Research Article

Significance of measurement of corrected calcium in patients with normoalbuminemia

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ABSTRACT

Background: Total calcium (TC) level is influenced by the serum albumin level. Calcium is corrected for the lower range of albumin using different formula. While corrected calcium (CC) is frequently reported by laboratory when there is hypoalbuminemia, similar variation in albumin even in patients with normal albumin will result variation in total serum calcium. **Objectives:** This study is conducted to analyze the effect of CC measurement in clinical decision-making in patient with normal albumin level. **Materials and Methods:** In 579 patients with serum albumin between 3.2 and 5.5 g/dl by bromocresol green dye method, TC by Arsenazo III method were measured and CC were calculated. The discordance between TC and CC in relation to reference range is found in percentage. **Results:** The discordance between TC and CC was observed between 7.9-9.2 mg/dl and 10.3-10.7 mg/dl. Overall discordance rate in the range of 7.9-9.2 mg/dl was 20% and in the range of 10.3-10.7 mg/dl was 40%. **Conclusion:** When TC is around the upper and lower reference range, CC may affect clinical decision-making.

KEY WORDS: Corrected Calcium; Albumin; Normoalbuminemia; Measurement

INTRODUCTION

The total calcium (TC) of serum or plasma is distributed as free calcium, calcium bound to proteins, and calcium bound to inorganic anion. About half of the calcium in serum is bound to serum proteins, particularly albumin. Changes in albumin concentration cause changes in TC without affecting the physiologically and clinically important ionized calcium fraction.[1,2] Correction of calcium is done using different formulas when albumin is below the reference range. While correction of TC in patients with low serum albumin is frequently practiced, there are no data available as to effect of physiological variation in albumin on serum calcium. The current study compares serum calcium and corrected calcium (CC) in patients with normal serum albumin.

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About 80% of protein-bound calcium is associated with albumin, with the remaining 20% associated with globulins. Low total serum calcium (hypocalcemia) may be due to a reduction in albumin-bound calcium, the free fraction of calcium, or both. Hypoalbuminemia is the most common cause of apparent hypocalcemia on a standard biochemical profile, particularly in hospitalized patients, because 1 g/dl of albumin binds approximately 0.8 mg/dl of calcium.[1,3,4]

Adjusted or Corrected TC

Wide variation in the concentrations of compounds that bind calcium in blood will affect the measured TC concentration without changing the free calcium fraction. Several types of calculation have been suggested to "adjust" the measured calcium concentration. The goal is to produce a corrected

result that would have been found if the concentrations of all compounds that bind calcium had been within their respective reference intervals. In practice, only adjustments based on albumin are used.

The following two equations are used for results expressed as mg/dl and mmol/L, respectively:[1]
CC mg/dl = TC mg/dl + 0.8 [4 - measured albumin g/dl]
CC mmol/L = TC mmol/L + 0.02 [40 - measured albumin g/L]

Apart from above equation various other formula are also used.[2,3]
CC (mg/dl) = Calcium (mg/dl) - albumin (g/dl) + 4
CC (mg/dl) = Calcium - (0.676 × total protein (g/dl)) + 4.87
CC = Calcium (mmol/L) - (0.25 × albumin (g/l)) + 1.0

MATERIALS AND METHODS

The study is performed at New Civil Hospital, Surat Laboratory Services, an NABL accredited laboratory. Eight hundred consecutive serum specimens received in the laboratory with a request for calcium estimation were analyzed for calcium and albumin in Erba XL 640 AutoAnalyzer by Arsenazo III method for calcium and bromocresol green in succinic acid buffer at pH 4.2 for albumin.

Specimens included in this study were from different wards and outpatient departments. No account was taken of age, sex, or provisional diagnosis. Quality was satisfactory during the study period and assured by the use of multi-rule quality control procedures at two levels.[5] From this eight hundred samples, samples with normal range of albumin (3.2-5.2 mg/dl)[1] were selected for measurement of CC. CC concentrations were calculated by the following formula:
CC = 0.8(4 - serum albumin g/dl) + Total serum calcium mg/dl.

Sample containing albumin level <3.2 g/dl and >5.2 g/dl are not included in the study. Calcium reference range of 8.5-10.5 mg/dl is used.

