ORIGINAL ARTICLE

# A Retrospective Study of Serum Calcium Levels in a Hospital Population in Malaysia

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## Summary

A retrospective six-month study of serum calcium and albumin in patients treated at the Kuala Lumpur Hospital was carried out. There were 19,291 subjects, of which the prevalences of hypocalcemia (corrected serum calcium of ≤ 2.1 mmol/l) and hypercalcemia (corrected serum calcium of > 2.7 mmol/l) were 18.0% (3460 subjects) and 2.4% (468 subjects) respectively. Persistent hypocalcemia (a minimum of first two consecutive corrected serum calcium of ≤2.1 mmol/l) was found in 408/19,291 subjects (2.1%). Serum calcium values of < 2.00 mmol/l were found in 98.5% of this group. Persistent hypercalcemia (a minimum of first two consecutive corrected serum calcium of > 2.7 mmol/l) was found in 108/19,291 subjects (0.5%) and 52/108 subjects (48.1%) had serum calcium values of ≥ 3.0 mmol/l. 2902/3460 subjects (83.8%) and 313/468 subjects (66.9%) the hypocalcemia and hypercalcemia groups respectively failed to be retested (singletons). In the hypocalcemia group, 1115/2902 (38.4%) showed corrected serum calcium values of < 2.00 mmol/1), whilst 100/313 subjects (31.9%) of the hypercalcemia group had corrected serum calcium values of ≥ 3.00 mmol/l.

There were no significant differences between the mean corrected serum calcium between 3 age groups of the test population, namely in childhood (≤18 years), adults (19-64 years) and the elderly (≥ 65 years).

*Key Words:* Hypocalcemia, Hypercalcemia, Serum calcium

## Introduction

Disorders of calcium homeostasis are common in hospital populations. The advent of profiling, rapid and reliable automated methods for measuring serum calcium makes it possible to detect abnormalities early in the course of the disease process, when patients may be asymptomatic. If derangements of calcium metabolism are detected early and adequate treatment is started promptly, the complications of hypo- and hypercalcemia could be prevented.

## Materials and Methods

All calcium and albumin measurements done on patient's sera over the period between 1st December 1991 and 15th June 1992 were retrieved from the laboratory computer. Subjects of the study came from the outpatient clinics and wards of the Kuala Lumpur Hospital as well as the polyclinics of the Universiti Kebangsaan Malaysia. The corrected serum calcium was calculated for each measurement using the formula, corrected serum calcium = total serum calcium + {(40 - serum albumin) x 0.02}.

Serum calcium and albumin measurements were done simultaneously on the Hitachi 717 analyzer. Serum albumin was analysed by the bromcresol green method. Serum calcium was analysed using the O-cresolphthalein dye-binding technique.

The actual number of patients investigated for calcium status was determined. The initial corrected serum calcium done on each patient was used to categorise hypocalcemia (defined as a corrected serum calcium of < 2.11 mmol/l) normocalcemia (a corrected serum calcium of 2.11 to 2.7 mmol/l) and hypercalcemia (a corrected serum calcium of > 2.7 mmol/l).

A study was made to determine 1) the prevalences of persistent hypo- and hypercalcemia defined as a minimum of first two consecutive low or high corrected serum calcium in the same subject respectively and 2) unverified hypo- and hypercalcemia. In the latter groups, the extent of abnormal results which were not followed by a retest (i.e. singletons) as well as non-persistent (different from the initial value) were identified.

The hypocalcemia and hypercalcemia were arbitrarily classified as mild, moderate and severe, as shown in Table I.

A study was made to see whether there were any significant differences in the mean corrected serum calcium in varying age groups, which were classified under childhood (≤ 18 years) adulthood (19-64 years) and the elderly (≥ 65 years).

## Results

During the period of study, the inter-assay and inter-assay coefficient of variation (cv) of serum albumin at 36.2 g/l were 1.2% and 3.0% respectively. The intra-assay cv of serum calcium at levels of 2.51 and 3.11 mmol/l were 0.7% and 0.6% respectively. The inter-assay cv of serum calcium of serum levels of 2.18 and 3.49 mmol/l are 2.2% and 2.9% respectively.

The test population consisted of 19,291 subjects. Based on the corrected serum calcium values, the prevalence of hypocalcemia, normocalcemia and hypercalcemia were 18.0%, 79.6% and 2.4% respectively. (Table II)

**Table I**
**Classification of hypocalcemia and hypercalcemia**

| Type | Hypocalcemia (mmol/l) | Hypercalcemia (mmol/l) |
|---|---|---|
| Mild | 2.0 - 2.1 | 2.71 - 2.99 |
| Moderate | 1.0 - 1.99 | 3.00 - 3.99 |
| Severe | < 1.0 | > 4.0 |

**Table II**
**Prevalence of hypocalcemia, normocalcemia and hypercalcemia**

| Classification | No. of patients | Per cent |
|---|---|---|
| Hypocalcemia (≤ 2.1 mmol/l) | 3460 | 18.0 |
| Normocalcemia (2.11 - 2.7 mmol/l) | 15363 | 79.6 |
| Hypercalcemia (> 2.7 mmol/l) | 468 | 2.4 |

