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A study to assess the clinicopathological spectrum of acute complications of diabetes mellitus type II

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ABSTRACT

Background: The acute metabolic complications of diabetes consist of diabetic ketoacidosis (DKA), hyperosmolar non-ketotic coma (HNC), lactic acidosis (LA), and hypoglycemia. All of these are associated with significant morbidity and mortality. These can easily be prevented by early recognition and prompt management. Therefore, this study was conducted to assess the clinicopathological spectrum of acute complications of diabetes mellitus type II.

Methods: This observational, analytical study was conducted on 100 patients aged more than 18 years admitted in the ICU with acute complication of Diabetes mellitus Type II. Medical history was recorded. Physical examination and investigations were done and recorded.

Results: The mean age of the study population was 55.26±13.13 years. Hypoglycemia was more common (63%) than DKA (37%). Fever and sweating had the overall highest incidence (and were more in patients with hypoglycemia) while stupor, nausea and abdominal pain had the lowest incidence (and were more in patients with DKA). On examination, only one patient of DKA was drowsy. Mean temperature, pulse and respiratory rate were higher in the patients having DKA while blood pressure was higher in patients having hypoglycemia.

Conclusions: It can be effectively concluded from the present study that DKA and hypoglycaemia have a broad spectrum of clinicopathological features. But the incidences vary widely. This may help in early recognition of the impending complication and thereby enabling prompt management of the same, reducing the associated morbidity and mortality.

Keywords: Diabetes mellitus type II, Diabetic ketoacidosis, Hypoglycemia, Hyperosmolar non-ketotic coma, Lactic acidosis

INTRODUCTION

The acute metabolic complications of diabetes consist of DKA, HNC, LA, and hypoglycemia. DKA and HNC are related to insulin deficiency. Hypoglycemia results from the treatment of diabetes, either with oral agents or Although hypoglycemia may occur in conjunction with oral hypoglycemic therapy, it is more common in patients treated with insulin. LA is usually associated with other factors that may be related to diabetes, such as cardiovascular disease

myocardial infarction) associated with hypoxia and excess lactic acid production.^{1,2} The incidence rate for DKA varies with definition, age, and sex. The rate from population-based studies ranges from 4.6 to 8 per 1,000 diabetic persons per year. It is more common in young diabetic people and may be more common in women than men. DKA may be the initial manifestation of diabetes in 20%-30% of cases. Incidence rates for HNC, LA, and hypoglycemia are not available from population-based studies. Hypoglycemic events varied in the Diabetes Control and Complications Trial (DCCT) between the treatment groups. These events were associated with the degree of normalization of glycemia.^{3,4}

DKA, HNC, and LA require hospitalization for treatment and thereby result in the use of significant health care resources with increased health care costs. Prevention is an important component in reducing health care cost for these disorders. Hypoglycemia can usually be treated in an ambulatory care setting without using significant health care resources. Severe hypoglycemia with loss of consciousness may necessitate hospitalization.⁵ Significant morbidity and mortality is associated with DKA, HNC, and LA. Prompt recognition and management of these disorders and their associated morbidity results in improvement. Mortality rates are ~9% to14% for DKA and 10% to 50% for HNC. The mortality rate for LA is >50% with serum concentrations of lactic acid >5 mmol/l when associated with circulatory failure or septic shock. Hypoglycemia is usually associated with symptoms that are reversible with prompt treatment. Severe and profound hypoglycemia may be associated with long-term neurologic impairment.⁶ Therefore, early recognition of precipitating factors and appropriate instruction, awareness, and self-care will decrease the occurrence of these complications.⁷

The present study was conducted with the aim to evaluate the clinicopathological profile of acute complications of diabetes mellitus type II.

METHODS

This observational, cross-sectional, analytical study was conducted in the department of general medicine, D.Y Patil hospital, Nerul, Navi Mumbai after obtaining approval of institutional ethics committee. A total of 100 patients aged 18 years or more, presenting with acute complications of diabetes mellitus type II (diabetic ketoacidosis, hyperosmolar non-ketotic coma, lactic acidosis or hypoglycemia), admitted in the emergency department or ICU and consenting to participate, were included in the study. Patients not consenting to participate or pregnant females were excluded.

A written informed consent was taken from all the participants. Detailed relevant medical history was recorded. Physical examination was done. Routine haematological and biochemical investigations were carried out. Any mortality was recorded. The diagnostic criteria used for diabetes mellitus were glycosylated hemo-globin (HbA1C) ≥6.5%, or fasting plasma glucose ≥126 mg/dl (7.0 mmol/l).⁸ Fasting is defined as no caloric intake for at least 8 hours, or 2-hour plasma glucose ≥200 mg/dL (11.1 mmol/l) during an OGTT (oral glucose tolerance test), or in a patient with classic symptoms of hyperglycemia or hyperglycemic crisis, a random plasma glucose ≥200 mg/dL (11.1 mmol/l). The diagnostic criteria used for diabetes ketoacidosis are listed in (Table 1).

