

Smoking associated with TSH receptor antibody and serum IL-17A elevation in hyperthyroid Graves' disease

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Introduction

Graves' ophthalmopathy is an autoimmune thyroid disease with local orbital inflammations and immune processes leading to periorbital edema, proptosis, corneal ulcers and loss of visual fields. Proinflammatory cytokines, such as IL-1, IL-6 and TNF α are involved in the orbital damages. Th17 cells are newly discovered CD4+ T cells producing predominantly IL-17A cytokine. IL-17A act as proinflammatory cytokine and chemokine. The role of IL-17A is demonstrated in acute and chronic inflammation, autoimmune and allergic diseases, as well as in the defense mechanism. The worsening effect of smoking on thyroid gland size and risk of Graves' ophthalmopathy has been confirmed by several reports.

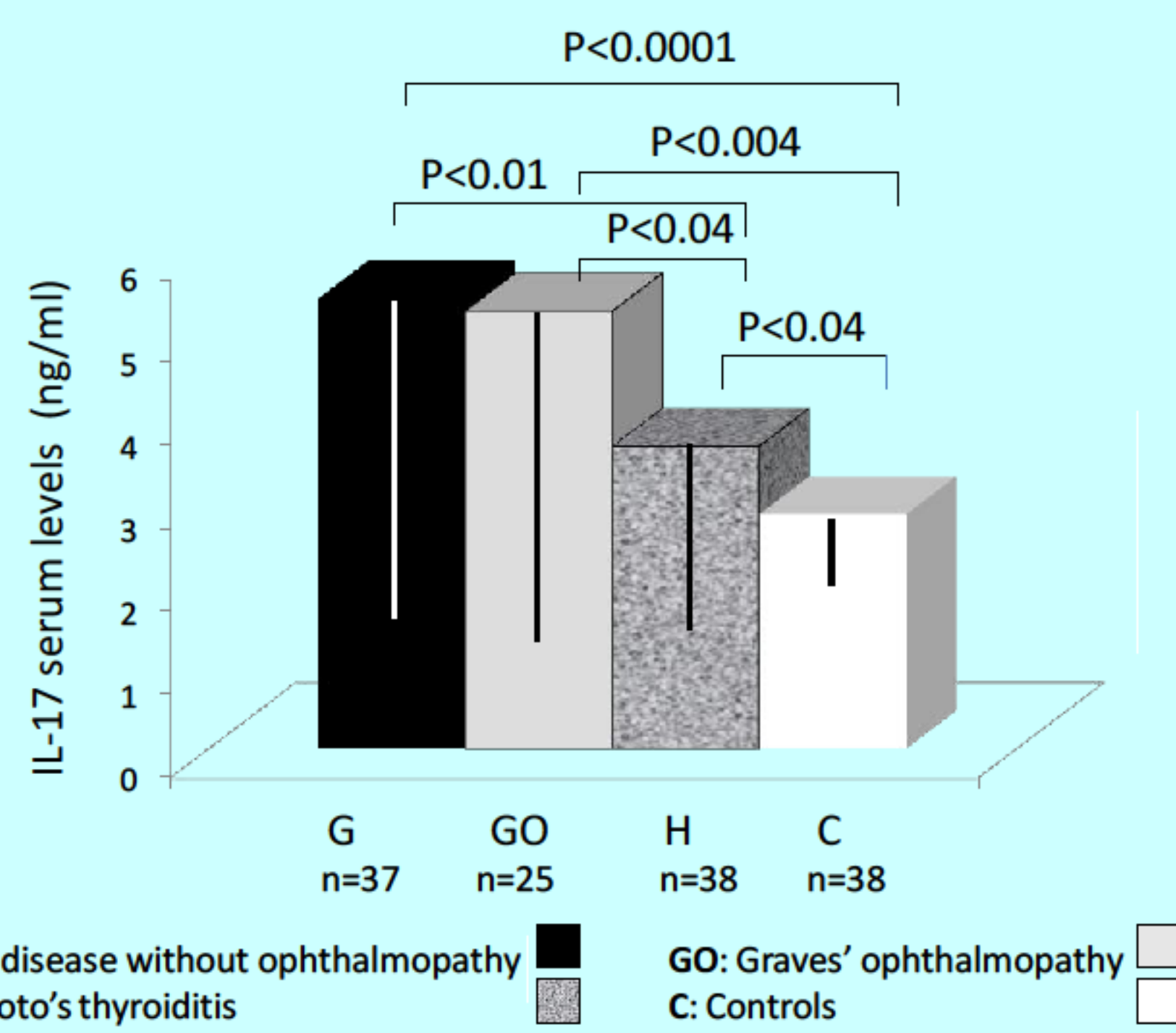


Figure 1: IL-17A serum levels in autoimmune thyroid diseases and controls.

Purpose of the study

- To investigate the IL-17A serum levels in autoimmune thyroid diseases and controls.
- To demonstrate smoking effect on IL-17A serum levels.
- To study the relationships among smoking and serum IL-17A, TSH receptor antibody, anti-TPO, anti-Htg levels in Graves' disease.
- To demonstrate the influencing effect of smoking on IL-17A serum level during thyrostatic therapy in Graves' hyperthyroidism.

