

Contributing Factors of DKA in patients of diabetes mellitus

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ABSTRACT

Objective: The objective is to define the occurrence of contributing factors of DKA in diabetes patients.

Study design: Descriptive cross sectional

Place and duration: At Institute of Child Health and Children's Hospital Lahore study was conducted out from 1st May 2018 to 30th April 2019.

Material and method: Those Patients were included in the study who were completing inclusion area. Informed agreement was taken from patients and their information was recorded. Complete medical record including non-compliance, infections and laboratory findings was also retrieved. Data was entered in Performa.

Results: The recorded mean age calculated was 7.79±4.24 years, 55.5 % (n=111) were females and 44.5 % (n=89) were males. Occurrence of contributing factors of DKA in patients of diabetes mellitus was recorded as 41% (n=82) infection, frequency of type of infection was calculated as 15% (n=30) had RTI, 13% (n=26) had CNS, 13% (n=26) had UTI while 59% (n=118) had no infection.

Conclusion: Frequency of infection was higher followed by non-compliance as contributing factors of DKA in patients of diabetes mellitus. However, respiratory tract infection was the commonest infection in our population.

Keywords: Diabetic ketoacidosis, contributing factors, infection.

INTRODUCTION

Diabetes Mellitus (DM) was developed every year almost in 6500 children of age 15 years in the whole world with DKA¹. Diabetic ketoacidosis (DKA) is an imbalance of metabolism that is occur due to the existence of low level of active action of insulin with the synchronization of acidosis, hyperglycemia and ketosis. This is the primary cause of death in diabetic children and is linked with sickness and high expenditures². It is in both children with established diabetes and with new onset, a prevalent illness. Though infections and increase rate of deaths in children with DKA was reported to precipitate DKA. Another major cause of deaths and morbidity in children was cerebral edema with DKA in developed world. However, renal failure, shock and infections are still main risk factors of deaths in DKA in many developing countries. Early identification and appropriate management of infections may prevent DKA and help decrease mortality in children. A systematic review of 46 studies, published in the British Medical Journal in 2011, was sought to recognize associated factors with DKA in young adults and children. They revealed that many aspects are related with high rate of risk of DKA such as diagnostic error, younger age, lack of health insurance, delayed treatment, ethnic minority status, preceding infection and lower body mass index. The occurrence of DKA is 12.8% to 80% in United Arab Emirates with the highest frequency and Romania and Saudi Arabia at the lowest level of frequency. Rowers and his colleagues stated prevalence of DKA at finding to be 25.5% in children of 20 years of age. To reduce the level of DKA in diabetic children, awareness and high medical alertness are compulsory. In most of the studies, risk factors for DKA were reported such as non-compliance to treatment, poor access to medical care, young age, infections and lack of medical insurance^{3, 5}. Limited studies have been carried out in Pakistan in order to investigate major causes of this life threatening complication of diabetes. Degree of hyper osmolality, severity of acidosis volume depletion were reported as clinical signs of DKA.⁶ Hyperglycemic hyperosmolar state at the onset of type 1 diabetes is more common in teenagers. Proper identification of more frequent risk factors is very important for better management of DKA and to make the policies for its prevention in the region in order to meet the sustainable development in the country. The most common endocrine illness in children is Type 1 diabetes. It is indistinct that what is the reason that some of the children acquire ketoacidosis diabetes but others do not develop this type of diabetes? It is also unknown that is it the result of delayed treatment or any aggressive form of diabetes. Therefore, it is important to understand the associated factors of diabetic ketoacidosis and significance of delayed treatment and diagnosis. Since there is very limited data available

on DKA occurrence in diabetic children of Punjab especially central and southern Punjab regions, this study is proposed to investigate major risk factors of DKA in children of these regions which mostly come to Lahore for the treatment.

MATERIAL AND METHODS

A cross sectional study was carried out at the Children's Hospital and The Institute of Child Health Lahore from 1st May 2018 to 30th April 2019. Inclusion criteria was patients of either gender who fulfilled the criteria of DKA and aged above 1 year and up to 15 years. While age > 15 years and < 1 year, patients with diabetes mellitus who did not fulfill the criteria of DKA and patients with any co-morbidities e.g. chronic kidney disease (GFR <50 ml/min), chronic liver disease (cirrhosis on ultrasound), stroke etc. were excluded.

A total of 200 cases were enrolled who were fulfilling the inclusion area. Informed agreement was taking from parents and approval from moral board their information including name, age, sex, address, date of admission and socio-economic class was recorded. Complete medical record including non-compliance, infections and laboratory findings (CBC, chest X-ray, CSF, blood culture, urine c/s) was also retrieved. Infections and non-compliance was labeled as per operational definitions. All the findings were documented in a standardized proforma and data was evaluated using SPSS. The variables to be analyzed included: quantitative variables (age, body mass index) and qualitative variables (gender, infection, type of infection, compliance/non-compliance to treatment, socio-economic class). Qualitative variables were obtainable as frequencies and percentages while quantitative variables were obtainable as means and standard deviations while Stratification for age, gender, socioeconomic status, BMI was done to control effect modifier. P value of <0.05 was taken as statistically important in Chi square test.

