ISSN: 0975-3583, 0976-2833 VOL14, ISSUE03, 2023

POST-OPERATIVE SERUM PARATHYROID HORMONE LEVELS AS A PREDICTOR OF HYPOCALCEMIA IN PATIENTS UNDERGOING TOTAL THYROIDECTOMY

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Received 9 th August 2022: Accepted 10 th September 2022: Published 21 th March 2023

ABSTRACT

Aims: To estimate serum PTH levels pre operatively and at 4th and 12th hour post operatively for patients undergoing total thyroidectomy.

Materials and methods: An Cross-sectional Analytical study in *33* patients who were planned for Total thyroidectomy is a frequently done surgery in the department of otorhinolaryngology in our hospital.

Results: Hypocalcemia is one of the complications of thyroid surgery which can be transient (3-30%) or permanent (0.5-10.6%). Clinically significant hypocalcemia may occur within 48 hours after thyroidectomy. However latent hypocalcemia may be delayed up to 4 days after the surgery. So, the onset and severity of hypocalcemia following total thyroidectomy is unpredictable and in order to monitor the serum calcium post operatively, patient may require multiple blood tests. Hypocalcemia can sometimes be life threatening. We aimed to estimate serum PTH levels pre operatively and at 4^{th} and 12^{th} hour post operatively for patients undergoing total thyroidectomy. we found that post-op 4 hour PTH is better predictor of transient hypocalcemia than the Post-op 12 th hour PTH. After total thyroidectomy a PTH value of $\leq$13.7 at 4^{th} hour or a PTH value of $\leq$12.4 at 12^{th} hour can be considered as cut-off for predicting transient hypocalcaemia.

Conclusions: Both post - op 4^{th} and 12^{th} hour PTH levels were found to have similar ability in predicting transient and prolonged hypocalcemia in the patients undergoing total thyroidectomy and either of them can be used as a predictor with similar results.

Keywords: Hypocalcemia, Total thyroidectomy, Vitamin-D supplementation,

INTRODUCTION

Total thyroidectomy is a frequently done surgery in the department of otorhinolaryngology in our hospital. Hypocalcemia is one of the complications of thyroid surgery which can be transient (3-30%) or permanent (0.5-10.6%).[1] Clinically significant hypocalcemia may occur within 48 hours after thyroidectomy. However latent hypocalcemia may be delayed up to 4 days after the surgery.[2] The onset and severity of hypocalcemia following total thyroidectomy is unpredictable. In order to monitor the serum calcium post operatively, patient may require multiple blood tests. Hypocalcemia can sometimes be life threatening. Various studies have been carried out to predict the onset and severity of hypocalcemia by

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estimating serum Parathyroid hormone (PTH) levels following total thyroidectomy.[3] However, there is no consensus among these studies regarding the time intervals and cut-off levels of serum PTH to predict hypocalcemia.

In this study we intend to estimate the serum PTH levels at three-time intervals for patients undergoing total thyroidectomy. These include preoperative level and postoperative levels at 4^{th} and 12^{th} hour after surgery. An attempt will be made to classify these total thyroidectomy patients as high risk or low risk for postoperative hypocalcemia after documentation and analysis of PTH cut-off levels. This study will therefore help in identifying patients developing hypocalcemia requiring calcium and vitamin-D supplementation following total thyroidectomy.

MATERIALS AND METHODS

An Cross-sectional Analytical study in *33* patients who were planned for Total thyroidectomy in the Department of Otorhinolaryngology Siddhartha medical college,Vijayawada were taken up for the study after fulfilling the inclusion criteria and signing the informed consent. The study took place during the period between December 2018 to May 2020.

Inclusion Criteria: Patients requiring Total Thyroidectomy.

Exclusion Criteria: Patients having parathyroid adenoma or hyperplasia, chronic renal disease, Lactating mothers and calcium and vitamin –D supplementation.

Sample Collection - Venous blood sample will be collected under sterile precautions, 12 hours preoperatively and 4 hours and 12 hours post-operatively, 2ml Venous blood sample will be collected in red vacutainer tube taking aseptic precautions, centrifuged at 3000rpm for 10 minutes to separate serum from the clot. The separated serum will be preserved at -20°C until analysis. The serum sample separated will be assayed for Parathyroid hormone, total protein, albumin and total calcium levels.

Sample Assay - Quantitative measurement of Parathyroid hormone in serum will be done by immunometric immunoassay technique using Vitros ECI Immunodiagnostic Systems. Parathyroid hormone present in the sample reacts with biotinylated antibody and horse-raddish peroxidase labelled antibody conjugate. The antigen antibody complex is captured by streptavidin on the wells. The bound HRP conjugate is measured by a Luminescent reaction. The light signals are read by the system. The amount of HRP conjugate bound is directly proportional to the concentration of PTH present in the sample. The Quantitative estimation of total protein in the sample will be determined by the Biuret reagent method, serum albumin levels by bromocresol green method and total calcium by Arsenazo lll dye method using Vitros 5.1 FS dry chemistry analyzer in the central clinical biochemistry section, CDLS. THE IONISED CALCIUM levels in the sample will be determined by calculation using the formula – Ionized Calcium = [0.9 + (0.55 × total calcium - 0.3 × albumin)] .

Statistical methods :

Hypocalcemia, High risk, Low risk were considered as primary outcome variables. Post-op 4^{th} hour PTH and 12^{th} hour PTH were primary explanatory variables.

Descriptive analysis: Descriptive analysis was carried out by mean and standard deviation for quantitative variables, frequency and proportion for categorical variables.

