ECRONICON OPEN ACCESS

EC ORTHOPAEDICS
Short Communication

# Ionized and Total Calcium, and the Secondary Hyperparathyroidism in Patients with Hypovitaminosis D

**Haider M Al Attia[1]* and Omran B Gatee[2]**

[1]*Department of Internal Medicine and Rheumatology, Universal Hospital, Abu Dhabi, UAE*

[2]*Department of Internal Medicine and Endocrinology, Burjeel Hospital, Abu Dhabi, UAE*

***Corresponding Author:** Haider M Al Attia, Department of Internal Medicine and Rheumatology, Universal Hospital, Abu Dhabi, UAE.

**Received:** December 05, 2017; **Published:** January 02, 2018

## Abstract

**Purpose:** In this retrospective study we tried to outline the relationship between the ionized calcium (iCa) and secondary hyperparathyroidism (SHPTH) in patients with hypovitaminosis D.

**Methods:** The records of 101 outpatients patients with hypovitaminosis D (25(OH)D < 30 ng /ml) who were also assayed for ionized calcium (iCa), total calcium (tCa) and PTH are presented. They were divided into two groups according to the level of their i Ca; subnormal iCa (G1) and another with normal levels (G2).

**Results:** 26 (25.5%) had i Ca < 1.16 mmol/l (G1) and 75 with normal levels (1.16 - 1.32 mmol/l) (G2), p = 0.0001. The age was not different in the two groups. The mean of iCa in G1 was significantly lower to that in G2 (1.10 +/- 0.11 vs. 1.23 +/- 0.12 mmol/l)respectively, p = 0.0001. The tCa was within normal values (eucalcemic range) in both groups respectively, yet 2 significantly lower in G1, (9.43 +/- 0.45, range 8.9 - 10.4 mg/dL vs.9.80 +/ -0.43, range 8.88 - 11.1 mg/dL) p = 0.0004. None a single case of hypocalcemia was identified. However, the mean of 25 (OH) D in both groups was not different. The R value was weakly positive in the correlation between the iCa and t Ca in both groups. The mean PTH was higher in G1, p = 0.007. 20 patients (20%) expressed secondary hyperparathyroidism (10 in each group, p = 0.009 with levels of 90.6 +/- 35.1 vs. 83.8 +/- 13.9 pg/ml respectively, p = 0.75). The R value was positive (0.2867) between the patients with subnormal iCa and SHPTH.

**Conclusion:** Subnormal ionized calcium exhibited higher degree of association/correlation with secondary hyperparathyroidism due to hypovitaminosis D than that of the total calcium. Ionized calcium to a great extent can be considered as the major stimulator of the PTH. Estimating it therefore should be considered essential in future studies addressing similar or other pertinent issues.

***Keywords:*** *Hypovitaminosis D; PTH; Ionized Calcium*

## Introduction

Serum (plasma) calcium exists in 3 distinct forms. Approximately 15% is complexed calcium bound to organic and inorganic anions, 40% is bound to albumin, and the remaining 45% circulates as free ionized calcium [1]. Serum total calcium (tCa) is routinely measured for diagnosing calcium disorders but may not reflect levels of the biologically active ionized calcium (iCa) in disease. Ionized calcium (iCa) is the form of calcium that is readily available to cells, and its measurement therefore is a more accurate reflection of the physiological calcium state than the total calcium. Specifically, reports suggest that ionized calcium is superior in identifying calcium disturbances in patients receiving transfusions with citrated blood, in critically ill patients, in patients with the late stages of chronic kidney disease (CKD), primary hyperparathyroidism and hypercalcemia of malignancy [2-5]. Low ionized calcium levels along with low total calcium may result from secondary hyperparathyroidism and from vitamin D deficiency [3].

## Patients and Methods

Records of 101 outpatients patients with hypovitaminosis D (25(OH)D < 30 ng /ml) were reviewed. The patients were also assayed for ionized calcium (iCa) by (direct ion selective electron method), total calcium (tCa) by (coloriometric method) and PTH by (ELICA). Data of patients with chronic renal failure, chronic liver disease, hypoalbuminemia, receiving loop diuretics, corticosteroids, calcium and vitamin D supplementation were not included. They were divided into two groups based on the level of iCa (normal level = 1.16 - 1.32 mmol/l). All patients were adult residents of Abu Dhabi, UAE.

