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Research article

IS POSTOPERATIVE HYPOCALCAEMIA A LIFE THREATENING COMPLICATION FOLLOWING THYROIDECTOMIES? A PROSPECTIVE STUDY IN THE RURAL POPULATION OF KANCHIPURAM

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ABSTRACT

Hypocalcaemia is one of the commonest complications that can occur after thyroidectomies. Permanent hypocalcaemia following thyroidectomy causes considerable morbidity. This prospective observational study aims to define the factors likely to predict hypocalcaemia following thyroidectomy. **Materials and Methods:** 59 Patients who were subjected to all types of thyroidectomy during February 2012 to January 2014 were studied retrospectively. Preoperative and postoperative Serum Calcium was estimated in all the patients. **Results:** The incidence of hypocalcaemia increased with increasing age groups. Out of 59 cases, 19 patients developed temporary hypocalcaemia postoperatively (32%). None of the patient had permanent hypocalcaemia. Of these cases 5% had hemithyroidectomy, 26% sub total thyroidectomy, 67% near total thyroidectomy**,** 64%total thyroidectomy and 67% completion thyroidectomy. **Conclusion:** Hypocalcaemia is a serious postoperative complication of thyroidectomies. It should be promptly diagnosed and treated early. All types of thyroidectomies should be investigated for hypocalcaemia. Care should be taken in exploring the parathyroid glands intraoperatively is an excellent method to prevent permanent hypocalcaemia.

Key words: Hypocalcaemia, Thyroidectomy, Serum Calcium, Parathyroids.

INTRODUCTION

Thyroidectomy is one of the commonest surgeries done in India. The two most common complications of thyroid surgeries are recurrent laryngeal nerve injury and hypocalcaemia. These and other major complications typically occur in less than 5% of the case. Thedor Kocher reported first 100 thyroidectomies in 1883 and noted the presence of tetany in many cases. William Halsted (1852-1922) was one of the first surgeons to advocate meticulous surgical techniques to prevent injuries to parathyroid glands and so greatly contributed to the prevention of this serious complication which together with bleeding and laryngeal nerve injury had made early thyroid surgeries so dangerous. In the 21st century, thyroidectomy has become safe and effective with improved outcomes and minimal morbidity. This is in part due to the awareness of the anatomical relationship of the parathyroid gland to the thyroid, which is important in preventing postoperative hypocalcaemia. Nonetheless, the incidence of

hypocalcaemia following thyroidectomy remains significantly high in the range of 1.6% to 50%, with permanent hypocalcaemia occurring in 1.5% to 4% of the cases. According to a study by Thomusch[1]et al, regardless of a surgeon's experience, an incidental parathyroid gland features occasionally in the pathology reports of thyroid specimens. The post-operative hypocalcaemia is frequently observed within 2-5 days after total or subtotal thyroidectomy, requiring exogenous replacement therapy to alleviate the clinical symptoms. We selected this study as we came across a few number of cases in the urban health center where we did the study. Many studies were done on this topic to stress the importance of postoperative hypocalcaemia in thyroidectomy cases. In a study by Herranzetal[2]showed the incidence and management of postoperative hypocalcaemia in total thyroidectomies. Our study was done in all types of thyroidectomies as post-operative hypocalcaemia can occur in any type of thyroidectomy.

The exact pathogenesis of hypocalcaemia in postoperative patients is difficult to explain. It is however, varies in different pathological conditions of thyroid gland and the type of surgical intervention. Grave's disease, malignancy, total thyroidectomy and parathyroid gland ischaemia/injury are the main causes of lowering serum calcium concentration. Hypoparathyroidism is an additional event whereas hypocalcaemia is relatively common after total thyroidectomy.According to a study by Sokouti Ma et al[3], hypocalcaemia is a common and usually transient but in some cases can become permanent due to loss of functioning parathyroid gland after total thyroidectomies. This can cause significant discomfort in affected patients who will eventually need to take oral calcium and Vitamin D for a long time.

To minimize parathyroid injury, an attempt to look for all the parathyroid glands and preserve their blood supply was done during the operation. However, it is difficult to find all parathyroid glands and to preserve these identified parathyroid glands due to the high probability of inflicting damage to their blood supply during the search process and dissection. Also, the extent of thyroidectomy and node dissection increases the likelihood of damaging the blood supply of the parathyroid glands. Intraoperative extensive handling, bleeding, distorted anatomy, fibrosis, adhesions and even surgeon's experience are related to parathyroid injuries.

