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Prognostic value of serum phosphorus levels in patients with diabetic ketoacidosis

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Abstract

Introduction: Diabetic ketoacidosis is characterised by hyperglycemia, ketonemia, ketonuria, high anion gap metabolic acidosis along with number of metabolic derangements. This study was undertaken to find out mainly the prognostic value of serum phosphorus levels in diabetic ketoacidosis patients to determine the severity and outcome.

Methodology: It was hospital based case control study in which 100 patients of DKA admitted in various medical wards of RNT Medical College, Udaipur were enrolled as cases and 100 healthy age and sex matched individuals were enrolled as controls. The study was carried out between Aug 2019 to Dec 2020.

Results: Out of 100 cases and 100 controls, 56% were males and 44% were female and 54% were male and 46% were female in case and control respectivaly. DKA had multiple precipitation factors among them 80 patients had poor patients compliance and 43 had infections. Many patients had more than one precipitating factors. Phosphorus levels were performed at time of admission, on day 3 and at discharge. Outcome measures including drowsiness at admission, duration of diabetic ketosis and duration of hospital stay were significantly higher in hypophosphatemics than euphosphatemics. There was statistically significant negative correlation between HbA1c levels and serum phosphorus levels.

Conclusion: From the present study it can be concluded that higher blood sugar value at the time of admission is associated with low phosphorus and low serum phosphorus levels were associated with poor mental status at admission, prolonged duration of diabetic ketosis and prolonged hospital stay.

Keywords: Diabetic ketoacidosis, Phosphorus, Mental status.

Introduction

Diabetic ketoacidosis is an acute complication of diabetes. Diabetic ketoacidosis is characterised by hyperglycemia, ketonemia, ketonuria, high anion gap metabolic acidosis along with a number of metabolic derangements. Diabetic ketoacidosis is often precipitated by intercurrent illness such as infection, inadequate insulin administration by the patient. Commonest presenting complaints were nausea, vomiting, polydipsia, polyuria, abdominal pain and altered sensorium[1].

A paradoxical metabolic imbalance in serum phosphorus occurs from the early onset of diabetes and may lead to a reduction of high energy phosphates and tissue hypoxia. These changes take place in the cells and tissues in which the entry of glucose is not controlled by insulin, and particularly in poorly regulated diabetes patients in whom long-term vascular complications are more likely to occur. The highest oxygen consumption is associated with the lowest content of inorganic phosphate, and lowering oxygen consumption is associated with higher concentration of inorganic phosphate. Since a reduction of high energy phosphates and tissue hypoxia may be important factors in the development of long-term diabetic complications, the effects of inorganic phosphate on the metabolism and function of the erythrocyte and renal tubular cell, as well as local and systemic consequences of serum phosphorus in and during recovery from diabetic ketoacidosis, have recently been reviewed[2].

Phosphate depletion is common in DKA. But the initial value may be high, normal or low. The study was therefore undertaken to find out mainly the relationship between serum phosphorus levels and its clinical correlation in diabetic ketoacidosis and serum phosphorus levels as a prognostic indicator in diabetic ketoacidosis patients.

Material and Methods

Study Site: 100 cases of diabetes ketoacidosis attending intensive care unit (ICU) and various medical wards of MB Govt Hospital and RNT Medical College, Udaipur were included in study group and 100 healthy persons matched with same age and sex were as control group.

Study Design: This is hospital based case control study of 200 patients (100 cases and 100 controls) showing the relationship between serum phosphorus levels and its clinical correlation in diabetic ketoacidosis and serum phosphorus levels as a prognostic indicator in diabetic ketoacidosis patients.

Blood samples were collected under aseptic precautions from controls and cases. Relevant investigations were carried out and results interpreted, reported and tabulated for controls and cases separately for statistical evaluation.

Study Period: Each and every eligible 100 consecutive cases of diabetic ketoacidosis admitted in ICU and IPD wards of RNT Medical College Hospital, Udaipur were studied from Aug 2019 to Dec 2020.

Study Population: A minimum of 100 patients with diabetic ketoacidosis and 100 healthy controls were included in the study. Baseline data were collected within 24 hours of admission.

Inclusion Criteria

- Patients who are > 18 years of age
- Patients admitted with diabetic ketoacidosis
- Patients who give written consent.

