

CLINICAL PROFILE OF PRIMARY HYPOTHYROIDISM- A COMPARISON OF AUTOIMMUNE THYROIDITIS WITH OTHER CAUSES (IATROGENIC)

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ABSTRACT

BACKGROUND

Primary Hypothyroidism is a common clinical condition. Majority of cases are autoimmune in nature. However iatrogenic causes like post thyroidectomy or post radio ablation cases are also present. This study was mainly conducted to evaluate the differences in the clinical features of both the groups. Autoimmune thyroiditis patients were selected based on the presence of antithyroid antibodies or histopathological diagnosis or both.

MATERIALS AND METHODS

This study was carried out in the Kasturba Hospital, Manipal, for a period of 2 years. A total of 101 cases of primary hypothyroidism were studied. Of these, 69 cases were autoimmune thyroiditis, while the rest 32 cases of hypothyroidism were non-autoimmune cases.

RESULTS

The average age of patients in autoimmune group was 40.1 years and in non-autoimmune group was 46.75 years. In autoimmune group, 70% of patients were in the age group of 20-30 years; with presence of family history in 5.8% patients. Comorbid conditions were common in autoimmune thyroiditis patients, with rheumatoid arthritis being the most commonly present in 14.5%, while such comorbid conditions were occasional in non-autoimmune group. Goitre was associated with autoimmune thyroiditis patients with presence in 59.4% patients. (Table-1)

CONCLUSION

At the end of the study, there were no major differences seen in demographics or clinical presentation in both the groups. Substantial proportion of patients with autoimmune thyroiditis have comorbid conditions such as rheumatoid arthritis, type I diabetes mellitus, ITP, megaloblastic anaemia, myasthenia gravis.

KEYWORDS

Clinical Features, Hypothyroidism, Autoimmune Thyroiditis.

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BACKGROUND

In areas of iodine sufficiency, autoimmune disease and iatrogenic causes are the most common causes of primary hypothyroidism.¹ Autoimmune thyroiditis is extensively studied organ specific autoimmune disorder in humans. It may be associated with goitre (Hashimoto's) or at the late stages minimal residual thyroid tissue (atrophic).² Up to 50% first-degree relatives of patients have thyroid antibodies apparently inherited as a dominant trait.³ Autoimmune thyroiditis is associated with other autoimmune diseases especially Type 1 diabetes mellitus, Addison's disease,

pernicious anaemia, vitiligo etc. less commonly with celiac disease, dermatitis herpetiformis, chronic active hepatitis, rheumatoid arthritis, systemic lupus erythematosus, Sjogren's disease etc.⁴

Women are 5-7 times more likely to be affected than men.^{5,6} Antithyroid peroxidase antibodies are reported in 95% of patients and antithyroglobulin antibodies in 60% of patients of hypothyroidism.⁷ The titers tend to be higher in patients with atrophic form than with goitrous form. In Whickham survey, after 45 years, rate for development of hypothyroidism increased with age.⁸ The clinical manifestations of hypothyroidism are largely independent of its cause.⁹ The present study was conducted to study compare the clinical presentation of patients with primary hypothyroidism, of Autoimmune Thyroiditis with other iatrogenic causes.

MATERIALS AND METHODS

This study was carried out in the Kasturba hospital, Manipal, for a period of 2 years. Institutional Ethics Committee was obtained. The patients with symptoms and signs of

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hypothyroidism were considered for the study. Patients were selected from inpatient and outpatient basis, from any medical or surgical speciality. Inclusion criteria included patients with history and clinical features suggestive of primary hypothyroidism and those with age above 15 years.

Data of patients were collected using case record form. Patient history and basic information was recorded. Hypothyroid status was assessed by high TSH and low T3 and T4 levels. The basic laboratory investigations like complete blood picture including platelet count and ESR were noted. Fasting lipid profile and thyroid scan were also done wherever possible. Chest X-ray and ECG were taken. Echocardiography was performed wherever possible.