OPERATIONAL DEFINITIONS

Diabetic Ketoacidosis: Biochemically diabetic ketoacidosis (DKA) is demarcated as serum bicarbonate concentration <15 mol/L, intravenous pH <7.3, blood glucose level > 200 mg/dL (11 mol/L) together with ketonuria and glycosuria and (+++ on dipstick)

CONTRIBUTING FACTORS

Infections (any of the followings)

1-Septis: 2 of the four SIRS (Systemic Inflammatory Response Syndrome i.e. temperature > 99F, TLC > 20000, heart rate > 100/min and respiratory rate > 40/min) criteria plus any of the following:

2-Respiratory Tract Infection (RTI): it was considered with consolidation in x-ray chest as reported by radiologist

3-Urinary Tract Infection (UTI): it was diagnosed with urine culture results with colony count more than 1 lakh

4-Central Nervous System (CNS) Infection: it was considered with CSF suggestive of infection. (Cells > 5, proteins > 100 mg/dl).

5-Non-compliance/Poor compliance: It was demonstrated as without medical indications in last 48 hours, missing one or more doses of insulin.

RESULTS

In study those 200 patients were enrolled who were fulfilling the inclusion area to define the occurrence of contributing factors of DKA in patients of diabetes mellitus. Age distributions of the participants was occurred, it shows that 41.5% (n=83) were among 2-6 years of age while 58.5% (n=117) were between 7-14 years of age, Mean+SD was considered as 7.87+4.24 years. Gender distribution shows that 55.5 % (n=111) were females and 44.5 % (n=89) were male. Mean body mass index was calculated as 28.85+3.33. Frequency of contributing factors of DKA in patients of diabetes was noted as 41%(n=82) infection while 14.5%(n=29) had non-compliance(Fig:1).Frequency of type of infection was calculated as 15%(n=30) had RTI, 13%(n=26) had CNS, 13%(n=26) had UTI while 59%(n=118) had no infection.(Fig:2).Frequency of socio-economic status in DKA in patients of diabetes mellitus was recorded as mentioned in fig:3. For age, gender, socioeconomic status data was stratified and BMI was done to control effect modifier. Chi square test was used. P value of <0.05 was taken as statistically significant. (Table No. 1-2).

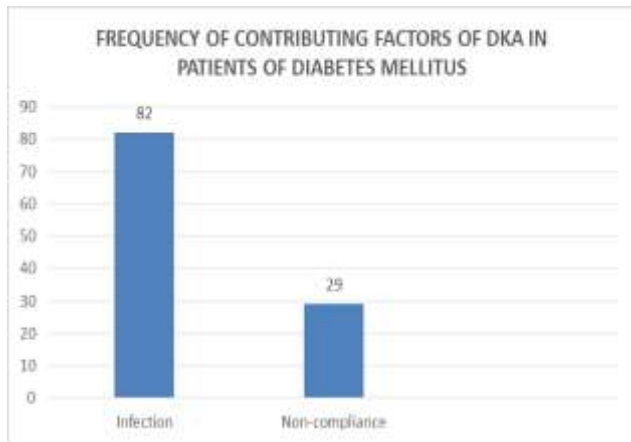
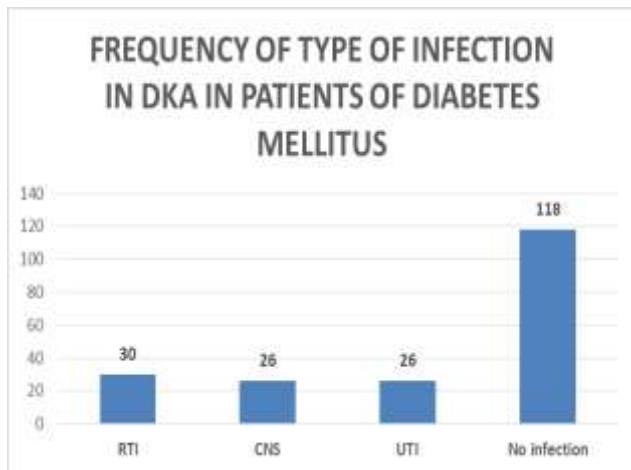


Fig. 1: Frequency of Contributing Factors of DKA



(n=200)