Exclusion Criteria

- Patients under the age of 18 years
- Patients with hyperosmolar hyperglycaemic states
- Patients with hyperemesis graviderum
- Patients with starvation ketosis
- Patients with chronic kidney diseases
- Patients with renal transplantation
- Patients who are alcoholics
- Patients with hyperparathyroidism
- Patients with pancreatitis, burns, volume expansion
- Who fails to give written consent

Statistical Analysis

Summary statistics were done by mean and standard deviation. The inferential statistics were done by student t test, chi-square test and person correlation. All measurements were done using SPSS version 21.0 with

p value <0.05 were considered as statistically significant.

Results and Observations

100 cases of diabetic ketoacidosis admitted to intensive care unit (ICU) and various medical wards in M.B. Govt. Hospital, Udaipur were taken as study group and 100 healthy persons matched with age and sex were taken as control group. The results of the study parameters were enclosed in appendix.

A correlation study with 200 individuals, 100 controls and 100 cases were undertaken to study the relationship between serum phosphorus levels and its clinical correlation in diabetic ketoacidosis and serum phosphorus levels as a prognostic indicator in diabetic ketoacidosis patients.

In our study the gender distribution of controls and cases were in ratio of male: female is 54: 46 in controls whereas the ratio of male: female is 56:44 in diabetic ketoacidosis cases. DKA was most commonly seen among males.

In our study the age distribution pattern of control and diabetic ketoacidosis cases ranges from 19 years to 80 years with mean age groups of 45.12 ± 12.43 years and 49.88 ± 16.57 years respectively and maximum patients were in age group between 41 to 70 years (59%).

Table 1: Comparison of Mental Status with Serum Phosphorus Level

Mental status	Phosphorus <2.5 mg/dl	Phosphorus 2.5-4.5 mg/dl	Phosphorus >4.5 mg/dl	Statistical Significance
Drowsy	16	2	0	Significant P<0.000
Normal	49	33	0	Significant P<0.000

There was a statistically significant association between mental status and serum phosphorus level at the time of admission of DKA patients. It is proven by chi square test.

Graph 1: Comparison of Mental Status with Serum Phosphorus Level

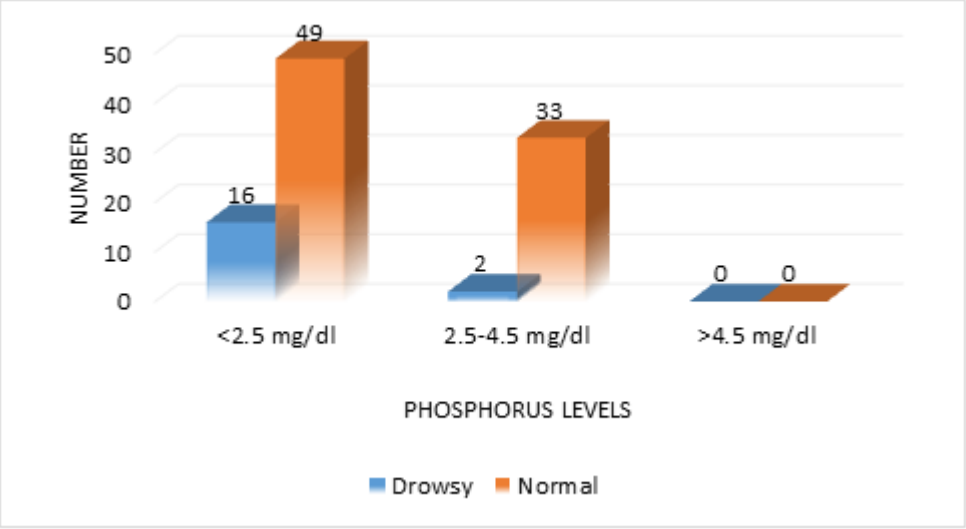


Table 2: Levels of serum phosphorus at the time of admission (D-1), after 48 hours (D-3) and at discharge in patients with Diabetic Ketoacidosis

Serum Phosphorus	Control	Cases		
		Day-1	Day-3	At discharge
Mild (2.0-2.4 mg/dl)	0	47 (47%)	8 (8%)	0
Moderate (1.0-1.9 mg/dl)	0	15 (15%)	5 (5%)	0
Severe (<1.0 mg/dl)	0	3 (3%)	0	0
Normal (2.5-4.5 mg/dl)	100(100%)	35 (35%)	87 (87%)	100 (100%)
Increased (>4.5 mg/dl)	0	0	0	0
Total	100(100%)	100 (100%)	100 (100%)	100 (100%)
Mean ± SD	3.16±0.27	2.27±0.55	2.78±0.48	3.39±2.30

