# Simultaneous Measurement of Ionized and Total Calcium in Intensive Care Unit Patients

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**Abstract**

**Purpose:** This study was undertaken to determine the relationship between total magnesium and ionized magnesium in critically ill and injured patients. **Methods:** Eighty consecutive intensive care unit (ICU) admissions were evaluated and 34 patients were enrolled in the study. Patients were enrolled who had in- dwelling arterial catheters and were within 4 days of ICU admission. Six milliliters of blood was collected and assayed simultaneously for total and ionized magnesium, total and ionized calcium, and albumin level. An Acute Physiology and Chronic Health Evaluation (APACHE II) score was calculated at the time of blood collection. **Results:** The results of our study show a strong correlation between ionized and total magnesium (R =.903) that was not seen between ionized and total calcium (R = 0.748). We found total hypomagnesemia in 18% and ionized hypomagnesemia in 21% of ICU patients. We also found that 14.7% (5 of 34) of our patients had ionized hypermagnesemia whereas none displayed total hypermagnesemia. We did not find a correlation between APACHE II, sex, race, albumin level, and any electrolyte level. The mortality rate in the subjects studied was 21% (7 of 34). **Conclusions:** Based on our results we would recommend that intensivists directly measure ionized calcium whereas ionized magnesium can be inferred from total magnesium.

**Keywords:** total magnesium; ionized magnesium; ICU; Ionized Calcium; Hypermagnesemia

## Introduction

Magnesium is essential for normal cellular functions and is the second most abundant intracellular cation.1 Magnesium serves as a cofactor for several enzymes required for electrolyte homeostasis and is also necessary for mem- brane stability, cell division, and generation of action potentials (**Walter, 2021**). Hypomagnesemia occurs in 40% of hospitalized patients **(Mekakas et al., 2022).** approximately 60% of postoperative patients,2 65% of medical intensive care unit (ICU) patients and up to 90% of surgical ICU patients **(Moris et al., 2021).** Hypomagnesemia has been implicated in the development of cardiovascular dysfunction and the systemic inflammatory response syndrome in ICU patients **(Kinesya et al., 2021)**. Ionized magnesium is the regulated and physio-logically active form of this electrolyte **(Crocker et al., 2020).** However, current magnesium supplementation is based on total serum magnesium measurement, although this might not accurately reflect ionized magnesium. This could be important because previous research with other cations, such as calcium, has shown that there is poor correlation between total and ionized electrolyte values, suggesting the need for ionized calcium measurement **(Cho et al., 2021).** Furthermore, the relaIonized magnesium is the regulated and physiologically active form of this electrolyte. However, current magnesium supplementation is based on total serum magnesium measurement, although this might not accurately reflect ionized magnesium. This could be important because previous research with other cations, such as calcium, has shown that there is poor correlation between total and ionized electrolyte values, suggesting the need for ionized calcium

measurement. **(Mittal et al., 2019).** Furthermore, the relationship between total serum magnesium and serum ionized magnesium in critically ill patients has not been studied. Presumably, similar to hypomagnesemia, ionized hypomagnesemia occurs in the critically ill though this must be inferred from intracellular or ultrafilterable magnesium values and not from direct ionized magnesium measurements **(Bom et al., 2021).** The ability to directly measure ionized magnesium.

