



Hypomagnesemia and Acute Kidney Injury in Critical Illness: Pathophysiology, Prognostic Value, and Clinical Implications

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Received: 28 October 2024, **Accepted:** 17 November 2024, **Published:** 20 November 2024

Abstract

Background: Acute kidney injury (AKI) is common in critical illness and remains difficult to detect before clinically apparent loss of filtration. Magnesium is central to cellular energy handling, vascular tone, inflammatory signaling, and tubular transport. Hypomagnesemia is frequent in intensive care and has been associated with AKI, but its clinical interpretation is complicated by illness severity, medications, renal losses, and the limitations of total serum magnesium measurement.

Aim: This review examines the biological rationale, prognostic evidence, measurement challenges, and practical implications of serum magnesium assessment in critically ill adults at risk of AKI.

Methods: A narrative review was developed from the thesis literature base, prioritizing guidelines, systematic reviews, critical-care cohorts, and renal-focused studies addressing magnesium homeostasis, AKI, and ICU outcomes.

Conclusion: Low serum magnesium is a plausible and potentially useful risk marker for AKI in critical illness, particularly when interpreted alongside hemodynamics, nephrotoxic exposure, sepsis, baseline kidney function, and serial creatinine and urine-output data. It should not be treated as a stand-alone diagnostic or as proof that empiric replacement prevents AKI. Standardized prospective studies using clinically meaningful magnesium phenotypes and intervention trials are needed before magnesium-guided renoprotection can be routinely recommended.

Keywords

acute kidney injury; critical illness; hypomagnesemia; intensive care unit; serum magnesium

Introduction

Acute kidney injury is a syndrome of abrupt impairment in kidney function that spans minor biochemical change through kidney failure requiring replacement therapy. In the intensive care unit (ICU), it commonly develops within a setting of sepsis, shock, respiratory failure, major surgery, exposure to nephrotoxins, or multiorgan dysfunction. Its importance extends well beyond a transient increase in serum creatinine: AKI modifies drug handling, complicates fluid and electrolyte management, increases short-term mortality, and may leave survivors with persistent kidney dysfunction or a higher subsequent risk of chronic kidney disease. The burden is especially high where preventive monitoring and timely supportive care are difficult to provide.¹⁻⁵

Magnesium deserves attention in this setting because it is both biologically active and routinely measurable. Hypomagnesemia is frequent among hospitalized and critically ill patients and may accompany poor intake, gastrointestinal loss, renal tubular wasting, diuretics, aminoglycosides, calcineurin inhibitors, osmotic diuresis, and the physiological stress response. A low concentration may therefore identify patients exposed to renal risk while also contributing to vascular, metabolic, and inflammatory instability. Yet magnesium is not incorporated into conventional AKI risk assessment, and the available evidence does not establish whether it is a causal mediator, a modifiable cofactor, or mainly a marker of severe illness.⁶⁻¹¹

This review considers serum magnesium as a component of clinical risk assessment rather than an isolated laboratory abnormality. It first summarizes magnesium distribution and renal handling, then links magnesium disturbance to the pathobiology of critical-illness AKI. The clinical evidence is assessed with attention to confounding, timing, and outcome definitions. Finally, a pragmatic approach to testing, replacement, and research priorities is proposed.¹²⁻¹⁵

AKI in Critical Illness: Why Early Risk Recognition Matters

KDIGO defines AKI using an increase in serum creatinine of at least 0.3 mg/dL within 48 hours, an increase to at least 1.5 times baseline within 7 days, or reduced urine output. These criteria standardize diagnosis but do not reveal the mechanism or the exact time of injury. Creatinine is influenced by baseline muscle mass, generation, fluid balance, and the delay between a fall in filtration and accumulation in blood. Urine output is sensitive to perfusion and treatment decisions but lacks specificity. Consequently, ICU clinicians often recognize AKI only after a period



during which hemodynamic, inflammatory, toxic, or obstructive injury has already occurred.^{1 3 33 34 35 36}

