signs and Symptoms of DKA?	Numbers (%)
Abdominal pain	60 (42)
Vomiting	30 (21)
rapid breathing	20 (14)
All of the above	29 (21)
Coma	3 (2)

Table 8: If positive history of DKA, then what were the signs and symptoms.

Mothers response	Numbers (%)
Directly went to the emergency	95 (67)
I did not go to the emergency until his condition worsened	27 (19)
Increase the dose of insulin	20 (14)

Table 9: Mothers' response and action after recognition.

Discussion

DKA is a medical emergency and life-threatening condition; and if not recognized early, with early management in emergency department, may lead to serious complications.

Illness and stress increases ketone bodies (acetoacetate, beta-hydroxybutyrate, and acetone) production due to inadequate insulin levels. Hence there are increased insulin requirements during the incubation period of an infection before the onset of the illness. Failure to increase the dose during illness may predispose to impending DKA. Furthermore, due to insulin resistance, the increased need for insulin may persist for a few days after the illness or infection has subsided. Pediatric type-1 diabetic patients are especially susceptible to these metabolic conditions. During this period, mothers of pediatric type-1 diabetics should pay special attention focusing diabetes management

at home with increased insulin dose and hydration. Hence, hyperglycemia crisis and development of DKA can be prevented by good diabetes education, for both the patient and mother [30-32]. Furthermore, visits to diabetes educator with family involvement is essential for better diabetes understanding and home management of diabetes [33,34]. To assess the patient or their parents' knowledge is an important aspect of diabetes health education or DSME [35,36]. Additionally, at the patient first visit, physician and diabetes health educator should counsel the patient regarding diabetes medications, including oral agents and insulin, diabetes acute and chronic complications and sick day management [37,38]. Hence, DKA is preventable if the family and the patient are well educated, especially for the newly diagnosed pediatric type-1 diabetics [39,40]. This can only be achieved by recording and developing questionnaire which can assess mothers' or the patients' knowledge in different societies and among different ethnic groups with different cultures [41].

Current research was conducted to assess knowledge pediatric type-1 diabetic mothers and their attitude, understanding, depth of knowledge and their action or responses during the emergency conditions when DKA initiates. This was not studied previously in our Aseer Region. It is very important to recognize emergency condition when it initiates such as impending DKA, when it can be managed easily at home, if metabolic conditions remain stable.

Our data has shown that 3.5% mothers were illiterate, while 38% mothers completed university level education. However, 46% patients (33%) responded that they do not know what is DKA. This was alarming figure and requires DSME at national levels in Saudi Arabia. According to table-5, overall 34.7% responded that DKA involves blood acidity (high levels ketone bodies with pH<7.3 mol/L). Remaining 65.3% gave different responses, indicating their unawareness of the severity of DKA. Regarding the source of information (Table 6), our data also demonstrated that overall 127 patients (89.6%) got general diabetes education and regarding DKA from diabetes educators and physicians. Although media and internet can play an important role, however, role of physicians and educators is important in DSME. Regarding Tables 7 and 8, it was observed that 68% of children had previously DKA with hospital admission; and 42% demonstrated abdominal pain, 21 % vomiting, with 14% demonstrating acidotic and rapid breathing.

One of the alarming facts was discovered while questioning the mothers regarding their emergency actions or responses. Only 14% increased the dose during impending DKA. Hence, we recommend diabetes educators to educate pediatric patients, their mothers and families regarding "sick day management", which not only includes increasing the dose of insulin, but also increased intake of fluids during the illness, infections or other stress related conditions.

It has been demonstrated that hyperglycemia, fever, excessive glycosuria and ketonuria increase fluid losses which must be replaced quickly and spontaneously to prevent dehydration. Fluids should also contain water with salt if there are ongoing losses of fluids such as vomiting or diarrhea. Additionally, in the presence of loss of appetite or decreased blood glucose below approximately 10 mmol/L (180 mg/dl), sugar-containing fluids should also be considered to avoid starvation ketosis.

