Journal of Chemical Health Risks

www.jchr.org

JCHR (2024) 14(6), 1623-1629 | ISSN:2251-6727

Serum Phosphate Levels and its Clinical Significance in Diabetic Ketoacidosis

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(Received: 16 September 2024 Revised: 11 October 2024 Accepted: 04 November 2024)

KEYWORDS

Diabetic ketoacidosis, Serum phosphate, Hyperglycemia, Hypophosphatemia, Glucose metabolism, Electrolyte imbalance

ABSTRACT:

Background: Diabetic ketoacidosis (DKA) is a severe complication of diabetes mellitus characterized by hyperglycemia, ketosis, and metabolic acidosis. Electrolyte imbalances, particularly in serum phosphate levels, significantly impact clinical outcomes in DKA. Phosphate disturbances are common due to insulin deficiency, hyperglycemia, osmotic diuresis, and the catabolic state of DKA, potentially leading to hypophosphatemia with serious consequences.

Objective: To investigate the clinical significance of serum phosphate levels in DKA patients, exploring their correlation with disease severity and treatment responses.

Methods: An observational cross-sectional study was conducted from June 2022 to June 2024 at Aarupadai Veedu Medical College, Puducherry. Forty-five adult patients with DKA, as per ADA guidelines, participated after providing informed consent. Data on demographics, clinical assessments, and laboratory tests were collected and analyzed using SPSS and Excel, with statistical significance determined by a p-value <0.05.

Results: The study population includes 45 patients with mean age of 52.91 years, with a slight female predominance (53.3%). High fasting and postprandial blood sugar levels were observed, indicative of severe hyperglycemia. A significant reduction in serum phosphate levels was noted from a mean of 3.77 mg/dL pre-treatment to 2.85 mg/dL post-treatment ($p=0.001$). There was no significant correlation between fasting blood sugar and serum phosphate levels (Pearson coefficient -0.081, $p=0.450$).

Conclusion: The study highlights a prevalence of Diabetic Ketoacidosis (DKA) among middle-aged to older adults with significant phosphate level reduction post-treatment. While no significant correlation was found between fasting blood sugar and serum phosphate levels, careful monitoring of phosphate is crucial to prevent complications. Individualized management of biochemical parameters remains essential in Diabetic Ketoacidosis (DKA) treatment.

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JCHR (2024) 14(6), 1623-1629 | ISSN:2251-6727

Introduction

Diabetic ketoacidosis (DKA) is a serious complication of diabetes, characterized by hyperglycemia, ketosis, and metabolic acidosis. Electrolyte imbalances, particularly alterations in serum phosphate levels, can significantly influence the clinical outcomes of this condition.(1) Although DKA primarily affects individuals with Type 1 diabetes, it may also occur in those with Type 2 diabetes. The pathophysiology of DKA involves a deficiency of insulin and an increase in counter-regulatory hormones such as glucagon, cortisol, catecholamines, and growth hormone.(2, 3) These hormonal imbalances drive processes including lipolysis, glycogenolysis, and gluconeogenesis, leading to an accumulation of ketone bodies and significant disruptions in acid-base balance.(2, 4)

Phosphate, an essential intracellular anion, plays a critical role in various biological processes, including energy metabolism, cell membrane integrity, and acid-base regulation. In DKA, phosphate homeostasis is frequently disturbed due to insulin deficiency, hyperglycemia, osmotic diuresis, and the catabolic state of the patient. Consequently, serum phosphate levels may fluctuate considerably during the onset and progression of DKA treatment.(5)

Initially, serum phosphate levels may appear normal or elevated due to the shift of phosphate from the intracellular to the extracellular compartment.(6) However, these levels typically decline following the initiation of insulin therapy and fluid resuscitation. Several mechanisms contribute to this reduction. Insulin promotes cellular uptake of both glucose and phosphate, lowering serum phosphate concentrations. Osmotic diuresis, driven by elevated glucose levels, results in significant phosphate losses through urine. Additionally, the catabolic state associated with DKA causes muscle protein breakdown, releasing phosphate, but the net phosphate balance remains negative due to increased urinary excretion.(7)

