

## Hypocalcemia Diagnosis in the Surgical Environment

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### ABSTRACT

Hypocalcemia, characterized by a total serum calcium level below 8.5 mg/dL (corrected for albumin) or an ionized serum calcium level below 4.65 mg/dL, presents a spectrum of clinical manifestations ranging from asymptomatic to life-threatening. Common after neck procedures, early detection and appropriate management are essential. Diagnostic tools include assessing calcium levels, correcting for albumin, and determining the underlying cause through tests like intact parathyroid hormone, serum phosphorus, magnesium, and creatinine. Treatment involves calcium replacement and addressing the root cause, with potential complications such as neuromuscular excitability and cardiac arrhythmias. Prognosis varies based on severity and underlying factors, emphasizing the importance of avoiding diagnostic pitfalls and overtreatment in chronic cases. ECG and genetic testing contribute to accurate diagnosis, aiding in differentiating causes like autosomal dominant hypocalcemia. Recognizing factitious hypocalcemia related to hypoalbuminemia or binding protein alterations is crucial. Understanding the pH-calcium relationship guides clinical evaluation. Holistic management requires a collaborative approach, emphasizing patient engagement and follow-up care.

**KEYWORDS:** Hypocalcemia, calcium levels, diagnostic tools, complications, prognosis, ECG, genetic testing, factitious hypocalcemia, pH-calcium relationship, management.

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### INTRODUCTION

Hypocalcemia arises when the total serum calcium level drops below 8.5 mg/dL (corrected for albumin) or when the ionized serum calcium level falls below 4.65 mg/dL (1.16 mmol/L)<sup>1, 2</sup>. This condition is commonly observed after bilateral neck procedures, such as parathyroidectomy or total thyroidectomy, but can be effectively managed prophylactically<sup>3</sup>. The clinical manifestations of hypocalcemia span from asymptomatic to life-threatening, depending on the severity of calcium deficiency<sup>3, 4</sup>. The primary diagnostic tool for detecting hypocalcemia is a laboratory test for total serum calcium or ionized calcium levels, with additional testing needed to determine the underlying cause. In severe or symptomatic cases, including any severe case, electrocardiogram (ECG) evaluation and hospital admission are indicated<sup>5, 6</sup>.

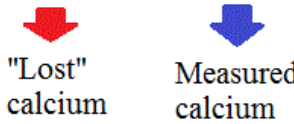
The primary treatment for hypocalcemia involves calcium replacement and addressing the underlying cause<sup>7</sup>. Complications associated with hypocalcemia include increased neuromuscular excitability or tetany, seizures, and cardiac arrhythmias<sup>3, 8</sup>. The prognosis varies based on the severity and underlying cause, with critically ill patients experiencing higher mortality rates in the presence of hypocalcemia<sup>9</sup>. It is crucial to avoid pitfalls such as failing to account for binding protein abnormalities, like hypoalbuminemia, which can lead to misinterpretation of serum calcium levels. Additionally, overtreatment in patients with chronic forms of hypocalcemia can result in ectopic calcifications, nephrolithiasis, and renal failure<sup>10</sup>.

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### CLASSIFICATION

Hypocalcemia is defined by a total serum calcium level below 8.5 mg/dL (corrected for albumin) or an ionized serum calcium level falling below 4.65 mg/dL (1.16 mmol/L)<sup>1</sup>. To correct for hypoalbuminemia, the formula for calculating the corrected total calcium level is as follows: Corrected total calcium level = measured total calcium level + (0.8 × [4 – measured albumin level in g/dL])<sup>11</sup>.

$$\begin{array}{l} \text{corrected Ca [mg/dl]} \\ = (4.0 - \text{albumin [g/dl]}) + \text{Ca [mg/dl]} \end{array}$$



This condition is classified into two categories:

**Mild Hypocalcemia:**

Total serum calcium level ranging from 8 to 8.5 mg/dL<sup>1</sup>.

Typically asymptomatic<sup>3,4</sup>.

**Severe Hypocalcemia:**

Total serum calcium level falls below 7.6 mg/dL<sup>1</sup>.

Symptoms are present at any level below the reference range<sup>5,6</sup>.