For each sample, TC and CC were compared to find out which of the following condition is satisfied.
- TC and CC within reference range (concordance).
- TC and CC outside reference range (concordance).
- TC outside and CC inside reference range (discordance).
- TC inside and CC outside reference range (discordance).

Frequency and percentage of discordance were calculated for each calcium value between 8.5 and 10.5 (at 0.1 mg/dl interval).

RESULT

Figure 1 shows % of discordance with relation to serum calcium.

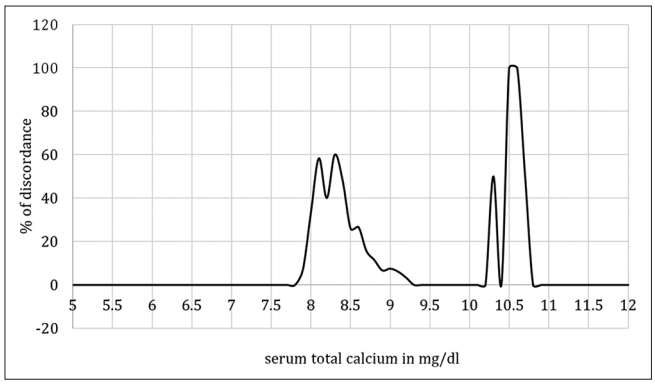

Figure 1: Relation of total serum calcium versus percentage of discordance

There are two distinct peaks of discordance between 7.9 and 9.2 (n = 353) mg/dl and 10.3 and 10.7 (n = 7) mg/dl. The discordance is concentrated around lower and upper limit of reference ranged (i.e., 8.5 and 10.5). Overall there is 20% discordance rate between 7.9-9.2 mg/dl and 40% discordance at 10.3-10.7 mg/dl. However, number of samples analyzed at 10.3-10.7 mg/dl range is very low, compared to 7.9-9.2 mg/dl range.

DISCUSSION

The study shows that if TC of a patient is within reference range but CC is not (and vice versa), clinicians need to make clinical decision based on TC or CC. Such situation may arise when TC and serum albumin are at both ends of their referenced range.

For example, in one patient in the study with serum calcium 8.0 mg/dl and serum albumin level 3.3 g/dl, CC was 8.56 mg/dl. Thus, in this patient, clinician looking at TC will consider the serum calcium abnormal, but actually, the lower result is due to albumin near lower limit of reference. In this patient, CC is within reference range; indicating that the patient's calcium homeostasis is normal.

Similarly, in another patient with serum calcium level 8.8 mg/dl and serum albumin level 4.4 g/dl, CC was 8.35 mg/dl. In this patient, serum albumin at upper range of reference, lower calcium is masked by higher value of albumin-bound calcium.

Both examples show that discordance in calcium and CC level with normal albumin level in patient may be clinically significant to make management decision.

Payne et al.[2] studied CC in 189 patients. The study included both normal and abnormal albumin. Seventy-five patients had normal calcium, which became abnormal on adjustment of albumin.

Payne et al.[3] concluded that it is impossible to interpret a patient's serum calcium concentration without some measurement of protein concentration.

However, parent X[6] concluded that the clinically justified adjustment due to hypoalbuminemia should not be extended to other situations, particularly, when albumin is increased.

The high rate of discordance at 7.9-9.2 mg/dl and 10.3-10.7 mg/dl between TC and CC indicates that clinical interpretation of laboratory data by clinician will differ if only TC is reported versus both TC and CC are reported. The study also shows that discordance becomes more obvious on borderline of the reference range. The laboratory may choose to report CC even when patient albumin is with in reference range, thereby giving a clearer idea to clinician about how to interpret serum calcium reports in patients.

CC was done only by using single formula. The other equations based on different parameters (e.g. total protein) needs to be evaluated similarly. This is of importance because calcium in serum also binds other serum proteins. It is an ionized form of calcium, which gives truly idea about the status of calcium homeostasis. Measurement of ionized calcium can improve conclusions of the study.

CONCLUSION

There is discordance between total and CC even when patient albumin is within normal range. Such discordance may be of clinical significance and routine use of CC at all ranges of albumin is advised.

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