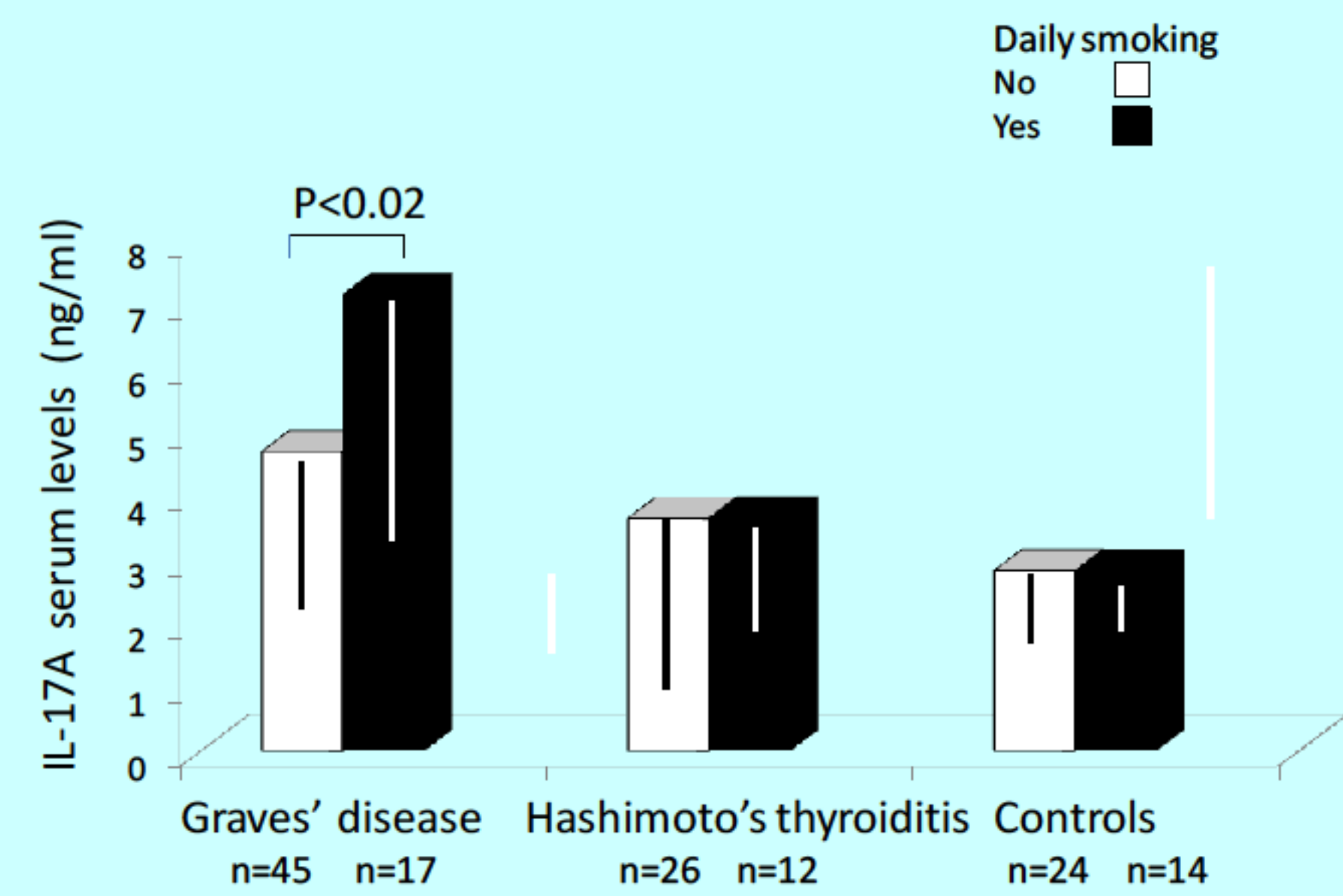


Figure 2: Smoking effect on IL-17A levels in autoimmune thyroid diseases and controls.

Patients and methods

One-hundred-thirty-eight patients, 62 with Graves' disease (25 with ophthalmopathy, 33 with hyperthyroidism, 17 have daily smoking), 38 with Hashimoto's thyroiditis and 38 healthy controls were investigated.

Serum IL-17A levels were measured with enzyme-linked immunosorbent assay; thyroid hormones, anti-thyroid antibodies in a fully automated way, but TSH receptor antibodies with radioimmunoassay.

Student's paired t-test was used for the statistical analysis.

Table 1: Clinical parameters in patients with autoimmune thyroid diseases and controls.