Patients were grouped as Group 1 – autoimmune thyroiditis: cases proven by thyroid peroxidase antibody positivity and/or FNAC (Histopathology) confirming autoimmunity. The test for thyroid peroxidase antibody was performed by the ELISA technique at the Ranbaxy laboratory. As per the lab standardisation, a value more than 50 u/mL was taken as positive; Group 2 – cases who

developed hypothyroidism post thyroid surgery or post radio-ablation of the thyroid gland.

Data was entered and analysed using a Microsoft excel sheet. Descriptive statistics were expressed as frequencies and percentages.

RESULTS

Table 1 describes the demographics and characteristics of the patients with auto-immune and non-autoimmune thyroiditis. In auto-immune group, 70% of patients were in the age group of 20-30 years with presence of family history was present in 5.8% patients. Comorbid conditions were common in autoimmune thyroiditis patients, with rheumatoid arthritis being the most common present in 14.5%, while such comorbid conditions were occasional in non-autoimmune group. Goitre was associated with autoimmune thyroiditis patients with presence in 59.4% patients.

	Autoimmune Thyroiditis (n=69)	Surgery/Radio Ablation Induced Hypothyroidism (n=32)
Age Distribution		
11-20	5 (7.24%)	1(3.125%)
21-30	15 (21.73%)	6(18.75%)
31-40	17 (24.63%)	5(15.62%)
41-50	16 (23.18%)	7(21.87%)
51-60	11 (15.94%)	5(15.62%)
61-70	3 (4.34%)	6(18.75%)
71-80	2 (2.89%)	2(6.52%)
Sex Distribution		
Male	17 (24.6%)	10 (31.30%)
Female	52 (75.4%)	22 (68.80%)
Family History		
Present	4 (5.8%)	-
Absent	65 (94.2%)	-
Associated Conditions		
Diabetes Mellitus 1	3 (4.30%)	-
Diabetes Mellitus 2	2 (3%)	3 (9.6%)
Rheumatoid Arthritis	10 (14.50%)	3 (9.6%)
Iron Deficiency Anaemia	4 (5.80%)	3 (9.6%)
Megaloblastic Anaemia	1 (1.45%)	-
Idiopathic Thrombocytopenic	1 (1.45%)	-
Purpura	1 (1.45%)	-
Osteoarthritis	4 (5.80%)	-
Carpal Tunnel Syndrome	1 (1.45%)	-
Myasthenia Gravis	1 (1.45%)	-
Membranous GN	1 (1.45%)	-
Clinical Features		
Cold Intolerance	38 (55.10%)	12 (37.50%)
Voice Change	27 (39.10%)	15 (46.90%)
Fatigue	53 (76.80%)	26 (81.3%)
Wt. Gain	39 (56.50%)	17(53.10%)
Muscle Stiffness	16 (23.20%)	5(15.6%)
Dry Skin	39 (56.50%)	10(31.30%)
Alopecia	9 (13%)	1 (3.10%)
Appetite	33 (47.80%)	15 (46.90%)

Constipation	32 (46.40%)	10(31.30%)
Chest Pain	9 (13%)	1 (3.10%)
Hypertension	13 (18.80%)	10(31.30%)
Dyspnea	11 (15.90%)	5 (15.6%)
Menstrual	22 (31.90%)	4 (12.50%)
Infertility	1 (1.40%)	-
Psychiatry	8 (11.60%)	1 (3.10%)
Pallor	16 (23.20%)	9 (28.10%)
Oedema	16 (23.20%)	3 (9.40%)
Goitre	41 (59.40%)	1 (3.10%)
Vitiligo	1 (1.40%)	-
Xanthoma	2 (2.90%)	1 (3.10%)
Cardiovascular Related Symptoms	6 (8.70%)	-
Memory	5 (7.20%)	2(6.30%)
Prox. Weakness	13 (18.80%)	3 (9.40%)
Delayed Refluxes	27 (39.10%)	5 (15.6%)
Menstrual Disturbances		
Menorrhagia	15 (21.7%)	-
Amenorrhea	6 (8.7%)	-
Oligomenorrhea	1 (1.4%)	-
Absent	47 (68%)	-
Goiter		
Present	41 (59.4%)	-
Absent	28 (40.6%)	-
Chest X-Ray		
Normal	64 (92.8%)	31(96.9%)
Cardiomegaly	3(4.3%)	1(3.1%)
Unfolding Aorta	1(1.4%)	-
Pneumonia	1(1.4%)	-
ECG		
Normal	55 (79.70%)	27 (84.4%)
LVH	2 (2.90%)	2 (6.25%)
IHD	9 (13%)	2 (6.25%)
Arrhythmias	3 (4.30%)	1 (3.1%)
Echo		
Not done	47(68.11%)	17(53.12%)
Normal	11(7.59%)	7(21.85%)
Diastolic Dysfunction	6(8.70%)	2(6.25%)
IHD	1(1.45%)	1 (3.1%)
LVH	3(4.3%)	-
Peri effusion	1(1.45%)	-
Histology (FNAC %)		
Not Done	49 (71%)	-
Hashimoto's/Lymphocytic	20 (29%)	-