Fig. 2: Frequency of Type of Infection In DKA

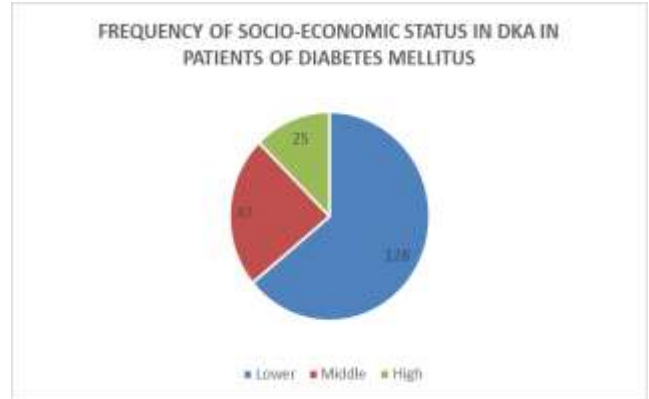


Fig. 3: Frequency of Socio Economic Status in DKA

Table 1: Stratification for Age

Contributory factors	Age(in years)		P value
	2-6	7-14	
Infection	Yes	33	0.76
	No	50	
Non-compliance	Yes	13	0.69
	No	70	

Table 2: Stratification for Socioeconomic Status

Contributory factors	Socioeconomic status			P value
	Low	Middle	High	
Infection	Yes	59	12	0.04
	No	69	35	
Non-compliance	Yes	20	5	0.69
	No	108	42	

DISCUSSION

In children the most common endocrine diseases is Type 1 diabetes. Diabetic ketoacidosis (DKA) is the acute metabolic complications of diabetes mellitus (DM) which is fatal if not accurately treated. Worldwide, frequency of DKA at T1DM diagnosis significantly differs ranges in different countries are between 13% and 80%. According to finding of a scientific study, lowest frequency of DKA in 29000 children was reported in Canada, Sweden, Finland and Slovak Republic. Highest frequency was reported in Saudi Arabia, Romania and United Arab Emirates. Frequency of T1DM was negatively linked with frequency of DKA in the regional and Latitude background. We recorded mean age as considered as 7.87±4.24 years, 55.5% (n=111) were females and 44.5 % (n=89) were male. Occurrence of contributing factors of DKA in patients of diabetes mellitus was recorded as 41%(n=82) infection, frequency of type of infection was calculated as 15%(n=30) had RTI, 13%(n=26) had CNS, 13%(n=26) had UTI while 59%(n=118) had no infection. We compared our results with Naveed et al¹⁰ who conducted a study at Pakistan Institute of Medical Sciences (PIMS) in order to determine the major risk factors of DKA in patients of Islamabad and they reported that infections (50%) at the time of presentation was the major risk factor followed by non-compliance to the treatment (11%) and other co-morbidities such as stroke and pancreatitis etc. (9%). They also found that DKA was more frequent in females (55%) as compared to males (45%). Worldwide, diagnosis of diabetes in girls and boys was at similar rate of DKA.¹¹ .Though, a study in Germany suggested that the frequency of diabetes is most prevalent in girls. Another study reported that increased prevalence of diabetes is in girls, under 2 years of age. Similarly, Syeda et al.¹² conducted a study at Aga Khan Hospital, Karachi and reported that severity of DKA was significantly linked with the poor passivity, presence of shock at time of presentation, length of stay in the hospital, presence of infection and Glasgow Coma Scale score. However, they found in their study that DKA was more frequent in male children in contrast to Naveed et al.¹⁰. An important risk factor associated with DKA is consistently identified

diabetes at younger age¹³. Another study¹⁴ revealed that in 128 patents with diabetes in hospitals, 80% (n=103) were mentioned for first time and 19.5 % (n=25) were treated in the past with insulin. . Out of 128 diabetic patents, 36 patients were with severe degree of ketoacidosis a d 71 with some degree of ketoacidosis. In a number of small studies, it was revealed that lower BMI or weight loss have also been linked with increased risk for DKA^{11, 15}. At onset of T1DM, children from racial subgroups are at increased risk for DKA¹¹. Commonly, the disposing factors of ketoacidosis were observed in 39 (54.9%) patients. This was due to insulin therapy discontinuation and infection in 30.76(n=12) and 69.23 % (n=27) respectively. In patients with history of admission with diabetic ketoacidosis and previous diagnosis of diabetes mellitus, 70.58% had preceding management termination. The above research study is agreed with our findings regarding higher frequency of infections as predisposing factors of ketoacidosis. Sheykhoul Eslami and his colleagues indicated that out of all patients 40% were having infections and mostly of them were with urinary tract infection. All efforts for the reduction of death rates from DKA should focus on the specific causes of deaths. Reasons of mortality from DKA were examined in many studies.¹⁷⁻¹⁹. Most common causes were sepsis and cerebral edema. From Greece, a study reported 12.9% death rate from DKA. An analysis recognized that there are different predictors of deaths from DKA such as high dose of insulin, persistence of hyperglycemia, comorbidities, development of coma or fever during treatment and severe academia at presentation (arterial blood pH < 7.0). We agreed with the incidence of infection but UTI was higher than our study. The findings of our study are helpful for development of patients, understanding of the disease, interventions based on population and professional for reducing the likelihood of ketoacidosis diabetic children.