Data was also represented using appropriate diagrams like bar diagram, pie diagram. All Quantitative variables were checked for normal distribution within each category of

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explanatory variable by using visual inspection of histograms and normality Q-Q plots. Shapiro- wilk test was also conducted to assess normal distribution. Shapiro wilk test p value of >0.05 was considered as normal distribution.

The association between variables for non-normally distributed Quantitative parameters, Medians and Interquartile range (IQR) were compared between study groups using Wilcoxon Signed Rank test, Mann Whitney U test and Kendall's W test.

X was considered as gold standard. Y was considered as screening test. The sensitivity, specificity, predictive values and diagnostic accuracy of the screening test along with their 95% CI were presented. Reliability of the screening test was assessed by kappa statistics along with its 95% CI and p Value.

Graphical representation of data: MS Excel and MS word was used to obtain various types of graphs such as bar diagram and Scatter plots.

p value (Probability that the result is true) of <0.05 was considered as statistically significant after assuming all the rules of statistical tests.

Statistical software: IBM Corp. Released 2017. IBM SPSS Statistics for Windows, Version 25.0. Armonk, NY: IBM Corp.

RESULTS

A total of 33 subjects were included in the final analysis. The mean age was 45 ± 10.37 in the study population, minimum was 21 and maximum was 64. Among the study population, 6 (18.18%) were male and 27 (81.82%) were female.

Table-1: Demographic details in the study population.

Gender	**Frequency**	**Percentages**
Male	6	18.18%
Female	27	81.82%
Thyroid Surgery In Past		
Yes	3	9.09%
No	30	90.91%
Thyroid Medications		
Taken	2	6.06%
Not taken	31	93.94%
Parathyroids Visualized		
2	9	27.27%
>2	24	72.73%
Parathyroids Saved		
2	25	75.76%
>2	8	24.24%
High Risk Cases (N=18)		
Normocalcemia	4	12.12%
Hypocalcemia	14	42.42%
Low Risk Cases (N=15)		

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Normocalcemia	12	37.50%
Hypocalcemia	3	9.38%

Among the study population, 3 (9.09%) had thyroid surgery in past, 2 patients (6.06%) had taken thyroid medications.

In 9 patients (27.27%) 2 parathyroids were visualized whereas in 24 (72.73%) > 2 parathyroid were visualized. 25 cases (75.76%) 2 parathyroids were saved while in 8 cases (24.24%) > 2 parathyroids were saved.

High risk cases, 4 (12.12%) of the participants had Normocalcemia, 14 (42.42%) of the participants had Hypocalcemia. In the low risk cases, 12 (37.50%) of the participants had Normocalcemia, 3 (9.38%) of the participants had Hypocalcemia.

Table-2: Descriptive analysis of PTH, Total calcium, albumin and Ionized calcium in study population.

	Mean ± SD	**Median**	**Minimum**	**Maximum**	**95% C.I**	
					Lower	**Upper**
Pre-Op PTH	18.16 ± 10.18	17	4.3	47.5	14.55	21.77
Post-Op 4Th Hour	12.77 ± 7.25	11	3.4	29.1	10.2	15.34
Post-Op 12Th Hour	9.71 ± 5.31	8.9	3.4	26.1	7.82	11.59
Pre-Op Total calcium	9.3 ± 0.84	9.5	7.2	10.8	9	9.6
Post-Op 4Th Hour Total Calcium	8.45 ± 0.96	8.4	6.2	10	8.1	8.79
Post-Op 12Th Hour Total Calcium	8.17 ± 1.17	8.3	4	9.8	7.75	8.58
Serum. Albumin	3.97 ± 0.3	3.9	3.5	4.5	3.87	4.08
Post-Op 4Th Hour Ionized Ca2+	4.35 ± 0.53	4.3	3.17	5.17	4.17	4.54
Post-Op 12Th Hour Ionized Ca2+	4.2 ± 0.65	4.22	1.9	5.1	3.97	4.43

Among the study population, 10 (31.25%) of the participants had hypocalcemia after 1 month of follow-up while 22 (68.75%) of the participants were found to be Normocalcemic.

Table-3: Comparison of diagnosis between follow-up ionized calcium.

Diagnosis	**Follow-Up Ionized Calcium**	
	Hypocalcemia (N=10)	**Normocalcemic (N=22)**
PTC	6 (60%)	7 (31.82%)
MTC	0 (0%)	1 (4.55%)
FTC	2 (20%)	0 (0%)
MNG	1 (10%)	7 (31.82%)
Others (Inflammatory/Infectious Cause)	1 (10%)	7 (31.82%)

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In hypocalcemic participants, 6 (60%) had PTC, 2 (20%) had FTC. For MNG and others each had 1 (10%). In normocalcemic participants, 7 (31.82%) had PTC, 1 (4.55%) had MTC, 7 (31.82%) had MNG, 7 (31.82%) had Others (Inflammatory Causes).

Table-4: Comparison of diagnosis between risk.

Diagnosis	**Risk**	
	High (N=18)	**Low (N=15)**
PTC	10 (55.5%)	4 (26.67%)
MTC	1 (5.56%)	0 (0%)
FTC	2 (11.11%)	0 (0%)
MNG	2 (11.11%)	6 (40%)
Others (Inflammatory/ Infectious Cause)	3 (16.67%)	5 (33.33%)

In high-risk participants, 10 (55.5%) had PTC, 1 (5.56%) had MTC, 2 (11.11%) had FTC, 2 (11.11%) had MNG and 3 (16.67%) had Others (Inflammatory). In low risk participants, 4 (26.67%) had PTC, 6 (40%) had MNG, 5 (33.33%) had Others (Inflammatory Cause).

