ORIGINAL RESEARCH ARTICLE

JUVE NILE LYMPHOCYTIC THYROIDITIS - AN EXPERIENCE IN OUR INSTITUTE

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ABSTRACT

BACKGROUND
Chronic lymphocytic thyroiditis (Hashimoto’s thyroiditis) is one of the most common causes of goitre and hypothyroidism in children. In this study an attempt has been made to correlate the cytological findings with biochemical levels and ultrasonography findings.

MATERIALS AND METHODS
This is a prospective study conducted for a period of two years. The various parameters like patient’s clinical presentation, biochemical levels and thyroid ultrasound were studied. Fine needle aspiration of thyroid gland was done and correlated with biochemical and ultrasound findings.

RESULTS
Juvenile lymphocytic thyroiditis constituted 64/300 (21.33%) of cases; 60.93% were asymptomatic, 15.7% performed poorly in academics and 23.43% presented with diffuse enlargement of thyroid; 64.06% were hypothyroid and 12.5 were subclinically hypothyroid. Ultrasonographic features of hypoechoic micronodules (28.12%) and diffuse hypoechogenicity (23.43%) was definitely associated with hypothyroid state.

CONCLUSION
FNAC is a simple, safe and cost effective procedure and is a sensitive and specific diagnostic tool in diagnosing chronic lymphocytic thyroiditis. A combined approach of cytology with ultrasonography and biochemical levels can detect subclinical hypothyroid states and provide a guide to therapy. There is a definitive need for screening school children for chronic lymphocytic thyroiditis.

KEYWORDS
Thyroiditis, Juvenile, Cytology, Thyroid Function Tests, USG.

(Tregs), results in some way in a change in the thyroid microenvironment leading to decreased inhibition of Th1 cells and the overproduction of Th1 cytokines.[3]

Fine needle aspiration is a simple and cost effective procedure and plays a significant role in the diagnosis of chronic lymphocytic thyroiditis, which is a non-surgical condition. Clinically, chronic lymphocytic thyroiditis can present as a diffuse or nodular swelling being totally asymptomatic.

MATERIALS AND METHODS

This is a prospective study conducted in the Department of Pathology, at a tertiary care for a period of two years. Out of 1673 thyroid aspirations done during this study period, 300 cases of chronic lymphocytic thyroiditis were diagnosed on cytology, of which 64 cases were juvenile lymphocytic thyroiditis. Children till 18 years of age and newly diagnosed cases of chronic lymphocytic thyroiditis were included in the study. Subjects receiving either thyroxin or any other drug known to interfere with thyroid function at the time of evaluation, old cases of chronic lymphocytic thyroiditis and any other additional lesions observed in association with chronic lymphocytic thyroiditis diagnosed on cytology were excluded from study.

Thyroid function tests were used to determine blood concentrations of thyroid hormones. The reference range used was T4 (55 - 135 ng/mL), T3 (0.7 - 2 ng/mL) and TSH (0.17 - 4.05 μIU/mL). Depending on these results patients were considered euthyroid, hyperthyroid and hypothyroid. Ultrasonography of thyroid gland was performed by a single sonologist who was blinded to the clinical and biochemical status of the subjects using high resolution ultrasound machine with 5 - 10 MHz broadband linear transducer. A preselected set of sonographic features (hypoechogenicity, micronodularity, echogenic septa, echogenic nodules < 5 mm and hyperechoic nodules > 5 mm) were taken for sonographic analysis.

Fine needle aspiration of the thyroid was done by using non-aspiration technique. In case the material obtained was not satisfactory a repeat aspiration was done, but not more than 2 aspirations were tried on each patient. The cytology smears were seen by two independent pathologists. Qualitative criteria used for cytologic diagnosis were lymphocytes and plasma cells infiltrating the thyroid follicles and increased number of lymphocytes in the background with or without lymphoid follicles, Hurthle cell change, multinucleated giant cells, epithelioid cell clusters, interlobular fibrosis that is the presence of fibrous tissue or scattered fibroblasts in the aspirate.

RESULTS

Non-neoplastic lesions to be 91.3% of thyroid lesions diagnosed on FNAC and neoplastic lesions being 8.6%. The commonest non-neoplastic lesion in children and adolescents being nodular goitre 13.1% and lymphocytic thyroiditis 21.33%.

Our criteria for diagnosing thyroiditis was based on the typical features of lymphocytic thyroiditis on FNAC. We tried to include thyroid antibody titre of all cases, but it was not possible because of cost effectiveness.

