Post-Thyroidectomy Hypocalcaemia: Truncal Versus Branch Ligation of Inferior Thyroid Artery

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Abstract

Background: Post-thyroidectomy hypoparathyroidism is a common complication of thyroid surgery, characterized by low Parathyroid hormone (PTH) levels, which increases treatment costs and hospital stays.

Objectives: This study aimed to compare the effects of truncal and branch ligation of inferior thyroid arteries (ITA) near the thyroid capsule on serum calcium and PTH levels after surgery.

Patients and methods: This was a prospective clinical randomization trial conducted on 100 multi-nodular goiter patients underwent thyroidectomy, 34 were males and 66 were females. The assessments of PTH and Ca. levels were done on the 1st, 3rd day and 30th days post-thyroidectomy.

Results: There was no significant difference between the two groups Regarding age, sex, residence. The main trunk ITA ligation group showed a significant increase in the need for replacement with calcium and vitamin D, as well as a decrease in Ca and PTH at the first and second assessments compared to pre-operative results. However, there was no significant difference between the pre-operative and third assessments regarding Ca level and PTH. The selective branch ITA ligation group showed a significant decrease in PTH at the second assessment but insignificant-decrease in Ca level.

Conclusion: Ligation of the inferior thyroid artery (ITA) reduces the likelihood of postoperative hypocalcemia compared to trunk ligation. However, it was limited to the immediate postoperative period, as outcomes were similar in subsequent days.

Keywords: Post-thyroidectomy; Hypocalcemia; Truncal ligation; Branch ligation.

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Introduction

Thyroidectomy is a surgical procedure that involves the removal of the thyroid gland, and it poses a significant risk of postoperative hypoparathyroidism. Hypoparathyroidism is characterized by low intact parathormone (PTH) and hypocalcaemia, which can be either temporary or persistent **(Maralcan et al., 2010; Mattoo and Agarwal, 2019).** Several factors were accused, including devascularization, ischemia, venous congestion, accidental parathyroid removal, and insufficient surgical competence **(Dionigi et al., 2008; Jin et al., 2013; Mattoo and Agarwal, 2019).**

Patients who undergo total thyroidectomy, central neck dissection, or substernal goiters are more likely to experience hypoparathyroidism **(Abou-Amra and Abdel-Rahman, 2011; Eismontas et al., 2018).**

Hypocalcemia is a reliable indicator of hypoparathyroidism after thyroidectomy, and it affects patients' quality of life while also increasing hospital fees and stays. The incidence of postoperative hypocalcemia varies from 6% to 55% across studies **(Abou-Amra and Abdel-Rahman, 2011; Mattoo and Agarwal, 2019).** Several methods have been attempted to alleviate hypocalcemia, including surgical techniques that safeguard the blood supply of the glands **(Eismontas et al., 2018; Shen, 2013).**

To avoid main ITA truncal ligation and postoperative hypocalcemia, some researchers recommend forcing the closure of secondary and tertiary ITA branches medial to the gland. This approach did not reduce patient hypocalcemia, according to previous research **(Abou-Amra and Abdel-Rahman, 2011; Shen et al., 2013).**

Previous studies showed different findings, **Romano et al., (2016)** compared ~~between~~ ITA truncal and branch ligation and reported insignificant difference between both groups. In contrast studies by **Waseem et al., (2021)** and **Cocchiara et al., (2010)** found that truncal ligation is associated with post-thyroidectomy hypocalcemia.

This study aimed to compare the effect of truncal ITA ligation versus branch ligation on the post-thyroidectomy follow-up serum calcium and PTH levels.

Patients and methods

This was a prospective trial conducted on 100 subjects from Qena University Hospital – General Surgery Department from April 2022 to February 2023.

Inclusion criteria: All patients presented by multi-nodular goiter.

Exclusion criteria: History of neck surgery or irradiation, malignancy, and toxic goiter.

Randomization and allocation

The study population was randomized using a cmputer-generated randomization system into two groups by a 1:1 ratio:

Group (1) (Main Trunk Group) Included 50 patients underwent ITA truncal ligation.

Group (2) (Selective Branch Group) Included 50 patients underwent ITA branch ligation.

