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Remission in Graves' Disease: Predictive Value of Biochemical And Systemic Inflammatory Indices – A Single-Center Retrospective Cohort Study

Sezin Dogan Cakir, Mine Adas

Department of Endocrinology and Metabolism, University of Health Sciences, Prof. Dr. Cemil Tascioglu City Hospital, Istanbul, Türkiye

ABSTRACT

Objective: This study addresses the association of hematological inflammatory indices with remission in patients with Graves' disease (GD) and their potential contribution as remission-related markers.

Materials and Methods: This retrospective cohort study was conducted at a single tertiary endocrinology center. The study cohort consisted of 78 adults with GD who were admitted to a tertiary endocrinology clinic from September 2022 to September 2023. Demographic, clinical, and laboratory data, including thyroid function tests and thyrotropin receptor antibody (TRAb) levels, were collected. Indices reflecting systemic inflammation, namely, aggregate index of systemic inflammation, systemic inflammation response index, systemic immune-inflammation index, platelet-to-lymphocyte ratio, neutrophil-to-lymphocyte ratio, and monocyte-to-lymphocyte ratio, were calculated using complete blood count parameters. Remission was defined as achieving clinical and biochemical euthyroidism following 12–18 months of continuous antithyroid drug therapy, maintained without relapse for at least 12 months after treatment discontinuation. Subjects were stratified by remission status, and six separate binary logistic regression models were constructed, each including TRAb, age, and sex as core covariates alongside one inflammatory index, to avoid quasi-complete separation arising from a low events-per-variable ratio.

Results: Remission was achieved in 44.9% of patients. Baseline T3, T4, and TRAb levels were significantly elevated in patients without remission (all $p<0.001$). Age, sex, and inflammatory indices were comparable between groups (all $p>0.05$). In all six logistic regression models, TRAb was the only independent predictor of non-remission (Odds ratio: 1.267, 95% confidence interval [CI]: 1.144–1.403, $p<0.001$ across models), while no inflammatory index achieved statistical significance. Receiver operating characteristic analysis demonstrated excellent discriminatory performance for TRAb (area under the curve=0.897, 95% CI: 0.824–0.971, $p<0.001$), with a cohort-derived cut-off of 13.6 IU/L (sensitivity 91.4%, specificity 83.7%). This cut-off should be regarded as exploratory because it was derived from a small, single-center cohort without external validation.

Conclusion: TRAb is the most reliable predictor of remission in GD, whereas hematological inflammatory indices do not appear to have significant predictive value. These findings highlight the limited clinical utility of non-specific inflammatory markers and reinforce the importance of disease-specific autoantibodies in determining prognosis.

Keywords: Antithyroid drugs, graves' disease, hyperthyroidism, neutrophil-to-lymphocyte ratio, systemic immune-inflammation index

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Address for correspondence: Sezin Dogan Cakir. Department of Endocrinology and Metabolism, University of Health Sciences, Prof. Dr. Cemil Tascioglu City Hospital, Istanbul, Türkiye

E-mail: sezin.dogan@gmail.com **ORCID ID:** 0000-0001-6641-7827

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INTRODUCTION

As an autoimmune condition, Graves' disease (GD) is the leading cause of endogenous hyperthyroidism, driven by thyrotropin receptor antibody (TRAb) that stimulates the thyroid-stimulating hormone receptor and increases thyroid hormone production.[1-3]

Therapeutic options involve antithyroid medications to reduce hormone synthesis, in addition to permanent treatment modalities, including radioactive iodine administration and thyroidectomy.[4] Even though antithyroid medications are the preferred initial approach, disease recurrence following discontinuation continues to represent a major clinical problem, with rates of up to 50–60%.[5,6] Therefore, identifying reliable predictors of remission and relapse remains an important clinical challenge.