The syndrome is heterogeneous. Sepsis-associated AKI can occur despite preserved or increased renal blood flow and reflects microcirculatory dysfunction, endothelial activation, mitochondrial stress, tubular-cell metabolic adaptation, and immune dysregulation. In other patients, sustained hypotension, congestion, hypovolemia, rhabdomyolysis, contrast exposure, or drugs predominate. Such diversity explains why a single biomarker is unlikely to perform equally well across all ICU populations. Risk identification is more useful when it combines susceptibility, exposures, serial physiological data, and evidence of kidney stress or damage.^{4 6 31 37 38 39}

Even apparently reversible AKI has long-term implications. Severe episodes may lead to incomplete recovery, recurrent AKI, acute kidney disease, and chronic kidney disease through capillary loss, persistent inflammation, maladaptive tubular repair, fibrosis, and reduced renal reserve. These consequences reinforce the value of identifying low-cost markers that may help flag patients for closer surveillance, although association with later outcomes must not be mistaken for proof of a direct pathogenic role.^{8 9 40 41}

The clinical trajectory is rarely linear. A patient may arrive with normal creatinine but reduced renal reserve, receive large-volume resuscitation that dilutes creatinine, then develop oliguria during vasopressor treatment or after exposure to a nephrotoxic drug. Conversely, a transient creatinine change can reflect hemodynamic adaptation without sustained structural damage. Serial assessment is therefore more informative than a single measurement. It also explains why the timing of magnesium assessment matters: a value obtained before resuscitation answers a different question from one obtained after several days of ICU therapy.^{3 4 6 33 35}

Current prevention guidance emphasizes identifying susceptible patients, avoiding secondary insults, optimizing hemodynamics, and monitoring kidney function closely. These measures are inherently multifactorial. No electrolyte value can replace a careful evaluation of effective circulating volume, congestion, infection control, drug exposure, and obstruction. The potential contribution of magnesium is best understood within this framework: it may add a visible sign of altered tubular handling or systemic stress, but it cannot specify the dominant mechanism of AKI without clinical context.^{4 6 31 37}

Magnesium Biology and Renal Homeostasis

Magnesium is the fourth most abundant cation in the body and the second most abundant intracellular cation. Most body magnesium is located in bone and soft tissue; only a very small fraction is present in extracellular fluid. In plasma, magnesium circulates in ionized, protein-bound, and complexed forms. It participates in ATP-dependent reactions, nucleic-acid and protein synthesis, membrane stability, ion-channel function, neuromuscular transmission, and regulation of calcium and potassium transport. These wide-ranging roles make deficiency clinically relevant even when symptoms are nonspecific.^{11 12 13 15}

Intestinal absorption and renal excretion together maintain magnesium balance. The kidney filters magnesium freely and reabsorbs most of the filtered load along the nephron, with the thick ascending limb and distal convoluted tubule making particularly important contributions to regulated reabsorption. Volume status, sodium handling, hormones, acid-base state, and tubular integrity can alter this balance. In stable chronic kidney disease, declining filtration may promote magnesium retention; however, tubular dysfunction, poor intake, medication exposure, and dialysis can still produce depletion. The direction of serum change therefore cannot be inferred from glomerular filtration alone.^{13 14 15 42 43 44}

In critical illness, the determinants of magnesium concentration multiply. Catecholamine excess and insulin treatment can shift magnesium into cells. Diuretics, aminoglycosides, proton-pump inhibitors, osmotic diuresis, and high distal sodium delivery may increase renal loss. Diarrhea, nasogastric suction, inadequate nutrition, and refeeding can reduce available magnesium. Hypoalbuminemia affects total magnesium interpretation, while acidosis, alkalosis, and changes in circulating ligands may alter the relation between total and ionized fractions. A single low total concentration therefore represents a biochemical phenotype rather than a complete measure of body stores.^{10 16 17 18 19}

