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# Incidence and Clinical Outcomes of Hypophosphatemia in Patients with Diabetic Ketoacidosis Admitted to a Tertiary Care Hospital.

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## ABSTRACT

**Background:** Diabetic ketoacidosis (DKA) is a life-threatening complication of diabetes mellitus characterized by hyperglycemia, ketosis, and acidosis. Hypophosphatemia is a frequently overlooked yet clinically significant electrolyte disturbance during DKA management. This study aimed to determine the incidence of hypophosphatemia in DKA patients and assess its association with clinical outcomes.

**Method:** A descriptive cross-sectional study was conducted over six months 1st February 2025 to 31st July 2025, at Lady Reading Hospital and Khyber Teaching Hospital, Peshawar. A total of 150 patients aged ≥15 years admitted with DKA were enrolled using non-probability consecutive sampling. Serum phosphate levels were measured at admission and 24 hours after insulin therapy. Hypophosphatemia was defined as serum phosphate <2.5 mg/dL. Clinical outcomes such as muscle weakness, respiratory distress, altered consciousness, arrhythmias, ICU admission, and duration of hospitalization were recorded. Data were analyzed using SPSS version 26. Chi-square test and Mann–Whitney U test were applied.

**Results:** Hypophosphatemia was observed in 58.7% of DKA patients. Muscle weakness was significantly more common in hypophosphatemic patients ($p = 0.026$). Although altered consciousness, arrhythmias, and respiratory distress were more prevalent in this group, the differences were not statistically significant. Mean hospital stay was significantly longer among hypophosphatemic patients ($p < 0.001$). A significant association was also found between the severity of hypophosphatemia and muscle weakness ($p = 0.027$).

**Conclusions:** Hypophosphatemia is a prevalent and clinically relevant complication in DKA, associated with increased morbidity and prolonged hospitalization. Routine monitoring and timely management may improve outcomes.

**Keywords:** Diabetic Ketoacidosis, Hypophosphatemia, Phosphates, Electrolyte Imbalance.
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## INTRODUCTION

The symptoms of diabetic ketoacidosis (DKA), a severe and potentially fatal consequence of diabetes mellitus, include hyperglycemia, metabolic acidosis, and ketonemia[1]. Patients with type 1 diabetes frequently exhibit it; however, under specific stressors, people with type 2 diabetes may also show it.[2] With an estimated yearly incidence of 8 per 1,000 diabetic patients in wealthy nations, the incidence of DKA is rising worldwide[3]. Every year in the United States alone, DKA causes over 500,000 hospital days and costs more than $5 billion.[4] In developing countries like Pakistan, limited healthcare access and late diagnosis further elevate the morbidity and mortality associated with DKA[5].

Electrolyte disturbances are hallmark features of DKA, with hypokalemia and hyponatremia receiving the most clinical attention.[6] However, hypophosphatemia, though often overlooked, is a common and potentially serious complication. During insulin therapy, phosphate shifts intracellularly, leading to a marked drop in serum phosphate levels.[7] The reported incidence of hypophosphatemia in DKA varies between 45% and 80% depending on definitions and timing of measurement[8]. Severe hypophosphatemia can result in muscle weakness, hemolysis, impaired cardiac function, and respiratory failure[9].

Internationally, studies have highlighted the clinical impact of hypophosphatemia in DKA. A large cohort study from the UK reported an increased risk of prolonged hospital stay and complications in patients with moderate to severe hypophosphatemia[10]. In Saudi Arabia, a study revealed that 62% of patients with DKA developed significant hypophosphatemia, and among them, 18% required intensive care management.[11] In South Asia, regional data are sparse. A study from India reported a 54% incidence of hypophosphatemia in adult DKA patients, correlating it with worsened neurological outcomes[12].

In Pakistan, the burden of diabetes continues to rise, with over 33 million adults currently living with the disease, and an increasing trend in DKA admissions has been noted[13]. Despite this, there is a significant paucity of local data specifically focusing on hypophosphatemia in DKA. Most local studies concentrate on general electrolyte imbalances or acid-base disturbances without emphasizing phosphate derangements[14, 15]. This lack of detailed epidemiological and outcome-based information on hypophosphatemia hinders appropriate monitoring and management in routine DKA care.

