

FREQUENCY OF COMMON RISK FACTORS OF RECURRENT DIABETIC KETOACIDOSIS AMONG CHILDREN

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ABSTRACT

OBJECTIVE: To determine the frequency of common risk factors leading to recurrent diabetic ketoacidosis among children.

MATERIAL AND METHODS: This descriptive cross sectional study was conducted at the department of pediatric medicine Hayatabad Medical Complex, Peshawar from March 2017 to September 2018. In this study a total of 290 patients were observed. All with recurrent DKA were assessed for the risk factors. The patient's risk factors including RTI, diarrhea, UTI and typhoid in the last one week and information obtained about the timing, dose and frequency of insulin therapy were assessed on the basis of history, clinical examinations and investigations. Sample of blood and urine sent to hospital laboratory for various risk factor identifications including typhidotIgM and IgG status, urine R/E and culture for confirmation of current infection. All the laboratory investigations were done from hospital laboratory under the supervision of an expert pathologist.

RESULTS: The study showed that mean age was 9 years with standard deviation ± 4.761 . Sixty five percent patients were male while 35% patients were female. UTI was the most common found risk factor constituting 48% of cases followed by typhoid detected in 38% children. Acute diarrhea was found in 35% children while RTI was found in 33% children and inadequate insulin was found in 24% children.

CONCLUSION: Infections are one of the leading causes for the exacerbation of recurrent diabetic ketoacidosis among children with urinary tract infection as the most common one

KEYWORDS: Common risk factors, diabetes mellitus, Ketoacidosis.

ABBREVIATIONS: Diabetes Mellitus: DM, Insulin dependent diabetes mellitus: IDDM, Diabetic ketoacidosis: DKA, Urinary tract infections: UTI, Respiratory tract infections RTI.

INTRODUCTION

Diabetes Mellitus (DM) is one of the major health issue and leading cause of deaths amongst the non-communicable diseases¹. Diabetes is prevalent in both urban and rural areas of Pakistan and is affecting both genders. Due to rapid increase in current status of the diabetes Pakistan may become one the four leading countries with maximum diabetic populations by 2025⁵.

Type 1 diabetes mellitus (T1D) is caused by immune mediated destruction of beta-cells⁶. By the time of diagnosis of T1DM almost 60-80% of beta cell function is lost⁷.

Diabetic Ketoacidosis (DKA) is a metabolic decompensation state which is characterized by high blood glucose level with hepatic ketones production and acidosis⁸. Although diabetic ketoacidosis is one of the most occurring complications of Insulin Dependent diabetes mellitus still the mortality is less than 5% in these patients⁹. DKA in itself can have several complications hypoglycemia (due to overtreatment), hypokalemia, cerebral edema, fluid overload, thrombotic events, and acute respiratory distress syndrome¹⁰. Cerebral edema is though rare yet very serious condition associated with DKA and is having poor outcome^{11, 12}. The incidence of DKA is very high in children and adolescent period of life¹³. Inadequate insulin therapy, infection and drugs like corticosteroids are the most common DKA precipitating factors of recurrent DKA^{14, 15, 16}.

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Internationally studies have been conducted about the risk factors precipitating DKA but such studies lacking in our setup especially pediatric population of Khyber Pakhtunkhwa. Therefore we conducted this study to determine various risk factors precipitating diabetic ketoacidosis in children with type 1 diabetes mellitus.

MATERIAL AND METHODS

This descriptive cross sectional study was conducted at Pediatric and Endocrinology departments Hayatabad Medical Complex, Peshawar from March 2017 to September 2018. A total of 290 cases fulfilling the inclusion criteria were included in the study. Inclusion criteria included all patients having recurrent DKA, both gender and age \leq 18 years. Patients who had developed or having chronic kidney disease or chronic liver disorders were excluded from the study. Patients included in the study were assessed for precipitating factors like enteric fever, diarrhea, respiratory and urinary tract infections in the last one week. At the same time dose, timing and frequency of insulin therapy also confirmed. For confirmation of the diagnosis x ray chest, blood, urine and stool specimens were also collected as needed. All the relevant investigations for the confirmation of the diagnosis were done from hospital laboratory.

