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Original Research Article

Post-thyroidectomy permanent hypocalcemia and hypoparathyroidism: frequency and risk factors

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ABSTRACT:

Background: Hypoparathyroidism is the most common complication after thyroidectomy and the main reason for frequent outpatients' visits; however, there is a poor understanding of its outcomes, and no clear follow-up strategies are available. We aimed to evaluate the frequency and risk factors of post-thyroidectomy hypocalcemia hypoparathyroidism in Libyan patients.

Methods: A case series study was conducted. The serum calcium and parathyroid hormone level (PTH) were measured at least 8 months post thyroidectomy.

Results: 124 patients were reviewed in this study; 19 (15.3 %) were males and 105 (84.7 %) were females. 30.6 % of males and 13.7% of females developed hypocalcemia and hypoparathyroidism. Total thyroidectomy (TT) was performed in 62.9 % of all patients, while 24.2% of all patients underwent near total thyroidectomy (NTT). 12.1% of all patients underwent bilateral subtotal thyroidectomy (BST) and 1 patient underwent hemi thyroidectomy (0.8%). The risk of hypocalcemia was higher in patients with malignant thyroid disease in comparison to benign thyroids (45.8 % vs. 27% of patients). Papillary thyroid carcinoma (PTC) was the most common cause of both hypocalcemia and hypoparathyroidism (45.5% for both) followed by Graves' disease (22.2% and 14.8% for hypocalcemia and hypoparathyroidism respectively). Hypocalcemia and hypoparathyroidism were more frequent in patients who underwent TT (19.2%), as compared to patients who underwent NTT (6.6 %). Among nine

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patients who were operated on twice, three patients had hypocalcemia, and two of them were found to be hypoparathyroid; one case is diagnosed with Graves' disease, while the other was diagnosed as PTC.

Conclusion: Total thyroidectomy, and re-operation are associated with increased prevalence of permanent hypocalcemia and hypoparathyroidism when compared to less extensive thyroid resection modes.

Keywords: hypocalcemia, hypoparathyroidism, post thyroidectomy, Libya.

INTRODUCTION

Hypocalcemia is the most common significant complication after thyroidectomy [1]. It is mostly caused by hypoparathyroidism, which usually occurs as a result of inadvertent gland injury, removal, or de-vascularization [2]. Because of its complexity, it represents the main reason for prolonged postoperative follow-up. Post-thyroidectomy hypocalcemia requires frequent serum calcium monitoring and dose management, which adds to the patient's discomfort and increases in the cost of care [3].

Parathyroid insufficiency can be transient or permanent [4]. Transient hypoparathyroidism is a well-recognized complication of thyroid surgery and is easily treated when it occurs. In most cases, serum calcium levels normalize within a few months with the spontaneous recovery of parathyroid function. In a few patients, however, hypoparathyroidism persists after six months to one year and must be considered permanent. There is a controversy regarding the exact definition of transient and permanent post-thyroidectomy hypocalcemia and hypoparathyroidism, as well as the appropriate duration of resulting follow-up [5]. While most literatures consider six months postoperatively as a cutoff time to differentiate between transient and permanent [6]. The risk of permanent hypoparathyroidism following thyroidectomy remains unclear, varying among recent series from 0 up to 10 % [7].

Although the vast majority of thyroid operations are not associated with hypoparathyroidism, this complication can occur

in about 1% to 3% of cases following a total thyroidectomy [8]. The British Association of Endocrine and Thyroid Surgeons audit reported rates of 27.4 and 12.1 per cent for transient and permanent post-thyroidectomy hypocalcemia respectively [9]. El-Shinawi et al, in their review of 401 patients found that Permanent HPT following surgery on the thyroid gland occurred in 8.5% of the patients while permanent hypocalcemia occurred in 8% of them [10]. A number of research studies have shown that surgeons with little experience in thyroid surgery are much more likely to accidentally remove the parathyroid glands [11]; these studies have shown that surgeons performing more than 100 thyroid operations per year are much less likely to have these complications. This is why most endocrinologists will explain to their patients that they should find the most experienced thyroid surgeon available [12]. The current study aimed to investigate the frequency and risk factors of permanent hypocalcemia and hypoparathyroidism among patients subjected to thyroidectomy in two general hospitals in Benghazi, Libya.

