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Quick Intra-operative Parathyroid Hormone Assay in Predicting Hypocalcemia after Thyroidectomy

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Abstract

Background: Despite the higher morbidity, total thyroidectomy is emerging as an attractive surgical option even for benign thyroid disease due to the risk of subclinical (occult) malignancy, the possibility of goiter relapse as well as of the increased risk of complications following reoperation **(1).** Total thyroidectomy is now being performed as a short-stay or even an outpatient procedure at some medical centers. Postoperative hypocalcemia is common after total thyroidectomy, and perioperative monitoring of serum calcium levels is arguably the primary reason for overnight hospitalization. This study aimed to evaluate the accuracy and reliability of quick parathyroid hormone level measurement in predicting clinically relevant hypocalcaemia after total thyroidectomy. **Methods:** This was a prospective study carried out from January 2016 to December 2020 that included all patients who underwent either a total or a completion total thyroidectomy for benign or malignant disease. All patients were operated on and cared for by the same surgical team in Aswan University Hospital. Sixty out of three-hundreds cases who underwent thyroid surgery for abnormal thyroid disorder and fulfil the criteria of total thyroidectomy were enrolled in the study. Preoperative assessment: History: Physical examination, Investigations: Routine preoperative assessment, Free T3, T4 and TSH assessment, Ionized serum calcium. PTH assay. Patients included in this study has been divided into two groups according to post thyroidectomy symptoms of hypocalcemia: Group I: asymptomatic (no symptoms or signs of hypocalcaemia within 48 hours postoperatively). Group II: Symptomatic (positive symptoms or signs of hypocalcaemia within 48 hours postoperatively). Measurement of serum calcium and parathyroid hormone levels.Postoperative Management.**Results:** Statistical significance between Group Iand Group II according to Parathormone Hormone level and serum ionized calcium level. The ROC curve cut-off value of parathormonepre-operatively to detect post-operative symptomatic group of hypocalcemia (Group II) after thyroidectomy is ≤ 74.3, Sensitivity 87.5%, Specificity64.64%, Positive predictive value 46.7%, and Negative predictive value 93.3%. The ROC curve cut-off value of serum ionized calcium pre-operatively to detect post-operative symptomatic group of hypocalcemia**(**Group II**)** after thyroidectomy is <1.11, Sensitivity 100%, Specificity 59.09%, Positive predictive value 47.1%, and Negative predictive value 100%. The ROC curve cut-off value of serum ionized calcium results to detect post-operative symptomatic group of hypocalcemia after thyroidectomy **(**Group II**)** is ≤ 1.06, Sensitivity 87.5%, Specificity 95.45%, Positive predictive value 87.5%, and Negative predictive value 95.5%. The changes of parathormone and ionized calcium levels between the preoperative and postoperative state in non-symptomatic group (Group I) and symptomatic group (Group II) of post thyroidectomy hypocalcemia; there was more changes in parathormone and ionized calcium (decline) in symptomatic group (Group II), but the change is more significant in ionized calcium level (p-

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value 0.001).**Conclusion:** Quick parathyroid hormone level measurement in accurate and reliabile in predicting clinically relevant hypocalcaemia after total thyroidectomy.
Key words: Parathyroid Hormone- Hypocalcemia- Thyroidectomy.

Introduction:
Despite the higher morbidity, total thyroidectomy is emerging as an attractive surgical option even for benign thyroid disease due to the risk of subclinical (occult) malignancy, the possibility of goiter relapse as well as of the increased risk of complications following reoperation [(1)].

Total thyroidectomy is now being performed as a short-stay or even an outpatient procedure at some medical centers [(2)]. However, this shift in management has occurred in the absence of consensus and evidence-based parameters for defining the population of patients eligible to undergo outpatient total thyroidectomy [(3)].

