

## Original Research Article

## The effect of RLN identification technique on post-thyroidectomy initial hypocalcaemia and the role of peri-operative PTH measurement as a predictor

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**Abstract:** Thyroidectomy is a very common elective procedure in Sudan. This is why critical analysis of early and late postoperative complications is necessary to assure the quality of surgery for benign thyroid diseases. A identification of the RLN has become a standard step that should be followed during total thyroidectomy; this study was meant to show how far this technique is effective in post-thyroidectomy hypocalcemia. We also aimed to study the role of peri-operative PTH measurement on the prediction of post-thyroidectomy hypocalcaemia. It's a prospective descriptive hospital base study, done on patients who underwent total thyroidectomy in the Military hospital (Omdurman). Recorded data include; gender, age, presenting history, associated illness, operator, technique and procedure, post-operative complication, post-operative serum calcium, perioperative PTH, follow up and compliance of the patient. In results A seventy two consecutive patients underwent total thyroidectomy for benign goiter were studied and analyzed for post-operative hypocalcaemia. The majority of patients were females (83.3%), with male to female ratio of (1:5). The mean age + SD were  $48 \pm 12$  years. Post thyroidectomy hypocalcaemia ( $< 8\text{mg/dl}$ ) with in the first 72 hours was found in 18 (25%) patients, nine (50%) of them were symptomatic. From the seven patients under the study with toxic goiters, three patients developed hypocalcaemia (p-value=0.047). RLN was identified and preserved in 65 patients thirteen (20.0%) of them developed hypocalcaemia.(P-value= 0.211).The inferior thyroid artery (ITA) ligated and cut near the thyroid capsule in 66 (91.7%) patients, 13 (19.7%) developed hypocalcaemia(p- value= 0.051). During surgery, the four parathyroid glands were seen and preserved in 57 (79.2%) patients, 13 (22.8%) of them developed hypocalcaemia (p-value= 0.712). All of the 18 hypocalcemic patients had significant drop of more than 50% in the PTH (p-value= 0.013). Vitamin D and Calcium supplemented for all of them. Fourteen from the hypocalcemic patients returned to normal serum calcium, nine of them within 4 weeks, while five required  $>$  one month. In conclusion There was no significant effect of RLN identification on post-thyroidectomy hypocalcemia (p-value=0.211). Identification and ligation of ITA near the thyroid capsule to achieve delicate hemostasis during surgery was found to have a role in decreasing post-thyroidectomy hypocalcemia (p-value=0.051).The role of PTH drop after surgery was the most significant factor in early detection of post-thyroidectomy hypocalcaemia with a sensitivity of 100% if the drop exceeded 50% of T0 value with symptoms manifestation if it was more than 60%.

**Keywords:** Thyroidectomy, PTH, RLN

### INTRODUCTION

The main postoperative complications of thyroidectomy are recurrent laryngeal nerve (RLN) palsy and hypo-para thyroidism. Post-operative hypocalcaemia after thyroidectomy leads to patient discomfort and prolonged hospital stay. The variety of causes and multi-factorial elements, make the avoidance of post-thyroidectomy hypocalcaemia practically doubtful. However, the trends are now stressing on the prediction and early management of hypocalcaemia. This is why many of the researches now studying the sensitivity of PTH for predicting post-thyroidectomy hypocalcaemia.

### Identification technique of the recurrent laryngeal nerve:

Permanent RLN paralysis occurs in 1-2% of thyroidectomies in experienced hands [1,2]. These cases may be underestimated, as not all patients undergo postoperative laryngeal evaluation.

Injury to the recurrent laryngeal nerve (RLN) can yield vocal fold paresis or paralysis. The implementation of nerve monitoring has not been proven to lower this risk, but may provide prognostic value [3]. Studies showed that identifying the RLN is associated with lower rates of injury.

During surgery, a few anatomic landmarks can assist in identification of the nerves. The Tubercle of Zuckerkandl marks the posterolateral aspect of the thyroid lobe and is most often found lateral to the recurrent laryngeal nerve. The tubercle can be found in 80% of thyroids and when found can lead directly to the recurrent laryngeal nerve, as 93% of the nerves are found medial to this tubercle [3,4]. Most often, the nerve is found in a groove between the tubercle and the lobe of the thyroid gland [5].