Hypophosphatemia, defined as serum phosphate levels below 2.5 mg/dL, is a common complication of DKA treatment. This condition has serious clinical implications because phosphate is essential for the synthesis of adenosine triphosphate (ATP), the primary energy source for cellular functions. Severe hypophosphatemia can lead to respiratory failure caused by weakened respiratory muscles, cardiac dysfunction manifesting as arrhythmias and impaired contractility, neurological symptoms such as irritability, confusion, seizures, and coma, as well as muscle weakness and rhabdomyolysis due to ATP depletion in muscle cells.(8)

Several studies have examined the prevalence, causes, and consequences of hypophosphatemia in DKA.(9) Although phosphate supplementation has been shown to increase serum phosphate levels, its impact on DKA resolution, insulin requirements, or clinical outcomes remains unclear. Recent research suggests that hypophosphatemia is associated with severe acidosis and occurs in approximately 74% of patients with DKA. However, the absence of adverse effects in untreated hypophosphatemia has also been reported. In contrast, a case of respiratory failure in a DKA patient highlights the potential severity of this complication.(10, 11)

Understanding the role of serum phosphate in DKA is essential for optimizing treatment strategies and improving patient outcomes. Disturbances in phosphate levels may affect the severity of the condition and the recovery process. This study aims to evaluate the clinical significance of serum phosphate levels in DKA, investigating their correlation with disease severity and treatment responses.

Materials and Methods

This observational cross-sectional study was conducted from June 2022 to June 2024 at Aarupadai Veedu Medical College, a tertiary care center in Puducherry, within the Outpatient and Inpatient Departments of General Medicine. Written informed consent was obtained from all participants prior to their inclusion in the study. Ethical approval for the study was obtained from the Institutional Human Ethics Committee of Aarupadai Veedu Medical College and Hospital, Kirumampakam, Puducherry, with the approval number IHEC No.AV/IHEC/2022/088.

Eligible participants were adults aged 18 years or older, of both genders, diagnosed with either Type 1 or Type 2 diabetes mellitus and with a confirmed diagnosis of Diabetic Ketoacidosis (DKA) based on the American Diabetes Association (ADA) guidelines. Participants were required to provide consent and demonstrate

Journal of Chemical Health Risks

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JCHR (2024) 14(6), 1623-1629 | ISSN:2251-6727

willingness to participate in the study. Exclusion criteria included a history of hypo- or hyperparathyroidism, cell lysis syndromes, renal failure, recent bolus dextrose infusion, respiratory acidosis or alkalosis, and acute alcohol intoxication.

A total of 45 participants were recruited through consecutive sampling of eligible cases from both outpatient and inpatient departments. The sample size was calculated based on a study by van der Vaart A et al. (2021).(12) Data collection involved obtaining informed consent, detailed history-taking, clinical examinations, and laboratory investigations. Data were recorded on a pre-designed proforma and analyzed statistically.

Data entry and analysis were performed using SPSS software (IBM SPSS Statistics for Windows, Version 26.0, Armonk, NY: IBM Corp., 2019) and Microsoft Excel. Normality of the data distribution was assessed using the Kolmogorov-Smirnov and Shapiro-Wilk tests, which confirmed that the data followed a normal distribution. Consequently, parametric tests were applied for analysis. Descriptive statistics, including frequency, percentage, mean, and standard deviation, were used to summarize the variables. A paired t-test was conducted to determine the statistical significance of serum phosphate levels. The significance level was set at 5% ($\alpha = 0.05$), with a p-value < 0.05 considered statistically significant.

Results

The findings of this study provide a detailed overview of the demographic, physiological, and biochemical characteristics of participants with Diabetic Ketoacidosis (DKA). The age distribution of participants reveals that the largest proportion, 28.9%, falls within the 41–50 years age group, followed closely by those aged 51–60 years and 61–70 years, each comprising 24.4% of the sample. Participants aged 31–40 years account for 15.6%, while those aged 30 years or younger and over 70 years represent smaller proportions at 2.2% and 4.4%, respectively. These findings suggest a higher prevalence of DKA among middle-aged to older adults in this study population. Gender distribution shows a slightly higher prevalence of DKA among females (53.3%) compared to males (46.7%). While the distribution is relatively balanced, the data indicates a marginal female predominance within the sample.