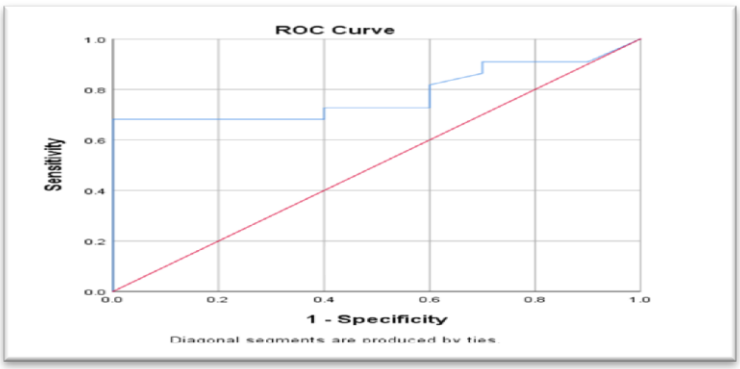
Table-5: Comparison of type of thyroidectomy between risk.

Type Of Thyroidectomy	**Risk**		**Fisher exact P value**
	High (N=18)	**Low (N=15)**	
Total Thyroidectomy	16 (88.89%)	12 (80%)	0.639
Completion Thyroidectomy	2 (11.11%)	3 (20%)	
Central Compartment Clearance			
Yes	12 (66.67%)	1 (6.67%)	<0.001
No	6 (33.33%)	14 (93.33%)	

In high-risk participants, 16 (88.89%) had Total Thyroidectomy and 2 (11.11%) had Completion Thyroidectomy. In low-risk participants, 12 (80%) had Total Thyroidectomy and 3 (20%) had Completion Thyroidectomy. There was no statistically significant difference between type of thyoidectomy and risk groups (P value 0.639).

In high risk participants, 12 (66.67%) had Central Compartment Clearance and in low risk participants, 1 (6.67%) had Central Compartment Clearance. There was statistically significant difference in Central Compartment Clearance between risks. (P value <0.001)

Figure-1: Predictive validity of Post Op 4Th Hour PTH in predicting follow-up ionized calcium (ROC analysis).



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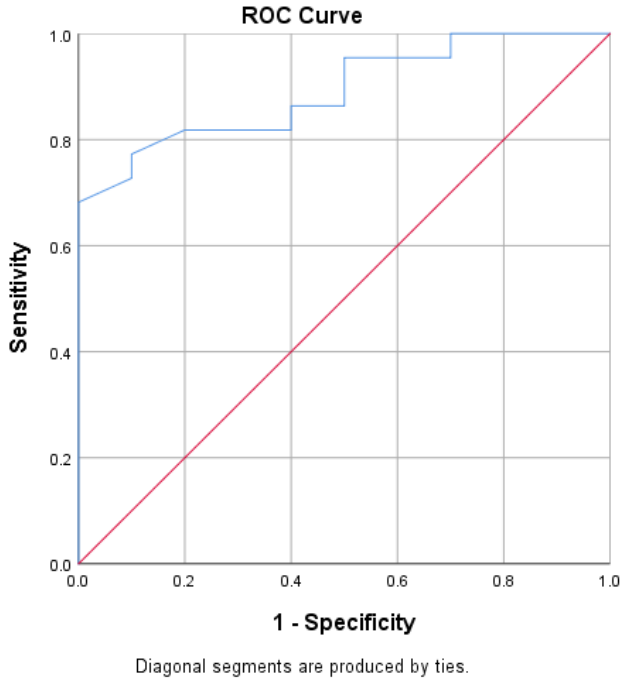
the study population, PTH median was 17 (IQR 9.75 to 26.25) of pre-operative, PTH median was 11 (IQR 7.05 to 16.60) of post-operative 4^{th} Hour and PTH median was 8.9 (IQR 5.05 to 13.60) of post-operative 12^{th}Hour.There exists a statistically significant difference in PTH between different time periods of operation. (P Value <0.001).

The Post Op 4Th Hour had fair predictive validity in predicting follow-up ionized calcium, as indicated by area under the curve of 0.780 (95% CI 0.621 to 0.938, P value 0.012).

Table-6: Predictive validity of Post Op 4Th Hour in predicting Follow-up ionized calcium

Parameter	Value	95% CI	
		Lower	Upper
Sensitivity	70.00%	34.75%	93.33%
Specificity	68.18%	45.13%	86.14%
False positive rate	31.82%	13.86%	54.87%
False negative rate	30.00%	6.67%	65.25%
Positive predictive value	50.00%	23.04%	76.96%
Negative predictive value	83.33%	58.58%	96.42%
Diagnostic accuracy	68.75%	49.99%	83.88%

Figure-2: Predictive validity of Post Op 12Th Hour in predicting follow-up ionized calcium (ROC analysis).