Before being exposed to the operation, every patient provided their informed consent. All cases were subjected to complete history taking, physical examination, general examination, and local neck examination.

All patients were subjected to laboratory investigations including: CBC, Coagulation profile, and Calcium level.

For blood sampling, six millilitres of venous blood were obtained, divided into 2 ml for the CBC,

2 ml for the coagulation profile, and 2 ml for serum separation for calcium and PTH levels.

Calcium level detection: using ARCHITECT c4000 clinical chemistry analyzer (Abbott, Chicago, Illinois, United States). The blood sample was collected in a sterile, dry tube and left to clot for at least 30 minutes at room temperature. The sample was then centrifuged at 3500 rounds per minute for 10min and serum was used for calcium level measurement. Calcium normal reference range: 8.5-10.5 mg/dL.

PTH examination: ELISA was used to estimate PTH concentration. We used Human BioActive PTH 1-84 ELISA kit (LSBio, Seattle, Washington, USA). PTH normal reference range: 10 to 69 pg/mL.

Hypocalcemia is defined as a serum calcium concentration below the normal range of 8.5-10.5 mg/dL and clinical hypocalcemia is present when patient had symptoms such as muscle cramps, tingling, fatigue, and confusion **(Mehanna et al., 2010).** Furthermore, hypocalcemia refers to a transient decrease in calcium levels in the blood that is typically reversible and can be caused by factors such as medication or low magnesium levels. whereas hypocalcemia, is usually due to a chronic medical condition that affects the body's ability to maintain calcium levels, such as hypoparathyroidism **(Seo et al., 2015)**

The diagnostic criterion for transient postoperative hypocalcemia was a calcium level of 8 mg/dl. It was recommended to monitor the clinical symptoms of hypocalcemia as well. In this study, low levels of parathyroid hormone were defined as hormone level below the reference range (10 to 69 pg/mL).

Surgical procedure

- All operations followed the standard protocol for administering general anesthesia. A typical complete thyroidectomy was performed on all patients with a collar incision measuring between 30 and 50 millimeters in length, two centimeters above the sternal notch. We followed **Waseem et al. (2021)** general descriptions in our study.
- For each patient, skin incision and upper and lower flaps elevated as shown in **(Fig.1),** complete bilateral extracapsular thyroidectomies were performed as part of the procedure. To treat the upper pedicle, the upper thyroid pole was moved laterally, and the inter-cricothyroidal gap was explored. This was done to ensure that no damage was done to any nerves that were located further down. It was necessary to individually ligate the branches of the superior thyroid artery at the lowest possible level.

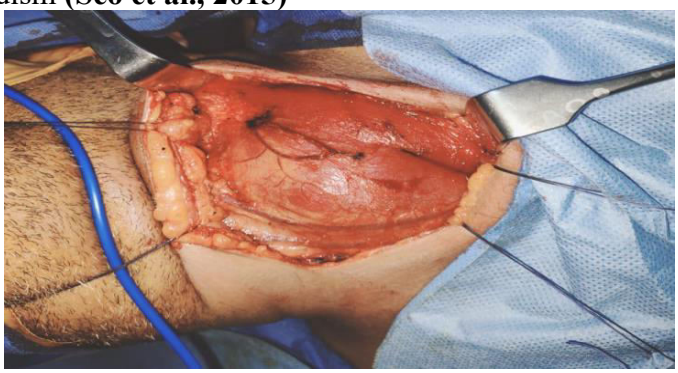

Fig. 1: Elevation of upper and lower flaps

- In the main ITA trunk ligation group we follwo **Maralcan et al. (2006)** procedure, the truncal ITA was identified and ligated before looking for the artery **(Figs 2, 3)**, but in the Selective Branch group we follow **(Cocchiara et al., 2010)** procedure, the terminal branches of the ITA were ligated separately **(Fig.4).** Both groups underwent the exploration of the artery. If the artery had previously been split into many branches, each of those branches would have been situated medially to the carotids and laterally to the recurrent laryngeal nerves. The artery was located adjacent to the thyroid capsule.

