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Comparison of outcome of total thyroidectomy with and without pre-operative calcium and vitamin D supplements in terms of post-operative hypocalcemia.

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ABSTRACT… Objective: The objective of this study is to compare the effect of pre-operative calcium and vitamin D supplements in terms of hypocalcemia in patients with total thyroidectomy. **Study Design:** Comparative study. **Setting:** EAST Surgical Ward, MAYO Hospital Lahore, Pakistan. **Period:** 1st July 2018 to 30th June 2020. **Material & Methods:** Sample size of 342 patients and duration of 2 years. 2 groups were created including 171 patients each. Group A patients received calcium and vitamin D supplements 1 week prior to total thyroidectomy while Group B patients didn't receive any supplements. The results of both groups were compared. Data was collected by pre designed proforma and evaluated by SPSS 21. **Results:** 164 (47.9%) patients were male and 178 (52.0%) were females. Most common age group which undergone total thyroidectomy was between 31 years to 40 years. Total 140 patients (40.93%) experienced hypocalcemia. In group A, 32 (18.71%) experienced hypocalcemia while in group B 108 (63.1%) experienced hypocalcemia. The most common occurrence of hypocalcemia was noted on 1st post-operative day where 52 (37.14%) cases of hypocalcemia were reported. **Conclusion:** In a country with prevalent calcium and vitamin D deficiency the addition of these supplements one week prior to total thyroidectomy will lead to lesser incidence of hypocalcemia after total thyroidectomy and early discharge of the patient.

Key words: Calcium, Hypocalcemia, Supplements, Surgery, Thyroidectomy, Vitamin D.

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INTRODUCTION

The thyroid gland is one of the most important endocrine organs in the human body.[1] Worldwide thyroid diseases are very common from benign conditions to rapidly growing malignant conditions. It has been approximated that about 42 million people around the globe are suffering from thyroid problems.[2] Thyroid surgery is one of the most commonly performed surgery in the surgical residency as well as the surgical career of a general surgeon. There are many types of thyroidectomy including lobectomy, subtotal, near total and total thyroidectomy depending upon the condition of thyroid disease.[3]

The most common post-operative complication of thyroid surgery is damage to the recurrent laryngeal nerve and hypocalcemia. Hypocalcemia as a result of hypoparathyroidism is very common complication of total thyroidectomy.[4] It may be transient which get recovered before 6 months and permanent if it does not get recover within 6 months after surgery. Hypocalcemia is seen in about 0.3% to 49% of patients undergoing thyroidectomy.[5] It occurs because of transient hypo-parathyroidism due to parathyroid gland manipulation or impairment of its blood supply. The development of postoperative hypocalcemia after total thyroidectomy is unfavorable not only since it is a cause of morbidity but also because it occurs 24 to 72 hours postoperatively and hence necessitates prolonged hospital stay with intravenous calcium supplementation and at times repeated biochemical testing.[6]

The use of calcium and vitamin D supplements after total thyroidectomy is controversial. Some thyroid surgeons routinely start calcium

supplements from the first postoperative day while some wait for development of sign and symptoms of calcium deficiency confirmed by laboratory investigations of serum calcium levels and serum Parathyroid hormone levels.[7]

The development of hypocalcemia post operatively after total thyroidectomy is unpredictable and preoperatively it is impossible to say which patient develop hypocalcemia in the post-operative period.[8] It has been proposed that malnourished patients or patients with increased calcium and vitamin D demands like teenage, pregnancy and patients with any bone disorder are those who are at high risk of developing hypocalcemia in the post-operative period after total thyroidectomy.[9]

Many risk factors have been identified for postoperative hypocalcemia including age >50 years, female gender, thyroid malignancy, Grave's disease, lymph node dissection, non-identification of parathyroid glands intra operatively, reoperation, and Vitamin D deficiency.[10] The prediction of patients who can be discharged early or those who would require close monitoring and postoperative calcium and Vitamin D supplementation is difficult. Although 1 hourly and 4 hourly postoperative intact parathormone (iPTH) testing has been shown to stratify patients into high- and low-risk for hypocalcemia and expedite an early discharge after total thyroidectomy, rapid iPTH measurement facility is not routinely available in many resource-poor settings and is hence not feasible.[11]

A high prevalence of Vitamin D deficiency has been demonstrated in some Northern Pakistani states and is a known risk factor for postoperative hypocalcemia after total thyroidectomy.[12] To prevent postoperative hypocalcemia, routine Vitamin D supplementation as a standard protocol merits consideration. Although routine postoperative oral calcium and Vitamin D supplementation has been shown to prevent the development of hypocalcemia after total thyroidectomy and facilitate an early discharge the role of preoperative supplementation has seldom been tested.[13] Ozturk UI et al reported that the incidence of hypocalcemia was lower in the treatment group receiving the supplement than in the control group not receiving the supplement: 24% versus 44%.[14]

So, this study was conducted to assess the role of pre-operative calcium and vitamin D supplements before total thyroidectomy. We hypothesize that a 1-week preoperative Vitamin D and calcium supplementation to a cohort of patients belonging to our setting of Vitamin D deficiency would reduce the rates of hypocalcemia and associated morbidity.

