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Original Article

Frequency of Post-Operative Hypocalcemia after Total Thyroidectomy for Graves' Disease versus Multinodular Goiter

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ABSTRACT

Objective: To compare the frequency of post-operative hypocalcemia after total thyroidectomy for Graves' disease compared with multinodular goiter.
Study Design: Quasi experimental study.
Place and Duration of Study: Department of Surgery, Pak-Emirates Military Hospital, Rawalpindi Pakistan, from Mar 2022 to Feb 2023.
Methodology: A total of 161 patients were enrolled and divided into two groups, where Group-A consisted of 110 patients, undergoing total thyroidectomy for multinodular goiter, while Group-B had 51 patients, undergoing total thyroidectomy for Graves' disease. Participants were enrolled using non-probability sequential sampling. All data was collected on a self-designed data collection tool and manually entered into data analysis software for final analysis.
Results: Our study found hypocalcemia after 24 hours of total thyroidectomy in 11(10.0%) patients of Group-A and 9(17.6%) patients of Group-B, with an additional 21(19.1%) patients from Group-A and 13(25.4%) patients of Group-B when 48 hours had elapsed (p-value=0.06). Serum calcium levels performed two months after surgery detected low levels in 4(3.6%) patients of multinodular goiter and in 7(13.7%) patients with Graves' disease (p=0.034).
Conclusion: Patients with Graves' disease have greater likelihood than patients of multinodular goiter, of experiencing transient hypocalcemia and persistent hypocalcemia after total thyroidectomy, warranting more careful monitoring in these patients.

Keywords: Graves' Disease, Hypocalcemia, Multinodular Goiter, Total Thyroidectomy.

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INTRODUCTION

Thyroidectomy is a commonly performed procedure for different diseases of the thyroid gland.[1,2] In cases of benign multinodular goiter, total thyroidectomy is preferred due to its low recurrence rate,[3] and fewer complications.[4] For Graves' disease, the initial treatment may be anti-thyroid medications or radioactive iodine but surgery is the definitive treatment and may be indicated because of local compressive symptoms, or nodules that could harbor malignancy.[5] Hypocalcemia is a major post-operative complication after total thyroidectomy, due to intraoperative damage to the parathyroid gland, which can be because of de-vascularization, direct or dissection injury and accidental removal of parathyroid gland, causing transient asymptomatic hypocalcemia, acute symptomatic hypocalcaemia and permanent hypocalcemia.[6-9] Hypocalcemia typically occurs at around 24-48 hours post-operatively with a series of symptoms, ranging from mild paresthesia and tingling to more severe cramps, tetany, convulsions and cardiac arrest, however, hypocalcemia symptoms are uncommon unless serum calcium level drops below 2mmol/l (8mg/dl), although it is lower than the reference range.[10] With this study, we aimed to determine the occurrence of persistent hypocalcemia after 2 months among patients undergoing total thyroidectomy for multinodular goiter and Graves' disease.

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METHODOLOGY

This quasi-experimental study was carried out in the Female Ward of the Department of Surgery, at Pakistan Emirates Military Hospital (PEMH) and Combined Military Hospital (CMH), Rawalpindi Pakistan, from March 2022 to February 2023, after gaining approval from the Institutional Review Board via Ethics Review Committee letter 357, dated 28 February 2022. The sample size for single proportion, with a confidence level of 95% and precision of 7.5%,

was found to be 123. In a previously published observational study, hypocalcemia was diagnosed when serum corrected calcium level dropped below 8mg/dl, with an overall incidence of hypocalcemia in 161 patients, after total thyroidectomy, found to be 23.6%.[11] A total of 191 patients were enrolled in our study initially, of which 27 were lost to follow up and 3 patients left on the 3rd post-operative day, with plans to follow up in peripheral hospitals. Thus, total sample size comprised of 161 patients. We divided our enrolled participants into two groups, after taking informed, written consent. Group-A comprised 110 patients of Multinodular Goiter on whom total thyroidectomy was performed while Group-B comprised of 51 patients with Graves' disease. The surgeons who performed the surgeries were experienced surgeons and parathyroid glands were identified and spared in all the surgeries.

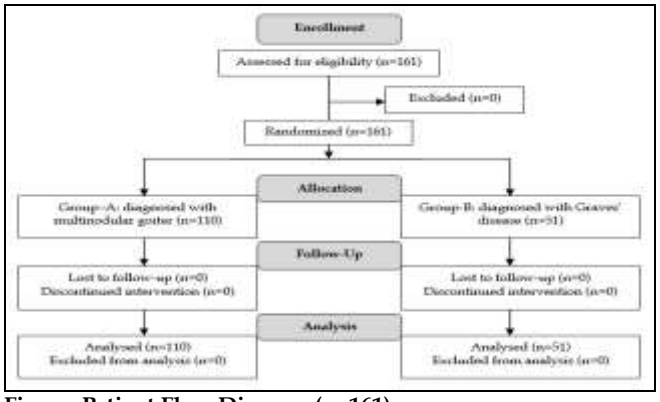

Figure: Patient Flow Diagram (n=161)

Inclusion Criteria: Patients diagnosed with multinodular goiter and Graves' disease admitted for total thyroidectomy were included.