**Table III**
**Frequency of persistent and unverified hypocalcemia**

| Serum calcium (mmol/l) | Persistent | Unverified | |
|---|---|---|---|
| | | Singletons | Non-persistent |
| (2.0 - 2.1) | 6 | 1787 | 74 |
| (1.0 - 1.99) | 228 | 1064 | 70 |
| < 1.0 | 174 | 51 | 6 |
| Total | 408 | 2902 | 150 |

The prevalences of persistent and unverified hypocalcemia and hypercalcemia are shown in Table III and Table IV respectively. The ratio of singleton hypocalcemia to persistent hypocalcemia was 7.1:1, whereas the ratio of singleton hypercalcemia to persistent hypercalcemia is 2.9:1.

Persistent hypocalcemia was found in 408/19,291 subjects (2.1%). Serum calcium values of < 2.00 mmol/l was found in 98.5% of this group. Persistent hypercalcemia was found in 108/19,291 subjects (0.5%) and 52/108 (48.1%) had serum calcium values of ≥ 3.0 mmol/l.

In the hypocalcemia and hypercalcemia groups, 83.8% and 66.9% respectively failed to be retested (singletons). Serum calcium of < 2.00 mmol/l was found in about 38.4% of the singleton hypocalcemic subjects, whilst 31.9% of the singleton hypercalcemia group had serum calcium of ≥ 3.00 mmol/l.

Only 15,528 subjects of the study population had their ages known. There were no significant differences in the mean corrected serum calcium between the three populations, (Table V), indicating a similar mixture of patients with normal and abnormal calcium values in each of the three groups.

## Discussion

The prevalence of hypocalcemia in a hospital population as shown in this study was about 18.0%. No similar study of a Malaysian population or a foreign population was available for comparison. A search through the literature had shown an incidence of hypocalcemia in malignancy of about 10.8% in a survey of 158 patients with malignancy[1], and between 5 to 13% in malignancies with bone metastases in another study[2].

The prevalence of hypercalcemia in this study was about 2.4%, which was lower than earlier reports[3,4] although higher than the prevalence of 0.6% reported in 2 papers[5,6] and comparable to 2.6% reported in another paper[7]. There were several studies which showed that clinically unsuspected hypercalcemia may often be detected[8,9]. The prevalence rate had been reported to vary between 0.1 and 0.7%[10-13] in outpatients or general population and between 3.0 - 3.6% in hospital populations[3,4].

**Table IV**
**Frequency of persistent and unverified hypercalcemia**

| Serum calcium (mmol/l) | Persistent | Unverified | |
|---|---|---|---|
| | | Singletons | Non-persistent |
| (2.71 - 2.99) | 56 | 213 | 34 |
| (3.00 - 3.99) | 48 | 93 | 13 |
| > 4.0 | 4 | 7 | 0 |
| Total | 108 | 313 | 47 |

**Table V**
**Distribution of serum corrected calcium according to age groups**

| Subject | Mean | 2S.D. | Range | No. of Patients |
|---|---|---|---|---|
| Children ≤ 18 years | 2.26 | 0.55 | 1.71 - 2.81 | 3,442 |
| Adults 19 - 64 years | 2.24 | 0.48 | 1.76 - 2.72 | 10,317 |
| Adults ≥ 65 years | 2.28 | 0.42 | 1.86 - 2.87 | 1,769 |

There was a high incidence of singleton abnormal corrected serum calcium, 83.8% of the hypocalcemic group and 66.9% of the hypercalcemic group. In addition, 7.1 and 2.9 patients were not retested for every one with persistent hypocalcemia and hypercalcemia respectively. Mild hypocalcemia and hypercalcemia were less likely to be investigated, as shown by a low percentage of retesting (hypocalcemia - 4.3%; hypercalcemia - 29.7%) whereas in the severe hypocalcemia group 77.9% of the subjects were retested. These observations are related to issues of action limits and factors influencing the decisions of the physicians, which are outside the scope of this study.

Being a retrospective study and recognising the magnitude of the problem in obtaining the correct diagnoses, no attempts were made to study the underlying causes of hypocalcemia and hypercalcemia in this population.

Both hypocalcemia and hypercalcemia have severe consequences on the health of the patient, increasing morbidity, mortality and health costs. Proper investigations and correct treatment are warranted. Mild disturbances of calcium metabolism are usually asymptomatic but may progress in severity if no treatment is received. In times of limited and diminishing resources, it is hoped that this exercise would initiate a prospective study in delineating the common causes of serum calcium abnormalities in a hospital population in Malaysia. Consequently, optimal utilisation of the facilities made available by the chemical pathology laboratory would be enhanced.

## Acknowledgement

The authors wish to thank the staff of the Chemical Pathology Laboratory, Universiti Kebangsaan Malaysia, for their dedicated involvement in the analysis of serum calcium and albumin during the period of study.

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