

Original Research Article

Incidence of postoperative hypocalcaemia in patients with preoperative cytological evidence of Hashimoto's thyroiditis undergoing thyroidectomy

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ABSTRACT

Background: Hashimoto's thyroiditis is an autoimmune pathology presents as a painless goiterogenous condition. It manifests as hypothyroidism, occurring in females of the age group 30-40. Patients are operated for cosmetic symptoms or suspicions of malignancy. The surrounding adhesions and fibrosis of the gland makes it more prone for hypocalcaemia post operatively. This study was conducted to find the incidence of hypocalcaemia postoperatively in patients with Hashimoto's thyroiditis.

Methods: Patients above 13 years undergoing total thyroidectomy where completion thyroidectomy after hemithyroidectomy, concurrent lymph node dissection, patients on calcium therapy or the ones with preexisting hypocalcaemia were excluded from the study. 100 patients were studied from 1 January 2018 to 1 January 2019 and corrected serum calcium levels at 24 hours, 48 hours and 2 weeks estimated postoperatively. Analysis was done using CSC sepi-info software. Qualitative data were analyzed with Chi square, Z test and ANOVA test.

Results: Though 32/100 patients had hypocalcemic symptoms only 26 (26%) had low calcium biochemically. The association between Hashimoto's thyroiditis and post thyroidectomy hypocalcaemia had significant association ($p < 0.0001$). 11.53% (3/26) had recovered in 48 hours and at two weeks 10 patients remained hypocalcemic with a recovery of 61.53%.

Conclusions: Hypocalcaemia after total thyroidectomy in Hashimoto's thyroiditis occurs due to fibrosis in gland, adhesions to the adjacent structures, injury to the parathyroid glands during surgery and non-identification of parathyroid glands.

Keywords: Hashimoto's thyroiditis, Total thyroidectomy, Postoperative hypocalcaemia

INTRODUCTION

Hashimoto's thyroiditis is a painless goiterogenous condition which can manifest as hypothyroidism, usually occurring in females in the age group between 30 and 40.¹ Considered as an autoimmune pathology Hashimoto's thyroiditis is caused due to an interplay of genetic and environmental risk factors. The thyroid follicles are atrophic and the stroma is infiltrated with

lymphocytes, arranged in germinal follicles.² The anti TPO antibodies and anti TG antibodies can be demonstrated in the serum. Patient may be euthyroid but can present with cosmetic disturbances due to the goiter, pain, hoarseness or compression symptoms. Although medically treated with thyroid hormone replacement, the suspicion of malignancy, the local symptoms and cosmesis demands surgical treatment. The thyroid gland is firm and adherent to the adjacent structures making

operative treatment more prone for post thyroidectomy complications such as hypocalcaemia.³ This study attempted to find the incidence of hypocalcaemia following thyroidectomy in the cases of Hashimoto's thyroiditis requiring surgery.

METHODS

This prospective study was conducted on patients who underwent total thyroidectomy during the period from 1 January 2018 to 1 January 2019. Patients above the age of 13 years admitted to government medical college, Thrissur, Kerala who were diagnosed with Hashimoto's thyroiditis/chronic lymphocytic thyroiditis by fine needle aspiration cytology (FNAC) who underwent total thyroidectomy by bilateral exploration were included in the study.

The exclusion criteria included completion thyroidectomy following hemi-thyroidectomy; concurrent lymph node dissection; patients who were on calcium supplementation and those with preexisting hypocalcaemia.

The sample size was calculated using the formula,

$$N = \frac{4PQ}{d^2},$$

where,

P denotes the prevalence of hypocalcaemia after total thyroidectomy in patients with Hashimoto's thyroiditis according to the study by Nair et al hypocalcaemia following total thyroidectomy; an analysis of 806 patients which was equal to 33 %,

$Q = 100 - P$,

d is allowable error which was taken as 20% of P.

The calculated sample size was 203. Our institute had only 100 cases of Hashimoto's thyroiditis in the year proposed for the study, hence sample size was taken as 100.

Preliminary work up included complete clinical examination, biochemical assay of the thyroid hormone profile and ultrasound imaging of the thyroid gland and neck. Aspiration cytology was done from all solitary nodules and nodules showing suspicious features of malignancy. Contrast enhanced computerized tomography was done when the goiter showed clinical evidence of retrosternal extension. The patients were rendered euthyroid prior to surgery. Vocal cords were assessed prior to surgery with direct laryngoscope.