Hypomagnesemia often coexists with hypokalemia and hypocalcemia. Magnesium deficiency impairs potassium conservation and can make hypokalemia refractory to potassium administration; severe deficiency may also impair parathyroid hormone secretion or action. These linked abnormalities are clinically important in the ICU because arrhythmia risk, muscle weakness, vasopressor requirements, and replacement strategies may be influenced by the entire electrolyte pattern. Interpretation should therefore document potassium, calcium, phosphate, renal function, nutrition, acid-base status, and current medications rather than reporting magnesium in isolation.^{11 16 17}

The distinction between total and ionized magnesium has practical implications. Total magnesium is affected by the protein-bound fraction, whereas ionized magnesium represents the physiologically active circulating form. Neither measurement fully describes intracellular magnesium, where many enzymatic actions occur. In critically ill patients, the relation among these compartments can be altered by hypoalbuminemia, citrate exposure, acid-base disturbance, and rapid fluid shifts. A normal total value should thus be interpreted as reassuring only in context, while a low value should lead to confirmation of the clinical setting and a review of losses rather than automatic attribution



to nutritional deficiency alone.^{10 11 13 16}

Renal magnesium handling also provides a reason why AKI and magnesium cannot be separated conceptually. Intact tubules normally conserve magnesium efficiently when intake is inadequate. Tubular injury, high flow states, osmotic diuresis, and drug toxicity may disrupt that response and promote urinary wasting before filtration falls sufficiently to raise creatinine. Once severe filtration impairment occurs, the balance may reverse and excretion becomes limited. This dynamic helps explain reports of both low and high magnesium in patients who meet AKI criteria at different stages of illness.^{13 14 15 24 45}

How Magnesium Could Influence AKI Susceptibility

Several mechanisms make a contribution of magnesium deficiency to AKI biologically credible. Magnesium is required for ATP utilization and mitochondrial function, so depletion may lower the metabolic reserve of tubular cells exposed to ischemia, oxidative stress, or toxins. It also modulates calcium entry and vascular smooth-muscle tone; deficiency may favor vasoconstriction, endothelial dysfunction, and impaired microvascular perfusion. In a critically ill patient whose renal circulation is already vulnerable to shock, congestion, or vasopressor exposure, these effects could reduce tolerance to an additional insult.^{11 12 15 42}

Inflammatory and immune pathways may provide another link. Experimental AKI involves activation of resident renal cells, leukocyte recruitment, cytokine signaling, oxidative stress, and a transition from adaptive repair to persistent inflammation in some patients. Magnesium has been associated with modulation of inflammatory signaling and membrane stability, while hypomagnesemia in sepsis often accompanies a more severe physiological disturbance. The literature supports plausibility, but it does not establish that a measured serum decrease is the proximal driver of tubular injury in humans.^{18 38 39 40}

Magnesium may also interact with hemodynamic and metabolic pathways. Deficiency has been associated with insulin resistance, dysglycemia, arrhythmias, and altered vasomotor responses, all of which may complicate resuscitation. Conversely, AKI itself can alter magnesium excretion and create hypermagnesemia, particularly when intake or replacement continues during declining filtration. The association may therefore be bidirectional: low magnesium can accompany a vulnerable patient before AKI, whereas high magnesium may arise after renal dysfunction has developed. Timing of blood sampling is essential when interpreting either pattern.^{13 15 24 25 45}

Oxidative stress may be another relevant pathway. Renal tubular cells are highly dependent on mitochondrial ATP production and are particularly vulnerable to ischemia-reperfusion, inflammatory mediators, and toxic injury. Experimental work on AKI has highlighted mitochondrial dysfunction, autophagy, endoplasmic-reticulum stress, and oxidant injury as interacting processes. Magnesium participates in reactions that stabilize ATP and cellular membranes; depletion could plausibly amplify stress responses, although translating these mechanisms into a clinically actionable serum threshold remains difficult.^{12 38 39 40}