In a study by Rajeev Parameswaran[4], parathyroid auto transplantation can reduce the incidence of hypocalcaemia, when unintentionally removed or devascularised parathyroid glands were found intra-operatively. Sometimes, parathyroid gland may be found within the postoperative specimen, when it was unknowingly removed with the thyroid or lymph node during the operation.

Aims and objectives

The aims of our study were

1. To identify the incidence of parathyroid gland injuries.
2. To analyze the reasons for injuries.
3. To analyze the serum calcium level postoperatively.

MATERIALS AND METHODS

This prospective study was carried out from February 2012 to January 2014 in Meenakshi Medical College and Research Institute, Kanchipuram. After obtaining Ethical Committee clearance and consent from the patients, 59 cases of goiters who underwent thyroidectomies in our hospital were studied.

Inclusion criteria: 1. All thyroidectomise 2. All age groups 3. Both genders 4. Euthyroid patients

Exclusion criteria: 1. Patients with chemotherapy and radiotherapy 2. Recurrent thyroid surgeries 3. Cardiac patients

As this study was performed in different units in the Departments of General Surgery and ENT, patients were operated by different surgeons performing or not preferring the active identification of the parathyroid glands to avoid injury to parathyroid glands. Along with a brief history and clinical examination and routine laboratory investigations, Ultrasonogram of thyroid, Fine Needle Aspiration Cytology (FNAC) were performed in all the patients, Baseline total serum calcium was done in all the patients on the preoperative day, second and seventh postoperative days. Normal range for total serum calcium 8.5 to 10.5 mg/dl and ionized serum calcium 4.5 to 5.6 mg/dl were considered in all the cases (Davidson's Principles and Practice of Medicine).Depending on the extent of resection of thyroid tissue, surgery was categorized as hemi, subtotal, near total or total thyroidectomy. Identification and preservation of

parathyroid glands were done. Reasons for non-identifications or sacrifice of parathyroid glands was surgeon's choice, adhesions, distorted anatomy, bleeding or fibrosis. In this study, we also studied the experience of the operating surgeons playing a role in outcome of thyroid surgery and incidence of parathyroid gland injuries.

The following symptoms of hypocalcaemia were observed

1. Oral, perioral or acral paraesthesia
2. Carpopedal spasm
3. Tetany
4. Hyperactive tendon reflexes
5. Laryngospasm
6. ECG changes

Postoperative total serum calcium was measured after 48 hours and on 7th day or at the time of discharge for biochemical evidence of early and delayed onset hypocalcaemia as the evidence of parathyroid gland injury either in the form of devascularisation or its removal. Iodized calcium levels were done in all cases that had low total serum calcium levels or had signs and symptoms of hypocalcaemia and in cases where serum calcium level was low but patients were asymptomatic. Patients developing symptoms of hypocalcaemia were asked to continue calcium and vitamin D supplements for additional seven days after discharge. Patients were asked for follow up after 3 months or earlier if symptoms of hypocalcaemia occur. None of our patients came with symptoms of hypocalcaemia. These patients were assumed to have normocalcaemia both clinically and biochemically, therefore calcium levels were not repeated in these patients.Measurement of postoperative serum parathormone (PTH) as the evidence of parathyroid gland injury was not taken into account due to inaccessibility and high cost of this investigation at our centre because majority of our patients were from poor socio-economic strata.

Then patients were followed for histopathology report (HPR) to see for accidental removal of parathyroid glands as reason for hypocalcaemia. In the rest of all cases of hypocalcaemias, possibility of parathyroid gland injuries were considered due to devascularisation or ischemia or direct trauma to parathyroid glands rather than its complete removal.

The handling of the parathyroid glands during operation was divided into 5 types:

1. The preserved type – a grossly tan parathyroid gland with intact blood supply.
2. The color changed type – a grossly congested and having a low chance of survival.
3. The auto-transplantation type – an isolated parathyroid gland implanted into the sternocleidomastoid muscle.
4. The removed type – a parathyroid gland being removed with the thyroid gland due to its proximity to the cancer or were incidentally found in the biopsy report.
5. The non-identified type - parathyroid gland not found during operation.