Recently, easily accessible and cost-effective inflammatory indices based on blood counts (neutrophil-to-lymphocyte ratio [NLR], monocyte-to-lymphocyte ratio [MLR], platelet-to-lymphocyte ratio [PLR], systemic immune-inflammation index [SII], systemic inflammation response index [SIRI], aggregate index of systemic inflammation [AISI]) have been investigated in various inflammatory and metabolic diseases. However, studies evaluating their role in GD have yielded inconsistent and controversial results.[7-9] The inconsistency in prior findings may be attributable to heterogeneous study populations, small sample sizes, differences in disease activity at the time of blood sampling, variability in antithyroid drug (ATD) dosing, and whether indices were measured at diagnosis or during follow-up. Our study contributes to the literature by systematically evaluating multiple hematological inflammatory indices in a well-characterized cohort of GD patients, using multivariate analysis to control for confounders, with remission as the primary outcome.

We hypothesized that elevated hematological inflammatory indices at baseline would be associated with a lower likelihood of achieving remission in GD patients treated with ATD. The primary aim of this study was to evaluate whether hematological inflammatory indices (NLR, MLR, PLR, SII, SIRI, and AISI) are independent predictors of remission in GD, and to assess the comparative predictive utility of these markers alongside TRAb and thyroid hormone levels.

MATERIALS AND METHODS

This retrospective, single-center cohort study was conducted at Endocrinology Department of Prof. Dr. Cemil Tascioglu City Hospital,Hospital using data from the hospital electronic medical record system. Patients were identified using the International Classification of Diseases, 10th Revision (ICD-10) code E05.0 who were admitted between September 2022 and September 2023. A total of 322 patients were initially identified using the ICD-10 code E05.0. After applying the exclusion criteria, 244 patients were excluded due to pregnancy (n=42), insufficient follow-up data (n=114), acute or chronic infections (n=24), hematological or rheumatological diseases (n=18), history of malignancy (n=34), and chronic renal failure (n=12). Consequently, 78 patients aged ≥18 years with a diagnosis of GD and complete medical records were included in the final analysis. (Fig. 1) No patients were lost to follow-up, as the study was retrospective and data were extracted from complete electronic medical records. Patients were diagnosed with GD between January 2019 and August 2022. Medical records were reviewed retrospectively between September 2022 and September 30, 2023 (data cut-off date). Total follow-up duration was calculated from the date of initial GD diagnosis to the date of the last recorded clinical visit or the data cut-off date, whichever occurred first.

Demographic characteristics (age and sex), biochemical parameters including thyroid-stimulating hormone (TSH), free thyroxine (T4), triiodothyronine (T3), and TRAb, as well as ATD treatment duration and total follow-up duration (from diagnosis to the last recorded clinical visit) were recorded.

Systemic inflammatory indices calculation was based on:

- AISI=(neutrophil×monocyte×platelet)/lymphocyte
- SIRI=(neutrophil×monocyte)/lymphocyte
- SII=(platelet×neutrophil)/lymphocyte
- PLR=platelet count/lymphocyte count
- NLR=neutrophil count/lymphocyte count
- MLR=monocyte count/lymphocyte count.

Hematological inflammatory indices were calculated using complete blood count parameters obtained at the time of initial diagnosis, before initiation of ATD therapy, to avoid confounding effects of ATD-related hematological changes such as leukopenia.

The diagnosis of GD was based on clinical findings of thyrotoxicosis together with biochemical evidence of hyperthyroidism, including suppressed TSH, elevated free T4 and/or T3 levels, accompanied by positive TRAb. Diagnosis was further supported by increased thyroid uptake on 99mTc-pertechnetate scintigraphy and/or ultrasonographic findings consistent with diffuse thyroid enlargement and increased vascularity.