Postoperative hypocalcemia is common after total thyroidectomy, and perioperative monitoring of serum calcium levels is arguably the primary reason for overnight hospitalization. Confidently predicting which patients will not develop significant hypocalcemia may allow for a safe earlier discharge. Defining a framework for safe outpatient thyroidectomy is crucial, especially given that the complication rates following thyroidectomy are not insignificant (7.4%–13.8%) [(4)]. Hypocalcemia after thyroidectomy is the most common complication, with the reported incidence of transient and permanent hypocalcemia ranging from 3% to 52% and 0.4% to 13%, respectively[(5)]. Various strategies for diagnosing and managing postoperative hypocalcemia have been used. The traditional approach of 2-day hospitalization and monitoring of serum calcium levels after surgery is still being used by many institutions worldwide because hypocalcemia typically occurs within 48 hours after surgery[(6)].

The routine-use of postoperative oral calcium and/or vitamin D supplementation has been advocated by some surgeons to minimize the incidence of hypocalcemia and shorten hospital stays. Such routine use is particularly common in the outpatient or short stay setting, where there is limited time available to correct hypocalcemia once it is discovered. Others have advocated sending patients home with prescriptions for elemental calcium supplementation to be filled if symptoms of hypocalcemia develop [(7)].With the aim of finding an earlier predictor for hypocalcemia, the short half-life of the parathyroid hormone has led to increased interest in postoperative intact parathyroid hormone (IPTH) as an early marker of hypocalcemia[(8)]. However, the routine measurement of IPTH to assess the risk of postoperative hypocalcemia has yet to become accepted as standard practice. The variability in assays, timing of measurements, and cutoff levels makes comparisons between studies difficult [(9)].

It is crucial to identify the most reliable early determinants of hypocalcemia to help surgeons distinguish those patients who are at low risk for developing hypocalcemia from those who need calcium supplementation therapy and inpatient observation. The ability to discriminate between these groups may allow for an up to 50% cost reduction compared with traditional postoperative hospital stays [(2)].
This study aimed to evaluate the accuracy and reliability of quick parathyroid hormone level measurement in predicting clinically relevant hypocalcaemia after total thyroidectomy.

Patients and Methods

This was a prospective study carried out from January 2016 to December 2020 that included all patients who underwent either a total or a completion total thyroidectomy for benign or malignant disease. All patients were operated on and cared for by the same surgical team in Aswan University Hospital.

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Sixty out of three-hundreds cases who underwent thyroid surgery for abnormal thyroid disorder and fulfil the criteria of total thyroidectomy were enrolled in the study.

Ethical consideration

Ethical committee approval was done before starting the study. Verbal and written consent was obtained from all the patients regarding the nature of the operation and its possible complications.

Inclusion criteria

All patients with thyroid diseases who underwent total thyroidectomy.

Exclusion criteria

All patients with thyroid diseases who underwent thyroid nodules excision, lobectomy, subtotal thyroidectomy, or malignant goiter with cervical lymphadenopathy that necessitate neck dissection.

Methodology:

Preoperative assessment:

🕮**History**: Through history of all patients including age, six, symptoms of pressure manifestation, toxicity, or malignancy. Also, history of chronic medical diseases, previous operations or thyroid surgery, metabolic bone disease, and medications, such as oral calcium / vitamin D supplementation, hormone replacement therapy for postmenopausal women, anabolic agents, thiazide type diuretics, or antiepileptic agents, known to affect serum calcium metabolism. **Physical examination:**

General: Including the body built, weight, pulse, and blood pressure, as well as toxic manifestations or manifestations suggestive of distant metastases.

Local: Inspection, palpation, percussion, and auscultation with the aim to determine the following:

- Size of the thyroid gland and its consistency.
- Which thyroid lobe is involved.
- Mobility or fixation to the surrounding structures.
- Presence of palpable thrill or audible bruit,
- Presence of retrosternal extension.
- Presence or absence of enlarged cervical lymph nodes.

Investigations:

Indirect laryngoscopy: routinely done to assess any abnormal mobility or lesions of the vocal cords.

Radiological examinations:

- Chest x-ray posteroanterior view.
- Neck ultrasound examination,
- Thyroid scan if indicated.