PATIENTS AND METHODS

Study design and setting: This study included all patients registered at endocrine clinics at Alhawary General Hospital and Benghazi Medical Center and underwent different types of thyroidectomy for different thyroid diseases. 136 files were reviewed, 11 of them were excluded because of insufficient data about final histopathologic diagnosis, and the final analysis covered 124 thyroidectomy procedures performed in the period from February 1990 up to

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February 2013. The various types of thyroidectomy included: total thyroidectomy (TT); near total thyroidectomy (NTT); hemithyroidectomy (HT); and bilateral subtotal thyroidectomy (BST).

Biochemical variables: Serum total calcium (reference range 8.5-10.5 mg/dL) was measured with routine methods while levels of plasma PTH were analyzed by an assay for intact PTH (reference range 10–60 pg/ml), eight months post-operatively. Based on our clinical experience, we chose the definition of permanent hypocalcemia and/or permanent hypoparathyroidism, if after six months of thyroid surgery serum corrected calcium level was below 8 mg/dl and serum PTH level was below 10 pg/ml or inappropriately normal levels in the setting of low serum calcium.

Statistical Analysis: The data was summarized using Microsoft excels 2010 then coded and processed on IBM compatible computers, using the Statistical Package for Social Sciences (SPSS) software (version 17). Descriptive statistics of the

different variables were presented either as frequencies and percentages or as means $\pm$ SD. For statistical comparisons, independent samples Chi-square test was employed for testing statistical significance of association between two discrete variables. Significant value is set up at $P < 0.05$.

RESULTS

Of 124 patients, 19 were males and 105 were females, with a male-to-female ratio of 1:6. TT was performed in 78 patients (62.9 %), while 30 patients (24.2 %) underwent NTT, 15 patients underwent BST (12.1 %) and 1 patient underwent HT (0.8%) (Table 1). Surgical indication was benign thyroid disease (BTD) in 100 patients (80.6 %), that included 36 patients with toxic MNG, 27 patients with Graves' disease, 18 patients with thyroiditis, and 19 patients with Non TMNG. 24 patients (19.4%) showed various types of malignant thyroid tumors (MTT) (Table 1), including papillary thyroid carcinoma in 22, medullary carcinoma in 1, and anaplastic thyroid carcinoma in 1 patient.

Table 1: Descriptive of patients who went different types of thyroidectomy and their surgical indications (see text for details)

Gender	Patients Frequency (%)	Types of Thyroidectomy Frequency (%)				Surgical indication Frequency (%)	
		TT	NTT	BST	HT	BTD	MTT
Male	19 (15.3%)						
Female	105 (84.7%)						
Total	124 (100%)	78 (62.9)	30 (24.2%)	15 (12.1)	1 (0.8%)	100 (80.6%)	24 (19.4)

Mean serum Ca^{++} was 8.7 mg/dl $\pm$ 1.13 mg/dl (range 4.1–11.8 mg/dl), while mean serum PTH was 40.1 pg/ml $\pm$ 37.3 pg/ml (range 2–378 pg/ml) (Table 2). Hypocalcemia was prevalent in 38 (30.6 %), 17 of them have hypoparathyroidism (13.7 % of the total patients). Among the hypocalcemic group, female patients experienced postoperative hypocalcemia more frequently than male patients

(32.4 and 21%, respectively) with no significant difference between both groups. Similar results were seen in hypoparathyroid patients (Table 2). The risk of hypocalcemia was higher in patients with malignant thyroid disease in comparison to benign thyroids (45.8 % vs. 27% of patients). However, this difference was not statistically different ($P \geq 0.05$).



Table 2: Number of patients developed hypocalcemia and hypoparathyroidism post thyroidectomy.

