

Risk Factors Associated with Diabetic Ketoacidosis at the Onset of Type 1 Diabetes Mellitus

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ABSTRACT

Background: There are various factors which increase the risk of diabetic ketoacidosis at the onset of type 1 diabetes mellitus. There have not been any such studies in our setting. This study was done to find the prevalence and risk factors associated with the development of diabetic ketoacidosis at onset of type 1 diabetes mellitus.

Methods: Children and young adults with type 1 diabetes mellitus being treated at Patan hospital were approached and after obtaining an informed consent, all the patient information on various risk factors for diabetic ketoacidosis were collected in a pre-developed proforma. Data was entered in Microsoft Excel and analysis was done using statistical package for the social sciences-16. Ethical approval was taken from Institutional Review Committee- Patan Academy of Health Sciences.

Results: Out of 99 patients with type 1 diabetes enrolled in the study, 52.5% presented in diabetic ketoacidosis at the onset. The duration of symptoms was significantly less in patient presenting with diabetic ketoacidosis than without diabetic ketoacidosis (6.45 ± 7.57 vs 9.13 ± 10.12 , $p=0.04$). There was no significant difference in the mean age, mean glycosylated hemoglobin, mean body mass index, gender, parents' literacy and medical consultations prior to diagnosis.

Conclusions: More than half of the patients with type 1 diabetes presented in diabetic ketoacidosis. The shorter duration of symptoms prior to presentation was the only significant factor leading to presentation as diabetic ketoacidosis.

Keywords: Diabetic ketoacidosis; risk factors; type 1 diabetes mellitus.

INTRODUCTION

Type 1 diabetes mellitus (T1DM) is the most common form of diabetes in children and young adults worldwide and annually more than 100,000 patients are diagnosed.¹

Diabetic ketoacidosis (DKA) is the most common cause of death in T1DM.² Incidence of DKA at the onset of T1DM ranges from 13-80%.³ Various risk factors and protective factors have been identified for DKA at initial presentation of T1DM. Few studies on diabetes in children and young adults have been done in Nepal but no study assessing risk factors for DKA at onset of T1DM has been done.⁴⁻⁶ This study was done to find out the prevalence and risk factors associated with DKA at onset of T1DM.

METHODS

This was a cross sectional study which was carried out in children and young adults with T1DM being treated at Patan Hospital Diabetic Clinic. Data collection was done over the period of October 1, 2019 to September 30, 2020. Ethical approval was taken from the institutional review committee (IRC) of Patan Academy of Health Sciences (PAHS), Patan Hospital. All patients who presented to the clinic were approached. Patients or patients' relatives who denied consent and those with incomplete information were excluded from the study. After obtaining consent, data collection was started. Hospital number was retrieved from the diabetic register kept in the out-patient department (OPD). Files of patients were reviewed from the medical record department. Files were extracted to see if DKA was

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present or absent at the initial presentation. Information like age at diagnosis, gender, weight, height, duration of illness at initial presentation and initial glycosylated haemoglobin (HbA1c) were also retrieved from the files. Information like maternal/paternal education (literate or illiterate) at the time of diagnosis, number of medical consultations prior to diagnosis was asked during OPD visits. All the information was filled out in the proforma. Data was entered in the Microsoft excel and analysis was done using SPSS 16. Qualitative variable like gender, maternal/paternal education and medical consultations prior to diagnosis was expressed in frequencies and percentage. Quantitative variables like age, duration of illness, body mass index (BMI) and HbA1c was expressed as mean and standard deviation. The difference in the parameters in children presenting with or without DKA at initial presentation was compared using t- test for quantitative data and Chi- square test for qualitative data. P-value <0.05 was considered significant.

RESULTS

There were 110 patients on regular follow up in the

diabetic clinic. Data could not be obtained for 11 patients who were excluded from the study. So, 99 patients were enrolled in the study. The mean and median age at diagnosis was 11.65 ± 4.96 and 12 years respectively ranging from 3 months to 23 years. There were 54(54.5%) males and 45(45.5%) females with the male to female ratio of 1.2. The duration of symptoms before presentation was a 7.84 ± 8.99 week ranging from being asymptomatic at presentation to up to one year of symptoms. The mean HbA1c at presentation was $10.72 \pm 2.47\%$.

