International Journal of Innovative Research in Medical Science (IJIRMS)
Volume 03 Issue 06 June 2018, ISSN No. - 2455-8737
Available online at - www.ijirms.in

Open Access Journal | Research Paper | DOI: 10.23958/ijirms/vol03-i06/05

Significance of Lymphocytic Infiltrate in the Development of Hypothyroidism Following Thyroidectomy for Benign Thyroid Lesions

Dr. Gloria Venissa Quadros[*1], Dr. Prema Saldanha[2], Ms. Mandara T. P.[3]

[1]Resident, Department of Pathology, [2]Professor, Department of Pathology, [3]MBBS Student
Yenepoya Medical College, Mangalore, 575018, Karnataka, India

Abstract

Multinodular Goitre (MNG) is a common disorder and the incidence of hypothyroidism following thyroidectomy varies in different studies. Of the many factors which determine the post-operative thyroid hypofunction, the presence of an inflammatory infiltrate in the thyroid gland may have a significant role. The objective was to study the association of post-operative hypothyroidism and lymphocytic infiltration in the thyroid gland. This was a retrospective study of patients who underwent thyroidectomy. Detection of hypothyroidism was based on thyroid function test values. The lymphocytic infiltrate within the thyroid gland was graded as 0,1,2,3 & 4. Correlations between the grade of lymphocytic infiltration and the patient's age, type of surgery and hypothyroid status was assessed. In our patients, 59 (57.2%) cases developed hypothyroidism post-operatively, of which 72.3% had a high lymphocytic grade. Out of the cases having a high lymphocytic infiltration who developed hypothyroidism, 63.8% were above 40 years of age. There was statistically significant correlation between the grade of lymphocytic infiltration and hypothyroid status post-operatively (p = 0.017). This suggests its role in the progressive development of post-operative hypothyroidism.

Keywords: Hypothyroidism, Lymphocytic infiltrate, Thyroidectomy

Introduction

Thyroid gland disease is considered to be the second most frequent endocrinological disease after diabetes mellitus.[1] Thyroidectomy is often performed for patients with nontoxic goitre. Hypothyroidism is an obvious sequela of near-total/subtotal thyroidectomy as well as total thyroidectomy, reported to occur in up to 60% of patients.[2] Hemithyroidectomy is also a common surgical procedure done in patients with a solitary thyroid nodule that is either symptomatic or suspicious of malignancy. The reported incidence of hypothyroidism following hemi thyroidectomy in various studies including those from India ranges from 5-6.5% to 35-60%.[1-8]

Hypothyroidism causes significant morbidity in the patient. It is important to identify clinical as well as subclinical hypothyroidism in patients following thyroid surgery. At the same time unnecessary supplementation with thyroid hormone is unwarranted as there are serious complications with this therapy. Various studies have found that there may be many factors which determine the development of thyroid hypofunction postoperatively. There is evidence to suggest that patients with glandular lymphocytic infiltration have an increased risk of developing hypothyroidism. This study was undertaken to assess the significance of lymphocytic infiltrate in the development of hypothyroidism following thyroidectomy.

Materials and Methods

Study Design: Retrospective analysis of patients' records and histopathology slides available in the archives of the Department of Pathology over a period of 28 months from January 2015 to May 2017.

Study Population: Patients who were admitted in our hospital and who underwent thyroidectomy.

Inclusion criteria:

- Patients who underwent thyroidectomy for benign thyroid lesions and who were euthyroid preoperatively.

Exclusion criteria:

- Patients with known hypothyroidism on thyroid hormone replacement therapy.
- Patients with known hyperthyroidism.
- Patients who underwent thyroidectomy/completion thyroidectomy for malignancy.
- Patients who were empirically started on thyroxine postoperatively.

Data Collection Procedure and Methodology:

Histopathological assessment: The thyroidectomy specimens are sent to the Department of Pathology in 10% formalin and are grossed according to the standard protocol. The tissue bits are paraffin embedded and the sections are stained with Haematoxylin and Eosin.

The slides from the benign thyroid lesions were retrieved from the archives and all the slides were carefully scrutinized for the presence of a chronic inflammatory cell infiltrate.

