ORIGINAL ARTICLE

A STUDY SELECTIVE INDICATOR LEVEL AS A PROGNOSTIC INDICATOR IN DIABETIC KETOACIDOSIS

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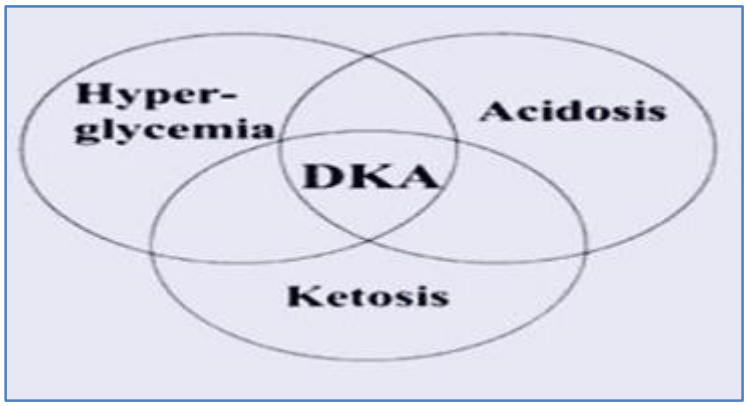
HOW TO CITE THIS ARTICLE:
M. Narayanaswamy, Sonali Appaiah, Nagappa H. Handargal. "A Study Selective Indicator Level as a Prognostic Indicator in Diabetic Ketoacidosis". Journal of Evidence based Medicine and Healthcare; Volume 2, Issue 6, February 09, 2015; Page: 629-637.

ABSTRACT: BACKGROUND: The correlation of serum phosphorus levels in DKA with prognosis of patient remains controversial; we prospectively evaluated the correlation in 50 consecutive patients with DKA. **METHODS:** This study was done on patients of DKA admitted to Victoria & Bowring & Lady Curzon hospitals attached to Bangalore Medical College, Bangalore. The total duration of the study was 2 years. A total of 50 patients of DKA were taken into the study. The diagnosis of DKA was based on ADA criteria. Venous blood samples were obtained from each patient and serum phosphorous levels were estimated at admission, day 2 and on day of improvement and discharge or at worsening /death of the patient. The correlation of serum phosphorus levels in DKA with prognosis of patient was studied using the One-Way Analysis of Variance test and Fisher LSD test. **RESULTS:** Type 1 DM constituted 30% while type 2DM made up 70% of the study group. In type 1 DM 53% were in the age group 18-28, while 47% were 29-38 in age group range. In type 2DM maximum patients were in age group 39-48 yrs accounting about 40%; 28% in range 49-58yrs and 29% in range >59yrs. In type 1 DM the most common precipitating cause of DKA was infection and noncompliance each accounting for 41%, with new onset DM seen in 18% of patients. In type 2 DM infection was the most common cause accounting for 42%, closely followed by noncompliance to treatment which came up to 41% of the patients of the precipitating infections UTI was the most common cause around 33%, while pneumonia accounted for 19%. The mean duration of hospitalization of DKA patients was 6.2days. On day 0, 72% of population had normal or high values of Phosphorous and hypophosphatemia was seen in 28% had hypophosphatemia at admission. On Day 2 of admission, incidence of hypophosphatemia increased to 69%. At discharge phosphorous values returned to normal with 95% of patients having normal levels. Significant correlation was observed in phosphorous levels in DKA patients between phosphorous levels on day 2 and phosphorous levels at discharge in type 1 and 2 DM. In study group 10% mortality was seen. Type 2 DM patients accounted for 80%, while Type 1DM patients accounted for 20% of the mortality. Among patients with DKA at death, hypophosphatemia was seen 60%. No significant correlation was observed between phosphorous level and duration of stay of patient in hospital. Significant correlation was observed between phosphorous level at Day discharge/Death and outcome of the patient i.e., recovery or death of the patient with point estimation values of 0.086 (CI= 0.008 – 0.93). **CONCLUSION:** The correlation of the serum phosphorous and prognosis of patient during hospital stay was significant as shown in our study and other studies as well. Hypophosphatemia is commonly encountered at diagnosis and during treatment of a patient with DKA. Serum phosphate levels do not accurately reflect intracellular phosphorus stores; hence symptoms may be present even with mild or moderate hypophosphatemia. The assessment of

the serum phosphorous of these patients during treatment could be a useful predictor of the clinical outcome in DKA. With the high prevalence of hypophosphatemia in DKA, and risk for poor prognosis in such patients, frequent laboratory monitoring is recommended, especially in high-risk groups.
KEYWORDS: DKA, Prevalence, Type-I diabetics, UTI, Hypophosphatemia.