It is equally possible that magnesium reflects disease severity rather than mediates injury. Patients with septic shock may have low magnesium because of poor intake, catecholamine surge, insulin treatment, renal losses, diuretics, and fluid shifts; the same patient is at high risk of AKI for many independent reasons. Multivariable adjustment can reduce but not remove such confounding, particularly in small cohorts. The appropriate interpretation is therefore that hypomagnesemia may identify a biologically and clinically vulnerable state, not that every low result indicates a magnesium-driven renal lesion.^{18 22 23 25}

Evidence Linking Serum Magnesium to AKI and ICU Outcomes

Observational ICU studies consistently show that magnesium abnormalities are common, although prevalence estimates differ because of variable thresholds, case mix, timing, and use of total rather than ionized magnesium. Older laboratory work emphasized that total serum magnesium does not necessarily reflect intracellular status. More recent prospective ICU cohorts similarly report frequent hypomagnesemia and associations with greater illness burden or prolonged admission. Such studies support routine awareness of magnesium disturbance but cannot reliably separate magnesium effects from the conditions and treatments that caused the disturbance.^{10 16 19 20 21 45}

The most relevant signal for this review comes from studies that examined incident AKI. Cheungpasitporn et al. reported that both admission hypomagnesemia and hypermagnesemia were associated with AKI risk, suggesting a nonlinear relationship rather than a simple deficiency model. Studies in patients with malignancy, traumatic brain injury, and ST-segment elevation myocardial infarction have also associated lower magnesium concentrations with subsequent AKI. These findings are clinically coherent across different acute settings, but the populations, thresholds, covariate adjustment, and AKI definitions vary substantially, precluding a universal cutoff or a common effect estimate.^{24 26 27 28}

The thesis cohort adds local prospective observational evidence. Among 52 critically ill patients with preserved kidney function at ICU admission, hypomagnesemia was common and AKI occurred more often in the low-magnesium group than in the normomagnesemic group. In multivariable analysis, hypomagnesemia remained associated with incident AKI after adjustment for selected clinical covariates. This supports magnesium as a candidate risk marker, but the small single-center sample, wide confidence intervals, residual confounding, and



reliance on total serum magnesium mean that the result should be viewed as hypothesis-supporting rather than practice-changing.

Whether hypomagnesemia predicts mortality independently is less clear. Meta-analyses and several cohorts have associated low admission magnesium with higher ICU mortality, longer stay, mechanical ventilation, or hemodynamic instability. However, death in the ICU is strongly determined by sepsis, neurologic injury, organ support, baseline frailty, and treatment limitations. Magnesium abnormalities may lie on the pathway from severity to outcome, may be induced by therapy, or may simply co-occur with poor nutrition and multiorgan failure. Prognostic language should therefore remain cautious unless studies demonstrate incremental value beyond validated severity and kidney-risk models.^{20 21 22 23 25}

A particularly important limitation is reverse causation. Patients may have occult kidney injury before the first creatinine-defined AKI event, and reduced magnesium excretion can subsequently cause hypermagnesemia. Fluid administration may dilute creatinine and total magnesium simultaneously, while diuretics or nephrotoxic antibiotics can affect both magnesium handling and renal risk. Baseline chronic kidney disease, diabetes, sepsis, hypoalbuminemia, urinary losses, and replacement practices are additional confounders. Studies that do not establish temporality, quantify exposures, and adjust for baseline renal function may overestimate an independent relationship.^{3 6 24 33 35 36}

Variation in cutoffs is a further barrier to translation. Some studies label magnesium below approximately 1.5–1.8 mg/dL as low, while others use laboratory-specific mmol/L limits, and few distinguish moderate biochemical reductions from severe symptomatic deficiency. An odds ratio from one threshold should not be applied directly to another ICU population. Similarly, an association observed at admission may not apply to a new reduction that develops during diuretic therapy or kidney replacement therapy. Standardized definitions and repeated measurements are needed before a threshold can be used for protocolized renal-risk stratification.^{10 16 19 21 24}

The literature also contains discordant signals. Some cohorts find associations with AKI or mortality, whereas others show no independent association once severity variables are considered. This inconsistency is not surprising given differences in enrollment, referral setting, baseline kidney function, illness acuity, measurement methods, treatment era, and follow-up. It does not negate the signal, but it argues against presenting magnesium as a validated predictor with a fixed clinical effect. External validation and careful calibration are more informative than repeated single-center associations.^{20 22 23 25 46}

Measurement: What Should Be Tested and When?