Successful preservation of parathyroid glands was considered for the first type and the remaining were considered non-preservation of parathyroid gland.

Data derived in this study was in the form of mean or percentages. In one place Fisher's Exact Test was applied to know the significance of the identification of parathyroid glands intra-operatively.

RESULTS

In this study, 59 cases with goitres that underwent thyroid surgeries in our hospital were studied.

Age distribution in our study, the maximum age recorded was 69 years and minimum age recorded was 21 years. The number of patients who developed hypocalcaemia in our study was 19. The following Graph 1 shows the relationship between age and hypocalcaemia.

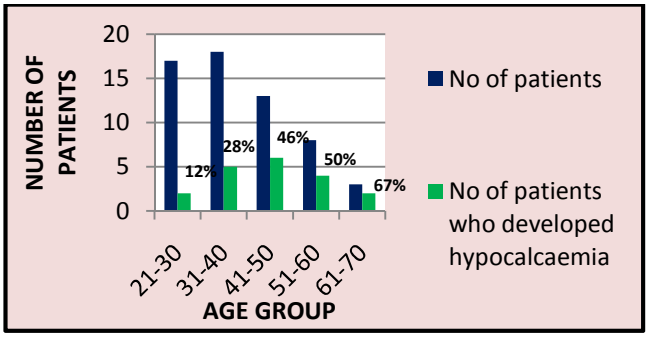

Fig-1: Relationship between age and the number of patients who developed hypocalcaemia.

Out of 19 cases who developed symptoms of hypocalcaemia in 48 hours postoperatively, 16 cases had low total and ionized serum calcium and 3 cases had normal total serum calcium but low iodized serum calcium level. Out of remaining 40 cases, 3 cases found to have low total serum calcium level but normal iodized calcium level.

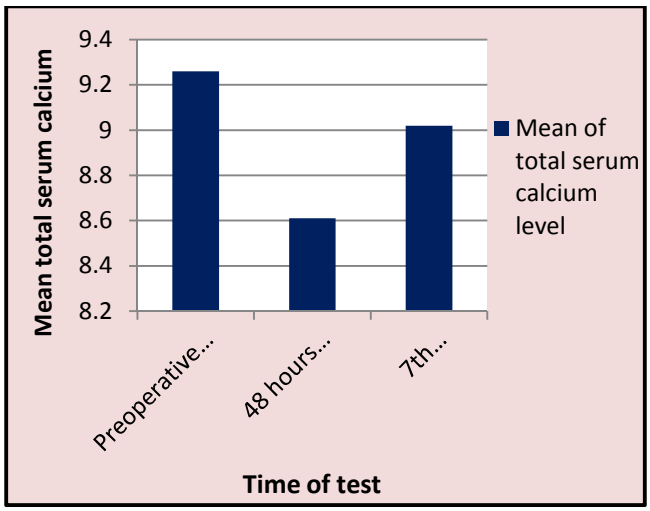

Fig 2: Mean total serum calcium levels

Diagnosis and hypocalcaemia, In this study all 59 patients were in euthyroid state. 19 patients had hypocalcaemia (32%). The table 1 shows the different diagnosis and its relationship to hypocalcaemia.

Table 1: Relationship between diagnosis and patients who developed hypocalcaemia

Diagnosis	No. of patients	No of patients developed hypocalcaemia	%
Colloid goitre	16	03	19
Solitary Nodule (adenoma)	09	01	11
MNG	10	04	40
Papillary Carcinoma	12	07	58
Follicular carcinoma	02	01	50
Hashimoto's thyroiditis	10	03	30

Table 2: Patients who developed hypocalcaemia after different type of operation

Type of operation	Number of patients	Number of patients who developed hypocalcaemia	%
Hemithyroide-ctomy	20	01	05
Subtotal thyroidectomy	19	05	26
Near-total thyroidectomy	03	02	67
Total thyroidectomy	14	09	64
Completion thyroidectomy	03	02	67
Total	59	19	-

Table 2 shows the relationship between type of operation done and the number of patients who developed hypocalcaemia. All the patients who developed hypocalcaemia were temporary only. On the 7th postoperative day all patients reverted to normocalcaemia.

