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Original Article

Surgery Section

Effect of Preoperative Hypovitaminosis D on Post-Total Thyroidectomy Transient Hypocalcaemia: A Retrospective Cross-sectional Study

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ABSTRACT

Introduction: Total Thyroidectomy (TT) is a standard surgical procedure for Multinodular Goiter (MNG). Transient hypocalcaemia is a frequent complication of TT with significant postoperative morbidity and long-term consequences. Many patient and surgical factors are attributed to postoperative hypocalcaemia. Vitamin D deficiency is one of the contributory factors in few of the studies, which is a modifiable risk factor. However, there is limited data to support the same.

Aim: To evaluate the effect of preoperative vitamin D deficiency on postoperative hypocalcaemia in patients undergoing TT surgery.

Materials and Methods: This was a retrospective cross-sectional, descriptive study done on patients undergoing TT for MNG in a single general surgical unit at a tertiary care teaching hospital in Southern India. The data pertaining to patients undergoing TT for MNG between January 2017 to February 2018 were collected. Patients who had low preoperative vitamin D levels before surgery were included. The preoperative vitamin D levels were correlated with postsurgery total serum calcium using pearson correlation and the association of preoperative serum total calcium was examined with postoperative serum total calcium by using paired t-test. The results were analysed using Statistical Package for the Social Sciences (SPSS) Version 20. The p-value<0.05 was considered statistically significant.

Results: Thirty-two patients had preoperative documented vitamin D deficiency. Preoperative mean serum vitamin D level was 15.42 ng/mL (R=3.21 to 29 ng/mL). Mean preoperative calcium level was 9.28±0.51 mg/dL at admission. Postoperatively mean serum total calcium level was 8.54±0.47 mg/dL. There was no correlation between preoperative vitamin D levels and postoperative low serum calcium levels (Pearson R=0.154).

Conclusion: There was no influence of preoperative vitamin D levels on postoperative transient hypocalcaemia. Prospective studies with well-defined controls in a larger cohort are needed for ascertaining the same, as it has wider clinical implications.

Keywords: Low vitamin D, Multinodular goiter, Postoperative hypocalcaemia

INTRODUCTION

The TT is a standard surgical procedure for MNG. After TT, the hypocalcaemia is a much troublesome complication [1,2]. The hypocalcaemic symptoms range from mild perioral numbness or distal acral paresthesia to more severe symptoms such as carpopedal spasm, tetany, laryngospasm, cardiac arrhythmias [3]. After thyroidectomy, the incidence of transient hypocalcaemia is up to 50% and permanent hypocalcaemia is up to 4% [4,5].

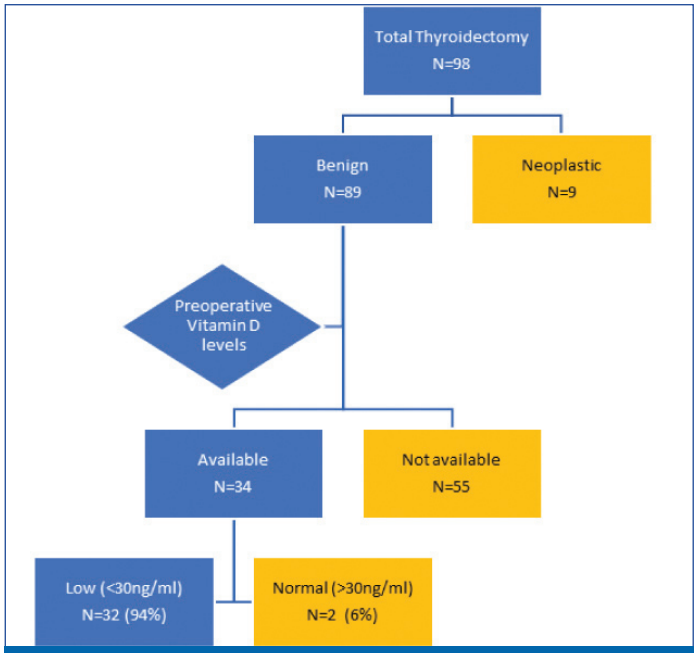
The assumed factors for post-TT hypocalcaemia are biochemical blood parameters before and after surgery, factors related to surgery, surgical technique, surgeon's experience, the patient, and the disease [6]. But the exact cause and mechanisms of post-thyroidectomy hypocalcaemia remains unclear. The importance of vitamin D in serum calcium regulation is well-known. Vitamin D is required for maintaining normal serum calcium levels. However, whether patients with vitamin D levels are predisposed to postsurgery low serum calcium levels is not fully known.