Seven of these formulas estimated iCa and 15 were directed toward predicting a "corrected" totCa. Adult patients admitted to the trauma intensive care unit who received specialized nutrition support were consecutively recruited for study. Patients who received blood products, i.v. calcium, or therapeutic doses of heparin within 24 hours before the laboratory measurements or had a history of cancer, bone disease, parathyroid disease, hyperphosphatemia (> or = 6 mg/dL), hyperbilirubinemia (> 3.5 mg/dL), or renal failure requiring dialysis were excluded. The 22 published methods were analyzed for sensitivity, specificity, percentage false negatives, and percentage false positives for predicting hypocalcemia or hypercalcemia. RESULTS: One hundred patients were studied 4.9 +/- 3.3 days postinjury and were receiving enteral nutrition (n = 81), parenteral nutrition (n = 18), or both (n = 1) at the time of study. Twenty-one patients were hypocalcemic (iCa < or = 1.12 mmol/L) and 6 were hypercalcemic (iCa > or = 1.32 mmol/L). The mean sensitivity of the 22 methods for assessing hypocalcemia was 25% +/- 32% and the specificity was 90% +/- 18%. Although the average percentage of false positives for assessing hypocalcemia was 10% +/- 18%, the mean percentage of false negatives was inordinately high at 75% +/- 32%. The most common method for determination of "corrected" totCa concentration ["corrected" calcium = totCa + (0.8 x (4-serum albumin concentration))] had a sensitivity of only 5%. The McLean-Hastings nomogram method, the most common method for estimating serum iCa concentration, had a sensitivity of 67% but unfortunately also had a significant false-positive rate of 27%. Serum totCa correlated modestly with iCa (r2 =.334, p <.001). Those patients with a serum albumin < or = 2 g/dL (n = 43) had a significantly higher prevalence of hypocalcemia than those with a higher serum albumin concentration (37% incidence of hypocalcemia vs 10%, respectively, p <.002). Aberrations in calcium homeostasis are frequent (27%) in postresuscitative critically ill multiple trauma patients. Methods for predicting hypocalcemia lack sensitivity and are often associated with an unacceptable rate of false negatives. Predictive methods for estimating ionized or corrected serum concentrations should not be used. Direct measurement of serum iCa concentration is indicated for assessing calcium status for this population.

The ability to directly measure ionized magnesium has been difficult before the development of ionspecific electrodes. However, recently available blood gas analyzers have magnesium-selective electrodes that will enable the intensivist to measure ionized magnesium in critically ill and injured patients. Thus, the purpose of this study was to determine the relationship between simultaneous measurement of total and ionized magnesium in ICU patients by using a commercially available electrode.

## 1. Patient and methods

### 2.1 Design of the Study

This study is a retrospective cross-sectional study. All of the acute appendicitis patients at our hospital had open appendectomy due to the facility availability of equipment.

### 2.2 Setting of the study

This study included the patients who referred from 01/2024 to 06/2025.

### 2.3 The study instruments and sampling

We evaluated all the patients who had undergone open appendectomy, with Alvarado scores between 4-7 and divided them in two groups: (group A) were those patients that had abdominopelvic ultrasound as an accessory modality for diagnosing AA which was carried out by radiology resident prior to their surgery and (group B) were those who did not have any imaging study before their surgeries. Diagnosis of AA was made through "acute appendicitis" or "gangrenous appendix" written in the histopathology results of the appendectomy.

### 2.4 Inclusion criteria

Patients age below 15 and above 60, patients with no medical disease (past medical history negative).

### 2.5 Exclusion criteria

Lack of histopathological report, Alvarado score below 4 and above 7 and incomplete information needed for calculating the Alvarado score.

### 2.6 Study protocol

After approval by the Committee for the Protection of Human Subjects of the University of Texas Health Sciences Center, we obtained informed consent from 34 acutely ill and injured patients who met study criteria. Eighty consecutive patients who met admission criteria to the neurologic and shocktrauma ICUs, had indwelling

