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SUBTOTAL THYROIDECTOMY;
CHANGES IN THE THYROID AUTOANTIBODY LEVEL FOLLOWING SURGERY & RADIOIODINE THERAPY

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ABSTRACT ... kraqur21@hotmail.com **Objective:** Autoimmunity is common in thyroid diseases. Antibody level is affected after subtotal thyroidectomy and radio iodine treatment. We studied microsomal & thyroglobulin autoantibody level in patients with toxic diffuse goitre and multinodular goitre before and after surgery & radio iodine to determine effects of therapy. **Design:** Prospective study. **Settings:** Postgraduate Medical Institute, Lahore. **Material & Methods:** Three serial blood samples from each of a total of 30 seropositive patients (15 of multinodular goitre, undergoing thyroid surgery. 15 of toxic diffuse goitre receiving radioiodine) were analyzed for microsomal & thyroglobulin autoantibody using tagged red cell haemagglutination technique. **Results:** We found a female preponderance in thyroid diseases. The microsomal & thyroglobulin autoantibody level in patients with multinodular goitre, decreased gradually and progressively after subtotal thyroidectomy while subjects with toxic diffuse goitre receiving radioiodine showed a rise in antibody level as compared to pretreatment period. The change became evident just after 10 days of therapy. **Conclusion:** The autoimmune status of thyroid disease patients is altered after subtotal thyroidectomy & radioiodine therapy. The autoantibody levels after subtotal thyroidectomy are gradually decreased while after radioiodine therapy the antibody levels have been found to increase.
Key Words: 1. Thyroid auto antibodies 2.Subtotal thyroidectomy 3. Radioiodine treatment

INTRODUCTION

Around one in 20 people will experience some form of thyroid dysfunction in their life time.[1] The autoimmune nature of the human thyroid disease was described in 1956 by Roitt et al.[2] Overall prevalence of autoimmune thyroid disease comprising toxic diffuse goiter (TDG), Hashimoto' thyroiditis and primary hypothyroidism approaches 1.0% in the Western population.[3]

Presently apart from these conditions, most of the other thyroid diseases like multinodular goiter (MNG) and solitary toxic nodule are also thought to immunologically mediated.[4.6] Thyroid autoimmunity involves both the cell mediated as well as humoral response (antibodies). Autoanitibodies in autoimmune thyroiditis are generally directed against thyroid microsomal antigen and/or thyroglobulin.[7] Microsomal autoantibody (MS Ab) is more specific than thyroglobulin autoantibody (TG Ab) as a marker of autoimmunity in thyroid diseases.[8.9] Positive serum antithyroid antibodies may indicate the existence of lymphocytic infiltration in the thyroid gland.[10]

Subtotal thyroidectomy and radioiodine therapy (RAI) are two therapeutic modalities for TDG and MNG. In the USA. 70-90% of the patients with hyperthyroidism are treated with RAI as first line of therapy.[11] In Europe the surgical approach is often preferred and considered safer than RAI.[12] Thyroid surgery i.e., subtotal thyroidectomy results in a rapid and reliable resolution of hyperthyroidism and removal of goiter with low morbidity and mortality.[13] RAI is safe and effective for the treatment of hyperthyroidism, usually a single dose is required.[14.15] But the results are delayed and there is a possible risk of relapse of hyperthyroidism and thyroid cancer.[12.16]

Additional doses of RAI, however, may be administered if first dose fails. Goiter is usually not affected by this therapy. Various studies have demonstrated the prognostic significance of changes in the autoantibody level following the treatment by surgery and radioiodine. [16-17] The patients with TDG who have high levels of MS Ab after RAI, suffer more frequently from hypothyoidism.[18.19] Relapse of hyperthyroidism may occur in patients with persistent levels of thyroid stimulating antibody.[12.20] So far no study has been conducted in Pakistan on the autoimmune status in patients with thyroid diseases after treatment. Therefore, in this prospective study we measured MS Ab and TG Ab level in patients with thyroid disease following subtotal thyroidectomy and RAI to determine their effects on thyroid autoimmunity.

MATERIAL & METHODS

This prospective study included 30 patients with thyroid disease who were positive for thyroid autoantibody, half of them received RAI and second half underwent subtotal thyroidectomy.

Subjects were recruited from the Services Hospital, Mayo Hospital and INMOL, Lahore after informed consent. A uniform physical examination was done for all patients after taking a thorough clinical history. Patients receiving RAI suffered from TDG while those undergoing subtotal thyroidectomy had non-toxic MNG.

For measurement of MS Ab and TG Ab, three blood samples were drawn from each patient, first at the initiation of therapy, second 10 days later and third after two months, Serum was separated and preserved at-20^{o} C until assay. Antibodies were measured by tagged red cell haemagglutination technique[21] using commercial kits Thymune-M, and Thymune-T supplied by Wellcome Diagnostics, Antibody titre of 100 units for MS Ab and 20 units for TG Ab were considered positive. Subjects positive for any of the two antibodies or for both were taken as positive.

For the purpose of statistical analysis, antibody titres were assigned numerical values (i.e 1;100=1, 1:400=2, 1:600=3etc for MS Ab and 1:10=1, 1:20=2, 1:40=3 etc for TG Ab).[10] Student T test was used for comparison of numeric data. The comparison of antibody level was done using Sign test and the Mann-Whitney U test. The level of significance was set at 0.05.