DATA COLLECTION PROCEDURE

The sample technique adopted was consecutive non probability. The study was conducted after approval from Institutional Ethical Research Board (IERB) of Medical Teaching Institute Hayatabad Medical Complex, Peshawar (No: 1136). In all cases informed written consent was obtained from the guardians of the patients. The diagnosis of recurrent DKA was made as per criteria mentioned. History was taken from the

patient's attendants who were fitting into criteria as per operational definitions. Patients were examined and investigated for the risk factors by expert. The laboratory investigations were also done from hospital laboratory by an expert fellow. The informations related to all patients were recorded on already designed proforma. All the patients were treated with standard protocol.

DATA ANALYSIS

All the data collected was finally entered into and analyzed by statistical package for social sciences (SPSS) version 17. For numerical values like age and duration of type 1 diabetes mellitus Mean and standard deviations were calculated. For categorical values like gender and risk factors frequency was calculated. For effect of modifiers common factors were stratified. All the results were ultimately presented in tabulated form.

RESULTS

A total of 290 patients were included in this study. The majority of the patients were in age range of 2-10 year, followed by i.e. 180 (62%) and 110 (38%) 10 to 18 years. Female patients exceeded male patients in the study making 157 (65%) and 133 (35%) respectively. Duration of diabetes was less than five years in 81 (28%) and more than five years in 209(72%) of cases. Mean duration was 5years with standard deviation \pm 2.81.

Frequency of risk factors in patients with recurrent episode of DKA was 33%, 48%, 38%, 35% and 24% for RTI, UTI, Typhoid Fever, acute diarrhea and inadequate insulin respectively as shown in table 1.

Frequency of risk factors in patients with recurrent episode of DKA, stratification with age and gender has been shown in table 2 and 3 respectively.

Table no 1: Common risk factors in recurrent diabetic ketoacidosis (n=290)

| RISK FACTORS | FREQUENCY | PERCENTAGE |
|--------------------|-----------|------------|
| RTI | 96 | 33% |
| UTI | 139 | 48% |
| Typhoid Fever | 110 | 38% |
| Acute Diarrhea | 102 | 35% |
| Inadequate Insulin | 70 | 24% |

Table no 2: Stratification of common risk factors with respect to age distribution (n=290)

| RISK FACTORS | | 1-10 years | 11-18 years | Total | P Values |
|--------------------|-----|------------|-------------|-------|----------|
| RTI | Yes | 59 | 37 | 96 | 0.8801 |
| | No | 121 | 73 | 194 | |
| Total | | 180 | 110 | 290 | |
| UTI | Yes | 86 | 53 | 139 | 0.9467 |
| | No | 94 | 57 | 151 | |
| Total | | 180 | 110 | 290 | |
| Typhoid Fever | Yes | 68 | 42 | 110 | 0.9541 |
| | No | 112 | 68 | 180 | |
| Total | | 180 | 110 | 290 | |
| Acute Diarrhea | Yes | 63 | 39 | 102 | 0.9373 |
| | No | 117 | 71 | 188 | |
| Total | | 180 | 110 | 290 | |
| Inadequate Insulin | Yes | 43 | 27 | 70 | 0.5645 |
| | No | 137 | 83 | 220 | |
| Total | | 180 | 110 | 290 | |

