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CLINICO-EPIDEMIOLOGICAL PROFILE AND ASSOCIATED RISK FACTORS IN PATIENTS PRESENTING WITH DIABETIC KETOACIDOSIS AT A TERTIARY CARE CENTRE OF UTTARAKHAND

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Abstract:

Background: Diabetic Ketoacidosis (DKA) is an acute, severe disorder associated with absolute or relative insulin deficiency, volume depletion, and acid–base abnormalities, which can result in potentially serious complications if not promptly diagnosed and treated.

Aim: To study the clinico-epidemiological profile and associated risk factors in patient presenting with diabetic ketoacidosis in Dr. Susheela Tiwari Government Hospital, a tertiary care centre of Uttarakhand.

Design: A cross-sectional and observational study was conducted in the Department of General Medicine, Government Medical College and associated Dr Susheela Tiwari Hospital, Haldwani for a period of 18 months from January 2023 to June 2024.

Materials and methods: 64 patients were diagnosed as Diabetic Ketoacidosis by the presence of (1) Venous blood pH of 7.30 or lower or a serum bicarbonate concentration of 18 mEq/L or lower (2) Plasma glucose level of 250 mg/dL or higher (3) Presence of urine ketones.

Results: In this study, the minimum age of presentation was 17 years and the maximum age of 81 years with mean age of 49.2±13.60 years, maximum number of patients belonged to age group of 46 to 60 years (n=28,43.75 %). 39 were male and 25 were female with a ratio of 1.56:1. 57 were Type 2 and 7 were Type 1 Diabetes Mellitus with mean duration of Diabetes Mellitus as 7.18 years and mean value of HbA1C level as 10.57%. 56.25% were on oral hypoglycemic agents, 26.56% were on insulin, 7.81% were not on any treatment and 9.38% were newly diagnosed at presentation. 40 participants were urban residents and 24 were rural residents with 63% belonging to upper lower socioeconomic class. 48.43% had Systemic Hypertension as a comorbidity and 38% were found to be overweight. Nausea/ vomiting were the most common clinical presentation (n=17,26.56%) and infections were the most common precipitating factor (n=32,50%) of DKA in these patients.

Conclusion: Early diagnosis and prompt treatment can reduce the life threatening complications of the disease. Easy access to healthcare services, public awareness and seeking early intervention are the key elements concerning the disease and its burden.

Keywords: Diabetic Ketoacidosis (DKA), Type 1 Diabetes Mellitus (T1DM), Type 2 Diabetes Mellitus (T2DM), Uttarakhand.

INTRODUCTION

Diabetic Ketoacidosis is an acute, severe disorder directly related to diabetes. It occurs in both type 1 and type 2 diabetes mellitus although it was previously considered as a 'hallmark of type 1 Diabetes Mellitus'. It is associated with absolute or relative insulin deficiency, volume depletion, and acid–base abnormalities. If Diabetic Ketoacidosis is not promptly diagnosed and treated, it can result in potentially serious complications [1].

As per World Health Organization Global report on diabetes in 2016, the number of people in the world with diabetes increases from 108 million in 1980 to 422 million in 2014[2]. The prevalence of diabetes in countries with low and middle income has been found to be leaping more speedily than in those countries with high income[2]. Majority of people including more than 95% with diabetes are found to have type 2 diabetes in 2019; globally there were 9 million people with type 1 diabetes in 2017 with majority of them living in countries with high-income[2]. 1.5 million deaths were attributed to Diabetes in the year 2012; rates of diabetes mortality by age increases by 3% between 2000 and 2019[2]. The overall incidence of Diabetic Ketoacidosis is 4-8% with a mortality of <1% with intensive management in developed countries. However, Indian studies have shown a higher incidence with mortality reaching up to 30% [3-16]. As Diabetes mellitus takes over 17% of total global cases, it is a noteworthy and dense public health issue; especially with India being the diabetic capital of the world [3].