Laboratory assessment:

Blood samples were collected using conventional venipuncture for:

1. Routine preoperative assessment.
2. Free T3, T4 and TSH assessment.
3. Ionized serum calcium.
4. PTH assay.

Patients included in this study has been divided into two groups according to post thyroidectomy symptoms of hypocalcemia:

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- -Group I: asymptomatic (no symptoms or signs of hypocalcaemia within 48 hours postoperatively).
- -Group II: Symptomatic (positive symptoms or signs of hypocalcaemia within 48 hours postoperatively).

Operative technique:

1. Under general endotracheal anesthesia, the patient was placed in a supine position with the neck extended. A low collar incision was made and carried down through the subcutaneous tissue and platysma muscle.
2. Superior subplatysmal flap was developed, and the strap muscles were divided vertically in the midline and retracted laterally and dissected from the relevant thyroid lobe.
3. The middle thyroid vein was divided and ligated.
4. The superior pole of the thyroid was dissected free, and care was taken to identify and preserve the external branch of the superior laryngeal nerve. The superior pole vessels were ligated very close to the upper pole of the thyroid lobe.
5. The inferior thyroid artery and recurrent laryngeal nerve were identified to preserve blood supply to the parathyroid glands, the inferior thyroid artery was not ligated laterally as a single trunk; rather, its branches were ligated individually on the capsule of the lobe after they have supplied the parathyroid glands.
6. The parathyroid glands were identified, and an attempt was made to leave each with an adequate blood supply while moving the gland off the thyroid lobe.
7. Care was taken to identify the recurrent laryngeal nerve along its course if a total lobectomy is to be done. The nerve was gently unroofed from surrounding tissue, with care taken to avoid trauma to it. The nerve is in greatest danger near the junction of the trachea with the larynx at the ligament of Berry where it is adjacent to the thyroid gland. Once the nerve and parathyroid glands have been identified and preserved, the thyroid lobe was then removed from its tracheal attachments by dividing the ligament of Berry The contralateral thyroid lobe was removed in a similar manner.
8. Careful hemostasis and visualization of all important anatomic structures were mandatory for success.
9. A small suction drain was inserted through a small stab wound; it was generally removed within 24 hours.
10. The strap muscles sutured transversely. Platysma was closed by interrupted sutures and the skin edges were approximated with a running subcuticular 5-0 absorbable suture. Sterile paper tapes (Steri-strips) were then applied and left in place for about a week.

Measurement of serum calcium and parathyroid hormone levels:

A preoperative blood sample was drawn after the induction of anesthesia for baseline measurement of serum ionized calcium and PTH levels. Another sample was also drawn at the end of operation for measurement of serum ionized calcium and PTH levels during skin closure.

Serum intact PTH level were measured with the standard **enzyme-linked immunosorbent assay (ELISA)**. Expected values in normal adults are 15 to 65 pg/ml. Ionized calcium detected by **ion selective electrode technique**. The expected range of ionized calcium in normal adult is from 1.15 to 1.30 mmol/L. Significant hypocalcemia was defined as patient with diffuse perioral, fingertip paresthesia, numbness, tetany, a newly positive Chvostek sign, plasma ionized calcium concentration level of less than 1.15 mmol/l during the hospital stay or at any time after discharge from the hospital.

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Postoperative Management:

During the postoperative period, the patients were assessed carefully for the clinical symptoms and signs of hypocalcemia (fatigue, weakness, numbness around the lips or the tips of the extremities and positive Chvostek's or Trousseau's signs were considered, to be compatible with mild hypocalcemia while the carpopedal spasm, convulsions and laryngospasm were considered, to be associated with advanced hypocalcemia). Patients who developed symptoms and signs of hypocalcemia were treated by IV calcium gluconate infusion till improvement of symptoms followed by oral calcium 500–1,500-mg calcium tablets daily and oral active vitamin D (calcitriol) 0.25 mcg twice daily was added if the 1,500-mg calcium tablets alone failed to maintain normocalcemia till disappearance of symptoms.

The decision to continue or discontinue use of these medications was based on physical examination, laboratory results, and clinical judgment of the surgeon at postoperative encounters. Patients were categorized as permanently hypocalcemic when calcium supplementation therapy was required to maintain normocalcemia beyond 6 months following surgery.

