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CLINICAL PROFILE OF DIABETIC KETOACIDOSIS IN ADULTS IN SUB HIMALAYAN REGION: HOSPITAL BASED STUDY

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ABSTRACT

Diabetic ketoacidosis (DKA) is a serious acute complication of diabetes mellitus and has significant morbidity and mortality. This study was done to observe the clinical profile and Outcome of the adult patients with DKA from our state from sub Himalayan region. Total 42 patients observed: (42.85%) were males and 24 (57.14%) were females Average age of presentation was 44.78years \pm 15.92 years with range from 18 years to 82 years. 12 (28.57%) patients were of type 1DM and 30 patients (71.42 %) of type 2DM. 33.33% patients newly diagnosed. Commonest presenting complaint was vomiting in 45.23% patients. Severe DKA was seen in 50% patients and mortality in 7 patients (16.66%). Average duration of hospital stay was 9.4 \pm 5.83 days. In 76.19 % patients precipitating factors was seen. Commonest precipitating factor was infection in 33.33% % patients followed by poor compliance in 30.95%. DKA is now a recognised acute complication in type 2dm adults also. There is need among physicians to educate patients regarding need for regular follow up, proper adherence to treatment and management during an intercurrent illness.

Keywords: *Diabetes Mellitus, Diabetic Ketoacidosis, Sub-Himalayan Region and Mortality*

INTRODUCTION

Diabetic ketoacidosis (DKA) is an acute life threatening complication of diabetes mellitus (DM). Earlier thought to be a hallmark of type 1DM, DKA now is being recognised in type 2DM also (Powers, 2015). About 26-34% of total DKA cases are seen in type2DM nowadays (Westphal, 1996; Kitabchi *et al.*, 2009). In fact, as the prevalence of diabetes mellitus worldwide is increasing in with total global burden of disease being 382million (90% type2DM), prevalence of DKA has also risen in the past two decades. India is home to 65.1 million (17.04%) of total global burden of diabetic patients (Powers, 2015). Acute complications like DKA increase the cost of treatment, and also stress the limited hospital facilities available. In USA, the crude and age-adjusted admission rates with DKA were 7.1 and 22.0 per 1,000 diabetic population and average duration of hospital stay 3.4 days (Centers for Disease Control and Prevention, 2014). There are few epidemiological studies on DKA from India based on adult population and none from our sub Himalayan state. So, this study was planned to observe the clinical profile and, recognise the common precipitating factors so that information can be used to sensitize the physician for better care, early recognition and prevention in the diabetic patients.

MATERIALS AND METHODS

Methodology

This was an observational study done in the department of medicine in IGMCM, Shimla. All the adults aged 18 years and above presenting with primary diagnosis of DKA during three years period from January 2011 to December 2014 were included in the study. The diagnosis of DKA was made by the presence of plasma glucose \geq 250mg/dl, serum bicarbonate \leq 18 meq/L or an arterial pH \leq 7.30 along with presence of ketones in blood or urine (Kitabchi *et al.*, 2009). Those presenting with ketosis without acidosis were excluded. Patients were evaluated for the demographic features such as age and sex, diabetic status prior to admission, presenting complaints, precipitating factors, severity of acidosis (Kitabchi *et al.*, 2009), biochemical profile, and the outcome in hospital. Treatment of DKA was as per the standard guidelines of the American Diabetes Association and the institution protocol where required. Statistic were done using Microsoft excel window 8.

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RESULTS AND DISCUSSION

Results

There were total 63 patients who were admitted with suspected DKA during three years period, out of which only 42 patients were turned out to be DKA meeting the criteria. Rest 21 were excluded for having only ketosis without acidosis. Profile of the patients has been tabulated in table 1, 2.

Table 1: Profile of Patients with DKA

S. No	Parameter	Total N=42 (%)	Male N=18 (%)	Female N=24(%)
1.	Mean Age(yr)	44.78±15.9	43.66±13.92	45.6±17.52
2.	Age Distribution			
	≤30yrs	11(26.19)	7(38.88)	4(16.66)
	31-50yrs	18(42.85)	4(22.22)	14(58.33)
	51-70 yrs	11(26.19)	6(33.33)	5(20.83)
	>70 yrs	2(4.76)	1(5.55)	1(4.16)
3.	Duration of Diabetes(yr)	4.47±6.67	4.51±8.67	4.43±4.87
4.	Type of Diabetes			
	1	12 (28.57)	7(38.88)	5(20.83)
	2	30 (71.42)	13(72.22)	17(70.83)
5.	First Time Diagnosed	14 (33.33)	7 (38.88)	7(29.16)
6.	Mortality	7 (16.66%)	4(22.22%)	3(12.5%)
7.	Average Duration of Hospital Stay(days)	9.4±5.83	9.77±6.26	9.125±5.61
8.	Severity			
	Mild	11 (26.19)	4 (22.22)	7(29.16)
	Moderate	10(23.80)	3(16.66)	7 (29.16)
	Severe	21(50)	11(61.11)	10(41.66)

