

Calcium Correction for Hypoalbuminemia and Hyperalbuminemia

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Abstract

Serum calcium levels are influenced by several physiological factors, particularly the concentration of albumin, to which a significant portion of calcium is bound. This dependency can lead to misleading total calcium values in patients with hypoalbuminemia or hyperalbuminemia, where ionized calcium, the biologically active form, remains unchanged. A correction formula for serum calcium, accounting for abnormal albumin levels, enables clinicians to more accurately assess calcium status, avoiding misdiagnosis of pseudohypocalcemia or pseudohypercalcemia. Additionally, conditions such as multiple myeloma (via elevated gamma globulins) or shifts in extracellular pH can alter the balance between bound and ionized calcium, complicating the interpretation of total calcium measurements. In such cases, direct measurement of ionized calcium is recommended when corrected calcium suggests abnormality.

Corrected calcium values assist in determining when further evaluation is warranted for true hypo- or hypercalcemia. Common causes of hypocalcemia include vitamin D deficiency or resistance, hypoparathyroidism, renal or hepatic dysfunction, malabsorption syndromes, and certain medications or toxic exposures. Conversely, hypercalcemia may result from primary hyperparathyroidism, malignancy, excessive vitamin D or A intake, granulomatous diseases like sarcoidosis, specific medications, dehydration, or rare genetic disorders such as familial hypocalciuric hypercalcemia. Recognizing when total calcium levels misrepresent ionized calcium is essential for accurate diagnosis, appropriate testing, and management of the underlying condition.

HOW TO USE

When to Use

Use in patients with albumin below the laboratory value of lower limit of normal or in those with albumin above the laboratory value of upper limit of normal.

Pearls and Pitfalls

The total amount of calcium in the serum is found bound to albumin and multiple organic and inorganic anions, while some circulates as ionized or free calcium. Changes in albumin can result in a decrease in total calcium (pseudohypocalcemia) or increase in total calcium (pseudohypercalcemia), without changing ionized calcium. Rarely, changes in gamma globulins (in multiple myeloma) can result in pseudohypercalcemia.

An increase in extracellular pH can result in changes in ionized calcium without changing total calcium. The formula assumes stable physiological conditions and may

misclassify true calcium status in certain patients, such as those with abnormal pH, critical illness, or paraproteinemia. Alternative methods, including direct ionized calcium measurement or newer adjustment formulas, may offer greater accuracy.

The number of validation studies in diverse patient populations, such as the critically ill or those with acid-base disorders, are limited, and the formula's performance remains inconsistent in these groups.^{1-3, 4}

Why to Use

Correcting serum calcium levels for levels of albumin outside of the normal range will allow clinicians to identify patients whose ionized calcium levels may be out of normal range despite total calcium levels appearing to be within normal range; or those whose ionized calcium levels are likely in normal range while their total calcium levels appear abnormal.

NEXT STEPS

Advice

Consider measuring ionized calcium to confirm conclusions drawn after correcting for serum calcium.

Management

If calcium is confirmed to be outside of normal range, consider a diagnostic evaluation to determine the etiology. Common causes of Hypocalcemia include vitamin D inadequacy or resistance, hypoparathyroidism, renal disease or end-stage liver disease causing vitamin D inadequacy, malabsorption, post-gastric bypass surgery, drugs and toxic ingestions, hypomagnesemia.

Common Causes of Hypercalcemia include primary hyperparathyroidism, vitamin D toxicity, vitamin A toxicity cancer, sarcoidosis, medications (e.g. lithium and thiazide diuretics), dehydration or volume depletion, genetic conditions (e.g. familial hypocalciuric hypercalcemia), and little or no movement.

EVIDENCE

Evidence Appraisal

Validity: The formula is based on well-established physiological principles of calcium binding to albumin, but

its derivation was not rigorously documented in a broad population, and comparisons to ionized calcium (the gold standard) are limited in quality and scope.

Reliability: As validation studies across diverse patient populations (e.g., critically ill, those with acid-base disorders) are lacking, and its performance is inconsistent in these groups.

Applicability: The formula is easy to calculate, widely used in clinical practice, and often included in lab reports. However, its usefulness is limited in situations where direct ionized calcium measurement is feasible.

Limitations and sources of error: The formula assumes stable physiological conditions and may misclassify true calcium status in certain patients (such as those with abnormal pH, critical illness, or paraproteinemia), and alternative approaches like direct ionized calcium measurement or newer adjustment formulas may provide greater accuracy.

Formula

Corrected Calcium = $(0.8 * (\text{Normal Albumin} - \text{Pt's Albumin})) + \text{Serum Ca}$

Note: formula assumes albumin units in g/dL.

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