Criteria	DKA mild	DKA moderate	DKA severe	HNC
Plasma glucose	>250 mg/dl	>250 mg/dl	>250 mg/dl	>600
Arterial pH	7.25-7.30	7.00-7.25	< 7.00	>7.3
Bicarbonate	15-18	10 to <15	<10	>15
Urine ketone	Positive	Positive	Positive	Small
Serum ketone	Positive	Positive	Positive	Small
Effective serum	Variable	Variable	Variable	>320 mOsm/kg
Anion gap	>10	>12	>12	<12
Mental status	Alert	Alert/drowsy	Stupor/coma	Stupor/coma
Typical deficits				
Total water (l)	6			9
Water (ml/kg)	100			100-200
Na ⁺ (mEq/kg)	7-10			5-13
Cl ⁻ (mEq/kg)	3-5			5-15
K+(mEq/kg)	3-5			4-6
PO ₄ (mmol/kg)	5-7			3-7
Mg ⁺⁺ (mEq/kg)	1-2			1-2
Ca ⁺⁺ (mEq/kg)	1-2			1-2

Table 1: Diagnostic criteria for diabetic ketoacidosis.9

The diagnostic criteria used, for hypoglycemia were¹⁰, alert value for hypoglycemia ≤70 mg/dl (≤3.9 mmol/l) plasma concentration, severe hypoglycaemia, requiring assistance of another person to actively administer carbohydrates, glucagon, or take other corrective actions

or plasma glucose concentrations may not be available during an event of neurological recovery following plasma glucose levels returning to normal considered sufficient evidence that event was induced by low plasma glucose concentration, documented symptomatic hypoglycemia with typical hypoglycemia symptoms accompanied by measured plasma glucose \leq 70 mg/dl (\leq 3.9 mmol/l), asymptomatic hypoglycemia not accompanied by typical hypoglycemia symptoms but with measured plasma glucose \leq 70 mg/dl (\leq 3.9 mmol/l), probable symptomatic hypoglycemia with typical hypoglycemia symptoms not accompanied by plasma glucose determination but likely caused by plasma glucose \leq 70 mg/dl (\leq 3.9 mmol/l), pseudo-hypoglycemia with reports of typical hypoglycemia symptoms with measured plasma glucose \geq 70 mg/d (\geq 3.9 mmol/l) but approaching that threshold.

Statistical analysis

The descriptive and analytical statistics were done. All the data was analyzed using statistical software (IBM SPSS

V20.1, IBM corporation, Armonk, NY, USA). Results was expressed as mean±standard deviation and proportions. Comparisons between categorical variables was performed with chi-square test (Fisher's exact test when any cell value was less than 5). For quantitative data, student's t-test was used. The statistical significance was determined at p<0.05.

RESULTS

The mean age of the study population was 55.26±13.13 years with a range of 24 to 84 years. There were equal proportions of male and female population. 37% of the diabetic patients suffered from DKA and 63% of the patients suffered from hypoglycemia. There were no cases of lactic acidosis or HNC.

Table 2: Distribution of the study group as per the symptoms and the type of complication.

Symptom		DKA (%)	Hypoglycemia	P value	Statistical significance
Fever	Present	12 (32.4)	53 (84.1)	< 0.001	Significant
rever	Absent	25 (67.6)	10 (15.9)		Significant
Sweating	Present	12 (32.4)	44 (69.8)	< 0.001	Significant
	Absent	25 (67.6)	19 (30.2)		Significant
Dolmitotion	Present	23 (62.2)	1 (1.6)	< 0.001	Significant
Palpitation	Absent	14 (37.8)	62 (98.4)		Significant
Headache	Present	4 (10.8)	8 (12.7)	0.524	Not significant
Headache	Absent	33 (89.2)	55 (87.2)		Not significant
Nausea	Present	2 (5.4)	1 (1.6)	0.308	Not significant
	Absent	35 (94.6)	62 (98.4)		Not significant
Vomiting	Present	31 (83.8)	1 (1.6)	< 0.001	- Significant
Volinting	Absent	6 (16.2)	62 (98.4)		Significant
Abdominal pain	Present	6 (16.2)	1 (1.6)	0.010	- Significant
Abuommai pam	Absent	31 (83.8)	62 (98.4)		Significant
Tachycardia	Present	33 (89.2)	5 (7.9)	< 0.001	- Significant
1 active at the	Absent	4 (10.8)	58 (92.1)		Significant
Breathlessness	Present	7 (18.9)	5 (7.9)	0.096	Not significant
	Absent	30 (81.1)	58 (92.1)		Not significant
Stupor	Present	2 (5.4)	0 (0)	0.135	Not significant
	Absent	35 (94.6)	63 (100)		Not significant