Table 2: Symptoms, Signs and Biochemical Profile in Patients with DKA

S. No	Parameter	Total N=42 (%)	Male N=18 (%)	Female N=24(%)
1	Presenting Complaints			
	Vomiting	19 (45.23)	8(44.44)	11(45.83)
	Altered Sensorium	7 (16.66)	3(16.66)	4(16.66)
	Pain Abdomen	8 (19)	5(27.77)	3(12.5)
	Osmotic Symptoms	6(14.28)	3(16.66)	3(12.5)
	Fever	6(14.28)	3(16.66)	3(12.5)
	Loose Stools	3(7.14)	1(5.55)	2(8.33)
	Chest Pain	1(2.38)	1(5.55)	1(4.16)
	SOB	2(4.76)	0(0)	2(8.33)
	Weakness	2(4.76)	2(11.11)	0(0)
	Cough	2(4.76)	1(5.55)	1(4.16)
	Localised Infection	4(9.52)	2(11.11)	2(8.33)
2	Signs			
	Signs of Dehydration	38(90.47)	17(94.44)	21(87.5)
	Kussmauls Breathing	9(21.42)	2(11.11)	7(29.16)
	Ketotic Breath	6(14.2)	4(22.22)	2(8.33)
3	Biochemistry			
	Average RBS at Presentation (mg/dl)	381.9±84.59	390.61±84.95	375.37±85.54
	Arterial pH at Presentation	7.13±0.22	7.04±0.29	7.2±0.12
	HCO ₃ at Presentation (meq/L)	10.54±4.44	10.27±4.72	10.26±4.31

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Out of total 42 patients 18 (42.85%) were males and 24 (57.14%) were females (male: female:: 1:1.3). Average age of presentation was 44.78 years \pm 15.92 years with range from 18 years to 82 years. Total 12 (28.57%) patients were of type1DM and 30 patients (71.42 %) were of type 2DM. 11(26.19%) patients were of age \leq 30 years out of which 3 were of type1DM and 8 were of type2DM and only 2(4.76%) patients were of age \geq 70 years, both of type2DM.

14(33.33%) patents presented for the first time in DKA and out of these 4 (28.57%) turned out to be of type1DM and 10 (71.42%) patients turned out to be type 2DM on investigations done later (C-peptide, anti-GAD).

The most common presenting complaint was vomiting present in 45.23% patients followed by pain abdomen in 19% and altered sensorium in 16.66% patients. Osmotic symptoms were present in 14.28% patients. Other complaints were fever, loose stools, chest pain, shortness of breath, weakness, cough and localised infection.

Average RBS, pH and HCO₃ were 381.9 \pm 84.59mg/dl, 7.13 \pm 0.22 and 10.54 \pm 4.44meq/l respectively at presentation. Severe DKA was seen in 21 patients (50%) patients and mortality in 7 patients (16.66%). Average duration of hospital stay was 9.4 \pm 5.83 days.

In total 76.19 % patients precipitating factors could be found out and in rest 23.8 % patients no precipitating factors could be ascertained (table 3).

Table 3: Precipitating Factors in DKA

S. No	Precipitating Cause	Total N=42(%)	Male N=18(%)	Female N=24(%)
1.	Poor Compliance	13(30.95)	9(50%)	4 (16.6)
2.	Infection	14 (33.33)	6 (33.33)	8 (33.33)
3.	Acute Coronary Syndrome	3(7.14)	2(11.11)	1(4.16)
4.	Pregnancy	1(2.38)	0(0)	1(4.16)
5.	CVA	4(9.52)	2(11.11)	2(11.11)
6.	Unknown	10 (23.8)	3(16.66)	7 (29.1)

Commonest precipitating factor was infection seen in 33.33% % patients followed by poor compliance in 30.95%. Other causes were acute coronary syndrome 7.14%, CVA 9.52% and pregnancy in 2.38% patients.

Among infections, UTI and pneumonia were commonest with 28.57% frequency each followed by cellulites, sepsis, infected diabetic foot, abdominal abscess, gluteal abscess a, mastoid abscess in 7.14 % each.

We compared the data of DKA in type1DM with type2DM patients (table 4) and found that average age of presentation in type1DM was (24.41 years) significantly less ($p < 0.01$) as compared to that of patients with type2DM (52.93years).

There were more severe cases in type1DM (83.33%) as compared to type2DM (36.66%) ($P < 0.05$) and average duration of hospital stay was 11.16 days in type1DM as compared to type2DM with 8.7 days. Rest of the profile was similar in both the groups.

Profile of the patients who died is tabulated in Table 5. Overall mortality was 16.66% and more mortality was seen in type2DM group (85.7%) and all the cases had moderate or severe DKA.