Identification of parathyroid glands

In our study, identification of parathyroid glands was done according to the type of surgery done, i.e. all 4 parathyroid glands were attempted to identify in all thyroidectomies, but parathyroid glands of only respective sides were identified and preserved in case of right or left hemithyroidectomy and completion thyroidectomy. Out of 59 cases all parathyroid glands with respect to operative procedure were identified in 39 cases.

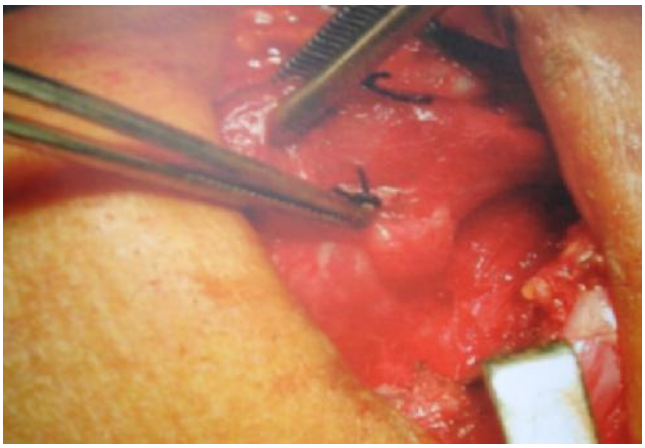

Fig 3: Left superior thyroid seen during subtotal thyroidectomy

Of these 39 cases, in 36 cases all parathyroid glands with respect to operative procedure were attempted to identify and preserve. In 2 cases parathyroid glands were identified, but 1 was sacrificed in each due to proximity to the tumor. In 1 case, accidentally removed parathyroid gland was identified on table and was autotransplanted in ipsilateral sternocleidomastoid.

Table 3: Hypocalcaemia when parathyroid gland is seen

Parathyroid gland	Seen	Temporary hypocalcaemia	Seen in HPR With hypocalcaemia	Seen in HPR Without hypocalcaemia
All preserved	36	7	1	0
Sacrificed	2	1	0	0
Autotransplanted	1	0	0	0
Total	39	8	1	0

Out of 39 cases where parathyroid glands were seen and identified, 8 cases developed hypocalcaemia (21%).

In remaining 20 cases, parathyroid glands were not seen. Out of which in 16 cases parathyroid glands were not seen due to Surgeon's choice; 2 cases due bleeding and in 2 cases due to fibrosis and distorted anatomy.

Table 4: Hypocalcaemia when parathyroid gland is not seen

Parathyroid Gland	Not seen	Temporary hypocalcaemia	Seen in HPR With hypocalcaemia	Seen in HPR Without hypocalcaemia
Surgeon's Choice	16	8	2	1
Bleeding	2	1	1	0
Fibrosis/ distorted anatomy	2	2	0	0
Total	20	11	3	1

In 20 cases were parathyroid glands were not seen during surgery 11 developed hypocalcaemia (55%).

The following Graph 3explains the significance of identifying the parathyroid glands during surgery.

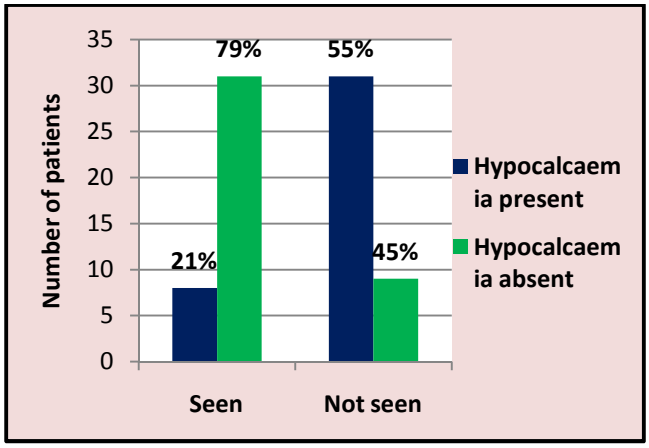

Fig 4: Significance of identifying parathyroid glands

Reasons for hypocalcaemia

In our study, intraoperative identification of parathyroid glands carries 0.677 times risk of developing hypocalcaemia. But after the application of Fischer's Exact Test (p value = 0.3), this difference is found to be statistically insignificant. Graph 4 shows the comparison of identification of parathyroid gland in HPR and hypocalcaemia