Total serum magnesium is inexpensive and widely available, so it is the most practical first test. Yet its convenience should not be confused with completeness. Because the extracellular compartment contains only a small portion of total-body magnesium, normal total magnesium cannot exclude depletion, and hypoalbuminemia can complicate its interpretation. Ionized magnesium may better reflect the biologically active fraction, but availability, analytical standardization, sample handling, and reference intervals remain limiting in many ICUs. Intracellular assays are primarily research tools and are not ready for routine risk stratification.^{10 13 16 44}

Testing is most informative when timed to a clinical decision. An admission measurement establishes a baseline phenotype before large shifts from fluids, diuretics, nutrition, or renal replacement therapy. Repeat testing is appropriate with ongoing gastrointestinal losses, aggressive diuresis, aminoglycoside or calcineurin exposure, refractory hypokalemia, ventricular arrhythmia, major transfusion, severe sepsis, or continuous kidney replacement therapy. In each case, the result should be interpreted with creatinine trajectory, urine output, fluid balance, potassium, calcium, phosphate, albumin, acid-base status, and medication timing.^{10 17 18 30 32}

Magnesium should complement, not replace, established AKI surveillance. A creatinine rise and oliguria retain central roles in diagnosis, while risk assessment should include prior kidney disease, diabetes, heart failure, shock, infection, surgery, nephrotoxins, and severity of illness. Novel injury and stress biomarkers may improve earlier identification in selected settings, but their clinical value depends on whether a result prompts an effective response. Magnesium is attractive precisely because it is already available; its value may be greatest as one element of a bundled electrolyte and renal-risk review rather than as a standalone predictive test.^{1 31 33 34 36 37}

Where clinically appropriate, urinary magnesium excretion can help separate renal wasting from reduced intake or gastrointestinal loss, although its interpretation is difficult during AKI, diuretic use, and changing urine output. A focused evaluation is often more useful than indiscriminate testing: review medication charts, nutrition, and gastrointestinal losses; repeat serum values after stabilization; and consider urinary indices only when the answer will alter management. This approach avoids both under-recognition of important deficiency and overinterpretation of isolated laboratory variation.^{13 14 15 19}

Clinical Implications and a Pragmatic ICU Approach

For a critically ill adult with hypomagnesemia, the first task is to identify the context. Clinicians should review pre-existing kidney function, nutritional intake, gastrointestinal losses, glycemic control, acid-base disturbance, alcohol use where relevant, and drugs that promote magnesium wasting. They should also assess whether the patient has



concurrent hypokalemia, hypocalcemia, arrhythmia, seizures, neuromuscular irritability, or a need for therapies that may magnify electrolyte loss. This approach treats a laboratory result as a prompt for clinical reassessment rather than as a direct AKI diagnosis.^{10 11 17 18 43}

Correction is appropriate for clinically meaningful deficiency, symptoms, arrhythmia risk, or associated difficult-to-correct electrolyte disturbances, while the route and dose should reflect severity, enteral tolerance, renal function, and urgency. Intravenous replacement is often used in unstable ICU patients, but dosing must be individualized and monitored because impaired filtration increases the risk of overcorrection. In patients receiving continuous kidney replacement therapy, magnesium losses can occur depending on the prescribed fluids and replacement strategy; regular monitoring and protocol-based supplementation are particularly important.^{10 11 30 32 44}

Evidence is not yet sufficient to state that magnesium replacement prevents AKI in unselected ICU patients. A small report by Barbosa et al. suggested a lower AKI incidence after correction of asymptomatic hypomagnesemia, but this signal requires confirmation in adequately powered randomized trials with standardized replacement, clear timing, and patient-centered renal outcomes. Magnesium administration may be beneficial for other recognized indications, but those indications should not be extrapolated automatically into a renoprotective claim.^{29 37 42 44}

