

# ANTI DEOXYRIBONUCLEIC ACID AND ANTINUCLEAR ANTIGEN ANTIBODIES IN GRAVES' DISEASE

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**Abstract-** Graves' disease is an autoimmune disorder characterized by presence of antibodies directed against thyroid stimulating hormone (TSH) receptor or nearby region. Other serological abnormalities like antibodies to double stranded DNA (ds-DNA) and antinuclear antibodies (ANA) have also been observed. We studied antibodies to ds-DNA and ANA in our patients with Graves' disease and compared them with control group. Sera of 84 patients (29 males, 55 females) with diagnosis of Graves' disease were prepared and level of antibodies to ds-DNA and ANA were measured and compared with 41 healthy persons (15 males, 26 females). The level of antibodies to ds-DNA and ANA in patients and control group did not show any significant difference. Our results were different from other studies in other countries. The difference may be explained by difference in our method of antibody measurement or genetic background which needs to be confirmed by HLA studies of our population.

*Acta Medica Iranica*, 43(2): 140-142; 2005

**Key words:** Graves' disease, anti deoxyribonucleic acid, antinuclear antigen antibodies, immunofluorescent method

## INTRODUCTION

Graves' disease is an autoimmune disorder with organ specific antibodies directed against antigens of thyroid stimulating hormone (TSH) receptor or close proximity to TSH receptor which cause hyperplasia and increased functional activity of thyroid follicular cells (1). Recently, Katakura *et al.* reported that 88% of untreated patients with Graves' disease had detectable antibodies to double stranded DNA (ds-DNA), quantitated by RIA (2). Antibodies to ds-DNA are considered to be a highly specific for systemic lupus erythematosus (SLE) (3).

Conflicting reports exists about positivity of anti DNA antibodies in Graves' disease. Antinuclear antibodies (ANA) were more frequent in patients with autoimmune thyroid disease than controls in one study but rheumatologic symptoms have not been reported to more frequent (2, 4-8).

## MATERIALS AND METHODS

From 102 patients who were referred to our endocrine clinic, 84 patients were accepted as having Graves' disease according to one of the following criteria.

1. Patients who clinically were hyperthyroid with diffuse thyroid enlargement and elevated T4, T3, T3 resin uptake and radioactive iodine uptake (RAIU) accompanied by suppressed TSH level.

2. Patients who clinically and by laboratory data confirmed to be hyperthyroid with CT scan or MRI in favor of Graves' ophthalmopathy.

3. Those who had ophthalmopathy of Graves' disease, confirmed by CT scan or MRI of orbit or TRH test and diagnosed as euthyroid Graves' ophthalmopathy.

A total of 41 persons with negative past history of hyperthyroidism who did not have collagen vascular disease, SLE or any other rheumatologic disease and were not on any medication and had normal laboratory thyroid function tests were selected as control group.

Five ml of blood of patients and controls was prepared. Antibodies to ds-DNA was measured by

Received: 17 Jan. 2004, Revised: 7 Aug. 2004, Accepted: 31 Aug. 2004

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ELISA method and ANA was measured by indirect immunofluorescent. Subjects were mainly patients with active Graves' disease except for a few patients which only had euthyroid Graves' ophthalmopathy.

Patients were treated with methimazole for one year, with starting dose of 40 mg/day and maintenance dose of 5-10 mg/day, till they became euthyroid.

Data were analyzed by SPSS Win 6; comparison of mean values in both groups was performed by variance analysis. We used Pearson correlation coefficients for determination of correlation and Chi square and Fisher exact test for quantitative variables analysis. A  $P$  value  $< 0.05$  was considered to be significant.

## RESULTS

A total of 84 patients, 29 males (34.5%, with mean age of 38.2 years) and 55 females (65.5%, with mean age of 34.01 years) were compared with 41 healthy persons, 15 males (36.6%, with mean age of 37.3 years) and 26 females (63.4%, mean age of 33.5 years) (Table 1).

The results of hormonal assay are shown in table 2. Mean ds-DNA antibody measured by ELISA method was not significantly different in patients and controls of both sexes. Mean antibody levels in patients and controls were 6.6 and 7.68, respectively. Considering age and sex in patients with Graves' disease, level of ds-DNA antibody was higher in 30-34 years old females while in other age groups there was no significant difference (Table 3).

Measurement of ANA by immunofluorescent method showed positive results in 3 patients and one control with a titer of 1:20 (homogenous pattern). which were not different statistically ( $P > 0.05$ ).

**Table 1.** Distribution of patients and control groups according to age and sex

Sex	Patients (n=84)		Controls (n=41)	
	No (%)	Mean age $\pm$ SD	No (%)	Mean age $\pm$ SD
Male	29 (34.5%)	38.2 $\pm$ 12.1	15 (36.6%)	37.3 $\pm$ 11.9
Female	55 (65.5%)	34.01 $\pm$ 13.4	26 (63.4%)	33.5 $\pm$ 10.2

Abbreviation: SD, standard deviation.