## Results

26 (25.5%) had i Ca < 1.16 mmol/l (Group 1, G1) and 75 with normal levels (1.16 - 1.32 mmol/l) (Group 2, G2), p = 0.0001. The age was not different in the two groups (43.3 +/- 9.35 in G1 vs. 41.6 +/- 13.2 years in G2, p = 0.54. M: F 1.3:1 in G1 and G2. Table 1, is showing all relevant comparisons between the 2 groups. The R value was weakly positive in the correlation between the iCa and tCa in both groups (R = 0.2264 and 0.2876 respectively). The R value was positive (0.2867) between subnormal iCa and SHPTH in G1 patients (Figure 1), whereas another but rather unusual correlation was observed between higher levels of t Ca and SHPTH (Figure 2) in the same group.

| | G1 (26) | G2 (75) | P |
|---|---|---|---|
| Age (yrs) | 43.3+/-9.35 | 41.6+/-13.2 | 0.54 |
| Mean ( iCa), N (1.16-1.32n mol/L) | 1.10 +/-0.11 | 1.23 +/-0.12 | 0.0001 |
| Mean (t Ca), N (8.4-10.5 mg/dL) | 9.43+/-0.45 | 9.80+/-0.43 | 0.004 |
| Mean 25(OH)D,N > 30 ng/ml | 17.77 +/-5.33 | 18.5+/-5.47 | 0.52 |
| Patients with 25(OH)D < 10 ng/ml (deficient) | 3(11.5%) | 8 (10.5%) | 1.00 |
| Mean of PTH, N 15 - 65 pg/ml | 63.3+/-31.7 | 49.6 +/-17.6 | 0.007 |
| Number of patients with secondary HPTH | 10/26 | 10/75 | 0.009 |

***Table 1***

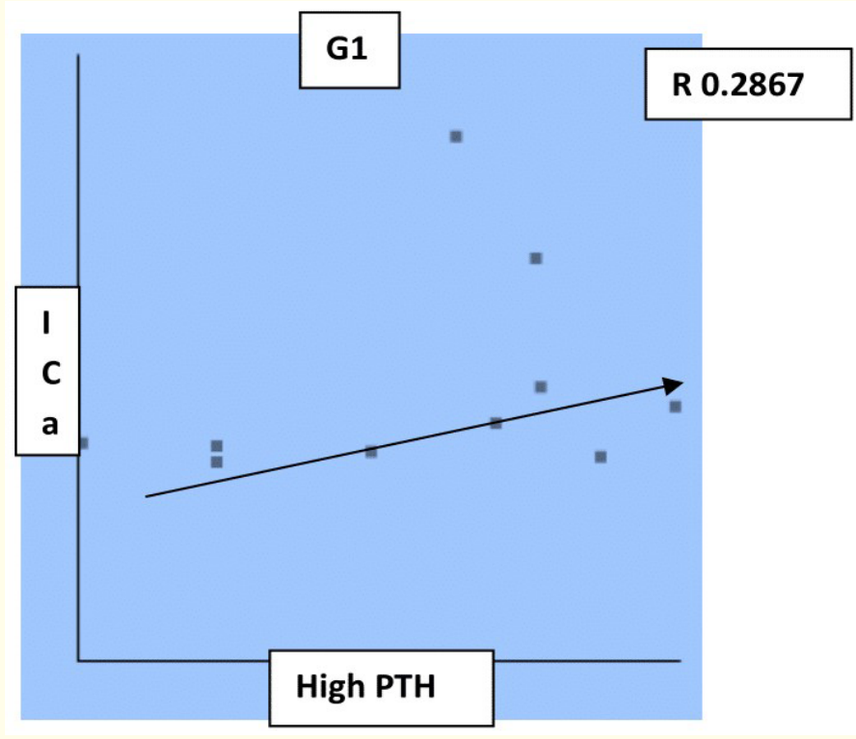


***Figure 1:*** *Demonstrating the correlation between iCa and high PTH levels in G1.*

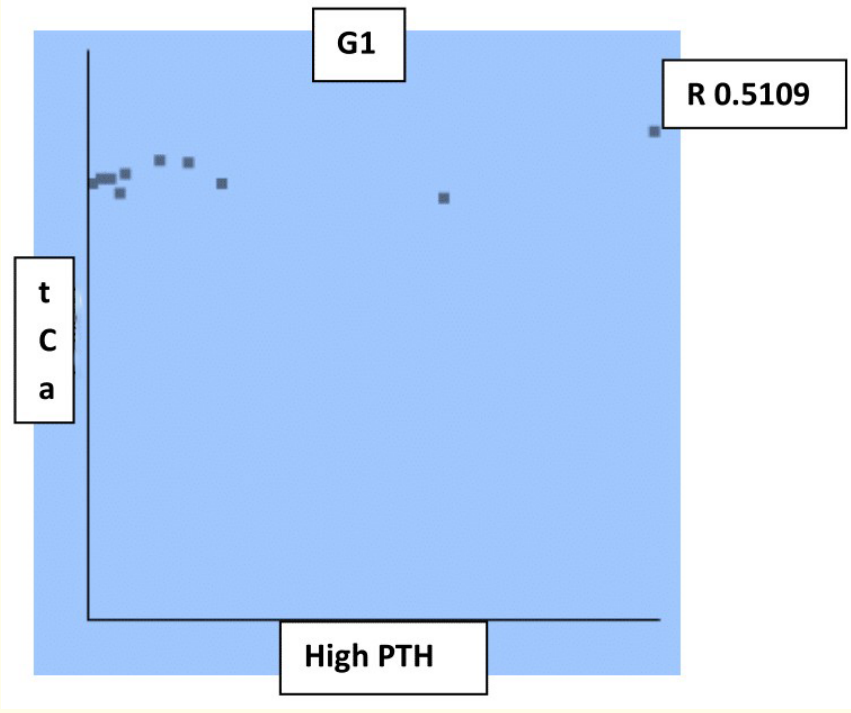


***Figure 2:*** *The value of R is 0.5109. This is a moderate positive correlation, which means there is a tendency for high PTH variable scores go with high tCa variable scores (and vice versa).*