MATERIAL & METHODS

It was an observational cross-sectional study conducted in Surgery department of MAYO Hospital which is the tertiary care hospital of Punjab and teaching hospital of King Edward Medical University (KEMU) Lahore Pakistan. The duration of the study was 2 years, from 1st July 2018 to 30th June 2020. The study was approved by the Institutional Review Board of King Edward Medical University 232/KEMU/RC. A total of 342 patients were selected for this study by consecutive non probability sampling technique. These 342 patients were divided into 2 groups, Group A and Group B each containing 171 patients. Group A patients were given Calcium and vitamin D supplements, started 7 days before total thyroidectomy while no supplementations were given to Group B patients. Calcium supplements were given in the form of 500 milligrams of elemental calcium tablet per oral three times per day. Vitamin D supplements were given as 600 IU (15mcg) per day for 7 days pre operatively as a single dose as oral solution. All those patients were selected in this study who presented in outdoor department of MAYO Hospital Lahore and were aged 20 and above including both genders and having simple or drug controlled multi nodular goiter. Exclusion criteria include patients with both type 1 and type II diabetes, concomitant parathyroid disease, any type of carcinoma thyroid, toxic multi nodular goiter, chronic renal failure, hypoalbuminemia, any respiratory disease, cardiovascular disease or peripheral occlusive disease and patients taking any calcium or vitamin D supplementation

previously for any other chronic disease. Hypocalcemia was defined as serum calcium level of < 8 mg/dl and symptomatic hypocalcemia was defined as patients having calcium level of < 8 mg/dl with signs and symptoms of hypocalcemia like cheveostic sign, trosseus sign, cramps and numbness of extremities. Written and informed consent was taken from all the patients for including them in study and for total thyroidectomy under general anesthesia. Total thyroidectomy was performed by different consultant general surgeons with experience of more than 5 years and whole of the thyroid gland was removed from the neck of the patients. Serum calcium profile was measured one day before surgery and then on 1st,3rd,7th and 4th postoperative day. Hypocalcemia observed in postoperative period was treated as standard protocol mentioned by Arer et al. Standard Chvostek's and Trousseau's signs will be monitored in the postoperative period every 6th hourly.[15] In severe cases intravenous calcium gluconate 10% in normal saline will be administered at dose of 1 mg calcium/kg body weight per hour. Data was analyzed on SPSS 20 and was expressed as mean ± standard deviation (minimum – maximum). Multivariate analysis was done using logistic regression analysis. Categorical data analysis was done using Chi-square test and Student's t-test. P <0.05 was considered statistically significant. Comparison of proportions between both groups was made by using the $\chi 2$ test and The Fisher's exact test was used when applicable.

RESULTS

Total 342 patients were included in this study out of which 164 (47.9%) patients were male and 178 (52.0%) were females. Most common age group which undergone total thyroidectomy is between 31 years to 40 years (Table-I). The mean age of the patients was 38 years with standard deviation of ±5 years. The minimum age of patient included in this study was 24 years while maximum age was 68 years. Total 140 patients experienced hypocalcemia. Out of 171 patients included in group A, 32 (18.71%) experienced hypocalcemia while in group B 108 (63.1%) experienced hypocalcemia (Table-II). The most common occurrence of hypocalcemia was noted on 1st post-operative day where 52 (37.14%) cases of hypocalcemia was reported. The incidence of hypocalcemia reduced to 14 (10%) after 7th post-operative day (Table-III).

Age Group	No of Patients	Percentage
20 years – 30 years	32	9.35 %
31 years – 40 years	114	33.33 %
41 years – 50 years	92	26.9 %
51 years – 60 years	68	19.88 %
61 years – 70 years	36	10.52 %
Total	342	100%

Table-I. Age distribution of the patients.