Remission was defined according to clinical guidelines as the achievement of clinical and biochemical euthyroidism (normal TSH, free T4, and T3 levels) following 12–18 months

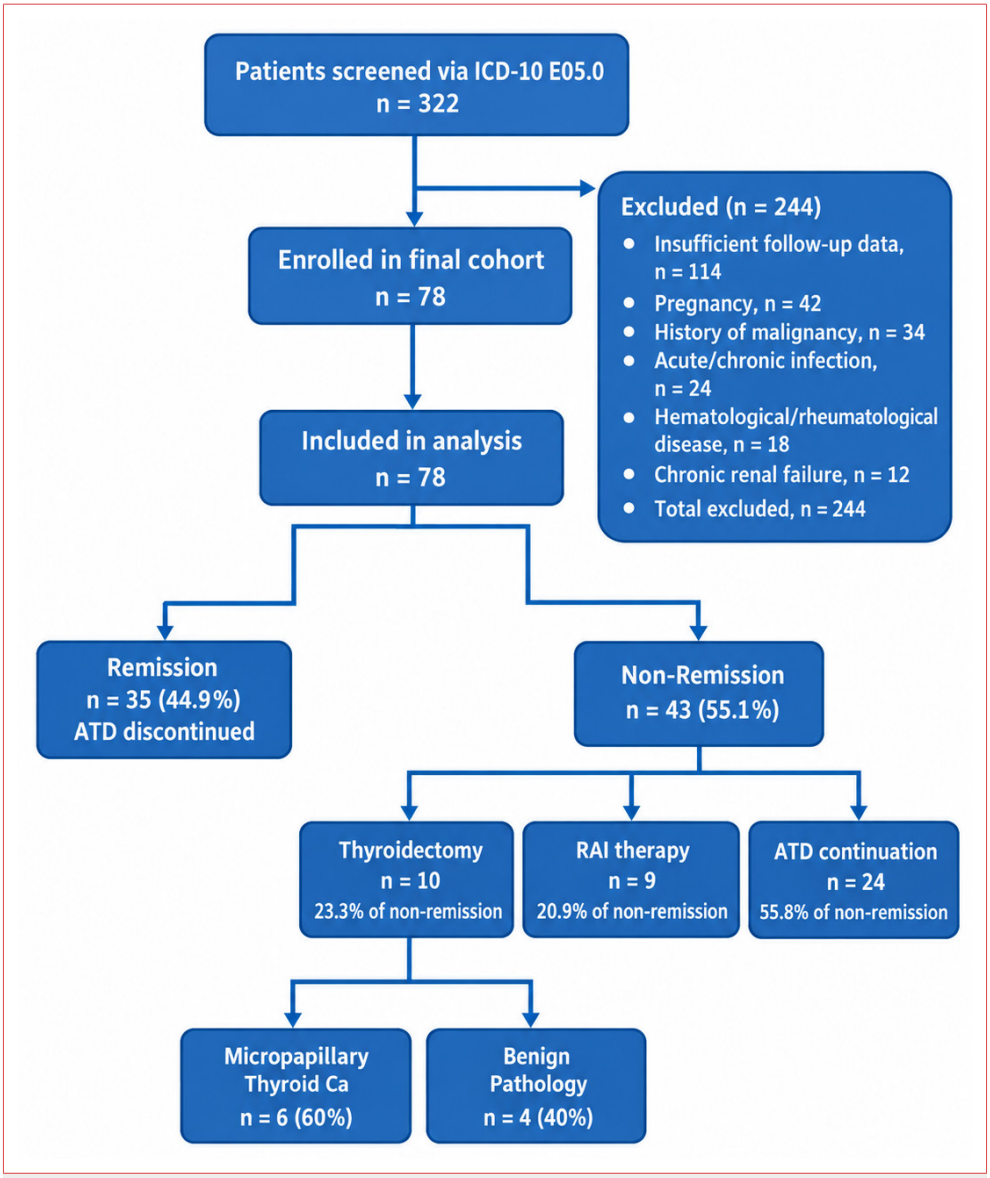

Figure 1. STROBE flow diagram. STROBE flow diagram illustrating patient screening, exclusion, and allocation. A total of 322 patients were initially identified using ICD-10 code E05.0. After applying exclusion criteria (n=244), 78 patients were included in the final analysis. Non-remission patients were further categorized by treatment modality. All papillary thyroid carcinomas identified in the thyroidectomy group were micropapillary (≤1 cm) incidental findings. ATD: Antithyroid drug; RAI: Radioactive iodine; Ca: Carcinoma

