Original Article

Seasonal variations in serum levels of vitamin D and other biochemical markers among KSA patients prior to thyroid surgery

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Abstract

Objectives: Serum levels of vitamin D can vary between seasons, which may affect serum calcium levels in post-thyroidectomy patients. This study aimed to determine seasonal variations in serum levels of vitamin D and other biochemical markers in patients prior to thyroid surgery in a KSA hospital.

Methods: In this study, we analysed the data of 685 post-thyroidectomy patients. The preoperative laboratory values of all patients were collected, and the patients were categorized into groups based on the month when the surgical procedure was performed as follows: cold (November–February) and warm/hot groups (March–October).

Results: Serum vitamin D levels were deficient in 70% of the patients, insufficient in 18%, and optimal in 12%. The mean age of patients in the deficient group was significantly lower than that in the optimal group. There were significantly more patients who had vitamin D deficiency during the cold season than during the warm/hot season (p = 0.024). Serum vitamin D levels did not vary between seasons (p = 0.836); however, the preoperative magnesium and thyroid stimulating hormone (TSH) levels were significantly higher during the warm/hot season than during the cold season (p = 0.039 and

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Introduction

Vitamin D is a fat-soluble steroid vitamin that plays a key
role in calcium homeostasis by increasing the intestinal ab-
sorption and metabolism of calcium, magnesium, and
phosphorus.1,2 The majority of vitamin D in the body is
obtained through cutaneous synthesis (80%–100%), and the
ability of the body to synthesise vitamin D depends on
the amount of sunlight the skin receives.3,4 The day length,
which is the period between sunrise and sunset, varies with
latitude and the time of the year. People living at the
equator experience approximately 12 h of daytime throughout
the year.5 In contrast, people living at the Polar Circle latitudes of 66.33\(^\circ\), north or south, experience at least one day per year when the sun is above the horizon
for 24 h, and at least one day per year when the sun is
below the horizon for 24 h. During winter, exposure to
natural sunlight diminishes with increasing latitude.5

Recently, there has been growing interest in the vitamin D
levels of thyroid patients because of its impact on post-
thyroideectomy hypocalcaemia and hypocalcaemia treat-
ment. Several recent studies have recognised vitamin D
deficiency as a risk factor for post-thyroideectomy hypo-
calcemia and the importance of vitamin D status in
directing post-thyroideectomy hypocalcaemia manage-
ment.7–11 This interest is driven by the impact of post-
thyroideectomy hypocalcaemia on patients’ postoperative
quality of life, and by the financial burden imposed by
hypocalcaemia on patients and the health care system.12,13 It
has been reported that the median hospital stay increases by
51.5 h if the patient develops hypocalcaemia, and the
estimated cost of bed utilisation in a local hospital is
$23US per hour.12

Because of seasonal variations in sunlight exposure, var-
iations in vitamin D levels have been proposed to occur.
However, the phenomenon of variation in vitamin D levels
over the year remains controversial. Several studies have
concluded that vitamin D levels fluctuate over the year,14–17
whereas other studies have concluded the opposite.18 Several
factors might account for the inconsistency in the reported
results regarding the prevalence of vitamin D deficiency.
The most important of these factors is the lack of a
standard definition of vitamin D deficiency based on a
serum vitamin D cut-off value. Thus, to date, there is no
clear consensus regarding acceptable seasonal variation in
vitamin D levels.

Apart from the seasonal variation of vitamin D, several
other factors also include higher levels of parathyroid hor-
mones (PTH) in the cold when vitamin D levels are low
causing an increase in bone resorption and fractures.19–22
Serum calcium and phosphate were reported to decrease
whereas alkaline phosphatase and PTH were reported to
increase during the cold season, although some studies
showed no significant seasonal variations in serum calcium
and urinary excretion of calcium especially among
hypercalciuria prone patients.23,24 Reports also showed
that vitamin D deficiency was correlated with magnesium
deficiency.25

KSA is well known for receiving abundant sunlight all
year long. Therefore, we hypothesised that a seasonal vari-
ation in vitamin D levels might not occur in Saudi Arabian
residents since they are exposed to adequate sunlight. To test
this hypothesis and to determine the prevalence of vitamin D
deficiency in the Saudi population, we investigated seasonal
variations in vitamin D levels and the correlation between
vitamin D levels and other laboratory values in patients prior
to thyroid surgery in Riyadh, KSA.