Both the left and right nerve follow closely with the course of the inferior thyroid artery, and this landmark can also help identify the nerve. Veyseller *et al.*; compared identifying the nerve from a superior-to-inferior approach (from its insertion into the larynx) to an inferior-to-superior approach (identification at the inferior pole) and found a lower rate of hypoparathyroidism using the superior-to-inferior approach for identifying the RLN. However, while this was a prospective trial, it was not randomized and could be confounded by both surgeon preference, experience and the indication for the thyroidectomy [6].

Many variations of the anatomic relationship between the artery and the nerves exist. Additionally, Berry's ligament can be used for identification, since the nerves are found in close proximity to the ligament; however, the literature describes various anatomic relationships between the two structures [6].

Berlin described the nerve penetrating the ligament in 25% of cases; however, a recent study by Sasou *et al.*; described 24 cases showing the nerve travelling posteriorly and dorsally to the ligament [7]. The inferior thyroid artery can also be used as a landmark for the RLN, with its close association with the pathway of the nerve. Again variations exist, and the branches of the inferior thyroid artery can be anterior or posterior to the nerve, or the nerve can run in between the branches of the artery.

Once the nerve is identified anatomically, its identity and integrity may be confirmed with nerve stimulation. A threshold value may be obtained to determine the minimum current necessary to stimulate the nerve. The course of the nerve should be bluntly dissected using the Reinhoff or a right angle clamp. A sufficient portion of the nerve should be dissected to ensure its safety during dissection and removal of the thyroid gland. Of note, too extensive of a dissection of the nerve can increase the risk of neurapraxia or injury to the nerve.

#### **Identifying Para-thyroid gland:**

Reported rates of transient hypocalcaemia vary in the literature from between 5-50%, but the rate of permanent hypocalcaemia secondary to hypoparathyroidism (i.e., lasting more than 6 months) is between 0.5-2percent. The pathophysiology behind

transient hypoparathyroidism and hypocalcaemia is not well understood but is thought to be related to a transient ischemia to the parathyroid glands or perhaps an increased release of the acute phase reactant endothelin 1[8]. Patients who are at increased risk for this complication are those with Graves' disease or malignancy or those undergoing total thyroidectomy, or total thyroidectomy with central compartment neck dissection.

Once the dissection of the posterior aspect of the thyroid lobe begins, the surgeon and assistants should be vigilant in identifying the parathyroid glands. The superior parathyroid gland can often be found cephalic to the tubercle of Zuckerkandl and can also be found adjacent to the superior pole. The inferior parathyroid gland is usually located in a 1 cm radius around the inferior pole of the thyroid gland and almost always anterior to the plane of the recurrent laryngeal nerve. Of note, 3-7% of patients may have supernumerary glands [9]. After identifying the glands, they should be carefully dissected from the thyroid and left in the thyroid bed.

#### **Relation between post-thyroidectomy hypocalcaemia and RLN identification:**

In 2008, the Journal of Zhejiang University Science was published an article titled with "Total thyroidectomy is safer with identification of recurrent laryngeal nerve". It discussed the importance of RLN as the main issue for the article and also noticed the relation and the effect of that technique on post-operative hypofunction of the parathyroid glands.

They compared the major complications of thyroidectomies in two groups by identifying and not identifying RLN. The results showed that the delicate surgical technique identifying and exposing the whole course and branches of the RLN during total thyroidectomy increased the rate of temporary hypocalcaemia and parathyroid gland auto transplantation, but decreased the rate of total permanent major postoperative complications and prevented RLN injury [10].

Another study published on August 15, 2011, by 'American Medical Association', the article titled with "Effect of recurrent laryngeal nerve identification technique in thyroidectomy on recurrent laryngeal Nerve paralysis and hypo-para thyroidism". Patients were allocated into two groups according to the thyroidectomy technique used to identify the RLN: (1) superior-inferior direction, exploring the nerve where it enters the larynx, followed by superior pedicle ligation; and (2) inferior-superior direction, following the inferior pedicle ligation and identifying the nerve in the tracheoesophageal groove. The first and second groups included 67 and 128 patients, respectively. In the first group, 19 patients underwent lobectomy, and 48 underwent total thyroidectomy. In the second group, 42

patients underwent lobo-isthmectomy, and 86 underwent total thyroidectomy. They performed 115 and 214 RLN dissections in the first and second groups, respectively. Comparing the two groups based on the frequencies of RLN paralysis and hypo-pa thyroidism, they found that complications were significantly lower in the first group ( $P_{.05}$ ) in terms of hypoparathyroidism. The rate of hypo-pa thyroidism was significantly lower in the thyroidectomies that located the RLN using the superior-inferior approach, so the superior-inferior approach was a safer technique, in terms of avoiding complications [11].

