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Original Research Article

Comparative study of female hypothyroid patients having autoimmune thyroiditis with the clinico-pathological parameters

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ABSTRACT

Introduction: Hypothyroidism during reproductive age group is responsible for menstrual irregularities, infertility along with miscarriages and congenital malformation s during pregnancy. It has a prevalence of 5-20% in child bearing age. Autoimmune thyroiditis is the common cause of subclinical hypothyroidism in adult female population. Presence of thyroid autoantibodies is high in subclinical hypothyroidism. American Thyroid Association (ATA) & American Association of Clinical Endocrinologist (AACE) recommends for treatment of these patients. Lack of obvious signs and symptoms in subclinical hypothyroidism creates dilemma and challenge for diagnosis.

Hypothesis: This was a retrospective study conducted in Kalinga Institute of Medical Sciences (KIMS), Bhubaneswar during the period from January 2017 to January 2019. Women of reproductive age group having thyroid swellings were subjected to Fine needle aspiration cytology (FNAC), Thyroid function test and Anti TPO Ab levels in serum. Cytological grading was done and it was correlated with clinical presentation and serological parameters.

Results: Out of 120 cases, 56.7% patients were hypothyroid. Increased titre of Anti- TPO Ab levels in serum was observed in 91.4%, 95.3% and 95% cases of Grade I, Grade II & Grade III categories of autoimmune thyroiditis respectively.

Conclusion: Autoimmune thyroiditis is the common cause of hypothyroidism in adult females. Early detection and management with low dose of thyroxine will prevent the complications during reproductive period.

1. Introduction

Thyroid disorders are one of the most common endocrine disorders in India. Incidence of hypothyroidism in India is 30–60/1, 00,000 populations per year with a prevalence rate of 1– 4%.[1] Prevalence of hypothyroidism in women of reproductive age is 2–4%.[2] Autoimmune thyroiditis is the most common type of thyroiditis and the second most common benign thyroid lesion next to colloid goiter.[3,4] It's prevalence is more common among Asian population.[5] Women are more commonly affected. It is the common cause of hypothyroidism. Hypothyroidism in reproductive age group is responsible for menstrual irregularities and infertility along with miscarriages and congenital malformation during pregnancy.[6,7] Patients of autoimmune thyroiditis may present in a hypothyroid, euthyroid or hyperthyroid state. However, mostly patients present with hypothyroidism. It is important to establish it's diagnosis as these patients require lifelong supplementation with thyroxin.[8]

The clinical presentation may be diffuse or nodular asymptomatic thyroid swelling.[1] Hurtle cell changes of follicular cells, increased number of reactive lymphoid cells & plasma cells in the background along with impingement of lymphocytes into thyroid follicular cells are characteristic cytological features.[9]The most commonly detected auto-antibody in the serum is Anti Thyroid P eroxidase Antibody (Anti TPO Ab), however at times in 10 to 15% cases

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antibody may not be detected in serum.[10,11]

Lack of obvious signs and symptoms in subclinical hypothyroidism creates dilemma and challenge for diagnosis. Presence of thyroid auto-Ab in serum is high in most of these cases. American Thyroid Association (ATA) & American Association of Clinical Endocrinologist (AACE) recommends for treatment of these patients [AACE/ACE G4GAC, Endocr Pract. 2017; 23(No. 8)]. Despite availability of several tests, FNAC remains the gold standard with a diagnostic accuracy of 92%.[12] FNAC is a simple, cost effective, safe and sensitive diagnostic tool.[13]

2. Aims and Objectives

1. To study the incidence of hypothyroidism in reproductive age group of women.

2. To correlate it with cytomorphological grading, clinical presentation, thyroid function tests (TFT) and Anti-Thyroid Peroxidase Antibody (Anti TPO Ab) levels in serum.

3. Materials and Methods

This was a retro spective study conducted in the Department of Pathology, Kalinga Institute of Medical Sciences, Bhubaneswar, and Odisha from January 2017 to January 2019. 120 newly diagnosed cases of autoimmune thyroiditis on FNAC were included in this study. Informed consent was taken from all the se patients. Women of reproductive age group presenting with diffuse and nodular thyroid swellings were subjected to FNAC of thyroid gland by non-aspiration and aspiration techniques using 23 G needle and 10 ml syringe. Air-dried smears were stained with Leishman's stain and wet, ethanol fixed smears were stained with Haematoxylin and Eosinstain. TFT and Anti TPO Ab levels were simultaneously estimated in Cobase 441 automated hormone analyser. Cytological grading of the FNAC smears was done according to density of lymphocytic infiltration, Hurthle cell changes, degree of anisonucleosis, presence of giant cells along with impingement of thyroid follicular cells by lymphocytes [as per the criteria mentioned in Table no- 3]. I t was correlated with clinical presentation, TFT and anti-TPO antibody levels.

3.1. Inclusion Criteria

All cases of thyroid swellings in women of reproductive age group coming to Pathology Department for FNAC were included in the study.