Materials and Methods

Study participants

The study protocol was approved by King Saud Uni-
versity Hospital Institutional Review Board (Research
Project No. E-16-1813). The need for informed consent was
waived owing to the retrospective design of this study. We
reviewed the charts of all patients who underwent thyroid
surgery between 2010 and 2015 at King Abdulaziz Univer-
sity Hospital (KAUH) and King Fahad Medical City
(KFMC). Thyroid surgery includes total thyroidectomy,
completion thyroidectomy, and hemithyroidectomy. Patient
demographic data, including age, gender, and body mass
index (BMI), were collected. Histopathology reports and
laboratory levels of corrected calcium, vitamin D, para-
thyroid hormone, phosphorus, and magnesium were
reviewed. The exclusion criteria were as follows: missing
vitamin D level data, a history of vitamin D or calcium
supplement use in the three months prior to surgery, and
comorbidities affecting calcium and vitamin D levels,
including renal and parathyroid disease. In KSA, the cold
season typically start in November and continue until
February. Based on the records available from 1980 to
2016, a report of the typical weather in Riyadh defined the
winter season from the end of November until the end of
February. Based on this report, we divided the year into
cold season (November to February) and warm season
(March to October).26 Patients were classified based on the
month in which the surgery was performed as the cold and
warm/hot groups.

Conclusion: This study suggests a non-significant sea-
nonal fluctuation in serum levels of vitamin D with
insignificant variation in serum calcium levels during cold
and warm/hot seasons. The findings necessitate a careful
review of the patients’ biochemical status prior to sur-
gery. Future prospective longitudinal studies are needed
to confirm this variability.

Keywords: KSA; Middle East; Seasonal variation; Thyroid-
ectomy; Vitamin D

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Biochemical tests

According to our protocol at KAUH and KFMC, all patients admitted for thyroid surgery undergo tests to determine the preoperative serum levels of the following: corrected calcium, vitamin D (25-hydroxyvitamin D), parathyroid hormone, phosphorus, and magnesium. Corrected calcium, phosphate, and magnesium levels were measured using an autoanalyzer, whereas 25-hydroxyvitamin D levels were measured using an immunoassay. We used the following normal laboratory reference values: corrected calcium 2.25–2.5 mmol/L, parathyroid hormone 1.6–6.9 pmol/L, phosphate 2.5–4.5 mg/dL, and magnesium 0.7–1 mmol/L, and we evaluated the vitamin D status in patients based on the Endocrine Society clinical practice guidelines. According to the guidelines, a vitamin D level <50 nmol/L is considered deficient, 50–74 nmol/L is considered insufficient, and ≥75 nmol/L is considered optimal.

Statistical analysis

Descriptive statistical data are presented as mean ± standard deviation (SD). An independent-samples t-test was used to compare the mean age between patients with deficient, insufficient, and optimal vitamin D levels. The Spearman correlation test was used to correlate vitamin D levels with other preoperative markers. The independent-samples t-test was used to compare vitamin D and PTH levels between the cold and warm season. The data were analysed using the Statistical Package for the Social Sciences version 16.0 (SPSS, Chicago, IL, USA). The significance level was set at \( p < 0.05 \).

Results

Subjects' characteristics

Of the 943 patients who underwent thyroidectomy, 258 were excluded. Of those excluded, 183 patients had missing vitamin D level, 7 had a history of hyperparathyroidism, and 68 had a history of vitamin D or calcium supplement use (22 patients were taking concomitant vitamin D and calcium supplements, 29 were taking vitamin D supplements alone, and 17 were taking calcium supplements alone). The remaining 685 were included in the analysis. The demographic characteristics are shown in Table 1. The mean (SD) patient age was 41 (14) years (with range from 9 to 90 years), and 548 (80%) patients were female. The mean (SD) height, weight, and BMI values were 1.59 (0.09) m, 78.93 (19.15) kg, and 30.93 (7.09) kg/m², respectively. The final histopathology revealed benign lesions in 349 patients (50.9%) and malignant lesions in 336 patients (49.1%).

Preoperative biochemical parameters

The results of the preoperative laboratory tests are shown in Table 2. Vitamin D levels were deficient in 70% of patients, insufficient in 18%, and optimal in 12%. The mean (SD) age of patients in the deficient group was significantly lower than that of the optimal group (39.68 ± 13.37 years vs 46.67 ± 12.37 years, respectively; \( p = 0.022 \)). Spearman’s correlation coefficient analysis revealed a significant negative correlation between preoperative vitamin D and parathyroid hormone levels \( (r = -0.115, p = 0.003) \). In contrast, no significant correlation was found between preoperative vitamin D levels and preoperative levels of magnesium \( (r = -0.003, p = 0.9) \), phosphorus \( (r = 0.052, p = 0.3) \), and corrected calcium \( (r = 0.065, p = 0.10) \).