Diabetes Educators must inform that during the illness never stop insulin, may increase the insulin dose depending on SMBG, more frequent monitoring of blood glucose and ketones. And if symptoms

persist, or ketones become significantly positive, then emergency visit is essential to prevent further complications of DKA.

Sick day management reduces worsening of DKA with reduced hospital or emergency department visits. Sick day management also involves with frequent self-monitoring of blood glucose (SMBG) and blood (beta-hydroxybutyrate) or urine ketone testing [42-47]. Diabetes educators should focus on all aspects of diabetes management on each visit, and to follow and assessment up periodically.

Conclusion and Recommendations

Our data has demonstrated that although mothers of pediatric type-1 diabetic children have the knowledge of DKA, however they need further education from the diabetes health educators and diabetes care team as most of them do not know about the sick day management.

The diabetes care team and health educators should provide clear guidance to patients and families on how to manage diabetes during sick days or illnesses to avoid the complications of ketoacidosis, uncontrolled or symptomatic hyperglycemia, hypoglycemia and dehydration, never stop insulin, and the insulin dose may need to be increased or decreased and adjusted according to SMBG.

A multidisciplinary team approach with arrangement of group education at tertiary care diabetes centers of Aseer Region of Saudi Arabia is required for better understanding type-1 DKA and its prevention to reduce economic burden.

Insulin pump would be a better option for pediatric type-1 diabetics with recurrent DKA and uncontrolled diabetes. It is recommended using evidence based guidelines for the better management of diabetes [48-54].