	Group A With Pre-operative Calcium and Vitamin D supplementation (N = 171)	Group B Without Pre-operative Calcium and Vitamin D supplementation (N = 171)	Total (N = 342)	P- Value
Post-operative hypocalcemia	32 (18.71%)	108 (63.1%)	140 (40.93%)	0.04

Table-II. Comparison of group A and group B.

Post-Operative Day of Hypocalcemia	No of Patients with Percentage
1st Post-Operative day	52 (37.14%)
3rd Post-Operative day	40 (28.57%)
7th Post-operative day	34 (24.2%)
14th Post-operative day	14 (10%)
TOTAL	140 (40.93%)

Table-III. Relation between incidence and number of hypocalcemia cases to post-operative day.

DISCUSSION

The major source of calcium and vitamin D for the human body is through diet. That is the reason diseases due to calcium and vitamin D deficiency are rare in countries where there is full availability of the well-balanced diet.[16] This is exactly opposite to the under developed countries where poverty is the very common and the reach to well-balanced diet is impossible for many people. Also, there are conditions where there is increased demand of calcium and vitamin D levels like pregnancy and teenage. Females require more calcium and vitamin D rich diet as compared to males.[17] Unfortunately, Asia and particularly Pakistan is among those developing countries where calcium and vitamin D deficiency is prevalent. Vitamin D

deficiency is pervasive in South Asian population and in Pakistan it has been estimated that a high number of asymptomatic adult patients have low vitamin d level.[18] Females have comparatively lesser mean vitamin D levels (56.2%) as compared to males (15.3%).It has been reported that calcium and vitamin D deficiency in 11.3% of population with 9.65% females and 1.65%males.[19] This shows the extent of hypocalcemia in Pakistan and when these calcium and vitamin D deficient have thyroid or parathyroid disease as well which require total thyroidectomy then the chances of getting hypocalcemia post operatively is more as compared to the patient without deficiency.[20]

In clinical practice hypocalcemia is the most common complication encountered after total thyroidectomy. Many surgical techniques are now discovered to preserve the parathyroid gland but still transient hypocalcemia occurs in about one third of total thyroidectomies performed worldwide.[21] The main per operative cause identified during total thyroidectomy is hypoparathyroidism which is caused by DE vascularization or injury to the parathyroid gland. Though it is multifactorial problem many authors mentioned the postoperative decline in the serum calcium levels and parathyroid hormone levels.[22] In a study done by Unsal et al, it was discovered that the administration of early pre-operative calcium supplements to the patients who will have parathyroid surgery or total thyroidectomy, prevents the post-operative hypocalcemia spells and early discharge of the patients.[23] While on the hand in a study done by Wang et al, there is no role of pre-operative calcium supplements and the incidence of post-operative hypocalcemia is almost same in patient with and without preoperative calcium supplements.[24]

In this study we assessed the incidence of hypocalcemia in patients after total thyroidectomy after giving one group pre-operative calcium and vitamin D one week prior to the operation and compared this group with other group who didn't received any calcium and vitamin D supplements. Out of total 342 patients, hypocalcemia was observed in 140 patients (40.93%). We found that group A patients who received calcium and vitamin D supplements had lower incidence of post-operative hypocalcemia (32 (18.71%)) as compared to the group B who didn't received any supplements (108 (63.1%)) (P Value = 0.04). The results of this study were same as the previous study done by Elsaeiti et al, which states that pre- and post-operative oral calcium and vitamin D supplements can prevent the post-operative hypocalcemia and hence leads to early and safe discharge of the patients.[25] This will ultimately lead to improved patient satisfaction and significant cost savings. Another study done by Jaan et al also state the significance of pre-operative calcium and vitamin D supplementation.[26]

In our study out of 140 patients who experienced hypocalcemia, most of the patients experienced hypocalcemia on the first post-operative day 52 (37.14%). This shows the already depleted calcium and vitamin D reserves among these patients and local population. In a study done by Benkhadoura er al, peaked hypocalcemia was observed on first operative day while based on serum calcium level third post-operative day is crucial for the decision of discharge of patient.[27]

CONCLUSION

This study clearly states the importance of pre-operative calcium and vitamin D supplements in Pakistani population. The administration of oral calcium and vitamin D supplements one week prior to total thyroidectomy not only decreases the incidence of post-operative hypocalcemia but also allows early discharge of the patient. More local studies and easy provision of calcium rich diet and oral calcium supplements are required to get knowledge of other factors of post-operative hypocalcemia.

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AUTHORSHIP AND CONTRIBUTION DECLARATION

Sr. #	Author(s) Full Name	Contribution to the paper	Author(s) Signature
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