Seasonal variations in biochemical parameters

Of the 685 patients, 225 (32.8%) underwent surgery in the cold season, and 460 (67.2%) underwent surgery in the warm season. Figure 1 shows the distribution of patients across the vitamin D categories for every month of the year. The independent-samples t-test revealed no significant differences in the levels of vitamin D (39.61 ± 23.89 nmol/L vs. 39.89 ± 27.07 nmol/L) and parathyroid hormone (13.37 ± 7.07 years vs. 12.37 ± 6.54 years) between cold and warm seasons.
40.03 \pm 25.66 \text{nmol/L}, \quad p = 0.836) \text{ or parathyroid hormone (6.49 \pm 4.83 \text{pmol/L vs. 6.65 } \pm 4.19 \text{pmol/L}, \quad p = 0.668) between patients who underwent surgery in the warm and cold seasons.}

There were significantly more patients with vitamin D deficiency during the cold season than during warm/hot season \((n = 335, 72.8\% \text{ versus } n = 145, 64.4\%, \quad p = 0.024).\) The preoperative Mg level was also significantly higher during the warm/hot season than during the cold season \((0.84 \pm 0.08 \text{ versus } 0.81 \pm 0.08, \quad p = 0.039).\) The preoperative TSH level was also significantly higher in the warm/hot season than in the cold season \((4.34 \pm 2.86 \text{ versus } 2.25 \pm 2.65, \quad p < 0.001).\) Preoperative calcium was not significantly different between the cold and warm/hot seasons \((p = 0.282).\) There were no other significant differences in biochemical parameters between the warm/hot and cold seasons \((Table 3).\)

There were significant correlations between vitamin D deficiency and the investigated parameters. Vitamin D deficiency was significantly correlated with the male gender \((r = -0.088, \quad p = 0.022),\) increased PTH levels \((r = 0.171, \quad p = 0.037),\) decreased preoperative calcium level, \((r = -0.099, \quad p = 0.015),\) larger tumour size \((r = 0.121, \quad p = 0.032),\) and heavier thyroid weight \((r = 0.128, \quad p = 0.004).\) No significant correlations were found between vitamin D deficiency and magnesium \((r = -0.009, \quad p = 0.879),\) TSH \((r = -0.044, \quad p = 0.265),\) and phosphate \((r = -0.068, \quad p = 0.251).\)

### Discussion

In this study, we found no significant seasonal variation in the vitamin D levels detected in the study population of pre-thyroidectomy patients. In contrast, we found a high prevalence of vitamin D deficiency; further, the mean age of patients in the deficient group was significantly lower than that of patients in the optimal group. A significant negative correlation between preoperative vitamin D level and parathyroid hormone level was found; however, that significant correlation was not present when correlated with other preoperative laboratory values.

An important finding in our study was the high prevalence of vitamin D deficiency (70%). Despite campaigns in KSA to raise awareness, the incidence of vitamin D deficiency continue to show an upward trend. Compared to other local reports, our findings show that the prevalence of vitamin D deficiency in patients with thyroid dysfunction is higher than that in the general population of KSA. In a study that included 3475 patients, Alfawaz et al. reported a similar prevalence of vitamin D deficiency: 78.1% in women and 72.4% in men. A randomised study with similar cut-off values conducted on healthy individuals who were accompanying patients to primary healthcare centres in Al-Qaseem province found the prevalence of vitamin D deficiency, insufficiency, and optimal levels to be 28.3%, 39.4%, and 32.2%, respectively. Another study with similar cut-off values performed in Eastern KSA on randomly selected healthy individuals found the prevalence of vitamin D deficiency to be 10% in young individuals and 12% in adults. A likely explanation for this prominent dissimilarity in the prevalence of vitamin D deficiency among studies conducted in different regions of the country could be selection bias. It is well known that Al-Qaseem is an agricultural province, and its inhabitants stay outdoors relatively longer than those in the other regions of the country. Moreover, because of their location on the seacoast, Eastern province residents rely heavily on vitamin D rich fish as a source of food, compared to residents of the Riyadh metropolitan area.

Although most studies have revealed a higher prevalence of vitamin D deficiency in the older population, we found that the mean age of patients who were deficient in vitamin D was significantly lower than the mean age of those with optimal levels. This finding could be explained by the fact that in Saudi Arabian culture, older people generally have healthier lifestyle habits than the younger generation, including spending more time outdoors and eating healthier food. A higher prevalence of vitamin D deficiency in younger people has also been identified in other studies conducted in non-Saudi populations.

