

Association of Hypomagnesemia with Hypocalcemia after Thyroidectomy

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Abstract

Background: Hypocalcemia is one of the most common acceptable complications in postoperative period after thyroidectomy. Hypomagnesemia has been recognized after parathyroid surgery, and it has not been studied extensively after thyroidectomy. The aim of this study was to estimate magnesium and calcium ion levels in patients undergoing thyroidectomy and to evaluate the association of hypomagnesemia with hypocalcemia after thyroidectomy. A prospective study was conducted in Government Medical College, Calicut, from December 2012 to November 2013. **Materials and Methods:** all patients had undergone total/near-total/subtotal thyroidectomy. Pre- and postoperative at 24 h and serum calcium and magnesium were measured by automate electrolyte analyzer. Clinical findings of hypocalcemia were recorded. Statistical analysis was done using SPSS software, version 17.0. Unpaired student *t*-test was used. Pearson Chi-square test or Fisher's exact test was used to compare the percentage for categorical variables. **Results:** In our study, 58% of the patients developed hypocalcemia, biochemical and/or symptomatic (S. Ca <8.5). About 34% of patients developed hypomagnesemia, biochemical and/or symptomatic (S. Mg <1.7). About 30% of patients developed both hypocalcemia and hypomagnesemia. About 24% of patients developed symptoms of both hypocalcemia and hypomagnesemia. **Discussion:** Thyroidectomy patients were at a risk of transient and permanent hypoparathyroidism because of chances of parathyroid resection during operation. Transient hypocalcemia and hypomagnesemia occur frequently after total thyroidectomy. It is important to monitor both calcium and magnesium levels after total thyroidectomy and to correct deficiencies to facilitate prompt resolution of symptoms. **Conclusion:** There is an association of hypomagnesemia with hypocalcemia after thyroidectomy.

Keywords: Hypomagnesemia and hypocalcemia, thyroid gland, thyroidectomy

INTRODUCTION

Thyroidectomy is a clean surgical procedure with minimal blood and fluid loss. Total thyroidectomy has been established as the preferred operation for a range of thyroid pathologies. The most common postoperative complications are hypocalcemia. Homeostasis of magnesium ions is directly related to calcium levels.^[1] An abrupt fall in magnesium concentration leads to a reduction in the production and release of parathyroid hormone (PTH) and secondarily exacerbates the clinical manifestations of hypocalcemia. Therefore, hypocalcemic patients with hypomagnesemia will present with relative hypoparathyroidism.^[2] Plasma calcium correction without concurrent normalization of magnesium may prolong the clinical manifestations.^[3] The aim of this study was to estimate magnesium and calcium ion levels in patients undergoing thyroidectomy and to evaluate the association of hypomagnesemia with hypocalcemia after thyroidectomy.

MATERIALS AND METHODS

A total of 50 new patients who underwent thyroidectomy in Medical College Hospital, Calicut, from December 2012 to November 2013 were enrolled into this prospective study.

Inclusion criteria

All patients with benign/malignant thyroid disorder undergoing total/near-total/subtotal thyroidectomy with or without neck dissection in Medical College, Calicut.

Exclusion criteria

Coexisting hypo/hyperparathyroidism, patients with renal dysfunction and hypoalbuminemia.

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Procedure

This study involved determination of serum calcium and serum magnesium preoperatively and serum magnesium and serum calcium level 24 h postoperatively. After taking informed consent, under all aseptic precautions, about 4 ml of venous blood will be collected in a vacutainer. It will be subjected for centrifugation, and serum will be separated. Serum calcium and magnesium were measured by ion-selective electrode method by automate electrolyte analyzer. Estimation is done within 2 hours. If there occurs delay in processing, serum sample stored at 4 degree celcius in deep freezer. Clinical findings suggestive of hypocalcemia, that is, perioral numbness, paresthesias, tetany, Chvostek sign, Trousseau sign, seizures, and electrocardiogram changes, are also watched for and recorded.

Concentrations that were below the reference values for the ions evaluated were considered to be cases of hypocalcemia and hypomagnesemia.

- Total calcium – reference value: 8.5 mg/dl to 10.5 mg/dl, hypocalcemia: S. Ca <8.5 mg/dl
- Magnesium – reference value: 1.8 mg/dl to 2.2 mg/dl, hypomagnesemia: S. Mg <1.7 mg/dl.