The clinical significance of hypophosphatemia lies in its silent progression and potential for life-threatening complications if left unrecognized. Despite international guidelines acknowledging its occurrence, the routine monitoring and replacement of phosphate remains controversial due to

inconsistent findings in the literature regarding its true impact on clinical outcomes. While hypophosphatemia is a recognized complication of diabetic ketoacidosis (DKA), it often remains underdiagnosed and undertreated, particularly in low-resource settings like Pakistan. International studies have linked hypophosphatemia with adverse clinical outcomes such as muscle weakness, cardiac dysfunction, and prolonged hospital stay. However, local data specific to its incidence and impact on clinical outcomes in DKA patients are scarce.

This knowledge gap limits the ability of clinicians to develop targeted monitoring and management protocols. Given the rising burden of diabetes and the increasing number of DKA admissions in tertiary care hospitals in Pakistan, it is essential to evaluate the frequency and clinical consequences of hypophosphatemia in this population. A deeper comprehension of these results can help direct evidence-based therapies and early detection, possibly enhance patient outcomes, and lower medical expenses. The purpose of the current investigation was to assess the prevalence of hypophosphatemia and evaluate its clinical consequences in patients with diabetic ketoacidosis.

## METHODS

This cross-sectional study was conducted at the Department of Medicine, Lady Reading Hospital and Khyber Teaching Hospital for six months, from 1st February, 2025 to 31st July, 2025. The Institutional Research and Ethical Review Board (IREB) of Khyber Medical College/Khyber Teaching Hospital, Peshawar, provided the ethical approval of the study (Approval No: 23/DME/KMC Dated:30th January, 2025).

All individuals with a diagnosis of diabetic ketoacidosis (DKA) who had been admitted through the emergency room or medical ward during the study period and who were at least 15 years old were deemed eligible. All eligible patients who fulfilled the inclusion criteria were recruited using a non-probability consecutive sampling technique. To determine the sample size, OpenEpi Version 3.01 was utilized. The minimum required sample size was determined to be 150, assuming a '95% confidence level, a 7% margin of error', and an expected incidence of hypophosphatemia in DKA patients of 74%, based on prior literature[8].

Participants had to be ≥15 years old, diagnosed with diabetic ketoacidosis (as defined by the American Diabetes Association; 'blood glucose >250 mg/dL', arterial pH <7.3, serum bicarbonate <18 mEq/L, and positive serum or urine ketones), admitted within 24 hours of the onset of symptoms, and give informed consent. Pregnant women, patients with incomplete medical records, patients with chronic liver disease, cancer, or sepsis, patients on dialysis or with chronic kidney illness, and patients taking phosphate supplements before admission.

Patients who satisfied the inclusion criteria were enrolled one after the other after giving their informed consent. Patient demographic information, clinical presentation, laboratory results (including serum phosphate at admission and 24 hours after insulin administration), and hospital outcomes were all gathered using a pre-made proforma. Standard laboratory procedures were used to test blood samples that were obtained in an aseptic environment. Serum phosphate levels below 2.5 mg/dL were considered hypophosphatemia. Throughout their hospital stay, patients were watched for issues like cardiac arrhythmias, respiratory distress, muscle weakness, altered consciousness, and length of hospitalization. The lead investigator oversaw the qualified medical officers who collected the data.

SPSS version 26 was utilized for data entry and analysis. Descriptive calculations were used to summarize baseline parameters such as: mean ± SD for continuous variables and frequencies/percentages for categorical variables. Hypophosphatemia incidence was expressed as a percentage. The relationship between hypophosphatemia and categorical outcomes was assessed using the chi-square test. Where appropriate, means were compared using the Mann-Whitney U test. P-values less than 0.05 were regarded as statistically significant.

## RESULTS

**Table 1: Baseline Characteristics of DKA Patients (n = 150)**

| Variable | Mean ± SD / n (%) |
|---|---|
| **Age (years)** | 36.2 ± 14.7 |
| **Gender** | |
| Male | 81 (54.0%) |
| Female | 69 (46.0%) |
| **Diabetes Type** | |
| Type 1 | 96 (64%) |
| Type 2 | 54 (36%) |
| **Diabetes Duration** | 5.8 ± 4.2 years |
| **Mean Blood Glucose at Admission** | 468.5 ± 105.3 mg/dL |
| **Serum pH** | 7.12 ± 0.08 |
| **Bicarbonate (mEq/L)** | 12.4 ± 3.2 |
| **Anion Gap** | 22.7 ± 4.5 |

| | |
|---|---|
| **Serum Phosphate at Admission** | 2.8 ± 0.9 mg/dL |
| **Serum Phosphate at 24h post-insulin** | 2.2 ± 0.7 mg/dL |
| **Hypophosphatemia (<2.5 mg/dL)** | 88 (58.7%) |