The presence and the degree of chronic (lymphocytic/lymphoplasmacytic) infiltration was recorded.

The degree of infiltration was subjectively quantified and graded into five grades as follows based on the methodology in previous studies:[1,3,14-17,22]

Grade 0 - Complete absence of glandular lymphocytic infiltration
Grade 1 - Scattered (minimal) lymphocytes
Grade 2 - Moderate number of lymphocytes (less than 4 aggregates* per high power field)
Grade 3 - Moderate to marked number of lymphocytes without the occurrence of germinal centres (four or more aggregates per high power field)
Grade 4 - Occurrence of diffuse infiltration and germinal centre formation (the diagnostic clue of lymphocytic thyroiditis)

*An aggregate was defined as a focus with approximately 50 or more lymphocytes.

Biochemical values: Details of the thyroid function tests (serum levels of total triiodothyronine T3 and thyroxine T4, and TSH [thyroid stimulating hormone]) were obtained from the patients' records. The normal levels considered in our hospital laboratory are T3 - 0.97 - 1.69 nanogm/ml; T4 - 5.5 - 11 microgm/dl; TSH - 0.4 - 4.6 mIU/L.

Statistical Tool: Application of Chi Square test using SPSS package version 22.

Ethical clearance: The study was started after obtaining permission from the Institutional Ethics Committee (IEC).

Results

During the study period, 152 patients underwent thyroidectomy for benign thyroid lesions. Out of these, 49 were excluded from the study as they did not return to the hospital after thyroidectomy.

A total of 103 patients satisfied the inclusion-exclusion criteria described in the methodology. The age of the patients ranged from 19-76 years, with a female: male ratio of 10.4:1.

There were 62 cases diagnosed as multinodular goitre, 14 cases of solitary colloid nodule, 6 cases of follicular adenoma, and 14 cases of Hashimoto's thyroiditis. Sixty eight patients had subtotal thyroidectomy and thirty five patients underwent hemithyroidectomy.

The thyroid function tests results were categorised as hypothyroid, and normothyroid. Of these patients, 59 (57.2%) cases developed hypothyroidism post-operatively, and 44 cases remained normothyroid. The detailed evaluation of the cases is shown in Table 1.

Histopathological assessment of the degree of lymphocytic infiltration was done and arbitrarily categorised into low (Grade 0 - Complete absence of glandular lymphocytic infiltration, Grade 1 - Scattered (minimal) lymphocytes and Grade 2 - Moderate number of lymphocytes i.e. less than 4 aggregates* per high power field) and high (Grade 3 - Moderate to marked number of lymphocytes without the occurrence of germinal centres and Grade 4 - Occurrence of diffuse infiltration and germinal centre formation) grades. Figures 1 & 2 show low grade and high grade lymphocytic infiltrates respectively.

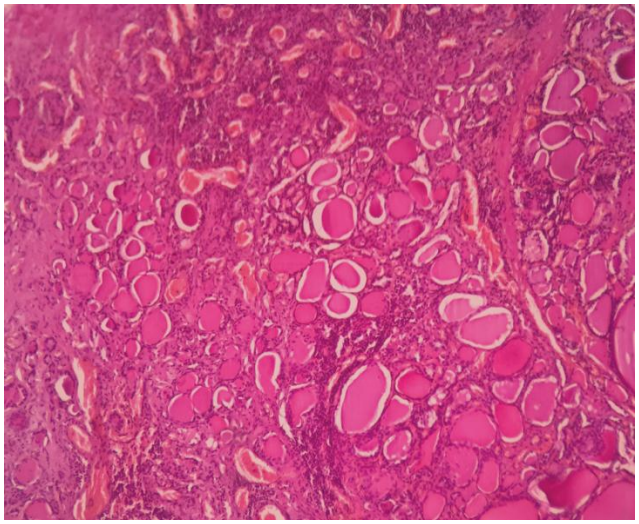

Figure 1: showing a low grade lymphocytic infiltrate in a multinodular goitre [H&E x100]