Diabetic Ketoacidosis is a result of insulin deficiency (relative or absolute) combined with excess of counter regulatory hormones like glucagon, thus promoting the process of gluconeogenesis, glycogenolysis, and ketone body formation in the liver. Although it occurs more frequently in 'individuals with established diabetes', DKA could be the initial symptom complex leading to type 1 DM diagnosis. It is characterized by hyperglycemia (serum glucose >250 mg/dL], ketosis, and metabolic acidosis along with a number of secondary metabolic derangement. The symptoms of DKA include nausea and vomiting, abdominal pain, thirst, polyuria, shortness of breath. Physical findings include tachycardia, dehydration, hypotension, tachypnea, respiratory distress, classic signs like Kussmaul respirations and a fruity odor on the patient's breath, abdominal tenderness, lethargy, obduntation, cerebral edema and even coma with severe DKA. The two most common precipitating factors remain inadequate insulin administration or poor compliance to treatment and infections like respiratory tract infection, urinary tract infection, gastrointestinal infection, sepsis. Infarction (cerebral, coronary, mesenteric, peripheral), pancreatitis, drugs (cocaine) and pregnancy are the other precipitating factors[1]. Previous Indian studies found infection as a principal recognized cause of DKA precipitations [3-12]. Acute management includes aggressive fluid resuscitation, insulin infusion, correction of electrolyte disturbances and care of treatable precipitant factor like an infection. Untreated or ineffectively treated patients have invariably high mortality[4].

MATERIALS AND METHODS

The study was a cross-sectional and observational study conducted in the Department of General Medicine, Government Medical College Haldwani and associated Dr. Susheela Tiwari Government Hospital, Haldwani, Uttarakhand after obtaining approval from Institutional Ethics Committee for a period of 18 months (January 2023 to June 2024) in a total of 64 patients of Type 1 and Type 2 Diabetes Mellitus with age more than 16 years presenting to emergency department. Diagnostic criteria for Diabetic Ketoacidosis[3]:

1. A venous blood pH of 7.30 or lower or a serum bicarbonate concentration of 18 mEq/L or lower
2. A plasma glucose level of 250 mg/dL or higher
3. Ketonuria

Patients on steroids, Cushing's Syndrome, Acromegaly which can also cause hyperglycaemia; patients with starvation, fasting, anorexia, alcohol intoxication which can also cause ketosis were excluded. **Statistical analysis:** The data was described in terms of frequencies (number of cases), relative frequencies (percentage of cases), mean and standard deviation as appropriate.

RESULTS AND OBSERVATION

In our study, the maximum number of DKA patients were between the age group of 46 to 60 years (n=28, 43.75 %) with the least number of patients belonging to age group of 16- 30 years (n=6,9.38%). The mean age of DKA was 49.2 years, minimum age being 17 years and maximum age being 81 years. Male to female ratio was 1.56:1 with 39 male participants (61%) and 25 female participants (39%).

S No.	Age group (in years)	Male	Female	tal num	al percent
		N (%)	N (%)		
1	16-30 years	4 (6.25%)	2 (3.125%)	6	9.38 %
2	31-45 years	12 (18.75%)	7 (10.93%)	19	29.69 %
3	46-60 years	16 (25%)	12 (18.75%)	28	43.75 %
4	More than 60	7 (19.93%)	4 (6.25%)	11	17.19 %
TOTAL		**39 (60.94%)**	**25 (39.06%)**	**64**	**100 %**

Figure 1.0: Age and Sex distribution in DKA

Type 2 Diabetes Mellitus (n=57, 89%) were more compared to Type 1 Diabetes Mellitus (n=7,10.94%). 40 participants were urban residents (62.5%) and 24 were rural residents (37.5%). Maximum participants (n=26) belonged to upper lower socioeconomic class (40.63%), followed by 20 participants of lower middle class (31.25%), lower class of 13 participants (20.31%), and upper middle class of 5 candidates (7.81%). In the treatment history, the

maximum number of patients were found to receive oral hypoglycemic agents (n= 36,56.25%) followed by insulin (n=17,26.56%), 5 were not on any treatment (7.81%) and 6 were newly diagnosed at the time of hospital presentation (9.38%) . 36 patients (56.25 %) were found to live with diabetes for less than 5 years, 15 patients (23.44%) lived with diabetes for 6 to 10 years, 6 patients (9.38%) for 11 to 15 years and 7 patients (10.94%) for more than 15 years. 31 patients (48.43%) were found to have Systemic Hypertension as a comorbidity, 24 DKA patients were found to be overweight (38%), 21 patients had normal BMI (33%) and 19 patients were obese (30%).