The Post Op 12Th Hour PTH had good predictive validity in predicting follow-up ionized calcium, as indicated by area under the curve of 0.891 (95% CI 0.782 to 1.000, P value <0.001)

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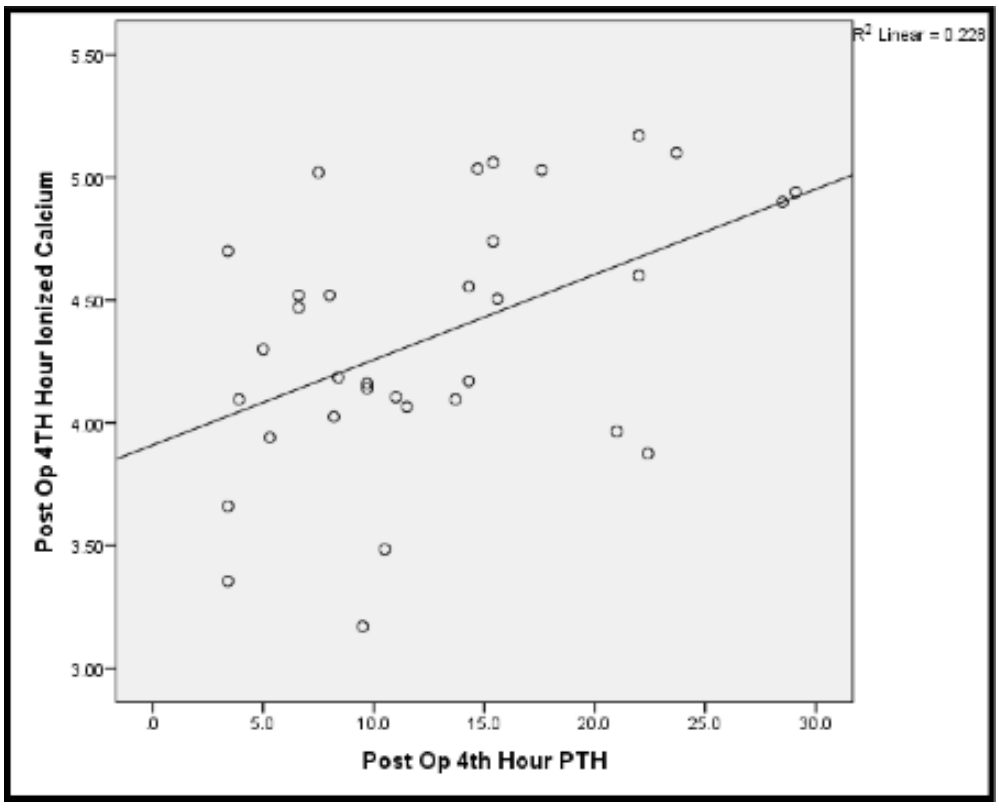
Table-7: Predictive validity of Post Op 12Th PTH Hour in predicting Follow-up ionized calcium.

Parameter	Value	95% CI	
		Lower	Upper
Sensitivity	70.00%	34.75%	93.33%
Specificity	68.18%	45.13%	86.14%
False positive rate	31.82%	13.86%	54.87%
False negative rate	30.00%	6.67%	65.25%
Positive predictive value	50.00%	23.04%	76.96%
Negative predictive value	83.33%	58.58%	96.42%
Diagnostic accuracy	68.75%	49.99%	83.88%

Figure-3: Scatter Plot showing Correlation between Post Op 4th hour PTH and Post Op 4th hour Ionized calcium



In the study there was significant correlation between Post Op PTH at 4th hour and Post Op 4th Hour Ionized Calcium i.e. with increase in PTH there was increase in Ionized calcium at post op 4th hour and vice versa.

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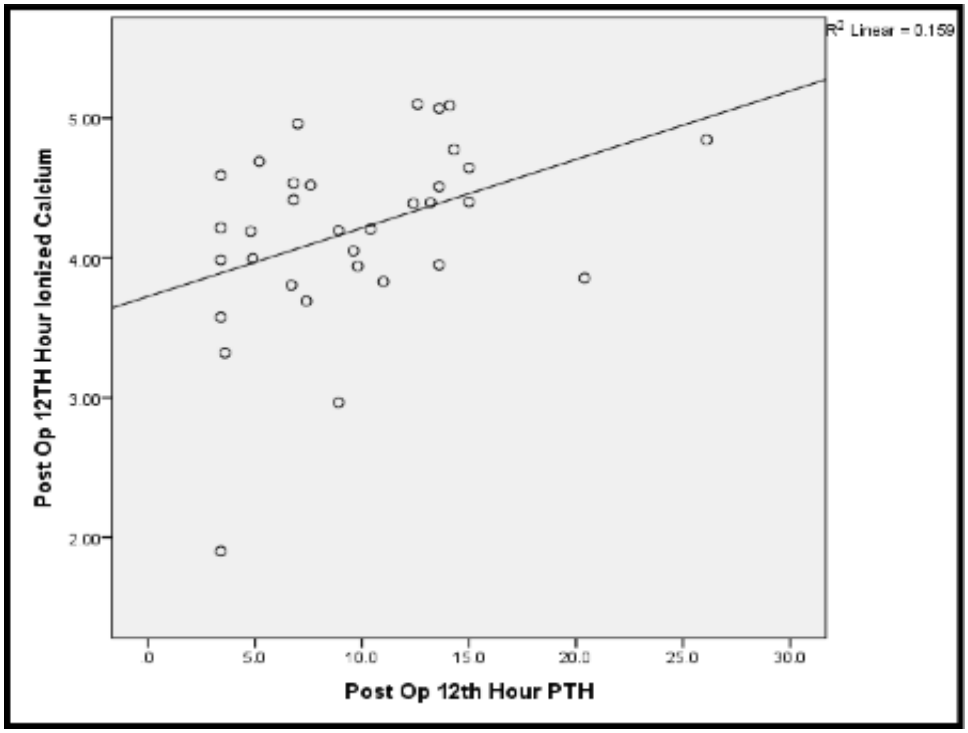
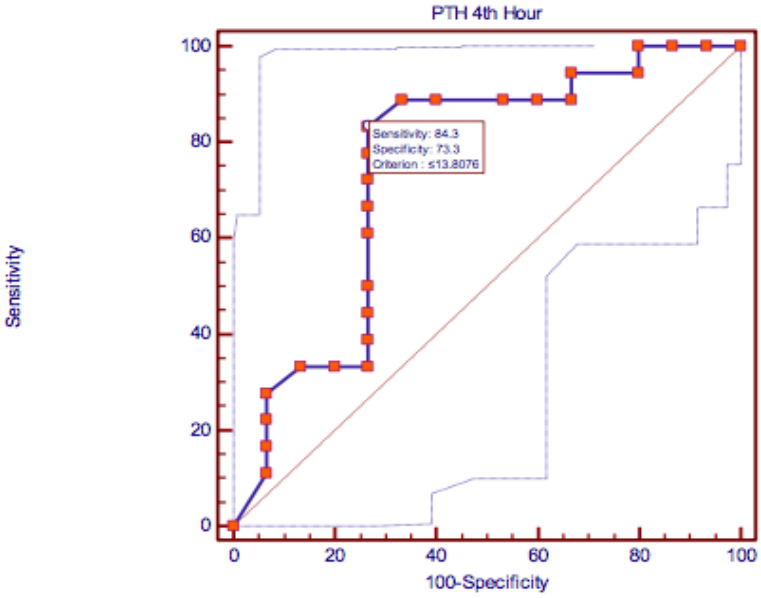
Figure-4: Scatter Plot showing Correlation between Post Op 12th hour PTH and Post Op 12th hour Ionized calcium