Operation was performed by the members of the surgical team under general anesthesia. The lateral mobilization was done by capsular dissection technique identifying the

parathyroid glands and recurrent laryngeal nerves. The parathyroid glands were inspected for signs of injury or ischemia before closure and auto transplantation into the sternocleidomastoid was done if the viability was suspicious. Vocal cords were assessed during extubation.

Corrected serum calcium was measured on the postoperative day 1 and day 2. Hypocalcaemia is defined as the corrected serum calcium below 8 mg/dl. Hypocalcemic patients were treated with oral calcium supplementation along with calcitriol. For those who developed neuromuscular and cardiac symptoms intravenous calcium gluconate was given. Patients who had hypocalcaemia was followed up after 2 weeks with corrected serum calcium levels to look for recovery.

A total number of 100 patients were studied who showed features of thyroiditis on fine needle aspiration who underwent total thyroidectomy. Variables collected included the corrected serum calcium levels at 24 hours, 48 hours and 2 weeks after surgery. It also included the age and sex of the patient and the thyroid status of the patient prior to correction.

Analysis was done using CSC sepi-info software. Qualitative data were analyzed with Chi-square test. Z test and ANOVA test were employed to evaluate the quantitative data.

RESULTS

A total number of 100 patients with Hashimoto's thyroiditis with a mean age of 37 who underwent total thyroidectomy were included in the study. The sex ratio studied was 1:5.67 in favor of the females.

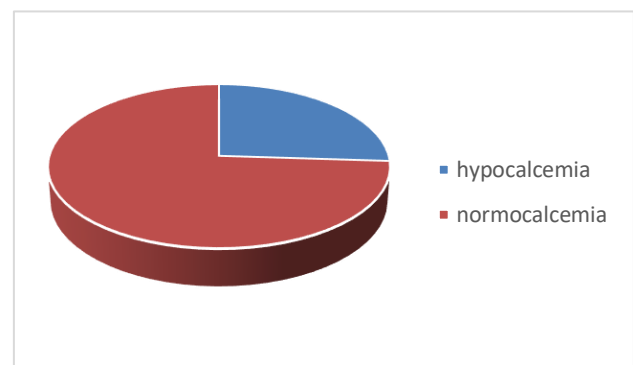


Figure 1: Incidence of hypocalcemia.

Of the 100 patients 32 showed clinical features suggestive of hypocalcaemia but only 26 showed biochemical correlation with low serum calcium levels on the first postoperative day. Hence the incidence of hypocalcaemia was 26 percent with an odds ratio of 2.3 with 95 percent confidence interval. The association between thyroiditis and post thyroidectomy hypocalcaemia showed a significant association with a p value of less than 0.0001.

23 of the 26 patients with hypocalcaemia still remained hypocalcaemic even at 48 hours with a recovery of only 11.53 percent. At 2 weeks only 10 remained hypocalcaemic with a recovery seen in 61.53 percent of the patients.

Among 26 patients who developed hypocalcaemia in the postoperative period, 16 (61.54%) patients were hyperthyroid as per the preoperative thyroid function test and 10 patients were euthyroid.

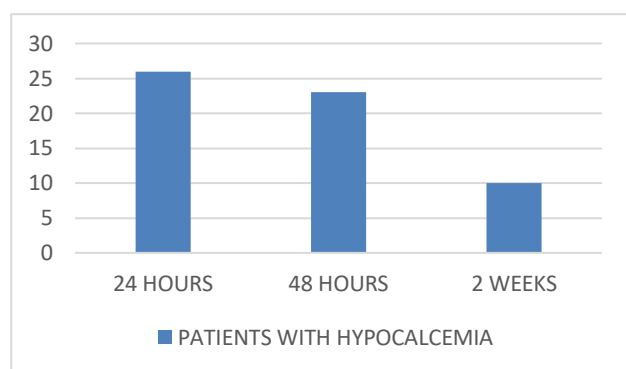


Figure 2: Patients with hypocalcemia.