A sensible preventive bundle remains focused on proven principles: optimize perfusion while avoiding unnecessary fluid overload; promptly treat infection and shock; review nephrotoxins and adjust doses; monitor creatinine and urine output; avoid preventable contrast or drug exposure; and seek early nephrology input for progressive AKI or complex electrolyte disturbance. Serum magnesium can be added to this bundle as a low-cost indicator of physiological vulnerability, particularly when repeated abnormalities coexist with other evidence of tubular stress or systemic deterioration.^{4 6 31 32 37}

The practical value of magnesium is likely greatest at the bedside during dynamic reassessment. A patient who develops low magnesium after admission should trigger a search for a change in physiology: increasing urine output after diuresis, new gastrointestinal loss, uncontrolled hyperglycemia, aminoglycoside exposure, a fall in albumin, or the onset of sepsis. This does not establish that magnesium caused the deterioration. It may, however, reveal a preventable loss process at the same time that other kidney-protective actions are considered. Repeating the measurement after correction or after a major treatment change helps distinguish persistent wasting from a transient shift.^{10 18 19 33}

Where serum magnesium is normal but clinical suspicion of depletion remains high, the result should be interpreted conservatively rather than used to dismiss risk. This situation can occur in patients with marked hypoalbuminemia, changing acid-base status, recent transfusion, or substantial intracellular shifts. The potential role of ionized magnesium is attractive, but routine measurement is not yet supported by consistent outcome data or universal analytical standards. Units that use it should establish local specimen-handling procedures and reference intervals before linking a result to treatment pathways.^{13 16 33 44}

Renal replacement therapy creates a separate clinical setting. Magnesium balance depends on the modality, dialysate or replacement-fluid composition, delivered dose, residual kidney function, and concurrent intravenous or enteral intake. Both depletion and accumulation can occur if treatment is not monitored carefully. Regular electrolyte review is therefore required throughout continuous kidney replacement therapy, particularly in patients with sepsis, ongoing gastrointestinal losses, or concurrent medications that affect tubular transport. Replacement should be documented as part of the overall fluid and electrolyte prescription.^{30 32 44}

Communication across the ICU team is important. The clinician ordering magnesium, the bedside team administering replacement, the pharmacist reviewing nephrotoxins, and the nephrologist assessing evolving AKI may each see a different part of the problem. A simple daily review can connect these elements: identify the magnesium trend, note replacement given, review filtration and urine output, list active losses and medications, and state whether further measurement is needed. This avoids the common pattern of repeated empiric replacement without identifying why the level remains low or whether renal function is deteriorating.^{6 10 31 32}

Magnesium results should also be interpreted with restraint in end-of-life care and severe multiorgan failure. Correction of a biochemical abnormality may be appropriate for symptoms or safety, but it should not obscure broader goals of care or create unrealistic expectations of renal recovery. In patients with rapidly worsening AKI, the priorities remain assessment of reversibility, appropriate support, medication adjustment, and timely decisions about kidney replacement therapy. Magnesium is supportive information within this broader management process.^{4 32 45}

Research Priorities

Future studies should define magnesium phenotypes more rigorously. This includes measuring total and, where feasible, ionized magnesium at prespecified times; distinguishing admission values from values after resuscitation; documenting albumin, acid-base state, urinary losses, nutrition, and magnesium-containing therapies; and using standardized KDIGO outcomes. Analyses should account for baseline kidney function and time-varying confounding, because both magnesium and AKI evolve rapidly during critical illness.^{16 24 33 36 37}

Prospective multicenter cohorts should test whether magnesium improves discrimination, calibration, or clinical



decision-making beyond established ICU severity scores and AKI risk factors. The key question is not whether magnesium has a statistically significant association in a model, but whether knowing it changes surveillance or treatment in a way that improves outcomes. Such studies should report the incremental value of magnesium and evaluate clinically meaningful endpoints, including persistent AKI, kidney replacement therapy, kidney recovery, major adverse kidney events, and longer-term kidney function.^{8 31 32 37 41}

Interventional trials are ultimately required. They should enroll patients with a clearly defined magnesium deficit before AKI has become established, use a reproducible replacement strategy, and balance potential benefit against the risk of hypermagnesemia in impaired filtration. Stratification by sepsis, diuretic exposure, baseline chronic kidney disease, and renal replacement therapy may be necessary. Until these data are available, magnesium measurement should be viewed as clinically useful supportive information, not as a validated trigger for kidney-protective pharmacotherapy.