Clinical parameters	Patient groups			
	Graves' disease (n=37)	Graves' ophthalmopathy (n=25)	Hashimoto's thyroiditis (n=38)	Control (n=38)
Gender (female/male)	32/5	22/3	38/0	34/4
Age (years)	41 ± 12	49 ± 13	43 ± 11	45 ± 12
Daily smoking (n)	11	6	12	14
TSH (mU/l)	1,65 ± 3,6	2,78 ± 5,71	3,51 ± 5,83	
FT ₄ (pmol/l)	19,8 ± 9,49	23,55 ± 14,5	15,22 ± 3,39	
FT ₃ (pmol/l)	8,38 ± 5,7	8,09 ± 7,43	4,19 ± 1,17	
TSH receptor antibodies (U/l)	5,89 ± 8,66	10,61 ± 12,33		
Anti-TPO antibodies (IU/l)	359,47 ± 414,51	298,64 ± 410,41	480,12 ± 313,8	
Anti-Htg antibodies (IU/l)	196,72 ± 322,8	34,34 ± 32,1	433,14 ± 976,92	
IL-17A (ng/ml)	5,43 ± 3,62 ^{a,b}	5,28 ± 3,8 ^{c,d}	3,65 ± 2,22 ^{b,d,e}	2,83 ± 0,73 ^{a,c,e}

^a P<0.0001 ^b P<0.02 ^c P<0.004 ^{d,e} P<0.04

Results

- IL-17A serum levels were higher in Graves' disease in comparison with Hashimoto's thyroiditis and controls.
- Smoking accompanied with higher IL-17A levels in hyperthyroid Graves' disease.
- Smoking was associated with higher serum levels of TSH receptor antibody (TRAK) in Graves' hyperthyroidism, particularly in patients with TRAK positivity.
- Smoking was connected to higher anti-TPO and anti-Htg antibody serum levels.
- Smoking resulted in relevant increase of IL-17A serum levels compared to those with nonsmoking patients or who did not receive any therapy in hyperthyroid Graves' patients.
- No remarkable elevated IL-17A serum levels was demonstrated in active ophthalmopathy but was connected to eye symptoms with periorbital edema, conjunctivitis, proptosis and eye muscle involvements.

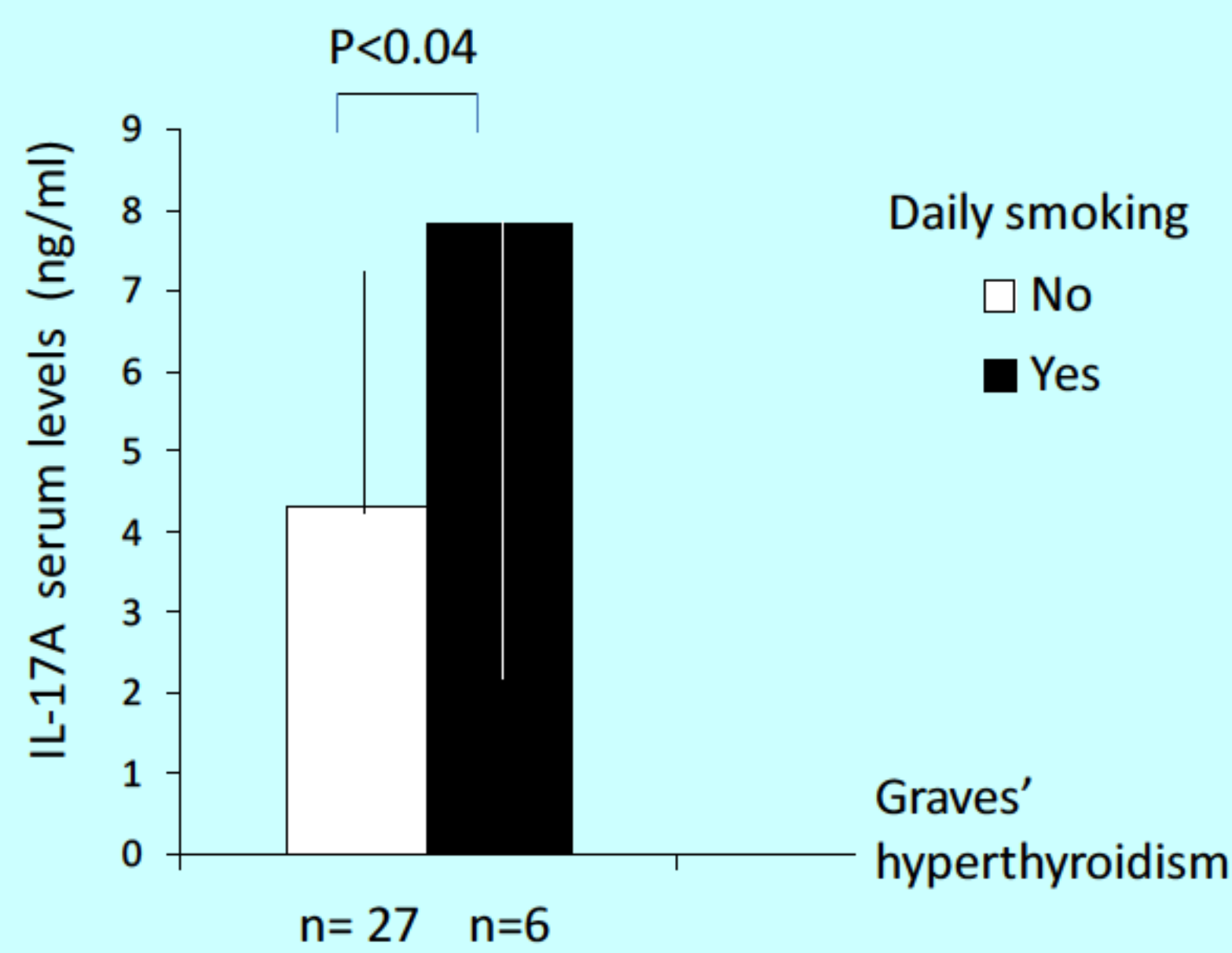


Figure 4: Effect of smoking on IL-17A in hyperthyroid Graves' disease.

