

'HYPOCALCEMIA FOLLOWING THYROID SURGERY '

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ABSTRACT

BACKGROUND

This was a prospective observational study of 18 months' duration. The purpose of this study is to compare preoperative serum calcium levels with postoperative serum calcium levels and to analyze post thyroid surgery hypocalcaemia with regards to prevalence, clinical presentation, and severity and to treat Hypocalcaemia if it occurs. In addition, we analyzed the correlation of postoperative Hypocalcaemia with relation to the type of surgery, diagnosis, duration of surgery and the quantity of blood loss. This study was conducted on consecutive patients who underwent thyroid surgery in the Department of General Surgery of a tertiary hospital in Puducherry for 18 months from November 2014 to April 2016. The median age of the patients was 40 years. The sex ratio was 17:2 in favour of females. Out of 38 patients, 18 patients were diagnosed with multinodular goitre, 8 were follicular carcinoma thyroid, 5 were papillary carcinoma thyroid, 2 were medullary carcinoma thyroid, 4 were adenomatoid nodule, and 1 patient was diagnosed to have thyroid abscess. In addition, 31 patients underwent total Thyroidectomy, 6 patients underwent hemithyroidectomy when 1 patient underwent incision and drainage for thyroid abscess.

RESULTS

39 % (n=15) of the patients developed Hypocalcaemia postoperatively. 87% (n=11) of the patients were symptomatic and required calcium correction. 2 patients had delayed presentation of Hypocalcaemia on postoperative day five. 1 patient who underwent hemithyroidectomy developed Hypocalcaemia in the postoperative period. Trousseau's sign was the most typical clinical feature seen in hypocalcaemia patients. In the present study, no significant association of Hypocalcaemia with the female gender was noted, and we did not find any association of Hypocalcaemia with advancing age. We did not find any association between Hypocalcaemia and prolonged surgery duration or increased blood loss in the present study. In addition, we did not see any increase in the incidence of Hypocalcaemia in patients who underwent Thyroidectomy combined with lymph node clearance.

CONCLUSIONS

The rate of postoperative Hypocalcaemia following thyroid surgery in this study was 39%. It coincides with the incidence reported elsewhere in the world. Although the risk of Hypocalcaemia was associated with increased blood loss,

prolonged surgery and extent of surgery, it was not statistically significant. If a similar study is conducted on a larger scale, including a broader spectrum of the population, important factors that influence postoperative Hypocalcaemia may be recognized.

KEYWORDS

Hypocalcemia, Thyroidectomy, carcinoma thyroid

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INTRODUCTION

Postoperative hypocalcemia is the most common complication after total Thyroidectomy, although vocal cord palsy and postoperative bleeding are more clinically apparent. The incidence of hypocalcemia following thyroid surgeries ranges from 1.7 to 68% [1,2,3]. The clinical syndrome usually presents 24–48 hours after surgery and requires strict monitoring. It could be the main factor determining the length of hospital stay after the surgery [4,5]. It is usually mild, but sometimes it may be severe. If it persists for six months or longer after surgery, then it is considered permanent hypocalcemia. Otherwise, it is called transient hypocalcemia. Patients must undergo close postoperative observation and laboratory evaluations. However, 0% to 33% of patients will experience permanent Hypoparathyroidism. The main reason for postoperative hypocalcemia is Hypoparathyroidism, caused by injury or devascularization of a parathyroid gland, accidental removal of one or more parathyroid glands and hematoma formations. Many factors contribute to the increased incidence of hypocalcemia and Hypoparathyroidism after Thyroidectomy, like- total Thyroidectomy, need for reoperations, combined neck dissection, preoperative hyperthyroidism and inexperienced surgeons performing Thyroidectomy [6,7].

There are many discussions in the literature regarding the role of parathormone in detecting postoperative hypocalcemia. Some studies have found that in post-thyroidectomy patients with clinical symptoms of tetany, the concentration of PTH was indeterminable and much lower in hypercalcemic patients [4,5]. However, there is only one official recommendation from the Australian Endocrine Surgeons Society in 2007, which advised measuring parathormone concentration as a means of postoperative hypocalcemia evaluation [8]. Hence postoperatively, we did not monitor serum parathormone levels.

Since hospital stay is always extended if hypocalcemia develops, some surgeons advocate a policy of early discharge by treating all patients with calcium supplements, with or without vitamin D supplements, regardless of they developing symptoms or not [9]. Unfortunately, this practice invariably results in many patients getting over treatment and could delay hypoparathyroidism diagnosis and appropriate treatment [10].