In the study there was significant correlation between Post Op PTH at 12th hour and Post Op 12th Hour Ionized Calcium i.e. with increase in PTH there was increase in Ionized calcium at post op 12th hour and vice versa.

Figure-5: Validity of PTH at 4th hour in predicting Hypocalcaemia at 4th Hour (ionized calcium)



PTH value of ≤13.7 at 4th hour had highest sensitivity and specificity in predicting hypocalcaemia at post op 4th hour. Sensitivity was 83.3%, specificity was 73.33%, PPV was 78.9% and NPV was 78.6%.

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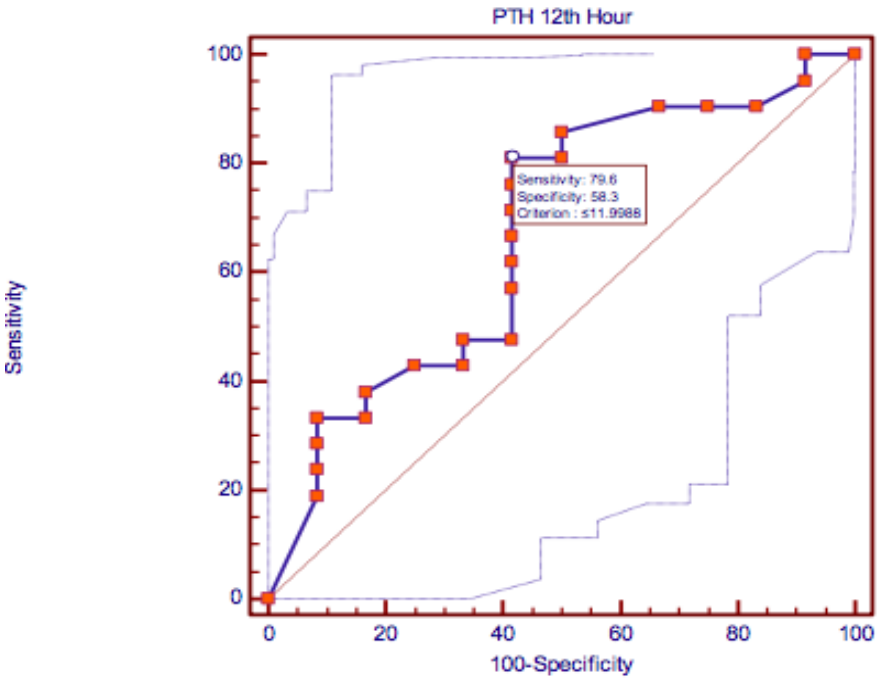
Figure- 6: Validity of PTH at 12th hour in predicting Hypocalcaemia at 12th Hour (ionized calcium)



PTH value of ≤12.4 at 12th hour had highest sensitivity and specificity in predicting hypocalcaemia at post op 12th hour. Sensitivity was **80.95**%, specificity was 58.33%, PPV was 77.3% and NPV was 63.6%.

DISCUSSION

Thyroidectomy though considered safe carries risks especially, in terms of hypo-functioning of the parathyroid glands. Along with thyroid surgeries, any surgery of the anterior neck (central compartment) predisposes the parathyroid glands to the risk of being inadvertently removed along with the thyroid specimen, or having vascular compromise leading to a fall in the serum parathormone (PTH, Parathyroid hormone) levels. The fall in serum parathyroid hormone levels post thyroidectomy often manifests as hypocalcemia with an incidence of 1-50%.[4]

In our study, the estimated rate of transient hypocalcemia was 42%. This hyposecretion of PTH can be relatively transient [1.6% – 68%] or permanent [0.4% – 33%]. Numerous theories have been described in the literature like, injury/removal or devascularization of the parathyroid glands, hemodilution secondary to intraoperative fluid administration, calcitonin release after manipulation of the thyroid or hungry bone syndrome, but the exact mechanism of transient hypocalcemia remains unclear.[5]

Some physicians follow routine administration of calcium and vitamin D supplementation to all total thyroidectomy patients, while others obtain serial calcium measurements in order to predict patients who can develop hypocalcemia. However, none are cost- -effective strategies since in former, all the patients are exposed to side effects of calcium (when less than half actually need the supplementation), and in the latter, there can be a delay in discharge and

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also the patient is subjected to the discomfort of multiple venipunctures. Some authors have suggested that protocols based on calcium slope are useful, but they still require serial blood sampling, can postpone treatment and may prolong hospital stay.