Descriptive statistics for physiological and biochemical variables indicate a mean age of 52.9 years with moderate variability (SD = 12). Blood pressure measurements show a mean systolic pressure of 124.88 mmHg and a diastolic pressure of 76.88 mmHg, with broad variability. Pulse rates average 90.6 beats per minute with significant variation, while respiratory rates show less variability, averaging 18.42 breaths per minute. Fasting and postprandial blood sugar levels are markedly elevated, with means of 310.2 mg/dL and 409.88 mg/dL, respectively, reflecting wide variability. Urea levels average 37.15 mg/dL, with substantial spread, while creatinine levels are comparatively lower but still variable. Uric acid levels have a mean of 4.84 mg/dL with moderate variability. The average pH is nearly stable at 7.32, showing minimal variation. Bicarbonate levels average 16.2 mmol/L with moderate spread, while PCO2 and PO2 levels exhibit moderate to high variability. Sodium levels, both blood and arterial, demonstrate relatively low variability compared to potassium and phosphate levels, which show moderate dispersion. Overall, the data highlights significant variability across physiological and biochemical measures, reflecting diverse profiles within the study population.

Post-treatment symptom analysis reveals that 80.0% of participants reported no symptoms. Among those who experienced symptoms, 8.9% reported breathlessness, while drowsiness, myoclonus, and a combination of myoclonus and palpitations were each reported by 2.2%. Palpitations alone were noted by 4.4% of participants. These results indicate that the majority of individuals experienced no symptoms post-treatment, with breathlessness being the most commonly reported among those who did.

The analysis of the relationship between fasting blood sugar (FBS) and serum phosphate levels reveals a Pearson correlation coefficient of -0.081, indicating a very weak inverse relationship. However, the significance value of 0.450 exceeds the commonly accepted threshold of 0.05, suggesting that this correlation is not statistically significant. Consequently, there is insufficient evidence to support a meaningful association between fasting blood sugar levels and serum phosphate levels in this study.

Journal of Chemical Health Risks

www.jchr.org

JCHR (2024) 14(6), 1623-1629 | ISSN:2251-6727

Discussion

Diabetic ketoacidosis (DKA) is a severe, potentially fatal complication primarily affecting people with type 1 diabetes, although it can also occur in those with type 2 diabetes. This condition is characterized by dangerously high blood sugar (hyperglycemia), excessive ketone production (ketosis), and metabolic acidosis. These abnormalities arise from an absolute or relative insulin deficiency.(13) This insulin deficiency stimulates excessive glucose production, fat breakdown, and ketone formation, leading to severe metabolic derangements. Of particular importance are the resulting disturbances in serum phosphate levels, given its critical roles in cellular energy production, bone integrity, and acid-base balance.(14) The present study includes 45 patients with an average age of 52.91 years, spanning from 28 to 85 years, illustrating the broad age range affected by DKA. The distribution was slightly skewed towards females (53.3%) compared to males (46.7%). These demographics are consistent with the literature indicating that middle-aged individuals are commonly affected by DKA. According to a study conducted by Navarro-González et al in the year 2022, similar age distributions were observed in related metabolic conditions, suggesting that age and gender may influence the presentation and management of DKA.(15)

Patients presented with varying degrees of hyperglycemia, reflected in fasting blood sugar (FBS) and postprandial blood sugar (PPBS) levels, with means 310.20mg/dL and 409.88mg/dL, respectively. This significant hyperglycemia is a hallmark of DKA. The average systolic blood pressure (SBP) was 124.88 mmHg, and diastolic blood pressure (DBP) was 76.88 mmHg, with pulse rate (PR) and respiratory rate (RR) averaging 90.60 beats per minute and 18.42 breaths per minute, respectively. These vital signs indicate the bodys compensatory mechanisms to address metabolic acidosis and dehydration. Similar clinical presentations have been reported in the study conducted by Zhang et al. (2022), who noted the importance of monitoring vital signs to manage acute metabolic conditions effectively.(16)