of continuous ATD therapy, maintained without relapse for at least 12 months after treatment discontinuation. Relapse was defined as recurrence of biochemical or clinical hyperthyroidism within the post-discontinuation follow-up period. All patients were treated with methimazole (MMI) as the first-line ATD, in accordance with guideline recommendations. Propylthiouracil was used only in cases of MMI intolerance or specific contraindications (e.g., first trimester of pregnancy), which were excluded from this study. Treatment was discontinued when patients achieved biochemical euthyroidism on the lowest effective MMI dose (typically ≤5 mg/day). TRAb negativity at the time of treatment discontinuation was additionally documented when available.

Patients were divided into remission and non-remission groups. Patients were classified as non-remission if they: (1) required ongoing ATD therapy (MMI >5 mg/day) beyond 24 months without achieving biochemical euthyroidism; (2) experienced disease relapse (recurrent hyperthyroidism) after initial ATD discontinuation; or (3) required definitive therapy (radioactive iodine or thyroidectomy) at any point during follow-up due to treatment failure or patient preference guided by shared decision-making.

TRAb levels were measured using the electrochemiluminescence immunoassay method (Elecsys Anti-TSHR assay, Roche Diagnostics), with a reference range of <1.75 IU/L.

Patients with pregnancy, insufficient follow-up data, or comorbid conditions known to influence hematological parameters, including acute or chronic infections, hematological or rheumatological diseases, a history of malignancy, and chronic renal failure, were excluded from the study.

To minimize selection bias, all consecutive patients meeting the inclusion criteria during the study period were enrolled without further selection. Standardized definitions for remission and non-remission were applied uniformly. Data were extracted from the structured electronic medical record system using predefined variables. Laboratory measurements were performed at the same certified central laboratory throughout the follow-up period.

Statistical Analysis

Data were analyzed using IBM Statistical Package for the Social Sciences Statistics for Windows, Version 26.0 (IBM Corp., Armonk, NY, USA). Continuous variables are presented as mean±standard deviation, whereas categorical variables are expressed as counts and percentages. Group differences were evaluated using either the independent samples t-test or the Mann–Whitney U test, depending on data distribution (assessed using the Shapiro–Wilk test). The Chi-square test was employed for categorical comparisons. Due to the low events-per-variable ratio (EPV) (EPV=35/11=3.2, below the recommended minimum of 10), simultaneous entry of all candidate variables was not appropriate. Therefore, six separate binary logistic regression models were constructed, each including TRAb, age, and sex as core covariates alongside one inflammatory index (NLR, MLR, PLR, SII, SIRI, or AISI). This strategy was used to limit model overparameterization. However, given the small sample size and limited number of events, estimates for some inflammatory indices were imprecise, as reflected by wide confidence intervals (CI). Results are expressed as odds ratios (OR) with 95% CI. For all binary logistic regression models, non-remission was coded as 1 and remission as 0; therefore, ORs >1 indicate higher odds of non-remission. Receiver operating characteristic (ROC) curve analysis was performed for TRAb and other significant continuous predictors to determine optimal diagnostic cut-off values using the Youden index. Statistical significance was defined as $p<0.05$.

The study protocol was approved by the Clinical Research Ethics Committee of University of Health Sciences, Prof. Dr. Cemil Tascioglu City Hospital (approval date: September 26, 2023; decision number: 184), and the study adhered to the Declaration of Helsinki.

RESULTS

Baseline Characteristics

Seventy-eight individuals were incorporated into the study cohort. The mean age was 40.4±11.4 years. The cohort was predominantly female (82.1%). The mean ATD treatment duration was 30.1±11.7 months (range: 8–59 months). The enrollment period (September 2022–September 2023) refers to the data extraction period; patients diagnosed at earlier time points were included if follow-up data were available within this period. The data cut-off was September 30, 2023. The mean total follow-up duration (from diagnosis to last recorded visit, including the post-treatment observation period) was 45.4±12.1 months (remission group: 44.2±8.2 months; non-remission group: 46.4±14.9 months; P=0.395). Baseline laboratory values included mean T4 of 28.9±11.3 pmol/L, T3 of 10.6±5.6 pmol/L, and TRAb of 15.9±11.4 IU/L (Table 1).