Statistical analysis

Data analysis was performed by SPSS, version 17 (IBM Company, Chicago). If normal distributed, continuous variables were presented as the mean \pm standard deviation (SD) and compared by *t*-test. Pearson Chi-square test or Fisher's exact test was used to compare frequency (percentage) for categorical variables. *P* < 0.05 indicated statistically significant difference.

RESULTS AND DISCUSSION

The study included 50 patients, of both genders and all the age groups, who underwent thyroidectomy. The patients were of varied age group, the youngest being 14 years and the oldest 63 years of age. The mean age was 40.12 years. About 68% of the patients were in the age group of 31–50 years. The age did not have any significant correlation with postoperative hypomagnesemia (Pearson's correlation 0.110).

Among these 50 patients, 8 (16%) were male and 42 (84%) were female. Three out of five males and 14 of 28 females developed postoperative hypomagnesemia. There was no any statistically significant difference in the occurrence of hypomagnesemia between males and females (*P* = 0.820).

Case group was selected on fine-needle aspiration cytology report and confirmed on postoperative histopathology report. In this study, 39 (78%) patients were diagnosed as multinodular goiter, 6 (12%) patients follicular neoplasm, 3 (6%) patients papillary carcinoma, 1 (2%) patient Hurthle cell neoplasm, and 1 (2%) patient solitary nodular goiter. Patients underwent different types of surgeries. Ten (20%) patients underwent total thyroidectomy, 36 (72%) patients were treated with near-total thyroidectomy, and 4 (8%) of them underwent subtotal thyroidectomy. 12 out of the total 39 patients of multinodular goiter, 2 of 6 patients of

follicular neoplasm, 2 of 3 of papillary carcinoma and the sole case of SNT developed hypomagnesemia. Demographic and clinical characteristics of the study population with occurrence of hypomagnesemia are summarized in Table 1.

Among the study group, 29 patients (58%) developed hypocalcemia, biochemical (S. Ca <8.5) [Figure 1] and among them 15 patients (51.7%) developed symptomatic hypocalcemia. In study group, 17 patients (34%) developed hypomagnesemia, biochemical and/or symptomatic (S. Mg <1.7) [Figure 2]. Of the 17 patients who developed hypomagnesemia postoperatively, 13 (86.7%) patients were symptomatic. In contrast, even though the serum magnesium level was >1.7, 2 (13.3%) patients developed symptoms [Table 2]. Hypomagnesemia present with symptoms such as muscle cramps, muscle fasciculation and tremors, convulsions, carpopedal spasm-positive Chvostek's sign, and Trousseau's sign.^[4,5]

Fifteen (30%) patients developed both hypocalcemia and hypomagnesemia with biochemical value S. Ca <8.5 and

Table 1: Demographic and clinical characteristics of the study population with occurrence of hypomagnesemia

| Variable | Normomagnesemia | Hypomagnesemia | <i>P</i> |
|-----------------------|-----------------|----------------|----------|
| Sex | | | |
| Male | 5 | 3 | 0.820 |
| Female | 28 | 14 | |
| Diagnosis | | | |
| Follicular neoplasm | 4 | 2 | 0.397 |
| Hurthle cell neoplasm | 1 | 0 | |
| MNG | 27 | 12 | |
| Papillary carcinoma | 1 | 2 | |
| SNT | 0 | 1 | |
| Type of surgery | | | |
| TT | 25 | 11 | 0.668 |
| NTT | 2 | 2 | |
| STT | 6 | 4 | |

MNG: Multinodular goiter, SNT: Solitary nodule of thyroid, TT: Total thyroidectomy, NTT: Near total thyroidectomy, STT: Sub total thyroidectomy

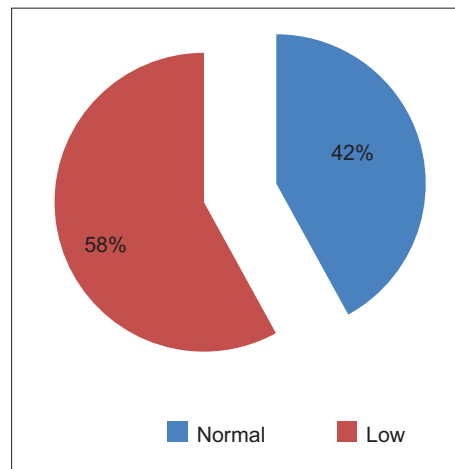


Figure 1: Hypocalcemia

S. Mg <1.7 [Figure 3]. 12 out of 15 patients show symptoms of both hypocalcemia and hypomagnesemia [Table 3]. A total of 24% from study patients developed symptoms with both hypocalcemia and hypomagnesemia.