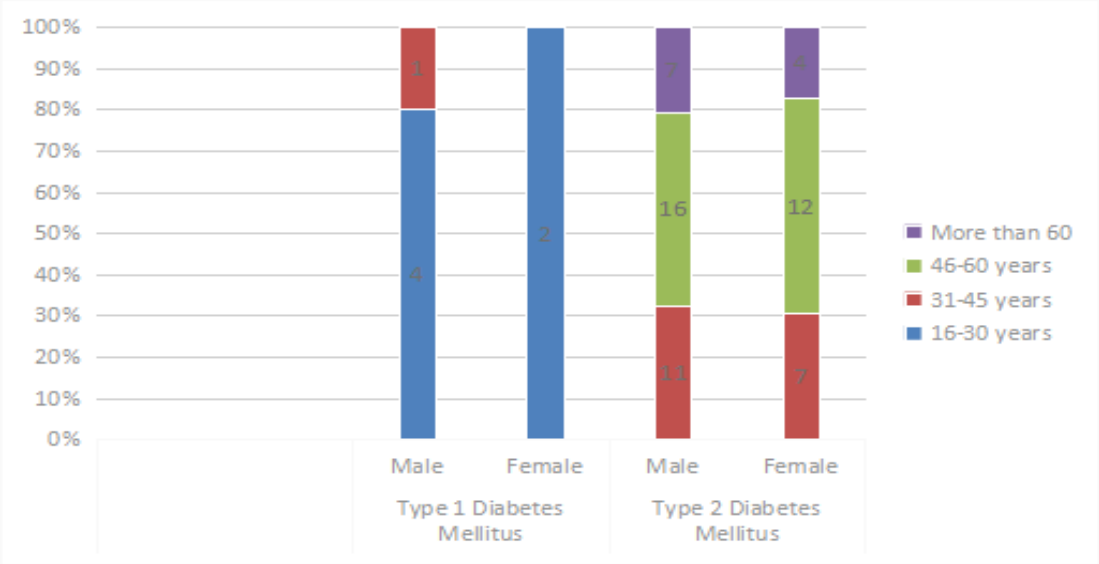

Figure 2.0: Distribution of type of diabetes according to gender and age in DKA

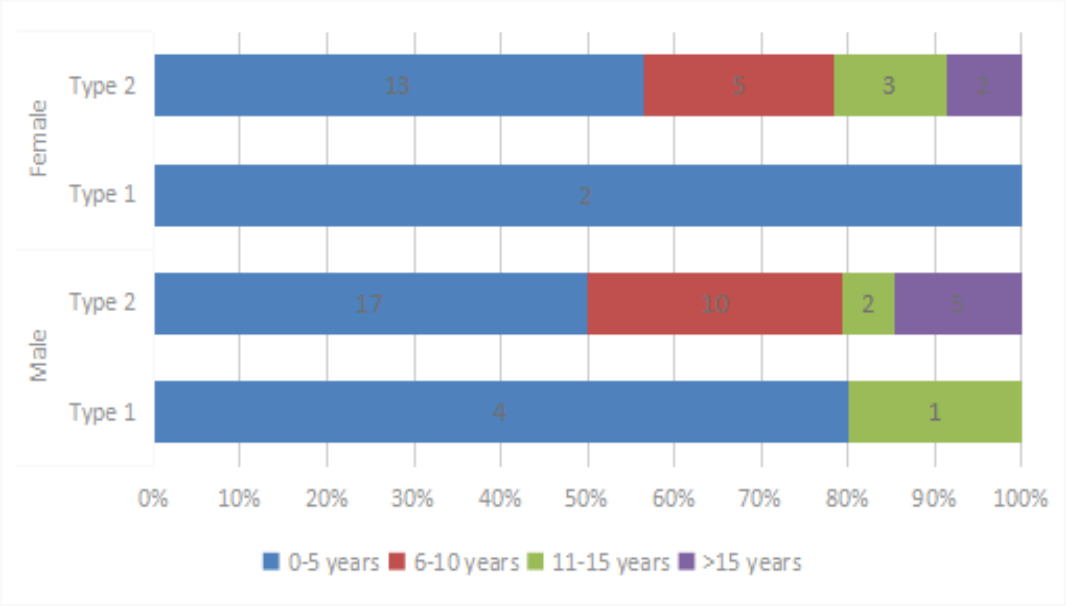

Figure 3.0: Duration of diabetes mellitus distributed according to sex and type of Diabetes in DKA

The most common clinical presentation among DKA in this study was nausea/vomiting (n=17,26.56%), followed by thirst/polyuria (n=11,17.19%), abdominal pain (n=10,15.63%), shortness of breath (n=9,14.06%), altered sensorium (n=8,12.50), fever (n=8,12.50 %) and others (1.56%). In physical examination, hypotension was found in 12 participants (18.75%), tachycardia in 31.25%, low oxygen saturation in 28.125%, >100^{o}F temperature in 6.25%, focal neurological deficit in 3.125%, chest crepitation in 27 patients (42.18%).