### DIAGNOSIS

Confirmation of hypocalcemia involves assessing the serum total or ionized calcium levels as the primary diagnostic tool. It is crucial to correct for albumin or acid-base abnormalities during the diagnostic process<sup>12</sup>. Determining the cause of hypocalcemia can be approached based on the likelihood of a specific diagnosis suggested by the patient's history and physical examination or through a stepwise examination<sup>13</sup>. First-line tests for all patients include assessing intact parathyroid hormone, serum phosphorus, serum magnesium, and creatinine. Additional tests, such as serum 25-hydroxyvitamin D, amylase, and creatine kinase, should be obtained based on the initial results<sup>14</sup>.



**Figure 1. ECG of a male with hypocalcemia. Characteristic elongation of ST-segment and QT prolongation**

Different scenarios may arise based on the test outcomes:

If there are high intact parathyroid hormone and low phosphorus levels, considerations may include vitamin D deficiency, acute pancreatitis, or drug-related causes<sup>15</sup>.

In cases of high intact parathyroid hormone and high phosphorus levels, potential causes such as tumor lysis or rhabdomyolysis should be considered<sup>15</sup>.

Low intact parathyroid hormone and high phosphorus levels may suggest hypoparathyroidism as the likely underlying cause<sup>16</sup>.

Measuring serum magnesium level is essential, and if normal, rare causes such as autosomal dominant hypocalcemia should be considered<sup>5</sup>.

In the laboratory, a serum calcium level below 8.5 mg/dL (corrected for albumin) confirms a diagnosis of hypocalcemia. The corrected total calcium level is calculated using the formula: Corrected total calcium level = measured total calcium level + (0.8 × [4 – measured albumin level in g/dL]). An ionized serum calcium level below 4.65 mg/dL further confirms the diagnosis, with a preference for this measurement in the presence of suspected binding protein abnormalities or acid-base disturbances<sup>1,11</sup>.

Assessing intact parathyroid hormone levels helps differentiate potential causes, including vitamin D deficiency, renal disease, pseudohypoparathyroidism, hypoparathyroidism, hypomagnesemia, and rare genetic causes such as autosomal dominant hypocalcemia or hungry bone syndrome. Additional tests, such as serum phosphorus, renal function, serum 25-hydroxyvitamin D, serum magnesium, and serum alkaline phosphatase, provide further discrimination of the underlying cause of hypocalcemia, considering conditions like severe vitamin D deficiency, secondary hyperparathyroidism, osteomalacia, and osteoblastic bone metastasis. If pancreatitis is suspected, assessing serum amylase levels is recommended<sup>15,16</sup>.

In cases of severe hypocalcemia, an electrocardiogram (ECG) is indicated for all patients. Acute hypocalcemia is known to cause the lengthening of the ST segment and prolongation of the QT interval, with the duration of the ST segment being inversely related to the serum calcium level. However, correlations between serum calcium levels and the length of the corrected QT interval can vary. It is essential to note that QT prolongation resulting from hypocalcemia can lead to ventricular arrhythmias<sup>5,6,13</sup>.

Apart from ECG, additional diagnostic tools may include genetic testing, especially in identifying cases of autosomal dominant hypocalcemia. Mutational analysis of the CASR gene is a common approach, requiring a venous blood sample from which DNA is extracted<sup>17</sup>.

### CONCLUSION

In terms of the differential diagnosis, the most common consideration is factitious (spurious) hypocalcemia. This can be caused by factors such as hypoalbuminemia or alterations in binding proteins. Acute respiratory alkalosis is highlighted as a potential cause, as it increases the avidity of albumin for calcium, transiently causing hypocalcemia. It's worth noting that for every 0.1 increase in pH, the ionized calcium level decreases by 0.14 mg/dL.

## Hypocalcemia Diagnosis in the Surgical Environment

In conclusion, hypocalcemia is a condition characterized by a total serum calcium level falling below 8.5 mg/dL (corrected for albumin) or an ionized serum calcium level falling below 4.65 mg/dL. It commonly occurs after bilateral neck procedures but can range from asymptomatic to life-threatening, depending on its severity. Proper diagnosis involves assessing total or ionized calcium levels and correcting for albumin or acid-base abnormalities. Initial tests include intact parathyroid hormone, serum phosphorus, serum magnesium, creatinine, and additional tests based on initial results.