References

1. American Diabetes Association. (2014) Diagnosis and classification of diabetes mellitus. *Diabetes care*. Jan 1: 81-90.
2. Craig ME, Hattersley A, Donaghue KC (2009) Definition, epidemiology and classification of diabetes in children and adolescents. *Pedi dia* 10: 3-12.
3. Galtier F (2010) Definition, epidemiology, risk factors. *Diabetes Metab* 36: 628-651.
4. Møller N, Jørgensen JO (2009) Effects of growth hormone on glucose, lipid, and protein metabolism in human subjects. *Endo reviews* 30: 152-177.
5. Randle PJ, Garland PB, Hales CN, Newsholme EA (1963) the glucose fatty-acid cycle its role in insulin sensitivity and the metabolic disturbances of diabetes mellitus. *The Lancet* 13: 785-789.
6. Zierler KL, Rabinowitz D (1963) Roles of insulin and growth hormone, based on studies on forearm metabolism in man. *Medicine* 6: 385-402.
7. Aziz KMA (2014) Association of microalbuminuria with ischemic heart disease, dyslipidemia and obesity among diabetic patients: Experience from 5 year follow up study of 1415 patients. *Bioenergetics* 3: 118
8. Aziz KM (2013) The diabetic foot syndrome an ignored and potential problem in medical practice. *Int J Diabetol Vasc Dis Res* 11: 1-3.
9. Aziz KMA (2010) Association between high risk foot, retinopathy and HbA1C in Saudi diabetic population. *Pak J Physiol* 6: 22-28.
10. Aziz KMA (2015) Correlation of urine biomarkers: Microalbuminuria and spot urine protein among diabetic patients. Application of spot urine protein in diabetic kidney disease, nephropathy, proteinuria estimation, diagnosing and monitoring. *Recent Pat Endocr Metab Immune Drug Discov* 9: 121-33.
11. Aziz KMA (2016) Association between hypothyroidism, body mass index, systolic blood pressure and proteinuria in diabetic patients: Does treated hypothyroid with thyroxine replacement therapy prevent nephropathy/chronic renal disease? *Curr Diabetes Rev* 12: 297-306.
12. Centers for Disease Control and Prevention (2014) Estimates of diabetes and its burden in the United States. National Diabetes Statistics Report. Atlanta, GA: US Department of Health and Human Services.
13. Boulton AJ, Vileikyte L, Ragnarson-Tennvall G, Apelqvist J (2005) The global burden of diabetic foot disease. *The Lancet*. 12:1719-24.
14. Cleary P, Crofford O, Davis M, Rand L, Siebert C, et al. (1996) Effect of intensive treatment of diabetes on the development and progression of long-term complications in insulin-dependent diabetes mellitus. *N Engl J Med* 14: 977-986.
15. Fowler MJ (2008) Microvascular and macrovascular complications of diabetes. *Clinical diabetes* 2: 77-82.
16. Hoerger TJ, Segel JE, Gregg EW, Saaddine JB (2008) Is glycemic control improving in US adults?. *Diabetes care* 31: 81-6.
17. Van Belle TL, Coppieters KT, Von Herrath MG (2011) Type 1 diabetes: etiology, immunology, and therapeutic strategies. *Physiol Rev* 91: 79-118.
18. Eisenbarth GS (1986) Type I diabetes mellitus. *New England N Engl J Med* 22: 1360-1368.
19. Maahs DM, West NA, Lawrence JM (2010) Epidemiology of type 1 diabetes. *Endocrinol Metab Clin North Am* 39: 481-497.
20. Nyenwe EA, Kitabchi AE (2016) The evolution of diabetic ketoacidosis: An update of its etiology, pathogenesis and management. *Metabolism*. 65: 507-521
21. Kitabchi AE, Umpierrez GE, Murphy MB, Barrett EJ (2004) Hyperglycemic crises in diabetes. *Diabetes care*. 27: S94-S102
22. Agarwal A, Yadav A, Gutch M, Consul S, Kumar S (2016) Prognostic factors in patients hospitalized with Diabetic Ketoacidosis. *Endocrinol Metab* 31: 424-432
23. Eledrisi MS, Alshanti MS, Shah ME, Brolosy B, Jaha N (2006) Overview of the diagnosis and management of diabetic ketoacidosis. *Am J Med Sci* 5: 243-251.
24. Weinstock RS, Xing D, Maahs DM, Michels A, Rickels MR, et al. (2013) Severe hypoglycemia and diabetic ketoacidosis in adults with type 1 diabetes: results from the T1D Exchange clinic registry. *J Clin Endocrinol Metab* 8: 3411-3419.
25. American Diabetes Association. (2006). Standards of medical care in diabetes. *Diabetes Care*. 29: S4-S42.
26. Brink SJ, Chiarelli FG (2004) Education and multidisciplinary team approach in childhood diabetes. *Acta Bio Medica Atenei Parmensis* 75: 7-21.
27. Majumder N, Majumder N, Datta S (2013) Knowledge and perception of mothers of under five children regarding etiology of type-II diabetes mellitus in Agartala. Tripura. *Health* 1: 64-70.
28. Al-Odayani AN, Alsharqi OZ, Ahmad AE, Al-Asmari AK, Al-Borie HM (2013) Children's glycemic control: Mother's knowledge and socioeconomic status. *Global J of health sci* 5: 214.
29. Albertyn R (2012) A multi-disciplinary education clinic for rural diabetics in KwaZulu. *South Afric Family Pract* 2: 8.
30. Speight J, Bradley C (2001) The ADKnowl: Identifying knowledge deficits in diabetes care. *Diabetic medicine* 18: 626-33.
31. Moodley LM (2007) An assessment of the level of knowledge about diabetes mellitus among diabetic patients in a primary healthcare setting. *South Afric Family Pract* 49: 6-16.
32. Wu YP, Hilliard ME, Rausch J (2013) Family involvement with the diabetes regimen in young people: The role of adolescent depressive symptoms. *Diabet Med* 30: 596-602.
33. Keough L, Sullivan-Bolyai S, Crawford S, Schilling L, Dixon J (2011) Self-management of type 1 diabetes across adolescence. *The Diabetes Educator*. 37: 486-500.
34. Noohu Khan AN, Venkatachalam VV, Akhali KM, Alavudeen SS, Dhanapal CK (2015) Overview of glycemic control, knowledge,