INTRODUCTION: Globally more than 371 million people are found to be living with diabetes. An estimated 90 per cent of the cases are of Type 2 diabetes mellitus.[1] India with 63 million diabetic patients is just next to China (92.3 million) in the race to become the diabetes capital of the world, according to the International Diabetes Federation (IDF) Atlas released on November 14, 2012.DKA is a common and serious acute metabolic complication that affects patients with diabetes[2] and is an expensive complication of diabetes[3,4] DKA remains the prominent cause of mortality in diabetic patients. The mortality from DKA remains low at <5%, but it is the most common cause of death in young people with diabetes and is high in those >65 years of age.[5,6] The present study aims to study of phosphorous levels as a prognostic indicator in diabetic ketoacidosis and correlate phosphorous levels with morbidity and mortality in DKA.

Diabetic Ketoacidosis: DKA is a triad of hyperglycaemia, ketosis and acidaemia, and the diagnostic criteria, as defined by the American Diabetes Association, are blood glucose >13.8 mmol/l (250 mg/dl), pH <7.30, serum bicarbonate <18 mmol/l, anion gap >10, and ketonaemia.[7]Dehydration and hyperosmolarity may be present as well. There is no "typical" presentation and individual patients may present with a range of clinical findings not clearly meeting the above criteria.



The triad of DKA (hyperglycemia, acidemia, and ketonemia). From Kitabchi and Wall.

	DKA	HHS
Total water (liters)	6	9
Water (ml/kg body wt)	100	100-200
Na+ (mEq/Kg)	7-10	5-13
Cl-(mEq/Kg)	3-5	5-15
K+ (mEq/Kg)	3-5	4-6

PO4- (mmol/kg)	5-7	3-7
Mg2+ (mEq/Kg)	1-2	1-2
Ca2+ (mEq/Kg)	1-2	1-2

Table 1: Typical total body deficits of water and electrolytes in DKA and HHS

	DKA			HHS
	Mild	**Moderate**	**Severe**	
Plasma glucose (mg/dl)	>250	>250	>250	>600
Arterial pH	7.25-7.30	7.00-<7.24	<700	<7.30
Serum bicarbonate (mEq/1)	15-18	10-<15	<10	<15
Urine ketones*	Positive	Positive	Positive	Small
Serum ketones*	Positive	Positive	Positive	Small
Effective serum osmolality (mOsm/kg)	Variable	Variable	Variable	>320
Anion gap	>10	>12	>12	<12
Alteration in sensorial or mental obtundation	Alert	Alert/drowsy	Stupor/ Coma	Stupor/ Coma

Table2: Diagnostic Criteria of DKA .Adapted from Kitabchi AE et al. Diabetes Care 2006; 29: 2739–2748

DIFFERENTIAL DIAGNOSIS: The diagnostic criteria for DKA include a glucose greater than 250 mg/dl, a pH lower than 7.30-7.35, a low HCO3, and positive ketonuria or ketonemia greater than 1: 2 dilution with the nitroprusside reaction.

MATERIALS AND METHODS: Study was done on patients of Diabetic ketoacidosis admitted to Victoria & Bowring & Lady Curzon hospitals attached to Bangalore Medical College & Research Institute, Bangalore. The total duration of the study was 2 years. A total of 50 patients of Diabetic ketoacidosis were taken into the study. Phosphorous levels will be estimated on day one, after 48 hours of admission or worsening of patient's condition and at discharge. It will be correlated to prognosis of patient in diabetic ketoacidosis

INCLUSION CRITERIA: 1. Patients who have given written informed consent with diabetic ketoacidosis. Type 1 & 2 diabetes mellitus and who are >18 years age.

EXCLUSION CRITERIA: Patients who have not given written informed consent. Malnutrition, malabsorption syndromes, on diuretics, steroids, phosphate binding antacids. With renal transplantation with hyperparathyroidism. Pancreatitis, burns, volume expansion. Alcoholics Respiratory alkalosis–hyperventilation, panic attacks, salicylate poisoning Rapid cellular uptake–refeeding syndrome, leukemic blast cell crises, hungry bone syndrome.

RESULT AND ANALYSIS: Study was done on patients of Hepatic encephalopathy admitted to Victoria & Bowring & Lady Curzon hospitals attached to Bangalore Medical College & Research Institute, Bangalore. A total of 50 patients of DKA were taken into the study. Type 1 DM constituted 30% while type 2DM made up 70% of the study group.