Table 1. Demographics and Characteristics of Patients

DISCUSSION

Hypothyroidism is the most common clinical disorder of thyroid function. Primary hypothyroidism may result from diseases or treatments that destroy thyroid tissue or interfere with thyroid hormone biosynthesis. Hypothyroidism holds its importance for a physician, as it forms a reversible cause for many of the varied systemic manifestations it produces. In areas where iodine intake is adequate, the most common cause of primary hypothyroidism is ascertained as chronic autoimmune thyroiditis.

In present study, maximum patients were in the age group of 31-50 in the autoimmune group (total of 33 patients) and a similar finding in the iatrogenic group (total of 12 patients). This was in accordance with the Whickham Survey,⁸ wherein peak incidence of hypothyroidism was seen in 31-50 years age group.

Present study showed female dominance as expected. The ratio of female to males were 3:1 in the autoimmune group and 2.2:1 in the other group. The female predominance in thyroid disorders is well known. In the

original series of 109 patients reported by the Myxoedema Commission of the Clinical Society of London, 15 of the patients were men, 94 were women.¹⁰ About 80% of patients with hypothyroidism have been women, when the patients were in areas endemic for goiter or in non-endemic areas.¹¹

The family history was noted in the autoimmune hypothyroid group as its heritability and prevalence in families is well known. Pathogenesis of autoimmune thyroiditis suggests that each patient has a background inherited predisposition to autoimmunity, with additional environmental and hormonal factors contributing to it.¹² Even the heritability of thyroid antibodies like Tg and TPO were shown in some studies.¹³ But on the contrary, in this study group only 5.8 percentage of patients had family history positive. This may be due to the subclinical cases unnoticed in families, the newer nuclear family system coming up and also the less advance in genetic and chromosomal detection facilities compared to the west.

In this study, in the autoimmune group, the commonest mode of presentation was fatigability in 76.8% of patients. The above mentioned studies and other studies by Wayne¹⁴ and Larson et al,¹⁵ all state that it is the major symptom. Goiter was the next major finding (59.4%) in the autoimmune group. As mentioned in the review, autoimmune thyroiditis exists in two major form – goitrous (Hashimoto's) and atrophic. This study has shown that the goitrous form is predominant. Dry skin and weight gain were next in the order (56.5%). The percentage of dry skin in this humid part of the world also was correlating with some western study data of about 77%. The weight gain data was closely matching with the Larsen¹⁵ study figure of 59%, though Wayne,¹⁴ observed it to be 76%.

Symptom of cold intolerance were noted in 55% in this study, but in Western studies of Wayne¹⁴ and Larsen,¹⁵ the figures were 95% and 89% respectively. This difference could probably be explained by the climatic differences experienced by the Western study population as compared to ours. The figures of decreased appetite and constipation were almost similar with 47.8% and 46.4% respectively. Nine patients had alopecia and memory disturbance, vitiligo and xanthelasma were seen in a minor group.

