Cohort Study

Role of perioperative parathormone hormone level assay after total thyroidectomy as a predictor of transient and permanent hypocalcemia: Prospective study

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ABSTRACT

Background: The researchers are trying to evaluate the measurement of: Intact parathyroid hormone (iPTH) and serum total calcium (sCa) levels for predicting hypocalcemia after total thyroidectomy (TT).

Methods: The sample of this single center prospective study consists of (100) patients, where (77) females and (23) males with an age range between (28) and (65) (the mean level is, 48.17 ± 6.54). These selected patients underwent total thyroidectomy (TT) in the general surgery department, Benha university hospital from the period of June 2019 to February 2020. Levels of sCa and iPTH were measured at several times preoperatively, 10 min, 48 h, 3, 6, 9 months, and 1 year after being after gone TT.

Results: Among the entire study sample, 23 patients (23%) developed transient hypoparathyroidism and hypocalcemia (<8.5 mg/dl), none of them developed permanent hypoparathyroidism and hypocalcemia. The cut-off point of PTH has been 10 min after TT was at 23 pg/mL as it was the best compromise between sensitivity and specificity for predicting hypocalcaemia. It has been found that Patients who have a PTH greater than 23 pg/ml can be discharged safely after 24 h. Patients who have PTH of less than 23 pg/mL were observed for an additional 24 h, and the study found that timely treatment initiation is recommended. A PTH < 10 pg/mL measured at 48 h after surgery had a sensitivity, specificity as well as an accuracy of 100%, for predicting hypocalcemia after TT. The accuracy of a single PTH concentration at 48 h was useful for predicting hypocalcemia [Area under receiver–operator characteristic curve (AUC) 1; confidence interval (CI), 95%, 0.85–0.94].

Conclusion: Patients with iPTH < 10 pg/mL, and sCa levels < 7.4 mg/dl are at higher risk of developing hypoparathyroidism and hypocalcemia after TT.

1. Introduction

Thyroid surgery can result in serious morbidities such as recurrent laryngeal nerve (RLN) injury, leading to transient or permanent vocal cord paralysis and hematoma that may result in airway compromise. Hypocalcemia is the most common complication after thyroidectomy, which may be temporary or permanent [1–4].

Hypocalcemia after thyroid surgery occurs for several reasons, such as removing the parathyroid gland and injury to its blood supply, leading to transient or permanent hypoparathyroidism. Furthermore, deficiency of vitamin D, hungry bone syndrome, acute rising in serum calcitonin level, hypocalcemia induced by postoperative alkalosis due to hyperventilation from postoperative pain, and postoperative dilutional hypocalcemia can all lead to or exacerbate post-thyroidectomy hypocalcemia [5–10].

Post-thyroidectomy incidence of transient hypoparathyroidism ranges between 0.3 and 49%, whereas permanent hypoparathyroidism is up to 13% [11]. Intraoperative PTH assay has been suggested to have value in predicting and identifying the patients being at risk of post-thyroidectomy hypoparathyroidism and hypocalcemia. Furthermore, intraoperative PTH results can affect postoperative management, such as patients who need early calcium supplementation and eligible for early safe discharge [12,13].

Post-thyroidectomy PTH predicts hypocalcemia accurately.

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The high incidence of post-thyroidectomy hypoparathyroidism and the fact that it is associated with a considerable morbidity rate results in sustained efforts for reliable markers to be found out for prediction of hypoparathyroidism. Many studies demonstrate that PTH is a highly sensitive indicator, with high specificity to predict hypocalcemia after TT [15]. Our study aims to find out if an early reduction of PTH after TT can predict hypocalcemia.

1.1. Patients and methods

1.1.1. Study design, setting and period

This is a prospective study of 100 new consecutive patients undergoing TT with preoperative and postoperative time-serial analysis of total calcium and PTH levels, it is implemented from June 2019 to February 2020 in the general surgery department, Benha university hospital.

Inclusion criteria:

1. Benign multinodular goiter (37%).
2. Graves’ disease (20%).
3. Papillary thyroid cancer (PTC) (16%).
4. Follicular thyroid cancer (10%).
5. Recurrent goiter (10%).
6. Thyroiditis (7%).

1.1.2. Exclusion criteria

- Patients with concomitant primary hyperparathyroidism.