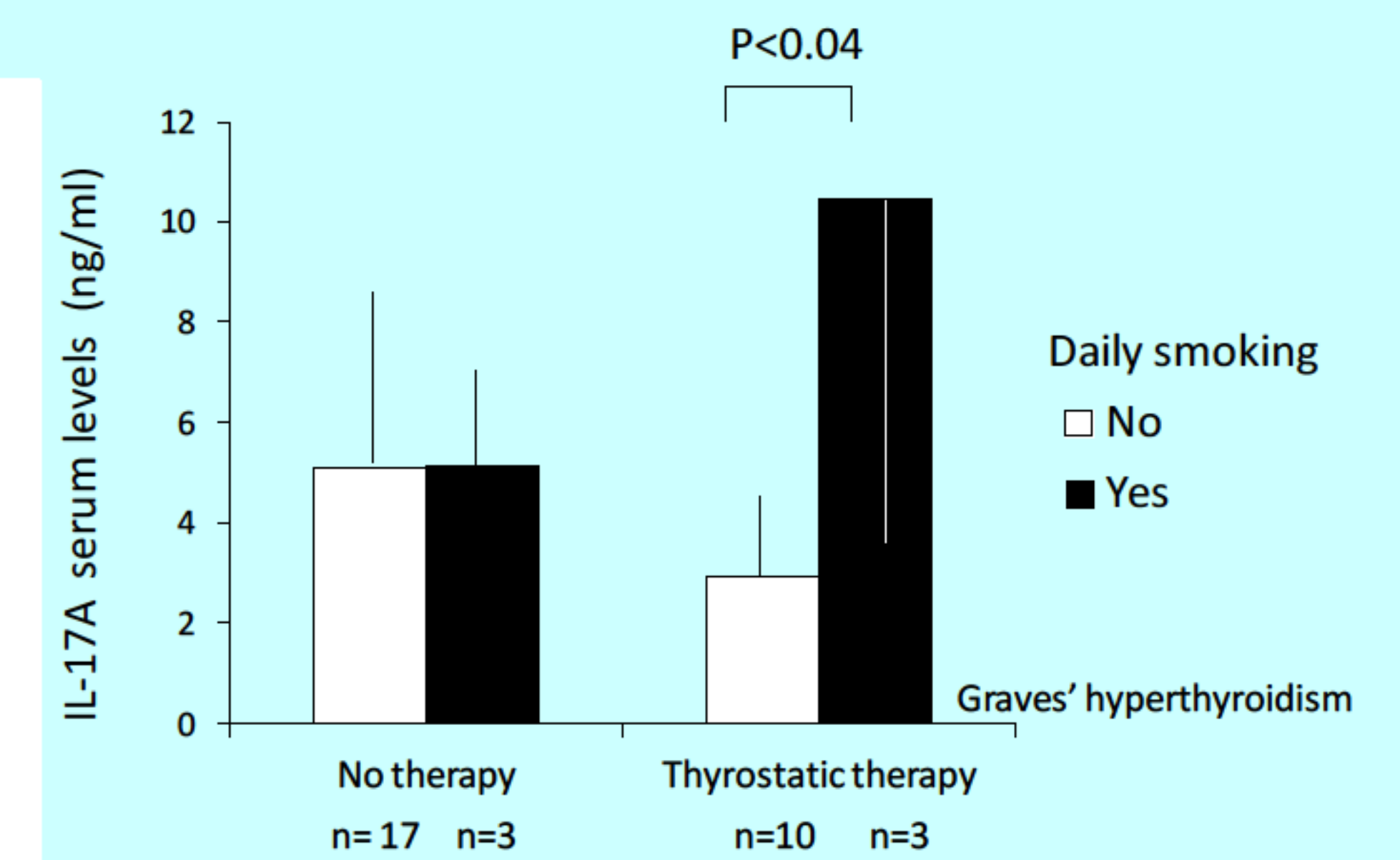


Figure 3: Effect of thyrostatic therapy and smoking on IL-17A levels in Graves' hyperthyroidism.