- awareness and attitude among type-2 diabetes male patient's. *J App Pharm* 7: 75-82.
35. Charron PD, Fischl AR, Choi J, Schmitt PL, White NH (2014) Mother-daughter dyadic approach for starting preconception counseling at puberty in girls with diabetes. *Res J Womens Health* 29: 1.
 36. Murugesan N, Snehalatha C, Shobhana R, Roglic G, Ramachandran A (2007) Awareness about diabetes and its complications in the general and diabetic population in a city in southern India. *Diabetes Res Clin Pract* 77: 433-437.
 37. Schillinger D, Grumbach K, Piette J, Wang F, Osmond D, et al. (2002) Association of health literacy with diabetes outcomes. *Jama* 288: 475-482.
 38. Golden MP, Herrold AJ, Orr DP (1985) An approach to prevention of recurrent diabetic ketoacidosis in the pediatric population. *J Pediatr* 1: 195-200.
 39. Smith CP, Firth D, Bennett S, Howard C, Chisholm P (1998) Ketoacidosis occurring in newly diagnosed and established diabetic children. *Acta Paediatrica* 5: 537-541.
 40. Al Shafae MA, Al-Shukaili S, Rizvi SG, Al Farsi Y, Khan MA, et al. (2008) Knowledge and perceptions of diabetes in a semi-urban Omani population. *BMC Public Health* 8: 249.
 41. Laffel LM, Wentzell K, Loughlin C, Tovar A, Moltz K, et al. (2006) Sick day management using blood 3-hydroxybutyrate (3-OHB) compared with urine ketone monitoring reduces hospital visits in young people with T1DM: A randomized clinical trial. *Diabet Med* 23: 278-284.
 42. Laffel L (2000) Sick-day management in type 1 diabetes. *Endocrinol Metab Clin North Am* 4: 707-23.
 43. Brink S, Laffel L, Likitmaskul S, Liu L, Maguire AM, et al. (2009) Sick day management in children and adolescents with diabetes. *Pediatric Diabetes* 10: 146-153.
 44. Clement S (1995) Diabetes self-management education. *Diabetes care* 18: 1204-1214.
 45. Murase Y, Imagawa A, Hanafusa T (2006) Sick-day management in elderly patients with diabetes mellitus. *Nihon rinsho*. 71: 2020-2024.
 46. Pichert JW, Snyder GM, Kinzer CK, Boswell EJ (1992) Tool chest: Sydney meets the ketone challenge-a videodisc for teaching diabetes sick-day management through problem solving. *The Diabetes Educator*. 18: 476-479.
 47. Realsen J, Goettle H, Chase HP (2012) Morbidity and mortality of diabetic ketoacidosis with and without insulin pump care. *Diabetes Technol Ther* 14: 1149-1154.
 48. Weissberg BJ, Antisdell LJ, Seshadri R (2003) Insulin pump therapy: A meta-analysis. *Diabetes care* 26: 1079-1087.
 49. DiMeglio LA, Pottorff TM, Boyd SR, France L, Fineberg N, (2004) A randomized, controlled study of insulin pump therapy in diabetic preschoolers. *J Pediatr* 145: 380-384.
 50. Hanas R, Ludvigsson J (2006) Hypoglycemia and ketoacidosis with insulin pump therapy in children and adolescents. *Pediatr Diabetes* 7:32-38.
 51. Phillip M, Battelino T, Rodriguez H, Danne T, Kaufman F (2007) Use of insulin pump therapy in the pediatric age-group: Consensus statement from the European Society for Paediatric Endocrinology, the Lawson Wilkins Pediatric Endocrine Society, and the International Society for Pediatric and Adolescent Diabetes, endorsed by the American Diabetes Association and the European Association for the Study of Diabetes. *Diabetes care* 30: 1653-1662.
 52. Johnson SR, Cooper MN, Jones TW, Davis EA (2013) Long-term outcome of insulin pump therapy in children with type 1 diabetes assessed in a large population-based case-control study. *Diabetologia* 56: 2392-2400.
 53. Plotnick LP, Clark LM, Brancati FL, Erlinger T (2003) Safety and effectiveness of insulin pump therapy in children and adolescents with type 1 diabetes. *Clinical Diabetology* 4: 245-52.
 54. Aziz KMA (2012) Management of type-1 and type-2 diabetes by insulin injections in diabetology clinics-a scientific research review. *Recent patents on endocrine, metabolic & immune drug discovery* 6: 148-170