After obtaining the approval of the Institutional ethical committee’s study proposal (IRB No: RC.December.1, 2020) in the form of a written informed consent from the patients for purpose of participation in this study, patients were fully informed about the hazards and benefits of the surgery. The sample size of the study was calculated using online software (https://clincalc.com/stats/samplesize.aspx). The current study has been reported in line with the STROCSS criteria [16]. Registration unique identifying number (UIN): 6941 (https://www.researchregistry.com/browse-the-registry#home/).

Therefore, all selected patients underwent the following:

A-Preoperative assessment including
1. Full detailed history, including any history suggestive of hypocalcemia.
2. General and local physical examination.
3. Laboratory investigation includes routine preoperative assessment, free T3, T4, thyroid-stimulating hormone (TSH), total and ionized serum calcium, PTH, creatinine, and serum albumin. At the time of surgery. It has been found out that renal panel and albumin were normal in all patients.

Table 1

| Variable                          | Total number Of patients (100) |
|-----------------------------------|--------------------------------|
| Age, range, (Mean ± SD)           | 28.65 (48.17 ± 6.54)           |
| Sex                               |                                |
| Male                              | 23 (23%)                       |
| Female                            | 43 (43%)                       |
| Post-menopausal                   |                                |
| Indications of thyroidectomy      |                                |
| PTC                               | 16 (16%)                       |
| FTC                               | 10 (10%)                       |
| Benign goiter                     | 37 (37%)                       |
| Multinodular goiter               |                                |
| Recurrent goiter                  | 10 (10%)                       |
| Thyrotoxicosis                    | 20 (20%)                       |
| Diabetes Mellitus                 | 31 (31%)                       |
| Hyperension                       | 42 (42%)                       |
| Number of parathyroid glands      |                                |
| identified during operation       |                                |
| 0                                 | 1 (1%)                         |
| 1                                 | 5 (5%)                         |
| 2                                 | 27 (27%)                       |
| 3                                 | 55 (55%)                       |
| 4                                 | 7 (7%)                         |

Table 2

| Variable                          | Total calcium levels between normocalcemic and hypocalcemic group. |
|-----------------------------------|-------------------------------------------------------------------|
|                                  | Total Calcium (mg/dL)                                             |
|                                  | Normocalcemic group (n = 77)                                      |
|                                  | Hypocalcemic group (n = 23)                                       |
|                                  | P value                                                           |
| Pre-operative                    | 9.45 ± 0.48                                                       |
| After 10 min                     | 9.39 ± 0.43                                                       |
| After 6 months                   | 9.22 ± 0.56                                                       |
| After 9 months                   | 9.32 ± 0.39                                                       |
| After 1 year                     | 9.42 ± 0.50                                                       |

Table 3

| Variable                          | PTH level in normocalcemic and hypocalcemic groups. |
|-----------------------------------|-----------------------------------------------------|
|                                  | PTH (pg/ml)                                         |
|                                  | Normocalcemic group (n = 77)                        |
|                                  | Hypocalcemic group (n = 23)                         |
|                                  | P value                                             |
| Pre-operative                    | 50.12 ± 4.82                                        |
| After 10 min                     | 49.11 ± 1.25                                        |
| After 48 h months                | 41.29 ± 5.57                                        |
| After 9 months                   | 40.71 ± 7.13                                        |
| After 1 year                     | 44.83 ± 5.46                                        |

Hypocalcemia is less likely in the presence of a normal PTH level, so PTH can facilitate the patient’s discharge within 24 h. Furthermore, PTH levels can be followed to guide early postoperative treatment with calcium and/or cholecalciferol supplements to decrease the incidence and severity of hypocalcemia. Measurement of PTH at any time from 10 min to several hours after thyroideectomy will accurately predict post-operative hypocalcemia. Some surgeons advise oral calcium supplementation routinely to all patients who underwent hypoparathyroidism. Some surgeons advise oral calcium supplementation routinely to all patients who underwent TT to prevent hypocalcemia [11,14].

PPV: Positive Predictive Value, NPV: Negative Predictive Value.
Radiological assessment has been conducted, including neck ultrasonography (U/S) and thyroid scan for those with low TSH.

Indirect laryngoscopy.