Total number of cases with chronic lymphocytic thyroiditis were 300. Juvenile lymphocytic thyroiditis constituted 64/300 (21.33%) of cases; 4.68% of cases presented before 10 years of age and 95.31% of cases occurred between 11 and 18 years.

Almost all presented with goitre enlargement except for one case, a male aged 10 years who presented with congenital hypothyroidism with delayed mile stones in the form of defective speech and learning abilities. He was on eltroxin therapy since the age of 4 years. Clinical presentation of cases: 60.93% were asymptomatic, 15.7% performed poorly in academics and 23.43% presented with diffuse enlargement of thyroid (Table 2).

Thyroid function tests in juvenile lymphocytic thyroiditis: 64.06% were hypothyroid, 23.43% were euthyroid and 12.5% were subclinically hypothyroid (Table 3).

USG findings in juvenile lymphocytic thyroiditis: Normal study was seen in 42.18% of cases, hypoechoic micronodules (28.12%) and diffuse hypoechogenicity (23.43%) was definitely associated with hypothyroid state (Table 4).

On cytology, the predominant features were reactive population of lymphocytes, epithelioid cells, few thyroid follicular epithelial cells, foreign body giant cells, plasma cells and Hurthle cells (Fig. 1, 2).

<table>
<thead>
<tr>
<th>Age</th>
<th>Male</th>
<th>Female</th>
<th>Total</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 - 10 years</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4.68</td>
</tr>
<tr>
<td>11 - 18 years</td>
<td>5</td>
<td>56</td>
<td>61</td>
<td>95.31</td>
</tr>
<tr>
<td>Total</td>
<td>6</td>
<td>58</td>
<td>64</td>
<td>100</td>
</tr>
</tbody>
</table>

**Table 1. Age and Sex Distribution of Cases with Juvenile Lymphocytic Thyroiditis - 64**

<table>
<thead>
<tr>
<th>Clinical Presentation</th>
<th>Number of Cases</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Asymptomatic</td>
<td>39</td>
<td>60.93</td>
</tr>
<tr>
<td>Poor performance at school</td>
<td>10</td>
<td>15.7</td>
</tr>
<tr>
<td>Thyroid enlargement</td>
<td>15</td>
<td>23.43</td>
</tr>
</tbody>
</table>

**Table 2. Clinical Presentation in Juvenile Lymphocytic Thyroiditis**

<table>
<thead>
<tr>
<th>Thyroid Function Tests</th>
<th>Number of Cases</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypothyroid</td>
<td>41</td>
<td>64.06</td>
</tr>
<tr>
<td>Euthyroid</td>
<td>15</td>
<td>23.43</td>
</tr>
<tr>
<td>Subclinical Hypothyroid</td>
<td>08</td>
<td>12.5</td>
</tr>
</tbody>
</table>

**Table 3. Thyroid Function Tests in Juvenile Lymphocytic Thyroiditis**

<table>
<thead>
<tr>
<th>USG Findings</th>
<th>Number of Cases</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diffuse Hypoechogenicity</td>
<td>15</td>
<td>23.43</td>
</tr>
<tr>
<td>Hypoechic Micronodules</td>
<td>18</td>
<td>28.12</td>
</tr>
<tr>
<td>Echogenic Septa</td>
<td>04</td>
<td>6.25</td>
</tr>
<tr>
<td>Normal Study</td>
<td>27</td>
<td>42.18</td>
</tr>
</tbody>
</table>

**Table 4. USG Findings in Juvenile Lymphocytic Thyroiditis**
thyroid management of euthyroidism or subclinical or overt forms of hypothyroidism and less commonly hyperthyroidism. There is considerable debate regarding the common presenting complaint, especially in older children and adolescents. Thyroid function can vary from euthyroidism in children usually there is asymptomatic enlargement of gland with gain in weight. Thyroid function can vary from euthyroidism to hypothyroid state. The most important subgroup is subclinical hypothyroid state, which needs periodic monitoring.\cite{4,5,6}

Subclinical Hypothyroidism (SH) is biochemically defined as a serum TSH concentration above the statistically defined upper limit of the reference range when serum-free thyroxine (FT4) concentration is within its reference range. The clinical presentation varies widely, ranging from no manifestations to clear signs or symptoms of hypothyroidism. SH prevalence in the adult population is reported to be 1-10%, being higher in the elderly population, in females and in white subjects. In the paediatric population SH prevalence is reported to be slightly lower than 2%, even if epidemiological studies concerning childhood and adolescence are scanty. Therefore, SH is quite a common disorder in paediatric patients and both primary care physicians and paediatric endocrinologists frequently face the decision of what to do regarding these children.\cite{7}