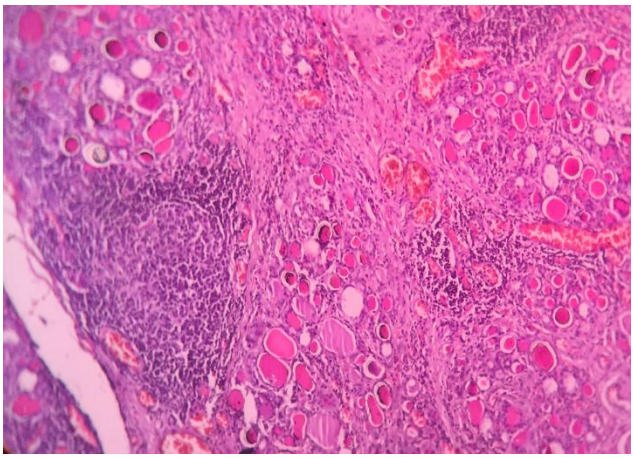

Figure 2: showing a lymphoid follicle with germinal centre (high grade) [H&E x100]

Evaluation of the lymphoid infiltrate showed 46 cases (Grade 3 = 25 cases and Grade 4 = 21 cases) with a significant (high) lymphocytic infiltrate and 57 cases (Grade 0 = 3 cases and Grade 1 = 30 cases, Grade 2 = 24 cases) with a mild (low) degree of lymphocytic infiltration.

Majority (72.3 %) of the patients who had a high degree of lymphocytic infiltration were found to have developed hypothyroidism post-operatively.

Table 1: showing details of the cases in the various categories.

		High grade lymphocytic infiltrate (n=47)			Low grade lymphocytic infiltrate (n=56)			
		Hypothyroid (n=34)	Normo thyroid (n=13)		Hypo thyroid (n=25)	Normo thyroid (n=31)		
Age	**≤ 40**	13	4	17	14	14	28	45
	>40	21	9	30	11	17	28	58
Gender	**Female**	32	12	44	21	29	50	94
	Male	4	2	6	2	1	3	9
Thyroid-ectomy	**Sub-total**	25	9	34	18	16	34	68
	Hemi	9	4	13	7	15	22	35

The ages of the patients with hypothyroidism ranged from 19 – 76 years and in the normothyroid case it was 19-58 years. There was only minimal difference in the age distribution. Out of the cases having a high lymphocytic infiltration who developed hypothyroidism, 63.8% were above 40 years of age. Out of 9 male patients, 6 showed high grade lymphocytic infiltration and were found to be hypothyroid.

There was statistically significant correlation between the grade of lymphocytic infiltration and hypothyroid status post-operatively (p = 0.017). There was no statistically significant correlation between whereas the patient's age and type of thyroid surgery, and the development of postoperative hypothyroidism.

Discussion

Nontoxic goitre is a common disorder of the thyroid gland and thyroidectomy is often performed for these patients. Hypothyroidism is a potentially debilitating consequence of thyroid surgery and occurs postoperatively in most patients who have undergone subtotal thyroidectomy and many patients with hemithyroidectomy. The hypothyroidism may be clinical or subclinical. Subclinical hypothyroidism remains undetected for a long period of time as the patient does not come for medical help unlike in the case of patients with overt symptoms. Also the symptoms in subclinical hypothyroidism may be nonspecific. The incidence of hypothyroidism following thyroidectomy in various studies ranges from 5-6.5% to 35-60%. This depends on how the investigators define hypothyroidism and also on the duration of follow-up.[1-8] The occurrence of hypothyroidism significantly affects the postoperative outcome and the patient's quality of life.

Studies have found that there may be many factors which determine the thyroid function. At present, there is evidence to suggest that patients with glandular lymphocytic infiltration have an increased risk of developing hypothyroidism.[1-3,5,10-24] Some of these studies recorded only the presence or absence of the lymphoid infiltrate,[2,5,10-13] but in some others a semi-quantitative analysis in the form of histopathological grading of the lymphocytic infiltrate was performed.[1,3,14-16] This semi-quantitative analysis was also followed in our study as it results in a more objective method of assessment.

One study found that the impact of lymphocytic infiltrate on hypothyroidism after thyroidectomy was age dependent.[3] The predictive value of lymphocytic infiltration on development of post-operative hypothyroidism was found to be most useful in younger patients.[3] Age as a factor was taken into account in other studies, but there was found to be no statistical significance.[1,2,10,18,19] In our study we found that there were more number of patients above the age of forty years than younger patients.

