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RESEARCH ARTICLE

ASSESSMENT OF CYTOLOGY GRADING AND CLINICAL PARAMETERS IN PREDICTING THE EXTENT OF DAMAGE TO THE THYROID GLAND IN CASES OF CHRONIC LYMPHOCYTIC THYROIDITIS: A PROSPECTIVE STUDY

Ommini Sirisha[1], P. Yujwal Raj[2]

[1]*Assistant Professor, Department of Pathology, Bhaskar Medical College, Telangana, India, 501101*
[2]*Consultant Public health expert & epidemiologist, Telangana, India, 500075.*

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ABSTRACT: Background: Chronic lymphocytic thyroiditis presents with a highly variable range of presentation and varying degrees of damage to the thyroid at the time of diagnosis. For most of the patients, duration of symptoms is the main criterion for consulting a medical practitioner. The present study is conducted in the rural area of Moinabad which has a high incidence of chronic lymphocytic thyroiditis and the clinical parameters, cytology grading are compared with the biochemical parameters (considered as gold standard in assessing the degree of thyroid damage) and their efficacy in predicting the degree of thyroid damage was assessed. The role of cytology grading and duration of symptoms in substituting the thyroid function tests as a method of assessment was thus being evaluated. **Materials& methods**: 63 cases were included in the study, conducted between January 2017 to June 2017. Clinical details, cytology findings & biochemical parameters were obtained and compared with each other using Chi-square test. **Results:** On comparison and statistical evaluation, cytology grading proved to be more sensitive and more predictive of damage to the thyroid gland. **Conclusion:** Patients can be educated that duration of symptoms can be misleading in case of Chronic Lymphocytic Thyroiditis and can be advised to consult a medical practitioner with the onset of symptoms so that damage to the thyroid gland can be prevented.

KEYWORDS: Thyroid, assessment, severity, biochemical parameters, cytology.

INTRODUCTION:

Hashimotos thyroiditis/Chronic Lymphocytic thyroiditis is an autoimmune disorder where there is gradual destruction of the thyroid follicular cells leading to inevitable hypothyroidism in the future. The disease has a striking female preponderance and is more commonin the 20 – 40 year age group, but case reports of children as young as 9 years of age have been documented[1].Biochemical evidence of hypothyroidism or subclinical hypothyroidism necessitates hormone

Corresponding Author:
Ommini Sirisha
Department of Pathology, Bhaskar Medical College, Moinabad, Telangana-500075

supplementation. Antibodies tothyroid peroxidase & Thyroglobulin are confirmatory to the diagnosis. There were many studies comparing the demographic parameters, the biochemical parameters and the clinical findings[2]. There were also many studies comparing the cytological findings, sonographic features and biochemical parameters. The present study is an attempt to compare the clinical parameters, cyto-morphological findings and biochemical parameters and evaluate the sensitivity, specificity and predictive values of the parameters in predicting the course of the disease. Thy thyroid function tests namely biochemical parameters were taken as Gold standard in the present study.

MATERIALS & METHODS:

The present study was conducted at the Department of Pathology, Bhaskar Medical College, Moinabad for a period of 6 months from January 2017 to June 2017. Clinical details, biochemical parameters and cytology findings of all the cases were recorded in detail in a structured performa. The duration of the symptoms was the main clinical parameter compared with the cytology & biochemical findings. Cytology findings were graded by a grading system designed by Bhatia et al into Grade 1, Grade 2 & Grade 3. Grade 1was considered as a mild grade & Grade 2 & 3were considered as Moderate and severe Grades respectively. Biochemical parameters were evaluated and the patients were classified as **EUTHYROID and NOT EUTHYROID**. Duration of symptoms were classified as Acute symptoms (duration less than 4 months) & Chronic symptoms (duration greater than 4 months). The sensitivity, specificity and positive & negative predictive values were calculated using the Chi-square test.