Gender	Number of patients with hypocalcemia (frequency % per gender)	Number of patients with hypoparathyroidism (frequency % per gender)
Male (19)	4 (21%)	2 (10.5%)
Female (105)	34 (32.3)	15 (14.3%).
Total (124)	38 (30.6)	17 (13.7%)
Mean±SD	(Ca ⁺⁺)=8.7 mg/dl±1.13 mg/dl	PTH=40.1 pg/ml±37.3 pg/ml

PTC was the most common cause of both hypocalcemia and hypoparathyroidism (45.5% for both) followed by Graves' disease (22.2% and 14.8% for hypocalcemia and hypoparathyroidism respectively) (Table 3).

Hypocalcemia and hypoparathyroidism were significantly more frequent in patients who underwent total thyroidectomy (15 out of 78 patients - 19.2%), as compared to two patients out of 30 who underwent near total thyroidectomy (6.6 %) ($P<0.05$) (Table 4).

Table 3: Distribution of hypocalcemia and HPT patients according to causes of thyroidectomy

Indication of thyroidectomy (Frequency)	Number of patients with hypocalcemia	Number of patients with HPT
Toxic MNG (36)	13 (36.1%)	3 (8.3%)
Graves' disease (27)	6 (22.2%)	4 (14.8%)
Thyroiditis (18)	4 (22.2%)	0 (0%)
Non TMNG (19)	4 (21%)	0 (0%)
PTC (22)	10 (45.5%)	10 (45.5%)
Medullary carcinoma (1)	1 (100%)	0 (0%)
Anaplastic thyroid carcinoma (1)	0 (0%)	0 (0%)
Total (124)	38 (30.6%)	17 (13.7%)

Table 4: Distribution of hypocalcemia and HPT patients according to type of thyroidectomy.

Number of patients with hypocalcemia & HPT	
TT (78)	NTT (30)
15 (19.5%)	2 (6.6%) *

* $P<0.05$

DISCUSSION

Permanent hypocalcemia and hypoparathyroidism is a debilitating morbidity following thyroidectomy. According to

literature, the risk of permanent hypoparathyroidism is up to 17.3% following thyroid surgery [13]. In one meta-analysis study the median incidence of permanent hypocalcemia was 1 (0–3) per cent [14]. El-

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Shinawi et.al, in their review of 401 patients found that Permanent HPT following surgery on the thyroid gland occurred in 8.5% of the patients, while permanent hypocalcemia occurred in 8% of them [10]. Compared to literature, the overall permanent HPT rate in the present study was high, at 13.7%; also that of hypocalcemia was relatively high at 30.6%.

Our analysis focused on the effects of risk factors for the development of post thyroidectomy hypoparathyroidism described in the literatures; these factors include indication of surgery, and the extent of thyroidectomy. Many published studies suggest that the incidence of permanent HPT as a postoperative complication is significantly affected by the underlying thyroid disease [15-17]. Many authors indicate that Graves' disease is an independent risk factor for postoperative hypoparathyroidism [16-18]. Thus, Witte et al. found a high rate of permanent HPT (5.3%) in patients with the diagnosis of Graves' disease [19]. In the study by Yip et al., 4% of permanent HPT cases were reported after thyroidectomy for Graves' disease [6]. In this study we found high frequency of permanent hypocalcemia and permanent HPT in patients with PTC which was 45.5% of both group of patients, followed by patients diagnosed with Graves' disease (22.2% and 14.8% for hypocalcemia and hypoparathyroidism respectively).

In the study by Songun et al., permanent HPT was observed in 5.2% of the patients and there were no significant differences in its occurrence following either subtotal or total resection of the two thyroid lobes [20]. El-Shinawi et al, found that total thyroidectomy was associated with increased prevalence of permanent hypoparathyroidism when compared to less extensive thyroid resection modes (20.2% for TT, 6.7% near-total thyroidectomy and 4.2% subtotal thyroidectomy [10]. Our results showed significant differences in the hypocalcemia and hypoparathyroidism between TT (19.2%) and near total thyroidectomy (6.7%) ($P<0.001$). On the other hand, according to Citation DOI: [10.21502/limuj.011.02.2017](https://doi.org/10.21502/limuj.011.02.2017)



numerous published reports, goiter recurrence and radical re-operative surgery for thyroid carcinoma are associated with higher rates of parathyroid gland insufficiency compared to primary thyroidectomy [21]. Youssef et al., in their analysis of 210 thyroidectomies, found reoperation for recurrent goiter is a significant independent risk factor for development of permanent HPT [22]. Pappalardo et al. reported a high permanent HPT rate in a study of 141 patients. Out of 9 patients who had undergone reoperative surgery for goiter recurrence, 1 was diagnosed with permanent HPT (11%) [23]. In the present study, the rate was even higher, at 22 % (2/9 patients), although it should be emphasized that this group was very small.

