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ORIGINAL ARTICLE

Frequency of post-operative hypoparathyroidism after subtotal thyroidectomy for treating benign multinodular goiter.

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ABSTRACT… Objective: To determine the frequency of post-operative hypoparathyroidism after subtotal thyroidectomy in benign multinodular goiter. **Study Design:** Descriptive Study. **Setting:** Department of Surgery, Madinah Teaching Hospital, Faisalabad. **Period:** 20th March, 2024 to 19th September, 2024. **Methods:** 140 patients of benign multinodular goiter fulfilling the inclusion criteria were enrolled. Patients with toxic goiter, recurrent goiter, any malignancy, pregnant females, autoimmune thyroiditis and vocal cord paralysis prior to the surgery were excluded. All patients underwent subtotal thyroidectomy performed by senior surgeon. Serum calcium and parathyroid hormone levels after 72 hours of surgery during the hospital stay were tested and reported by pathology laboratory of hospital. Post-operative hypoparathyroidism (serum calcium level < 2mmol/L (hypocalcemia) with parathyroid hormone < 15 pg/ml after 72 hours of the surgical procedure) was assessed. The data was analyzed in SPSS version 26. Chi-square test ($p \leq 0.05$) was applied to test significance of statistics. **Results:** The study's age range was 25 to 75 years old, with a mean age of 49.31 ± 11.40 years. Majority of patients i.e. 57.86%, were between 25 to 50 years of age. Of these 140 patients, 80 (57.14%) were females and 60 (42.86%) were males with female to male ratio of 1.3:1. Frequency of post-operative hypoparathyroidism after subtotal thyroidectomy for treating benign multinodular goiter was found in 14 (10.0%) patients. **Conclusion:** Study concluded a higher chance of transient hypoparathyroidism and hypocalcemia following thyroid surgery more likely in young female patients. A cautious surgical approach is advised to lower the risk of postoperative-complications.

Key words: Goiter, Hypocalcemia, Hypoparathyroidism, Subtotal Thyroidectomy.

INTRODUCTION

Thyroid diseases are a common worldwide health issue with different percentage of thyroid dysfunction.[1] Morphologically goiter may either be diffuse or nodular. Generally, goiter proceeds as diffuse form and then becomes nodular.[2] In Pakistan, goiter is more prevalent in hilly area (69.9%) as compared to that of plain area (30.1%).[3] During the late stages of illness, multinodular goiter (MNG) has been found as a common clinical disorder. Though MNG refers to benign and asymptomatic type, however it may incline the patients to a stage with compressive-symptoms i.e. it may grow as independently functioning-nodules or doubtful nodules.[4] The global prevalence of multinodular goiter is 4-7%.[5] For the treatment of thyroid related issues, thyroidectomy is commonly employed as a safe procedure.[6] Thyroidectomy procedures are categorized from lobectomy to total thyroidectomy. The most commonly used methods by surgeons for MNG are subtotal thyroidectomy and total thyroidectomy. Subtotal thyroidectomy involves the bilateral removal of the thyroid tissue as well as the isthmus with residual bilateral 3g remnants of healthy thyroid tissue.[4] Wound infection, hypocalcemia, hemorrhage causing airway obstruction, thyroid storm and recurrent or superior laryngeal nerve injury are the most common complications postoperatively. But, the most common complication of total thyroidectomy is hypocalcemia and is presented as low-ionized serum-calcium levels (<8mg/dl while normal calcium ranges 8.0-10.3 mg/dl). The decrease in parathyroid hormone (PTH) in circulation due to post-operative hypoparathyroidism occurs

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because of devascularization or accidental resection of one or more parathyroid glands by thermal or mechanical surgical trauma.[7] Hypoparathyroidism took place in 6(20%) of the patients undergone total thyroidectomy compared to 3(9.9%) of the patients treated with subtotal thyroidectomy.[8] The normal PTH level ranges between 10-72 pg/ml.

The patients are considered euparathyroid in the absence of hypocalcemic symptoms with PTH levels 10pg/ml. The PTH measurement less than 10 pg/ml recorded within 24 hours post-surgery is demarcated as low PTH. Muscle cramps, perioral paresthesia, laryngospasm, carpopedal spasm, tetany or bronchospasm shows signs and symptoms of hypocalcemia with low PTH.