According to Becker KL et al., Chvostek's sign is no longer considered a reliable indicator of hypocalcemia since it only indicates neuromuscular irritability and is not a reliable indicator of hypocalcemia [11]. A study done by Fonseca OA mentions that 29% of patients with hypocalcemia (confirmed by laboratory reports) had a negative Chvostek's sign [12]. On the other hand, in his study, Hoffman E demonstrated a positive Chvostek's sign-in for nearly 25% of healthy individuals [13]. Becker KL et al. and Bushinsky DA mentions in their research that, Trousseau's sign is both sensitive and specific for hypercalcemic tetany [14] and according to Bushinsky DA, in patients with positive Trousseau's sign, the visual manifestations are apparent, and sometimes patients may also experience upper limb extremity paresthesia, fasciculation or twitches. Therefore, Trousseau's sign is more sensitive and specific for hypocalcemia than Chvostek's sign.

The purpose of this study was to compare preoperative serum calcium levels with postoperative serum calcium levels and to analyze post thyroid surgery hypocalcaemia with regards to prevalence, clinical presentation, and

severity and to treat Hypocalcaemia if it occurs. In addition, the correlation of postoperative Hypocalcaemia with respect to the type of surgery, the diagnosis, the duration of surgery and the quantity of blood loss was also analyzed in our study.

MATERIALS AND METHODS

This was a prospective observational study of 18 months duration. This study was conducted on consecutive patients who underwent thyroid surgery in the Department of General Surgery in a tertiary hospital for 18 months. Patients aged more than 12 years, both men and women, were included in this study. If they had concomitant parathyroid diseases or were already on calcium supplementation, such patients were excluded from the study. The parameters studied were

- Pre-operative & post-operative serum calcium (corrected calcium)
- Preoperative & Postoperative magnesium level
- Preoperative & Postoperative phosphate level
- Serum albumin level

METHODOLOGY

During 18 months, 38 consecutive patients older than 12 years of age undergoing all thyroid surgeries were prospectively followed up, and they underwent analysis regarding postoperative hypocalcemia. The ethical committee approved the study, and all patients gave their informed consent to participate. The surgeries were performed by a team consisting of consultants and residents. Demographic and clinical characteristics of the patients were obtained using a structural proforma. All the patients were evaluated preoperatively with complete blood investigations, thyroid function tests, ultrasound study of the neck and thyroid and fine-needle aspiration cytology. In addition, specific blood investigations like serum calcium levels, serum albumin levels, serum magnesium levels and serum phosphorus levels were measured and documented preoperatively. In addition, operative details like the extent of surgery, blood loss, the number of parathyroid glands identified, and the time duration of surgery were documented. Postoperatively, the patients were closely monitored for any clinical features suggestive of hypocalcemia, viz oral and perioral paraesthesia, acral paraesthesia, Trousseau's sign, Chvostek's sign, abnormal tendon reflexes or laryngospasm. Serum calcium, magnesium, phosphorus and albumin were checked and documented after 24 hours on postoperative day 1. Corrected calcium was calculated with the help of the formula

Corrected $[Ca^{2+}] = \text{Serum } [Ca^{2+}] + \{0.8 \times (4 - \text{Serum albumin})\}$

Serum calcium, magnesium, phosphorus and albumin were estimated again on postoperative day five. If the serum corrected calcium level was less than 8.5 mg /decilitre at any of the above said times, such patients were deemed to have Hypocalcaemia.

RESULTS

A total of 38 patients who had undergone thyroid surgeries for various thyroid diseases were included in this study. The median age of the patients was 40 years. The sex ratio was 17:2 in favour of females. Patients with different thyroid diseases were included in this study. Out of 38 patients, 18 patients were diagnosed to have a multinodular goitre, 8 were follicular carcinoma thyroid, 5 were papillary carcinoma thyroid, 2 were medullary carcinoma thyroid, 4 were adenomatoid nodule, and 1 patient was diagnosed to have thyroid abscess. 31 patients underwent total Thyroidectomy, 6 patients underwent hemithyroidectomy, and 1 patient underwent incision and drainage for thyroid abscess. We identified at least 2 parathyroid glands in 34 patients.