Case 1 (Truncal ITA Ligation Group)

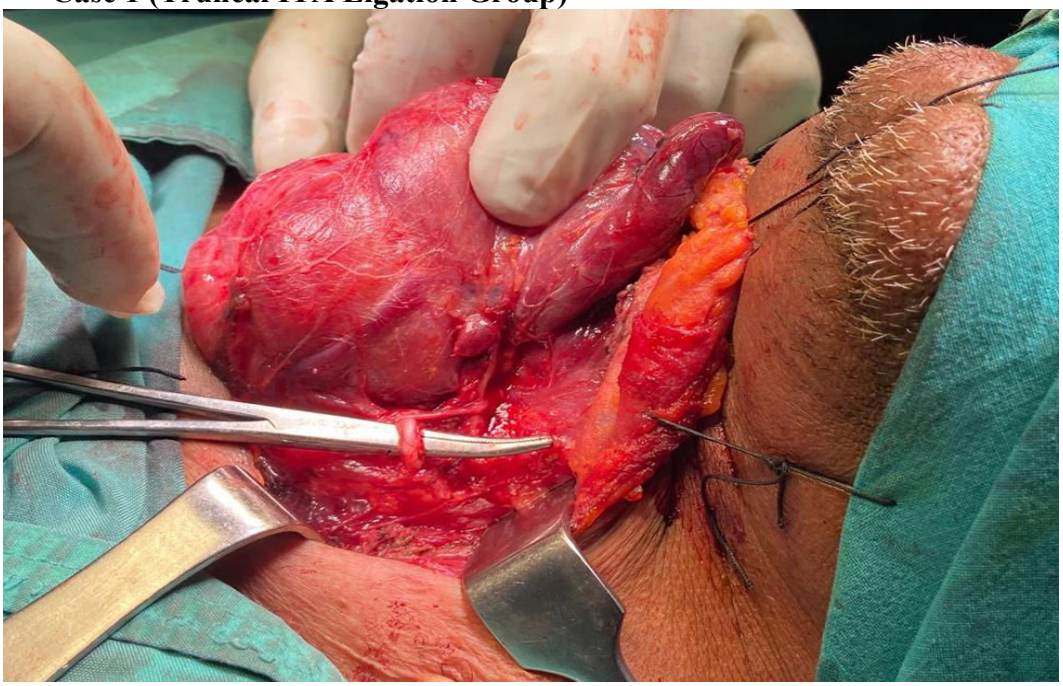

Fig. 2. Identification of the inferior thyroid artery, for main trunk ligation

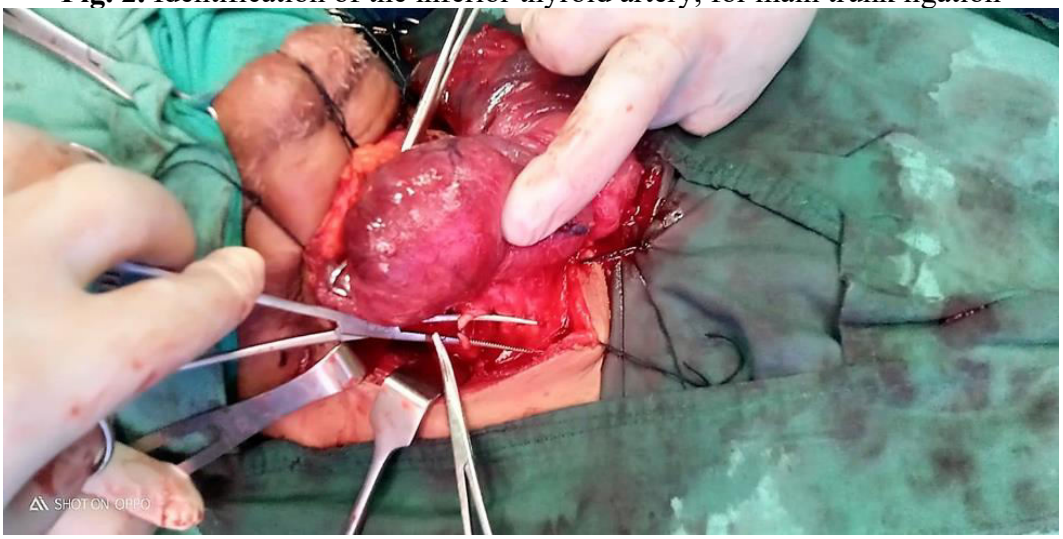

Fig. 3. Ligation in the continuity of the inferior thyroid artery using 2/0 VICRYL (polyglactin) in the main trunk ligation case