Data Management and Analysis:

The collected data was revised, coded, tabulated, and introduced to a PC using Statistical package for Social Science **(SPSS 25).** Data was presented and suitable analysis was done according to the type of data obtained for each parameter.

i.Descriptive statistics:

1. Mean, Standard deviation (± SD) and range for parametric numerical data, while Median and Interquartile range (IQR) for non-parametric numerical data.
2. Frequency and percentage of non-numerical data.

ii.***Analytical statistics: Paired t-test. Wilcoxon signed rank test. Student T Test. Mann Whitney Test (U test). The ROC Curve (Receiver Operating Characteristic)*** provides a useful way to evaluate the Sensitivity and Specificity for quantitative diagnostic measures that categorize cases into one of two groups.

P- value: level of significance -P>0.05: Non-significant (NS). -P< 0.05: Significant (S). -P<0.01: Highly significant (HS).

Results

Fifty patients underwent total thyroidectomy for multinodular goiter, six cases for controlled toxic goiter (4) cases primary toxic goiter and 2 cases for secondary toxic goiter) and four cases for suspicious solitary thyroid nodules. Postoperatively, forty-four patients (73.3%) had no symptoms of hypocalcemia(GroupI), while sixteen patients (26.7%) had symptoms of hypocalcemia (Group II) (Group II) (**Table 1 and 2).**

This table shows statistical significance betweenGroup Iand Group IIaccording toParathormone Hormone level**(Table 3).**

This table shows statistical significance between Group Iand Group II according to serum ionized calcium level (**Table 4).**

This Roc curve shows cut-off value of parathormonepre-operatively to detect post-operative symptomatic group of hypocalcemia(Group II) after thyroidectomy is ≤ 74.3,Sensitivity 87.5%, Specificity64.64%, Positive predictive value 46.7%, and Negative predictive value 93.3%**(Table 5).**

This Roc curve shows cut-off value of serum ionized calcium pre-operatively to detect post-operative symptomatic group of hypocalcemia**(**Group II**)** after thyroidectomy is <1.11, Sensitivity 100%, Specificity 59.09%, Positive predictive value 47.1%, and Negative predictive value 100%**(Table 6).**

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This Roc curve shows cut-off value of parathormone to detect post-operative symptomatic group of hypocalcemia (Group II) after thyroidectomy is ≤ 24.6,Sensitivity 75%, Specificity 95.45%, Positive predictive value 85.7%, and Negative predictive value 91.3%(**Table 7).**

This Roc curve shows cut-off value of serum ionized calcium results to detect post-operative symptomatic group of hypocalcemia after thyroidectomy **(**Group II**)** is ≤ 1.06, Sensitivity 87.5%, Specificity 95.45%, Positive predictive value 87.5%, and Negative predictive value 95.5%**(Table 8).**

These two tables show the changes of parathormone and ionized calcium levels between the preoperative and postoperative state in non- symptomatic group (Group I) and symptomatic group (Group II) of post thyroidectomy hypocalcemia; there was more changes in parathormone and ionized calcium (decline) in symptomatic group (Group II), but the change is more significant in ionized calcium level (p-value 0.001).

The decline of PTH in Group II post operatively was 78.3% which was more significant than the changes in Group I(**Table 9 and 10).**

This Roc curve shows Cut-off value of the percentage of parathormone decline postoperatively in (Group II) after thyroidectomy; is 62.9%, Sensitivity 62.5%, Specificity 100 %, Positive predictive value 100%, and Negative predictive value 88% (**Table 11).**

This Roc curve shows Cut-off value of the percentage of serum ionized calcium decline postoperatively in (Group II) after thyroidectomy; is ≤ -9.4%, Sensitivity 87.5 %, Specificity 100 %, Positive predictive value 100%, and Negative predictive value 95.7% (**Table 12).**

Table 1: Age among the study group.

	Mean	SD	Median (IQR)	Range
Age	42.15	9.78	40.5 (35 - 50)	(25 - 65)

SD: Standard Deviation. (IQR): Interquartile range.