Serum phosphorus levels of control and cases were shown in the Table 2. 100% of the controls showed normal serum phosphorus level in the range of 2.5-4.5 mg/dl and in diabetic ketoacidosis cases, out of 100 patients, 47 (47%) patients had mild hypophosphatemia, 15 (15%) patients had moderate hypophosphatemia and 3 (3%) patients had severe hypophosphatemia and remaining 35 (35%) of them were in the normal range at the time of admission. On day 3, 8 (8%) patients had mild hypophosphatemia and 5 (5%) patients had moderate hypophosphatemia and remaining 87 (87%) patients had normal serum phosphorous levels. At the time of discharge all patients had normal serum phosphorous levels. When chi square test was applied, results were statistically significant. (P<0.000).

Graph 2: Levels of serum phosphorus at the time of admission (D-1), after 48 hours (D-3) and at discharge in patients with Diabetic Ketoacidosis

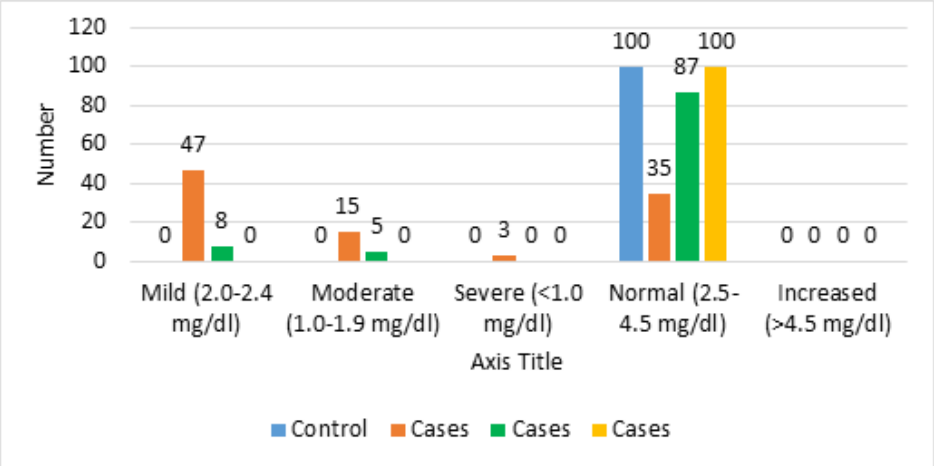


Table 3: Comparison of Admission RBS Value with Serum Phosphorus

Admission RBS (mg/dl)	Phosphorus <2.5 mg/dl	Phosphorus 2.5-4.5 mg/dl	Phosphorus >4.5 mg/dl	Statistical Significance
200 to 300	5	2	0	Significant P<0.100
301 to 400	39	21	0	Significant P<0.000
401 to 500	21	12	0	Significant P<0.001

There was a statistically significant negative association between serum phosphorus level at the time of admission and initial random blood sugar value of DKA patients. It is proven by chi square test.

Graph 3: Comparison of Admission RBS Value with Serum Phosphorus.