Several studies have highlighted the importance of monitoring serum phosphate in DKA.(17) Similarly, the study conducted by Zhang et al in the year 2022 found that lower serum phosphate levels on admission predicted acute hydrocephalus following aneurysmal subarachnoid hemorrhage, emphasizing the critical need for early phosphate correction in acute settings.(16) The comparison of serum phosphate levels before and after management in patients with diabetic ketoacidosis (DKA) reveals significant changes.(18) Pre-treatment, the mean serum phosphate level was 3.77 mg/dL, which decreased to 2.85 mg/dL post-treatment. This reduction is statistically significant, with a p-value of 0.001, indicating the treatments complication in producing hypophosphatemia, a common complication in DKA.(19) Proper management of phosphate levels is critical in DKA to prevent complications such as muscle weakness and hemolytic anemia. Hypophosphatemia can occur due to insulin therapy, which promotes the uptake of phosphate into cells. Therefore, monitoring and managing phosphate levels are crucial to ensuring that phosphate levels remain within the normal range during and after treatment.(20)

The analysis of the correlation between fasting blood sugar (FBS) and serum phosphate levels reveals a Pearson correlation coefficient of -0.081 with a p-value of 0.450. This result indicates no significant correlation between FBS and serum phosphate levels. Understanding these correlations, or lack thereof, is essential for comprehensively managing DKA and its biochemical derangements. While phosphate levels do not correlate significantly with FBS, it highlights the importance of individually monitoring various biochemical parameters in patients with DKA to tailor treatment and management plans effectively.(21)

Conclusion

In conclusion, this study highlights the prevalence of Diabetic Ketoacidosis (DKA) among middle-aged to older adults, with a slight female predominance. Elevated fasting and postprandial blood sugar levels were observed, reflecting severe hyperglycemia typical of DKA. Vital signs indicated the bodys compensatory responses to metabolic imbalances. The significant reduction in serum phosphate levels post-treatment underscores the need for careful phosphate monitoring to prevent complications. Although there was no significant correlation between fasting blood sugar and serum phosphate levels, this study underscores the importance of individualized management of biochemical parameters in DKA.

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JCHR (2024) 14(6), 1623-1629 | ISSN:2251-6727

Table 1: Age and gender distribution of the study participants

	Frequency	**Percentage**
Age (in years)		
≤30	1	2.2
31 – 40	7	15.6
41 – 50	13	28.9
51 – 60	11	24.4
61 – 70	11	24.4
>70	2	4.4
Gender		
Male	21	46.7
Female	24	53.3

Table 2: Mean and standard deviation for measurable variables

Variable	**Minimum**	**Maximum**	**Mean ± SD**
Age	28.00	85.00	52.91 ± 12.00
Duration	0.00	30.00	8.22 ± 6.31
SBP	70.00	180.00	124.88 ± 20.29
DBP	40.00	100.00	76.88 ± 11.83
PR	62.00	128.00	90.60 ± 16.22
RR	14.00	26.00	18.42 ± 2.52
FBS	140.00	570.00	310.20 ± 107.17
PPBS	204.00	680.00	409.88 ± 117.10
Urea	15.00	154.00	37.15 ± 27.48
Creatinine	0.00	8.80	1.07 ± 1.38
Uric Acid	1.60	13.20	4.84 ± 2.41
PH	7.12	7.50	7.32 ± 0.06
Bicarb	6.20	25.00	16.20 ± 3.31
PCO2	15.50	56.00	33.88 ± 9.56
PO2	45.00	150.00	87.15 ± 19.89
B.Na+	115.00	146.00	133.08 ± 6.05
A.Na+	126.00	147.00	136.64 ± 4.72
B.K+	3.10	5.70	4.22 ± 0.66
A.K+	2.80	4.80	3.74 ± 0.50
B.Phos	1.60	9.40	3.77 ± 1.58
A.Phos	1.00	8.80	2.85 ± 1.37

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Table 3: Frequency and percentage of Post RX Symptoms among the study participants

Post RX Symptoms	F	Percentage
NA	36	80.0
Breathlessness	4	8.9
Drowsiness	1	2.2
Myoclonus	1	2.2
Myolocnus / Palpitations	1	2.2
Palpitations	2	4.4
Total	**45**	**100**

Table 4: Association of Serum Phosphate, pre and post treatment

Variable	Mean	Std Deviation	Paired sample t test	P value
Pretreatment	3.7733	1.58321	-3.745	0.001*
Post treatment	2.8511	1.37057		

Figure 1: Correlation between serum phosphate levels and fasting blood glucose