

Lymphocytic Thyroiditis with Associated Lesions in Coastal Areas of Alappuzha - A 2-Year Study

K. Jayasree¹, T S. Sudhiraj², M B. Jayaraman³

¹Assistant Professor, Department of Pathology, Government Medical College, Thrissur, Kerala, India, ²Assistant Professor, Department of Community Medicine, Government Medical College, Thrissur, Kerala, India, ³Associate Professor, Department of Radiotherapy, Government Medical College, Thrissur, Kerala, India

Abstract

Introduction: The prevalence of goiter and thyroid disorders is influenced by low iodide intake as seen in areas far remote from seacoast. Around 400 cases of goiter were reported in MCH, Alappuzha, every year. The present study was done to know the increase in lymphocytic thyroiditis (LT) cases and associated lesions like coexistent papillary carcinoma in such iodine sufficient coastal areas.

Aim: This study aims to assess the frequency of LT and study the associated lesions.

Methods: The study was done in all thyroidectomy specimens during a period of 2 years. Clinical details were collected with a standard pro forma. Specimens were fixed with 10% formalin and histological sections were stained with hematoxylin and eosin. Grading of LT was done using histologic criteria of Williams and Doniach.

Results: Of the total biopsies received in our Histopathology Department (TDMC, Alappuzha) in a 2-year period (2005 and 2006), 5.19% were thyroid lesions and among the total 683 thyroidectomy specimens, LT constituted 208 cases (30.45%). In our study, incidence of LT in females is 18.63% compared to males 0.874% and the age peaked around 3rd–4th decade. The major proportion (96.4%) belongs to the very severe (Grade 4) category. In our study, out of the 58 carcinomas, 51 were papillary thyroid carcinomas and 26 of them had coexistent lymphocytic thyroiditis.

Conclusion: The increased frequency of LT in coastal areas of Alappuzha may be due to excess intake of iodide. Prognostic influence of papillary carcinoma in coexistent lesions has to be studied further. Iodine supplementation should be maintained at a safe level to prevent autoimmune diseases.

Key words: Coastal areas, Iodide, Lymphocytic thyroiditis

INTRODUCTION

The prevalence and spectrum of thyroid disorders are influenced by various environmental factors, the most important being low iodide intake.^[1] The high incidence of goiter among the people in remote hilly areas, far remote from seacoast has been found to be apparently associated with this problem.^[2] Studies indicated that the environmental occurrence of iodine in these areas is relatively much lower as reflected in its content in soil, water, and the

common food items that people consume.^[3] Conversely, iodine as a micronutrient is abundantly available in coastal areas.^[4] Alappuzha is a coastal district, a narrow strip of land covering an area of 200 sq. km. Arabian sea forms the western boundary. Vast majority of the people in this area are non-vegetarian with a high per capita consumption of seafood, particularly fish. It is found that Indian marine fishes are rich in iodine content.^[5] However, it is observed that the incidence of goiter is very high among the people of this district. A total of about 350–400 cases are reported in the Department of Pathology, TDMC, Alappuzha, every year. This accounts for >17% of all the major surgeries done in MCH, Alappuzha. Among these thyroid lesions, the frequency of lymphocytic thyroiditis (LT) was found to be increased. Reports are available which indicates that high intake of iodide can induce thyroid autoimmunity and that iodide prophylaxis by salt iodization can result in higher prevalence of lymphocytic thyroiditis.^[6] It is well known

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Corresponding Author: Dr. T S. Sudhiraj, Department of Community Medicine, Government Medical College, Thrissur, Kerala, India

that LT can predispose to malignant lesions of thyroid, especially papillary thyroid carcinoma.^[7]

Aim

This study aims to assess the frequency of thyroiditis among thyroidectomy specimens and to study the associated lesions in lymphocytic thyroiditis.