Rationale of the Current Study

Subtotal thyroidectomy i.e. leaving a wafer of thyroid tissue to inhibit hypoparathyroidism, is commonly adopted to avoid inadvertent injures to the parathyroid glands and its blood supply. Keeping in view the said benefits of subtotal thyroidectomy, the present study was planned to assess the rate of hypocalcemia and permanent hypoparathyroidism using a reasonable study sample size. The current study outcomes will help better management of disease and will propose guidelines for clinicians regarding timely diagnosis, evaluation and management of hypoparathyroidism. Ultimately, it will lead to decrease hospitalization time, morbidity and cost of healthcare. Moreover, this study will be helpful in assessing the magnitude of hypoparathyroidism after subtotal thyroidectomy, that may attract attention of the surgeons in the early treatment of this complication.

METHODS

After taking approval from hospital ethical committee (TuF/IRB/247), this descriptive study was conducted from 20th March 2024 to 19th September 2024 at Department of Surgery, Madinah Teaching Hospital, Faisalabad. Patients coming through OPD fulfilling the inclusion criteria i.e. benign multinodular goiter having subtotal thyroidectomy were enrolled through non-probability, consecutive sampling technique along with informed consent. Moreover, the WHO sample proportion calculator yields a sample size of 140 with a 95% confidence level, at 4.9% margin of error, and taking frequency of post-operative hypoparathyroidism after subtotal thyroidectomy for treating benign multinodular goiter of 9.9%.[8] Patients with toxic goiter, recurrent goiter, any malignancy, pregnant females, autoimmune thyroiditis and with vocal cord paralysis prior to the surgery were excluded. All the patients underwent subtotal thyroidectomy and it was performed by senior surgeon. For evaluation of serum calcium and parathyroid hormone after 72 hours of surgery sample was sent to pathology laboratory of the hospital and result was reported by pathologist. Post-operative hypoparathyroidism (serum calcium level < 2mmol/L) with parathyroid hormone (< 15 pg/ml) after 72 hours of the surgical procedure was assessed. All the information was collected on a specially designed proforma.

For statistical analysis, data was entered and analyzed in SPSS software version 26. Descriptive statistical analysis was applied to quantitative variables like age and mean ± SD (standard deviation) were calculated. Percentage and frequency were also computed for variables i.e. gender, hormonal status and hypoparathyroidism. Stratification was used to control the effect modifiers including age, gender and hormonal status. Hereafter a post-stratification chi-square test was applied to the recorded data and p-value ≤ 0.05 was considered as significant.

RESULTS

In the study group, the patient age ranged from 25 to 75 years, while mean age was 49.31 ± 11.40 years. A relatively high number of patients i.e. 57.86%, were of 25-50 years of age. Out of total 140 patients included in the study, 80 (57.14%) were females and 60 (42.86%) were males (Table-I) indicating female to male ratio of 1.3:1. Frequency of post-operative hypoparathyroidism after subtotal thyroidectomy for treating benign multinodular goiter was found in 14 (10.0%) patients as shown in Figure-1. Stratification of post-operative hypoparathyroidism with respect to gender (p = 0.255), age (p = 0.026), and

hormonal status (p = 0.341) is presented in Table-II.

Variables	Patient	Frequency	%age
Age (years)	25-50	81	57.86
	51-75	59	42.14
Gender	Male	60	42.86
	Female	80	57.14
Hormonal status	Euthyroid	67	47.86
	Hypothyroid	46	32.86
	Hyperthyroid	27	19.29

Table-I. Distribution of patients in different groups based on studied variables (n=140)

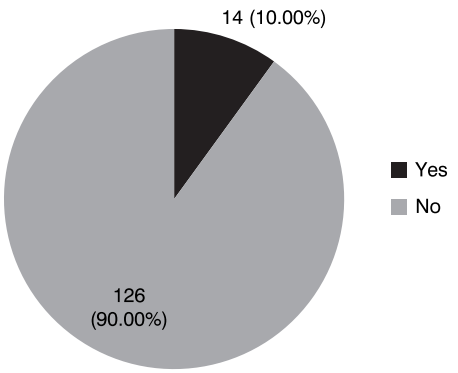

Figure-1. Frequency of post-operative hypoparathyroidism after subtotal thyroidectomy for treating benign multinodular goiter (n=140)