Case 2 (Branch ITA Ligation Group)

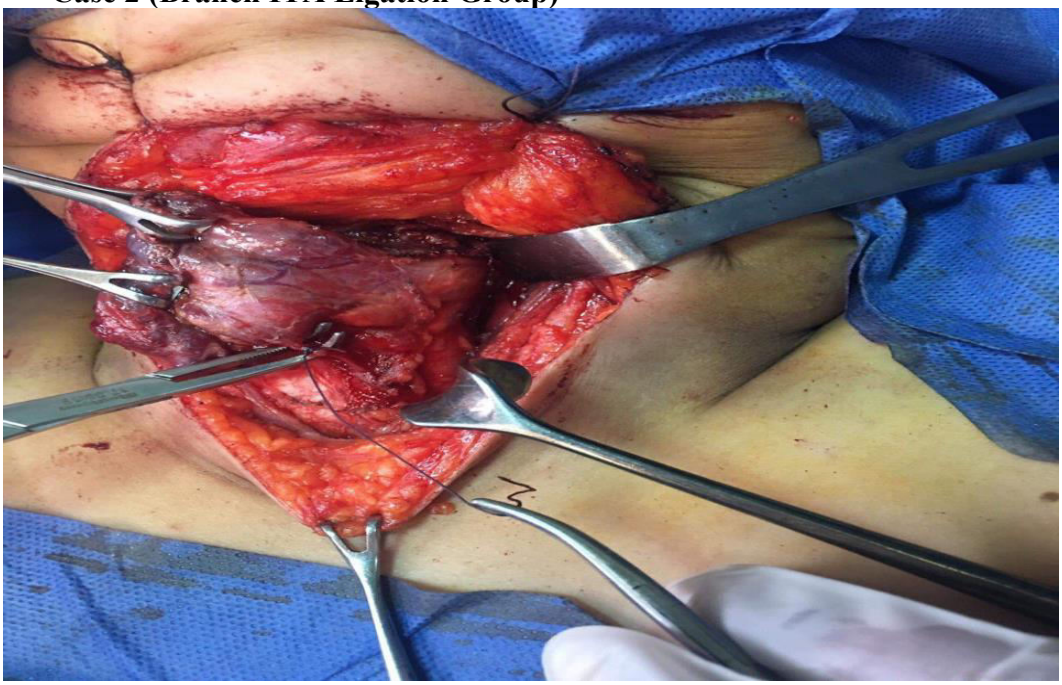

Fig.4. Inferior thyroid artery ligation medial to the parathyroid gland

Fig. 5. Identification of parathyroid gland in the branch ligation group

- By carefully pinpointing the characteristic markers associated with each structure, the superior and inferior laryngeal nerves, plus the inferior and superior parathyroid glands, were successfully identified. The Zuckerkandl's tuberculum and the trachea-oesophageal groove were utilized to find the inferior and superior parathyroid glands on both sides. On the left side, Zuckerkandl's tuberculum was also employed. In addition, the technique was carried out to identify both the inferior and the superior parathyroid glands **(Fig. 5).** At the end of the surgery, we inserted a suction drain **(Fig.6).**

Fig. 6. Closure of the operation wound after removal of the thyroid and insertion of the suction drain.

- The duration of the whole surgical procedure was determined by adding up the intervals that passed between the initial skin incision and the last skin suture.
- **Re-assessments:** Following assessments were done on the 1st day (first assessment) and 3rd day (second assessment) and 30th day (third assessment).
- Ethical committee approval Code: SVU-MED-SUR011-1-22-4-383.