In the present study, 12.5% were with subclinical hypothyroid. In these cases, Fine Needle Aspiration Cytology (FNAC) and ultrasound examination of thyroid contributed to the diagnosis of thyroiditis. Gopalakrishnan et al\cite{8} analysed 98 subjects with age range of 8 - 18 years with diagnosis of autoimmune thyroiditis; 24.55% were euthyroid, 32.6% had subclinical hypothyroidism and 42.9% hypothyroidism. Meena P. Desai et al\cite{9} analysed 96 children with suspected juvenile autoimmune thyroiditis, 77% had hypothyroidism, 10% had thyrotoxicosis and only 13% were euthyroid. Family history of thyroid disease was elicited in 33% of the series. In the present study, 64.06% were hypothyroid and 23.43% were euthyroid. In two cases, both the siblings had juvenile lymphocytic thyroiditis with positive history in the mother.

Thyroid ultrasonography is a useful tool to support the diagnosis and classical sonographic findings are present in 20% - 95% of affected individuals. Furthermore, their presence is related to subclinical hypothyroidism and levels of thyroid autoantibodies and ultrasonography has been used for the follow-up of patients. Thyroid ultrasonography is usually heterogeneous because of fibrosis and hypoechoic areas, it is not necessary for diagnosis but it is recommended to confirm the presence of a thyroid nodule, solitary or multiple

DISCUSSION
Thyroid hormones play a crucial role as a regulator of growth, of nervous system myelination, of common endocrinopathies in childhood. Disorders affecting the thyroid gland represent the most disorders in children and adolescents differ from that of adults. Thus paediatric medical care requires an appreciation of distinct characteristics of thyroid function and dysfunction in childhood and adolescence. Early diagnosis and treatment are essential to prevent irreversible and permanent nervous system damage and developmental delay, as they are extremely vulnerable to thyroid dysfunction. Regions where iodine intake is highest have higher incidence of thyroiditis, eg in Japan and United States.

Patients with juvenile autoimmune thyroiditis can present due to thyroid enlargement or symptoms arising due to hypothyroidism. Asymptomatic enlargement of thyroid gland is a common presenting complaint, especially in older children and adolescents. Thyroid function can vary from euthyroidism to subclinical or overt forms of hypothyroidism and less commonly hyperthyroidism. Accordingly, patients can be asymptomatic. There is considerable debate regarding the management of euthyroidism or subclinical hypothyroidism.

Autoimmune thyroiditis is a frequent cause of goitre in children. Clinically, it manifests as presence or absence of goitre depending on goitrous and atrophic forms. Thyroid autoimmunity in susceptible children depends on genetic, endogenous and environmental factors.\cite{2}

Kaur J et al\cite{3} in their study lymphocytic thyroiditis constituted 49.3% of cases in children on fine needle aspiration cytology; it provides a tissue diagnosis, thereby avoiding more invasive procedure for merely diagnostic purposes. In the present study, juvenile lymphocytic thyroiditis constituted 21.33% of cases.

The precise environmental trigger(s) leading to the development of disease is not known with certainty, but infection, drugs (lithium, amiodarone, interferon-alpha), hormones (oestrogen), dietary substances (iodine, selenium), stress, smoking and most recently environmental toxins have all been implicated. An epigenetic mechanism has been postulated in some cases low birth weight, sex hormones, glucocorticoids contribute to the development of lymphocytic thyroiditis. In younger children common complaints are growth retardation, difficulty in learning at school with short attention span and poor performance at school. In older children usually there is asymptomatic enlargement of gland with gain in weight. Thyroid function can vary from euthyroid to hypothyroid state. The most important subgroup is subclinical hypothyroid state, which needs periodic monitoring.\cite{4,5,6}

Subclinical Hypothyroidism (SH) is biochemically defined as a serum TSH concentration above the statistically defined upper limit of the reference range when serum-free thyroxine (FT4) concentration is within its reference range. The clinical presentation varies widely, ranging from no manifestations to clear signs or symptoms of hypothyroidism. SH prevalence in the adult population is reported to be 1-10%, being higher in the elderly population, in females and in white subjects. In the paediatric population SH prevalence is reported to be slightly lower than 2%, even if epidemiological studies concerning childhood and adolescence are scanty. Therefore, SH is quite a common disorder in paediatric patients and both primary care physicians and paediatric endocrinologists frequently face the decision of what to do regarding these children.\cite{7}
nodule can be detected in both hypothyroid or euthyroid patients. During disease progression, reduced echo levels develop gradually, reflecting either reduction of colloid content and increased intrathyroidal blood flow or lymphocytic tissue infiltration, which induces diffuse fibrosis. The appearance of thyroid gland on ultrasonography may be normal at diagnosis, but characteristic changes evolve over time.