Age (yrs)	Type 1DM	%
18-28	8	53
29-38	7	47
39-48	0	0
49-58	0	0
>59	0	0

Table 3: Age distribution of patients studied with % in type 1 DM

Age (yrs)	Type 2DM	%
18-28	0	0
29-38	1	3
39-48	14	40
49-58	10	28
>59	10	29

Table 4: Age distribution of patients studied with % in type 2 DM

In type 1 DM 53% were in the age group 18-28, while 47% were 29-38 in age group range. In type 2DM maximum patients were in age group 39-48yrs accounting about 40%; 28% in range 49-58 yrs and 29% in range >59yrs.In our study male patients constituted 51% and female patients constituted 49% of the population.

Precipitating Cause of DKA	No. of patients in	
	Type 1 DM	Type 2 DM
New Onset	3	0
Non-compliance/Inadequate Treatment	7	15
Infection	7	15
Cardiovascular comorbidities	0	6

Table 5: Precipitating Cause of DKA in type 1 and type 2 DM

In type 1 DM the most common precipitating cause of DKA was infection and noncompliance each accounting for 41%, with new onset DM seen in 18% of patients. In type 2 DM infection was the most common cause accounting for 42%, closely followed by noncompliance to treatment which came up to 41% of the patients.

Infections	No. of patients	%
UTI	7	33
Pneumonia	4	19
Gastroenteritis	2	14
Diabetic foot with sepsis	3	10
typhoid	2	10
febrile thrombocytopenia	3	14

Table 6: Precipitating Infection in DKA

Of the precipitating infections UTI was the most common cause around 33%, while pneumonia accounted for 19%.

Result	Minimum	Maximum	Mean	Standard Deviation ±
Pulse/min	80	132	104.48	13.337
RR/min	18	36	23.92	3.896
RBS-D0	358	700	585.92	104.167
RBS-D2	168	530	327.68	75.909
RBS-At Dis/Dth	120	320	211.10	37.230
ABG- ph	6.8	7.3	7.077	.1495
pCO2(mmHg)	9.0	30.0	16.688	5.1604
HCO3(mmol/dl)	2	20	11.42	4.789
Na-D0	128	157	138.24	7.006
Na-D2	128	162	135.34	5.397
Na-	130	146	137.08	2.927
Discharge/Death				
K-D0	2.1	5.6	3.808	.6395
K-D2	2.6	5.7	3.720	.5079
K-	3.2	5.0	3.866	.3311
Discharge/Death				
Cl-D0	98	120	107.64	4.421
Cl-D2	100	118	106.72	3.456
Cl-	98	114	106.12	3.485
Discharge/Death				
P-D0	1.2	6.5	3.112	1.1471
P-D2	1.0	3.6	2.142	.6048
P-	1	4	3.01	.539

Table 7: Minimum and maximum values with mean and standard deviation of Clinical and laboratory values of DKA patients

Discharge/Death	Minimum	Maximum	Mean	SD
Ca-D0	5.6	9.8	8.382	.5742
Ca-D2	7	9	8.16	.465
Ca-	7.0	9.2	8.272	.3676
Discharge/Death				
Blood Urea	8	74	34.50	11.503
creatinine	.2	1.3	.951	.2459
Hb	8.1	18.0	13.416	2.1730
WBC	5330	29120	12886.78	5038.234

Table 8: Mean and Standard Deviation of Duration of DM and Duration of Current Hospitalization of DKA patient

In our study the mean duration of DM in DKA patients at admission was 8.8 years. The mean duration of hospitalization of DKA patients was 6.2days

Type of DM	Mean Duration DM
type1	9.14Yrs
type2	8.26 Yrs

Table 9: Mean Duration of DM in type 1 and 2 DM

Clinical Feautes (Vitals)	95% C. I. for EXP (B)		
	Exp (B)	Lower	Upper
Pulse	.975	.920	1.034
Systolic BP	1.021	.984	1.060
Diastolic BP	.961	.893	1.034
RR	1.009	.838	1.216
Temperature	.856	.212	3.457

Table 10: Clinical Features in DKA patients in Type 1 and Type 2 DM

No significant difference was noticed in clinical features (vitals) at admission between type1 and type2 Diabetes patients.