Distribution of the symptoms according to the type of complication is shown in (Table 2). Fever and sweating had the overall highest incidence (and were more in patients with hypoglycemia) while stupor, nausea and abdominal pain had the lowest incidence (and were more in patients with DKA). The incidences of nausea, headache and stupor were not significantly different in the two groups. There were no cases of mental confusion, blurred vision, tremors, polyuria, polydipsia, ketotic smell, syncope and coma in the study group.

On examination, only one patient of DKA was drowsy. Per abdomen examination of all the patients was soft, no

abnormality was detected on the examination of respiratory system. Mean temperature, mean pulse and mean respiratory rate were higher in the patients having DKA while mean blood pressure (systolic and diastolic) was higher in patients having hypoglycemia (Table 3).

Amongst the haematological and biochemical parameters showing significant difference between the two complications, all the parameters, viz., mean total leucocyte count, mean fasting and post lunch blood sugar and mean HbA1c were higher in the patients having DKA compared to hypoglycemia (Table 4). There was no mortality in the study group.

Table 3: Distribution of the study population as per the physical examination and type of complication.

Parameter	DKA		Hypoglycemia		P	Statistical
raranietei	Mean	SD	Mean	SD	value	significance
Temperature (in degrees)	97.40	1.48	96.88	1.40	0.085	Not significant
Pulse (per minute)	100.45	10.21	82.87	8.20	< 0.001	Significant
Respiratory rate (per minute)	25.62	5.94	20.61	3.77	< 0.001	Significant
Systolic BP (in mmHg)	110.91	13.17	121.01	12.46	0.002	Significant
Diastolic BP (in mmHg)	74.27	5.01	77.74	5.52	< 0.001	Significant

Table 4: Distribution of the study population according to investigations and type of complication.

Parameter	DKA		Hypoglycemia		P	Statistical
raranieter	Mean	SD	Mean	SD	value	significance
Hemoglobin (in gm/dl)	11.95	2.03	11.97	1.74	0.957	Not significant
Total leucocyte count (in thousands/μl)	9.90	5.95	7.31	2.07	0.002	Significant
Platelets (in lakhs/µl)	242.02	84.83	251.52	73.83	0.558	Not significant
Creatinine (in mg/dl)	1.04	0.73	0.88	0.53	0.209	Not significant
Fasting blood sugar (in mg/dl)	176.66	74.47	145.09	49.31	0.012	Significant
Post lunch blood sugar (in mg/dl)	214.95	75.25	156.74	53.76	< 0.001	Significant
HbA1c (in percent)	8.92	2.40	7.32	1.56	< 0.001	Significant

DISCUSSION

India is the prototypical underdeveloped nation that has undergone a dramatic socioeconomic and demo-graphic transition in the past couple of decades. The far-reaching effects of industrialization and urbanization have combined with an increasingly ageing population to create a fertile milieu for the development of chronic NCDs such as diabetes mellitus.

The acute metabolic complications of diabetes consist of DKA, HNC, LA and hypoglycemia. DKA and HNC are related to insulin deficiency. In the present study, the clinicopathological profiles of acute complications of diabetes mellitus type II have been compared.

Mean age of patients in the present study was 55.25 years. Diabetic ketoacidosis occurs more in type II diabetic patients. Many studies support this finding. In the study by Adhikari et al the mean age was 44.78 years. 11 Studies conducted by Faich et al and Kreisberg reported that the mean age of patients admitted for DKA was between 40-50 years. 12,13 Beigelman study reported 47 years as the mean age of presentation for DKA. 14