	Characteristics	Patients (n=38)
1	Age in years	41 ± 12
2	Duration of surgery in minutes	175 ± 53
3	Blood loss in milliliters	26 ± 8
4	Preop corrected ca2+ In mg/dl	9 ± 0.6
5	Pod 1 corrected ca2+ In mg/dl	8.7 ± 0.9
6	Pod 5 corrected ca2+ In mg/dl	9.0 ± 0.7

Table 1- Baseline Characteristics

Incidence of Hypocalcaemia:

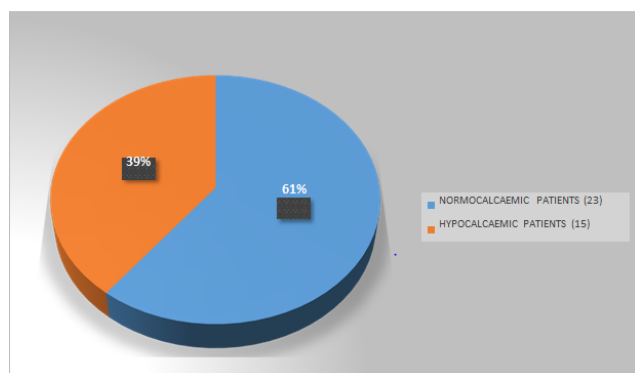


FIG 2: Incidence of Hypocalcaemia.

39 % (n=15) of the patients developed Hypocalcaemia postoperatively.
CONFIDENCE INTERNAL- ±15.5

Out of 25 patients with age less than or equal to 45 years, 7 patients developed Hypocalcaemia. Out of 13 patients with age more than 45 years, 8 developed Hypocalcaemia. The mean value of preoperative corrected calcium was 9.1 mg and, at the time of discharge, was 9 mg. Symptomatic Hypocalcaemia was seen in 13 patients. Delayed presentation of Hypocalcaemia was noted in 2 patients. (POD 5).11 patients required oral calcium supplementation, and 2 patients required intravenous calcium supplementation. The most typical clinical sign elicited in hypocalcaemia patients was Trousseau's sign (n=11). Perioral paraesthesia was noted in 4 patients. Chvostek's

sign was elicited in 2 patients

Hypocalcaemia Association With Other Clinical Parameters:

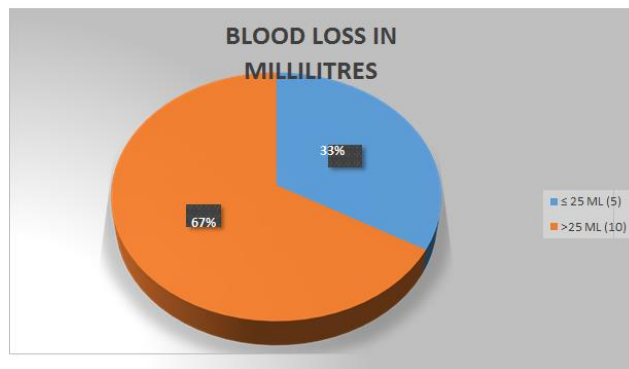


FIG 32: Association Of Hypocalcaemia With Blood Loss (P-Value- 0.880)

In 10 hypocalcaemia patients, blood loss was more than 25 millilitres. Conversely, in 5 hypocalcaemia patients, blood loss was less than or equal to 25 millilitres.

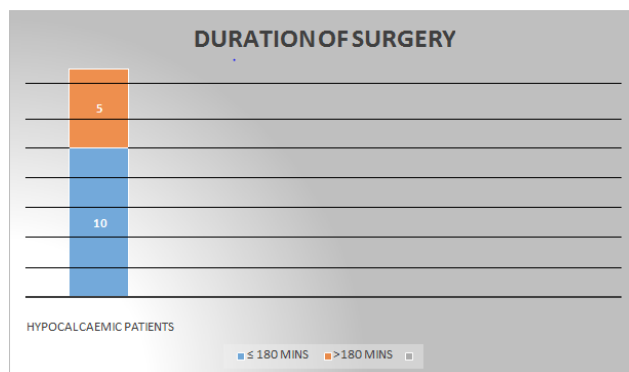


FIG 33: The Association of Hypocalcaemia With The Duration Of Surgery. (P-Value- 0.139)

5 out of 15 hypocalcaemia patients had prolonged surgery. (Duration more than 180 minutes.)