Serum Calcium is not an accurate predictor for Hypocalcemia as levels do not undergo significant change until one to two days post thyroidectomy and also the hypocalcemia symptoms might not appear for 24 to 48 hours post-operatively.

Hence, post-operatively it is difficult to predict whether a patient is at a greater risk of developing hypocalcemia based upon only calcium levels or surgical events.[5,6] So, as a common practice in our center, calcium and/or calcitriol are administered prophylactically to patients following total thyroidectomy surgery.[7] Symptomatic hypocalcemia can be an emergency condition and therefore a cause for significant distress to the patient. Hence there is always a preferred need for a method that can reliably identify patients who are at risk for developing hypoparathyroidism in the post- operative period.

In order to reliably predict the risk of development of hypocalcemia in patients undergoing total thyroidectomy more specific biochemical tests can be done, like serum parathyroid hormone level estimation, as it has been shown by studies that the post-operative serum PTH levels can be a predictor of occurrence as well as severity of hypocalcemia after thyroidectomy.

Numerous studies have utilized either absolute values or relative percentage decrease of PTH for diagnosis and in addition, various timings for measurement of serum PTH levels have also been suggested by some studies, ranging from intraoperative measurements to measurements in the early postoperative period (generally 1-4 hours after surgery) and even up to 24 hours postoperatively. In almost all of these settings, PTH has been found to be a reliable early marker for postoperative hypocalcemia.

During the last several years, a number of researchers have measured PTH levels within minutes or hours of the thyroidectomy procedure in an attempt to predict postoperative hypocalcemia. Most of these studies suggested that PTH assays performed within hours of the surgery may identify patients with hypocalcemia who require medical attention. Some of these studies showed that PTH levels had a predictive value of about 100%.

A large meta-analysis done in 2014, suggested that lower postoperative PTH levels 30 minutes to 5 days after surgery are associated with transient hypocalcaemia. It also showed that low postoperative PTH between 1 hour and 1 day after surgery had a sensitivity ranging from 69%-100% in predicting transient hypocalcaemia. [7]

In a prospective study done in Canada, 42 patients were followed postoperatively with serial PTH and Calcium measurements and it was found that patients who exhibited a PTH level ≤ 9 pg/mL at post-op 1 hour, developed hypocalcemia requiring treatment with calcium and vitamin D whereas, none of the patients with PTH ≥ 9 developed hypocalcemia. Subsequent study conducted at same center (100 total and completion thyroidectomy patients), stated that more than half of the patients with 1-hour post-surgery PTH levels in the range of 9–12 pg/ml developed transient hypocalcemia.

Our study categorizes post-thyroidectomy patients as high risk for developing hypocalcemia based on Post-op 4^{th} hour PTH of less than 12 pg/ml. The high-risk group was started on prophylactic treatment with calcium and vitamin D whereas those with Post-op 4^{th} Hour

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PTH levels of 12 pg/ml or higher were classified as low risk, and were not given prophylactic treatment.

The outcomes of PTH determinations after a total thyroidectomy, led some investigators to evaluate its usefulness to predict hypocalcemia following thyroid surgery. Studies have found that all patients with PTH level less than 8 pg/mL measured one hour after the surgery became hypocalcaemic, and all patients with PTH level greater than 9 pg/mL did not. Similarly, some have stated that, PTH less than 10 pg/mL measured four or six hours after surgery predicted hypocalcemia with an overall accuracy of 98%.

Few studies also state that a postoperative PTH level of 12 pg/mL or less was also a good predictor of hypocalcemia. The Australian Endocrine Guidelines has adopted the recommendations of Lombardi and colleagues to standardize obtaining a PTH level 4 hours after a thyroidectomy. The wide variability of the predictors for the development of hypocalcemia across centres suggests that the measurement of PTH at any time in the postoperative period may be a reliable predictor of hypocalcemia. Almost all studies define hypocalcemia as either low levels of serum calcium or development of symptoms of hypocalcemia. Our study was in accordance with these studies.[8,9]

Despite all favorable outcomes, however, no common guidelines regarding the use of PTH have been established, nor has its use been universally adopted in common practice, also the widespread application of PTH assay is expensive and many centers do not have access to the PTH assay kits or the technical feasibility to run the tests.

Studies have evaluated the possible risk factors that include patient characteristics, disease related factors or surgical procedures which can influence the development of post-thyroidectomy hypoparathyroidism. In literature, different opinions have been stated about the correlation between development of postoperative hypocalcemia and patient age. A systematic review observed no correlation between patient's age and post-operative hypocalcemia. In most studies female gender has been identified as a significant risk factor for hypocalcemia. In fact, females have been found to be more prone for developing this complication. In our study, female patients developed transient hypocalcemia in 44% (12/27) of cases, which was significantly greater than that detected in men, 33% of the cases (2/6).[10,11]

There can be variations in the serum calcium levels in women due to hormonal changes during the time of menopause. Hence evaluations of bone mineral density, menstruation status, and hormone levels (estrogen, progesterone) may be necessary. Almost all the previous studies, including ours, did not take into consideration, these possible confounding factors.[12]

In accordance with other studies, we did not find a relationship between patient demographic characteristics and development of hypocalcemia. In our study we found that in both High and Low risk group there was significant decrease in mean Calcium levels at 4^{th} hour and 12^{th} hour compared to pre op Calcium levels and that the mean perioperative variation in serum calcium levels (difference between preoperative level and 4 h or 12 h postoperative level) was significantly higher in patients that developed transient hypocalcemia ($p < 0.001$) These findings clearly show that peri-operative variation of calcium levels plays an important

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role in development of transient hypocalcemia. This finding is also confirmed by other studies in which a larger decrease in post-operative calcium (measured within 6 hours of surgery) from preoperative levels was associated with transient hypocalcemia. The extent of the thyroidectomy, and malignant neoplasm are commonly considered to be risk factors for post-thyroidectomy hypocalcemia. Multivariate analyses by various authors confirmed that extent of resection is a major risk factor for both transient and permanent hypoparathyroidism after thyroid surgery even when surgical technique and surgeon expertise are controlled for.