Table no 3: Stratification of common risk factors with respect to gender distribution (n=290)

| RISK FACTORS | | Male | Female | Total | P Values |
|--------------------|-----|------|--------|-------|----------|
| RTI | Yes | 44 | 52 | 96 | 0.9944 |
| | No | 89 | 105 | 194 | |
| Total | | 133 | 157 | 290 | |
| UTI | Yes | 64 | 75 | 139 | 0.9526 |
| | No | 69 | 82 | 151 | |
| Total | | 133 | 157 | 290 | |
| Typhoid | Yes | 51 | 59 | 110 | 0.8934 |
| | No | 82 | 98 | 180 | |
| Total | | 133 | 157 | 290 | |
| acute diarrhea | Yes | 47 | 55 | 102 | 0.9565 |
| | No | 86 | 102 | 188 | |
| Total | | 133 | 157 | 290 | |
| Inadequate Insulin | Yes | 32 | 38 | 70 | 0.9772 |
| | No | 101 | 119 | 220 | |
| Total | | 133 | 157 | 290 | |

DISCUSSION

Diabetes Mellitus cases are increasing globally enormously day by day. The prevalence of the condition is quite high in Pakistan and is affecting all ages, both gender and both urban and rural populations. Type 1 Diabetes Mellitus (T1DM) is mainly present in pediatric age group¹⁷.

In our study mean age was 9 ± 4.761 years. The majority of our patients were males which coincide with other local and international studies. UTI was the leading risk factor for recurrent DKA. Other risk factors were typhoid fever, acute diarrhea, acute respiratory tract infections respectively. Almost similar results were documented by Fritsch M et al where UTI was found in 45%, Typhoid fever in 34% of cases, acute diarrhea and respiratory tract infections in 34% and 30% respectively¹⁵.

Alourfi Z et al et al results were also not different from our result who documented infection as the most common cause of recurrent DKA (48%), followed by inadequate insulin therapy (24%), unknown cause (21%) and other medical conditions (8%) respectively¹⁶. UTIs, skin infections, pneumonia, bronchitis and sepsis accounted for 61 cases (56%) in a study¹⁸. The study found that infections were the cause of recurrent DKA in 35% of all new diagnosed cases of diabetes. In 48% of cases with recurrent diabetic ketoacidosis coexisting infection was reported in patients with known diabetes. The study also found that in 14% of cases, infection and poor compliance were recorded as the causes; and in 36% of cases, poor compliance with insulin therapy was the sole cause¹⁸.

Poor compliance with insulin therapy was also one of the precipitating factors. Studies have documented higher frequency of recurrent DKA association with high HbA1c level as compared to controlled levels¹⁹. Studies have also related increased episodes of recurrent DKA where patients had stopped insulin or had developed lipodystrophy at injection sites²⁰.

CONCLUSION

Infections are one of the leading causes for the exacerbation of recurrent diabetic ketoacidosis among children with urinary tract infection as the most common one.

RECOMMENDATION

Diabetic ketoacidosis is one of the important metabolic and endocrine causes having a high

impact on quality of life of the patient and attendants. The study conducted within limited resources at our regional setup. We recommend further studies on this important topic at much larger scale for the health of the patients with type 1 diabetes mellitus with best glucose control and without short and long term complications of this serious and manageable health problem.

DECLARATION

AUTHOR'S CONTRIBUTION

It is to certify that in the original article titled "FREQUENCY OF COMMON RISK FACTORS OF RECURRENT DIABETIC KETOACIDOSIS AMONG CHILDREN" the contribution of the authors is as follow:

Dr. Gul-e-Lala: Conception of the work,

Dr. Mohammad Imran: Data Collection and analysis

Dr. Arshia Munir: Drafting and critical review

Dr. Muhammad Aqeel Khan: Drafting and critical review

Dr. Madiha Gul: Proof Reading

Dr Bilal Noor: Proof Reading

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REFERENCE

- 1 Dunstan DW, Zimmet PZ, Welborn TA, de Courten MP, Cameron AJ, Sicree RA. The Rising Prevalence of Diabetes and Impaired Glucose Tolerance. *Diabetes Care* 2012; 25(5):829-834.
- 2 Susan D, Beulensa JWG, Van-dera SYT, Grobbee DE, Nealbb B. The global burden of diabetes and its complications: an emerging pandemic. *Europ J PrevCardiol* 2010; 17(1):suppl s3-s8.
- 3 Huang ES, Basu A, O'Grady M, Capretta JC. Projecting the Future Diabetes

Population Size and Related Costs for the U.S. Diabetes Care 2009;32(12):2225-2229.