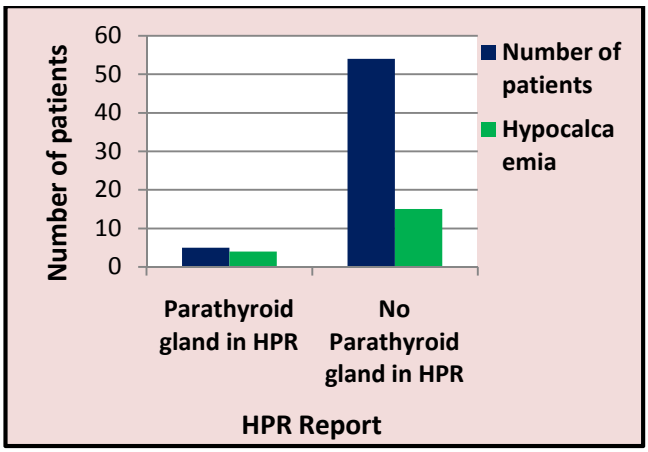

Fig 5: Parathyroid gland in HPR and hypocalcaemia

Out of 19 cases developing hypocalcaemia, 4 cases were considered due to accidental removal as seen in histopathology report and 15 cases were probably due to devascularisation or injury to parathyroid glands.

DISCUSSION

Inadvertent parathyroid excision and hypocalcaemia are well recognized complications of thyroid surgery. The exact pathogenesis of hypocalcaemia in postoperative patients is difficult to explain. Grave's disease, malignancy, total thyroidectomy and parathyroid gland ischemia / injury are the main causes of lowering serum calcium concentration.

In a study by Baldassarre R L et al[5], the incidence of hypocalcaemia increases with age group. In our study also the incidence of hypocalcaemia was more in the later age group, almost 50% in cases between 40 and 70 years of age group.

Amongst 59 patients studied, preoperatively all were within normal limits. Postoperatively 19 patients (32%) developed only temporary hypocalcaemia which all reverted back to normal on the 7th postoperative day owing to oral calcium and Vitamin D supplements for a short period. None of our patients developed permanent hypocalcaemia. In a study by Rajnikanthetal[6] in 364 patients showed 28% of patients developing hypocalcaemia. This is on par with our study. In another study by PfleidererA Get al[7] 43% of patients developed temporary hypocalcaemia and 5% developed permanent hypocalcaemia. This study had high incidence when compared to ours.

In a study by Moore et al[8] confirmed that iodized calcium accounts for the biologically active form of

serum calcium and subsequently demonstrated the crucial role of iodized calcium in the calcium homeostasis of healthy individuals and patients with parathyroid abnormalities. In our study also out of 19 cases who developed symptoms of hypocalcaemia 48 hrs postoperatively, 16 patients had low total and iodized calcium levels and 3 cases had normal serum calcium and low iodized calcium levels. Out of the remaining 40 cases, 3 cases had low total calcium and normal iodized calcium levels.

In our study, out of 59 patients, maximum number of patients operated was colloid goitre, MNG and Papillary carcinoma of thyroid accounting for 64% of cases. In our study, the number of malignant cases was24% and benign cases were 76%. In a study by Rajnikanthetal[6], 59% were benign and 41% were malignant.

In a study by HanyAlyetal[9], the incidence of postoperative hypocalcaemia was higher in malignant cases (25%) and in toxic goitre (11%), while in MNG it was 4% and 10% in Hashimoto's thyroiditis. In our study 57% of malignant cases had hypocalcaemia and only 24% of benign cases suffered from hypocalcaemia. This is owing to other factors like age, bleeding, adhesions or a distorted anatomy.

In our study, maximum number of patients underwent hemithyroidectomy (34%) and minimum number of patients underwent near total and completion thyroidectomies (each 5%); subtotal thyroidectomy (32%); total thyroidectomy (24%). In our study hypocalcaemia was seen in 67% of patients undergoing completion thyroidectomy; 67% in near total thyroidectomy; 26% in subtotal thyroidectomy; 64% in total thyroidectomy and 5% in hemithyroidectomy. In a study by Akram Rajput et al[10], transient hypocalcaemia was seen in 54% of patients undergoing total thyroidectomy; 50% with completion thyroidectomy; 29% with subtotal thyroidectomy and 23% with hemithyroidectomy. In our study only 5% of patients developed hypoglycaemia after hemithyroidectomy. In a study by PfleidererA G et al[7], completion thyroidectomy was performed in patients found to have a malignancy in the thyroid lobe previously removed. Patients having a completion thyroidectomy appeared to be less likely to develop hypocalcaemia. According to them this two stage procedure may have resulted in lower incidence of hypocalcaemia since the parathyroids on the side of the previous lobectomy may have had time to recover their function prior to the completion thyroidectomy.