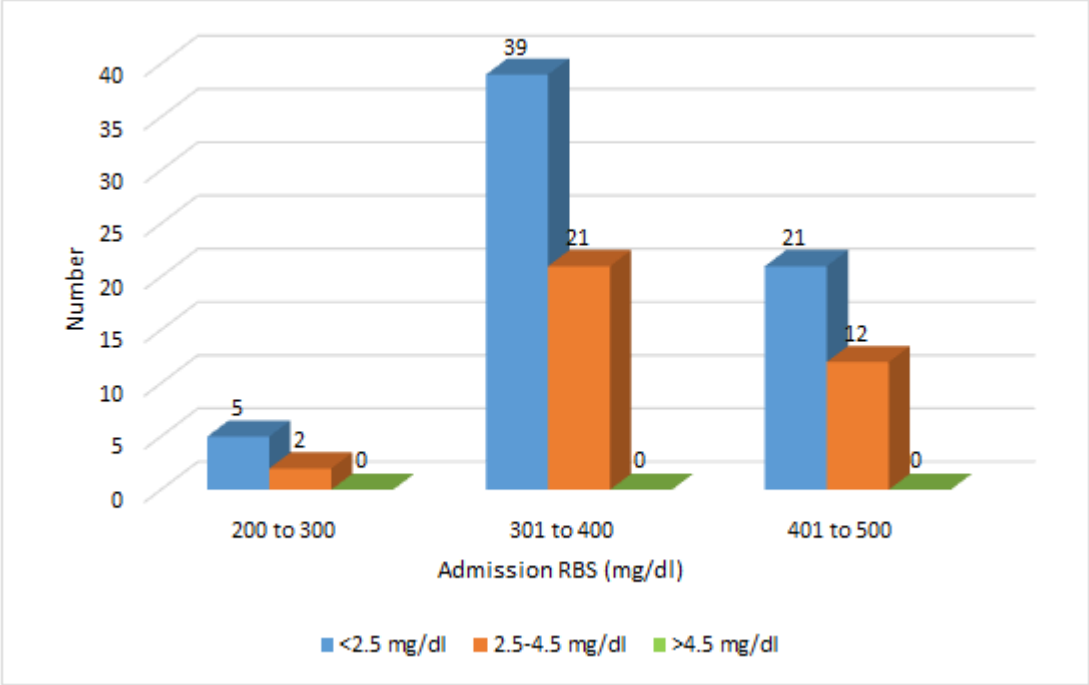


Table 4. Comparison of duration of diabetic ketosis with Serum Phosphorus Levels

Duration of diabetic ketosis (in days)	Phosphorus <2.5 mg/dl	Phosphorus 2.5-4.5 mg/dl	Phosphorus >4.5 mg/dl	Statistical Significance
1	20	35	0	Significant P<0.001
2	28	0	0	Significant P<0.000
3	12	0	0	Significant P<0.000
4	5	0	0	Significant P<0.007

There was a statistically significant negative association between duration of diabetic ketosis and serum phosphorus levels in DKA patients. It is proven by chi square test.