Remission Rates

Remission was achieved in 35 patients (44.9%), whereas 43 patients (55.1%) did not achieve remission. In the non-remission group, 79.1% of patients were female, while 20.9% were male. Radioactive iodine (RAI) therapy was administered in 20.9% of non-remission patients, and 23.3% underwent surgical treatment. Among surgically treated patients, 60% had papillary thyroid carcinoma (PTC) (all micropapillary, ≤1 cm, identified as incidental findings on pathological examination; no preoperative nodules were identified on ultrasonography) and 40% had benign pathology.

The non-remission group had significantly higher T4 levels (33.0±12.7 vs. 23.9±6.4 pmol/L, $p<0.001$). Similarly, T3 levels were elevated (12.7±6.5 vs. 8.1±2.8 pmol/L, $p<0.001$), and TRAb levels were substantially higher (22.9±9.9 vs. 7.2±6.1 IU/L, $p<0.001$).

There were no significant differences between groups in terms of age (p=0.474), sex distribution (p=0.453), or TSH levels (p=1.00). There were no significant differences in systemic inflammatory indices between patients who achieved remission and those who did not (all $p>0.05$). The

Table 1. Baseline characteristics and group comparisons

Variable	Overall (n=78)	No remission (n=43)	Remission (n=35)	p
Age (years)	40.4±11.4	39.6±12.3	41.4±10.4	0.474
Sex (female) (%)	82.1	79.1	85.7	0.453
TSH (mIU/L)	0.01±0.00	0.01±0.00	0.01±0.00	1.00
T4 (pmol/L)	28.9±11.3	33.0±12.7	23.9±6.4	**<0.001**
T3 (pmol/L)	10.6±5.6	12.7±6.5	8.1±2.8	**<0.001**
TRAb (IU/L)	15.9±11.4	22.9±9.9	7.2±6.1	**<0.001**
NLR	1.63±0.58	1.57±0.56	1.71±0.60	0.308
MLR	0.21±0.07	0.21±0.07	0.22±0.08	0.455
PLR	122.3±41.7	122.9±42.3	121.6±41.2	0.892
SII	454.7±195.2	442.3±177.8	468.9±212.6	0.557
SIRI	0.81±0.41	0.77±0.36	0.87±0.46	0.300
AISI	229.3±137.5	217.6±110.4	243.3±163.3	0.430
ATD treatment duration (months)	30.1±11.7	35.5±12.5	23.4±5.6	**<0.001**
Total follow-up duration (months)	45.4±12.1	46.4±14.9	44.2±8.2	0.395

Data are presented as mean±standard deviation or percentages. P-values calculated using an independent-samples *t*-test or Mann–Whitney U test, where appropriate. ATD: Antithyroid drug; TRAb: Thyrotropin receptor antibody; NLR: Neutrophil-to-lymphocyte ratio; MLR: Monocyte-to-lymphocyte ratio; PLR: Platelet-to-lymphocyte ratio; SII: Systemic immune-inflammation index; SIRI: Systemic inflammation response index; AISI: Aggregate index of systemic inflammation

non-remission group had a significantly longer ATD treatment duration than those in remission (35.5±12.5 vs. 23.4±5.6 months, p<0.001). Total follow-up duration was comparable between groups (non-remission: 46.4±14.9 months vs. remission: 44.2±8.2 months, p=0.395).