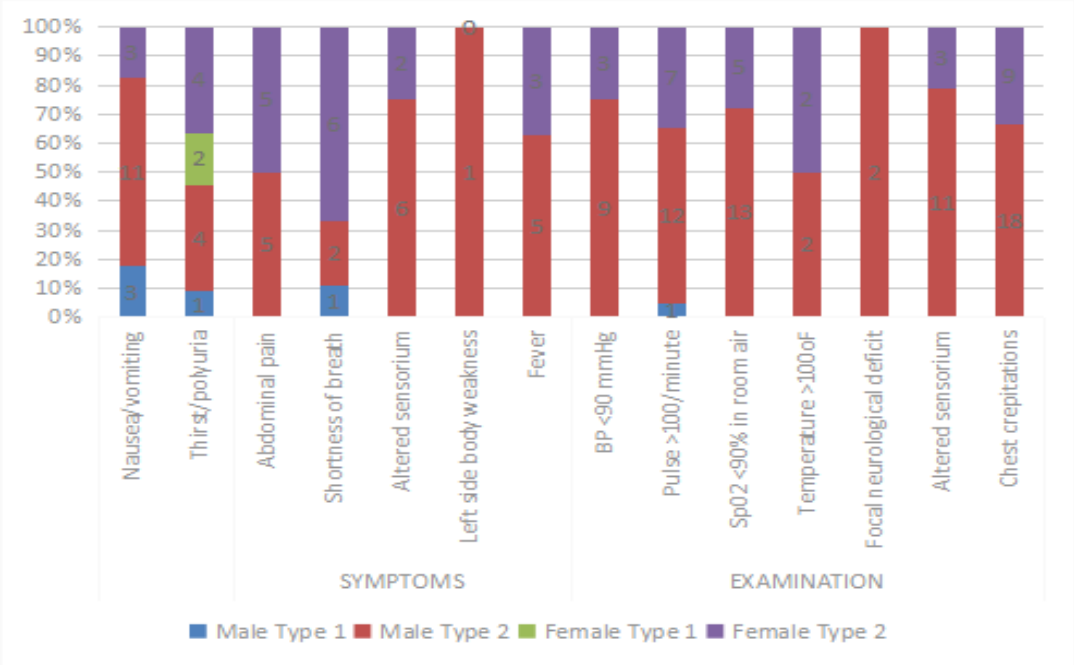

Figure 4.0: Distribution of clinical features of DKA

The most common precipitating factor of DKA in this study was infection (n=32,50%), followed by poor compliance to treatment (n=23, 35.94%), cerebrovascular accident (n=2,3.125%), acute coronary syndrome (n=5,7.81%) and others. Among infections, respiratory tract infection (n=19, 29.68%) was the most common precipitating factor, followed by gastrointestinal infections (n=5,16%), urinary tract infection (n=2,3.125%) and other infections (n=6,9.375%).