In this study, 17 patients show hypomagnesemia. Six out of 17 patients were having preoperative low calcium with the mean calcium of 7.8 (SD-0.5924). Eleven patients were having normal calcium with the mean calcium of 9.3 (SD-0.5732). The occurrence of hypomagnesemia with preoperative low calcium is statistically not significant ($P = 0.052$) [Table 4 and Figure 4].

Of the 17 postoperative hypomagnesemia patients, 15 were having postoperative low calcium with a mean calcium level of 7.7 (SD-0.5876). Two patients were having normal postoperative calcium with the mean calcium of 8.6 (SD-0.7174). By this study, simultaneous occurrence of hypomagnesemia and hypocalcemia is statistically significant ($P = 0.002$) [Table 5].

Of the 17 patients, who developed postoperative hypomagnesemia, 1 patient had preoperative low magnesium level (S. Mg mean value 1.847, SD-0.2939). Sixteen patients had normal preoperative magnesium level with a mean value of 2.106 (SD-0.2499). By this study, occurrence of postoperative hypomagnesemia with preoperative low magnesium is statistically not significant ($P = 0.626$) [Table 6]. By this study, hypomagnesemia is not statistically significant with S. albumin level ($P = 0.233$).

There was no significant difference statistically in the occurrence of hypomagnesemia with regard to diagnosis ($P = 0.397$). 11 patients out of the 36 NTT, 4 patients of 6 TT, and 2 of 4 STT developed hypomagnesemia. There was no statistically significant difference in the occurrence of hypomagnesemia with regard to the type of surgery ($P = 0.668$).

Table 2: Symptomatic hypomagnesemia

| Symptoms | Frequency (%) |
|----------------|---------------|
| No | |
| Hypomagnesemia | 4 (11.4) |
| Normal | 31 (88.6) |
| Total | 35 (100.0) |
| Yes | |
| Hypomagnesemia | 13 (86.7) |
| Normal | 2 (13.3) |
| Total | 15 (100.0) |

Table 3: Both hypocalcemia and hypomagnesemia with symptom

| Both | Frequency (%) |
|-------------|---------------|
| Symptoms | 12 (80) |
| No symptoms | 3 (20) |
| Total | 15 (100) |

DISCUSSION

Standard treatment for benign thyroid disorder is used to be subtotal thyroidectomy, but nowadays near-total and total thyroidectomies are becoming the most common operations for