#### **Role of PTH in prediction of post-thyroidectomy hypocalcaemia:**

A study discussing the evidence for the role of perioperative PTH measurement after total thyroidectomy as a predictor of hypocalcaemia was published in 2008 in the World Journal of Surgery. It concluded that Postoperative PTH can be used to stratify the risk of patients developing hypocalcaemia after thyroidectomy. In addition, the routine use of oral calcium supplements can lead to decreased incidence and severity of post-thyroidectomy hypocalcaemia. Protocols based on PTH and the routine use of oral calcium supplements can lead to improved patient outcomes after thyroidectomy [12].

#### **Patients and Methods**

##### **Study design:**

It's a prospective descriptive hospital base study, done on patients who underwent total thyroidectomy in the Military hospital (Omdurman), from Sep\2014 to July\2015

##### **Study area:**

The study conducted at the Military Hospital (Omdurman).It's a teaching hospital, with a capacity of 800 beds and an accident and emergency hospital.

**Study duration:** Prospective: from Sep\ 2014 to July\ 2015.

**Study population** All patients underwent total thyroidectomy at our unit in the Military Hospital within the study duration.

**Sample size:** The size will be bound by the study duration.

**Inclusion criteria:** All adult patients with thyroid enlargement who underwent total thyroidectomy

**Exclusion criteria:** No exclusion criteria.

**Sampling:** Non probability sampling.

**Data collection tools:** A predesigned and pretested questionnaire.

#### **Data variables:**

Variables include; gender, age, presenting history, associated illness, operator, technique and procedure, post-operative complication, follow up and compliance of the patient

#### **PROCEDURE:**

Patients, who planned to undergo total thyroidectomy, were selected from the general surgical lists of our units. Total thyroidectomy was performed for all of the patients. RLN identification, ITA ligation and numbers of parathyroid gland seen were the targets during surgery, however, some patients didn't subject to these techniques. Samples for serum calcium were collected after thyroidectomy at different times within the first 72 hours. We identified the hypocalcemic patients, gave them treatment in the form of calcium supplements and vitamin D and followed them till normalization of calcium level. For the PTH assay, we collected blood samples from the patients after intubation and before starting the surgery, and we called them T- zero (T0) samples. Other samples were picked up after ten minutes from the surgery and we called them T-ten (T10) samples. Change value was obtained from the PTH samples and we defined it as the difference between T0 and T10. We identified any drop from T0 to T10 in the PTH and we called it significant drop when it was more than 50%. All the samples were sent to the central laboratory of the hospital and all were tested by the head of department of chemistry.

#### **Data analysis:**

Data analyzed using computer program statistical package of social sciences (SPSS) version 20. Frequencies, descriptive statistic and tests of significance Chi square, t test will be used when appropriate. The P value will be considered significant if  $\leq 0.05$ .

#### **Ethical consideration:**

- Verbal consent was obtained from patients after explanation of the study, its nature and the confidential keeping of data.
- Ethical clearance was obtained from the Ethical clearance committee of Sudan Medical Specialization Board, Ethical Clearance Committee.
- Approval of the hospital administration.

#### **RESULTS**

Seventy two consecutive patients underwent total thyroidectomy for benign goiters were studied and analyzed for post-operative hypocalcaemia. The majority of patients were females (83.3%), with male to female ratio of (1:5). The mean age + SD were  $48 \pm 12$  years.

All the 72 patients had a normal serum calcium and serum albumin before the surgery and all of them underwent total thyroidectomy. Post thyroidectomy

hypocalcaemia (< 8mg/dl) with in the first 72 hours was found in 18 (25%) patients, nine (50%) of them were symptomatic.

The majority of hypocalcemic patients were females (88.9%), with female to male ratio (8:1) (p-value= 0.227). The mean age +SD were 46 ± 15 years and 62.6% were above 40 years (p-value= 0.568). The mean duration + SD of goiter was 6 ± 4.7 years with maximum duration of 20 years, compared to 7.8 ± 7.3 years with maximum duration of 40 years for the non-hypocalcemic patients (p-value=0.664).