In our statistical analysis, the pathologic finding of malignancy was significantly associated with the development of hypocalcemia as can be shown by comparison of risk groups.[13]

The high risk group had majority of patients (75%) with thyroid malignancy, most of them had diagnosis of PTC (77%), 80 % of whom developed transient hypocalcemia, out of which 6 remained hypocalcemic at the end of 1 month.

Similarly, majority of the patients constituting the low risk group had benign pathology (73%) with Multinodular Goitre being the most common diagnosis. 3 patients, with MNG developed transient hypocalcemia. However all of them became normocalcemic by the end of 1 month. The current study also demonstrates that extent of resection remains the strongest independent risk factor for postoperative hypoparathyroidism. In the study all patients who developed transient hypocalcemia and were hypocalcemic after 1 month of follow-up (i.e prolonged hypocalcemia) had undergone total thyroidectomy.

According to a meta-analysis, the incidence of transient and permanent hypocalcemia in a group that underwent prophylactic central compartment clearance were 26.0 and 2.0 %, respectively, when compared to 10.8 and 1.2 %, in the group that did not undergo prophylactic central compartment clearance. Also, one of the largest series in the literature on complications of Central compartment clearance done in 1087 patients over a 30-year period, found that bilateral central compartment clearance had a significantly higher rate of transient (51.9% vs. 27.7%, respectively) and permanent hypoparathyroidism (16.2% vs. 6.3%, respectively) than total thyroidectomy alone.

In our study, patients undergoing TT with Central compartment clearance had a higher rate of Transient [69.2% vs. 20%, respectively] and Prolonged hypoparathyroidism [46% vs. 20%, respectively] than patients undergoing total thyroidectomy alone. However, central compartment clearance was found to be a significant risk factor for only transient hypoparathyroidism. (P value <0.001)

In our practice, 65% of patients with thyroid malignancy and 12.5% of patients with benign pathology (routine Central compartment clearance was done) underwent Central compartment clearance, out of which among the former, 91% had diagnosis as Papillary thyroid carcinoma whereas, in the later 1 had MNG while other patient Hashimoto's thyroiditis.[14,15]

Preservation of the parathyroid glands in situ by careful dissection and preservation of their blood supply is a recommended surgical strategy in thyroid surgery to decrease the rate of postoperative hypoparathyroidism. Removal of a single parathyroid gland is not associated with postoperative hypocalcemia whereas resection of at least 2 parathyroid glands increases the risk of transient and permanent hypoparathyroidism.[16,17]

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Another study states that number of Parathyroid identified during surgery does not influence the occurrence of hypocalcemia.[2] Similar results were obtained in our study where, less than 2 parathyroids were visualized among 9 patients (27.27%) while in the rest 24 patients (72.73%) 2 or more parathyroids were visualized. In 25 (75.76%) patients less than or equal to 2 parathyroids were saved and in 8 (24.24%) of them more than 2 parathyroids were saved. There was no statistically significant difference in the occurrence of hypocalcemia with respect to the number of parathyroid visualized or saved within the risk groups. (P value 0.697) and (P value 0.101) respectively.

Additionally, we have also taken into account another time interval i.e. Post-op 12^{th} hour PTH, for evaluating its ability to predict hypocalcemia. Based upon the ROC the Post Op 12Th Hour PTH had good predictive validity in predicting the risk, as indicated by area under the curve of 0.906 (95% CI 0.779 to 1.000, P value <0.001).

The Post Op 12Th Hour PTH had good predictive validity in predicting follow-up ionized calcium levels, as indicated by area under the curve of 0.891 (95% CI 0.782 to 1.000, P value <0.001). Hence utility of Post-op 12^{th} hour PTH as an additional time interval to predict hypocalcemia following total thyroidectomy can be considered. Similarly, The Post Op 4Th Hour had fair predictive validity in predicting follow-up ionized calcium, as indicated by area under the curve of 0.780 (95% CI 0.621 to 0.938, P value 0.012).

In our study we found out that, in predicting the risk of development of hypocalcemia after 1 month of surgery, Post-op 4^{th} hour PTH and Post-op 12^{th} hour PTH have similar, sensitivity; specificity and Diagnostic accuracy (70%, 68.18%, and 68.75% each respectively) for predicting hypocalcemia at the end of 1month follow-up period. While to predict the risk of development of transient hypocalcemia we found that post-op 4^{th} hour PTH is a better predictor than the Post-op 12^{th} hour PTH, as the association of former with development of hypocalcemia in the immediate post-operative period is statistically more significant than the latter. Hence both post - op 4^{th} and 12^{th} hour PTH levels were found to have almost similar ability in predicting transient and prolonged hypocalcemia in the patients undergoing total thyroidectomy and either of them can be used as a predictor with similar results. Additionally, with further analysis of our results, we suggest that PTH value of ≤ 13.7 at 4^{th} hour and PTH value of ≤ 12.4 at 12^{th} hour can be taken into consideration as cut-offs to predict hypocalcemia, however prospective studies with larger sample size are required to prove the reliability of each of these predictors of hypocalcemia. Similar results have been observed in other studies with minimal variation of cut-off levels of serum parathyroid and serum calcium in the post-operative period.

