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PRECIPITATING FACTORS AND CLINICAL PRESENTATION AT THE TIME OF ADMISSION FOR DIABETIC KETOACIDOSIS IN NANGARHAR, AFGHANISTAN

Abstract. The publication is devoted to the study of the frequency of various factors provoking the development of diabetic ketoacidosis (DKA), and the initial clinical signs at the time of admission.

Diabetic ketoacidosis (DKA) is known to be one of the life-threatening acute complications of diabetes mellitus (DM), resulting from a decrease in insulin levels, a decrease in glucose intake by peripheral tissues and an increase in glucose production. The annual incidence of DKA ranges from 4.6-8 episodes per thousand diabetic patients. DKA most often occurs in type 1 diabetes mellitus (DM1), but also affects patients with type 2 diabetes in the presence of provoking factors.

We conducted a descriptive prospective cross-sectional study based on a targeted sample. The study was conducted in the medical department of the Nangarhar University Teaching Hospital from 12/28/2019 to 10/22/2021, including both female and male patients with any type of DM with DKA at the time of admission.

Key words: Diabetic Ketoacidosis (DKA), acute complication, diabetes mellitus, Nangarhar.

Introduction

The aim of the study was to determine the frequency of different DKA precipitating factors and the initial clinical feature at the time of admission.

This descriptive prospective cross sectional study based on purposive sampling, was conducted in the medical ward of Nangarhar University Teaching Hospital from 28/12/2019 to 10/2/2021 including both female and male patients of any type of DM with DKA at the time of admission. After thorough history taking, physical examination and investigations such as lab, radiological and ECG, precipitating factors were found out.

Diabetic Ketoacidosis (DKA) is one of the life threatening acute complications of diabetes mellitus (DM) [1] resulting from decreased insulin level either relative or absolute, decreased glucose consumption by peripheral tissues and increased glucose production (gluconeogenesis) due to the increased level of counter regulatory hormones such as cathecolamines, glucagon, cortisol and growth hormone [2]. The annual incidence of DKA ranges from 4.6-8 episodes per thousand diabetic patients [3]. DKA most often occurs in type 1 diabetes mellitus (T1DM) but also affects patients with type 2 DM in the presence of precipitating factors such as insulin discontinuation, infection and alcohol abuse [4]. Moreover, 6-7% incidences of DKA are reported in pregnancy, 90% of which are gestational DM (GDM) [5] [6]. The Mortality rate in DKA has significantly fallen to less than 1% in adult patients in USA due to improvement

in the diagnosis, patient education and treatment although it is still greater than 5% in the elderly patients due to concomitant disease [7] [8]. However, up to 30% deaths are reported in hospitalized DKA patients in India [9]. Hospital admission with the diagnosis of DKA at intensive care unit is 7.4% [10], in fact, there were 120000 hospital discharges in the year 2005 with an estimated annual cost of 2.4 billion dollars which reached 140000 discharges by 2009 [11] [12]. The clinical presentation of DKA is that of the acute clinical presentation of DM including polyurea, polydepsia and weight loss accompanied by nausea/vomiting, diffuse abdominal pain (>50%) which may mimic acute pancreatitis, kussmaul breathing, acetone smell, altered mental status and signs of dehydration [1] [13]; DKA patients can be euthermic despite the presence of its common precipitating factor, infection, while hypothermia is indicator of poor prognosis [14].

Arterial PH less than 7.3, positive ketones in urine or serum, hyperglycemia > 250 mg/dl and bicarbonate < 18mEq/L are diagnostic of diabetic Ketoacidosis [1], however, about 10% of DKA patients present with ≤250 mg/dl serum glucose known as euglycemic DKA [15]. The aforementioned diagnostic criteria and altered mental status classify DKA severity as mild, moderate and severe [1]. Furthermore, investigations such as ECG, chest X ray, urine exam, blood exam, sputum, urine and blood cultures and history taking should be ordered to find the precipitating factors of which insulin withdrawal, infection and stress are the most common ones [1] [16][17]. DKA should

be treated in intense care unit (ICU) regarding a comprehensive flow chart with fluid, insulin, potassium and/or bicarbonate and the precipitating factor should be resolved; fluid restoration should be considered first as fluid from all compartments including intravascular, interstitial and intracellular are depleted because of hyperglycemia, moreover, clinical trials suggest that insulin is the mainstay of the treatment regardless of its route of administration [18] [19]. Cerebral edema, a very rare complication in adults, is responsible for 57-87% of all deaths in children with DKA and results from rapid decline in serum glucose [20] [21].