From the seven patients under the study with toxic goiters, three patients developed hypocalcaemia (p-value=0.047), while there were two out of three patients (p-value=0.233) with recurrent goiter (p and only 13 from the total 62 patients with SMG (p – value=0.122).

The recurrent laryngeal nerve (RLN) identified and preserved using the anatomical inferior-superior technique at both side of the gland in 65 (90.3%) patients, thirteen (20.0%) of them developed hypocalcaemia. It was not identified or identified at one side in seven (9.7%) patients; five of them developed hypocalcaemia (p-value= 0.211). (Table 1)

The inferior thyroid artery (ITA) ligated and cut near the thyroid capsule in 66 (91.7%) patients, 13 (19.7%) developed hypocalcaemia. It was not identified or cut in six (8.3%) patients, three of them developed hypocalcaemia (p- value= 0.051). (Table 2)

During surgery, the four parathyroid glands were seen and preserved in 57 (79.2%) patients, 13

(22.8%) of them developed hypocalcaemia. Identification of less than four glands was noticed in 11 patients. The parathyroid glands were not seen or looked for in four patients, all of them developed hypocalcaemia (p-value= 0.712).

PTH before surgery (time zero), was found to be normal (zero - 65ng/l) in 47 (65.2%) patients. It was > 65ng/l in 25 (34.7%) patients. Vitamin D deficiency (25OHD < 30ng/ml) and insufficiency (25OHD < 20ng/ml) were noticed in five random samples taken from this group. After ten minutes of the removal of thyroid gland, PTH was found to be normal in 58(80.6%) patients and > 65ng/l in14 (19.4%).

In general the PTH decreased form time zero (T0) to ten minutes after surgery (T10) in 63 (87.5%) patients. It was increased or not changed in nine (12.5%) patients. We called this change in PTH level from T0to T10 as the ' Change value'. This change value reached maximum of 124 and minimum of -36.

All of the18 hypocalcemic patients had significant drop of more than 50% in the PTH(p-value= 0.013). (Table 3) Of the 18 hypocalcemic patients, nine were symptomatic; one of them required hospitalization for more than three weeks. Vitamin D and Calcium supplemented for all of them with 12 patients took ≤ 2gram/day calcium carbonate, and the rest took more than 2gram reaching up to 4gram/day. Two patients had 0.5mcg/day of vitamin D and the rest 0.25mcg/day. Fourteen from the hypocalcemic patients returned to normal serum calcium, nine of them within 4 weeks, while five required > one month.

**Table 1: RLN identification and post-thyroidectomy hypocalcaemia**

RLN Identification	Frequency	Hypocalcaemia	Symptomatic
Both side	65	13	6
One side or no side	7	5	3
Total	54	18	9

P –value 0.211

**Table 2: ligation and cut of the ITA and post-thyroidectomy hypocalcaemia;**

Yes\No	Frequency	Hypocalcaemia	Symptomatic
Ligation with cut	66	13	6
No ligation or cut	6	3	3

P-value 0.051

**Table 3: PTH reduction (change value) more than 50% and post-thyroidectomy hypocalcaemia:**

	Frequency	Hypocalcaemia	Symptomatic
Change value >50%	27	18	9
Change value <50%	45	0	0
Total	72	9	9

P-value 0.013

## DISCUSSION

### **Incidence of hypocalcaemia post-thyroidectomy:**

Reported rates of transient hypocalcaemia vary in the literature between 5-50%, but the rate of permanent hypocalcaemia (i.e. lasting more than 6 months) is between 0.5-2% [13]. In our study we reported 18 (25%) patients who developed post thyroidectomy hypocalcaemia.

Comparing with other studies, there is no marked difference. On June/2003, an article published in the Archives of surgery talked about intraoperative PTH assay as a predictor of postoperative hypocalcaemia. From 30 patients who underwent total thyroidectomy, ten (33.3%) had post-operative hypocalcaemia [13]. Another similar article done by a Chinese group, in 2010, reported 85 (51%) from 165 patients [14]. In 2014, Pakistani an group studied 99 patients who underwent bilateral thyroidectomy, 47 of them (47.5%) developed hypocalcaemia [15]. Also in 2014, the Canadian journal of surgery published an article on the same issue reported 38 of 149(25.7%) patients developed post-thyroidectomy hypocalcaemia [16].