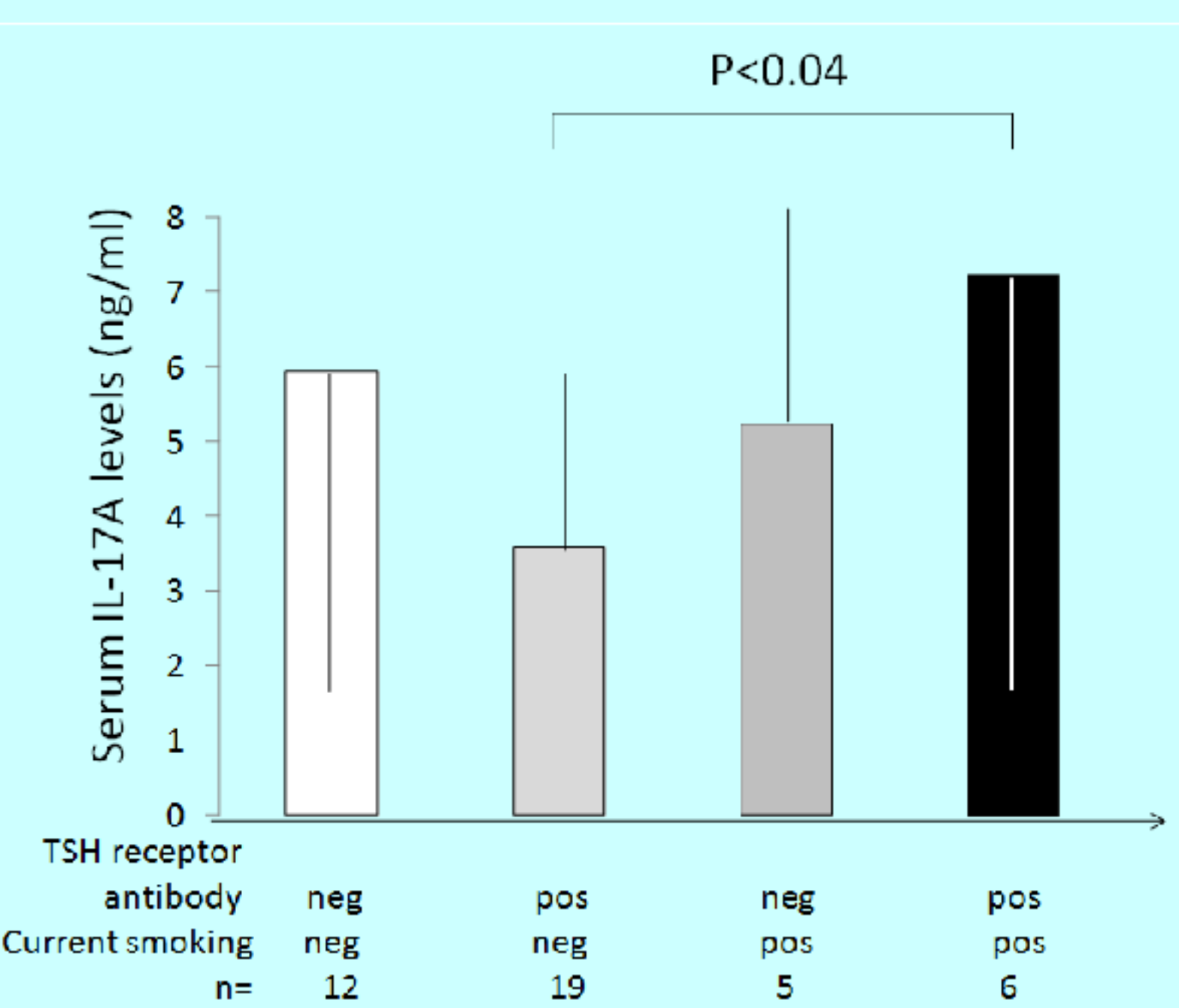


Figure 7: Effect of smoking and TSH receptor antibody serum levels on IL-17A serum levels in Graves' disease.