Despite the advances in the recognition and management of DKA, recent data on the prevalence of precipitating factors lack especially in developing countries which in fact, there is no published local data in Afghanistan, so we aimed to find the data regarding the prevalence of precipitating factors and initial clinical presentation at the time of admission which could be used for effective patient education programs to enhance public awareness and promote the DKA management in the area.

All 72 patients had DKA. 52 (72.2%) patients were female and 20 (27.8%) were male. 11 patients (15.3%) were type 1 and 61 (84.7%) were type 2 DM. The median age of the patients was 50; median weight was 61; median systolic blood pressure 120 mmHg and the median FBS was 272 mg/dl at the time of admission. Nausea/vomiting (49, 68.1%), tachycardia (46, 63.9%), dry tongue (42, 58.3%), and epigastric tenderness (40, 55.6%), were the most frequent clinical presentation. Infection specifically UTI (68.1%) was the most frequent precipitating factor followed by IHD (11.1%) and insulin withdrawal (5.6%) respectively. UTI distribution across gender (52.8% vs 15.2% two sided P value 0.14 CI 0.95), DM type (58.33% T2DM vs 9.72% in T1DM out of 68% two sided P value 0.7 CI 0.95) and age category was different, however not significant due to the small sample size where the same story occurred with FBS difference across gender (two sided P value 0.035, CI 95%).

Infection especially UTI, ischemic heart disease and insulin withdrawal are the leading precipitating factors; and clinical presentation of gastrointestinal tract (nausea/vomiting), dehydration (dry tongue),

cardiovascular system and urinary tract are the most prevalent in DKA patients at the time of admission in Nangarhar Afghanistan.

Methodology

This descriptive prospective cross sectional study based on purposive sampling was carried out in the medical ward of Nangarhar University Teaching hospital located in Nangarhar province, eastern Afghanistan over 72 patients for a period of 14 months from 28/12/2019 to 10/2/2021. All patients met the American Diabetic Association DKA diagnostic criteria as serum glucose >250 mg/dl, PH <7.35, bicarbonate <18 mEq/L and positive serum or urine ketones. In addition, the study included both male and female patients greater than 10 years of age with either type of DM. Patients with diagnosis other than DKA were excluded from the study. Patients' demographics (age, gender, marital status, etc) and symptoms and signs and the existing precipitating factors at the time of admission to the medical ward were noted after thorough history taking, physical examination, and investigations such as blood, urine and sputum exam and culture, radiological (chest X ray, ultrasound) and electrocardiographic tests.

Data was stored in excel sheet and analyzed in IBM SPSS (Statistical Program for Social Sciences version 22). Both descriptive qualitative and quantitative analysis were used as mean and standard deviation were used for continuous variables. Frequency/percentages were used for categorical variables. Chi square test, Fisher's exact test and T tests were used to compare difference in groups. P value less than 0.05 was considered significant.

Results

All 72 patients included in the study had DKA at the time of hospital admission of whom 52 patients (72.2%) were female and 20 patients (27.8%) were male. Further patient demographics and DM types are described in Table 1. Our data was found abnormally distributed after running Kolmogorov test. The median age was 50, median weight was 61, median systolic blood pressure was 120 and the median FBS was 271.

Table 1 – Patient Demographics and DM Type

Patient Demographic		Frequency	Percentage
Sex	Male	20	27.8
	Female	52	72.2
Age Group (in year)	Lower than 21	10	13.9
	21-40	7	9.7
	41-60	45	62.5
	Greater than 60	10	13.9

DM Type	Type 1	11	15.3
	Type 2	61	84.7
Residency	Nangarhar	61	84.7
	Laghman	8	11.1
	Konar	3	4.2
Marital Status	Married	62	86.1
	Unmarried	10	13.9
Religion	Islam	72	100
	Other	0	0
Income	Low	58	80.5
	Middle	12	16.7
	High	2	12.8

The initial clinical presentation comprising of both signs and symptoms were elicited after curious history taking and physical examination; gastrointestinal clinical feature, signs of dehydration, cardiovascular symptoms and signs, signs and symptoms related to UTI were respectively predominant as shown in table 2.