The study included a total of 150 patients diagnosed with diabetic ketoacidosis (DKA). The cohort had a balanced gender distribution, with a slightly higher proportion of males. Most patients were diagnosed with type 1 diabetes mellitus, and the average duration of diabetes indicated a relatively early onset and progression of the disease. On admission, laboratory parameters confirmed the presence of metabolic acidosis, with elevated anion gap and reduced serum bicarbonate and pH levels, consistent with the biochemical profile of DKA. Serum phosphate levels were within the expected range at presentation but showed a notable decline within the first 24 hours of insulin therapy. Overall, more than half of the patients developed hypophosphatemia during their hospital stay, highlighting the need for close monitoring of phosphate levels during DKA management **(Table 1)**.

**Table 2: Comparison of Clinical Outcomes Between Hypophosphatemia and Non-Hypophosphatemia Patients (n = 150)**

| Clinical Outcome | Hypophosphatemia (n = 88) | No Hypophosphatemia (n = 62) | p-value |
|---|---|---|---|
| Muscle Weakness | 28 (31.8%) | 9 (14.5%) | 0.026* |
| Respiratory Distress | 14 (15.9%) | 4 (6.5%) | 0.134 |
| Altered Consciousness | 22 (25.0%) | 7 (11.3%) | 0.060 |
| Cardiac Arrhythmias | 10 (11.4%) | 2 (3.2%) | 0.133 |
| ICU Admission | 18 (20.5%) | 6 (9.7%) | 0.122 |
| Mean Duration of Stay (days) | 5.6 ± 2.1 | 4.2 ± 1.6 | <0.001* |

**p-value ≤0.05 considered statistically significant.*
*'Mann–Whitney U test was applied for the mean duration of hospital stay'*

When comparing clinical outcomes between hypophosphatemia and non-hypophosphatemia patients, muscle weakness was significantly more common among those with hypophosphatemia (p = 0.026). Although higher rates of respiratory distress, altered consciousness, cardiac arrhythmias, and ICU admissions were observed in the hypophosphatemia group, these differences did not reach

statistical significance. Notably, the mean duration of hospital stay was significantly longer in hypophosphatemia patients compared to those with normal phosphate levels ($p < 0.001$), indicating a potential association between phosphate depletion and prolonged recovery.

**Table 3: Association Between Severity of Hypophosphatemia and Major Complications (n = 88)**

| Severity of Hypophosphatemia | Muscle Weakness | Altered Consciousness | Cardiac Arrhythmia |
|---|---|---|---|
| **Mild (2.0–2.4 mg/dL)** | 10 (20.8%) | 8 (16.7%) | 2 (4.2%) |
| **Moderate (1.5–1.9 mg/dL)** | 12 (40.0%) | 10 (33.3%) | 6 (20.0%) |
| **Severe (<1.5 mg/dL)** | 6 (60.0%) | 4 (40.0%) | 2 (20.0%) |
| **p-value** | 0.027* | 0.129 | 0.066 |

**p-value ≤ 0.05 considered statistically significant.*
*'The chi-square and Fisher Exact test were used'*

Among patients with hypophosphatemia, the increasing severity of phosphate depletion was associated with a higher frequency of complications. A statistically significant association was observed between the severity of hypophosphatemia and the occurrence of muscle weakness ($p = 0.027$), with the highest rate (60%) seen in those with severe hypophosphatemia (<1.5 mg/dL). Although altered consciousness and cardiac arrhythmias were also more frequent with worsening hypophosphatemia, these associations did not reach statistical significance ($p = 0.129$ and $p = 0.066$, respectively), though the trends suggest possible clinical relevance.

## DISCUSSION

This study found that hypophosphatemia occurred in over half (58.7%) of patients admitted with diabetic ketoacidosis (DKA), aligning with previous research that has reported prevalence rates ranging from 15-77% in DKA patients globally [8, 16, 17]. The high frequency of hypophosphatemia in this cohort supports the pathophysiological understanding that insulin therapy and intracellular phosphate shifting during DKA treatment significantly lower serum phosphate levels.

The association between hypophosphatemia and clinical complications was a key focus of this study. Muscle weakness was significantly more common in patients with low phosphate levels, which is consistent with earlier findings that identified muscle dysfunction as a hallmark manifestation of moderate to severe hypophosphatemia[18-20]. In our data, this complication showed a clear trend with increasing severity of hypophosphatemia, with up to 60% of severely hypophosphatemic patients

developing muscle weakness. This is in agreement with evidence from both critical care and endocrinology literature, which links phosphate depletion with reduced cellular energy stores and impaired neuromuscular function[21].