CONCLUSIONS

Hypocalcemia is a relatively common complication following total thyroidectomy and its risk increases following Central compartment clearance done for thyroid malignancies. Overall, hypocalcemia develops in about 50% of the patients undergoing total thyroidectomy. The patients were classified into high and low risk groups based upon the cut-off value of PTH as 12pg/ml, 4 hours following surgery. Risk factors for hypoparathyroidism after total thyroidectomy, include, female gender, malignancy, Total thyroidectomy and

ISSN: 0975-3583, 0976-2833 VOL14, ISSUE03, 2023

clearance of the central compartment nodes. Total thyroidectomy combined with central compartment clearance predisposes to development of both transient and prolonged hypocalcemia. Findings from our study can be incorporated in the management of patients undergoing total thyroidectomy, for early identification and initiation of prophylactic treatment to reduce the risk of development of hypocalcemia. PTH value of ≤ 13.7 at 4^{th} hour and PTH value of ≤ 12.4 at 12^{th} hour can be taken into consideration as cut-offs to predict hypocalcemia, however prospective studies with larger sample size are required to prove the reliability of each of these predictors of hypocalcemia.

REFERENCES

1. Carr AA, Yen TW, Fareau GG, Cayo AK, Misustin SM, Evans DB, Wang TS. A single parathyroid hormone level obtained 4 hours after total thyroidectomy predicts the need for postoperative calcium supplementation. JACS 2014;219:757-64.
2. Le TN, Kerr PD, Sutherland DE, Lambert P. Validation of 1-hour post-thyroidectomy parathyroid hormone level in predicting hypocalcemia. J otolaryngol Head Neck Surg 2014;43:5.
3. Saba A, Podda M, Campanella AM, Pisanu A. Early prediction of hypocalcemia following thyroid surgery. A prospective randomized clinical trial. Langenbeck's Arch surgery 2017;402:1119-25.
4. AlQahtani A, Parsyan A, Payne R, Tabah R. Parathyroid hormone levels 1 hour after thyroidectomy: an early predictor of postoperative hypocalcemia. Can J Surg [Internet]. 2014 Aug;57(4):237–40.
5. Grodski S, Farrell S. Early postoperative PTH levels as a predictor of hypocalcaemia and facilitating safe early discharge after total thyroidectomy. Asian J Surg. 2007 Jul;30(3):178–82.
6. Rao TUM. An early predictor of postoperative hypocalcemia : parathyroid hormone levels 1 hour after thyroidectomy. 2017;4(1):233–6.
7. Mazotas IG, Wang TS. The role and timing of parathyroid hormone determination after total thyroidectomy. Gland Surg [Internet]. 2017 Dec;6(Suppl 1):S38–48.
8. Sywak MS, Palazzo FF, Yeh M, Wilkinson M, Snook K, Sidhu SB, et al. Parathyroid hormone assay predicts hypocalcaemia after total thyroidectomy. ANZ J Surg. 2007 Aug;77(8):667–70.
9. Lombardi CP, Raffaelli M, Princi P, Santini S, Boscherini M, De Crea C, et al. Early prediction of postthyroidectomy hypocalcemia by one single iPTH measurement. Surgery. 2004 Dec;136(6):1236–41.
10. A. P. V. SK, G. V. A prospective study on parathyroid hormone levels in detecting early hypocalcemia after total thyroidectomy. Int Surg J. 2017;4(10):3242.
11. Del Rio P, Rossini M, Montana CM, Viani L, Pedrazzi G, Loderer T, Cozzani F. Postoperative hypocalcemia: analysis of factors influencing early hypocalcemia development following thyroid surgery. BMC surgery. 2019 Apr 1;18(1):25.
12. Augusto F, Vanderlei B, Gilberto J, Vieira H, Hojaij FC, Cervantes O, et al. Parathyroid hormone: an early predictor of symptomatic hypocalcemia after total thyroidectomy. 2012;56(3):5–9.

ISSN: 0975-3583, 0976-2833 VOL14, ISSUE03, 2023

13. Cho JN, Park WS, Min SY. Predictors and risk factors of hypoparathyroidism after total thyroidectomy. International Journal of Surgery. 2016 Oct 1;34:47-52.
14. Sasson AR, Pingpank JFJ, Wetherington RW, Hanlon AL, Ridge JA. Incidental parathyroidectomy during thyroid surgery does not cause transient symptomatic hypocalcemia. Arch Otolaryngol Head Neck Surg. 2001 Mar;127(3):304–8.
15. Higgins KM, Mandell DL, Govindaraj S, Genden EM, Mechanick JI, Bergman DA, et al. The role of intraoperative rapid parathyroid hormone monitoring for predicting thyroidectomy-related hypocalcemia. Arch Otolaryngol Head Neck Surg. 2004 Jan;130(1):63–7.
16. Thomusch O, Machens A, Sekulla C, Ukkat J, Brauckhoff M, Dralle H. The impact of surgical technique on postoperative hypoparathyroidism in bilateral thyroid surgery: a multivariate analysis of 5846 consecutive patients. Surgery. 2003 Feb 1;133(2):180-5.
17. Le TN, Kerr PD, Sutherland DE, Lambert P. Validation of 1-hour post-thyroidectomy parathyroid hormone level in predicting hypocalcemia. J Otolaryngol Head Neck Surg [Internet]. 2014 Jan 29;43(1):5.