Bhatia et al grading system

Grade I [Mild]: Few lymphoid cells infiltrating the follicles/increased number of lymphocytes in the background

Grade II [Moderate]: Moderate lymphocytic infiltration or mild lymphocytic infiltration with Hurthle cell change/giant cells/anisonucleosis

Grade III [Severe]: Florid lymphocytic inflammation with germinal centre formation, very few follicular cells left.

RESULTS:

A total of 63 cases of Chronic Lymphocytic Thyroiditis were included in the present study. The demographic parameters and correlation between duration of symptoms, cytology grading and biochemical parameters were tabulated and interpreted. 75% of the patients were in the age group of 21 to 40 years (Figure 1).

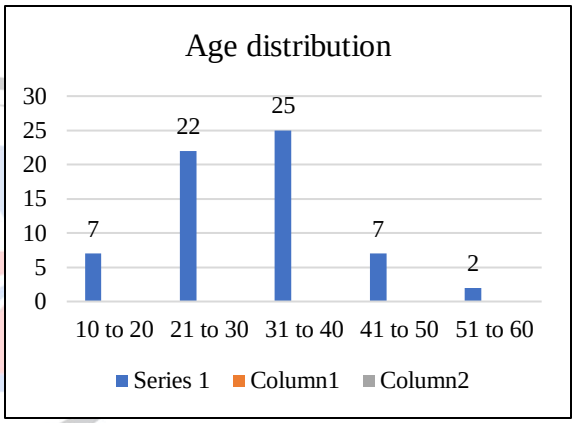

Figure1: Age distribution

Male: Female ratio was 1:20. 79% of the patients presented with thyromegaly, followed by 9% of the patients presenting with symptoms and signs of hypothyroidism (Figure 2).76% of the patients had symptom duration of more than 4 months out of which 53% of the patients had symptom duration of more than 1 year (Figure 3).57% of the patients were euthyroid biochemically, 25% of the patients were subclinically hypothyroid all of whom required supplementation with Thyroid hormone (Figure 4).

75% of the patients who were euthyroid on biochemical tests presented with symptom duration of more than 4 months. 3 out of 4 patients who were hypothyroid presented with a symptom