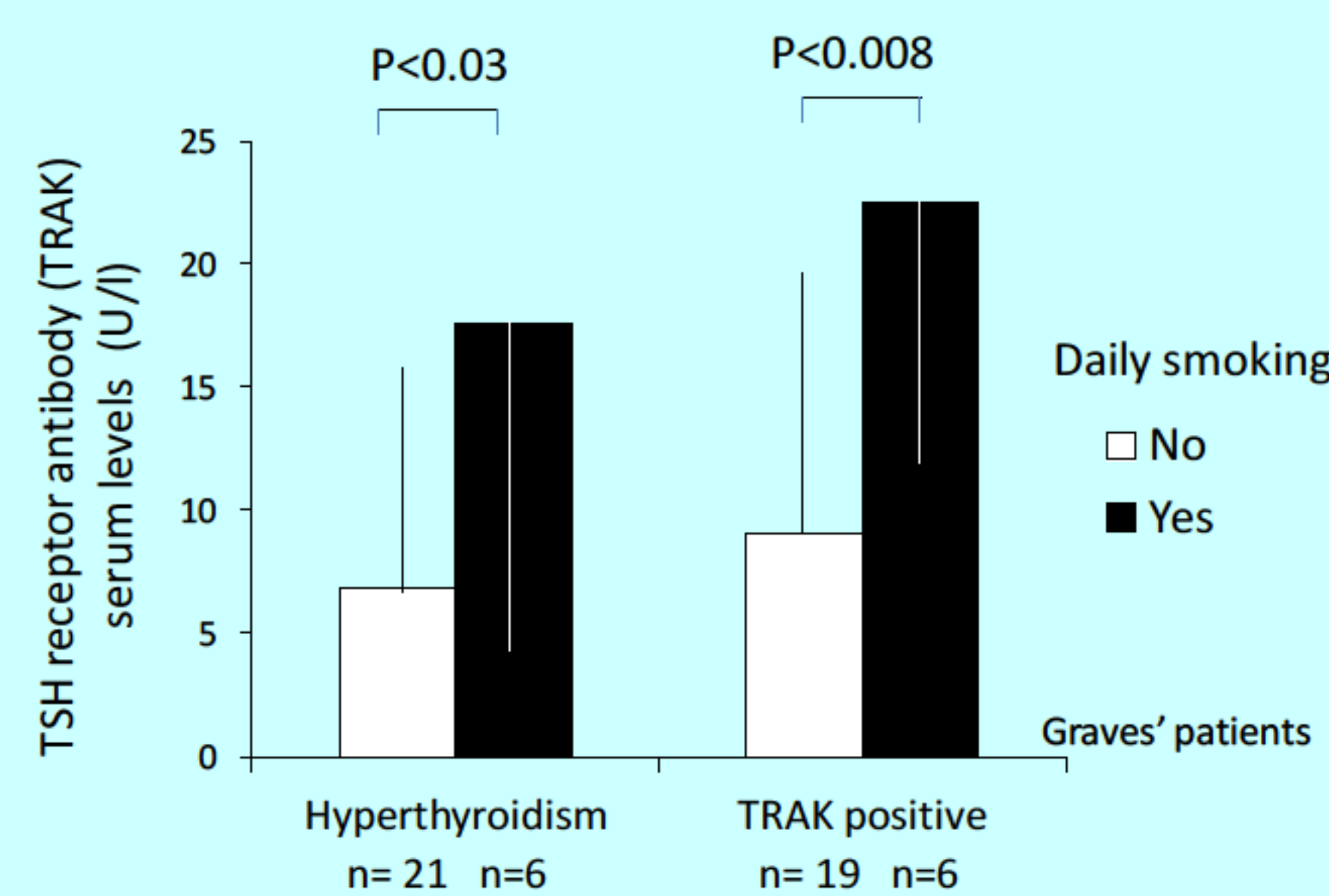


Figure 5: Smoking was connected to higher TSH receptor antibody levels in Graves' disease with hyperthyroidism or TSH receptor antibody (TRAK) positivity.