Table 2: Hypocalcaemia and types of goiter.

Types of goiters	Number of cases N	Percentage	Group I	Group II
Multinodular goiter	50	83.33%	40	10
Primary toxic goiter	4	6.66%	2	2
Secondary toxic goiter	2	3.33%	1	1
Solitary thyroid nodule	4	6.66%	1	3

Table 3: Level of Parathormone Hormone (PTH) before and after the operation.

	Symptoms of hypocalcaemia		Mann-Whitney test	
	Group I	GroupII		
	Median (IQR)	Median (IQR)	p-Value	Sig.
PTH (Pg/ml) before operation[1].	92.3 (57.5 - 147.1)	49.45 (35 - 72.9)	0.028	S
PTH (Pg/ml) after operation[2].	94.95 (65.2 - 228.8)	8.85 (3.7 - 57.65)	0.004	HS

P- value: level of significance (Sig.). (IQR): Interquartile range
-P>0.05: Non-significant (NS).
-P< 0.05: Significant (S).
-P<0.01: Highly significant (HS).

1-the blood sample taken at the induction of anesthesia.
2- the blood sample taken 10-15 minutes after thyroidectomy at skin closure.

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Table 4: Level of ionized calcium (i-CA) before and after the operation.

	Symptoms of hypocalcaemia		Student t-test	
	Group I	Group II		
	Mean ± SD	Mean ± SD	p-Value	Sig.
i-CA (mmol/l) before operation.	1.09 ± 0.12	1.21 ± 0.09	0.013	S
i-CA (mmol/l) after operation.	1.17 ± 0.12	0.97 ± 0.15	0.001	HS

Table 5: Roc curve to detect symptoms of hypocalcemia by parathormone pre-operatively.

AUC	95% CI	Sig.	Cut-off value	Sensitivity	Specificity	+LR	-LR	+PV	-PV
0.767	0.578 to 0.901	0.009	≤ 74.3	87.50	63.64	2.41	0.2	46.7	93.3

Table 6: Roc curve to detect symptoms of hypocalcemiaby i-CA pre-operatively.

AUC	95% CI	Sig.	Cut-off value	Sensitivity	Specificity	+LR	-LR	+PV	-PV
0.81	0.625 to 0.929	0.001	<1.11	100	59.09	2.44	0.0	47.1	100

Table 7: Roc curve to detect symptoms of hypocalcemia by parathormone post-operatively.

AUC	95% CI	Sig.	Cut-off value	Sensitivity	Specificity	+LR	-LR	+PV	-PV
0.852	0.675 to 0.955	<0.001	≤ 24.6	75	95.45	16.5	0.26	85.7	91.3

Table 8: Roc curve to detect symptoms of hypocalcemiaby i-CA post-operatively.

AUC	95% CI	Sig.	Cut-off value	Sensitivity	Specificity	+LR	-LR	+PV	-PV
0.889	0.721 to 0.974	<0.001	≤1.06	87.5	95.45	19.25	0.13	87.5	95.5

Table 9: Percentage of Parathormone Hormone (PTH) decline after the operation.

	Symptoms of hypo		Mann-Whitney test	
	Group I	Group II		
	Median (IQR)	Median (IQR)	p-Value	Sig.
PTH (Pg/ml) before operation	92.3 (57.5 - 147.1)	49.45 (35 - 72.9)	0.028	S
PTH (Pg/ml) after operation	94.95 (65.2 - 228.8)	8.85 (3.7 - 57.65)	0.004	HS
Change in Parathormone (Pg/ml)	7.65 ((-19.5) – 54.8)	-28.3 ((-45.25) – 8)	0.101	NS
Percent of change	-10.8% ((-42.5% - 23.02%)	-78.3% ((-3.9% – 93.7%)	0.013	S

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Table 10: Percentage of ionized calcium (i-CA) decline after the operation.