This retrospective study showed acceptable results of morbidity with hypocalcemia/hypoparathyroidism. However, this study suffers from many limitations. First, information on all risk factors for hypoparathyroidism was not collected for all patients. There was a lack of exact data on operation time, histopathological diagnosis, whether thyroid cancer patients underwent lymph node dissection and whether patients were on calcium-vitamin D supplements. Other limitations included patients who were operated on by different surgical teams, in different hospitals, with different surgical techniques. Other causes of hypocalcemia were not assessed and we didn't have an idea about serum levels of vitamin D, and no exact data about preoperative serum Ca^{+} levels. All blood samples were drawn at least 8 months post-operation, so we did not have any idea about transient hypocalcemia.

CONCLUSION

Permanent hypocalcemia and hypoparathyroidism is more prevalent among our study as compared with others, which requires further evaluation. Total thyroidectomy, and revision thyroidectomy are associated with increased prevalence of permanent hypoparathyroidism when

compared to less extensive thyroid resection modes.

RECOMMENDATIONS

- Permanent hypocalcemia / HPT requires further evaluation and more prolonged follow up by endocrinologist.
- Use of a less extensive thyroid surgery technique can help to decrease the risk of permanent hypocalcemia/HPT as surgeon can preserve parathyroid gland.

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ملخص باللغة العربية

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خلفية الدراسة: قصور نشاط الغدد المجاورة للدرقية من أكثر المضاعفات شيوعاً بعد عملية استئصال الغدة الدرقية، وهو سبب رئيسي للمراجعات المتكررة لعيادات الغدد الصماء في هذه الدراسة نسعى لمعرفة معدل ظهور هذه المضاعفات والعوامل التي تجعل المريض معرضاً لنقص الكالسيوم وقصور نشاط الغدد جارات الدرقية.

طرق الدراسة: قياس مستوى الكالسيوم وهرمون الغدد جارات الدرقية بعد 8 أشهر على الأقل من عملية استئصال الغدة الدرقية.

نتائج الدراسة: تمت دراسة 124 حالة، 19 (15.3%) ذكور و105 (84.7%) إناث، 38 (30.6%) كان لديهم نقص في معدل الكالسيوم، و17 (13.7%) قصور في نشاط الغدد المجاورة للدرقية. تم استئصال الغدة الدرقية بشكل كامل في 78 مريض (62.9%)، بينما استؤصلت بشكل شبه كامل في 30 مريض (24.2%) من المرضى. ظهر جلياً أن معدل ظهور نقص الكالسيوم كان مرتفعاً في حالات أمراض الغدة الدرقية السرطانية بنسبة (45.8%)، حيث كانت النسبة الأعلى لمرضى سرطان الغدة الدرقية الحليمي بنسبة 45.5%، كما ارتبط نقص الكالسيوم وهرمون الغدد المجاورة للدرقية بالاستئصال الكلي للغدة الدرقية بنسبة 19.8% مقارنة بـ 6.6% من حالات استئصالها بشكل أقل. العوامل التي تؤدي إلى زيادة احتمال الإصابة بقصور نشاط الغدد المجاورة للدرقية هي استئصال الغدة الدرقية بشكل كامل، أو إعادة إجراء عملية استئصالها.

الاستنتاج: الاستئصال الكلي للغدة الدرقية، وإعادة عملية استئصالها ترتبط بزيادة الإصابة بنقص الكالسيوم وقصور نشاط الغدد المجاورة للدرقية، إذا ما قورنت بعملية استئصالها بشكل أقل.

الكلمات المفتاحية: نقص الكالسيوم، نقص هرمون الغدد المجاورة للدرقية، استئصال الغدة الدرقية، ليبيا.