Table 2 – Frequency of Symptoms and Signs

Sign/Symptoms		Frequency	Percentage
Gastrointestinal system	Nausea/Vomiting	49	68.1
	Epigastric tenderness	40	55.6
	Abdominal pain	20	27.8
	Abdominal tenderness	3	4.2
	Epigastric pain	7	9.7
	Diarrhea	7	9.7
	Anorexia	2	2.8
Cardiovascular and Respiratory systems	Tachycardia	46	63.9
	Neck vein distension	5	6.9
	Hepatojugular reflex	1	1.4
	Cough	3	4.2
	Chest discomfort	7	9.7
	Creptiation	5	6.9
	Harsh breath sounds	2	2.8
	Dyspnea	1	1.4
Dehydration	Dry tongue	42	58.3
	Sunken eye	2	2.8
	Irritability	2	2.8
	Cold extremity	1	1.4
Urinary Tract	Flank tenderness	11	15.3
	Flank pain	8	11.1
	Dysurea	2	2.8
Others	Fever	17	23.6
	Headache	11	15.3
	Polyurea	3	4.2
	Polydepsia	2	2.8
	Kussmaul breathing	1	1.4
	Unconscious	3	4.2
	Vertigo	2	2.8
	Pallor	6	8.3
	Abortion	1	1.4
	Moonlike face	1	1.4
	One side weakness	1	1.4

UTI was the more prevalent precipitating factor among all the precipitating factors in the patients (68.1%) as shown in table 3.

Table 3 – Frequency of Precipitating Factors

Precipitating Factor	Frequency	Frequency	Percentage
Infection	UTI	49	68.1
	Gastrointestinal	13	18.1
	Respiratory	7	9.7
	Malaria	1	1.4
	Abscess	1	1.4
	Brain	1	1.4
Cardiovascular Disease	HTN	4	5.6
	IHD	8	11.1
	HF	2	2.8
	CVA	2	2.8
Miscellaneous	Insulin withdrawal	4	5.6
	Diabetic foot	3	4.2
	Peptic ulcer disease	2	2.8
	Anemia	1	1.4
	Pregnancy	1	1.4
	Surgery	1	1.4
	Unknown	1	1.4

Moreover, UTI was more prominent in the female gender {(Figure 1) two sided P value 0.14 CI 0.95}, type 2 DM (58.33% T2DM vs. 9.72% in T1DM out of 68% two sided P value 0.7 CI 0.95) and in the age category between 41 to 60 years {(Figure 2), two sided p value 0.4 CI 0.95}, however, they were not statistically significant due to the small sample size.
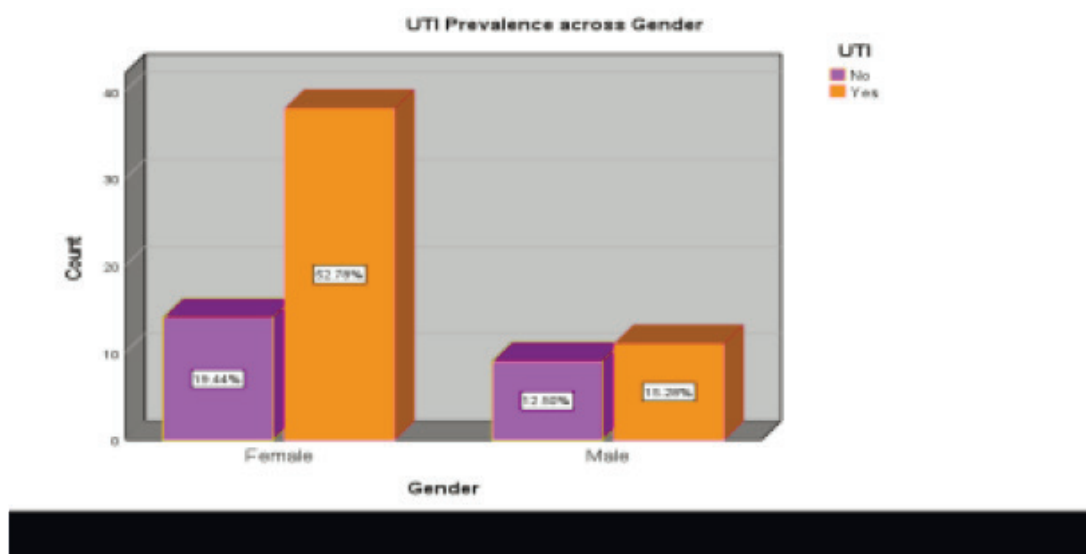

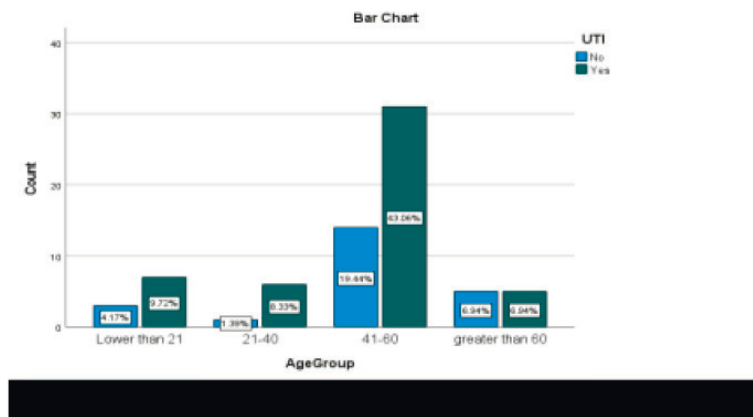**Figure 1 –** UTI Prevalence across Gender

Figure 2 – UTI Prevalence across Different Age Groups

There was difference of median FBS (271) across gender as shown in Figure 3 (two sided P value 0.035, CI 95%) but it was not considered statistically significant may be due to the very low sample size.