Furthermore, on evaluating the correlation in G2 between the 2 forms of calcium in relation to HPTH indicated a weak positive correlation between Ca and high PTH, R was 0.0172 (which is technically a positive correlation, yet the relationship between variables is weak) vs. a value of R of 0.1478 between tCa and high PTH (a technically a negative correlation, yet the relationship between variables is only weak). Two of the three patients with D deficiency exhibited SHPTH in G1 versus none in the 8 patients with G2 (P = 0.0545).

## Discussion

Interestingly, as shown here some one quarter of the patients with eucalcemia (based on the estimation of total calcium range) may turn out having subnormal levels of ionized calcium in hypovitaminosis D. This was a significant proportion that can be easily overlooked unless ionized calcium is being estimated. In those, the association with secondary HPTH appeared higher than in others with normal ionized calcium as over one third of former turned to have raised PTH. The latter primarily did not show relevance to the degree of vitamin deficiency itself. Eucalcemia (tCa) was a feature in this cohort. This not surprising as by and large the eucalcemia appeared to be the usual biochemical finding in patients studied locally or in other areas before [6-10]. The reliability of total calcium in the diagnosis of hypovitaminosis D has become very questionable. Furthermore, the correlation between the two forms of calcium was significantly weaker among G1 patients than that in G2 emphasizing the point that the two forms are not necessarily corresponding to each other in all clinical settings and divergence may occur. Hence, monitoring these patients, by estimating the two forms of calcium and the PTH after a good vitamin D supplementation would provide more understanding on this issue. The correlation between low ionized calcium, low vitamin D and higher PTH which as demonstrated here may not be a surprise as it reflects a normal metabolism. In a recent review that was published only lately, the interplay between these factors and the regulatory role of ionized calcium have well been texted and emphasized [6].

Finally, this report though extrapolated from relatively small number of patients, yet it stresses on the potentially important role of the ionized calcium particularly the subnormal one in stimulating the rise of PTH in hypovitaminosis D. Its measurement therefore seems more reliable than the total one. The latter is not a reliable predictor of hypovitaminosis D even when the deficiency is sufficient to produce secondary hyperparathyroidism. This may lead to consider replacing the estimation of total calcium by the ionized one in the panel of tests for diagnosing hypovitaminosis D in the clinical practice.

## Declaration

No conflict of interest declared between authors.

## Acknowledgement

We thank Mr. Mohamed Abu Shawish for his assistance in this work.

## Bibliography

1. Delmar's Guide to laboratory and diagnostic tests. 2nd Edition (2010).
2. Ong GS., *et al*. "The importance of measuring ionized calcium status and diagnosing primary hyperparathyroidism". *Journal of Clinical Endocrinology and Metabolism* 97.9 (2012): 3138-3145.
3. Jacques Wallach. "Interpretation of diagnostic test, 8th Edition". Lippincott Williams and Wilkins (2007).
4. Tee MC., *et al*. "Ionized vs serum calcium in the diagnosis and management of primary hyperparathyroidism: which is superior?" *American Journal of Surgery* 205.5 (2013): 591-596.
5. Calvi L M and Bushinsky DA. "When it is appropriate to measure ionized calcium". *Journal of the American Society of Nephrology* 19.7 (2008): 1257-1260.
6. Al Attia H M. "Vitamin D (25-OH) D status in Abu Dhabi: Is the wide screening needed". *Osteoporosis International* 23.1 (2012): S124.
7. Al Attia H M. "Is vitamin D insufficiency more common in males than in females in the sunny UAE?" *Osteoporosis International* 24.1 (2013): S87.
8. Al Attia H M and Ibrahim M A. "The high prevalence of vitamin D inadequacy and dress style of women in the sunny UAE". *Archives of Osteoporosis* 7 (2012): 307-310.
9. Smith GR., *et al*. "Diagnosing hypovitaminosis D: serum measurements of calcium, phosphate and alkaline phosphatase are unreliable even in the presence of secondary hyperparathyroidism". *Journal of Rheumatology* 32.4 (2005): 684-689.
10. Khundmiri S J., *et al*. "PTH and vitamin D". *Comprehensive Physiology* 6.2 (2016): 561-601.

**Volume 8 Issue 4 January 2018**