**B-Operative technique**

1. Under general anesthesia, the patient was placed in a supine position with the neck fully extended. A low collar incision was made and carried down through the subcutaneous tissue and platysma muscle.
2. Creation of subplatysmal flaps
3. Separation of strap muscles
4. Ligation of the middle thyroid vein.
5. Ligation of superior thyroid artery and external branch of SLN identified.
6. Ligation of branches of the inferior thyroid artery and RLN identified.
7. The parathyroid glands were identified, and effort was made to preserve each with an adequate blood supply while moving the gland away from the thyroid lobe.
8. The thyroid lobe was then removed from its attachments to the trachea by dividing Berry's ligament.
9. Careful hemostasis was ensured.
10. A small suction drain was inserted through a small stab wound; it was generally removed after 24 h.
11. Closure of strap muscles, platysma, and skin.

**C- Measurement of sCa and iPTH levels.**

A preoperative blood sample was drawn one day before TT for baseline measurement of total sCa and PTH levels. Postoperatively time-serval serum Ca levels were measured with an automated colorimetric method at: 10 min, 48 h, 3, 6, 9 months and one year after thyroidectomy. Besides, serum iPTH levels were measured with the two-site chemiluminescent enzyme-labeled immunometric assay one day before operation, 10 min, 48 h, 3-6-9 months, and a year after surgery. The reference ranges of serum Ca and PTH were 8.5–10.5 mg/dl and 15–65 pg/mL, respectively. The percentage change in Ca was defined as postoperative difference between the first two calcium levels (10 min and 48 h). In addition, the percentage change in PTH has been the difference between preoperative and postoperative PTH values.

**D-Postoperative Management:**

The study protocol required admission of all patients for at least 3 days postoperative for blood tests. All patients were clinically assessed for the manifestation of hypocalcemia. Hypocalcemia defined as a symptomatic patient or Ca level < 8.5 mg/dl during the hospital stay or at any time after discharge from hospital. Symptoms of hypocalcemia either mild: (easy fatigability, generalized weakness, perioral numbness,
numbness at the tips of fingers and toes, and positive Chvostek’s or Trousseau’s signs) or severe: (carpopedal spasm, convulsions, and laryngospasm). Patients with manifestation of hypocalcemia were treated by intravenous (IV) infusion of calcium gluconate until the improvement of symptoms, this is followed by oral supplementation of calcium and active form vitamin D until the symptoms disappeared totally. Patients were discharged with follow up in outpatient clinic at 3, 6, 9 months and 1 year for measurement of calcium and PTH.

1.2. Endpoints

1.2.1. Primary endpoint
Detection of the incidence of hypocalcemia, variation in perioperative calcium level, variation in perioperative PTH level and cut off level of PTH as a predictor of hypocalcemia after TT.

1.2.2. Secondary endpoint
An evaluation of predictive factors of hypocalcemia after TT.

1.2.3. Statistical analysis
Data were analyzed by applying Statistical Program for Social Science (SPSS) version 20.0. Quantitative data were expressed as a mean; it was expressed as frequency and percentage. Independent-samples t-test of significance was used when comparing two means. A one-way analysis of variance (ANOVA) applied when comparing more than two means. Post Hoc test: Least Significant Difference (LSD) was used for multiple comparisons among different variables. The confidence interval was set to (95%), whereas the margin of error accepted was set to (5%). The p-value was considered significant if ≤ 0.05.

2. Results

This study consists of 100 patients (77 women, 23 men) and underwent TT. Demographic characteristics of the patients are summarized and described in Table 1. All patients were normocalcemic preoperatively, none of them developed complications related to surgery and no patients missed follow up in outpatient clinic.

Primary endpoint.

There is a statistically significant variation in normocalcemia and hypocalcemia, according to indications of thyroidectomy (malignant versus benign) and operative procedures (lymph node dissection versus non-dissection), particularly the central group. Serum calcium levels continued to decrease to 48 h after surgery in the hypocalcemic group, but not in the normocalcemic group. There is a statistically significant difference between normocalcemic and hypocalcemic groups according to total calcium level after 48 h and 3 months (P = 0.001) [Table 1]. The low calcium levels slowly increased and recovered to a normal level at approximately 3 months in both groups of men and women after operation. The recovery rate of sCa levels was significantly lower in the hypocalcemic group than the normocalcemic group. All patients with hypocalcemia showed a higher drop in calcium level after an operation in comparison to the normocalcemic group.

Serum PTH concentrations in the hypocalcemic group decreased in most patients after 10 min and 48 h after surgery. Then, they were recovered into a normal level after 3 months of operation in all patients of the hypocalcemic group, therefore there is statistically significant variation between normocalcemic and hypocalcemic groups regarding PTH levels from after 10 min to after 3 months (P = 0.001) [Table 2].