CONCLUSION

Amongst children in this study, frequency of infection was higher followed by non-compliance as contributing factors of DKA . However, respiratory tract infection was the commonest among infections in our population.

REFERENCES

1. 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. *2012*;55:2878-94
2. Vanelli M, Chiari G, Lacava S, Iovane B. Campaign for diabetic ketoacidosis prevention still effective 8 years later. *Diabetes Care*. 2007;30:e12
3. Usher-Smith J, Thompson MJ, Sharp SJ, Walter FM. Factors associated with the presence of diabetic ketoacidosis at diagnosis of diabetes in children and young adults: A systematic review. *2011*;343:4092
4. Rewers A, Klingensmith G, Davis C, Pettitt DB, Pihoker C, Rodriguez B. Presence of diabetic ketoacidosis at diagnosis of diabetes mellitus in youth. *2008*;121(5):1258-66
5. Al-Hayek AA, Robert AA, Braham RB, Turki AS, Al-Sabaan FS. Frequency and associated risk factors of recurrent diabetic ketoacidosis among Saudi adolescents with type 1 diabetes mellitus. *2015*;36(2):216-20
6. Edge JA, Roy Y, Bergomi A. Conscious level in children with diabetic ketoacidosis is related to severity of acidosis and not to blood glucose concentration. *Pediatr Diabetes* 2006;7:11.
7. Zeitler P, Haqq A, Rosenbloom A. Hyperglycemic hyperosmolar syndrome in children: pathophysiological considerations and suggested guidelines for treatment. *J Pediatr* 2011;158:9.
8. Alvi NS, Davies P, Kirk JM, Shaw NJ. Diabetic ketoacidosis in Asian children. *Archives of disease in childhood*. 2001;85(1):60-1.
9. Usher-Smith JA, Thompson MJ, Sharp SJ, Walter FM. Factors associated with the presence of diabetic ketoacidosis at diagnosis of diabetes in children and young adults: a systematic review. *Bmj*. 2011;343:d4092.
10. Naveed D, Bilal N, Nasir B, Lodhi B. Precipitating factors for diabetic ketoacidosis. *2009*;1(1):6-8
11. Lokulo-Sodipe K, Moon RJ, Edge JA, Davies JH. Identifying targets to reduce the incidence of diabetic ketoacidosis at diagnosis of type 1 diabetes in the UK. *Archives of disease in childhood*. 2014;99(5):438-42.
12. Syeda M, Khawaja FB, Saleem T, Khalid U, Rashid A. Clinical profile and outcomes of paediatric patients with diabetic ketoacidosis at a tertiary care hospital in Pakistan. *2011*;61(11):1082-87.
13. Savoldelli RD, Farhat SC, Manna TD. Alternative management of diabetic ketoacidosis in a Brazilian pediatric emergency department. *Diabetology & metabolic syndrome*. 2010;2:41.
14. Alijanpour M, Shabanzadeh Z, Rezapour M. Incidence, predisposing factors and complications of Diabetic Ketoacidosis in diabetic patients. *Caspian J Pediatr* 2016;2(2):142-7.
15. Hekkala A, Reunanen A, Koski M, Knip M, Veijola R, Finnish Pediatric Diabetes R. Age-related differences in the frequency of ketoacidosis at diagnosis of type 1 diabetes in children and adolescents. *Diabetes care*. 2010;33(7):1500-2.
16. Sheikholeslami H, Ziaee A, Shariatmadari M. Evaluation of clinical manifestation, laboratory data and precipitating factors in patients with Diabetic ketoacidosis in educational and medical care center of Boali Sina in Ghazvin (1999-2004). *Birjand Uni Med Sci* 2008;15(2): 60-5.
17. Maletkovic J, Drexler A. Diabetic ketoacidosis and hyperglycemic hyperosmolar state. *Endocrinol Metab Clin North Am*. 2013;42:677-95.
18. Tzamaloukas AH, Sun Y, Konstantinov NK, Ing TS, Dorin RI, Malhotra D, Murata GH, Shapiro JI. Principles of quantitative fluid and cation replacement in extreme hyperglycemia. *Cureus*. 2013;5:e110.
19. Suwanto S, Sutrisna B, Waspadji S, Pohan HT. Predictors of five days mortality in diabetic ketoacidosis patients: a prospective cohort study. *Acta Med Indones*. 2014;46:18-23.