	Symptoms of hypo		Student t-test	
	Group I	Group II		
	Mean ± SD	Mean ± SD	p-Value	Sig.
i-CA (mmol/l) before operation.	1.09 ± 0.12	1.21 ± 0.09	0.013	S
i-CA (mmol/l) after operation.	1.17 ± 0.12	0.97 ± 0.15	0.001	HS
Change in i-CA (mmol/l)	0.08 ± 0.21	-0.23 ± 0.18	0.001	HS
Percent of change	4.8% ((-4.3%) – 13.9%)	-22.5% ((-30.2%) - (-9.5%))	0.001(M)	HS

Table 11: Roc curve to detect symptoms of hypocalcemia by percent of change in PTH.

AUC	95% CI	Sig.	Cut-off value	Sensitivity	Specificity	+LR	-LR	+PV	-PV
0.801	0.616 – 0.924	0.004	< -62.9%	62.5	100	∞	0.37	100	88

**62.9% decrease in PTH compared with preoperative level will detect appear of symptoms.*

Table 12: Roc curve to detect symptomsof hypocalcemia by percent of change in i-CA.

AUC	95% CI	Sig.	Cut-off value	Sensitivity	Specificity	+LR	-LR	+PV	-PV
0.92	0.762 – 0.987	0.001	≤ -9.4%	87.5	100	∞	0.13	100	95.7

**9.4% decrease in i-CA compared with preoperative level will detect appear of symptoms.*

Discussion

Over the last two decades, there has been a marked increase in outpatient and short stay thyroidectomies as the safety of the procedure improved and complication rates have decreased. Hypocalcemia has been a large factor in determining the need for hospitalization after surgery. Given the proximity of the parathyroid glands and the thyroid gland, even with careful sub-capsular dissection, one or more parathyroid glands may be inadvertently removed or have their blood supply compromised, which can then lead to hypocalcemia. It has been reported that transient hypocalcemia occurs in 27% of thyroidectomy patients **(10).**

There is consensus that the diagnosis and treatment of post-operative hypocalcemia must precede the development of symptoms and that PTH and/or serum calcium should be monitored after total thyroidectomy (TT) in -order to start treatment before symptoms occur. Timing of serum calcium measurement after thyroidectomy is critical because it has an impact on the prevalence of hypocalcemia rates: the closer the blood sampling is performed to surgery the lower the rates of hypocalcemia will be. On the other hand, if serum calcium is determined too late, patients may develop clinical symptoms before treatment is commenced **(11).**

Conventional approaches to manage post thyroidectomy hypocalcemia:

Strategies to manage post thyroidectomy hypocalcemia have been classified as preventive (routine calcium supplementation), reactive (therapy after demonstration of hypocalcemia) or predictive. While routine supplementation unnecessarily exposes many patients at low risk of hypocalcemia to adverse effects and economic burden of oral therapy, reactive therapy exposes them to the risks of life-threatening hypocalcemia. So, prediction of hypocalcemia using serum iPTH and selective use of calcium supplements seems to be a promising

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approach. Two issues related to iPTH still remain unresolved: one is the ideal cut- off value of serum iPTH and the timing of collection of the sample for serum iPTH[12].

IOPTH Assay and Parathyroid Gland auto transplantation:

IOPTH offers valuable information during total thyroidectomy (TT), correctly identifying patients at risk of postoperative hypocalcemia. **Barczyński et al., [13]** showed that: Selective IOPTH-guided parathyroid auto transplantation (PA) in patients with the plasma iPTH level <10 ng/L at 10–20 min after TT reduces the risk of permanent postoperative hypoparathyroidism to zero, and this approach seems to be as effective as elective PA of at least one parathyroid gland without IOPTH measurement. Moreover, selective IOPTH-guided PA significantly lowers the incidence of transient postoperative hypoparathyroidism and the need for calcium supplementation therapy compared with elective PA without IOPTH. **Tartaglia et al., [14]** showed that: In any case, it can certainly be useful to perform a rapid intraoperative PTH assay, they believed that it is a good rule, on realizing that when a parathyroid has been inadvertently removed, to reimplant the tissue, especially considering that this is an extremely easy procedure that does not significantly extend the surgical time. Also, **Iorio et al., [15]** recommend parathormone assay intraoperatively as it can help the surgeon to determine when reimplantation is indicated or not.