In the study by Marwaha RK et al.[10] 695 school children (244 boys and 451 girls) aged between 5 - 18 years were analysed. All the children were subjected to cytological and USG examination with estimation of thyroid function tests; 16% of children with thyroiditis showed hypoechogenicity on USG, 15.2% had thyroiditis on cytology and 25.2% had abnormal thyroid function tests. Thyroid with hypoechogenicity had higher percentage of thyroiditis on FNAC and thyroid function tests when compared to normal echogenicity.

Fang J et al[11] to find the accurate procedure in diagnosing diffuse goitre in children he examined 50 children with diffuse goitre and subjected them to fine needle aspiration biopsy cytology, thyroid antibody detection, thyroid hormone analysis and ultrasound imaging; 109 healthy children (control) were examined by ultrasound imaging. The results showed that thyroid imaging in health children was a smooth echo pattern with stronger homogenous echogram than surrounding muscle tissues. The patients with diffuse goitre showed an abnormally enlarged thyroid volume. In 22 (84.6%) of 26 children with chronic lymphocytic thyroiditis a varied patch hypoechogenicity was found, of whom 18 (81.8%) had positive results of antibody testing. On the contrary, echo pattern was normal in 17 (70.8%) of 24 patients with diffuse thyroid proliferation and only the remainder (7/24, 29.1%) had abnormal echo pattern as well as elevated autoantibody titres, of whom 2 were confirmed as chronic lymphocytic thyroiditis by a repeat fine needle aspiration biopsy 1 year later. By using combined ultrasound imaging and antibody determination, 92% of the cases with chronic lymphocytic thyroiditis could be diagnosed. Their study suggested that ultrasonic imaging is an easy, non-invasive, reproducible and effective procedure in the differential diagnosis of chronic lymphocytic thyroiditis in children.

Ivarsson SA et al[12] in 22 patients with suspected diffuse goitre, the diagnostic accuracy of ultrasonography was compared with that of aspiration biopsy cytology and thyroid antibody testing. Ultrasonography was abnormal in 100% of the patients with autoimmune thyroid disease. Thus, ultrasound imaging stands out as a valuable diagnostic tool for the differential diagnosis of diffuse thyroid disorders in children.

Poyhonen L et al[13] USG was abnormal in 97% of cases with thyroiditis and in most cases ultrasound was diagnostic. With antibody determinations, only 60% of the cases of thyroiditis could be diagnosed. Ultrasound imaging, a risk-free method should be included in the diagnostic investigation of thyroid disorders.

In the present study, 28.12% presented with hypoechoic micronodules and diffuse hypoechogenicity in 23.43% of cases and 42.18 with normal study. All the cases with hypoechoic micronodules and diffuse hypoechogenicity on USG were associated with hypothyroid state.

Krishna M et al[14] observed that lymphocytic thyroiditis was the most common cause of nontoxic goitre in childhood, comprised 20% of all goitres. The condition was common in preadolescent girls with or without symptoms of anxiety, nervousness and pressure in the neck. Majority were euthyroid. In the present study, 95.31% of cases were adolescent girls with 60.93% were asymptomatic and 23.43% presented as goitre.

CONCLUSION

Autoimmune thyroiditis is a frequent cause of goitre in children. Studies point to the increasing prevalence of Juvenile Autoimmune Thyroiditis (JAT) in children and adolescents. Clinically, JAT can manifest depending on the presence or absence of goitre as either a goitrous form or atrophic form. Both are characterised by the presence of thyroid antibodies in the serum with goitrous form being more common in children. Recent evidence suggests that thyroid autoimmunity originates from an interaction of genetic, endogenous, environmental factors which end up activating thyroid specific autoreactive T cells in susceptible children. In addition to underlying genetic/HLA predisposition factors including sex hormones, stress glucocorticoids, low birth weight (10%), radiation and drugs may play a role in thyroid autoimmunity. In the present study, juvenile lymphocytic thyroiditis constituted 21.33% of cases being more common between 11 - 18 years of age with female predominance. Majority of cases were asymptomatic. Subclinical hypothyroid cases were 12.5%, which can be easily diagnosed combining thyroid function tests, ultrasonography and fine needle aspiration cytology. Screening of school children for hypothyroid states due to thyroiditis is a must and should a part of school health programmes.

REFERENCES