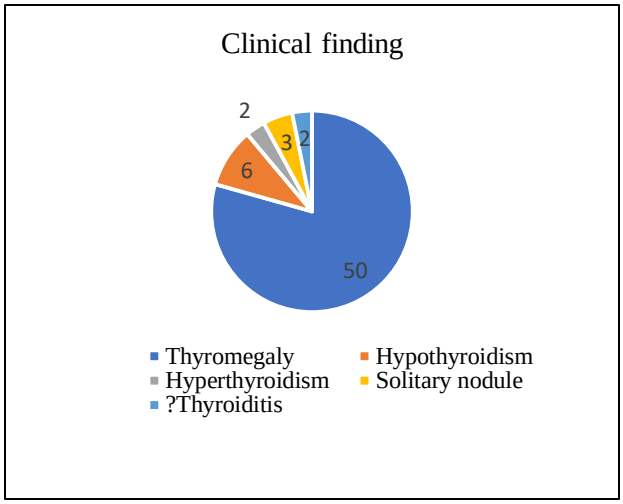

Figure 2: Clinical presentation

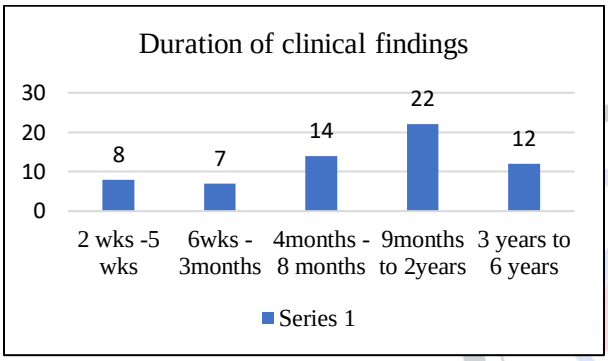

Figure3: Duration of clinical findings

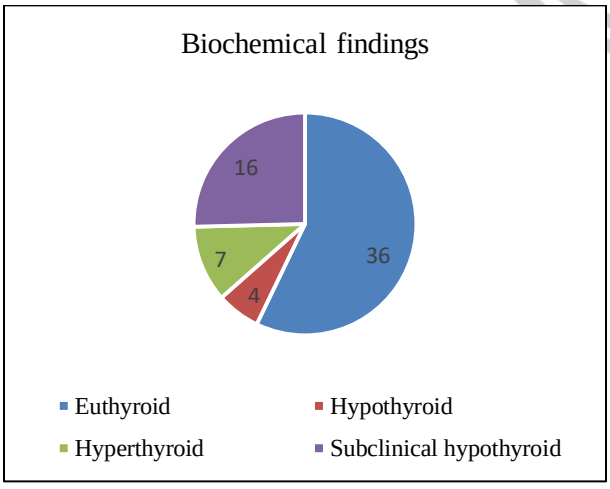

Figure 4: Biochemical Parameters

duration of more than 3 years, 81% of the patients who were subclinically hypothyroid had a symptom duration of more than 1 year (Table 1). 6/10 patients with grade 1 on FNAC presented with symptom duration of less than 1 year whereas 37/44 patients with grade 2 on FNAC presented with a symptom duration of more than 1 year. 6/9 patients with grade 3 on FNAC presented with a symptom duration of more than 1 year (Table 2). 7/10 patients with grade 1 on FNAC were biochemically euthyroid; 25/44 patients with grade 2 on FNAC were biochemically euthyroid, 10/44 patients with grade 2 on FNAC were subclinically hypothyroid; 6/9 patients with grade 3 on FNAC were biochemically subclinically hypothyroid (Table 3). Grade 1was considered as a mild grade & Grade 2 & 3were considered as Moderate and severe Grades respectively. Biochemical parameters were evaluated and the patients were classified as **EUTHYROID and NOT EUTHYROID**. Duration of symptoms were classified as **Acute symptoms** (duration less than 4 months) & **Chronic symptoms** (duration greater than 4 months).

Table 1: Correlation between Duration of symptoms & Biochemical parameters:

	Euthyroid	Hypothyroid	Hyperthyroid	Subclinical hypothyroidism
2 wks – 5 wks	5	0	1	2
6 wks – 3months	4	1	2	0
4 months – 1 year	8	0	3	1
1year – 2 years	14	0	1	7
3 years - 6 years	5	3	0	6

Table 2: Correlation between duration of symptoms and Cytology grading:

	Grade 1	Grade 2	Grade 3
2wks – 5 wks	0	3	2
6wks – 3 months	3	4	1
4 months – 1 year	3	11	4
1 year – 2years	4	11	2
3years- 6 years	0	15	0

Table 3: Correlation between Cytology grading and biochemical parameters:

	Grade 1	Grade 2	Grade 3
Euthyroid	7	25	3
Hypothyroid	0	4	0
Hyperthyroid	1	5	0
Subclinical hypothyroidism	2	10	6

Sensitivity, Specificity & Predictive values of various parameters:

Biochemical parameters were considered as a Gold Standard in the evaluation of various other parameters in predicting the severity of the disease. When duration of symptoms was correlated with the thyroid status of the patient, the sensitivity of the test was 78%, specificity – 25%, the positive and negative predictive values were 44% and 60% respectively. When duration of symptoms were correlated with cytology grades, the sensitivity and specificity were 81% and 70% respectively; the positive and negative predictive values were 86% and 23% respectively. When cytology grades were correlated with biochemical thyroid status, the sensitivity and specificity were 89% and 20% respectively. The positive and negative predictive values were 58% and 70% respectively.

DISCUSSION:

The present study conducted at Department of Pathology, Bhaskar Medical College, Moinabad is an attempt to study the various parameters in predicting the severity of damage to the thyroid gland. The duration of symptoms, the biochemical parameters (T3, T4 & TSH) and the cytological findings were compared with each other for their effectiveness in screening the disease as well as predicting the severity of damage.