MATERIALS AND METHODS

The study was done in all thyroidectomy specimens obtained in the histopathology division of the Department of Pathology, Medical College, Alappuzha, during a period of 2 years. Clinical details were collected directly from patients with a standard pro forma with regard to intake of iodized salt and their residential locality. Surgically removed thyroid specimens were fixed with 10°/0 formalin. Histological sections were obtained from the largest cut surface of the fixed materials. All whitish granular areas, nodules, and fibrotic areas were specifically studied to rule out malignancies and LT, respectively. The specimens stained with hematoxylin and eosin were used for analysis. Separate grading was done according to the severity of lymphocytic thyroiditis. The histologic criteria were those of Williams and Doniach. A “focus” was defined as an aggregate of 50 or more lymphocytes.

RESULTS

Of the total biopsies received in our Histopathology Department (TDMC) in 2-year period, 5.19% were thyroid lesions [Table 1]. Among the total major surgeries, thyroidectomy constituted 17.44% where it was next to appendicectomies (20.47%) [Figure 1].

Among the total of 683 thyroidectomy specimens studied in a 2-year period (2005 and 2006), LT constituted 208 cases (30.45%). In our study, incidence of LT in females is 18.63% compared to males 0.874% and the age peaked around 3rd–4th decade [Tables 2 and 3]. No single case of LT was not at below the age of 20 years age group of either gender.

The major proportion (96.4%) belongs to the very severe (Grade 4) category and the rest (3.6%) to the severe (Grade 3) category. 96% of the subjects were taking non-vegetarian diet and consumed lots of fish, which had high iodine content. Along with which we noticed, 94.6% of the patients had iodized salt in their staple food. TFT status, we assessed the T3, T4, and thyroid-stimulating hormone (TSH) values in 65% of the patients. Of this, 63.5% of patients had value confined to the normal range.

Table 1: Number of thyroid lesions in total biopsies

| Year | Biopsy | Thyroid lesion | Percentage |
|-------|--------|----------------|------------|
| 2005 | 7027 | 417 | 5.93 |
| 2006 | 7075 | 315 | 4.45 |
| Total | 14102 | 732 | 5.19 |

Table 2: Frequency of various thyroid lesions

| Lesions | Year | | Total | Percentage |
|-------------------------|------|------|-------|------------|
| | 2005 | 2006 | | |
| Nodular colloid goiter | 252 | 172 | 424 | 62.08 |
| Diffuse colloid goiter | 19 | 11 | 30 | 4.39 |
| Hashimoto's thyroiditis | 35 | 40 | 75 | 10.48 |
| Lymphocytic thyroiditis | 30 | 31 | 61 | 8.93 |
| Toxic goiter | 4 | 3 | 7 | 1.02 |
| Malignancies | 42 | 23 | 65 | 9.51 |

Table 3: Mean age and sex ratio of different thyroid lesions

| Type of thyroid disease | Mean (Years) age | | Sex ratio |
|-------------------------|------------------|-------|-----------|
| | M | F | |
| Nodular colloid goiter | 43.68 | 39.97 | 1:10.8 |
| Diffuse colloid goiter | 35.5 | 31.8 | 1:9 |
| Hashimoto's thyroiditis | 45.5 | 39.25 | 1:23 |
| Lymphocytic thyroiditis | 25.5 | 39.57 | 1:29.5 |
| Adenoma | 35.5 | 37.5 | 1:8.3 |
| Papillary carcinoma | 45.5 | 39.94 | 1:7 |

Rest 15 had borderline and 0.5% showed increased values of TSH only.

In our study, out of 58 carcinomas, 51 were papillary thyroid carcinomas and 26 of them had coexistent lymphocytic thyroiditis Table 4. 9 of 59 carcinomas were microcarcinomas and were of papillary type. There were two cases of malignant lymphomas in our study. Three medullary carcinomas were reported among which two were associated with lymphocytic thyroiditis.

DISCUSSION

Of the total biopsies received in our Histopathology Department (TDMC) in 2-year period, 5.19% were thyroid lesions. Among the total major surgeries, thyroidectomies constituted 17.44% where it was next to appendicectomies (20.47%).