As our study, all the above articles aimed to detect post-thyroidectomy hypocalcemia earlier and thereby giving treatment, rather than to follow and differentiate temporal from permanent hypocalcemia

### **RLN and post-thyroidectomy hypocalcaemia:**

Recent studies recommended that, on doing total thyroidectomy, identification of the RLN is mandatory to avoid its injury [9]. That was an issue carried by a group of surgeons produced an article titled with "total thyroidectomy is safer with identification of recurrent laryngeal nerve". The results of this study showed that delicate surgical technique identifying and exposing the whole course and branches of the RLN during total thyroidectomy increased the rate of temporary hypocalcaemia and parathyroid gland auto transplantation, but decreased the rate of total permanent major postoperative complications and prevented RLN injury [9]. In 2011 the American medical association, titled an article with "effect of recurrent laryngeal nerve identification technique in thyroidectomy on recurrent laryngeal nerve paralysis and hypo-para thyroidism". Patients were allocated into 2 groups according to the thyroidectomy technique used to identify the RLN: (1) superior-inferior direction, exploring the nerve where it enters the larynx, followed by superior pedicle ligation; and (2) inferior-superior direction, following the inferior pedicle ligation and identifying the nerve in the tracheoesophageal groove. The first and second groups included 67 and 128 patients, respectively. In the first group, 19 patients underwent lobo-isthmectomy, and 48 underwent total thyroidectomy. In the second group, 42 patients underwent lobo-isthmectomy, and 86 underwent total thyroidectomy. They performed 115 and 214 RLN

dissections in the first and second groups, respectively. Comparing the 2 groups based on the frequencies of RLN paralysis and hypoparathyroidism, they found that complications were significantly lower in the first group ( $P_{.05}$ ) in terms of hypoparathyroidism. The rate of hypoparathyroidism was significantly lower in the thyroidectomies that located the RLN using the superior-inferior approach. on other hands, the superior-inferior approach was a safer technique, in terms of avoiding complications [13]. They concluded that there is a significant effect of the recurrent laryngeal nerve identification technique on post thyroidectomy hypoparathyroidism [13].

In our study, however, that was different. The RLN was identified and preserved in 65 patients, all with inferior-superior technique and only 13 of them developed hypocalcemia. It was not identified in seven patients, five of them developed hypocalcemia. These results may reduce the significance of the effect of RLN identification on post thyroidectomy hypocalcemia ( $P$  value 0.211).

In fact, this technique required identifications  $\pm$  ligation of the ITA; this could be truncal or individual branch ligation. Some authors considered the ligation of ITA as major factor for the post-thyroidectomy hypocalcaemia [17], while others denied any relation between the two items [18,19]. In our study 66 (91.7%) patients had their ITA ligated and cut from the individual branches near the thyroid capsule, 13 (19.7%) of them had post-thyroidectomy hypocalcemia, while there were 50% from the patients who did not subject to this procedure were had hypocalcemia ( $P$  value is 0.051). So it was safer to identify, ligate then cut the artery near the thyroid capsule, than to do blind over-sewing to achieve hemostasis (blind over-sewing may increase the risk of ligation of individual branches to parathyroid gland and thereby ischemia and post-surgery hypocalcemia).

No significant relation was noticed between the numbers of parathyroid glands found during surgery and the effect on hypocalcaemia then. Thirteen patients, who suffered hypocalcaemia after surgery, had their four glands found during surgeries ( $P$  value is 0.900).

### **Other factors predicting post-thyroidectomy hypocalcaemia:**

Age ( $> 50$ years), diagnosis (toxic goiter or recurrent goiter), thyroid weight, thyrotropin level, and the number of preserved parathyroid glands, all were reported before as a negative predictor and effector in development of symptomatic hypocalcaemia [15]. However, some authors suggest that an age  $>50$  years, total thyroidectomy, reoperation, neck dissection and operative time, were have an impact on the development of post-thyroidectomy hypocalcaemia [21].