Statistical analysis

We employed version 24 of IBM's SPSS to carry out the statistical study that we needed to (May 2016). Shapiro-Wilk test was used to ensure normal distribution of continuous variable. To determine whether or not there were statistically significant differences between the groups, we employed the t- test for continuous data and chisquare test for categorical data. P-values that were lower than 0.05 were statistically significant.

Results

We studied 100 patients toxic multi-nodular goiter underwent thyroidectomy, 34 were males and 66 were females.(**Table.1**).

Table 1. Demographic data of included subjects in both groups

Variables	Main Trunk (N = 50)	Selective Branch (N = 50)	P-value
Age (Years)	42.32 ± 9.05	40.66 ± 9.01	0.36042[t]
Sex			
• **Male**	18 (36%)	16 (32%)	0.6729 [X]
• **Female**	32 (64%)	34 (68%)	
Residence			
• **Urban**	28 (56%)	25 (50%)	0.5478[X]
• **Rural**	22 (44%)	25 (50%)	
BMI (Kg/m^2)	19.94 ± 1	19.81 ± 1.14	0.53335[t]

BMI: Body Mass Index
t: t-test, X: Chi-Square

Regarding demographic data the mean age in the main trunk group, was 42.32 ± 9.05 years was statistically insignificant compared to the selective branch group 40.66 ± 9.01 years, (p =0.360).

The main trunk group comprised 18 (36%) males and 32 (64%) females, whereas was statistically insignificant compared to the selective branch group which consisted of 16 (32%) males and 34 (68%) females (p=0.673).

The main trunk group had 28 (56%) patients living in urban areas and 22 (44%) patients living in rural areas, which was statistically insignificant when compared to the selective branch group, which had 25 (50%) people living in urban areas and the other 25 (50%) people living in rural areas (P = 0.5478).

The mean body mass index (BMI) in the main trunk group, was 19.94 ± 1 kg/m^2 was statistically insignificant compared to the selective branch group 19.81 ± 1.14 kg/m^2 , (p=0.53335), (**Table.2**).

Table 2. Clinical signs appearance at postoperative follow up

Variables	Main Trunk group (N = 50)	Selective Branch group (N = 50)	P-value
Evaluation after the 2nd assessment			
Clinical Signs appearance	9 (18%)	1 (2%)	0.008*
Exogenous replacement with Ca. and Vit. D	12 (24%)	4 (8%)	0.029*
Hypocalcemia occurence	12 (24%)	4 (8%)	0.029*
Evaluation after the 3rd assessment			
Clinical Signs appearance	0	0	-
Exogenous replacement with Ca. and Vit. D	8 (16%)	2 (4%)	0.046*
Hypocalcemia occurence	8 (16%)	2 (4%)	0.046*

Ca: Calcium | PTH: Parathyroid Hormone; * significant, Chi square test

The main trunk group had a much higher prevalence of hypocalcemia and clinical complaints that require therapy with exogenous calcium and vitamin D after the second assessment. However, after the third assessment, there was no appearance of clinical signs, but significantly more cases in the trunk ligation group required exogenous replacement with calcium and vitamin D **(Table.3).**

Table 3. Main trunk group assessments data during the peroperative and post operative follow up

Variables	Pre-Operative (N = 50)	1st assessment (N = 50)	2nd assessment (N = 50)	3rd assessment (N = 50)	P-value
Ca level (mg/dL)	9.52 ± 0.49	8.98 ± 0.48	8.9 ± 0.48	9.44 ± 0.49	P1: <0.0001* P2: <0.0001* P3: 0.418

PTH (pg/mL)	42.12 ± 9.16	32.56 ± 9.28	31.22 ± 9.21	40.78 ± 9.13	P1: <0.0001* P2: <0.0001* P3: 0.467

Ca: Calcium | PTH: Parathyroid Hormone; *-significant, t-test; P1: Compare 1st post operative assessment results with Pre-Operative,; P2: Compare 2nd post operative assessment results with Pre-Operative,; P3: Compare 3rd post operative assessment results with Pre-Operative.1st assessment (1st day after operation), 2nd assessment (3rd day after operation), 3rd assessment (30th day after operation)