Treatment primarily involves calcium replacement and addressing the underlying cause. Complications can include neuromuscular excitability, tetany, seizures, and cardiac arrhythmias. The prognosis varies based on severity and underlying causes, with critically ill patients having higher mortality rates. It is crucial to avoid pitfalls like failing to account for binding protein abnormalities and overtreatment in chronic cases.

Diagnostic tools, including ECG and genetic testing, play a crucial role in confirming and identifying specific causes, such as autosomal dominant hypocalcemia. The differential diagnosis includes factitious hypocalcemia caused by hypoalbuminemia or binding protein alterations. Understanding the relationship between pH and ionized calcium levels is vital in the evaluation process. Overall, managing hypocalcemia requires a comprehensive approach, close collaboration between healthcare providers and patients, and appropriate follow-up care.

### REFERENCES

- I. Hakami, Y., & Khan, A. (2019). Hypoparathyroidism. *Parathyroid Disorders*, 51, 109-126.
- II. Goltzman, D., Rosen, C., & Mulder, J. (2013). Etiology of hypocalcemia in adults. *UpToDate*, Waltham, MA. (Accessed on April 13, 2014).
- III. Pepe, J., Colangelo, L., Biamonte, F., Sonato, C., Danese, V. C., Cecchetti, V., ... & Cipriani, C. (2020). Diagnosis and management of hypocalcemia. *Endocrine*, 69, 485-495.
- IV. Aul, A. J., Fischer, P. R., O'Grady, J. S., Mara, K. C., Maxson, J. A., Meek, A. M., ... & Thacher, T. D. (2019). Population-based incidence of potentially life-threatening complications of hypocalcemia and the role of vitamin D deficiency. *The Journal of pediatrics*, 211, 98-104.
- V. Schafer, A. L., & Shoback, D. M. (2015). Hypocalcemia: diagnosis and treatment.
- VI. Rosa, K. M., Matos, L. L. D., Cernea, C. R., Brandão, L. G., & Araújo Filho, V. J. F. D. (2015). Postoperative calcium levels as a diagnostic measure for hypoparathyroidism after total thyroidectomy. *Archives of endocrinology and metabolism*, 59, 428-433.
- VII. Cooper, M. S., & Gittoes, N. J. (2008). Diagnosis and management of hypocalcaemia. *Bmj*, 336(7656), 1298-1302.
- VIII. Vakharia, J. D., & Topor, L. S. (2021). Hypocalcemia. *Endocrine Conditions in Pediatrics: A Practical Guide*, 29-38.
- IX. Kelly, A., & Levine, M. A. (2013). Hypocalcemia in the critically ill patient. *Journal of intensive care medicine*, 28(3), 166-177.
- X. Prins, A. (2010). Nutritional assessment of the critically ill patient. *South African Journal of Clinical Nutrition*, 23(1), 11-18.
- XI. Clase, C. M., Norman, G. L., Beecroft, M. L., & Churchill, D. N. (2000). Albumin-corrected calcium and ionized calcium in stable haemodialysis patients. *Nephrology Dialysis Transplantation*, 15(11), 1841-1846.
- XII. Meng, Q. H., & Wagar, E. A. (2015). Laboratory approaches for the diagnosis and assessment of hypercalcemia. *Critical reviews in clinical laboratory sciences*, 52(3), 107-119.
- XIII. Asmar, A., Mohandas, R., & Wingo, C. S. (2012). A physiologic-based approach to the treatment of a patient with hypokalemia. *American journal of kidney diseases*, 60(3), 492-497.
- XIV. Deyrup, A. T., D'Ambrosio, D., Muir, J., Deyrup, A., Knollmann-Ritschel, B., Scordino, T., ... & Lin, A. (2022). Essential laboratory tests for medical education. *Academic pathology*, 9(1), 100046.
- XV. Schattner, A., Dubin, I., Huber, R., & Gelber, M. (2016). Hypocalcaemia of malignancy. *Neth J Med*, 74(6), 231-239.
- XVI. Abate, E. G., & Clarke, B. L. (2017). Review of hypoparathyroidism. *Frontiers in endocrinology*, 7, 172.
- XVII. Roszko, K. L., Stapleton Smith, L. M., Sridhar, A. V., Roberts, M. S., Hartley, I. R., Gafni, R. I., ... & Nemeth, E. F. (2022). Autosomal dominant hypocalcemia type 1: A systematic review. *Journal of Bone and Mineral Research*, 37(10), 1926-1935.