Around 16% had dyspnoea. Western studies have shown high percentage of dyspnoea (55%) in patients of hypothyroidism. In severe hypothyroidism, there is myxedematous infiltration of respiratory muscles and depression of both the hypoxic and the hypercapnic ventilatory drives. Pleural and pericardial effusions though are long standing and do not usually cause dyspnoea.

Nine patients in this study had complaints of chest pain. According to Larsen,¹⁵ a small percentage of patients (25%) can have precordial chest pain which may be due to associated hypertension and hypercholesterolemia leading to coronary artery disease or more commonly it may be due to starting of treatment with thyroid hormone replacement.

32% of patients had menstrual irregularities. The most common finding was menorrhagia occupying 21.7% of study group. The figure was closely correlating with Larsen¹⁵ of

35%. Primary hypothyroidism leads to decreased progesterone secretion. As a result, endometrial proliferation persists leading to excessive and irregular break through menstrual bleeding. These changes may be due to deficient secretion of LH. Rarely, secondary depression of pituitary function may lead to ovarian atrophy and amenorrhoea (8.7% in this study).

No difference was found in clinical presentation between two groups except in goiter incidence, which was obvious as the second group were thyroid devoid group. This was in accordance with the statement in 'the Thyroid'¹¹ that the clinical manifestations of hypothyroidism are independent of its cause.

In the autoimmune group, cardiomegaly was noted in 4.3%, while that in second group was 3.1%. The association of enlarged heart in hypothyroidism may be due to myxoedema heart, pericardial effusion, congestive cardiomyopathy etc.¹⁶

In autoimmune group, ECG changes of ST-T changes were present in 13% and LVH in 2.9%, while in second group, the ST-T changes and LVH were there in 6.3% each. The ST-T changes in hypothyroidism is reported in studies and the incidence of coronary artery disease is also well known.^{17,18}

In the autoimmune study group, histopathologic examination was done in 20 patients and all of them were reported to have Hashimoto's or lymphocytic thyroiditis changes. The thyroid scan was done in only 16 patients of the autoimmune group and a 31% out of that were demonstrated having thyroiditis. But thyroid imaging as a test in goitrous autoimmune thyroiditis is unnecessary.⁵

Comorbidities were common in these patients. 14.5% of patients had rheumatoid arthritis, which is also an autoimmune condition. In a study published in Rheumatology 2001, positive TPO antibody was detected in 10.9% of rheumatoid arthritis patients.¹⁹ The association has also been emphasized by Walker et al in his study.²⁰ Type I diabetes mellitus was present in 4.35% patients. In a study conducted on children with type I DM, 39% had Hashimoto's thyroiditis.²¹ Certain studies from UK and US also support the strong association between type I DM and autoimmune thyroiditis.²² Other minor associations were found with (1.45% each) megaloblastic anaemia, immune thrombocytopenic purpura, myasthenia gravis, membranous glomerulonephritis and osteoarthritis. The myasthenic case in this study had ocular myasthenia gravis. Studies also prove the association of Hashimoto's thyroiditis with pernicious anaemia, myasthenia gravis, ITP etc.^{23,24}

It can be observed that though the causes of hypothyroidism are different, such patients present with similar symptoms. Under such circumstances, it is important to identify the causes of hypothyroidism in such patients and treat them accordingly. Only clinical presentation is not enough to determine the cause and hence, doing detailed investigations along with identification of relevant history is important. Demonstration of anti-TPO antibodies helps to identify the cause of hypothyroidism as autoimmune. This a

limitation in India, as many of the places lack detection facilities and causes of hypothyroidism may go unidentified.

CONCLUSION

The patients with primary hypothyroidism of autoimmune thyroiditis and that due to other causes have similar demographics and clinical presentation. The common symptoms in these patients is fatigability and most of the patients with autoimmune thyroiditis have goitre. Substantial proportion of patients with autoimmune thyroiditis have comorbid conditions such as rheumatoid arthritis, type I diabetes mellitus, ITP, megaloblastic anaemia, myasthenia gravis.

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