Trial design deserves particular care. A magnesium-repletion trial that enrolls patients after creatinine has risen may be testing treatment of established injury rather than prevention. Conversely, a trial that includes patients with mild biochemical reductions unrelated to body depletion may dilute any treatment effect. Eligibility should combine a prespecified biochemical definition with a clinical exposure profile, such as sepsis, shock, nephrotoxin exposure, or major surgery. Randomization should occur early, and the protocol should address concurrent potassium replacement, fluid strategy, glycemic control, and kidney replacement therapy because each can modify magnesium balance and renal outcomes.^{1 31 37 42 44}

Outcome selection should also extend beyond a single peak creatinine value. Incident KDIGO AKI, severity stage, duration, persistent dysfunction, need for kidney replacement therapy, and kidney recovery capture different dimensions of clinically meaningful injury. Mortality remains important but is too nonspecific to serve as the only endpoint in a multifactorial ICU syndrome. Longer follow-up for chronic kidney disease and recurrent AKI would clarify whether magnesium status is linked to renal resilience after discharge. Transparent reporting of missing baseline creatinine and competing risks is essential.^{3 8 9 32 41}

Research should include resource-limited settings, where serum magnesium is more accessible than many emerging biomarkers and where AKI prevention strategies may have particular value. External validity requires enrollment across medical, surgical, neurologic, and mixed ICUs, with transparent reporting of laboratory methods and local replacement protocols. A low-cost test will improve care only if it leads to feasible action; studies should therefore evaluate implementation, workload, cost, and unintended consequences alongside predictive performance.^{7 33 34 37}

Strengths and Limitations of the Evidence

This literature offers a coherent biological rationale and a consistent observational signal that magnesium abnormalities identify a vulnerable ICU population. It also has major limitations: heterogeneous thresholds, use of total rather than ionized magnesium, variable sampling times, small cohorts, inconsistent adjustment for confounding, and mixed outcome definitions. The evidence for replacement as an AKI-prevention strategy is especially limited. These limitations explain why magnesium is promising as a component of risk assessment but is not yet a validated independent biomarker or therapeutic target for routine AKI prevention.

The current thesis contributes prospective data from a real-world ICU setting and appropriately focuses on incident AKI among patients who entered with preserved kidney function. Its findings should nevertheless be interpreted within the limitations of a small single-center observational cohort. A limited event count constrains the stability of multivariable models, and serum total magnesium may not reflect active or intracellular magnesium status. These limitations are common throughout the literature and should motivate confirmation, not premature clinical extrapolation.

A further strength of the evidence base is its consistency with renal physiology: magnesium disturbance is credible in patients exposed to diuresis, sepsis, drugs, nutritional compromise, and tubular stress. Its weakness is that these same factors are powerful causes of AKI. The research agenda must therefore move beyond documenting prevalence and unadjusted associations. It should demonstrate whether magnesium measurement adds predictive information after standard clinical assessment and whether correcting a deficit changes a patient-important renal trajectory.

Conclusion

Hypomagnesemia is frequent in critical illness and is associated with a higher risk of AKI across several observational settings. Its biological links to tubular energy metabolism, vascular function, electrolyte regulation, and inflammatory stress make this association plausible. In practice, serum magnesium should prompt a structured review of renal risk and correctable causes of deficiency, while serial AKI surveillance and established preventive measures remain essential. Larger prospective studies and randomized trials are needed to establish whether magnesium-guided management can improve kidney outcomes.^{10 24 27 28 29}



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