arterial lines, and were within 4 days of admission, were evaluated for inclusion in the study. Subjects were excluded from the study if they had a hemoglobin level of less than 10 g/dL, were receiving blood products, or were receiving magnesium or calcium infusions (n = 46). Six milliliters of blood was collected anaerobically from the arterial catheter by using a nonheparinized, 10-mL plastic syringe (Becton Dickinson, Lincoln Park, NJ). While being mixed by gentle inversion, 2 mL of blood was dispensed by use of a 3-way plastic stopcock (Baxter Edwards Healthcare, Valencia, CA) into our standard arterial blood gas syringe (Aspirator; Marquet Medical Products, Englewood, CO) for ionized calcium and ionized magnesium measurement. Three milliliters of e computed to examine the association among study variables. Simple linear regression analyses were conducted to investigate the relationships between total and ionized calcium and between total and ionized magnesium. Multiple linear regression analyses were also blood was dispensed into 3-mL tubes (Vacutainer; Becton Dickinson, Rutherford, NJ) for albumin, total magnesium, and total calcium measurement. Ionized magnesium and calcium were assayed within 5 minutes of blood collection (Stat Profile Ultra C; Nova Biomedical,Waltham, MA). Albumin, total magnesium, and total calcium were assayed in our hospital laboratory. Acute Physiology and Chronic Health Evaluation (APACHE II) scores were determined in each patient at the time blood was collected.

### 2.7 Statistical analysis

Data are represented as mean ± standard deviation. Pearson correlation coefficients were
performed to identify significant independent risk factors for ionized calcium and ionized magnesium. Statistical Analysis System (SAS; Cary, NC) software was used for the analysis.

## Results

Twenty-five of the subjects were men and 9 were women. Fifty-three percent of the patients were Caucasian, 20% Hispanic, 15% African American, and 12% Asian. Mean APACHE II score was 16.86 ± 8.31. The mortality rate in the subjects studied was 21% (7 of 34). A summary of electrolyte results and albumin is presented in Table 1. Fig 1 shows the linear regression fit between total magnesium and ionized magnesium. We did find a strong correlation between total magnesium and ionized magnesium ($R \leq .903$). Fig 2 shows the linear regression fit between total calcium and ionized calcium. The correlation between total calcium and ionized calcium ($R \leq .748$) is less than that between total magnesium and ionized magnesium. We did not find a significant correlation between APACHE II, sex, race, albumin level, and any elec- trolyte level.