Among the total of 683 thyroidectomy specimens studied in a 2-year period (2005 and 2006), LT constituted 208 cases (30.45%). This incidence shows a significant increase compared to the observed value done in a similar study in Calicut Medical College, 2 years earlier (5.2% for a 3-year period 2001–2003).^[8] Previous studies done by Okayasu *et*

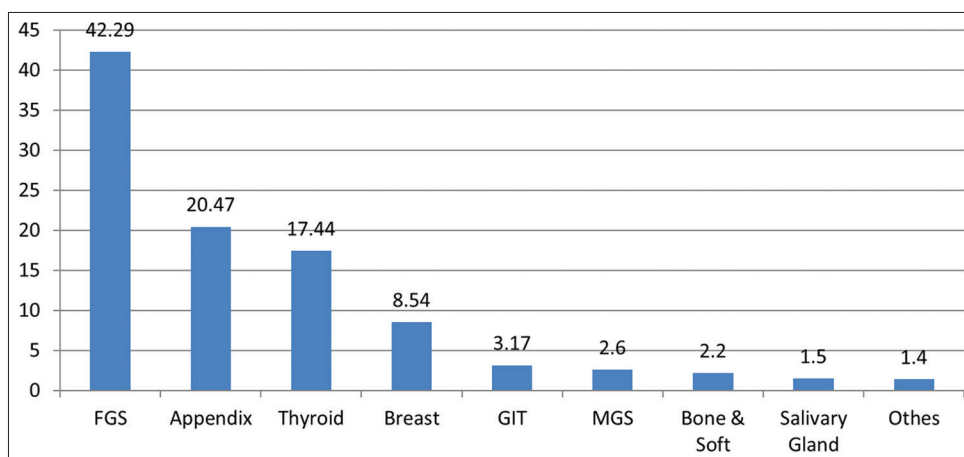


Figure 1: Thyroidectomies as proportion of major surgeries (%)

al. also show an increased incidence of LT in subjects aged >20 years (41.4% in American females, 7.4% in African Americans females).^[9,10]

In our study, incidence of LT in females is 18.63% compared to males 0.874% and the age peaked around 3rd–4th decade. This incidence is in concordance with studies done by Loh K *et al.* (1999).^[7] Studies done in the post-iodination phase in Delhi by Marwaha *et al.* (2000) also showed Hashimoto thyroiditis predominant in older girls (6.6%) compared to younger (4.2%).^[11]

Another reported study from Europe (Pescopagano, Italy) showed an overall prevalence of autoimmune thyroiditis (AIT) of 12.6% with females - 17.3% and males - 7%; this study showed a prevalence of 3.5% in children. However, in our study, no single case of LT was not at below the age of 20 years age group of either gender.

Cases were graded according to the degree of severity of the lymphocytic infiltration (Williams and Doniach).^[12]

The major proportion (96.4%) belongs to the very severe (Grade 4) category and the rest (3.6%) to the severe (Grade 3) category. This shows that the lymphocytic infiltration was significant in our cases.

As the specimens were from patients mostly residing in the coastal areas of Alappuzha district, the study was concentrated on dietary factors. Here, 96% of the subjects were taking non-vegetarian diet and consumed lots of fish, which had high iodine content. Along with which we noticed, 94.6% of the patients had iodized salt in their staple food.

Marine products such as shellfish and crustaceans are rich in iodine content. It was found that Indian marine fish are rich in iodine content (means of 193+82g/100g on wet weight basis).

Table 4: Relative frequency of different malignant lesions

| Type (carcinoma) | Year | | Total | % |
|------------------|------|------|-------|------|
| | 2005 | 2006 | | |
| Papillary | 31 | 20 | 51 | 8.35 |
| Follicular | 1 | 2 | 3 | 0.04 |
| Medullary | 1 | 2 | 3 | 0.04 |
| Anaplastic | 1 | 0 | 1 | 0.02 |

Furthermore, the iodine content of shellfish and crabs (0.7–2.5 mg/100 g on wet weight basis) was higher than that of other fish.