4 Sera AS, Jawad F, Maqsood A. Prevalence of diabetes in Pakistan. *Diabetes Res clinpract.* 2009;76:219-22.

5 World Health Organization. The World Health Report. Geneva Organization; 2011: World Health.

6 Van Belle TL, Coppieters KT, Von Herrath MG. Type 1 diabetes: etiology, immunology, and therapeutic strategies. *Physiological reviews* 2011; 91(1): 79-118.

7 Mortensen HB, Swiftb PG, Hollc RW, Hougaard P, Hansena L, Bjoerndalene H et al. Multinational study in children and adolescents with newly diagnosed type 1 diabetes: association of age, ketoacidosis, HLA status, and autoantibodies on residual beta-cell function and glycemic control 12 months after diagnosis. *Pediatric Diabetes* 2010;11: 218-226.

8 Brink, SJ. Paediatric and adolescent diabetic ketoacidosis. *Practical Diabetes*, 2014; 31(8):342-347.

9 Elliott J, Jacques RM, Kruger J, Campbell MJ, Amiel SA, Mansell P, et al. Research: Educational and Psychological Issues Substantial reductions in the number of diabetic ketoacidosis and severe hypoglycaemia episodes requiring emergency treatment lead to reduced costs after structured education in adults with Type 1 diabetes. *Diabetic Medicine*, 2014; 31(7):847.

10 Usher-Smith JA, Thompson M, Ercole A, Walter FM. Variation between countries in the frequency of diabetic ketoacidosis at first presentation of type 1 diabetes in children: a systematic review. *Diabetologia* 2012; 55: 2878-2894.

11 Kimura D, Raszynski A, Totapally BR. Admission and treatment factors associated with the duration of acidosis in children with diabetic ketoacidosis. *Pediatric emergency care* 2012;28(12):1302-1306.

12 Harris MA, Wagner DV, Heywood M, Hoehn D, Bahia H, Spiro K. Youth repeatedly hospitalized for DKA: proof of concept for novel interventions in children's healthcare (NICH). *Diabetes care* 2014; 37(6):e125-e126.

13 Gosmanov AR, Gosmanova EO, Dillard-Cannon E. Management of adult diabetic ketoacidosis. *Diabetes MetabSyndrObes.* 2014;7():255-64.

14 Limenis E, Shulman R, Daneman D. Is the frequency of ketoacidosis at onset of type 1 diabetes a child health indicator that is related to income inequality? *Diabetes Care.* 2012; 35:e5.

15 Fritsch M, Rosenbauer J, Schober E, Neu A, Placzek K, et al. Predictors of diabetic ketoacidosis in children and adolescents with type 1 diabetes. Experience from a large multicentre database. *Pediatric diabetes* 2011; 12(4pt1):307-312.

16 Alourfi Z, Homsi H. Precipitating factors, outcomes, and recurrence of diabetic ketoacidosis at a university hospital in Damascus. *Avicenna Journal of Medicine.* 2015;5(1):11-15.

17 Wallace TM, Matthews DR. Recent advances in the monitoring and management of diabetic ketoacidosis. *QJM.* Dec 2004;97(12):773-80.

18 Abbas W, Farman Ullah, Tariq A, Muhammad T, Jabeen N, Khan Z. Frequency of common risk factors of recurrent diabetic metabolic acidosis in children. *Pak J Med Haalht Sci.* 2023; 17(1):378-81

19 Brandenburg MA, Dire DJ. Comparison of arterial and venous blood gas values in the initial emergency department evaluation of patients with diabetic ketoacidosis. *Ann Emerg Med.* Apr 1998; 31(4):459-65.

20 Goyal N, Miller JB, Sankey SS, Mossallam U. Utility of initial bolus insulin in the treatment of diabetic ketoacidosis. *J Emerg Med.* May 2010; 38(4):422-7.