Multivariable Logistic Regression Analysis

Six separate logistic regression models were constructed as described in the Methods. In all models, non-remission was the dependent variable (coded as 1). Across all models, TRAb

Table 2. Multivariable logistic regression – six separate models (n=78)

Model	Index	TRAb OR (95% CI)	TRAb p	Age OR (95% CI)	Sex OR (95% CI)	Index OR (95% CI)/p
1	NLR	1.267 (1.144–1.403)	<0.001	1.045 (0.976–1.118)	2.156 (0.381–12.203)	0.624 (0.192–2.028)/ *P*=0.433
2	MLR	1.268 (1.144–1.405)	<0.001	1.045 (0.976–1.118)	2.411 (0.450–12.909)	0.679 (0.000–9647)/ *P*=0.937
3	PLR	1.268 (1.145–1.404)	<0.001	1.044 (0.976–1.117)	2.581 (0.427–15.606)	1.002 (0.985–1.018)/ *P*=0.848
4	SII	1.267 (1.144–1.404)	<0.001	1.046 (0.977–1.119)	2.279 (0.401–12.954)	1.000 (0.996–1.003)/ *P*=0.778
5	SIRI	1.265 (1.142–1.401)	<0.001	1.044 (0.976–1.117)	2.428 (0.447–13.190)	0.695 (0.123–3.911)/ *P*=0.679
6	AISI	1.267 (1.144–1.404)	<0.001	1.045 (0.977–1.118)	2.384 (0.440–12.914)	1.000 (0.995–1.004)/ *P*=0.877

The dependent variable was coded as non-remission=1 and remission=0. Accordingly, OR>1 indicates increased odds of non-remission, whereas OR<1 indicates decreased odds of non-remission. Each model included TRAb, age, sex, and one inflammatory index. All TRAb p<0.001. OR: Odds ratio; CI: Confidence interval; NLR: Neutrophil-to-lymphocyte ratio; MLR: Monocyte-to-lymphocyte ratio; PLR: Platelet-to-lymphocyte ratio; SII: Systemic immune-inflammation index; SIRI: Systemic inflammation response index; AISI: Aggregate index of systemic inflammation

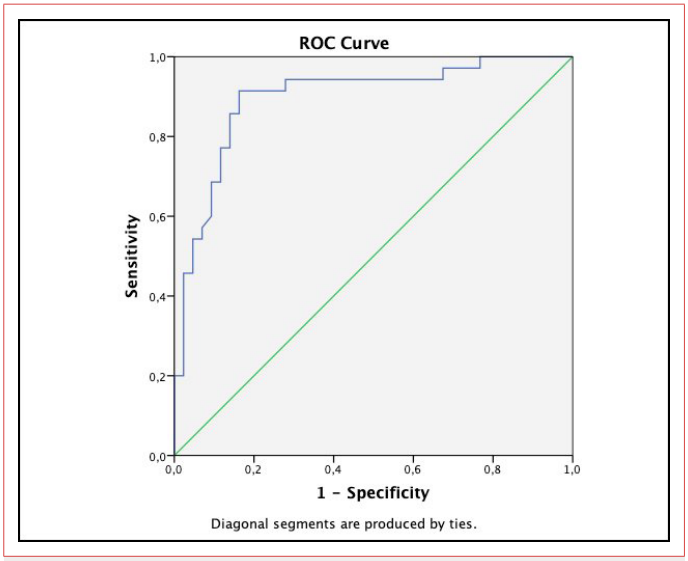

Figure 2. ROC curve for TRAb in predicting remission in Graves' disease. Receiver operating characteristic (ROC) curve for TRAb in predicting remission in patients with Graves' disease treated with antithyroid drugs. The area under the curve (AUC) was 0.897 (95% CI: 0.824–0.971, p<0.001), indicating excellent discriminatory performance. The optimal cut-off value, determined by the Youden index, was 13.6 IU/L (sensitivity: 91.4%, specificity: 83.7%). The diagonal reference line represents chance-level discrimination (AUC=0.5). TRAb: Thyrotropin receptor antibody, CI: Confidence interval

was the only statistically significant independent predictor of non-remission (OR: 1.267, 95% CI: 1.144–1.403, P<0.001 in all models). Each 1 IU/L increase in TRAb was associated with approximately 27% higher likelihood of non-remission. Age and sex were not significant in any model (all p>0.05). None of the six inflammatory indices achieved statistical significance in any model (all p>0.05). Full results are presented in Table 2.