Variable	Patient	Yes (n=14)	No (n=126)	P-Value
Age (years)	25-50	12 (14.81%)	69 (85.19%)	0.026
	51-75	02 (3.39%)	57 (96.61%)	
Gender	Male	04 (6.67%)	56 (93.33%)	0.255
	Female	10 (12.50%)	70 (87.50%)	
Hormonal status	Euthyroid	09 (13.43%)	58 (86.57%)	0.341
	Hypo-thyroid	04 (8.70%)	42 (91.30%)	
	Hyper-thyroid	01 (3.70%)	26 (96.30%)	

Table-II. Stratification of post-operative hypoparathyroidism in study group with gender, age and hormonal status

DISCUSSION

After a thyroid surgery, the true incidence of hypoparathyroidism is up for debate because of variations in analysis and documentation of this complication. However, it can effect up to 38% of patients.[9] A customized strategy to prevent symptomatic hypocalcemia and shorten the length of hospital stay would be possible with the premature stratification and identification of patients having higher threat of problems. There is an absence of agreement among physicians for patient selection, cut-off points and the timing for testing PTH levels. Despite this, monitoring serum calcium levels and PTH after thyroidectomy are the major analysts for detecting hypoparathyroidism and treating the consequential indicative hypocalcemia.[10]

Nagel et al.[11] while performing recent meta-analysis, assessed nature of postoperative hypoparathyroidism referring to variations in PTH and calcium levels and their inter dependence altogether with the presence of clinical-symptoms. They suggested that the occurrence of an untraceable or unusually low postoperative-PTH level in hypocalcemia with or without hypocalcemic indications, might be a characteristic of hypoparathyroidism. However, The American Thyroid Association states that a postoperative-PTH level of less than 15 pg/mL is classically indicative of hypocalcemia[10,12] and that the majority of studies have timed PTH measures between 10 minutes and 24 hours after thyroidectomy.[13] The spell of PTH measurements following surgical procedures can differ significantly; intraoperative, 1-4 hours after surgery, or one day postoperative. However, many authors reported to take early measurements of PTH within 4-6 hours of surgery as possible prognostic of interim postoperative-hypocalcemia.[14] Nevertheless, it makes sense that therapeutic calcium and vitamin D prescription would be administered earlier before clinical symptoms if PTH levels were measured sooner. However, it may rely on facilities unique to the area.[10]

Most of patients may be discharged without calcium supplementation as calcium ≥ 2.0 mmol/L and

PTH > 15 pg/mL at first postoperative day have been linked with low possibility of symptomatic hypocalcemia. A PTH level higher than 10 pg/mL postoperative day 1, can be considered as a harmless threshold for patient discharged without calcium supplementation according to numerous other studies in the literature.[10-15]

Many groups favored assessing postoperative or intraoperative intact PTH levels taken at different times during the early post-thyroidectomy period in order to improve the sensitivity and capacity of PTH concentration to predict the likelihood of the hypoparathyroidism.[10] In a cohort of 124 patients, Swift et al.[16] assessed the best time to monitor PTH. PTH levels were taken before surgery, 30 minutes after the procedure and 6 hours after the procedure. The most significant predictors of hypocalcemia were PTH-levels at 30 minutes and 6 hours after the procedure. Our results are in line with earlier reports by Schlottman et al.[17] as well as Lombardi et al.[18], who measured PTH at various consecutive time-intervals and discovered that postoperative hypocalcemia could be accurately predicted by only one PTH level measurement between 4 and 6 hours after surgery.