Average age and RBS were 52.57 years and 407.28 mg/dl which was more than that of overall average of 44.78 years and 381.9mg/dl respectively but was not statistically significant ($p = 0.46$, $p = 0.27$).

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Table 4: Profile of Patients in Type 1DM Vs. Type2DM Patients With DKA

Sr. No	Parameter	Type 1(n=12)	Type 2(n=30)
1.	Average Age (yrs)	24.41	52.93
2.	Age	≤30yrs	3 (25)
	Distribution	31-50yrs	6(50)
		51-70 yrs	3(25)
		>70 yrs	0(0)
3.	Duration(yrs)	3.58	4.82
4.	Newly Diagnosed	4 (33.33%)	10 (33.33%)
5.	Biochemistry	RBS(mg/dl)	376.91
		ph	7.12
		HCO ₃ (meq/L)	8.85
6.	Average Duration in Hospital Stay (Days)	11.16	8.7
7.	Mortality	1(8.33%)	6(20%)
8.	Severity	Mild	2(16.66%)
		Moderate	0(0)
		Severe	10(83.33%)

Table 5: Profile of Patients Who Died With DKA

Sr. No	Parameters	N= 7 (%)
1.	Type 1 (N)	1(14.28)
2.	Type 2(N)	6 (85.7)
3.	Average Age (yrs)	52.57
4.	RBS (mg/dl)	407.7
	Ph	7.13
	HCO ₃ (meq/L)	10.45
5.	Severity (N)	Mild
		Moderate
		Severe
6.	Precipitating factors(N)	Infection
		Poor Compliance
		CVA
		Unknown

Discussion

DKA is characterised by triad of hyperglycaemia, high anion gap metabolic acidosis and ketonemia (Fulop, 1985; Raghupathy, 2015). It occurs due to insulin deficiency along with increased glucose counter regulatory hormones: glucagon, catecholamines, cortisol and growth hormone associated with increased peripheral resistance to insulin. Insulin deficiency decreases the insulin mediated uptake in the insulin sensitive cells and fails to suppress the endogenous glucose formation leading to hyperglycaemia. In addition, there is increased lipolysis in the adipose tissue. Free fatty acids released are metabolised to ketone bodies. Hyperglycemia induces osmotic diuresis and hypovolemia and in association with ketoacidosis leads to other electrolyte disturbances characteristic of DKA (Kitabchi *et al.*, 2009; Gosmanov *et al.*, 2014; Hardern and Quinn, 2003).

In the present study we observed clinical profile of 42 patients admitted with primary diagnosis of DKA. Average age was 44.78years at presentation with mean duration of diabetes of 4.47 years. More number of females were present with ratio of 1:1.3 male:: female. This may be so because the health of females are neglected in the family and thus seek medical assistance at later stages of illness. Maximum patients

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were in the age group of 31-50 years (42.85%). There were 11 patients (26.19%) \leq 30 years of age out of which 8 were of type2DM suggesting the changing trends of type2DM being diagnosed in younger population also (Virmani and Kulkarni, 2012). In a study from India, by Rao *et al.*, (2012) done on 33 patients, more number of males 63% presented with DKA. Average of presentation was similar to our study 43.1 years and prevalence in age >70 years was 3.7% and 18.5% in less than 30 years. In study from Malaysia of 132 of patients 62.9% females and with mean age of 49.7years similar to our study (Usman *et al.*, 2015). In a study of 4807 episodes of DKA, 14 % occurred in patients older than 70 years, 23% in 30-50 years and 36% < 30 years of age (Henriksen *et al.*, 2007). Our study we had more number of type2DM patients 71.42% as compared to 28.57% patients of type 1DM. This change in scenario may be due to increasing prevalence of type2DM and more prevalence of type1DM among Caucasians and paediatric age. DKA is usually identified as complication in type1DM, it also occurs in type2DM during catabolic stress of acute illness. This group of patients are mainly black Latino, Asians, overweight/obese, males with family history of DM and commonly are newly diagnosed. This entity has been termed as ketosis prone DM and later after the termination of acute event these patients behave as type2DM (Kitabchi *et al.*, 2009; Dyanne and Westerberg, 2013). Rao *et al.*, (2012) had 81% type2DM and 19% type1DM in their study. In study of 643 patients from China, 45.7% were of type2DM, 47.9% type1DM, 6.4% atypical (Xu *et al.*, 2015). In another study of 60 patients from India type1DM were in 20% and type2DM in 80% cases of DKA (Seth *et al.*, 2015). One third of the patients (33.33%) we observed had the DKA as their first presentation of DM. These later turned out to be of type2DM in 71.42% and type1DM in 28.57% patients. Rest others were previously diagnosed with average duration of 4.47 years of DM. This figure is more than what observed in other studies (Rao *et al.*, 2012; Usman *et al.*, 2015; Seth *et al.*, 2015). This may be so because of less awareness about the disease and its symptoms among the masses in Himachal Pradesh. Also people ignore their early osmotic symptoms and consult the doctor quite late (Bajwa and Jindal, 2012). In a study on newly diagnosed DM cases in adults by Dhanwal *et al.*, (2014) 23.52% cases presented in DKA and almost half turned out to be of type1DM with positive immunological markers. Our findings matches the classic clinical presentation of DKA (Powers, 2015) with vomiting and nausea in 45.23%, pain abdomen in 19%, altered sensorium in 16.66%, osmotic symptoms in 14.28% patients, dehydration in 90.47%, kussmauls breathing in 21.42% and ketone breath in 14.2 % patients, serum RBS 381.9mg/dl, s. pH 7.13 and HCO_3^- 10.54 meq/l. Severity of the DKA was assessed using arterial pH, HCO_3^- and mental status (Gosmanov *et al.*, 2014). We had 50% of the patients presenting in severe DKA. This may be because of the failure of the patients to consult doctor at initiation of symptoms. More severe cases had more mortality also. Usman *et al.*, (2015) had less number of severe cases 21.2% as compared to our study. Mild cases were 48% and moderate 42.4%. Average length of hospital stay was 9.4 days in our study similar to other studies from southeast Asia ranging from 7-14 days (Rao *et al.*, 2012; Usman *et al.*, 2015; Xu *et al.*, 2015; Seth *et al.*, 2015). This duration is much longer than average stay of 3.4 days in the west (Centres for Disease Control and Prevention, 2014; Wang *et al.*, 2006) and is due to more admissions in severe DKA.