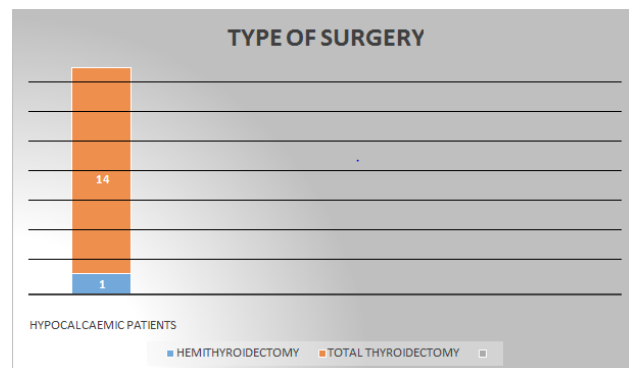


FIG 34: The Association Of Hypocalcaemia With The Type Of Surgery (P-Value- 0.301).

Out of 15 patients who developed Hypocalcaemia postoperatively, 14 patients underwent total Thyroidectomy,

and 1 patient underwent hemithyroidectomy. Out of 5 patients diagnosed with papillary carcinoma thyroid, 2 patients had undergone total Thyroidectomy with unilateral modified neck dissection, and 1 patient had undergone central lymph node clearance. One patient in this group developed postoperative Hypocalcaemia on day 2.

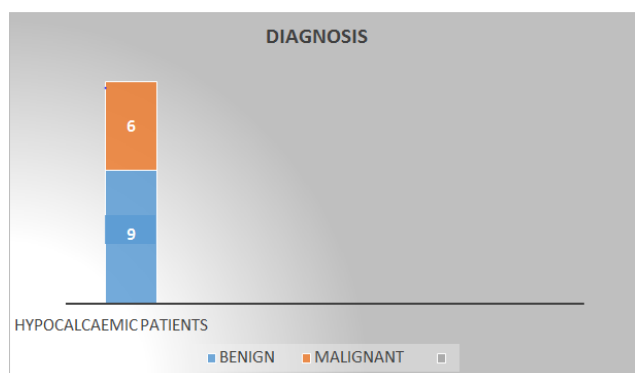


FIG 35: The Association Of Hypocalcaemia With The Diagnosis. (P-Value- 0.429)

9 Out of 15 patients who developed Hypocalcaemia postoperatively underwent surgery for benign diseases. 6 patients were operated on for malignant thyroid diseases.

DISCUSSION

No recent population studies are showing the prevalence of goitre in Tamil Nadu and Pondicherry. Our institutional statistics showed that 66% of thyroid surgeries are for benign diseases, comprising multinodular goitres, adenomatoid nodules, nodules with suspicious cytology and recurrent goitres. In the present study, the mean value of preoperative corrected calcium was 9.089; on postoperative day 2, it was reduced to 8.7. On postoperative day 5, there was an increase in mean corrected calcium to 9.03. In similar studies done by Nair CG et al. and Noureldine SI et al., 30.36% and 29.9% of patients developed Hypocalcaemia in the immediate postoperative period, respectively [15,16]. Another study by Shaha AR et al. had noted up to 50% of transient Hypocalcaemia after thyroidectomy [17]. In the present study, 34% (n=13) of patients developed Hypocalcaemia on postoperative day two. 29% (n=11) of the patients had symptomatic Hypocalcaemia for which calcium correction was given. Among them 81% (n=9) responded to oral calcium correction while 18 % (n=2) required intravenous calcium supplementation. In the present study, none of the patients developed permanent Hypocalcaemia. A study conducted by Nair CG et al. noted a three-day delay in the presentation of Hypocalcaemia after Thyroidectomy. There are reports of late-onset Hypocalcaemia following Thyroidectomy for Grave's disease [18]. In the present study, on postoperative day five, 2 new patients were diagnosed with Hypocalcaemia; both had undergone total Thyroidectomy, 1 female and 1 male patient, with the diagnosis of papillary carcinoma thyroid and follicular carcinoma thyroid, respectively. Baldassarre RL et al., in their meta-analysis, reported an incidence of 1.9 % postoperative Hypocalcaemia in patients who underwent hemithyroidectomy [19]. In the present study, one patient developed Hypocalcaemia on postoperative day 2 among the six patients who had undergone hemithyroidectomy. It was a female patient, and she was operated on for an