Analysis of the test cutoff values indicated much higher sensitivity for the PTH levels at 48 h (100%) than 10 min (89%) after thyroidectomy. The sensitivity of serum calcium levels at the cutoff point increased slightly at 48 h (100%) when compared with those obtained at 10 min after thyroidectomy (88%) [Tables 3 and 4, 5]. Receiver operating characteristics (ROC) curve was used to define the best cut off value of Total Calcium, and PTH, The accuracy of a single PTH concentration at 48 h was good for predicting hypocalcemia [AUC 1; CI,
Table 6
Clinical variables related to hypocalcemia

| Variables               | Normocalcemic group | Hypocalcemic group | P value |
|-------------------------|---------------------|--------------------|---------|
| Age (mean ± SD)         | 55 ± 11.86          | 56 ± 12.21         | 0.23    |
| Sex                     | Male                | Female             |         |
|                         | 16 (69.6%)          | 7 (30.4%)          | 0.34    |
| Post-menopause          | Yes (n = 42)        | No (n = 35)        | 0.002   |
|                         | 25 (71.4%)          | 10 (28.6%)         | 0.33    |
| Hyperthyroidism         | Yes (n = 24)        | No (n = 76)        | 0.001   |
|                         | 16 (66.7%)          | 8 (33.3%)          | 0.012   |
| Thyroiditis             | Yes (n = 10)        | No (n = 90)        | 0.35    |
|                         | 6 (60%)             | 4 (40%)            |         |
| Diabetes                | Yes (n = 31)        | No (n = 69)        | 0.45    |
|                         | 20 (64.5%)          | 11 (35.5%)         |         |
| Hypertension            | Yes (n = 42)        | No (n = 58)        | 0.49    |
|                         | 29 (69.0%)          | 13 (30.9%)         |         |
| Definitive histological | Malignant (n = 26)  | Benign (n = 74)    | 0.001   |
| diagnosis               | 15 (57.7%)          | 62 (83.8%)         |         |
| Central LN dissection   | Unilateral (n = 10) | Bilateral (n = 26) | 0.55    |
|                         | 3 (11.5%)           | 3 (11.5%)          |         |
| Total number of         | 0 (n = 1)           | 1 (n = 5)          | 0.44    |
| parathyroid glands      | 2 (40%)             | 3 (60%)            | 0.63    |
| identified              | 2 (n = 32)          | 10 (31.2%)         | 0.001   |
| during operation        | 3 (n = 55)          | 7 (12.7%)          | 0.32    |
| Preoperative calcium     | 4.82 ± 0.48         | 9.39 ± 0.43        | 0.44    |
| levels (mg/dL)          | 9.45 ± 0.48         | 9.39 ± 0.43        |         |
| Preoperative PTH level  | 50.12 ± 4.82        | 49.11 ± 1.25       | 0.38    |
| (pg/ml), (mean ± SD)    | 0.6 ± 0.02          | 2.85 ± 0.09        | 0.001   |

95%, 0.85–0.94] (Fig. 1 and 2). Clinical variables associated with hypocalcemia are illustrated in Table 6.

Secondary endpoint:
Analysis of the factors associated with hypocalcemia:
A univariate and multivariate analysis of the factors associated with hypocalcemia are summarized in Table 7.

3. Discussion

Hypocalcemia, after TT, results from either a removal of the parathyroid glands or damage to their blood supply. Incidence of hypocalcemia following TT ranging between (3%) and (40%)is usually transient. The incidence of permanent hypocalcemia in most centers with thyroid surgery experience is ≤2% [17–21]. Throughout the current study, the incidence of hypocalcemia was 23%, all were transient.

Monitoring of sCa levels is commonly used to detect post-thyroidectomy hypocalcemia. However, multiple blood samplings to at least the morning following surgery are required. Accordingly, early detection of hypocalcemia after thyroidectomy within the same day of operation is almost impossible due to the fact that PTH is well known to be a useful indicator of impending post-thyroidectomy hypocalcemia, rapid PTH assay has been used to measure intraoperative PTH levels [21].