It was seen by the Mizukami Y *et al.* that in 28 patients on exposure to excess dietary iodide, 13 patients had lymphocytic infiltration, and among them, 25 patients developed moderate to marked follicular hyperplasia.^[13] Similar studies done by Konno *et al.* in coastal areas of Japan which were previously iodine deficient, showed an increase in LT after iodine repletion.^[14] Japanese population is well known for consuming seaweeds (kelp) and reef fish having high iodine content. The daily iodine intake of Japanese is to the tune of 2000–3000 mg/day.

Studies done by Harach *et al.* in a 2-year period showed the frequency of moderate-to-severe LT in females rose from 2 to 12% (16%) in iodine pre-prophylaxis period to 34–114 (28 N in the past 25 years iodine prophylaxis).^[15] It has been found that the predominant lesion in school children in Greece, which was previously an endemic area, now in the post-iodization phase is autoimmune thyroiditis.^[16]

Similar studies in done in American workers in West Africa who were exposed to excess iodine through water purification units had an increased incidence of LT. However, on

removal of excess iodine, their free T4 value increased from 32.2 to 34.7 p mol/1 (normal value 22.5–49 p mol/1) - and TSH values decreased from 4.9 to 1.8 mU/K (normal value 0.4–4.2mU/L). There was no change in TFT values during sustained exposure to iodine. They formulated that acute excess of iodine results in decreased iodine organification (Wolff–Chaikoff effect). On sustained excess iodine exposure, usually, there is an escape from this effect which involves a decrease in Na/I symporter protein resulting in decreased thyroid iodine content. In some individuals, escape phenomenon would not occur and so develop iodine-induced hypothyroidism. Thus, iodine-induced hypothyroidism is reversible. This phenomenon is evidenced by the normal TFT values obtained in majority of the patients in our study. Same reasoning can be applied in studies done in Eastern Black Sea region in Turkey, which is an iodine sufficient area.^[17] In a 10-year follow-up study, Sato *et al.* found that 66.2% of their patients with Hashimoto's thyroiditis remained euthyroid and only 27% turned into hypothyroids.^[18]

In our study, out of 58 carcinomas, 51 were papillary thyroid carcinomas and 26 of them had coexistent lymphocytic thyroiditis. The incidence peaked around 30–50 years age group with a female preponderance as was shown in other studies.

Nine of 59 carcinomas were microcarcinomas and were of papillary type. Studies show association between iodine and carcinoma.^[19] Whether iodide has direct influence on the development of papillary carcinoma has to be studied further. Furthermore, being an iodine sufficient area and the major group of carcinomas occupied by papillary type, earlier studies have to be reviewed. These reveal that the tumor types and sex ratio distribution were modified after the introduction of iodine of the prophylaxis. More differentiated types emerged with a concurrent drop in undifferentiated aggressive types.^[20]

There were two cases of malignant lymphomas in our study. Both were associated with LT and satisfied the criteria put forth by Compagno and Oertel.^[21] Extension to extrathyroidal tissue, especially skeletal muscle and adipose tissue, was found in 60% of lymphomas. This feature was seen in both of our cases. It is seen that lymphomas with plasmacytoid differentiation display a more favorable prognosis. Those arising in a setting of autoimmune disease have a rapid fatal course. It is seen that 1.4% of patients with LT may develop thyroid lymphoma. Three medullary carcinomas were reported among which two were associated with lymphocytic thyroiditis. However, no lymphocytic infiltration was detected inside the tumor as in previous studies.^[22]

CONCLUSION

The increased frequency of LT in the coastal areas of Alappuzha district may be due to the high intake of iodide. The majority of population are consuming large amount of fish and food grown in soil rich in iodide. As association between lymphocytic thyroiditis and papillary thyroid carcinoma is well recognized, it is required to predict which foci will progress to papillary carcinoma. Whether coexistence of lymphocytic thyroiditis in papillary carcinoma has a good prognostic outcome has to be studied further. Iodine supplementation should be maintained at a safe level, especially for susceptible populations with potential for developing AIT disease.

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