There is limited data showing the role of vitamin D levels as a risk factor for hypocalcaemia after TT. Some studies [7] have found positive correlation of low vitamin D on postoperative hypocalcaemia while others [8] have not. In this context, we endeavor to study the effect of preoperative vitamin D deficiency (Hypovitaminosis D) on post-TT transient hypocalcaemia in the patients. This knowledge is important as correction of preoperative hypovitaminosis potentially can modify this risk factor preventing/reducing postoperative hypocalcaemia.

MATERIALS AND METHODS

This was a retrospective analysis of patients undergoing TT for MNG in a single general surgical unit at a tertiary care teaching hospital in hilly terrain of Southern India. The patient records between January-2017 and February-2018 were retrieved. As this was a retrospective study of descriptive, non-interventional nature without modification in their line of treatment or treatment outcomes and there being no harm, or intrusion into their privacy/infringement of rights of any kind, the ethical committee review and consent was not necessary.

The flow chart of selection process is given in [Table/Fig-1]. Ninety-eight records of patients undergoing TT during the study period were available. Patients who on final histopathological examination were having a neoplasm were excluded from the study as they would involve lymph node dissection and extensive surgery that might impact blood supply to parathyroid glands which can be a confounding factor. Of the 89 patients of MNG, 55 patients with no documented vitamin D levels were excluded. Of the remaining 34 patients with preoperative vitamin D level data, 32 had hypovitaminosis and only two of them had vitamin D values of 30.4 ng/mL and 32.0 ng/mL which is by definition is considered normal [9]. As they form a very small subset for any meaningful comparison they were excluded from the study. Hence, finally only 32 patients who had low preoperative vitamin D levels defined [9] as serum vitamin D less than 30 ng/mL were included in the study with no control group left.



[Table/Fig-1]: Flowchart showing the patient selection process. Total number (N) of patients undergoing Total Thyroidectomy (TTE) in the study period was 98. Number patients qualifying for analysis were 32.

Surgical Technique

Surgery was performed using a capsular dissection technique, with careful identification and conservation of all the parathyroid glands, together with the recurrent laryngeal nerve. Further, only patients operated by same unit were included to eliminate confounding factors related to technique of surgery, surgeon experience and methodology in data collection. We routinely do serum calcium levels between 48 to 72 hours after surgery or whenever the patients exhibit the symptoms of hypocalcaemia clinically. Symptoms observed being paresthesia, numbness, muscle cramps, carpopedal spasm or other symptoms that could be attributable to hypocalcaemia in the postoperative period. None of the patients had tetany, laryngospasm, cardiac arrhythmias. Hypocalcaemia was defined as serum calcium level below 8.5 mg/dL [9].

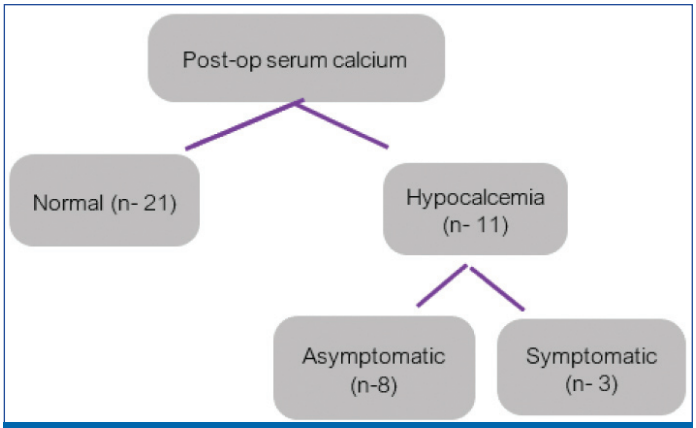
STATISTICAL ANALYSIS

The preoperative vitamin D levels were correlated with postsurgery serum calcium by using Pearson test. The association of preoperative serum calcium was examined with postoperative serum calcium by using paired t-test. SPSS Version 20 was used for statistical analysis. The p-value <0.05 was considered statistically significant.