In the main trunk ligation group, there was a significant decrease in Ca level and PTH at the first and second assessments compared to pre-operative results. There was no significant difference between pre-operative and the third assessment regarding Ca level and PTH **(Table.4).**

Table 4. Selective branch group assessments data during the peroperative and post operative follow up

Variables	Pre-Operative (N = 50)	1st assessment (N = 50)	2nd assessment (N = 50)	3rd assessment (N = 50)	P-value
Ca level (mg/dL)	9.41 ± 0.48	9.25 ± 0.48	9.22 ± 0.48	9.32 ± 0.48	P1: 0.102 P2: 0.053* P3: 0.353
PTH (pg/mL)	40.2 ± 10.18	36.84 ± 10.25	35.96 ± 10.14	38.66 ± 10.13	P1: 0.107 P2: 0.042* P3: 0.452

Ca: Calcium | PTH: Parathyroid Hormone; * significant, t-test; P1: Compare 1st post operative assessment results with Pre-Operative, P2: Compare 2nd post operative assessment results with Pre-Operative, P3: Compare 3rd post operative assessment results with Pre-Operative.

When compared to pre-operative data, PTH in the selective branch ligation group significantly decreased at the second examination. At the second assessment, the serum Ca level did not show significant decrease. At the third assessment, there was no significant difference with pre-operative Ca level or PTH **(Table .5).**

Table 5. Comparison between the two groups regarding calcium level through study period

Calcium level (mg/dL)	Main trunk (N = 50)	Selective branch (N = 50)	P- Value
Pre-Operative	9.52 ± 0.49	9.41 ± 0.48	0.26233
1st assessment	8.98 ± 0.48	9.25 ± 0.48	0.00705*
2nd assessment	8.9 ± 0.48	9.22 ± 0.48	0.00164*
3rd assessment	9.44 ± 0.49	9.32 ± 0.48	0.22197

* significant, t-test

Upon evaluating calcium and PTH levels over time in both groups, we found insignificant difference in pre-operative calcium levels (p=0.262). However, the main trunk group exhibited a statistically significant decrease in calcium levels during the first and second assessments (p=0.00705 and p=0.00164, respectively) compared to the selective branch group. By the third assessment, calcium levels did not significantly differ between the groups (p=0.22197) **(Table.6, Fig.7).**

Table 6. Comparison between the two groups regarding PTH hormone level through study period

PTH hormone (pg/mL)	Main trunk (N = 50)	Selective branch (N = 50)	P-Value
Pre-Operative	42.12 ± 9.16	40.2 ± 10.18	0.32637
1st assessment	32.56 ± 9.28	36.84 ± 10.25	0.03341*
2nd assessment	31.22 ± 9.21	35.96 ± 10.14	0.01805*
3rd assessment	40.78 ± 9.13	38.66 ± 10.13	0.27703