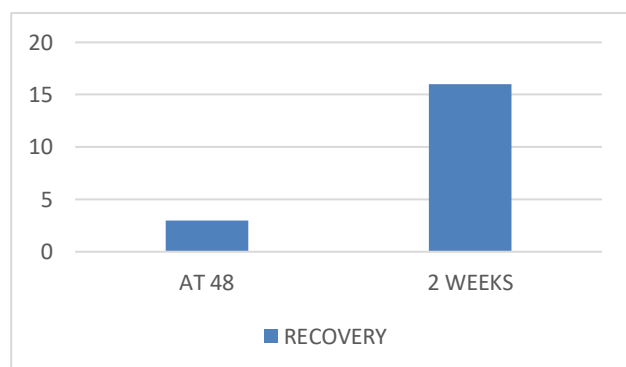


Figure 3: Recovery.

DISCUSSION

Hashimoto's thyroiditis is a commonly occurring painless, diffuse enlargement of the thyroid gland and are often euthyroid. Some may develop hypothyroidism. The incidence of Hashimoto's thyroiditis is unknown but is considered to be 0.3-1.5 cases per 1000 population. It is 15 to 20 times more frequent in women and is more common in the 4th and the 5th decade of life.¹ Hashimoto reported the first series of thyroid goiters featuring chronic lymphocytic thyroiditis in 1912. Hashimoto's thyroiditis is also known as autoimmune thyroiditis or chronic lymphocytic thyroiditis.³

This study showed a sex ratio of 1:5.67 in favor of females for thyroiditis and in case of Hashimoto's thyroiditis it was almost 6 times more common in females. Almost all the patients with Hashimoto's

thyroiditis belonged to the age group between 30 to 50 years.

Genetic predisposition along with environmental and endogenous factors decided the susceptibility to autoimmune thyroiditis. HLA-DR3, HLA-DR4, HLA-DR5 were studied for associations with Hashimoto's thyroiditis. Increasing age, female sex, infections, iodine intake and novel immunotherapeutic agents were also considered responsible for the etiology of the disease.⁴ Calder et al had suggested that antibody dependent and lymphocyte mediated cytotoxicity might be involved in the pathogenesis of thyroiditis.⁵ Although antimicrosomal antibodies had some cytotoxic potential to the thyroid cells, they were less common than antithyroglobulin antibodies. Hence it was not clear as to whether the antibodies were harmful to the gland.⁶

On histopathologic examination, lymphoplasmocytic infiltration consisting of lymphocytes and plasma cells usually arranging themselves into well-developed germinal centers with central macrophages were noted in the thyroid stroma between the atrophic thyroid follicles. In the fibrosing variant, the thyroid architecture was destroyed with marked follicular atrophy, dense keloid like fibrosis and prominent squamous metaplasia.² The thyroid cells were slightly larger and assume acidophilic staining and were packed with mitochondria called Hurthle cells or Askanazy cells.¹

Although most patients were asymptomatic, some develop flu like symptoms and some local symptoms like pain radiating to the ear, choking, hoarseness of voice, dysphagia and dyspnea. Clinically the thyroid may appear enlarged and firm and may be confused for malignancy. About 20 percent may show hypothyroidism and most of them were positive for anti TPO and TG antibodies. Some even showed antibodies against TSH receptor while a few may remain sero negative.^{3,4} Radio iodine uptake scan reveals a heterogeneous intake of iodine-hill and valley distribution. Iodine perchlorate test was usually abnormal.⁶ The diagnosis can be made clinically. Needle biopsy of the thyroid gave the diagnosis of thyroiditis with 90 percent accuracy.⁷

The mainstay of the treatment of Hashimoto's thyroiditis was treating the hypothyroidism. This was done with thyroid hormone replacement. The standard dose of thyroid replacement was 1.6-1.8 mcg/kg/day. There was very little evidence to support anti-inflammatory diet for treating thyroiditis.⁸ The suspicion of malignancy was the main reason for opting thyroidectomy as a treatment option in Hashimoto's thyroiditis. Surgery was also indicated in cases if significant pain, cosmetic or pressure symptoms remained after a fair trial of thyroid therapy with or without steroid therapy. Thyroidectomy reduced the local symptoms of thyroiditis, but the effects on the systemic effects were varied.^{1,3}

During thyroidectomy in Hashimoto's thyroiditis the thyroid was found to be firm and enlarged with adhesions to the adjacent structures. There may be numerous enlarged regional lymph nodes. Hence thyroidectomy in thyroiditis was expected to cause more surgical complications such as hypoparathyroidism and vocal cord palsy.³