Graph 4: Comparison of duration of diabetic ketosis with Serum Phosphorus Levels

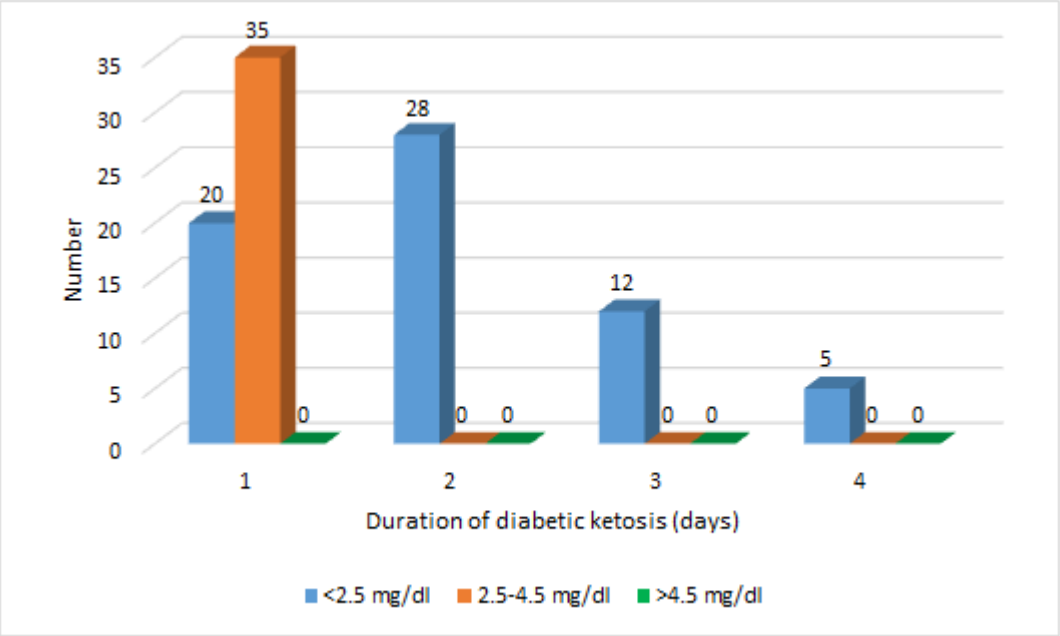
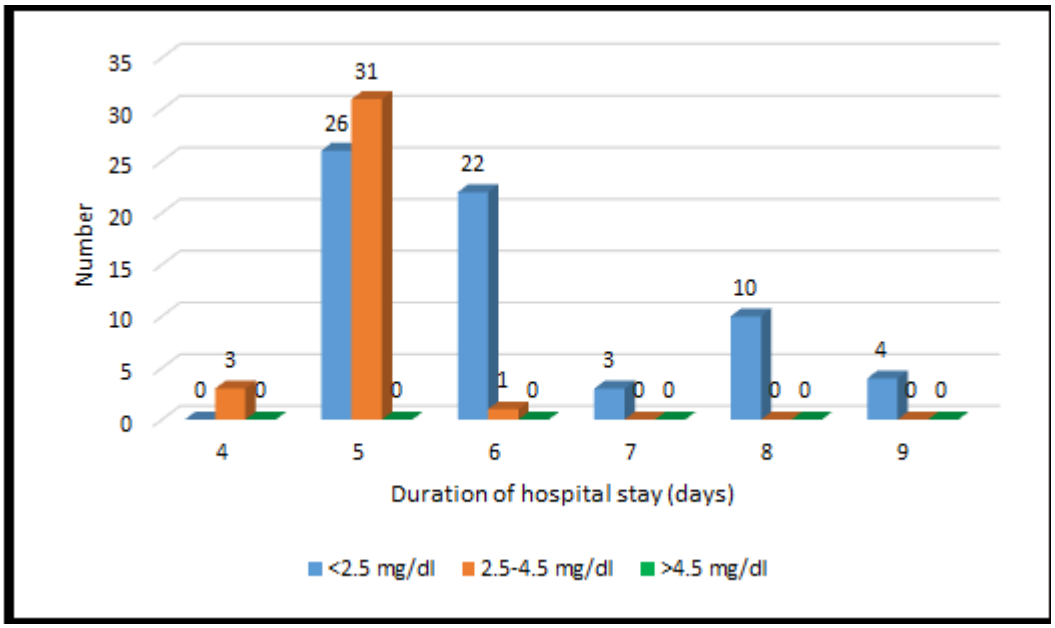


Table 5: Comparison of Duration of Hospital Stay with Serum Phosphorus Levels

Duration of Hospital stay (in days)	Phosphorus <2.5 mg/dl	Phosphorus 2.5-4.5 mg/dl	Phosphorus >4.5 mg/dl	Statistical Significance
4	0	3	0	Significant P<0.048
5	26	31	0	Significant P<0.001
6	22	1	0	Significant P<0.000
7	3	0	0	Significant P<0.048
8	10	0	0	Significant P<0.000
9	4	0	0	Significant P<0.018

There was a statistically significant negative association between duration of hospital stay and serum phosphorus levels at the time of admission in DKA patients. It is proven by chi square test.

Graph 5: Comparison of Duration of Hospital Stay with Serum Phosphorus Levels



Discussion

Diabetic ketoacidosis (DKA) is a serious acute complication of diabetes mellitus. This study has been done with regard to serum phosphorus levels and its clinical correlation in diabetic ketoacidosis patients and also serum phosphorus levels as a prognostic value in diabetic ketoacidosis patients.

In our study, we took 100 cases of diabetes ketoacidosis 56 (56%) were males and 44 (44%) were females and compared with 100 healthy controls 54 (54%) were males and 46 (46%) were females. In this study, male to female ratio is 56:44. DKA was most commonly seen among males.

In our study maximum number of patients of DKA were found in the age group of 41-70 years (59%). The mean age of patients was 49.88 ± 16.57 years and the mean age for controls group was 45.12±12.43 years. Centers for disease control and prevention data revealed more occurrence of diabetic ketoacidosis episodes among young diabetics[3]. This happened most probably because only adult patients (i.e. more than 18 years of age) were included in our study. So, patients less than 18 years of age having more prevalence of type 1 diabetes mellitus who are more prone for episodes of diabetic ketoacidosis were not taken into account.

In the study conducted by Dharma Rao et al[4] found that maximum numbers of patients in the age group of 41-50 years (45.3%). The mean age in Dharma Rao study was 43.1 years. The age group distribution results in present study were more in line with Dharma Rao study.