Phosphorous Level-Do	Patients with type 1	Patients with type 2	%
Hyperphosphatemia	3	3	12
Mild (2.5-2mg/dl)	1	7	16
Moderate(2-1mg/dl)	2	4	12
Severe(<1mg/dl)	0	0	0
Normal(2.5-4.5mg/dl)	9	21	60

Table 11: Phosphorous Levels at admission/Day-0 in type 1 and 2 DM

60% of DKA patients had normal levels of phosphorous at admission and 12% of the patients had hyperphosphatemia on day 0. 12% had moderate and 16% had mild hypophosphatemia. Hence 72% of population had normal or high values of Phosphorous at admission and hypophosphatemia was seen in 28% had hypophosphatemia at admission

Phosphorous Level-D2	Patients with type 1	Patients with type 2	%
Mild (2.5-2mg/dl)	5	8	28
Moderate (2-1mg/dl)	6	12	39
Normal (2.5-4.5mg/dl)	2	12	31
Severe (<1mg/dl)	1	0	2

Table 12: Phosphorous Levels at Day-2 in DKA

On Day 2 of admission, incidence of hypophosphatemia increased to 69% .Of which 28% had mild, 39% had moderate and 2% had severe hypophosphatemia, while 31% had normal phosphorous levels.

Phosphorous level at Discharge	Patients with type 1	Patients with type 2	%
Mild (2.5-2mg/dl)	1	0	3
Moderate (2-1mg/dl)	1	0	2
Severe (<1mg/dl)	0	0	0
Normal (2.5-4.5mg/dl)	11	29	95

Table 13: Phosphorous Levels at Discharge in type 1 and 2 DM

DISCUSSION: This study was done on patients with DKA admitted to Victoria & Bowring & Lady Curzon hospitals attached to Bangalore Medical College & Research Institute, Bangalore. The total duration of the study was 2 years. A total of 50 patients of DKA were taken into the study. Routine investigations like RBS, ABG urine ketone bodies and urine ketone bodies were used to diagnose DKA. RBS, serum electrolytes like sodium, potassium, chloride, phosphorous and chloride were recorded at admission. A repeat estimation of the serum electrolytes including Phosphorous were done on day of admission day 2 and at improvement and discharge or at worsening /death of the patient. The correlation of level of serum phosphorous and the prognosis of patient with was studied using the One-Way Analysis of Variance test and Fisher LSD test. Several studies have shown a correlation of serum phosphorous with prognosis, both in terms of morbidity and mortality of patient. Riley et al[8] found certain populations are likely to include a greater proportion of hypophosphatemic patients – for example, alcoholics (0.9%), septic patients (2.4%), malnourished patients (10.4%), and patients with diabetic ketoacidosis (14.6%). Severe hypophosphatemia was associated with fourfold increase in mortality. David W Miller et al[9] showed that hypophosphatemia may be seen in anywhere from 20% to 80% of patients who present to emergency department with alcoholic emergencies, diabetic ketoacidosis, and sepsis. In our study, the correlation of serum phosphorous with duration of stay was not significant

whereas serum phosphorous correlated significantly with prognosis of patient with DKA.72% of population had normal or high values of Phosphorous at admission and incidence of hypophosphatemia was 28% at admission, this increased to 69% 0n day2, with recovery and at discharge phosphorous values returned to normal range in 95% of patients. Among patients with DKA at death hypophosphatemia was seen in 60% of the study group. Significant correlation was observed between phosphorous level on Day of discharge/Death and outcome of the patient i.e., recovery or death of the patient with point estimation values of 0.086 (CI= 0.008 – 0.93). Thus improvement and normalization of serum phosphorous level at discharge was observed in patients who recovered from DKA. At worsening and death of patient with DKA significant correlation was found between hypophosphatemia and mortality. Hence the serum phosphorous levels correlated well with prognosis of the patient with DKA during their hospital stay, suggesting that the serum phosphorous level was an indicator of the clinical outcome of the patients during their hospital stay.

CONCLUSION: The correlation of the serum phosphorous and prognosis of patient during hospital stay was significant as shown in our study and other studies as well. Hypophosphatemia is commonly encountered at diagnosis and during treatment of a patient with DKA. Serum phosphate levels do not accurately reflect intracellular phosphorus stores; hence symptoms may be present even with mild or moderate hypophosphatemia. The assessment of the serum phosphorous of these patients during treatment could be a useful predictor of the clinical outcome in DKA. With the high prevalence of hypophosphatemia in DKA, and risk for poor prognosis in such patients, frequent laboratory monitoring is recommended, especially in high-risk groups.

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Date of Submission: 29/12/2014.
Date of Peer Review: 30/12/2014.
Date of Acceptance: 19/01/2015.
Date of Publishing: 03/02/2015.