The clinical features of the study population were as follows. A total of 12 (32.4%) DKA patients and 53 (84.1%) hypoglycemia patient had fever. Fever in DKA is primarily due to the precipitating factor or due to elevated counter regulatory hormones. Fever in the first 24 hours of onset of DKA is an independent risk factor for mortality in DKA. In a study done by Mahesh et al 31.81% of the patients had fever, out of which 22.9%

expired with a p<0.002 which is statistically very significant.¹⁵

Sweating was present in twelve (32.4%) DKA patients and forty-four (69.8%) hypoglycemia patients four (10.8%) DKA patients and eight (12.7%) hypoglycemia patient had headache. Nausea was present in two (5.4%) DKA patients and one (1.6%) hypoglycemia patient had nausea. Tachycardia was present in thirty-three (89.2%) DKA patients and five (7.9%) hypoglycemia patients had tachycardia. Seven (18.9%) DKA patients and five (7.9%) hypoglycemia patient had breathlessness. Only two (5.4%) DKA patients and none of the hypoglycemia patient had stupor. Only one (2.7%) DKA was drowsy. A total of thirty-one (83.8%) DKA patients and one (1.6%) hypoglycemia patient had vomiting. None of the reported patients had mental confusion, blurred vision, tremor, polyuria and polydipsia. A similar incidence of symptoms has been reported in previous studies by Adhikari et al, Munro et al and Umpierrez et al. 11,16,17

In a study done by Mahesh et al, the most common presenting symptom was found to be vomiting, seen in almost 50% of individuals, followed by generalized weakness, abdominal pain, symptoms of hyperglycaemia, fever, DMS and breathlessness. The most common presenting complaints were polyuria and polydipsia in 42 (80.7%), loss of weight in 48 (92.3%), fever in 31 (59.6%), and vomiting and abdominal pain in 28 (53.8%). In the present study, abdominal pain 62%, fast breathing 58%, polyuria 58% vomiting 55%, fever 45% and altered sensorium 44.8% were the predominant symptoms at admission.

A study done by Kanwal et al reported polyuria in 54.3%, vomiting 52.7%, abdominal pain 47.3%, fever in 40% and altered sensorium in 50% of the patients. In a study done by Seth et al, nausea and vomiting were present in maximum number of patients (63.33%). Pain abdomen was present in 43.33% of patients, while altered sensorium and polyuria/polydipsia were present in 30% and 26.66% of cases respectively. Twenty (33.33%) patients were dehydrated. Weakness was present in ten (16.66%) of patients. Kussmaul breathing was present in ten (16.66%) patients. Only eight (13.33%) patients had hypotension.

The findings of clinical presentation in the present study is contrary to the finding of the study in Kenya by Mbugua et al which showed more than 90% had altered level of consciousness, with almost a quarter in coma, one-third had systolic hypotension, and almost three-quarters had moderate to severe dehydration.²⁰

In the present study we did not found any case of lactic acidosis. In a study by Ramesh et al lactic acidosis was one the rare complications of diabetes mellitus.²¹ Richy et al found out that lactic acidosis was one of the rare complications of diabetes mellitus and mostly associated with the use of metformin and more commonly present in patients with renal impairment.²²

The overall mortality in the present stud, was zero. This finding did not coincide with the findings of other studies. Adhikari et al found mortality of 16.3%. 11 Faich et al and Beigelman found mortality rate of 9%.12,14 Westphal found mortality of 5.1% and the study by Matoo et al showed mortality of 23.7%. 23,24 Estimated mortality rate for DKA is between 4-10% showed by Chaisson et al.²⁵ This shows that DKA in patients with type-2 DM is a more severe disease with worse outcomes compared with type-1 DM. A comparative study in patients presenting with DKA also showed that type 2 DM patients who present in DKA have significantly severe presentation and worse outcome than those who have type 1 DM.26 Indian studies still report mortality figures in the range of 20 to 30%, and hence, may constitute preventable mortality. A study done by Basavanthappa et al reported 6 deaths (11% mortality rate).²⁷ Death occurred within 12 hours of hospital admission in 4 cases. The cause of death was cerebral edema in 4 of the cases and renal failure in 1 case and sepsis/peritonitis in 1 case.

This study was limited to the OPD attendance and ICU admission of the diabetic patients suffering from acute complications. Therefore, the results may not be generalised.

CONCLUSION

It can be effectively concluded from the present study that DKA and hypoglycaemia have a broad spectrum of clinicopathological features. But the incidences vary

widely. This may help in early recognition of the impending complication and thereby enabling prompt management of the same, reducing the associated morbidity and mortality. An active measure should be taken stressfully to rule out DKA in any diabetic and comatose patient to prevent complications and mortality, as the mortality mainly depends on the general condition of the patient, as well as the coexistent medical illness and time of onset of therapy. Therefore, education of a diabetic patient about warning symptoms of ketosis such as weakness, abdominal pain, vomiting and drowsiness are mandatory for early diagnosis and treatment. More studies on larger scale are required to detect complications of diabetes mellitus type II at an early stage, prevent complications and have a better outcome.

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Ethical approval: The study was approved by the

Institutional Ethics Committee

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