RESULTS

On of thirty, 15 patients with MNG (mean age= 42.4+7.3 years (33-55), M/F=6/9] underwent subtotal thyroidectomy whereas the other 15 patients with TDG (mean age= 36.8+14.1 years

(16-48), M/F=4/11) received RAI. Thyroid disease showed a female preponderance. The difference of age between different groups and sexes was not significant.

The changes in the thyroid autoantibody level in patients with thyroid disease following subtotal thyoidectomy are shown Table I. These patients showed a decrease in the MS Ab and TG Ab titre. The difference of MS Ab level before and after 2 months of treatment was highly significant ($p<0.01$).

The difference of TG Ab titre became significant just after10 days. This difference became more pronounced after 2 months. The changes in the thyroid autoantibody level in patients receiving RAI are shown in Table II. Both the MS Ab and TG Ab showed a rise after the therapy. The majority of patients had higher antibody level in the post treatment period. The difference of titre for both the antibodies was highly significant and it was more marked after 2 months.

Table-I. Comparison of Thyroid Autoantibody level in Patients with Multinodular Goitre before & after Subtotal Thyroidectomy

		No. of Patients		
	Antibody Titre	**Before Therapy (A)**	**Ten days after Therapy (B)**	**Two months after Therapy (C)**
Microsomal Antibody	100-400	7	9	12
	1600-6400	7	5	3
	25,000 & above	1	1	
Comparison	A vs B = S, A vs C = HS, B vs C = NS			
Thyroglobulin Antibody	20-160	4	6	7
	320-640	3	1	
	1280 & above	1	1	1
Comparison	A vs B = S, A vs C = HS, B vs C = NS			

S=significant ($p<0.05$), HS=highly significant ($p<0.01$), NS=non-significant ($p>0.05$)

DISCUSSION

Treatment of thyroid disease by subtotal thyroidectomy and radioiodine may directly affect the levels of thyroid autoantibodies as it has been observed that lymphocytes infiltrating thyroid itself acts as a major source of thyroid antibodies.[22-23] Therefore antibody titer and lymphocytic infiltration parallels during clinical course of autoimmune thyroid disease.[10] In this study, we observed a female preponderance in patients population (Having TDG as well as MNG). This is in accordance with other studies, which have found female dominance in all the thyroid disease.[10.24.25] The reason for this observation is not known. Roitt proposed that sex hormones might contribute to the increased frequency of autoimmunity in females.[26]

Table-II. Comparison of Thyroid Autoantibody level in Patients with Diffuse Toxic Goitre before & after Radioiodine Therapy.

		No. of Patients		
	Antibody Titre	**Before Therapy (A)**	**Ten days after Therapy (B)**	**Two months after Therapy (C)**
Microsomal Antibody	100-400	9	5	1
	1600-6400	4	7	9
	25,000 & above	2	3	4
Comparison	A vs B = S, A vs C = HS, B vs C = NS			
Thyroglobulin Antibody	20-160	7	6	6
	320-640	2	2	1
	1280 & above	2	3	4
Comparison	A vs B = S, A vs C = HS, B vs C = NS			

S=significant (p<0.05), HS=highly significant (p<0.01), NS=non-significant (p>0.05)

Following subtotal thyoidectomy, patients with MNG showed a gradual and progressive fall in thyroid autoantibody level. The reduction in antibody level was more marked after 2 months of surgery. Most of the studies support these findings.[22.23.27] It has been seen that the fall in the antibody titer was not immediate but slow and progressive. This change can be explained thus: As the thyroid is a major site of antibody production, the removal of a portion of the gland along with antibody producing lymphocytes results in reduction of antibody synthesis.[22.23]

In contrast, some researchers have demonstrated a dramatic fall of antibody level during first 24 hours after surgery[28] while others reported initial increase before the reduced levels were detected.[29] Transient increase may be due to leakage of antibodies from the manipulated gland. Although there is gradual and progressive fall after thyroidectomy, antibodies may not disappear altogether and perist indefinitely.[30] reflecting that the dysfunction responsible for their production was still there and the basis of this dysfunction could be genetic.

In this study. a rise in the thyroid autoantibody level was observed in patients with TDG after RAI. Both MS Ab and TG Ab titre rose significantly as compared to pretreatment levels. This became evident after 10 days. These findings are in agreement with other studies. Amino found a sharp rise in the thyroid autoantibody titre to many time of pretreatment level during 1-3 months of therapy.[31] Scherbaum showed that MS Ab & TG Ab titre may fluctuate from one on observation to the other.[32] There may be two reasons of increase in antibody level. Firstly, the radiation damage may release autoantigen from the thyroid that is able to stimulate the production of antibodies from extra thyroidal sites.[33] Secondly, the thyroid contains a population of helper and suppressor T calls and B cells.

Helper cells are radioresistent as compared to suppressor cells. Radiation kills the B cells as well as suppressor T cells. A population of T cells survives which produce the antibodies from the non-radiated cells, which populate the gland.[34] Some studies found association of occurrence of

hypothyroidism in TDG cases with high MS Ab & TG Ab titres in the post radiation period.[18.27] Some researchers have detected development of thyroid antibodies in some serongative subjects with thyroid diseases after treatment with RAI [25.35]

CONCLUSION

The autoimmune status of thyroid disease is altered after subtotal thyroidectomy & radioiodine therapy. The autoantibody levels after subtotal thyroidectomy, are gradually decreased while after radioiodine therapy the antibody levels have been found to increase. Further to this a large prospective study with a prolonged follow-up of autoantibody level and thyroid function is required to find the prognostic significance of the changes in autoimmunity in these patients.

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