Early attempts to detect patients at higher risk for post-thyroidectomy hypocalcemia were primarily dealt with to detect the change in sequential calcium level every time as well as calculating the slope to predict the risk of hypocalcemia. The main concern with this approach was that levels had to be taken over 8 h to be predictive. There was no significant correlation seen with early calcium levels, limiting the use of calcium slopes in facilitating early postoperative hospital discharge [22–24].

Within the current study, 10 min PTH measurement post-thyroidectomy can be used as an indicator of hypocalcemia with (95%) accuracy, which avoids postoperative calcium supplementation and favors early postoperative hospital discharge. A study reported by Lang et al., showed that PTH sensitivity and specificity on skin closure were 82.4 and (95.0%), respectively. In the current research, 10 min PTH level post-thyroidectomy had a sensitivity of (89%) and a specificity of (100%). In the study of Lang et al., PTH level measurement was withdrawn at the time of the closure of the skin (PTH-SC) because the patient was still anesthetized. So, PTH level results would be ready sooner to help ambulatory surgery. Furthermore, PTH-SC might be a more precise and reliable marker in predicting postoperative hypocalcemia than serial Ca level monitoring; it might also abolish the need for multiple withdrawal of blood samples during hospital stay overnight. In Lang et al.’s characteristic curve (AUC), there are different predictors such as sCa slopes, preoperative Ca, PTH-SC, PTH on the next day (PTH-D1), and a combination of preoperative Ca and PTH-SC score that are used for prediction for post-thyroidectomy hypocalcemia. The best cutoff values for PTH-SC and PTH-D1 were 1.0 pmol/L [20].

Noordzij et al., reported that a single PTH threshold (65% decrease in comparison to the level before surgery) measured 6 h post-thyroidectomy had a sensitivity and specificity of 96.4% and 91.4%, respectively. In the study of Lang et al., PTH level measurement was withdrawn at the time of the closure of the skin (PTH-SC) because the patient was still anesthetized. So, PTH level results would be ready sooner to help ambulatory surgery. Furthermore, PTH-SC might be a more precise and reliable marker in predicting postoperative hypocalcemia than serial Ca level monitoring; it might also abolish the need for multiple withdrawal of blood samples during hospital stay overnight. In Lang et al.’s characteristic curve (AUC), there are different predictors such as sCa slopes, preoperative Ca, PTH-SC, PTH on the next day (PTH-D1), and a combination of preoperative Ca and PTH-SC score that are used for prediction for post-thyroidectomy hypocalcemia. The best cutoff values for PTH-SC and PTH-D1 were 1.0 pmol/L [20].

Table 7
Factors associated with hypocalcemia.

| Variables              | Odds ratio | 95% CI |
|------------------------|------------|--------|
| Univariate             |            |        |
| Age ≥55                | 0.531      | 0.266–1.008 |
| Female gender          | 0.503      | 0.263–0.874 |
| Postmenopause          | 0.512      | 0.323–0.651 |
| Hypertension           | 0.462      | 0.342–0.759 |
| Diabetes mellitus      | 0.422      | 0.351–0.741 |
| Hyperthyroidism        | 0.359      | 0.438–0.871 |
| Thyroid cancer         | 0.419      | 0.487–0.776 |
| Bilateral central LN dissection | 0.532 | 0.502–0.864 |
| Preoperative calcium   | 0.442      | 0.364–0.797 |
| Preoperative PTH       | 0.443      | 0.541–0.679 |
| ≤2 parathyroid identified intraoperatively | 0.359 | 0.493–0.571 |
| Calcium drop from preoperative to postoperative (48 h) | 0.339 | 0.473–0.582 |
| Multivariate           |            |        |
| Age ≥55                | 0.642      | 0.352–1.083 |
| Female gender          | 0.663      | 0.357–0.767 |
| Hyperthyroidism        | 0.721      | 0.554–0.962 |
| Thyroid cancer         | 0.614      | 0.589–0.862 |
| Bilateral central LN dissection | 0.543 | 0.469–0.817 |
| ≤2 parathyroid identified intraoperatively | 0.431 | 0.651–0.733 |
| Postoperative PTH      | 0.437      | 0.663–0.854 |
| Calcium drop from preoperative to postoperative (48 h) | 0.445 | 0.599–0.752 |

CI: Confidence Interval.
cutoff was applied. The drawback of this approach is that patients in the middle (with a reduction in percent PTH between 50% and 90%) cannot be discharged early and should have traditional serum calcium level monitoring until their serum calcium leveled off [26].