The most commonly documented precipitating factor for DKA is insulin lack due non compliance or pump failure in 2/3 case (Hardern and Quinn, 2003). In our study commonest precipitating factor was infection in 33.33% patients followed closely poor compliance in 30.95% patients. CVA was found in 9.52% patients, MI in 7.14% patients and pregnancy in one patient (2.38%) patients. Cause could not found in 23.8% patients. CVA and ACS were found in type 2 dm patients only. Among infections, UTI and pneumonia were commonest with 28.57% frequency. Rao *et al.*, (2012) had 50% patients with poor compliance identified as precipitating event in 60% cases of type1DM and 33% cases of type2DM. Seth *et al.*, (2015) had infection (73.66%) as the commonest precipitating cause like ours followed by noncompliance in 66.66% and stress in 26.66%. Pneumonia was in 40.90%, tuberculosis in 9.09%, UTI in 27.27% patients, diabetic foot in 9.09%, GI infection in 4.54%.

On comparison of the profile of type1DM vs. type2DM, we found significant difference in age (24.1 years vs. 52.93years), duration of hospital stay (11.16 days vs. 8.7 days) and severity of cases (83.33% severe cases vs. 36.66%) and mortality (8.33% vs. 20%). This suggests that DKA has more adverse

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outcome in type2DM. However, this higher mortality cannot be completely attributed to DKA alone as prevalence of comorbid conditions like atherosclerotic diseases, and chronic kidney disease which are independent cause of mortality are more in type2DM. In a study of 138 patients by Newton and Raskin, (2013), 30 patients had type2DM. A greater proportion of the type2DM group was Latino American or African American. The type1DM group was more acidotic and type2DM patients required longer treatment periods. In another study of 201 patients, with 17.4% type2DM and 82.6% type1DM, type2DM patients were significantly older than patients with type1DM and more patients with severe forms of DKA were seen in the group with type2DM (Ambarski *et al.*, 2013). Chu *et al.*, (no date) and Maskey *et al.*, (2015) had finding similar to our study with higher age, more severity and higher mortality among type2DM group. Case fatality in DKA in developed countries ranges from 1-5% (Kitabchi *et al.*, 2009; Dhanwal *et al.*, 2014; Edo, 2012). Mortality up to 5% is seen in elderly with concomitant life threatening conditions (Kitabchi *et al.*, 2009). However, it is higher for developing countries ranging from 10% to 30% (Xu *et al.*, 2015; Maskey *et al.*, 2015; Matoo *et al.*, 1991). We had 16.66% overall fatality. This higher rate is likely due to less awareness among people, poor socio economic status, less hygienic surroundings, poor adherence to treatment, late presentation, failure of treating doctor to advise regarding compliance.

Conclusion

DKA is now a recognised acute complication in type2DM adults also. 50% of the patients presented in severe DKA. Mortality is more in type2DM group with DKA because of more association of co-morbid illnesses. Infections followed by poor compliance are the major precipitating causes. There is need among physicians to educate patients regarding need for regular follow up, proper adherence to treatment and management during an intercurrent illness, as DKA is potentially preventable complication.

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