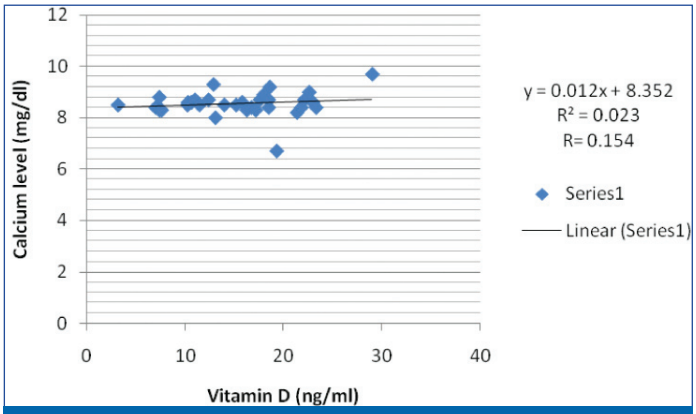
RESULTS

After selection process, 32 patients had preoperative documented Vitamin D deficiency were included for analysis. Twenty-seven patients (84%) were females. Mean patient age was 40.03±10.22 years (Range=27 to 64 years). Mean preoperative calcium level was 9.28±0.51 mg/dL at admission. None of the patients in low Vitamin D level group had preoperative biochemical or clinical hypocalcaemia in this study. Postoperatively mean serum total calcium level was 8.54±0.47 mg/dL. Preoperative mean serum vitamin D level was 15.42 ng/mL (R=3.21 to 29 ng/mL).

Out of 32 patients with low vitamin D levels, 21 (56%) patients had postoperative normal calcium levels, 11 (34%) developed hypocalcaemia, of whom only three patients (9%) were symptomatic [Table/Fig-2]. Scatter Plot shows linear correlation and hence, pearson coefficient R was deduced [Table/Fig-3]. It was found that the correlation between preoperative vitamin D levels and postoperative hypocalcaemia was weak [Table/Fig-4]. There was significant association between preoperative and post-TT serum calcium levels (p<0.001) [Table/Fig-5].



[Table/Fig-2]: Postoperative serum calcium levels and symptoms in patients undergoing Total Thyroidectomy (TT).



[Table/Fig-3]: Scatter plot showing correlation between preoperative vitamin D level with postoperative serum calcium. There was linearity between the continous variables tested. Hence, the coefficient R was calculated.

Parameters	R value	R^2 value	Pearson correlation
Preoperative serum Vitamin D levels	0.154	0.0237	Weak
Postoperative serum calcium levels			

[Table/Fig-4]: Correlation coefficient (R) between preoperative Vitamin D levels and postoperative serum calcium levels. The correlation was weak.

DISCUSSION

Hypocalcaemia is a frequent and concerned complication following thyroid surgery with spectrum of symptoms like perioral or distal acral paresthesia to more severe symptoms such as carpopedal spasm, laryngospasm, arrhythmias. None of the patients in this study had preoperative biochemical or clinical hypocalcaemia despite having low vitamin D levels. Variable food habits, different geographies, individual compensatory mechanisms do play a complex role when it comes why some patients exhibit symptoms at particular calcium levels and why others don't.

The incidence of transient hypocalcaemia in present study was 34% (N=11) [Table/Fig-2]. Many studies have shown that the

Pair	Paired differences					t	df	Sig. (2-tailed)
	Mean	Standard deviation	Standard error mean	95% confidence interval of the difference				
				Lower	Upper			
Pre-calcium and Postop calcium	0.7562500	0.6226569	0.1100712	0.5317582	0.9807418	6.871	31	0.001

[Table/Fig-5]: Paired t-test for association between pre and postoperative serum calcium levels. There was significant association between pre and postoperative serum calcium levels (p<0.001).

incidence of transient hypocalcaemia was between 3% to 50% of cases undergoing TT, with a permanent hypocalcaemia of 2-4% [4-6]. Multiple factors are attributed to cause hypocalcaemia which include devascularisation/inadvertent removal of the parathyroid glands, old age, surgical technique, surgical skills, surgeon experience, concurrent neck dissection. However, the exact cause and mechanisms are unclear [6,10,11]. No long-term follow-up data was there in present study to see whether these translates into permanent hypocalcaemia.