There are several studies in which PTH evaluated either rapid IOPTH or standard-length PTH assay as a predictor for postoperative hypocalcemia after TT which are summarized in Table 8. Blood supply of the parathyroid glands can be assessed through several methods, including the IOPTH levels routinely obtained at the end of thyroidectomy, visual inspection of vascular pedicles of the glands, and small incision of the glands to access bleeding. Because of PTH’s short half-life (2–5 min), low levels of PTH can develop within a few minutes following bilateral thyroidectomy and on postop. days 1, 7, 14, 21, 28, and 56 after TT, the 112 patients who had a PTH-D1 level ≤ 23 pg/mL at 4 h after TT required calcium. Another prospective study of 143 patients undergoing TT, the 112 patients who had a PTH-D1 level ≥ 10 pg/mL were discharged without calcium supplementation; only 10% developed symptomatic hypocalcemia. By contrast, almost 50% of the other 31 patients who had PTH-D1 level < 10 pg/mL developed hypocalcemic symptoms. In a meta-analysis of 15 studies, routine administration of calcium and vitamin D decreased both the incidence and severity of hypocalcemic symptoms. In a small randomized trial of 79 patients undergoing TT, routine supplementation with oral calcium and vitamin D decreased both the incidence and severity of hypocalcemic symptoms. In a meta-analysis of 15 studies, routine administration of calcium and vitamin D3 after TT was associated with a lower risk of both hypocalcemic symptoms (risk difference −0.24, 95% CI −0.32 to −0.18) and biochemical hypocalcemia (risk difference −0.17) in comparison to treatment based on measured calcium levels [14,40,41].

Other surgeons prescribe calcium routinely to all patients after thyroidectomy to avoid hypocalcemic symptoms. In a small randomized trial of 79 patients undergoing TT, routine supplementation with oral calcium and vitamin D decreased both the incidence and severity of hypocalcemic symptoms. In a meta-analysis of 15 studies, routine administration of calcium and vitamin D3 after TT was associated with a lower risk of both hypocalcemic symptoms (risk difference −0.24, 95% CI −0.31 to −0.17) in comparison to treatment based on measured calcium levels [14,40,41].

The current study has some limitations: first of all, it is a single center study in addition to small number of patients. Therefore, more studies including more cases from multiple centers should be conducted in the future.

### Table 8

| Author (year) | Study type | N | Incidence of hypocalcemia | Method of PTH assay, (type, reference range [pg/mL]) | Times PTH checked | PTH level that predict hypocalcemia | Sensitivity | Specificity |
|---------------|------------|---|--------------------------|-----------------------------------------------|------------------|-------------------------------------|------------|------------|
| Lang et al (2012) [22] | Prospective | 117 | 14.5% | Access immunoassay system (Range 1.2–5.7 pmol/L). | PTH-SC, PTH-D1 | ≤ 3 ng/L at 4 h | 82.4% | 95% |
| Syvak et al (2007) [23] | Prospective Cohort | 100 | 18% | Chemiluminescent assay was used (Immulite 2000 Immuno analyser) | Preop., 4 & 23 h after TT | PACU rPTH < 12 pg/mL | 100% | 92% |
| Macleod et al (2006) [24] | Prospective | 60 | 25% | Immulite (rapid; range 10–72) | Preop., intraop (5 min after TT), 1 h postop | IOPTH < 10 pg/mL | 88.9% | 92.9% |
| Friedman et al (2005) [25] | Prospective | 23 | Not reported | Automated two-site sandwich immunoassay chemiluminescence system | IOPTH, in the recovery room and on postop. days 1, 7, 14, 21, 28, and 56 | ≤ 28 ng/L at 6 h after TT | 100% | 100% |
| Payne et al (2005) [26] | Prospective | 70 | 24% | Roche Elecsys 2010 (rapid; range 10–70) | Preop, intraop (10 min after TT), 1H postop | < 10 pg/mL at 4 & 6 h | 94% | 100% |
| Lombardi et al (2004) [27] | Prospective | 53 | 30.2% | Roche Elecsys E170 (not rapid; range 10–65) | Postinduction, postisolation, 5, 10, 20 min after surgery | > 75% reduction in PTH at 20 min | Not reported | Not reported |
| Higgins et al (2004) [28] | Prospective | 104 | 23.1% | Quick-intra-operative intact PTH KIT | Preop, intraop (TT), 2, 4, 6, 24, and 48H postop | Not reported | Not reported |
| Warren et al (2004) [29] | Prospective | 27 | 11% | Immulite (rapid; range 10–72) | Preop, intraop (10 min after TT), 1H postop | ≥ 10 pg/mL 1H after TT | Not reported | Not reported |
| Lam et al (2003) [30] | Prospective | 40 | 30% | Immulite (rapid; range 10–72) | Postoperative (1 & 6 h) | ≤ 8 pg/mL 1H after TT | 100% | 100% |
| Richards et al (2003) [31] | Prospective | 30 | 33.3% | Immulite (rapid; range 10–72) | IOPTH-SC | IOPTH-SC < 10 pg/mL | 80% | 100% |
| Warren et al (2002) [32] | Retrospective case review | 23 | 17.4% | Immulite (rapid; range 10–72) | Preop, intraop (10 min after TT), 1H postop | < 15 pg/mL 10 min after TT | Not reported | Not reported |
| Lo et al (2002) [33] | Prospective | 100 | 11% | Immulite (rapid; range 10–72) | Intraoperative (at 0 & 10 min) | > 75% reduction in PTH at 0 and 10 min | 100% | 72% |
| Lindaism and et al (2002) [34] | Prospective | 38 | 26.3% | Immulite (rapid; range 10–72) | 1 day preop., after induction of anesthesia, after resection of 1st lobe, after resection of 2nd lobe, 1–3 days after TT and at 4th week. | IOPTH < 1.6 pmol/L | 90% | 75% |