In our study, we suggested some factors, in order to test as far their sensitivity to predict and thereby effect on incidence of post-thyroidectomy hypocalcaemia. From 72 patients, females represented 60 patients (83.3%), 16(22.2%) of them developed hypocalcaemia, while of the 12 males under the study there were two (16.6%). But the significant of this 16% in male might not be related to gender factor, when we noticed that one of the two patients had retrosternal extension on presentation and the other was above 80 years (i.e. so another predicting factors shared the cause of hypocalcaemia). According to our results, the age in particular didn't have a great effect on prediction of hypocalcemia. From the 18 hypocalcemic patients, eight were above 45 years and 10 were below. There was no considerable difference between the two groups.

Pressure symptoms were not an issue for developing post-thyroidectomy hypocalcaemia. Signs of retrosternal extension on imaging appeared in two patients one of them developed hypocalcaemia. A research done in 2006 by an Australian group of endocrine surgeons, studied 199 patients with retrosternal extension goiters. They found a postoperative morbidity of 30%, the majority being asymptomatic temporary hypocalcaemia [21], suggesting an appreciable association with retrosternal extension.

Clinical and histological diagnosis also had a considerable effect on post-thyroidectomy hypocalcaemia in some studies. An American group did a study in 2010 concluded that patients with Graves' disease are more likely to require increased dosages of calcium as well as experience tetany postoperatively than patients undergoing total thyroidectomy for other indications. This suggests that patients operated upon for Graves' disease warrant close follow-up as both inpatients and outpatients for signs and symptoms of hypocalcaemia [22]. In our study, the only patient who came with Graves' disease, underwent total thyroidectomy and developed post-thyroidectomy hypocalcaemia with no other suggested factors to affect the outcome of hypocalcaemia. From the seven patients of our group with control toxic goiters, three developed hypocalcaemia, the thing which supported the known relation between toxicity and hypocalcaemia post-surgery, (P value is 0.047). In fact sever symptomatic hypocalcemia after thyroidectomy was reported before as Hunger bone syndrome (HBS) and it was specifically for patients who were had Grave's disease [23]. In these patients there is pre-operative bone disease due to high bone turn-over induced by excess thyroid hormone. A Recurrent goiter also played a significant role when we noticed that from the three patients with recurrent goiter, two of them developed hypocalcaemia.

Surgeries were done by senior doctors in 53% of the hypocalcemic group, while 47% were done by junior surgeons. Lack of relation between surgeon's

experience in thyroid surgery and post-thyroidectomy hypocalcemia was noted in our study.

However, an Italian surgeons performed a study in 2006 described the effect of resection extension, surgical technique and thyroid pathology on post-operative hypo-para thyroidism [24]. They actually proved the importance of surgeon's experience and their technique on the percentage of post-thyroidectomy hypocalcemia

#### **Role of peri-operative Parathyroid hormone:**

Many studies talked about the PTH hormonal assay and its strong relation in the prediction of post thyroidectomy hypocalcaemia. Most the studies agreed that PTH should be measured peri-operatively and should be used as a predictor for calcium level post-thyroidectomy. The issues were when the actual time of sampling and how far the sensitivity will be in detecting hypocalcaemia earlier post-thyroidectomy?

In 2012, a study from Bangladesh suggested a sensitivity of 84% when the sample taken within 20 minutes after removal of the thyroid gland [25]. Another group in 2014 suggested a serial of PTH sampling starting from one, six and 24 hours intervals post removal of the gland, will carry sensitivity of 89% [15]. More over the sensitivity of PTH assay were found to be affected by the difference between two peri-operative samples rather than the post-operative value alone. That was the conclusion of study done in 2014 [26]. They said that; "measuring PTH levels after 24 hours post thyroidectomy is not reliable factor for predicting hypocalcaemia. Instead, it's more reliable to measure the serum PTH level before and after operation and calculate the reduction value and percentage of drop" [27].

In our study, all samples of PTH were taken at T0 (before surgery and patient on table) and T10 after removal of the gland. From the 72 patients under the study, 63 (87.5%) had a reduction in their PTH from T0 to T10, 27 of them (42.8%) had the reduction of more than 50% (significant reduction). Among this group (27 patients) emerged the 18 patients (66.7%) with hypocalcaemia. The significance of that appeared when we found that the rest 38 patients who had reduction of less than 50% in their PTH, did not have the significant reduction, and thereby didn't included in the hypocalcemic group. In another term, it needed a 'significant reduction value' to express hypocalcaemia after surgery and that assumed to be more than 50% of T0 value (P value is 0.013).