In the present study, patients were in the age range of 10 to 60 years; 75% of the patients were in the age group of 21 to 40 years. In the study by P. Uma et al, 88.34% of cases were in the age group of 11-40 years[3]. Studies by Bhatia et al, Singh et al, Kumar et al, Nguyen et al and Friedman et al showed age of the patients ranging from 6-60 years, 9-65 years, 7-45 years, 15-70 years, and 18-71 years respectively which was comparable with the present study[4,5,6,7]. In the study by N. Sood et al, maximum patients were in the age group of 21 to 30 years[8]. In the present study, the male -female ratio was 1: 20. In the study by P. Uma et al, females far outnumbered males in the ratio of 24.75:1; In the study by N. Sood et al, the M:F ratio was 1: 10; In the study by Anila et al, 92% of the patients were females[9].

The present study showed that 79% of the patients presented with thyromegaly, followed by 9% of the patients presenting with symptoms and signs of hypothyroidism. In the study by P. Uma et al, the patients were asymptomatic in 62.46% of cases and 31.71% of patients had symptoms of hypothyroidism, which is said to be the natural course of the disease.[4,6] Study by Singh et al showed 63.3% asymptomatic cases and 36.7% hypothyroid cases. Study by Bhatia et al showed 73.68% hypothyroid cases and 25% asymptomatic cases on clinical assessment. In the study by Anila et al, forty-six (77%) patients presented with diffuse enlargement of thyroid, and 14 (23%) cases presented with nodular disease. After extensive review of literature, the present study has considered as duration of symptoms less than 4 months as short duration (acute symptoms) & greater than 4 months as a chronic duration. In the present study, 76% of the patients had symptom duration of more than 4 months out of which 53%

of the patients had symptom duration of more than 1year. The reason to take duration of symptomatology in the present study as the main clinical parameter was that many patients present with a symptom duration of very long periods yet are not taking treatment unless it has a cosmetic effect or because of the pressure symptoms. The present study aimed to predict the efficacy of symptom duration as a screening tool as well as a predictor of severity of autoimmune damage to the thyroid gland.

In the present study, 57% of the patients were euthyroid biochemically, 25% of the patients were subclinically hypothyroid who also required supplementation with thyroid hormone. These findings contrasted with the findings in the study by P. Uma et al where 62.78% of the patients were found to be hypothyroid, with 22%of them having subclinical hypothyroidism. In the study by Suja et al, 25(64%) patients to be hypothyroid and 6(15%) had subclinical hypothyroidism, while the rest (21%) were euthyroid[10]. In the present study, 70% of the patients were having Grade 2 findings on cytomorphology, 16% had Grade 1 findings & 14% had Grade 3 findings on cytology. In the study by Suja et al, 49% were Grade 3 & 43% were Grade 2 on cytomorphology findings. In the study by N. Sood et al, GradeI lymphocytic thyroiditis was observed in 21.82% cases; Grade II was observed in 30.91% cases; Grade III thyroiditis was noted in twenty-six (47.27%) cases and characterized by dense lymphoid infiltrates with germinal centres and with few residual follicular cells, Hurthle cell change, giant cells, and granulomas. In the study by Anila et al, 45% of patients had Grade 1 findings on cytology and 36% of the patients had Grade 2 findings on cytology.

The present study assessed the efficacy of duration of symptoms, cytology grading as a screening tool and also their efficacy in predicting the severity of damage to the thyroid glandusing Chi-square tests. The Biochemical status of the patient was taken as the Gold Standard in assessing the parameters as the hormone status of the patient has the final say regarding the damage to the thyroid gland. The duration of symptoms was categorised as short – less than 4 months and long – more than 4 months. The cytology grades were classified as Mild (Grade 1) and Moderate to severe (Grade 2&3). The biochemical parameters were classified as Euthyroid & Not Euthyroid. When the duration of symptoms was compared with the biochemical status, the sensitivity was 78%, specificity – 25%, the positive predictive value was 44% and negative predictive value was 60%. When duration of symptoms was correlated with cytology grading, the sensitivity was 81% and positive predictive value was 86%. The duration of the symptoms correlated well with the cytology grading it is fairly sensitive in predicting the morphological damage to the thyroid gland. The specificity was 70% and negative predictive value was 23%. When cytology grading was correlated with the thyroid function tests,the sensitivity was 89% and the negative predictive value was 70%. The positive predictive value was 58% and specificity was only 20%.