In our study there was a significant association between mental status and serum phosphorus level at the time of admission of DKA patients. 16 (16%) patients had drowsy at the time of admission with low phosphorus value.

This is in concordance with a study done by E. I. Ugwuja[5], Severe hypophosphatemia is manifested with clinical symptoms like dizziness, dysartria, irritability, confusion and coma along with decreased concentration of 2,3-BPG(Bisphosphoglyceric acid)[6-9]. This acute changes in the blood glucose level of 2,3-BPG, as a result increased amount of glycated hemoglobin is

formed with high oxygen affinity to meet the tissue oxygen demand[10].

In our study out of 100 DKA patients, 35% of the patients had normal levels of serum phosphorous at admission and 65% of the patients had hypophosphatemia at admission, of which 47 (47%) had mild, 15 (15%) had moderate hypophosphatemia and 3 (3%) had severe hypophosphatemia. On Day 3 of admission, incidence of hypophosphatemia decreased to 13%, of which 8% had mild and 5% had moderate hypophosphatemia, while 87% had normal serum phosphorous levels. With recovery and at discharge serum phosphorous values returned to normal range.

Y Kanter et al[11] studied levels of 2,3-DPG (Diphosphoglyceric acid), nucleotide phosphate, organic and inorganic phosphate levels during early phases of diabetic ketoacidosis. They observed that steady drop in serum inorganic phosphate was found during first 24 hours of insulin treatment and was profound at 24 hours. In our study findings were similar to these findings, having maximum number of hypophosphatemia on day one.

In our study, the admission random blood sugar values were inversely proportional to the serum phosphorus levels.

In our study the duration of diabetic ketosis was prolonged in patients with low serum phosphorus levels at admission.

In our study the duration of hospital stay was prolonged in patients with low serum phosphorus levels at admission due to more frequent occurrence of complications and poor glycemic control.

Steven Brunelli et al[12] in their article "Hypophosphatemia: clinical consequences and management" found that in-hospital mortality was more in cases of hypophosphatemia than controls.

In a retrospective study conducted by Schibe J R, Mattu A[13] on 651 critically ill patients measured mortality was higher in hypophosphatemic group. We had no mortality in our study.

In severe, uncontrolled diabetes, increased HbA1c levels is accompanied by decreased phosphate levels which may further decrease with intravenous insulin therapy.

Summary and Conclusion

100 patients of diabetes ketoacidosis who admitted in the ICU and various medical wards at M.B. Govt. Hospital and RNT Medical College, Udaipur were taken as cases for the study and 100 numbers of age and sex matched healthy persons were taken as controls.

Following observations were recorded:

- In our study, higher blood sugar values was associated with lower serum phosphorus value and low serum phosphorus was associated with poor mental status at the time of admission and with prolonged duration of diabetic ketosis and hospital stay.
- There was decrease in serum phosphorus levels in diabetic ketoacidosis cases when compared to controls which was statistically significant.
- There was a positive correlation between the glycated hemoglobin (HbA1c) levels and serum phosphorus levels in controls whereas there was a negative correlation between HbA1c levels and serum phosphorus in diabetic ketoacidosis cases which indicates that as the HbA1c level increases serum phosphorus level decreases.
- Thus in diabetic ketoacidosis patients with poor glycemic control as shown by increase HbA1c level there was decrease in serum phosphorus levels. Insulin therapy in these patients causes phosphate

to shift intracellular which may further decreases the serum phosphorus levels leading to hypophosphatemia. Therefore diabetic ketoacidosis treated with insulin should be monitored for serum phosphorus levels.

Hence we concluded that serum phosphorus the neglected aspect of diabetic ketoacidosis needs due consideration. In our study high blood sugar was associated with a low phosphorus value and low serum phosphorus was associated with poor mental status at admission, prolonged duration of diabetic ketosis and hospital stay. Treatment mainly includes adequate fluid management, insulin administration, antibiotics and correction of electrolyte abnormality. Though phosphate therapy is not routinely required during the treatment of diabetic ketoacidosis, it should not be ignored. If the serum phosphate is less than 1 mg/dl, then phosphate supplement should be considered[14]. Identification and treatment of precipitating factors for diabetic ketoacidosis are more important and patient education plays an important role in prevention of diabetic ketoacidosis.

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