Differences in outcome after thyroidectomy in our study could be due to our centre being less in volume for neck surgeries; surgeons with less experience in neck surgeries and no new techniques are employed.

Out of 39 patients where parathyroid glands were attempted to identify and preserve, 8 patients developed hypocalcaemia (21%). In only one case the parathyroid gland was identified by the pathologist. Out of 2 cases where 1 parathyroid gland was sacrificed due to proximity to tumour mass. 1 patient developed hypocalcaemia but none showed parathyroid gland in the histopathology report. This indicates that there is a possibility of parathyroid gland being misidentified by the surgeon. So the hypocalcaemia developed in this case could be due to devascularisation of parathyroid glands.

In 1 case parathyroid gland was accidentally removed but was auto transplanted in ipsilateral sternocleidomastoid. This patient did not develop hypocalcaemia. This proves that auto transplantation is an important procedure if parathyroid gland was identified after accidental removal.

Out of 16 cases where parathyroid glands were not seen by surgeon's choice, 8 developed hypocalcaemia. In 2 cases parathyroid glands were not seen due to bleeding and one developed hypocalcaemia. In another 2 cases parathyroid glands were not seen due to distorted anatomy and fibrosis and both developed hypocalcaemia. This is a clear indicator of the importance of parathyroid gland identification during surgery.

In our study, intraoperative identification of parathyroid glands carries 0.677 times risk of developing hypocalcaemia postoperatively. But after the application of Fischer's Exact Test (p value = 0.3) this difference is found to be statistically insignificant. This may be due to the smaller sample size.

In our study, in 5 cases parathyroid glands were seen in histopathology report. So the incidence of inadvertent removal of parathyroid gland in our study was 8%. In a study by Rajnikanthetal[6], the incidence of in advertent removal of parathyroid gland was 13%. In another study by Gamal Ahmed Khairyetal[11]it was 16%.

The role of identifying parathyroid glands in the prevention of hypocalcaemia has been debated in literature. Rimpl and Wahl et[12]however advocated that identification of at least three parathyroid glands to avoid hypocalcaemia. Walsh et al[13] found no association with the number of parathyroid glands identified. On the other hand, a study by PfleidererA Get al[7] suggested that the identification of the parathyroid glands was not a safeguard and in fact, increased the risk of hypocalcaemia probably related to either direct trauma or disruption of the blood supply due to surgical manipulation. But our study clearly indicates that identification of parathyroid glands were important to avoid postoperative hypocalcaemia.

Thomusch et al[1] emphasized that at least 2 parathyroid glands should be identified and preserved to prevent hypoparathyroidism and they found that the additional benefit was evident by having more than two identified and preserved parathyroid glands. Our study also showed the same results.

The location of parathyroid glands may vary but unnecessary dissection to locate them should not be carried out as it may be more hazardous than not seeing them. We also did the same and the results were much better.

In general, the parathyroid injury should be avoided intraoperatively and this depends upon so many factors like age of the patient, thyroid status, experience of the surgeon, identification of parathyroid glands intraoperatively and so on.

CONCLUSION

In our study hypocalcaemia secondary to parathyroid gland injuries were due to devascularisation (79%) and rest of the patients (21%) were probably due to accidental removal of parathyroid glands.

Parathyroid injuries were more when parathyroid glands were not searched actively due to bleeding, distorted anatomy or fibrosis.

Identification and preservation of parathyroid glands during thyroidectomy has less chances of developing hypocalcaemia postoperatively.

The incidence of developing postoperative hypocalcaemia in all thyroid surgeries was 32%. The incidence of hypocalcaemia was 21% when parathyroid glands were attempted to identify and see intraoperatively.

Incidence of hypocalcaemia was 55% when parathyroid glands were not seen intraoperatively.

Iodized calcium levels rather than the total serum calcium levels are responsible for developing or not developing symptoms of hypocalcaemia.

Conflict of Interest: Nil

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