IOPTH-SC: Intraoperative PTH following skin closure. ICMA: Immunochemiluminesetric Assay. PTH-D1: PTH at first postoperative day 1., PACU rPTH: Post Anesthesia Care Unit Rapid PTH.
4. Conclusion

Measurement of the PTH level in the early postoperative period after TT accurately predicts if patients are likely to develop hypocalcemia, it allows the timely initiation of calcium supplementation and may reduce the length of postoperative hospital stay as well as decreasing unnecessary blood tests.

Ethical approval

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration with its later amendments or comparable ethical standards.

Consent to participate

Informed consent was obtained from all individual participants who took part in the study.

Consent for publication

A Written consent was obtained for publication of this study.

Availability of data and materials

The datasets used and/or analyzed during the current study available from the corresponding author on reasonable request.

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Authors’ contributions

Mohamed S. Essa: Study conception, acquisition of data design and Drafting of manuscript.
Khaled S. Ahmad: Literature review and revision of the manuscript.
Mohamed E. Zayed:Acquisition, analysis and interpretation of data.
Ahmed M.F. Salama: Drafting of manuscript and revision of manuscript.
Mohammed A. Fadey: Revision of the manuscript. Mohamed O. El-shaer:Revision of manuscript.

Guarantor

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List of abbreviations

| Abbreviation  | Description                              |
|---------------|------------------------------------------|
| iPTH          | Intact Parathormone Hormone              |
| sCa           | Serum Calcium                            |
| AUC           | Area Under The Curve                     |
| CI            | Confidence Interval                      |
| RLN           | Recurrent Laryngeal Nerve                |
| PTC           | Papillary Thyroid Cancer                 |
| MNG           | Multinodular Goiter                      |
| U/S           | Ultrasound                               |
| TSH           | Thyroid Stimulating Hormone              |
| SLN           | Superior Laryngeal Nerve                 |
| ANOVA         | A one-way analysis of variance           |
| LSD           | Least Significant Difference             |
| UIN           | Unique Identifying Number                |
| IOPTH-SC      | Intraoperative PTH following Skin Closure|
| ICMA          | Immunochemiluminometric Assay            |
| PTH-D1        | PTH at first postoperative day           |
| PACU rPTH     | Post Anesthesia Care Unit Rapid PTH      |

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.amsu.2021.102701.

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Research studies involving patients require ethical approval. Please state whether approval has been given, name the relevant ethics committee and the state the reference number for their judgement.

Current study approved by the ethical committee of the Faculty of Medicine, Benha University.

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Studies on patients or volunteers require ethics committee approval and fully informed written consent which should be documented in the paper.

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Mohamed S. Essa: Study conception, acquisition of data, design and drafting of manuscript.
Khaled S. Ahmad: Literature review and revision of the manuscript.
Mohamed E. Zayed: Acquisition, analysis and interpretation of data.

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