Discussion

This is the first paper published from Nangarhar Un

Independent-Samples Median Test Summary

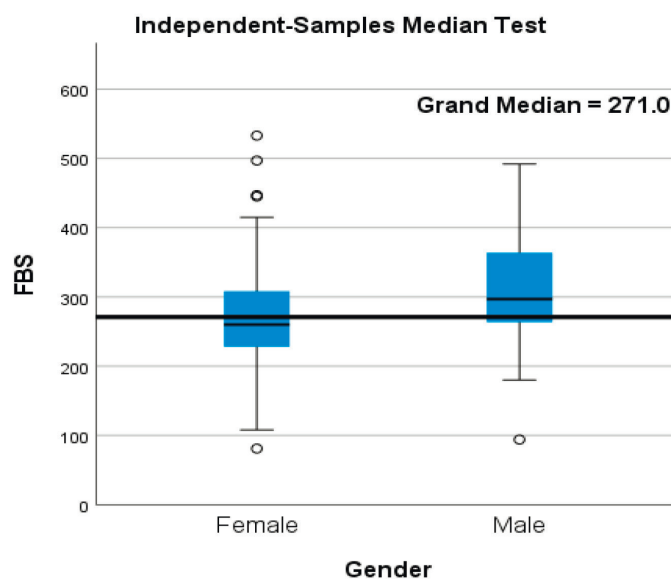|	
Total N	72
Median	271.000
Test Statistic	4.431a
Degree Of Freedom	1
Asymptotic Sig.(2-sided test)	.035
Yates's Continuity Correction Chi-Square	3.392
Degree Of Freedom	1
Asymptotic Sig.(2-sided test)	.066

Figure 3 – FBS Difference across Gender

University teaching hospital about the precipitating factors of DKA and the initial clinical presentation at the time of admission. The major findings of the current study are as the following:

Infection is the most prevalent precipitating factor of DKA at the time of diagnosis where UTI was in the top followed by gastrointestinal tract infections and respiratory tract infections. This finding is consistent with those of the China [22], Pakistan [17], India [23] and US [24]. On the contrary, insulin withdrawal has been reported being the most prevalent DKA precipitating factor as in Israel [25], Brazil [26] while in our study only 4 patients (5.6%) with DKA discontinued insulin due to the lack of awareness and education on their treatment and poor economy or either the efficacy of insulin was in doubt due to the unavailability of the refrigerator and power facility in the low income population in the province. Ischemic heart disease and insulin discontinuation were next. Only 11 patients in our study are type 1 DM having DKA (15.3% of the current study) but according to its global prevalence of around 5%; the prevalence of DKA is supposed to be 19 fold more than that of type 2 DM.

Gastrointestinal system signs and symptoms specifically nausea and vomiting were most prevalent in our patients in their initial presentation at the time of admission, which were concordant with that of the China [22]; in addition, clinical features of dehydration, cardiovascular comorbidity and urinary tract were respectively higher in the current study. Moreover, UTI as the dominant precipitating factor is more prevalent in females and type 2 DM which

is consistent with the study by Nitzan Orna et al. [27,28], however it is not statistically significant due to the low sample size in our study. Despite adequate management for DKA, proper education on diabetes, diet and personal hygiene especially in women is necessary to avoid the episodes of DKA in diabetic patients which could be best done by media and local healthcare staff in the rural areas.

Conclusion

Infection, especially UTI, heart disease and insulin withdrawal are the leading precipitating factors; and clinical presentation of gastrointestinal tract (nausea/vomiting), dehydration (dry tongue), cardiovascular system and urinary tract are the most prevalent in DKA patients at the time of admission in Nangarhar Afghanistan.

Limitation

There were a few limitations in our study, the first being the design of the study, cross sectional, in which we could not follow the patients for their management and awaiting complications and the outcome measures could have been biased. Second, the study was conducted in one setting in the medical ward of Nangarhar University teaching hospital which is not designed for pediatric patients while studies show that pediatric patients constitute 80% of all DKA admissions mainly because of type 1 DM [28]. Third, the low sample size significantly affected the results of the study.

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