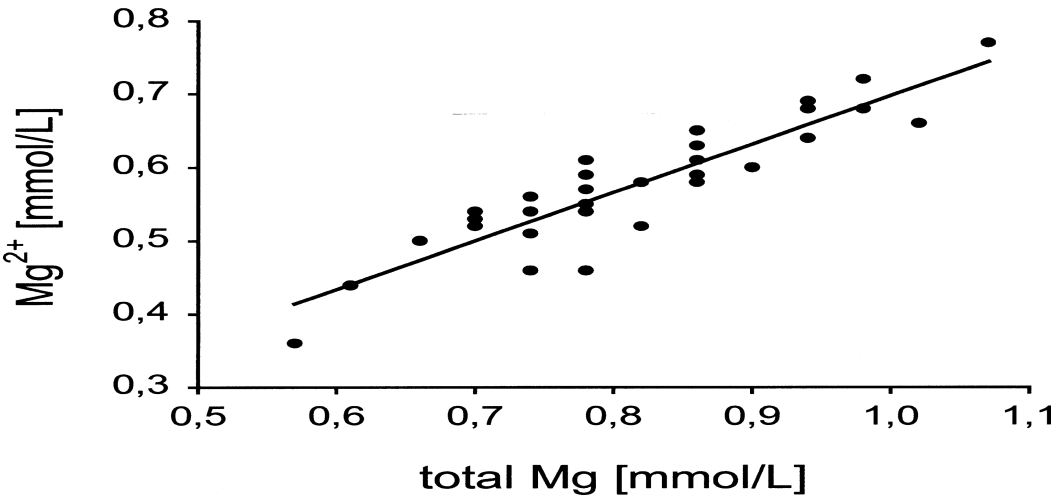


**Fig 1.** Ionized magnesium versus total magnesium. y = .66 × .039; P < .0001; r2 = .81; n = 34.

**Table 1.** Summary of Albumin and Electrolyte Data

| | Albumin mg/dL | Mg mmol/L | $Mg^{2+}$ mmol/L | Ca mmol/L | $Ca^{2+}$ mmol/L |
|---|---|---|---|---|---|
| Mean | 2.81 | 0.82 | 0.58 | 1.93 | 1.05 |
| SD | 0.77 | 0.12 | 0.08 | 0.19 | 0.08 |
| Range | 1.5–4.6 | 0.60–1.07 | 0.36–0.77 | 1.70–2.33 | 0.87–1.22 |
| Hyperelectrolyte | | 0 | 5 | 0 | 0 |
| Normal electrolyte | | 28 | 22 | 3 | 9 |
| Hypoelectrolyte | | 6 | 7 | 21 | 25 |
| Total electrolyte | | 34 | 34 | 24* | 34 |
| % Hypoelectrolyte | | 18 | 21 | 88 | 74 |

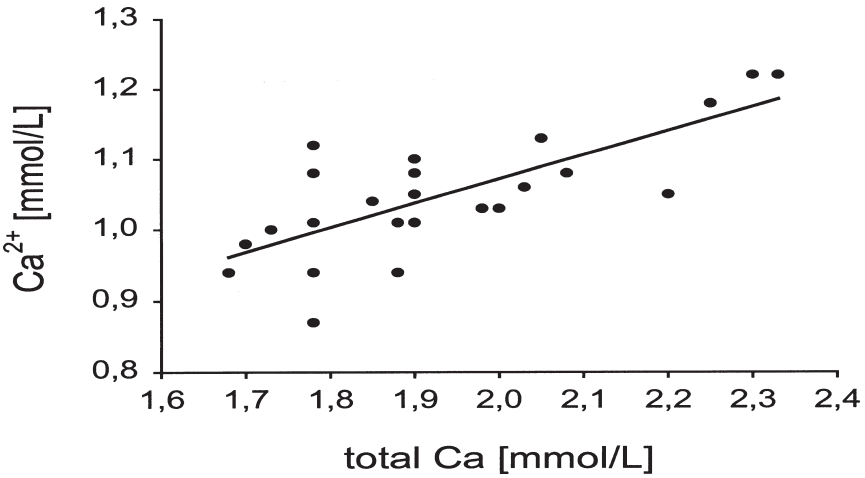


**Fig 2.** Ionized calcium versus total calcium. y = .34 × .038; P < .0001; r2 = .56; n = 34.

## Discussion

In the ICU, magnesium deficiency may occur as a result of poorly controlled diabetes, alcohol, diarrhea, or malabsorption, or owing to renal losses from drugs such as aminoglycosides indirect- ics.13 Magnesium deficiency is associated with a number of abnormalities including other electrolyte derangements, neuromuscular instability, respiratory muscle weakness, dysrhythmias, and myocardial ischemia. **(Kumar et al., 2020)**. Independent of severity of illness, as measured by APACHE II, hypomagnesemia is associated with a doubling of the mortality in medical ICU patients. Indeed, the correction of hypomagnesemia has decreased hypomagnesemia associated morbidity. Therefore, it is essential that early diagnosis of hypomagnesemia is made and treatment initiated **(Yilmaz et al., 2018).** Before recent technological advances, the serum magnesium concentration remained the only readily available test to assess magnesium status in most ICUs. Zaloga (**Zaloga, G. P., et al11997**), found that normal total serum calcium and magnesium concentrations essentially ruled out ionized hypocalcemia or ultra filterable hypomagnesemia. Thus, these patients did not re- quire routine measurements of ionized or ultrafilterable calcium or magnesium levels. Our data would support these conclusions as they relate to magnesium but not to calcium. Similar to Zaloga et al,[15] we found that total magnesium and ionized magnesium were closely correlated but we did not find a strong correlation between total calcium and ionized calcium.

We found total hypomagnesemia in 18% and ionized hypomagnesemia in 21% of ICU patients. We also found that 14.7% (5 of 34) of our patients had ionized hypermagnesemia whereas none of our patients displayed total hypermagnesemia. Similar to Chernow et al, we did not find a correlation be- tween total or ionized magnesium and severity of illness. Based on our results we would recommend that intensivists directly measure ionized calcium whereas ionized magnesium can be inferred from total magnesium.