Exclusion Criteria: Patients who had lobectomies, recurrent multinodular goiter, completion thyroidectomy following hemi-thyroidectomy, preoperative hypocalcemia or received calcium supplementation were excluded.

Calcium levels of all patients were noted at 24 and 48 hours post-operatively. All the patients were called for follow-up after 2 months and their calcium levels repeated. Our primary outcome was incidence of hypocalcemia post-total thyroidectomy. Statistical Package for Social Sciences (SPSS) version 26 was used for data analysis. Descriptive and inferential statistics were employed. Qualitative variables were analyzed in the form of frequencies, percentages. We applied t-test, for comparison between groups, and Pearson chi-square, to establish any statistically significant difference among both groups. The *p*-value ≤0.05 was considered as significant.

RESULTS

Out of 161 patients, 74(45.9%) were from CMH and 87(54.1%) were from PEMH. Out of these patients, 118(73.3%) were females and 43(26.7%) were males. Mean age of patients was 43.88±9.30 years, ranging from 28-67 years. Further details of demographic characteristics of participants is listed in Table-I.

Table-I: Comparison of Demographic Characteristics of Participants (n=161)

Variables	Group-A (n=110)	Group-B (n=51)	*p*-value (≤0.05)
Gender			
Female	88(72.7%)	38(74.5%)	0.821
Male	30(27.3%)	13(25.5%)	
Age (Years)			
Mean±SD	47.12±8.77	36.90±6.02	<0.001

Hypocalcemia was detected after 24 hours of total thyroidectomy among 11(10.0%) patients of Group-A and 9(17.6%) patients of Group-B although there was no statistically significant difference between these two values (*p*-value=0.107). Hypocalcemia was detected in an additional 21(19.1%) patients of Group-A and 13(25.4%) patients of Group-B after 48 hours and there was a statistically significant difference present (*p*-value=0.06). However, after two months, low levels were detected in 4(3.6%) patients Group-A and in 7(13.7%) patients of Group-B with a statistically significant difference noted (*p*=0.034) between both groups (Table-II).

Table-II: Presence of Hypocalcemia between Group-A and Group-B after 24 Hours, 48 Hours and 2 Months (n=161)

Hypocalcemia		Study Group		*p*-value (≤0.05)
		Group-A (n=110)	Group-B (n=51)	
24 Hours	Yes	11(10.0%)	9(17.6%)	0.107
	No	99(90.0%)	42(82.3%)	
48 Hours	Yes	21(19.1%)	13(25.4%)	0.06
	No	89(80.9%)	38(74.6%)	
2 Months	Yes	4(3.6%)	7(13.7%)	0.034
	No	106(96.4%)	44(86.3%)	

DISCUSSION

In our study, patients with multinodular goiter were in the age range of 31 to 67 years with a mean age of 45.31±8.9 years. In literature, the usual mean age of similar patients varies from 33.4 to 49.71 years[1,14] with a male to female ratio of 1:1.6[1] while in our study, the male to female ratio was 1:2.3.

Concurrently, patients with Graves' Disease were in the age range of 29 to 46 years with a mean of 39.90±6.67 years while the usual mean age of similar varies from 44.7 to 50 years according to recent studies[15,16] with a female to male ratio of 1:2.9[16] while in our study it was 1:2.6. The incidence of transient hypocalcemia in multinodular goiter was found to be 10.8% in one study,[17] which is comparable to our findings. In another study, the incidence of transient hypocalcemia after total thyroidectomy for multinodular goiter was found to be 20.6% which is similar to our findings.[18] In one study, an increased incidence of hypocalcemia, after total thyroidectomy for Graves' Disease, was noted with 39 out of 108 patients developing post-operative hypocalcemia,[19] which was also reported by another study,[18] similar to our findings. One meta-analysis done on 22,940 patients concluded that there was a significantly higher incidence of transient hypocalcemia in patients with Graves' disease who underwent total thyroidectomy.[20] As per our literature search, the incidence of permanent hypocalcemia after total thyroidectomy for multinodular goiter and Graves' disease was noted to be 0.85% and 9.52% respectively, with higher incidence of hypocalcemia after total thyroidectomy in patients of Graves' disease, which is comparable with our study.[20] Moreover, our findings indicated that increasing age and female gender were significantly associated with an increased risk of hypocalcemia after total thyroidectomy, which is consistent with the findings of previous studies.[22,23]

LIMITATIONS OF STUDY

Our study did not investigate other potential risk factors for hypocalcemia, such as surgical technique employed, extent of thyroidectomy and per operative mishaps. Future studies are needed to address these limitations and provide a more comprehensive understanding of the severity of hypocalcemia after total thyroidectomy.

CONCLUSION

Patients with Graves' disease have increased likelihood of transient hypoglycemia and persistent hypocalcemia after total thyroidectomy compared to patients of multinodular goiter which requires careful post-operative monitoring and calcium supplementation if required.

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Authors' Contribution

Following authors have made substantial contributions to the manuscript as under:

MIR & SRQN: Data acquisition, data analysis, critical review, approval of the final version to be published.

SQN & HAM: Study design, data interpretation, drafting the manuscript, critical review, approval of the final version to be published.

SMK & UMR: Conception, data acquisition, drafting the manuscript, approval of the final version to be published.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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