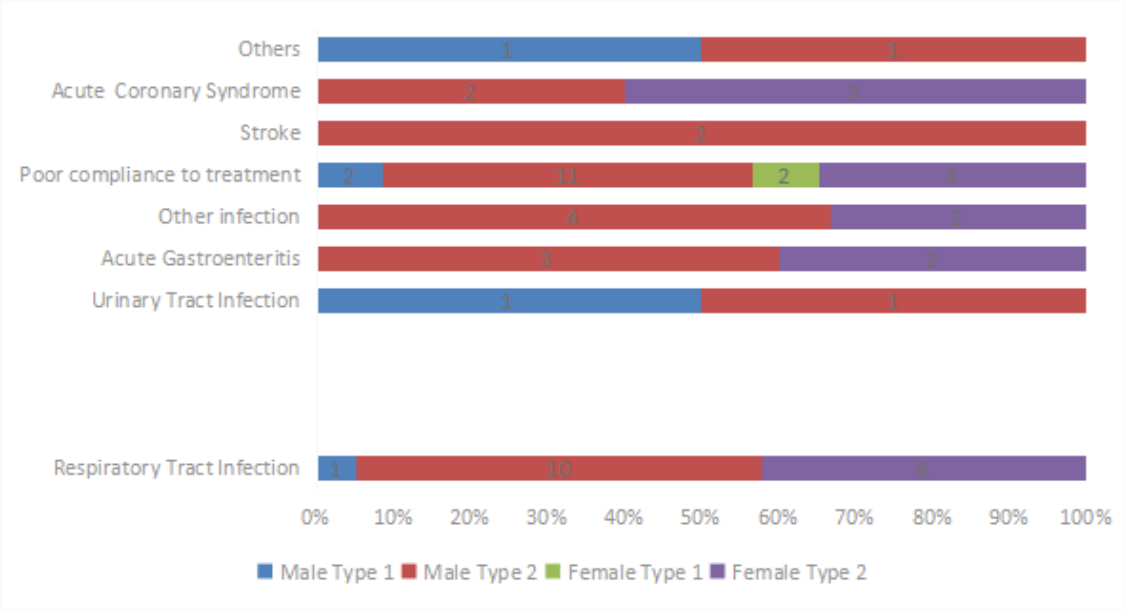

Figure 5.0: Distribution of precipitating factors in Diabetic Ketoacidosis

24 patients had HbA1C level of more than 11% (37.5%), 22 patients had HbA1C level of 9.1 to 11.0% (34.37%), 14 patients had HbA1C level of 7.0 to 9.0% (21.87%) and 4 patients had HbA1C level of less than 7% (6.25%). 41 Patients were found to have moderate Diabetic Ketoacidosis (64%), 15 mild (23%) and 8 severe (13%).

Parameters	Male		Female		Total Number	Total Percentage
	Type 1 (N)(%)	Type 2 (N)(%)	Type 1 (N)(%)	Type 2 (N)(%)		
Less than 7%	0	2 (3.125%)	0	2 (3.125%)	4	6.25%
7.0 to 9.0%	1 (1.56%)	7 (10.93%)	0	6 (9.37%)	14	21.87%
9.1 to 11.0%	1 (1.56%)	15 (24.43%)	0	6 (9.37%)	22	34.37%
More than 11%	3 (4.68%)	10 (15.62%)	2 (3.125%)	9 (14.06%)	24	37.5%

Figure 6.0: HbA1C level distribution in Diabetic Ketoacidosis

Parameters	Male		Female	
	Type 1 (Mean±SD)	Type 2 (Mean±SD)	Type 1 (Mean±SD)	Type 2 (Mean±SD)
SBP (mm Hg)	114±15.36	114.52±39.63	110±8.48	120.58±29.10
DBP (mm Hg)	80±9.38	68.82±23.01	78±0	73.39±20.08
Pulse	94±15.29	95.96±22.49	92.5±6.36	97.43±16.47

O2 saturation (%)	96.2±2.38	89.31±10.25	97±0	92.13±9.91
Temperature	97.56±0.91	98.06±1.46	97.5±1.83	98.29±1.31

Figure 7.0: Vitals parameters distribution in DKA at admission (Mean±SD)

Investigation	**Severity of Diabetic Ketoacidosis**		
	Mild (Mean±SD)	**Moderate (Mean±SD)**	**Severe (Mean±SD)**
Hb (g/dl)	12.47±2.05	12.15±2.93	12.36±2.65
TLC/ micro liters	10053.33±4429.42	11504.63±5326.31	10753.78±5209.4
Platelet (lacs)	2.178±0.76	2.197±1.04	2.244±1.033
Urea (mg/dl)	61.66±34.53	74.12±59.17	55.64±24.02
Creat (mg/dl)	1.66±1.13	1.67±1.49	1.21±0.51
Na^+ (mEq/L)	137.2±6.89	139.17±825	138.86±8.42
K^+ (mEq/L)	3.66±0.66	3.67±0.70	3.57±0.65
RBS (mg/dl)	299.8±100.6	373.46±103.84	365.18±117.28

Figure 8.0 Investigation distribution according to severity in DKA (Mean±SD)