Out of the 99 patients with T1DM, 52.5% patients presented in DKA at the onset of illness.

As seen in Table 1, the mean duration of symptoms among those presenting in DKA at the onset of T1DM was 6.45 ± 7.57 weeks and among those not presenting in DKA was 9.13 ± 10.12 weeks. The difference was statistically significant ($p=0.04$). There was no significant difference in the mean age, mean HbA1c and mean BMI between the patients presenting with and without DKA at the onset of illness as shown in Table 1.

Table 1. Comparison of mean age, duration of symptoms, mean HbA1c and BMI between T1DM presenting with and without DKA at onset.

| Parameters | DKA | No DKA | p- value |
|------------------------------------|------------------|------------------|----------|
| Number of patients (%) | 52(52.5) | 47(47.5) | |
| Mean age (in years) | 11.65 ± 4.88 | 11.80 ± 4.97 | 0.96 |
| Duration of symptoms (in weeks) | 6.45 ± 7.57 | 9.13 ± 10.12 | 0.04 |
| Mean HbA1c (%) | 10.88 ± 2.52 | 10.55 ± 2.43 | 0.52 |
| Mean BMI (kg/m ²) | 17.48 ± 3.90 | 17.7 ± 3.13 | 0.75 |

As shown in Table 2. there was no significant difference in the sex and parental education in the T1DM patients presenting with and without DKA. There was also no difference in the two groups if they had prior medical consultations or was diagnosed as T1DM in the first visit.

Table 2. Comparison of sex, parental literacy and prior medical consultations in T1DM presenting with and without DKA.

| Characteristic | Total | DKA | No DKA | p- value |
|--------------------|-------|-----|--------|----------|
| Sex | | | | |
| Male | 54 | 28 | 26 | 0.88 |
| Female | 45 | 24 | 21 | |
| Father's education | | | | |
| Literate | 74 | 35 | 39 | 0.07 |
| Illiterate | 25 | 17 | 8 | |

Table 2. Comparison of sex, parental literacy and prior medical consultations in T1DM presenting with and without DKA.

| | | | | |
|--|----|----|----|------|
| Mother's education | | | | |
| Literate | 50 | 25 | 25 | 0.61 |
| Illiterate | 49 | 27 | 22 | |
| Medical consultations prior to diagnosis | | | | |
| Yes | 55 | 28 | 27 | 0.72 |
| No | 44 | 24 | 20 | |

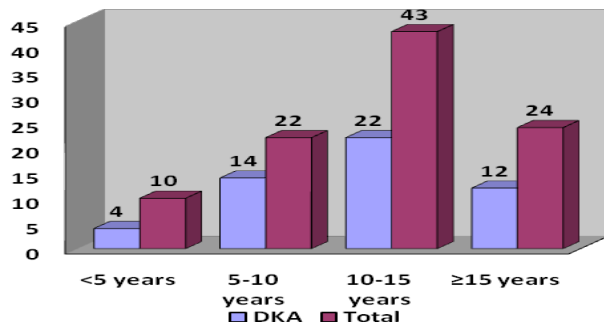
**Figure 1. Age- wise distribution of patients presenting with DKA.**

Figure 1 shows age- wise distribution of total patients and those presenting in DKA. Most of the patients were in the age group of 10-15 years. DKA at the onset of illness was lowest in the age group < 5 years (40%) and highest in the age group 5- 10 years (63%). There was no significant difference in DKA at onset in the different age group ($p=0.61$).