3.2. Exclusion Criteria

1. Cases diagnosed as colloid goitre on cytology.

2. Old cases of autoimmune thyroiditis on therapy.

3. Any other additional lesions along with autoimmune thyroiditis diagnosed on cytology.

4. Subjects receiving either thyroxine or any other drugs known to interfere with TFT.

4. Observation

Out of total 120 cases studied, w e observed that, the most common age group was 31-40 yrs [Table no-1]. Diffuse thyroid swelling was the commonest clinical presentation in 85 cases (70.8%), however, nodular & solitary thyroid swellings were observed in 22 cases (18.3%) and 13 cases (10.8%) respectively [Table no- 2]. Majority of patients were in Grade-II, 65 cases (54.2%). We observed that 35 cases (29.2%) were in Grade I & 20 cases (16.6%) were in Grade III [Table no- 4]. Hypothyroidism was the commonest presentation comprising of 68 cases (56.7%). Euthyroid and hyperthyroid cases were observed in 22 cases (18.3%) & 30 cases (25%) respectively [Table no- 5]. Correlating with cytological grading with hormone status, out of 35 cases of grade-I, 32 cases (91.4%), 65 cases of grade-II, 62 cases (95.3%) and 20 cases of Grade III, 19 cases (95%) had raised Anti -TPO antibody levels [Table no- 6]. However, 3 cases of Grade-I and 2 cases of Grade-II had no rise in Anti TPO antibody levels.

Table 1: Incidence ofAutoimmune thyroiditis according to different age groups (N=120)

Age Group	No of Cases	%
10-20	15	12.5
21-30	36	30.0
31-40	48	40.0
41-50	21	17.5
Total	120	100%

Table 2: Incidence ofAutoimmune thyroiditis according to clinical presentation (n=120)

Clinical Presentation	No of Cases	%
Diffuse swelling	85	70.8
Nodular swelling	22	18.3
Solitary nodule	13	10.8
Total	120	100%

Table 3: Cytomorphologicalgrading of Autoimmune thyroiditis

Grades	Cytomorhology
Grade-1	Mild lymphocytic infiltration in the thyroid follicles (Fig-I)
Grade-2	Moderate lymphocytic infiltration, presence of abundant Hurthle cells, giant cells, anisonucleosis of thyroid follicular cells, lymphocytes impinging into thyroid follicular cells (Fig-II)
Grade-3	Florid lymphocytic infiltration with germinal centre formation & follicular destruction (Fig-III)

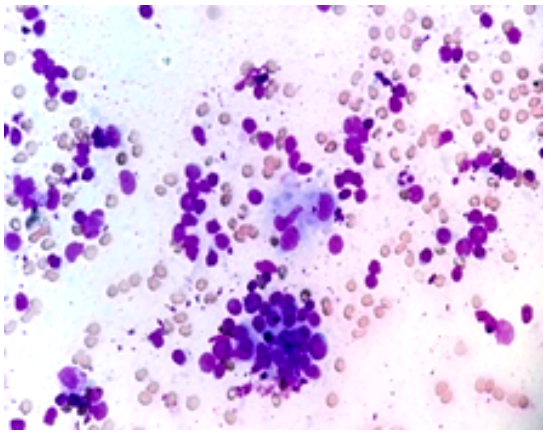

Fig. 1: (400x Leishman's stain) Grade-I Autoimmune thyroiditis-showing mild lymphocytic infiltration

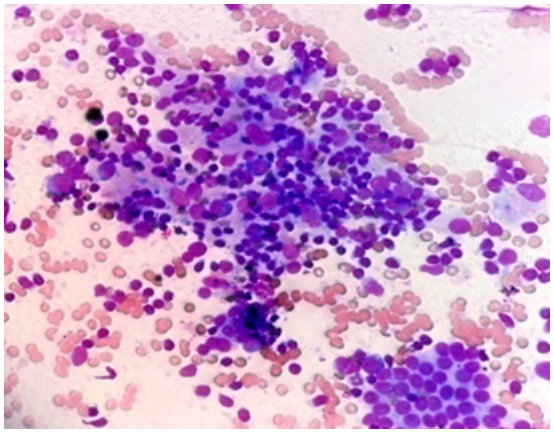

Fig. 2: (400x Leishman's stain) Grade-II Autoimmunethyroiditis showing, hurthle cell changes of thyroid follicular cells, and moderate lymphocytic infiltration

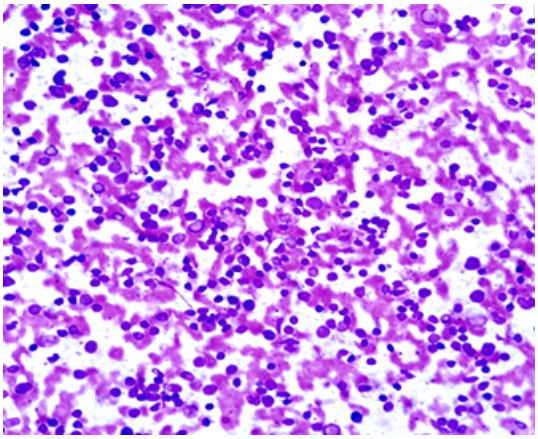

Fig. 3: (400x Leishman's stain) Grade-III Autoimmunethyroiditis showing Florid lymphocytic infiltration with germinal centre formation