Interpreting the above test results, duration of symptoms when taken into consideration would identify 78% of the patients likely to have biochemical thyroid dysfunction which necessitates treatment. But the positive & negative predictive values were 44% and 60% indicating that it is more useful for its negative predictive value more than its positive predictive value that is it would predict better patients who are unlikely to have damage to the thyroid. When duration of symptoms was used to assess the cytological damage to the thyroid gland, the test is fairly sensitive and the most significant result was obtained in the positive predictive value which was 86% indicating that when there is longer duration of symptoms, the likelihood of increased severity of cytological damage was also high. When cytology grading was used to assess the degree of biochemical thyroid dysfunction, the test was fairly sensitive with 89% sensitivity and the negative predictive value was 70% indicating that when the cytology grading is low, the likelihood

of biochemical thyroid dysfunction is also low. In a study by Kishore at al, the cytology grading was proved superior in predicting the severity of the damage than the clinical symptoms[11].

CONCLUSION:

When the 2 tests namely duration of symptoms, cytology grading were compared with the biochemical parameters in assessing the degree of thyroid dysfunction, cytology grading proved to be more sensitive than duration of symptoms. Also cytology grading proved to be more accurate in identifying the patients who are unlikely to have a biochemical thyroid dysfunction (high negative predictive value). The duration of symptoms in turn can predict with 86% positive predictive value the people with more severe cytological damage. The present study shows that patients can be assessed better by cytology grading than the duration of symptoms and can be used at community camps for screening purposes. At rural areas, where people have minimal access to standard lab facilities which is necessary to assess biochemical thyroid parameters, cytology grading can be used as an effective alternative to thyroid function tests.

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Microphotos

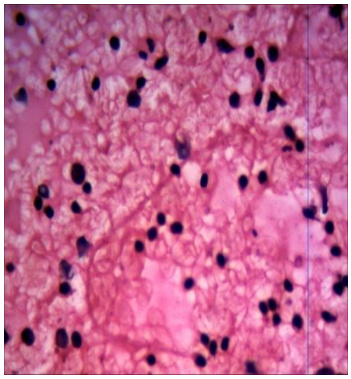

Fig. 5: Grade 1 cytology: H & E: 100 X

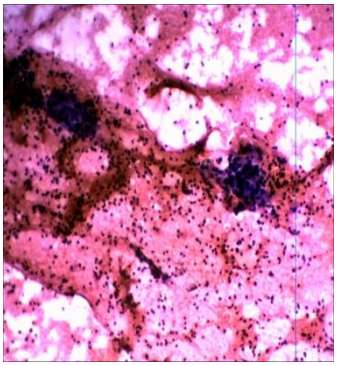

Fig. 7: Grade 3 cytology: H & E: 40X

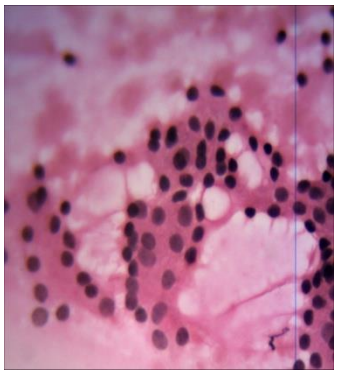

Fig. 6: Grade 2 cytology: H & E: 100X

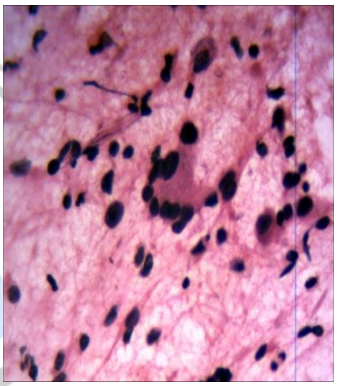

Fig. 8: Anisonucleosis; Giant cell;Hurtle cell: H & E:

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