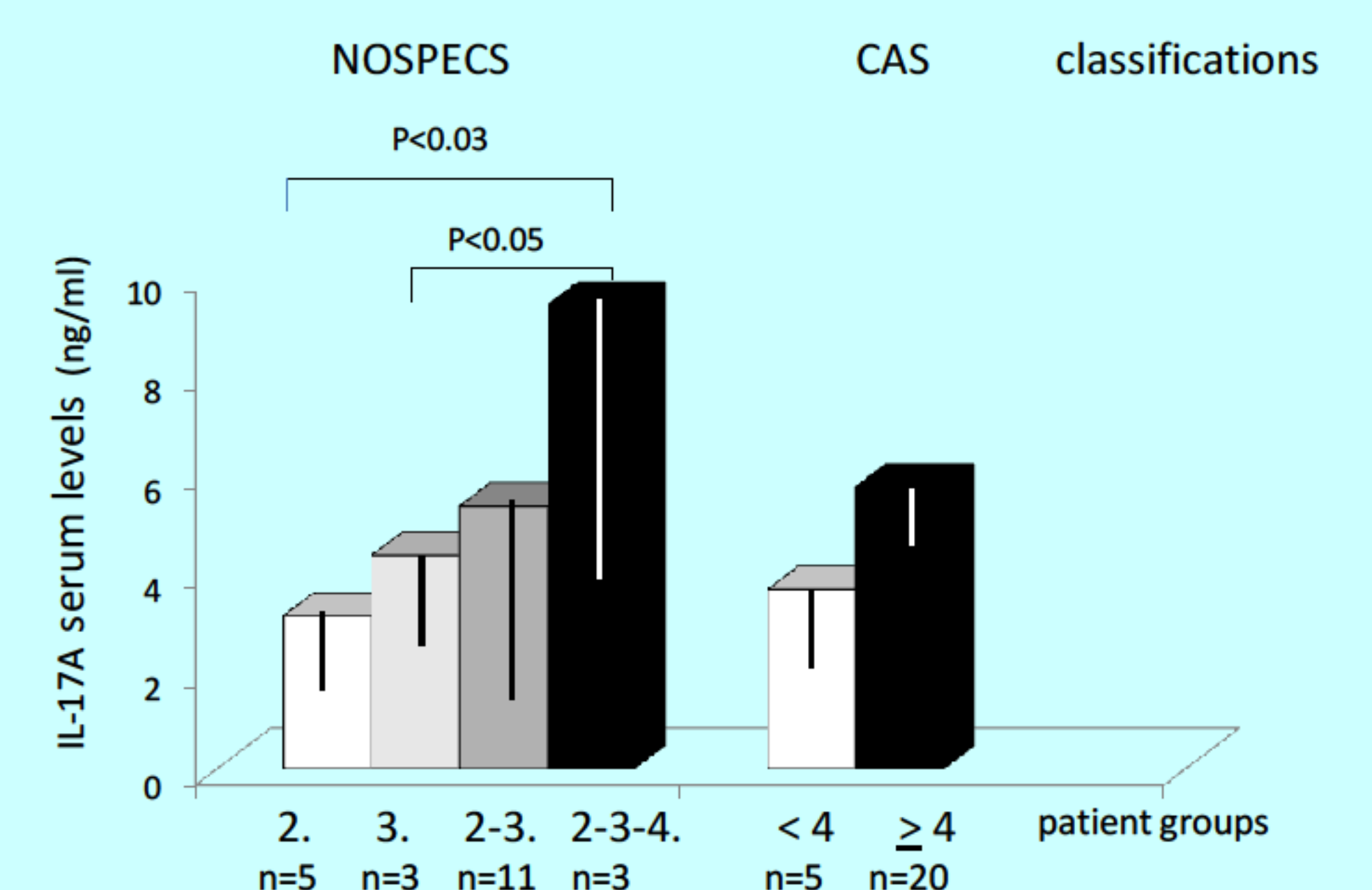


Figure 6: IL-17A serum levels with respect to the presence of ophthalmopathy based on NOSPECS and CAS (clinical activity score) classifications in Graves' disease.

Conclusions

- IL-17A cytokine was associated rather with hyperthyroid Graves' disease than in Hashimoto's thyroiditis.
- Smoking demonstrated aggravating effect on IL-17A serum levels.
- Smoking was associated with higher IL-17A and TSH receptor, anti-TPO, anti-Htg antibody serum levels in Graves' disease.
- The worsening effect of smoking may participate in Graves' ophthalmopathy via IL-17A and TSH receptor antibody elevation.
- Smoking can influence the low remission rate of Graves' ophthalmopathy through IL-17A elevation.