Because both vitamin D and PTH are calciotropic hormones that play an important role in calcium metabolism, vitamin D deficient patients become more dependent on PTH. It has been documented that a 25-hydroxyvitamin D level ≥40 \text{nmol/L} is associated with a low PTH level. Consistent with this relationship, the mean PTH level of our patients was in the upper normal range, and the mean vitamin D level was below 40 \text{nmol/L}. Moreover, our data showed a linear drop in vitamin D level associated with a rising PTH level. This inverse relationship between preoperative PTH and vitamin D levels further confirms the prevalent vitamin D deficiency in our study participants. Furthermore, our data showed no relationship between preoperative vitamin D levels and other preoperative laboratory values, including magnesium, corrected calcium, and phosphate.

Geographical areas located at latitudes closer to the equator are known to have daylight for approximately 12 h per day throughout the year; therefore, people residing in these areas are typically exposed to enough sunlight in both summer and winter to continue vitamin D production year-round. In contrast, people living closer to the poles, where daylight hours vary markedly between seasons,
experience greater seasonal variations in exposure to sunlight that negatively impact the production of vitamin D via the skin during winter. For instance, individuals living at latitudes greater than 33° north or south have been reported to produce little or no vitamin D during the winter season. A study on thyroid patients conducted in Beppu, Japan (located at 33.2846° N) revealed significant seasonal variations in the vitamin D levels of patients pre-thyroidectomy. Studies performed in northern latitudes (Evaston, USA (located at 42.0451° N)) and southern latitudes (Launceston, Australia (located at 41.4332°S)) reported similar findings.

However, the findings of this study support our original hypothesis that seasonal variations in vitamin D levels do not occur in Riyadh, KSA (located at 24.7136° N). One probable explanation is that the weather and daylight hours in Riyadh, KSA are less variable compared to the other parts of the world. Saudi patients who underwent thyroid surgery in the warm season had levels of preoperative vitamin D comparable to those who underwent surgery during the cold season. However, despite the absence of a seasonal variation in vitamin D levels, we found a significantly larger number of patients with vitamin D deficiency during the cold season.

This led us to ask, “Why is there a larger proportion of vitamin D deficient individuals in a non-significant, non-seasonal variation or fluctuation of vitamin D levels?” There are several possible explanations. Many studies have established the seasonal association and fluctuation of vitamin D levels and vitamin D deficiency. However, other factors including magnesium, phosphate, calcium, and TSH levels, which may have been inherently abnormal, may have affected the vitamin D levels in these patients. Higher magnesium and TSH levels during the warm/hot season were reported to be directly associated with a higher level of vitamin D, and a decrease in magnesium and TSH levels during cold season may cause bone resorption and fractures as numerous studies have reported.

However, we did not find any significant seasonal variation in the calcium level, though calcium levels were significantly associated with vitamin D deficiency. This study has also concurred with previous studies that calcium and phosphate had no significant seasonal variation as opposed to magnesium, PTH, and vitamin D levels. One probable reason why vitamin D deficiency does not generally cause malabsorption of calcium is that serum 1,25-dihydroxyvitamin D, which is the major determinant of calcium absorption, is maintained by secondary hyperparathyroidism until the serum 1,25(OH)2D falls to approximately 10 nM as suggested by Need et al. (2008). There could also be other factors that need to be investigated as to why these patients had vitamin D deficiency despite the non-seasonal variation of vitamin D levels.

This study has some limitations. First, we used a non-randomised sample which only included patients with thyroid dysfunction who visited our hospitals, and not the general population. Second, the higher number of patients who underwent surgery during the summer season compared to the winter season, and the exclusion of patients with missing vitamin D level data (19%), might have influenced our results. Our exclusion of patients who were on vitamin D supplementation and those who were taking calcium medications might have also affected the results.

Conclusion

This study found a non-significant seasonal fluctuation in vitamin D levels with no significant variation in serum calcium levels during the cold and warm/hot seasons, indicating the need for a careful review of the biochemical status of patients prior to surgery. Many other inherent factors should be considered that may cause variability in vitamin D levels prior to surgery. Future prospective longitudinal studies are needed to confirm this variability. Moreover, although daylight hours in KSA are long throughout the year, vitamin D deficiency is still prevalent. In Saudi patients, we suggest routine preoperative screening for vitamin D deficiency and correction of vitamin D levels accordingly.

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Conflict of interest

The authors have no conflicts of interest to declare.

Ethical approval

This manuscript has been approved by King Saud University Research Center (Project No. E-16-1813), 25 February, 2016. The support was non-financial, its logistic support such as consultation, provide the necessary programs such spss, endnote etc.

Authors contributions

TA conceived and designed the study, and assisted in drafting the manuscript; SA assisted in drafting the manuscript, conducted the research, and collected and organised the data; AA assisted in drafting the manuscript; SA designed the study and collected and organised the data; SD analysed and interpreted the data and provided logistic support and supervision. All authors have critically reviewed and approved the final draft and are responsible for the content and similarity index of the manuscript.

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