* significant, t-test

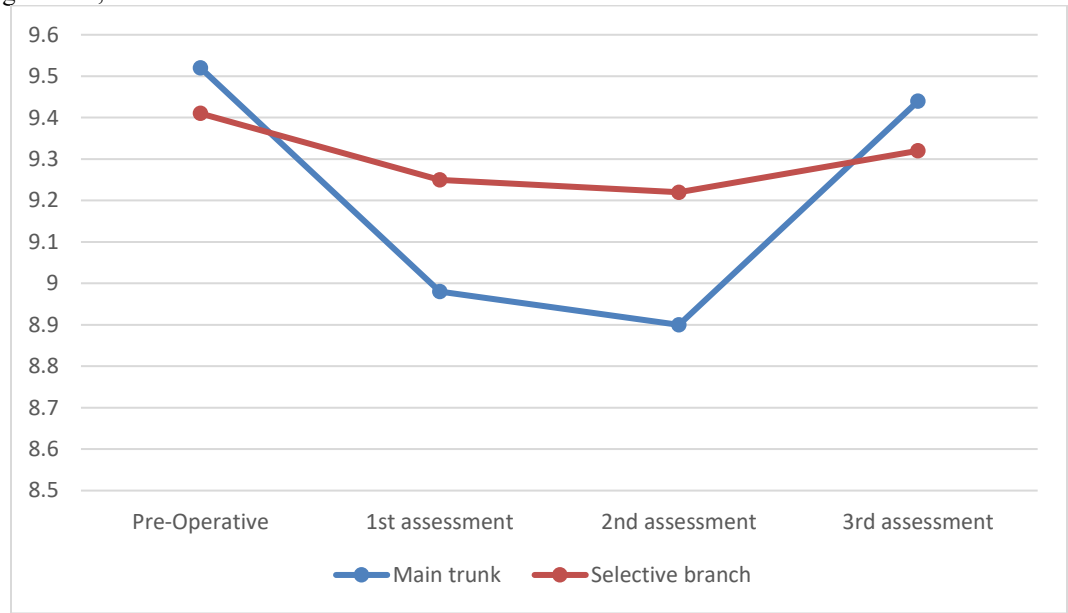

Fig. 7. Mean calcium level (mg/dL) through the study period in both groups

We found no significant difference in pre-operative PTH levels between the groups (p=0.32637). However, the main trunk group displayed a statistically significant decrease in PTH levels during the first and second assessments (p=0.03341 and p=0.01805, respectively) compared to the selective branch group. PTH levels did not significantly differ between the groups during the third assessment (p=0.27703) **(Table 6, Fig.8).**

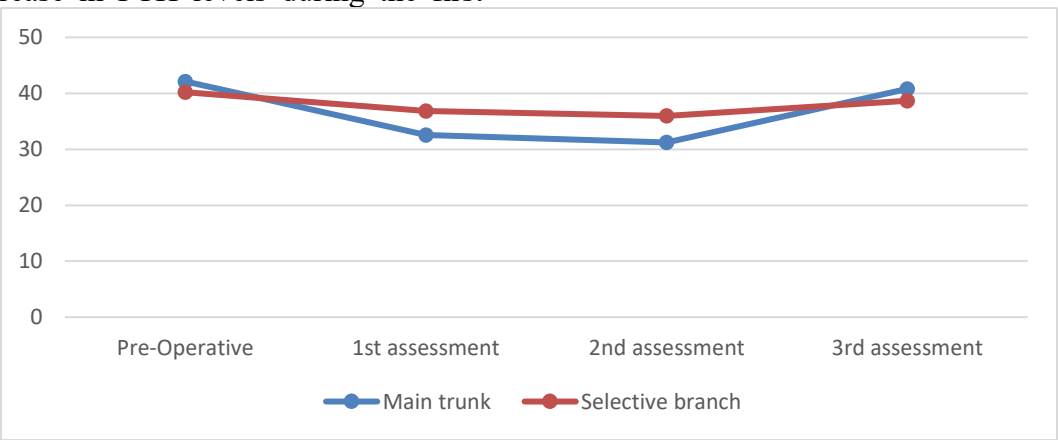

Fig.8. Mean parathyroid hormone level (pg/mL) through the study period in both groups

Discussion

In a case of a complete, partial, or near-total thyroidectomy, there is a possibility of developing hypoparathyroidism. This condition can occur due to the surgical removal of one or more parathyroid glands or disruption of their blood supply during the operation **(Waseem et al., 2021).**

Preserving parathyroid glands during surgery is important to avoid hypoparathyroidism. The gland's preservation depends on various factors such as anatomy, blood supply, and the surgeon's skill (**Shaari et al., 2022**). So, we aimed to compare the effect of truncal ITA ligation vs. branch ligation of inferior thyroid arteries on post-thyroidectomy serum calcium and PTH levels.

In our study, we found insignificant statistical difference between the two groups regarding demographic data or preoperative lab investigations. This–was in agreement with **Waseem et al. (2021)** who found insignificant———differences between patients who underwent truncal ITA (n = 157) and branch (n = 162) ligation.

Also**, Al Kordy et al., 2019**, observed that both groups had similar numbers, ages, sexes, and thyroidectomy reasons.

In our study, the main trunk ITA ligation group had substantial decreases in Ca and PTH at the first and second assessments compared to pre-operative data. However, the pre-operative and third Ca and PTH levels were similar.