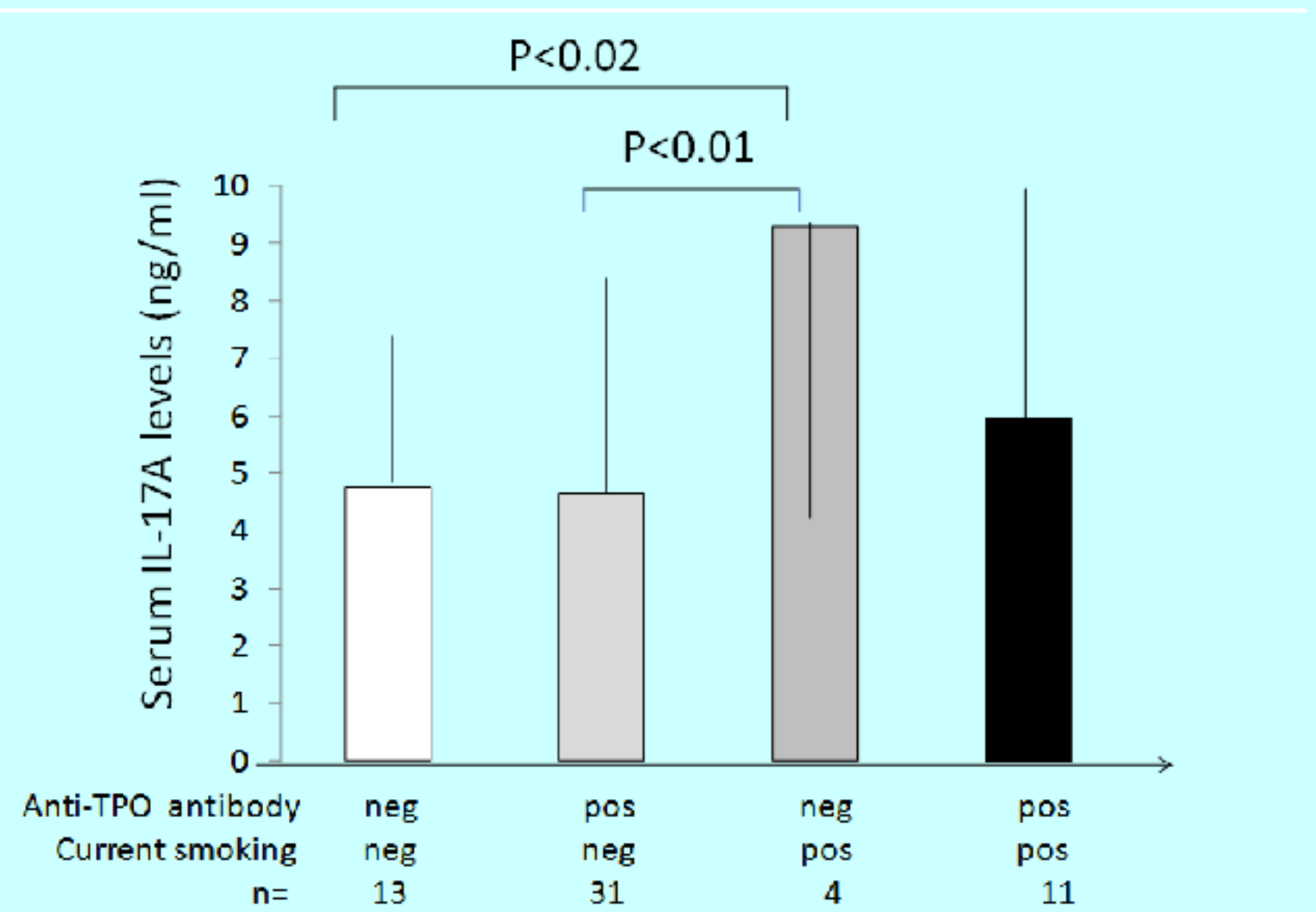


Figure 8: Effect of smoking and anti-thyroid peroxidase (TPO) antibody serum levels on IL-17A serum levels in Graves' disease.

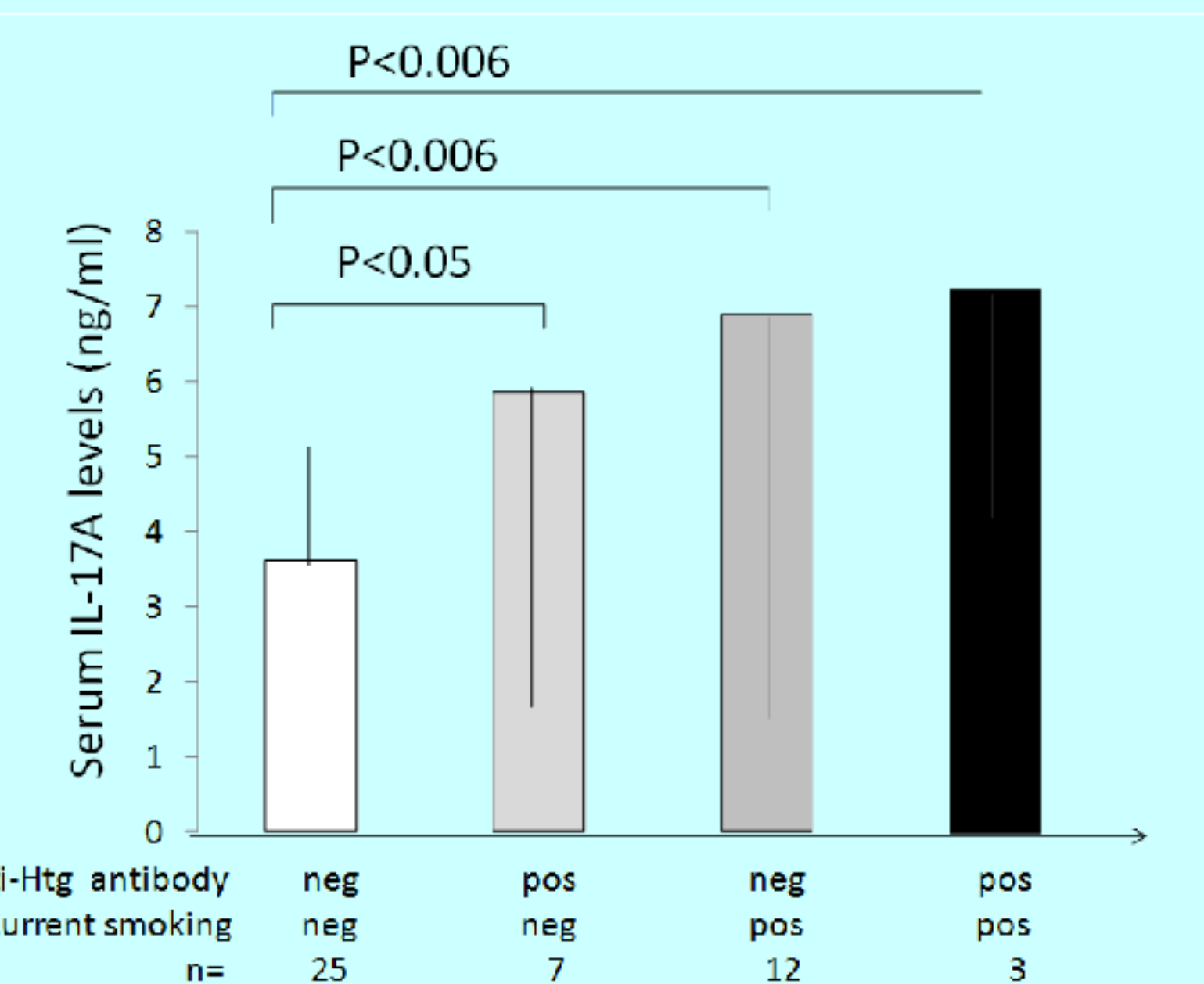


Figure 9: Effect of smoking and anti-thyroid thyroglobulin (Htg) antibody serum levels on IL-17A serum levels in Graves' disease.

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