Gender was not found to be statistically significant in those studies were it was taken into account as a factor influencing post-operative hypothyroidism.[1,2,10,18,19] In our study 94 (91.2%) of the patients were female. Six out of the nine male patients showed high grade lymphocytic infiltration and were found to be hypothyroid or had normal thyroid function status.

The indication for surgery was considered in one study, but was not statistically significant.[1] The type of surgery was not found to be statistically significant in the studies where it was taken into account.[14,21] The side of the hemithyroidectomy was found to be statistically significant in one study.[1] In our study, majority of the patients underwent subtotal thyroidectomy. Also the relationship to the presence of the lymphoid infiltrate was not statistically significant in these cases.

Studies found that there was a significant difference in thyroid function postoperatively between patients with no

or, only a slight degree of chronic inflammation, and patients with pronounced inflammation. This indicates that histologic grading of lymphocytic infiltration in the thyroid gland may be useful for predicting the risk of postoperative hypothyroidism. High lymphocytic infiltration in the resected gland increased the risk of post-operative hypothyroidism.[1-3,5,10-24] The presence of thyroiditis in the excised lobe in hemithyroidectomy would imply its presence in the opposite lobe. Therefore, such patients would definitely be at a higher risk of developing post-operative hypothyroidism.[6] Similar to these observations in nodular goitre, presence of lymphocytic infiltrate in patients operated on for Graves' disease had a higher risk of developing post-operative hypothyroidism[16]

In our study majority (72.3%) of the patients who had a high degree of lymphocytic infiltration were found to have developed hypothyroidism post-operatively. The grade of lymphocytic infiltration and hypothyroidism were found to be statistically significant in our study. Similar findings were seen in many studies where there were a large number of patients with high grade lymphocytic infiltration developing postoperative hypothyroidism.[10,15,16,18,21,22]

Conclusion

The lymphocytic infiltration of the thyroid tissue in pathologic specimens has been found to be an important risk factor for post-thyroidectomy hypothyroidism where the strongest association was found in some studies.[10,15,16,18,21,22] Lymphocytic infiltrate may help predict those who will become hypothyroid. The information may be helpful as a method of assessing postoperative hypothyroidism after hemithyroidectomy.[3] It may be prudent to consider the degree of lymphocytic infiltration when arranging patient follow-up and advisable to resort to early hormone replacement therapy in patients with lymphocytic infiltration before development of the signs and symptoms of hypothyroidism.[16]

Sources of Support: Part of this study was selected in ICMR – STS 2017-01744

References

[1] DeCarlucci D, Tavares MR, Obara MT, Martins LAL, Hojaij FC, Cernea CR. Thyroid Function After Unilateral Total Lobectomy. Risk Factors for Postoperative Hypothyroidism. Arch Otolaryngol Head Neck Surg 2008; 134: 1076-9.

[2] McHenry CR, Slusarczyk SJ. Hypothyroidisim following hemithyroidectomy: Incidence, risk factors, and management. Surgery 2000; 128: 994-8.

[3] Piper HG, Bugis SP, Wilkins GE, Walker BAM, Wiseman S, Baliski CR. Detecting and defining hypothyroidism after hemithyroidectomy. Am J Surg 2005; 189: 587-91.

[4] Vaiman M, Nagibin A, Hagag P, Kessler A, Gavriel H. Hypothyroidism following partial thyroidectomy. Otolaryngol Head Neck Surg 2008; 138: 98–100.

[5] Stoll SJ, Pitt SC, Liu J, Schaefer S, Sippel RS, Chen H. Thyroid hormone replacement after thyroid lobectomy. Surgery 2009; 146: 554-60.

[6] Chu KK-W, Lang BH-H. Clinicopathologic predictors for early and late biochemical hypothyroidism after hemithyroidectomy. Am J Surg 2012; 203:461-6.

[7] Dympep B, Kakar AK, Tanwar R, Shankar RL, Sen IB, Belho ES. Postoperative hypothyroidism after thyroidectomy for nontoxic multinodular goitre: Can we prevent it by leaving more?. Thyroid Res Pract 2014; 11: 49-54.