Table 4: Incidence ofAutoimmune thyroiditis according to cytomorphological grading (n=120)

Grades	No of Cases	% of Cases
Grade-1	35	29.2
Grade-2	65	54.2
Grade-3	20	16.6
Total	120	100%

Table 5: Incidence [Incidence ofAutoimmune thyroiditis according to hormone status (n=120)

Hormone Status	No of Cases	Percentage
Euthyroid	22	18.3
Hypothyroid	68	56.7
Hyperthyroid	30	25.0
Total	120	100%

Table 6: Correlation betweencytomorphological grading of Autoimmune thyroiditis with increased Anti TPO Ablevel (n=120)

Grades		Increased Anti-TPO Ab	
Grading	No of cases	No of cases	% of cases
I	35	32	91.4
II	65	62	95.3
III	20	19	95.0

5. Discussion

Thyroid hormones play important role on normal reproduction and pregnancy. Autoimmune thyroiditis is the most common cause of hypothyroidism. Undiagnosed and untreated hypothyroidism can cause abnormal sexual development, menstrual irregularities, infertility as well as sub-fertility in women of reproductive age group along with miscarriages and congenital malformation during pregnancy.[6,7] Prevalence of hypothyroidism due to autoimmune thyroiditis in child bearing age of women is rising in the present era. Lack of obvious signs and symptoms in subclinical hypothyroidism creates diagnostic dilemma. Level of auto Abs against thyroid in serum is usually high in subclinical hypothyroidism. Both cytological and serological investigations are essential for proper diagnosis and management.

In autoimmune thyroiditis there is infiltration of T and B lymphocytes which are reactive against thyroid antigens. Activated B cells secrete thyroid auto antibodies. Cytotoxic T lymphocytes are largely responsible for destruction of thyroid parenchyma. In the long run, follicular architecture of thyroid gland is totally destroyed and replaced by fibrosis. The active phase of the disease is transient with clinical manifestation of thyrotoxicosis. Evolution and destructive phases manifest with subclinical and overt hypothyroidism. Although the exact etiology of autoimmune thyroiditis is unknown; however, predisposing factors include iodine

deficiency, medication, infection, smoking, stress etc.[13] It has an increased risk of transforming into malignancy, most commonly extra nodal marginal B cell lymphoma and papillary carcinoma.[14,15] Hence, patients diagnosed as autoimmune thyroiditis need follow up.

We have included total 120 numbers of cases. The most common age-group in our study was 31- 40yrs which is similar to study conducted by S Bhatia et al[9] and Bajaj et al.[11] Ashwin et al[13] found common age group to be 20-40 yrs.

The common presentation in our study was diffuse thyroid swelling (70.8%) which bears resemblance with studies by KarthaS et al[12] (66%) and Ashwin et al[13] (50.81%).

Grading of autoimmune thyroiditis was done as per the criteria described in [Table-3]. Majority of our cases belonged to Grade II (54.2%). Ashwin et al[13] and P Agrawal et al[16] observed 41.3% and 50% Grade II cases.

On analyzing the TSH levels, we found 56.7 % patients to be hypothyroid which was in concordance with study by Rathi et al,[10] Ashwin P et al,[13] and P Agrawal et al[16] who observed hypothyroidism in 56.1%, 50% and 50% cases respectively. However Bhatia et al[9] reported hypothyroidism in 73.6% patients.

In our study Anti-TPO Antibody was raised in 91.4%, 95.3% and 95% cases of Grade I, Grade II & Grade III categories of auto immune thyroiditis respectively. Neelam Sood et al[17] also observed Anti-TPO Antibody and TSH to be elevated in 91.67%, 94.12% and 96.16% cases of Grade I, Grade II & Grade III autoimmune thyroiditis respectively.

5.1. Limitation of Our Study

We were unable to correlate our results with radiological findings as in majority of cases USG reports were not available.

6. Conclusion

Although autoimmune thyroiditis can affect any age group, it predominantly affects females of third to fourth decades. It is the most common cause of subclinical hypothyroidism in adult females. There is a strong association of raised Anti-thyroid Antibodies; especially Anti-TPO Antibody. Rise in Anti-TPO Ab and TSH together play a significant role as there may be minimal or no lymphocytic infiltration in FNAC cytosmears of autoimmune thyroiditis. This could be due to very early stage of autoimmune thyroiditis. Inspite of various diagnostic modalities available, FNAC still remains the gold standard. However, a multidisciplinary approach including clinico-radiological, serological and cytological parameters should be utilized for detecting subclinical hypothyroid state. Early detection and management with low dose of thyroxine will prevent the complications during reproductive period.

7. Source of funding

The researchers did not receive any grant from outside funding agencies. This was self funding.

8. Ethical approval

The study was retrospective and had not influenced the FNAC decision. Prior to FNAC, all participants were oriented about the technique and informed consents were obtained**.**

9. Conflict of interest

The authors declare that they have no conflict of interest.

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