DISCUSSION

In our study, the mean age of DKA is 49.2 years, minimum age being 17 years and maximum age being 81 years showing a wide range inclusion of age groups with maximum number of patients belonging to age group of 46 to 60 years (n=28,43.75 %) and least number of patients belonging to age group of 16- 30 years (n=6,9.38%). Sex distribution in our study showed that the number of male participants (n=39,61%) were more compared to the number of female participants (n=25,39%) in all age groups with male to female ratio of 1.56:1. The number of Type 2 Diabetes Mellitus (n=57,89%) were more compared to Type 1 Diabetes Mellitus (n=7,11%) reflecting a higher prevalence of T2DM. T1DM were found in 4 males (6.25%) and 2 females (3.125%) of 16-30 years age group reflecting younger age among T1DM and male predominance. The mean duration of Diabetes Mellitus is 7.18 years. Majority of patients (n=36,56.25 %) lived with diabetes for less than 5 years showing the aspects of wisdom regarding the disease and its related acute complications enhanced as you live longer with the disease; it also revealed that type 1 diabetes developed acute complication of diabetes like DKA much earlier during the course of the disease. Subsequently, 15 patients (23.44) lived with type 2 diabetes for 6 to 10 years, 6 patients (9.38%) had diabetes for 11 to 15 years, 7 patients of type 2 (10.94%) had diabetes for more than 15 years. The most common clinical presentation of DKA in this study was nausea/vomiting (n=17,26.56%) followed by thirst/polyuria (n=11,17.19%), abdominal pain (n=10,15.63%) and shortness of breath (n=9,14.06%). Other

presentations include fever (n=8,12.50%), altered sensorium (n=8,12.50) and left body weakness (n=1,1.56%). Blood pressure of less than 90 mm Hg was found in 12 participants (18.75%); the reason for low blood pressure/hypotension could be attributed to volume depletion state of diabetic ketoacidosis and conditions associated with precipitating factors including septic shock in infections and cardiogenic shock in acute coronary syndrome. Other findings in our study include tachycardia in 31.25%, low oxygen saturation in 28.125%, >100^{o}F temperature in 6.25%, focal neurological deficit 3.125%, chest crepitation in 27 patients (42.18%). The most common precipitating factor of DKA in this study was infection (n=32,50%), followed by poor compliance to treatment (n=23, 35.94%), cerebrovascular accident (n=2,3.125%), acute coronary syndrome (n=5,7.81%) and others. Among infections, respiratory tract infection (n=19, 29.68%) was the most common precipitating factor, followed by gastrointestinal infections (n=5,16%), urinary tract infection (n=2,3.125%) and other infections (n=6,9.375%). Although the most common precipitating factor of Diabetic Ketoacidosis in this study is infection, but as far as type 1 diabetes is concerned, poor compliance to treatment remained the most common precipitating factor.

These findings were comparative with studies conducted at Northern part of India by **Ravindran Kiran and his colleagues** showing mean age of 43.7±17.0 years, T2DM being the most common type (n=91, 53.8%) and mean duration of diabetes as 6 years[3]; **Parveen Bhardwaj et al** and **Harpreet Singh et al** showing male to female ratio of 1.4:1.0 and 3:2.10 respectively, nausea or vomiting as the most common symptoms with respiratory infection being the most site for infection precipitating DKA in the later study[5,6]. **Pankaj Seth et al** conducted a study at Southern part of India in which out of 60 patients, 12 were of T1 and 48 were T2DM, mean duration of diabetes 8.65 years, nausea or vomiting being the most common symptoms (63.33%), hypotension in 13.33% and infections (73.33%) being the most common precipitating factor[7]. **Maskey R et al** conducted a study at Eastern Nepal in which our of 16 participants, 7 were T1 and 9 were T2DM and infections (56.25%) were the most common precipitating factor[8]. **B. Anupama et al** showed mean duration of diabetes as 7.3 ± 4.6 years and infections as the most common precipitating factors[9].

In our study, the maximum number of participants were urban residents (n=40,62.5%) and a lesser amount were from rural residents (n=24,37.5%) with predominant male sex in both distribution. Geographic dispersion, transportation issues, provider shortage, poor health literacy, limited access to healthcare services, financial burden were some of the ascribed factors for fewer rural residents seeking medical attention in tertiary care, thus reflecting less population. A systematic review by **Priyanga Ranasinghe and her colleagues** showed that prevalence of diabetes increased in both rural and urban India from 2.4% and 3.3% in 1972 to 15.0% and 19.0% respectively in year 2015-2019 which was independently observed in both genders in North and the South of India [10].