With increasing of the percentage reaching > 60%, symptomatic hypocalcaemia were significantly noticed (P value is 0.059) in nine patients with calcium supplementation reaching > 2gram/day and duration of treatment > two weeks. This raised the suspicious of the

significant effect of this value upon post thyroidectomy hypocalcaemia.

When we tested the sensitivity of the significant reduction value, we found that any patient had hypocalcaemia post-surgery (18 patients); also had a positive reduction value of more than 50%, however not all the patients with more than 50% reduction (27 patients) developed hypocalcaemia. So it was sensitive 100%, but not specific.

Vitamin D deficiency and insufficiency was also suggested to have an impact on post thyroidectomy hypocalcemia. In our data results we noticed 25 patients were had abnormal increase in PTH at T0. Random samples from five of them revealed vitamin D deficiency and insufficiency. If we assumed that all the 25 patients were had vitamin D deficiency, we would find that more than half of the patients who developed hypocalcemia post-surgery were had pre-operative vitamin D deficiency or insufficiency and more than half of them were symptomatic (p-value 0.029). This will be considered as another effective predictor on post-thyroidectomy hypocalcemia.

#### REFERENCES

1. Gourin CG, Tufano RP, Forastiere AA, Koch WM, Pawlik TM, Bristow RE; Volume-based trends in thyroid surgery. *Arch Otolaryngol Head Neck Surg.* 2010; 136(12):1191-8.
2. Stavrikis AI, Ituarte PH, Ko CY, Yeh MW; Surgeon volume as a predictor of outcomes in inpatient and outpatient endocrine surgery. *Surgery.* 2007; 142(6):887-99; discussion 887-99.
3. Donnellan KA, Pitman KT, Cannon CR, Replogle WH, Simmons JD; Intraoperative laryngeal nerve monitoring during thyroidectomy. *Arch Otolaryngol Head Neck Surg.* 2009; 135(12):1196-8.
4. Gauger PG, Delbridge LW, Thompson NW, Crummer P, Reeve TS; Incidence and importance of the tubercle of Zuckerkandl in thyroid surgery. *Eur J Surg.* 2001; 167(4):249-54.
5. Gravante G, Delogu D, Rizzello A, Filingeri V; The Zuckerkandl tubercle. *Am J Surg.* 2007; 193(4):484-5.
6. Yun JS, Lee YS, Jung JJ, Nam KH, Chung WY, Chang HS; The Zuckerkandl's tubercle: a useful anatomical landmark for detecting both the recurrent laryngeal nerve and the superior parathyroid during thyroid surgery. *Endocr J.* 2008; 55(5):925-30.
7. Veyseller B, Aksoy F, Yildirim YS, Karatas A, Ozturan O; Effect of recurrent laryngeal nerve identification technique in thyroidectomy on recurrent laryngeal nerve paralysis and hypoparathyroidism. *Arch Otolaryngol Head Neck Surg.* 2011; 137(9):897-900.  
Leow CK, Webb AJ; The lateral thyroid ligament of Berry. *Int Surg.* 1998;83(1):75-
8. Sasou S, Nakamura S, Kurihara H; Suspensory ligament of Berry: its relationship to recurrent laryngeal nerve and anatomic examination of 24 autopsies. *Head Neck.* 1998; 20(8):695-8.
9. Nomura K, Yamashita J, Ogawa M; Endothelin-1 is involved in the transient hypoparathyroidism seen in patients undergoing thyroid surgery. *J Endocrinol.* 1994; 143(2):343-51.
10. Eisele DW; Intraoperative electro physiologic monitoring of the recurrent laryngeal nerve. *Laryngoscope.* 1996; 106(4):443-9.
11. Hakan Canbaz, Musa Dirlik, Tahsin Colak, Koray Ocal, Tamer Akca, Oner Bilgin et al.; total thyroidectomy is safer with identification of recurrent laryngeal nerve. *J Zhejiang UnivSci B.* 2008; 9(6): 482-488.
12. Bayram Veyseller, Fadlullah Aksoy, Yavuz Selim Y, Abdullah Karataş, Orhan Ozturan; Effect of Recurrent Laryngeal Nerve Identification Technique in Thyroidectomy on Recurrent Laryngeal Nerve Paralysis and Hypoparathyroidism. *Arch Otolaryngol Head Neck Surg.* 2011; 137(9):897-900.
13. Simon Grodski, Jonathan Serpell; Evidence for the Role of Perioperative PTH Measurement after Total Thyroidectomy as a Predictor of Hypocalcemia. *World Journal of Surgery.* 2008; 32(7):1367-1373.
14. Laurie Barclay; Intraoperative PTH Assay Predicts Hypocalcemia after Thyroidectomy, *Arch Surg.* 2003; 138:632-636.16.
15. An CM, Tang PZ, Xu ZG, Zhang B, Zhang ZM, Yan DG, et al.; Role of parathyroid hormone measurement in prediction for symptomatic hypocalcaemia after total thyroidectomy. *Zhonghua Er Bi Yan HouTou Jing Wai KeZaZhi.* 2010; 45(3):217-21
16. Mehrvarz S, Mohebbi HA, Kalantar Motamedi MH, Khatami SM, Rezaie R, Rasouli HR; Parathyroid hormone measurement in prediction of hypocalcaemia following thyroidectomy. *J Coll Physicians Surg Pak.* 2014; 24(2):82-7
17. AlQahtani A; Parsyan A; Payne R; Tabah R; Parathyroid hormone levels 1 hour after thyroidectomy: an early predictor of postoperative hypocalcemia. *Can J Surg.* 2014; 57(4):237-40
18. Antakia R, Edefe O, Uttley L; Balasubramanian SP. Effectiveness of preventative and other surgical measures on hypocalcemia following bilateral thyroid surgery: a systematic review and meta-analysis. *Thyroid.* 2015; 25(1):95-106
19. Maralcan G, Sayin Z, Başkonu I, Gökalp A, Aybasti N; Does truncal ligation of the inferior thyroid arteries during bilateral subtotal thyroidectomy affect serum calcium levels? A prospective, randomized, controlled study. *Int Surg.* 2006; 91(4):211-6
20. Chaudhary IA, Afridi ZD, Samiullah, Masood R, Mallhi AA; To ligate or not the inferior thyroid artery to avoid hypocalcaemia after thyroid