Of the 11 patients having biochemical hypocalcaemia, only three patients had symptomatic hypocalcaemia [Table/Fig-2]. The thresholds at which individual patient's exhibits symptoms are not known and always low serum calcium levels necessarily do not produce symptoms. Those patients who exhibited symptoms received three doses of injection calcium gluconate eight hours apart followed by oral calcium and vitamin D3 supplements, one patient required calcium infusion for persistent symptoms for three days. Those patients who had hypocalcaemia but were asymptomatic received only oral supplements. We do not universally give postoperative calcium supplementation as practised by a few surgeons.

In present study, preoperative vitamin D levels had weak correlation with postoperative serum calcium levels. In few recent studies, there was positive correlation of low vitamin D on hypocalcaemia following thyroidectomies [7] and in others there was no correlation [8]. Alkhalili E et al., found that preoperative vitamin D deficiency was associated with an increased risk of postoperative hypocalcaemia wherein others did not [12].

Danan D and Shonka DC, have found that vitamin D deficiency (<25 ng/mL) is a significant factor of postoperative hypocalcaemia in patients in whom three or more parathyroid glands identified intraoperatively, but not in patients in whom 0-2 parathyroid glands are identified (Odds ratio 5.8) [13]. In one study doing a sub-group analysis, 83% of the patients were symptomatic hypocalcaemia in low vitamin D (<14 ng/mL) versus 25% of patients with normal levels [14]. Similarly, Yamashita H et al., had more number of patients with low vitamin D (<10 ng/mL) who had developed symptomatic hypocalcaemia [15]. In contrast, correlation of preoperative vitamin D3 level to post TT serum calcium levels in present study was found, and concur findings by Lin Y et al., [16].

These variant observations are possibly due to different biochemical cut-off levels used, and also the patient's individual characteristics, postoperative high mobilisation of calcium in certain conditions (associated to hyperparathyroidism). Recently, Soares CSP et al., in their prospective study found that transitory hypocalcaemia is more related to low serum parathyroid hormone levels than preoperative low vitamin D levels [17]. Postoperative serum parathyroid hormone levels can help in knowing whether ischemia to glands is more important than vitamin D3 levels. No analysis in present study was done for patients in reference to parathyroid glands/PTH hormone.

Interestingly, there was a significant association between pre and postoperative serum calcium levels in this study [Table/Fig-5]. The likelihood of having transient hypocalcaemia was low if preoperative calcium were in higher normal range. The high incidence of Hypovitaminosis D is explained by geographical and socio religious factors. This terrain being a high altitude, high rainfall, low sunshine area, the total exposure to sunlight is low. Adding to it, is the majority of population here wearing black overgowns for religious reasons. Similar high incidence is also reported in geographies like Kashmir as reported by Zargar AH et al., wherein upto 94% of females have low vitamin D levels with 83% of overall population being deficient [18]. Similar figures are seen in eastern belt of Kolkata as reviewed by Ritu G and Gupta A [19].

Limitation(s)

Being a retrospective study there are limitations. As only two patients out of 32 had normal serum vitamin D levels, we could not compare the outcomes in this group as it makes a smaller denominator and no meaningful conclusion can be drawn. This is in addition to the confounding factors already described before herein. Further, we did not take into account if some of the elderly patients who were operated were already on calcium supplements.

With this background understanding, randomised control trial is required in group of patients with low vitamin D levels and group of patients following correction of low vitamin D to predict its effect on postoperative hypocalcaemia.

CONCLUSION(S)

There was no influence of preoperative vitamin D levels on postoperative transient hypocalcaemia. Prospective studies with well-defined controls in a larger cohort are needed for ascertaining the same, as it has wider clinical implications.

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