Following main trunk ITA ligation, Ca and PTH levels may drop as the main trunk ligation cuts off blood flow to the thyroid gland, reducing PTH synthesis that controls blood calcium. Hence, PTH reduction lowers blood calcium levels. Thyroidectomy may harm the parathyroid glands, lowering PTH levels **(Chisthi et al., 2017; Parthipan, 2020).**

Our results was in line with **Waseem et al., 2021** who found that the ITA truncal ligation decreased both the serum calcium and PTH levels on the first day after the operation. Serum calcium and PTH levels did not significantly vary between the two groups throughout the follow-up months 3, 6, and 12.

In our study, In the main trunk ligation group, there was a significant decrease in Ca level and PTH at the first and second assessments compared to pre-operative results. There was no significant difference between pre-operative and the third assessment regarding Ca level and PTH. This was also observed by **Al Kordy et al. (2019)**

In our investigation, main trunk ligation reduced Ca and PTH levels more than selective branch ligation in the first and second assessments. Ca, and PTH, levels were similar across groups on the third assessment.

Our results were in line with **Cocchiara et al. (2010)** who reported that patients with truncal ITA ligation had considerably lower postoperative ionized calcium and greater PTH levels than those with terminal ITA ligature.

In contrast to our results, **Romano et al. (2016)** reported that in prospective randomized study comprising 184 patients who underwent complete thyroidectomy found no significant difference in postoperative calcium or PTH levels between the mean trunk and terminal branches ligation of ITA groups. However, the study reported a higher incidence of immediate postoperative hypocalcemia, vocal cord palsy, and swallowing difficulties compared to our results.

Waseem et al. (2021) found a significant higher prevalence of transitory hypocalcaemia in truncal

(22.9%) than in branch (3.1%) ligation, (P <0.05).

Al Kordy et al. (2019) reported that the hypocalcemia revealed was related to thyroidectomy; however, it had no clinical impact in any other context. Similar to our results, the ITA main trunk ligation procedure was more likely to result in a significant decrease in Ca and PTH levels compared with ITA branch ligation.

In contrast to our findings, **Cakmakli et al., 1992** found no association between bilateral truncal ITA ligation and hypocalcaemia.

The third postoperative evaluation showed no clinical symptoms, however, main trunk ligation group had significantly recived more exogenous calcium and vitamin D replenishment than the selective branch ligation group.

Our results was in line to the finding of **Waseem et al. (2021)** who assessed 319 patients randomly assigned to two groups: the first group had a truncal ITA ligation (n=157), while the second group had a branch ITA ligation (n=162).; 36 (22.93%) patients with truncal ITA ligation needed exogenous calcium and vitamin D on the second postoperative day, while only 5 (3.09%) of the patients with branch ITA ligation required these supplements.

Naseem et al. (2015) concluded that peripheral ITA ligation reduces postoperative clinical tetany in subtotal thyroidectomy.

Bilateral ITA truncal ligation following partial thyroidectomy decreased PTH levels but did not increase clinically evident hypoparathyroidism, according to **(Kebsch et al., 2015).**

In our results, the main trunk group exhibited a statistically significant decrease in calcium levels during the first and second assessments compared to the selective branch group. By the third assessment, calcium levels did not significantly differ between the groups. The same results were reported by **Waseem et al., 2021** who noted that after surgery calcium level and parathyroid hormone decreased significantly in the main trunk ligation group when compared with the selective branch ligation group, but with follow-up, there was no significant difference between the two groups regarding calcium level or PHT.

Our study has some limitations as it was performed in a single center, so results may not be generalizable to other population. Also, the sample size is limited to only 100 participants. Multi-nodular toxic goiter only.

We recommend that those carrying out further studies considering multicenter study on bigger sample size. We also recommend further studies to be performed with different throid pathology and different ligation techinques.

Conclusion

Ligation of ITA branches near the thyroid capsule reduces the likelihood of postoperative hypocalcemia compared to trunk ligation. However, the benefits of distal ITA branch ligation seem limited to the immediate postoperative period as outcomes are similar in subsequent days.

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Author Consent and Conflict of Interest

We want to affirm that we do not know any potential conflicts of interest or substantial financial support that may have influenced the results of this publication.

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