- surgery. J Ayub Med Coll Abbottabad. 2007; 19(2):19-22
21. Sousa Ade A, Salles JM, Soares JM, Moraes GM, Carvalho JR, Savassi-Rocha PR; Predictors factors for post-thyroidectomy hypocalcaemia. Rev Col Bras Cir. 2012; 39(6):476-82
  22. Chauhan A; Serpell JW; Breast, Endocrine and Surgical Oncology Unit, Frankston Hospital, Melbourne, Victoria, Australia. Thyroidectomy is safe and effective for retrosternal goiter. ANZ J Surg. 2006; 76(4):238-42
  23. Pesce CE, Shiue Z, Tsai HL, Umbricht CB, Tufano RP, Dackiw AP, et al.; Department of Surgery, The Johns Hopkins University School of Medicine, Baltimore, Maryland 21287, USA. Postoperative hypocalcemia after thyroidectomy for Graves' disease. Thyroid. 2010; 20(11):1279-83
  24. Jeena Mary Varghese, Absalon Dennis Gutierrez, Jamie Olejarski, Philip R Orlander; Disorders of Parathyroid Hormone & Calcium Homeostasis Translational. Orals, Featured Poster Presentations, and Posters. 2013
  25. Sciumè C, Geraci G, Pisello F, Facella T, Li Volsi F, Licata A, et al.; Complications in thyroid surgery: symptomatic post-operative hypoparathyroidism incidence, surgical technique, and treatment. Ann ItalChir. 2006; 77(2):115-22
  26. Islam MS, Sultana T, Paul D, Huq AH, Chowdhury AA, Ferdous C, et al.; Intraoperative serum parathyroid hormone level is an indicator of hypocalcaemia in total thyroidectomy patients. Bangladesh Med Res Counc Bull. 2012; 38(3):84-9
  27. Mehrvarz S, Mohebbi HA, Kalantar Motamedi MH, Khatami SM, Rezaie R, Rasouli HR; Parathyroid hormone measurement in prediction of hypocalcaemia following thyroidectomy. J Coll Physicians Surg Pak. 2014; 24(2):82-7