**Table 2.** Mean hormone level in 84 patients with Grave's disease

Hormone	Mean level $\pm$ SD
TSH $\mu$ U/ml (NL= 0.3-3.8)	0.2 $\pm$ 0.3
T4 $\mu$ g/ml (NL= 4-12)	20.2 $\pm$ 5.3
T3RU (%) (NL= 25.5-34.4)	33.2 $\pm$ 11
T3 ng/dl (NL= 80-200)	459.9 $\pm$ 205
RAIU 2 hr % (NL= 5-20)	46.1 $\pm$ 18
RAIU 24 hr % (NL= 20-55%)	67.9 $\pm$ 20

Abbreviations: TSH, thyroid stimulating hormone; NL, normal level.

## DISCUSSION

Graves' disease is an autoimmune diseases in which defect in T lymphocyte suppressor cells lead to stimulation of B lymphocytes by T-helper lymphocytes and finally production of different types of autoantibodies either specific to thyroid including TPO, Tg and TSH receptor or non specific like ANA, ds-DNA and smooth muscles antibodies (4,10). In recent years many studies have been performed concerning these non specific antibodies but diverse results have been obtained. In this study mean antibody level to ds-DNA measured by ELISA method was 6.6 with SD of 4.13 in 84 patients (table 3) and 7.68 with SD of 5.32 in 41 controls and level of antibodies did not show significant difference in males and females of both patients and control groups (1). In another study, measurement of ds-DNA antibody in 42 patients with active Graves' disease revealed that the level of antibodies were undetectable (7), a finding greatly different from those obtained by Katakura *et al.* (2).

**Table 3.** Comparison of ds-DNA antibody in patients and control of sexes according to different age groups both sexes

Sex	Age group	Patients	Controls	P
Male	15-29	5.8 $\pm$ 5.38	7.88 $\pm$ 3.3	NS
	30-44	7.51 $\pm$ 3.72	8.86 $\pm$ 4.5	NS
	$\geq 45$	7.03 $\pm$ 7	7.42 $\pm$ 3.5	NS
Female	15-29	7.41 $\pm$ 3.63	9.53 $\pm$ 8.7	NS
	30-44	5.62 $\pm$ 2.27	8.35 $\pm$ 3.1	0.01
	$\geq 45$	8.19 $\pm$ 4.08	4.83 $\pm$ 0.7	NS

Abbreviation: NS, not significant.

\*Data are given as mean  $\pm$  SD.

## Antinuclear antibodies in Graves' disease

Baethge *et al.* (4) measured ds-DNA antibodies by more specific crithidia immunofluorescence assay and were unable to confirm their positive findings with Farr assay. In a study by Morita *et al.*, ANA was positive in 18% of Graves' patients versus 8% of control group, and in higher titers (10). The difference in results of antibody level may be due to different cell lines used in lab tests and methods of measurement by immunofluorescent. Finally, difference in genetic background of our population needs to be confirmed by HLA study.

## REFERENCES

1. Gossage AA, Munro DS. The pathogenesis of Graves' disease. *Clin Endocrinol Metab.* 1985 May; 14(2):299-330.
2. Katakura M, Yamada T, Aizawa T, Hiramatsu K, Yukimura Y, Ishihara M, Takasu N, Maruyama K, Kameko M, Kanai M, et al. Presence of antideoxyribonucleic acid antibody in patients with hyperthyroidism of Graves' disease. *J Clin Endocrinol Metab.* 1987 Mar; 64(3):405-408.
3. Koffler D, Carr RI, Agnello V, Fiezi T, Kunkel HG. Antibodies to polynucleotides: distribution in human serums. *Science.* 1969 Dec 26;166(913):1648-1649.
4. Baethge BA, Levine SN, Wolf RE. Antibodies to nuclear antigens in Graves' disease. *J Clin Endocrinol Metab.* 1988 Mar; 66(3):485-488.
5. Tajiri J, Higashi K, Morita M, Ohishi S, Umeda T, Sato T. Elevation of anti-DNA antibody titer during thyrotoxic phase of silent thyroiditis. *Arch Intern Med.* 1986 Aug; 146(8):1623-1624.
6. Murakami M, Koizumi Y, Aizawa T, Yamada T, Takahashi Y, Watanabe T, Kamoi K. Studies of thyroid function and immune parameters in patients with hyperthyroid Graves' disease in remission. *J Clin Endocrinol Metab.* 1988 Jan; 66(1):103-108.
7. McDermott MT, West SG, Emlen JW, Kidd GS. Antideoxyribonucleic acid antibodies in Graves' disease. *J Clin Endocrinol Metab.* 1990 Aug; 71(2):509-511.
8. Petri M, Karlson EW, Cooper DS, Ladenson PW. Autoantibody tests in autoimmune thyroid disease: a case-control study. *J Rheumatol.* 1991 Oct; 18(10):1529-1531.
9. Peng SL, Hardin JA, Craft J. Antinuclear antibodies. 5th edition. Philadelphia: Saunders; 1996.
10. Morita S, Arima T, Matsuda M. Prevalence of nonthyroid specific autoantibodies in autoimmune thyroid diseases. *J Clin Endocrinol Metab.* 1995 Apr; 80(4):1203-1206.
11. McDermott MT, West SG, Emlen JW, Kidd GS. Antideoxyribonucleic acid antibodies in Graves' disease. *J Clin Endocrinol Metab.* 1990 Aug; 71(2):509-511.