[8] Pradeep PV. Post Hemi Thyroidectomy Hypothyroidism: Risk Factors and Course. BMH Med J 2014; 1: 3-8.

[9] Nagarkar R, Roy S, Akheel M, Palwe V, Kulkarni N, Pandit P. Incidence of Thyroid Disorders in India: An Institutional Retrospective Analysis. Int J Dent Med Spec 2015; 2: 19-23.

[10] Seiberling KA, Dutra JC, Bajaramovic S. Hypothyroidism following hemithyroidectomy for benign nontoxic thyroid disease. Ear Nose Throat J 2007; 86: 295-9.

[11] Verloop H, Louwerens M, Schoones JW, Kievit J, Smit JWA, Dekkers OM. Risk of Hypothyroidism following Hemithyroidectomy: Systematic Review and Meta-Analysis of Prognostic Studies. J Clin Endocrinol Metab 2012; 97: 2243–55.

[12] Rosai J. Thyroid gland. In: Rosai & Ackerman's Surgical Pathology. 10th ed. Mosby Elsevier, New Delhi. 2012: 528.

[13] Miller FR, Paulson D, Prihoda TJ. Risk factors for the development of hypothyroidism after hemithyroidectomy. Arch Otolaryngol Head Neck Surg 2006; 132; 36-8.

[14] Bang U, Blichert-Toft M, Petersen PH, Nielsen BB, Hage E, Diederichsen H. Thyroid function after resection for non-toxic goitre with special reference to thyroid lymphocytic aggregation and circulating thyroid autoantibodies. Acta Endocrinol (Copenh) 1985; 109: 214-9.

[15] Berglund J, Bondeson L, Christensen SB, Tibblin S. The influence of different degrees of chronic lymphocytic thyroiditis on thyroid function after surgery for benign, non-toxic goiter. Eur J Surg 1991; 157: 257-60.

[16] Lankarani M, Mahmoodzadeh H, Poorpezeshk N, Soleimanpour B, Haghpanah V, Heshmat R, et al. Hypothyroidism following thyroid surgery. Acta Medica Iranica 2008; 46: 225–32.

[17] Koh YW, Lee SW, Choi EC, Lee JD, Mok JO, Kim HK. Prediction of hypothyroidism after hemithyroidectomy: a biochemical and pathological analysis. Eur Arch Otorhinolaryngol 2008; 265: 453.

[18] Johner A1, Griffith OL, Walker B, Wood L, Piper H, Wilkins G, et al. Detection and management of hypothyroidism following thyroid lobectomy: evaluation of a clinical algorithm . Ann Surg Oncol. 2011 Sep;18(9):2548-54. doi: 10.1245/s10434-011-1627-1. Epub 2011 Mar 10.

[19] Su SY, Grodski S, Serpell JW. Hypothyroidism following hemithyroidectomy: a retrospective review. Ann Surg 2009; 250: 991-4.

[20] Spanheimer PM, Sugg SL, Lal G, Howe JR, Weigel RJ. Surveillance and intervention after thyroid lobectomy. Ann Surg Oncol 2011; 18: 1729–33.

[21] Wormald R1, Sheahan P, Rowley S, Rizkalla H, Toner M, Timon C Hemithyroidectomy for benign thyroid disease: who needs follow-up for hypothyroidism? Clin Otolaryngol. 2008 Dec; 33(6):587-91. doi: 10.1111/j.1749-4486.2008.01794.x.

[22] Lee J. Hypothyroidism after Hemithyroidectomy: Incidence, Risk Factors. 2012. https://www.intechopen.com/download/pdf/27823.

[23] Kandil E, Krishnan B, Noureldine SI, Yao L, Tufano RP. Hemithyroidectomy: a meta-analysis of postoperative need for hormone replacement and complications. J Otorhinolaryngol Relat Spec. 2013; 75:6-17.

[24] Okayasu I, Hara BY, Nakamura K, Rose NR. Racial and age related differences in incidence and severity of focal autoimmune thyroiditis. Am J Clin Pathol 1994; 101: 698-702.