Majority of the study population belonged to the upper lower socioeconomic class in our study (n=26,40.63%), followed by lower class of 13 participants (20.31%), 20 participants of lower middle class (31.25%) and 5 upper middle class (7.81%). This is comparative with data from **National Family Health Survey of India (NFHS)**, 2019–2021 analyzed by **Maiti S and his colleagues** showing the extent of undiagnosed, untreated and uncontrolled diabetes being higher in the poorer states of India although high-income states had the highest prevalence rates, while some of the poorer states had a relatively lower prevalence of diabetes [11].

The maximum number of patients were found to receive oral hypoglycemic agents (n= 36,56.25%) followed by insulin (n=17,26.56%); 5 were not on any treatment (7.81%) and 6 were newly diagnosed at the time of hospital presentation (9.38%). A review of the medical literature with an Asian Indian context by **Shashank R** showed that 4% of patients were on diet therapy, 53.9% were receiving oral antidiabetic agents (OHA), 22% were receiving insulin, and 19.8% a combination of insulin and OHA[12].

In our study, the most common comorbidity was Systemic Hypertension found in 31 patients (48.43%): 19 (29.68%) males and 12 females (18.75) of type 2 diabetes with male gender and type 2 diabetes predominance. 2 patients of Coronary artery disease (3.13 %) and others. Maximum patients were found to be overweight (n=24,38%) with all 24 candidates belong to type 2 diabetes, 21 patients had normal BMI (33%) comprising of 6 type 1 diabetes (9.375%) and 19 patients were found to be obese (30%) with mean BMI of 26.89 kg/m^2 which is comparative with a studies by **Kiran S.R and her colleague** showing that the most common conditions in patients with T2DM included Systemic Hypertension in 82.1%, overweight/obesity in 78.2%[13]; **Vasanthakumar and his colleagues** in Southern part of India showing 25.89 Kg/m^2 as mean BMI of the study participants[14].

The mean value of HbA1C level in our study is 10.57%. Majority of the patients (n=24,37.5%) had HbA1C level of more than 11% showing that incidence of DKA is high with uncontrolled blood sugar; it also showed female gender and type 1 diabetes predominance in high HbA1C level. 22 patients had HbA1C level of 9.1 to 11.0% (34.37%), 14 patients had HbA1C level of 7.0 to 9.0% (21.87%) and 4 patients had HbA1C level of less than 7% (6.25%). This is comparative with a study by **Viswanathan M and his colleagues** in an observational A1chieve study that the mean HbA(1c) was 9.2% and diabetes control was worse in those with longer duration of diabetes (9.9 +/- 5.5 years)[15].

64 patients in our study were classified into mild, moderate and severe DKA according to American Diabetes Association criteria[3]:

1. Mild: pH=7.25-7.30/HCO3= 15-18 mEq/L

2. Moderate: pH=7.00- <7.25/HCO3= 10-<15 mEq/L

3. Severe: pH=<7.00/HCO3=<10 mEq/L

Large group comprising of more than half the population were found to have moderate DKA (n= 41,64%), 15 had mild (23%) and 8 had severe DKA (13%). The characteristics of severe DKA derived from the above data included predominant T2DM, longer duration of diabetes, altered mental status and uncontrolled diabetes, A study by **George JT and his colleagues** in South India showed maximum participants presented with severe DKA (51%) and seconded by moderate DKA[16].

CONCLUSION

The maximum number of DKA are between the age group of 46 to 60 years with male gender predominance. The most common clinical presentation was nausea/vomiting followed by thirst/polyuria. Infections like respiratory tract infection were the most common precipitating factor followed by poor compliance to treatment. Type 2 diabetes mellitus exceeded type 1 diabetes in large number with Systemic Hypertension and Overweight found as common comorbidities. Urban residents had the upper hand in geographical distribution. Maximum participants belonged to lower socioeconomic class and a large number of participants lived with diabetes for less than 5 years. The incidence of Diabetic Ketoacidosis was higher in patients with higher HbA1C level. Emphasizing on regular follow up, uplifting access to healthcare services, improvement in raising awareness and active participation related to its acute and chronic complications, compliance to treatment, discouraging underestimation of treatment for ongoing infections, seeking early intervention from health care centre, education and promotion of healthy lifestyles are the key elements concerning the disease and its burden.

LIMITATIONS

There was a small number of study population. The study was a hospital based observational study done in a single tertiary care centre. Majority of the patients belonged to type 2 Diabetes Mellitus and other types of diabetes were not included. Maximum number of patients were of urban residents. Urine ketone estimation was done instead of plasma ketones.

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