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Letter to the Editor
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The Forgotten Electrolyte in Dengue: Hypophosphatemia Matters

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Dear Editor,

Dengue is an acute viral illness from the family Flaviviridae that has caused significant morbidity and mortality worldwide, with a broad disease spectrum, ranging from asymptomatic infection to severe dengue hemorrhagic fever and dengue shock syndrome. With 2.5 billion people at risk globally, especially in endemic regions, the burden continues to rise, underscoring the need for early recognition and comprehensive monitoring as crucial parts of patient care (1).

Although various laboratory investigations have been performed to assess the severity and progression of disease, such as complete blood count (CBC), prothrombin time (PT), activated partial thromboplastin time (aPTT), and liver function test (LFT) (2), and serum electrolytes, mainly sodium and potassium, serum phosphate levels are almost entirely ignored despite their high clinical relevance. A pediatric study published in the Pakistan Journal of Medicine and Dentistry reported that 65.3% of dengue patients had decreased serum phosphate levels (3), highlighting the wide gap in critical care and the current literature, where only selected electrolytes are monitored, leaving unmonitored serum phosphate alterations unnoticed. However, adult data remains limited, highlighting the need for further prospective studies.

Hypophosphatemia is defined as a serum phosphate level below 0.80 mmol/L (≈ < 2.5 mg/dL). It is further classified as mild (0.60–0.79 mmol/L ≈ 1.9–2.4 mg/dL), moderate (0.32–0.59 mmol/L ≈ 1.0–1.8 mg/dL), and severe (< 0.32 mmol/L ≈ < 1.0 mg/dL) (4). Decreased serum phosphate levels are commonly observed in critically ill patients and have also been reported in patients with dengue infection. However, various causes, such as reduced intestinal phosphate absorption, increased renal excretion, osteolysis, intracellular changes, and metabolic abnormalities, can also result in hypophosphatemia. Numerous deleterious clinical outcomes have been observed due to low serum phosphate levels, including more extended hospital and intensive care unit stays and higher death rates because phosphate is primarily an intracellular anion that is essential for regular cellular activity, including nucleic acid structural proteins, important cellular energy sources, red blood cells, and bones and its depletion can cause severe adverse

effects such as irregular heart rhythm, hemolysis, delirium, convulsions, prolonged mechanical ventilation, coma, peripheral neuropathy, rhabdomyolysis, skeletal muscle weakness, and respiratory insufficiency (5). A case report by Nirada Siriyakorn observed fatal rhabdomyolysis in a patient with dengue hemorrhagic fever, linking hypophosphatemia as a potential mechanism of causing such illness (6). Phosphate is a primary electrolyte in genetic and metabolic pathways and drives mineralization of skeletal tissues (7). Moreover, this electrolyte plays a vital role in maintaining body homeostasis via FGF23, vitamin D, and parathyroid hormone, influencing energy balance, mineralization, rickets prevention, and treatment of phosphate-related disorders (8). It is pertinent to note that in critical illness, hypophosphatemia correlates with worse outcomes; whether targeted correction improves outcomes in dengue remains to be studied (9). Therefore, this issue warrants urgent attention from health authorities because changes in serum phosphate levels were not random but showed a consistent pattern in dengue fever.

In conclusion, several practical approaches should be implemented, such as monitoring serum phosphate levels in conjunction with dengue phases; baseline measurements on admission, daily during the critical phase, and serial tracking in the ICU or for rhabdomyolysis risk. Critical-phase alarms should serve as reminders to perform serum phosphate testing. Serum phosphate laboratory investigations should be integrated with existing chemistry panels, guided by clinical triggers. Specifically, the serum phosphate with platelet bundle test is prompted by a fall in platelet levels, requiring a single lab test co-ordering CBC with platelets and serum phosphate, thus reducing phlebotomy and costs. During the replacement protocol, oral phosphate should be preferred for mild to moderate cases, and intravenous phosphate for severe cases, with close monitoring of electrolytes and renal function to prevent complications. Therefore, integrating diligent strategies in critical care may reduce the length of hospital stay and potentially be life-saving.

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