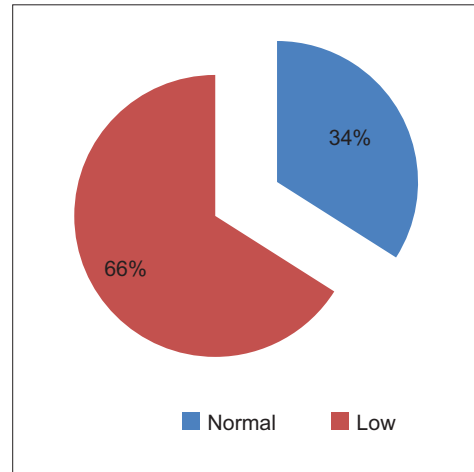


Figure 2: Hypomagnesemia

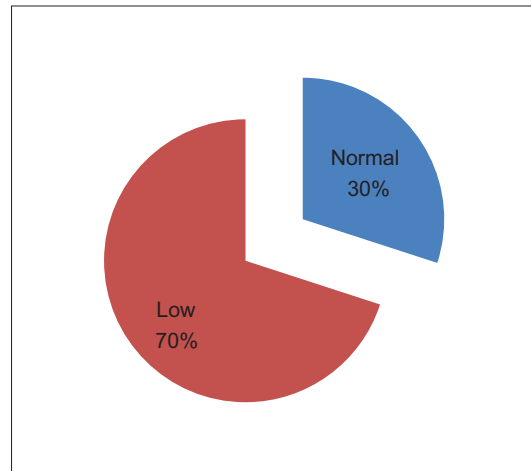


Figure 3: Both hypocalcemia and hypomagnesemia

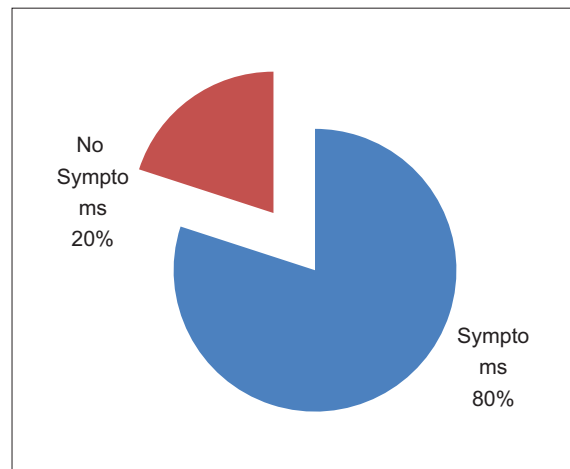


Figure 4: Both hypocalcemia and hypomagnesemia with symptom

Table 4: Association of postoperative magnesium with preoperative calcium

| Preoperative serum Ca | Comparison % of Pre-Operative S.Ca with Post-Operative S.Mg | Postoperative serum Mg | | Total, n (%) |
|-----------------------|---|------------------------|------------------------------------|--------------|
| | | Low, n (%) | Normal, n (%) | |
| Low | Count percentage within preoperative low Ca | 6 (60.0) | 4 (40.0) | 10 (100.0) |
| Normal | Count percentage within preoperative low Ca | 11 (27.5) | 29 (72.5) | 40 (100.0) |
| Total | Count percentage within preoperative low Ca | 17 (34.0) | 33 (66.0) | 50 (100.0) |
| | Value | df | Asymptotic significant (two-sided) | |
| Pearson χ^2 | 3.766 | 1 | 0.052 | |

Table 5: Association of postoperative magnesium with postoperative calcium

| Postoperative serum Ca | Comparison % of Post-Operative S.Ca with Post-Operative S.Mg | Postoperative serum Mg | | Total, n (%) |
|------------------------|--|------------------------|------------------------------------|--------------|
| | | Low, n (%) | Normal, n (%) | |
| Low | Count percentage within postoperative low Ca | 15 (51.7) | 14 (48.3) | 29 (100.0) |
| Normal | Count percentage within postoperative low Ca | 2 (9.5) | 19 (90.5) | 21 (100.0) |
| Total | Count percentage within postoperative Low Ca | 17 (34.0) | 33 (66.0) | 50 (100.0) |
| | Value | df | Asymptotic significant (two-sided) | |
| Pearson χ^2 | 9.666 | 1 | 0.002 | |

Table 6: Association of postoperative magnesium with preoperative magnesium

| Preoperative serum Mg | Comparison % of Pre-Operative S.Mg with Post-Operative S.Mg | Postoperative serum Mg | | Total |
|-----------------------|---|------------------------|------------------------------------|------------|
| | | Low, n (%) | Normal, n (%) | |
| Low | Count percentage within postoperative low Mg | 1 (50.0) | 1 (50.0) | 2 (100.0) |
| Normal | Count percentage within postoperative low Mg | 16 (33.3) | 32 (66.7) | 48 (100.0) |
| Total | Count percentage within postoperative low Mg | 17 (34.0) | 33 (66.0) | 50 (100.0) |
| | Value | df | Asymptotic significant (two sided) | |
| Pearson χ^2 | 0.238 | 1 | 0.626 | |

benign diseases of the thyroid gland. More extensive surgery is associated with more risk of damaging to parathyroid glands and may lead to transient or permanent hypoparathyroidism. According to the literature, the causes of parathyroid gland damage are multiple and associated mostly with their iatrogenic injury, extent of surgery, surgeon's experience, retrosternal goiter, neck lymphadenectomy, and thyroid cancer.^[6] Temporary hypoparathyroidism leads to a reduction in renal reabsorption of magnesium, and expansion of the extracellular volume increases magnesium excretion resulting in hypomagnesemia.^[7] Postthyroidectomy hypomagnesemia has been approved to reduce the production of PTH and decrease the affinity of PTH receptor and production of vitamin D, all of which may lead to hypocalcemia.^[8]

Hypocalcemia is defined as a serum total calcium of <8.5 mg/dl.^[9] Life-threatening complications can develop if serum calcium levels fall below 7 mg/dl. Hypocalcemia is one of the complications after total thyroidectomy. Transient hypocalcemia occurs in up to 50% of patients and permanent hypocalcemia in 2%.^[10]

In our study, 58% developed hypocalcemia (S. Ca <8.5). In literature, it was reported from 27% to 80%.^[11] In our study, 34% developed hypomagnesemia (S. Mg <1.7).