Kocher identified recurrent laryngeal nerve injury, myxedema and tetany as the main three postoperative complications of thyroidectomy as early as in 1883. Initially tetany was attributed to the deficiency of thyroid gland until Moussu could relieve the symptoms with an aqueous extract from the parathyroid glands in 1898.⁹

Hypocalcaemia is a common complication after thyroidectomy and usually occurs within the first few days after the surgery.¹⁰ The incidence of transient hypoparathyroidism following thyroidectomy was between 6.9 and 49 percent and that of permanent hypoparathyroidism was between 0.4 and 33 percent. Hypocalcaemia can be symptomatic, manifesting 24-48 hours after surgery or asymptomatic.^{10,11} This study showed an incidence of hypocalcaemia in 26 percent of the subjects studied and persistent hypocalcaemia at 2 weeks in 10 percent of the subjects. Sometimes patients may develop features suggestive of hypocalcaemia but the corrected serum values may remain normal.¹² Even though 32 of them showed symptoms suggestive of hypocalcaemia only 26 could be verified by biochemical analysis.

The hypocalcaemia was a manifestation of injury to the parathyroid gland or their blood supply during thyroidectomy. The mechanism of hypocalcaemia after thyroidectomy was considered multifactorial-surgical technique, iatrogenic trauma to the parathyroid, extent of thyroidectomy, hyperthyroidism, malignancy, presence of thyroiditis, no of parathyroid gland identified during surgery can be considered as etiological factors.^{10,13} The parathyroid gland secreted parathormone which mobilized calcium from bone, reabsorbed calcium from distal nephron and stimulated renal 1 α -hydroxylase activity thereby maintaining the calcium homeostasis in the body. Symptoms of hypocalcaemia included paresthesia, cramps or tetany. Some can present acutely with bronchospasm, laryngospasm or arrhythmias.¹⁴

Other causes of hypocalcaemia post thyroidectomy included alkalosis induced hypocalcaemia resulting from hyperventilation triggered by postoperative pain and hence causing dilutional hypocalcaemia. Vitamin D deficiency, an acute increase in serum calcitonin levels due to handling of the thyroid gland or hungry bone syndrome were also believed to contribute to this process.¹⁰

In this study we studied 100 patients with Hashimoto's thyroiditis and we found that a higher number of patients developed hypocalcaemia with an incidence of 26 percent

compared to 32.1% in a previous study conducted by Shih et al.³ Incidence of hypocalcaemia in an Indian study by Nair et al in patients who underwent thyroidectomy for Hashimoto's thyroiditis was 33.33%.⁹ This may be because patients with Hashimoto's thyroiditis were more susceptible to injury to the parathyroid glands due to the inflammation or due the additional retraction required to mobilize the firmer than normal thyroid gland. Hence there was a significant risk of hypocalcaemia in patients with Hashimoto's thyroiditis after thyroidectomy.

Another study by Riju et al showed the time taken for return of normocalcaemia after total thyroidectomy in benign thyroid diseases was 48 hours in 85% and 2 weeks in 96%.¹⁶ In present study, only 11.53 percent patients returns to normocalcaemia after 48 hours and 61.53 percent at 2 weeks. It showed that the recovery to normocalcaemia was significantly delayed in thyroiditis patients compared to other benign thyroid diseases.

Patients who were hyperthyroid prior to surgery had higher risk of hypocalcaemia. Hyperthyroidism may lead on to loss of bone mineral density. Transient hypocalcaemia may be related to osteodystrophy seen in hyperthyroidism.¹⁵

Out of 100 patients with Hashimoto's thyroiditis, 10 patients (10%) showed persisting hypocalcaemia after 2 weeks. Retrospective analysis of the data showed that all 40% of this patients were having documented disease for more than 20 years. So present study was strongly suggestive that chance for developing permanent hypoparathyroidism increases with duration of disease.

Limitation

Even though the calculated sample size was 203, during the proposed year of study only 100 cases of Hashimoto's thyroiditis underwent total thyroidectomy for various indications.

CONCLUSION

Hashimoto's thyroiditis is more common in females and occurs in the 4th and 5th decade of life. Thyroidectomy is only rarely indicated and has higher risk of developing hypocalcaemia after the procedure. Adequate care should be given to identify and preserve the parathyroid glands during the surgery. Hence thyroidectomy should be resorted only for selected cases of Hashimoto's thyroiditis.

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