Only 49 of the 101 patients who presented with blood calcium below 7.5 mg/dL recorded PTH levels below 12 pg/mL, while the PTH values were within the normal range in remaining 52 patients.[19] Del Rio et al.[19] further supported this supposition. In contrast, among current study group of patients having postoperative-PTH levels less than 12 pg/mL, a higher incidence of postoperative temporary hypocalcemia was observed. Additionally, a significant change was observed in PTH levels between current study group patients with postoperative-hypocalcemia (16.7 ± 5.13 pg/mL) as compared with those having normocalcemia (32.2 ± 24.4 pg/mL, $p < 0.001$). In general, patients having postoperative hypocalcemia displayed lower levels (65.7%) of PTH than preoperative ones. Moreover, this difference in hypocalcaemia was even more prominent (90.1%) in patients having a postoperative-PTH lower than 12 pg/mL.

The impact of age on the progress of postoperative-hypoparathyroidism remained inconsistent findings in the literature. In current study, the patient age ranged from 25 to 75 years, while mean age was 49.31 ± 11.40 years. A relatively high number of patients i.e. 57.86%, were of 25-50 years of age. Previously, younger age was found to have an impact in some research[20], although this link was not supported by many other studies.[19] Due to the higher susceptibility and frequency of thyroid pathology in the female sex, patients with this gender under 25-50 years of age were more likely to develop postoperative-hypocalcemia (Table II). The effects of sex-steroids on PTH-secretion may be a result of this higher predisposition[21], though this relationship has been reported with inconsistent findings.[10]

According to Privitera et al.[22], the rate of postoperative hypocalcemia in thyroid cancer patients is closely related with the degree of surgery, particularly neck dissection. This fact was supported by this study, which found that patients (5.2%, $p = 0.028$) having lymph node metastases undertaking neck dissection had a higher-risk (OR = 1.534 (95% CI 1.095–2.148), $p < 0.05$), of postoperative hypoparathyroidism. However, the diagnosis of thyroid cancer was not linked to a higher threat of hypoparathyroidism. Remarkably, the mean number of lymph nodes recovered was larger in individuals with low postoperative PTH levels than in those with greater PTH-levels (8.30 compared to 4.09, $p = 0.005$). The high incidence of incidental-parathyroidectomy in thyroid cancer patients[22], may help to explain this, where it can be difficult to distinguish between swollen lymph nodes and parathyroid glands. Although there appears to be a correlation between surgeon experience and center volume[23], neck-dissection in thyroid cancer patients has been linked to hypoparathyroidism.

The retrospective analysis of 511 patients receiving complete thyroidectomy, described that patients with more detected parathyroids had a higher prevalence of hypocalcemia[26]. This would imply that a thorough examination of parathyroid, even if they appear to be in good condition, could reveal a devascularization of parathyroids[27], ultimately resulting in hypoparathyroidism.

Our analysis further supported this apparent paradox, showing that patients with incidental parathyroidectomy experienced a significantly higher rate of temporary hypocalcemia. A noticeable percentage (27.9%) of patients without incidental-parathyroidectomy faced temporary hypocalcemia, while 1.7% (11 patients) experienced definitive-hypocalcemia. This clearly suggests that a postoperative normal parathyroid function cannot be guaranteed with 100 percent certainty, even if all glands are well preserved.[28]

Although this is the largest single-center study being reported in the medical literature. Yet main limitation may be, the field has previously been investigated. However, it needs confirmation. Furthermore, even though the study is descriptive, the data are homogeneous because the similar surgical team performed the surgeries in a high capacity institution, which may lessen the bias brought on by varying experiences of surgeons.

CONCLUSION

In conclusion, there may be a higher chance of transient hypoparathyroidism and hypocalcemia following thyroid surgery. Young female patients who have their neck dissected are more likely to experience transient hypoparathyroidism. Incidental-parathyroidectomy is linked to a high degree of postoperative-hypoparathyroidism, although a significant percentage of patients without incidental-parathyroidectomy can have temporary postoperative hypocalcemia. This suggests that a cautious surgical approach is advised to lower the risk of postoperative-complications.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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AUTHORSHIP AND CONTRIBUTION DECLARATION	
1	**Muhammad Ans:** Study Design, research, data collection and analysis, writing of manuscript.
2	**Saad Yaqub:** Data analysis.
3	**Tanvir Ahmad:** Topic proposal, study design, discussion.
4	**Sahabia Masood:** Writing, reference collection.
5	**Samina Ashfaq:** Data collection, analysis.