Although not statistically significant, other complications such as respiratory distress, altered mental status, and cardiac arrhythmias occurred more frequently in the hypophosphatemic group. These trends are in line with prior studies that have demonstrated associations between hypophosphatemia and impaired respiratory muscle function, encephalopathy, and arrhythmic events in critically ill and DKA patients[22, 23]. A study argues that even moderate reductions in phosphate levels can contribute to these complications, especially when comorbidities are present.[24]

Another significant finding in this study was the longer duration of hospitalization in hypophosphatemic patients. This outcome has been previously documented, with studies suggesting that complications related to hypophosphatemia, such as weakness and arrhythmias, may delay clinical stabilization and discharge[25]. The association between phosphate levels and length of stay underscores the clinical importance of monitoring and potentially correcting hypophosphatemia in DKA management protocols.

Interestingly, while some international guidelines recommend against routine phosphate replacement unless levels fall below 1.0 mg/dL or clinical symptoms develop, our findings support the notion that even mild to moderate hypophosphatemia may be clinically relevant in DKA. This reinforces the growing call for individualized phosphate monitoring during DKA treatment, particularly in settings where complications may go unrecognized[26].

In summary, our results are largely consistent with the existing literature and add to the growing body of evidence suggesting that hypophosphatemia is not only common in DKA but may also be associated with clinically important adverse outcomes. Given the high prevalence observed and its association with prolonged hospitalization and muscle weakness, clinicians should consider routine monitoring of phosphate levels during DKA treatment and assess patients carefully for early signs of complications.

The results of this study demonstrate the clinical importance of hypophosphatemia in diabetic ketoacidosis patients, especially its correlation with muscle weakness and extended hospitalization. These results underscore the need for routine monitoring of serum phosphate levels during DKA management, even in mild to moderate cases, to enable early identification of patients at risk for complications. Incorporating phosphate assessment into standard DKA protocols may improve patient outcomes and reduce healthcare burden through timely intervention.

This study does, however, have several limitations. Because the study was only carried out at one tertiary care facility, the results might not be as applicable in other contexts. The statistical ability to identify relationships with less common problems like arrhythmias or altered awareness may have been impacted by the sample size, which was quite small, especially in the subgroup with severe hypophosphatemia. Furthermore, the observational design limits causal inference, and potential confounders such as nutritional status or renal function were not controlled in detail.

Future research should focus on multicenter prospective studies with larger sample sizes and include long-term outcomes to assess better the impact of phosphate levels on morbidity and mortality. Interventional trials evaluating the benefits and risks of early phosphate supplementation in DKA patients with moderate hypophosphatemia are also warranted to guide evidence-based clinical practice.

## CONCLUSION

This study demonstrates that hypophosphatemia is a common electrolyte disturbance in patients with diabetic ketoacidosis, affecting more than half of the study population. It is significantly associated with muscle weakness and prolonged hospital stay, and its severity appears to correlate with an increased risk of clinical complications. Although other outcomes, such as altered consciousness and cardiac arrhythmias, were more frequent in hypophosphatemic patients, these did not reach statistical significance. These findings emphasize the importance of routinely monitoring serum phosphate levels during DKA management and recognizing the potential clinical consequences of even moderate phosphate depletion. Early identification and appropriate management of hypophosphatemia may contribute to improved patient outcomes and reduced hospitalization time.

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## CONFLICT OF INTEREST

None

## ETHICAL APPROVAL

The Institutional Research and Ethical Review Board (IREB) of Khyber Medical College/Khyber Teaching Hospital, Peshawar, provided the ethical approval of the study (Approval No: 23/DME/KMC Dated:30th January, 2025).

## AUTHORS' CONTRIBUTION

**SA:** Conceptualized and designed the study, supervised all aspects of the research, and critically revised the manuscript for important intellectual content. **SH:** Contributed to the study design, data acquisition, and assisted in the interpretation of results. **SHa:** Participated in literature review, drafted the initial manuscript, and contributed to data collection. **TA:** Performed data analysis, statistical interpretation, and contributed to results compilation. **UI:** Assisted in data entry and management, and supported manuscript formatting and referencing. **MA:** Contributed to drafting and reviewing the manuscript and assisted in preparing the final version for submission

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