Available literature:

Table I shows a review of various studies done so far across the world over the last one and a half decades. Majority of them have been prospective but the research methodology has been variable. While some have tried to identify the level of serum iPTH which could best predict hypocalcemia at a definite time- period in relation to surgery (1-15), others have endeavored to find out its statistical and clinical value corresponding to definite selected serum levels (16-22). Though both approaches are reasonable, the former is statistically more appropriate and can give a better cut- off value [12].We have used the same approach in this prospective study.

Table I Studies to predict post-thyroidectomy hypocalcemia using serum iPTH[12].

	Author	**Year**	**Type of study**	**Inclusion**	***N***	**S. iPTH cut-off**	**Timing**	**Sensitivity**	**Specificity**
1	Alia et al.	2007	Prospective	–	39	1.5 pmol/l	10 min	80	91.7
2	Roh et al.	2006	Prospective	–	92	15 pg/ml	1 h, 1 day, 3 day	85	84
3	Erbil et al.	2007	Prospective	Non-toxic	130	10 pg/ml	12 h	Odds ratio = 16.4	

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	Author	Year	Type of study	Inclusion	*N*	S. iPTH cut-off	Timing	Sensitivity	Specificity
4	Sywak et al.	2007	Prospective	–	100	10 ng/l	4 h, 23 h	90	84
5	Proczko-Markuszewska et al.	2010	Prospective	–	100	20 pg/ml	1 h, 24 h	93	84
6	Kim et al.	2013	Prospective	Non-toxic	50	10.6 pg/ml	6 h	89	88
7	AlQahtani et al.	2013	Retrospective		149	1.15 pmol/l	1 h, 6 h, 24 h	89	
8	Reddy et al.	2016	Prospective	–	100	9 pg/ml	20 min	92	83
9	Kolahdouzan et al.	2017	Prospective	-	83	15.39 pg/ml	1 h, 6 h, POD 1	88.2	77.5
10	Galy-Bernadoy C et al.	2018	Prospective	–	257	9 ng/l 19 ng/l	At skin closure	100 100	80.3 96
11	Sala et al.	2019	Prospective	Both toxic and non-toxic	134	11.2 pg/ml	POD1	82.3	71
12	Lang et al.	2012	Prospective	–	117	9.4 pg/ml	IOPTH, POD1	82	95

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	Author	Year	Type of study	Inclusion	*N*	S. iPTH cut-off	Timing	Sensitivity	Specificity
13	Lombardi et al.	2006	Prospective	–	53	10 pg/ml	2 h,4 h, 6 h, 24 h, 48 h	64.8	89.5
14	Toniato et al.	2008	Prospective	Both	160	9.6 pg/ml	POD1	NR	NR
15	Landry et al.	2012	Retrospective	–	156	6 pg/ml	2 h, 5PM, POD1	NR	NR
16	Grodski et al.	2009	Prospective	–	50	10 ng/l	4 h	NR	NR
17	Ezzat et al.	2010	Prospective	Both toxic and non-toxic	52	27 pg/ml	Intraop	100	68.2
18	Cayo et al.	2012	Prospective	–	143	10 pg/ml	POD 1	Odds ratio = 1.08	
19	Carr et al.	2014	Retrospective	–	77	10 pg/ml	4 h, POD 1	98	90
20	Inversini et al.	2016	Prospective	–	260	10 pg/ml		76 (Accuracy)	83
21	Sahli et al.	2018	Prospective	–	218	10 pg/ml 20 pg/ml	1 h, POD1	36.5 66.4	89.2 67.6

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	Author	Year	Type of study	Inclusion	*N*	S. iPTH cut-off	Timing	Sensitivity	Specificity
22	Selberherr et al.	2015	Prospective	Non-toxic	237	10 pg/ml 15 pg/ml	POD1	100 83	92 99

iPTH intact parathyroid hormone, *NR* not reported.

Conclusion:

Quick parathyroid hormone level measurement in accurate and reliabile in predicting clinically relevant hypocalcaemia after total thyroidectomy.

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