adenomatoid nodule. However, she did not have any symptoms of Hypocalcaemia. A study done by Noureldine SI et al. found that males had a 56% and 63% decreased risk of developing postoperative significant and mild Hypocalcaemia, respectively [16]. In the present study, among four men, all of them had undergone total Thyroidectomy. Two of them had medullary carcinoma thyroid, one of them was diagnosed with follicular carcinoma thyroid and the other with papillary carcinoma thyroid. The patient diagnosed with papillary carcinoma thyroid developed Hypocalcaemia on postoperative day two, it was severe, and he needed intravenous calcium correction. As mentioned above, the male patient diagnosed with follicular carcinoma thyroid developed delayed Hypocalcaemia on postoperative day five. He was managed with oral calcium supplementation. Four patients who developed postoperative Hypocalcaemia were below 35 years of age, and five were above 50. No significant association of Hypocalcaemia with the female gender was noted in the present study. We did not find any association of Hypocalcaemia with advancing age, unlike some similar studies done by Abboud B et al. and Bhattacharyya N et al. [20,21]. In the present study, Trousseau's sign was the commonest clinical feature observed in the patients who developed Hypocalcaemia. In 11 patients, Trousseau's sign was positive, whereas only 2 patients had positive Chvostek's sign. Nowadays, Chvostek's sign is no longer considered a reliable indicator of Hypocalcaemia since it only indicates neuromuscular irritability and is not a reliable indicator of Hypocalcaemia [11]. A study done by Fonseca OA showed that 29% of patients with Hypocalcaemia (confirmed by laboratory reports) had a negative Chvostek's sign [12]. Hoffman E, in his study, demonstrated a positive Chvostek's sign-in for nearly 25% of healthy individuals [13]. On the other hand, Trousseau's sign is thought to be both sensitive and specific for hypercalcaemic tetany. [14]. In positive Trousseau's sign, the visual manifestations are obvious, and sometimes patients may also experience upper limb extremity paraesthesia, fasciculation or twitches. Trousseau's sign is more sensitive and specific for Hypocalcaemia than Chvostek's sign. A study done by Ambe PC et al. on 305 patients showed that prolonged surgery or greater blood loss is not a surrogate marker for postoperative Hypocalcaemia following total thyroidectomy [22]. We did not find any association between Hypocalcaemia and prolonged surgery duration or increased blood loss in the present study. 64% (n=7) of patients who developed Hypocalcaemia postoperatively did not have a prolonged surgery (Duration<180 mins), while 36%(n=4) had a prolonged surgery (Duration>180 mins). In 39% of patients(n=5) who developed Hypocalcaemia postoperatively, the blood loss was less than 25 millilitres, while 62% (n=8) had blood loss of more than 25 millilitres. Puziello A et al. states that the rate of Hypocalcaemia following thyroid surgery is higher in patients who had undergone lymph node clearance than in the patients in which the lymph node clearance was not performed [23]. In the present study, out of five patients diagnosed with papillary carcinoma thyroid, two patients had undergone total Thyroidectomy with unilateral modified neck dissection, and one patient had undergone central lymph node clearance. One patient in this group developed postoperative Hypocalcaemia on day two. However, it was not statistically significant. But, we advise avoiding routine central neck dissection, at least in differentiated thyroid cancers, unless indicated.

SUMMARY

This study was conducted on consecutive patients who underwent thyroid surgery in the Department of General Surgery, Pondicherry Institute of Medical Sciences, Puducherry, for 18 months from November 2014 to April 2016. The median age of the patients was 40 years. The sex ratio was 17:2 in favour of females. Out of 38 patients, 18 patients were diagnosed with multinodular goitre, 8 were follicular carcinoma thyroid, 5 were papillary carcinoma thyroid, 2 were medullary carcinoma thyroid, 4 were adenomatoid nodule, and 1 patient was diagnosed to have thyroid abscess. 31 patients underwent total Thyroidectomy, 6 patients underwent hemithyroidectomy when 1 patient underwent incision and drainage for thyroid abscess. 39 % (n=15) of the patients developed hypocalcemia postoperatively. 87 % (n=11) of the patients were symptomatic and required calcium correction. 2 patients had delayed presentation of hypocalcemia on postoperative day five. 1 patient who underwent hemithyroidectomy developed hypocalcemia in the postoperative period. Trousseau's sign was the most typical clinical feature seen in hypocalcemia patients. In the present study, no significant association of hypocalcemia with the female gender was noted, and we did not find any association of hypocalcemia with advancing age. We did not find any association between hypocalcemia and prolonged surgery duration or increased blood loss in the present study. In the present study, we did not see any increase in the incidence of hypocalcemia in patients who underwent Thyroidectomy combined with lymph node clearance.

CONCLUSION

The rate of postoperative Hypocalcaemia following thyroid surgery in this study was 39%. It coincides with the incidence reported elsewhere in the world. Although the risk of Hypocalcaemia was associated with increased blood loss, prolonged surgery and extent of surgery, it was not statistically significant. If a similar study is conducted on a larger scale, including a broader spectrum of the population, important factors that influence postoperative Hypocalcaemia may be recognized.

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