Many previous studies show association of hypocalcemia with type of surgery and diagnosis. Randall *et al.*^[12] showed that hypocalcemia occurred more often after total thyroidectomy than after unilateral thyroid lobectomy. Sousa *et al.*^[13] showed that incidence of postoperative hypocalcemia is more in papillary carcinoma compared to follicular carcinoma as papillary carcinoma associated with neck dissection. The suspect nodule and the follicular adenoma are usually treated with partial thyroidectomy; therefore, the incidence of hypocalcemia was lower. However, our study shows that occurrence of hypocalcemia is independent of diagnosis and type of surgery done.

The study shows that 30% of patients developed both hypocalcemia and hypomagnesemia with biochemical value S. Ca <8.5 and S. Mg <1.7. About 24% of patients developed symptoms of both hypocalcemia and hypomagnesemia.

Magnesium is an essential cofactor of >300 enzymes. It also acts as a calcium channel antagonist and plays a key role in the modulation of any activity involving calcium, such as muscle contraction and insulin release.^[9] Temporary hypoparathyroidism leads to a reduction into renal reabsorption of magnesium, and expansion of the extracellular volume increases magnesium excretion. Magnesium deficiency reduces the PTH effect in the kidneys and bones and increases its degradation in the liver and kidneys.^[14]

The relation between calcium and magnesium metabolism is a complex one and relates mainly to the interaction of these cations with PTH. Levine and Coburn suggested that magnesium may mimic/antagonize calcium by competing with calcium for a binding site on the parathyroid cell.^[15]

Only few studies have been conducted worldwide to determine the association of hypomagnesemia with hypocalcemia after thyroidectomy. In a study conducted by Wilson *et al.*,^[7] immediate postoperative calcium and magnesium level were measured in 50 patients of undergoing thyroid surgery. There were 34 patients with hypocalcemia (68%) and 36 patients were hypomagnesemic (72%) and 18 (36%) patients were symptomatic during the postoperative period.

Rude *et al.*^[16] showed that administering intravenous magnesium to patients with hypocalcemia secondary to hypomagnesemia resulted in a dramatic rise in serum PTH levels within 1 min after injection. Thus, hypomagnesemia can inhibit PTH secretion. There is also evidence that hypomagnesemia contributes to increased catabolism of parathormone.^[17,18] Diminished end-organ responsiveness to PTH has also been demonstrated in several studies of magnesium deficiency in humans and experimental animals.^[19,20] Despite this experimental and clinical work, which demonstrates the importance of hypomagnesemia, particularly when it exists with hypocalcemia, there has been little published on the significance of hypomagnesemia after total thyroidectomy. It was found that both magnesium and calcium were associated with symptoms. This demonstrates that hypomagnesemia may well contribute to postoperative tetany after total thyroidectomy, especially with concomitant hypocalcemia. This finding was supported by Szubin *et al.*,^[21] who found that serum magnesium levels should be monitored after total thyroidectomy and corrected if low.

Limitation of the study

As sample size is small in our study, future studies with larger sample size can provide more information. We were unable to identify which patients went on to develop permanent, as opposed to transient, hypocalcemia. Prospective studies can differentiate permanent to transient hypocalcemia.

CONCLUSION

Hypomagnesemia is not a rare complication successive to thyroidectomy. In our study group, 58% of the patients developed hypocalcemia, 34% developed hypomagnesemia biochemical, and 30% of patients developed both hypocalcemia and hypomagnesemia. There is an association of hypomagnesemia with hypocalcemia after thyroidectomy. About 24% patients show symptomatic hypomagnesemia and hypocalcemia. Hence, if a patient had persistent symptoms postoperatively, then iv/oral magnesium supplementation can be given as a part in the management of hypocalcemia with hypomagnesemia.

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Conflicts of interest

There are no conflicts of interest.

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