## Conclusion:

The McLean-Hastings nomogram method, the most common method for estimating serum iCa concentration, had a sensitivity of 67% but unfortunately also had a significant false-positive rate of 27%. Serum totCa correlated modestly with iCa (r2 =.334, p <.001). Those patients with a serum albumin < or = 2 g/dL (n = 43) had a significantly higher prevalence of hypocalcemia than those with a higher serum albumin concentration (37% incidence of hypocalcemia vs 10%, respectively, p <.002). Aberrations in calcium homeostasis are frequent (27%) in postresuscitative critically ill multiple trauma patients. Methods for predicting hypocalcemia lack sensitivity and are often associated with an unacceptable rate of false negatives. Predictive methods for estimating ionized or corrected serum concentrations should not be used. Direct measurement of serum iCa concentration is indicated for assessing calcium status for this population.

**Conflict of Interest**

The authors declare no conflict of interest

**References:**

**Bom, W. J., Scheijmans, J. C., Salminen, P., & Boermeester, M. A. (2021).** Diagnosis of uncomplicated and complicated appendicitis in adults. *Scandinavian journal of surgery*, *110*(2), 170-179.

**Cho, S. U., & Oh, S. K. (2023).** Accuracy of ultrasound for the diagnosis of acute appendicitis in the emergency department: A systematic review. *Medicine*, *102*(13), e33397.

**Crocker, C., Akl, M., Abdolell, M., Kamali, M., & Costa, A. F. (2020).** Ultrasound and CT in the diagnosis of appendicitis: accuracy with consideration of indeterminate examinations according to STARD guidelines. American Journal of Roentgenology, 215(3), 639-644.

**Hadi Shalan, B., Tariq Hasson, Z., Hadi Shaalan, A., & Abd Elmohsen Abo El Nour, R. (2024).** Post-Operative Urinary Retention Beyond Spinal Anesthesia. *Egyptian Journal of Health Care*, *15*(3), 1020-1027.

**Kinesya, E., Cintya, E. P., Dorothy, M. J., Ennaidi, N. N., Rusti, H. F., Mannagalli, Y., & Pasaribu, E. A. (2022).** Diagnostic accuracy of Alvarado score components in patients with appendicitis: Systematic review and meta-analysis approach. *Health Sciences Review*, *2*, 100018.

**Kumar V, Abbas AK, Fausto N,** Aster JC. *Robbins & Cotran pathologic basis of disease.* 8th ed. Elsevier Health Sciences; 2020. pp. 826–827.

**Mekakas, A., Nagorni, E. A., & Tablaridis, T. (2022).** Complicated Appendicitis: A surgical controversy concerning risk factors, diagnostic algorithm and therapeutic management. *Doubts, problems and certainties about acute appendicitis*, *10*.

**Mittal MK, Dayan PS, Macias CG, Bachur RG, Bennett J, Dudley NC, et al.** Performance of ultrasound in the diagnosis of appendicitis in children in a multicenter cohort. *Acad Emerg Med.* 2019;20(7):697–702.

**Moris, D., Paulson, E. K., & Pappas, T. N. (2021).** Diagnosis and management of acute appendicitis in adults: a review. *Jama*, *326*(22), 2299-2311.

**Yilmaz M, Akbulut S, Kutluturk K, Sahin N, Arabaci E, Ara C, et al.** Unusual histopathological findings in appendectomy specimens from patients with suspected acute appendicitis. *World J Gastroenterol.* 2018;19(25):4015–22..

**ZALOGA, G. P., WILKENS, R., TOURVILLE, J., WOOD, D., & KLYME, D. M. (1987)**. A simple method for determining physiologically active calcium and magnesium concentrations in critically ill patients. Critical care medicine, 15(9), 813-816.