DISCUSSION

The median age of diagnosis in a study done at eastern region of Nepal was 11.5 years which was similar to our study.⁶ The mean age of diagnosis in other studies were less than our T1DM patients.⁷⁻⁹ This might be because they only included pediatric cases on follow up in the pediatric clinic while we included all T1DM presenting to our hospital upto the age of 23 years. The male: female ratio among the T1DM patients in our study was similar to various other studies.^{7,10-12} But, there were few studies with more female patients.^{6,9,13,14}

The incidence of DKA at the onset of T1DM is still very high not only in our setting but also in other countries. In our study out of the 99 patients, 52(52.5%) patients presented with DKA. Few studies in Nepal show incidence of DKA at the onset of T1DM ranging from 37.5% to 59.5%.^{5,6} In neighbouring countries like India, incidence upto 63.5% has been found.^{15,16} Countries like Brazil has incidence from 42.3 % to 67%.^{8,17} Developed countries in Europe and USA have frequency of DKA at diagnosis of T1DM ranging from 15-70%.^{8,10,18-22}

Many previous studies showed that the mean age of patients presenting with DKA was younger than without DKA.^{3,14,20-23} The inability of recognition of symptoms of diabetes like polyuria, polydipsia and polyphagia in younger children wearing diaper and breastfeeding can be the cause of the delay in diagnosis and increased risk of presenting in DKA. The patients presenting in DKA at the onset was also younger in our study but the difference was not significant. This finding was similar to other studies where the mean age of patients presenting in DKA was younger but no significant difference was found.^{19,24} The cause might be because of the less number of younger patients in our group and the inclusion of young adults unlike other studies.

Few studies have shown more DKA in female patients unlike our study.^{9,13,25,26} The reason for the higher rate of DKA in females has been attributed to less use of self monitoring of blood glucose(SMBG) and higher rate of nutritional and psychological problems in female patients.¹³ We did not see any difference in frequency of T1DM patients presenting in DKA among male and female. This finding was similar to other studies.^{12,24} No cause for the lack of difference in our study could be found.

Our study showed that the duration of symptoms was significantly less in patients presenting in DKA. Studies have found that diabetic patient with DKA had poor residual beta cell function than those presenting without DKA. This might be the reason for the increased severity leading to earlier presentation.^{19,23,24} DKA as the initial presentation of T1DM is a predictor of worse glycemic control, including higher levels of HbA1c. This similar findings was seen in many studies.^{7,20,27,28} Our study did not show significant difference in the HbA1c level among patients presenting with or without DKA which was similar to another study done in Italy.¹²

Previous studies indicate that parents' schooling as an indicator for children presenting with DKA at the onset of T1DM. They have indicated that worse understanding and limited access to healthcare system might be the cause of this observation.² Similarly, another study has shown that higher education level was protective and

more patients presented in DKA if the parents had lower education level.¹¹ Our study did not show that parents' education level affected the T1DM patients presenting in DKA. This finding was similar to a study done in the United States.²⁹ The education system in our settings still lacks education about chronic illnesses like diabetes. This might have caused the lack of difference in the knowledge about diabetes in literate and illiterate parents.

Prior visits to a physician before diagnosis of T1DM may lead to delay in diagnosis and might be one of the causes of a patient presenting in DKA. Our study showed no difference in DKA at presentation between patients who had prior medical consultations and those who were diagnosed in the first visit. This finding was similar to other studies.^{8,21} Many studies have shown that patients presenting in DKA have more frequent medical encounters prior to diagnosis compared to children without DKA.^{7,8,21,24} The difference might be in their study due to the difference in the incidence of DKA in their study and ours.

In our study we did not find any difference in BMI in patients presenting with or without DKA at the onset of T1DM. This finding was similar to a study done in South India.²⁴ Various studies have shown that patients with lower BMI presented in DKA.^{9,26} A study has shown that a higher BMI is associated with more residual β -cell function and a decrease in the incidence of DKA.³⁰

The limitation of our study was a small sample size.

CONCLUSIONS

More than half of the patients with T1DM presented in DKA at onset of illness. The shorter the duration of illness, higher the chances of DKA at the onset of T1DM. No significant difference in the mean age, mean HbA1c, mean BMI, gender, parents' literacy and medical consultations prior to diagnosis was observed as a risk factor to DKA at the onset of the disease. As the study sample was small, further studies are needed to confirm these findings.

ACKNOWLEDGEMENTS

I would like to acknowledge Life for a child (LFAC) programme who support monitoring and treatment of T1DM for last 30 years at Patan Hospital.

CONFLICT OF INTEREST

None.

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