In an exploratory ROC analysis, TRAb demonstrated excellent discriminatory ability for remission status (area under the curve=0.897, 95% CI: 0.824–0.971, p<0.001) (Fig. 2). The Youden index identified 13.6 IU/L as the optimal cut-off within the present cohort, yielding a sensitivity of 91.4% and a specificity of 83.7% for predicting non-remission. Given the small, single-center sample and absence of external validation, this cut-off should be regarded as exploratory.

Sensitivity Analysis

To assess whether the surgical subgroup influenced the results, analyses were repeated after excluding the 10 surgically treated patients (n=68; remission n=35, non-remission n=33). TRAb remained the only significant independent predictor across all six models (OR for non-remission: 1.258–1.261, 95% CI: 1.132–1.402, p<0.001), while no inflammatory index achieved significance (all p>0.05) (Suppl Table 1).

DISCUSSION

In the present study, we analyzed the biochemical and systemic inflammatory indices and remission status in patients with GD. Remission was achieved in 44.9% of patients. Higher baseline T3, T4, and TRAb levels were significantly associated with non-remission. Across the six multivariable models, TRAb was consistently associated with remission status, whereas none of the evaluated inflammatory indices reached statistical significance.

The predominance of female patients and the remission rate observed in our study are consistent with previous reports and current guidelines, indicating that approximately 40–50% of patients achieve remission following ATD therapy.[6,10] Despite improvements in diagnostic approaches and treatment accessibility, relapse remains a major clinical challenge, underscoring the need for reliable predictors of disease course.

Our results further reinforce the key role of TRAb in the pathophysiology and prognosis of GD.[11] TRAb stimulates the thyroid-stimulating hormone receptor, resulting in persistent hyperthyroidism, and has been consistently associated with disease activity and relapse risk. In our study, TRAb was the only independent predictor of remission, with every 1 IU/L increase associated with a 26% higher likelihood of non-remission (OR: 1.267, 95% CI: 1.144–1.403, p<0.001). Exploratory ROC analysis demonstrated good discriminatory performance of baseline TRAb for remission status. A cut-off of 13.6 IU/L provided the optimal combination of sensitivity and specificity within our cohort. However, this threshold was derived from a relatively small, single-center population and was not externally validated. It should therefore be regarded as a hypothesis-generating finding rather than an established clinical threshold. Larger prospective studies with external validation are required before a specific TRAb cut-off can be incorporated into treatment decisions. These results are in line with earlier studies indicating that elevated TRAb levels are strongly associated with poor treatment response and increased relapse rates.[12-14]

Baseline T3 and T4 levels were significantly higher in the non-remission group, indicating greater biochemical disease activity at presentation. However, T3 and T4 were not included in the revised multivariable regression models because the limited number of outcome events restricted the number of covariates that could be incorporated without overparameterization. Accordingly, no conclusions regarding their independent predictive value can be drawn from the present analysis.

In recent years, inflammatory indices have been investigated as potential prognostic markers in autoimmune and inflammatory diseases. However, their role in GD remains controversial. Some studies have suggested associations with disease activity or treatment response,[7,8,15] while others have reported no significant relationship.[9] Dasgupta et al.[7] evaluated PLR as a novel surrogate marker to differentiate between patients with GD and subacute thyroiditis. Kim et al.[15] reported that high NLR was associated with relapse in GD; however, this differs from our findings in that NLR was measured at treatment completion rather than at baseline, which may better reflect residual immune activity at that stage. Furthermore, their study focused on relapse after ATD withdrawal rather than overall remission status.

Furthermore, changes in hematological parameters following ATD treatment or differences between subgroups of thyrotoxicosis rather than GD alone were discussed in the literature[16-19] these studies primarily focused on disease activity or treatment-related changes rather than remission outcomes. Studies evaluating inflammatory markers in thyroid eye disease, which represents a distinct inflammatory phenotype from uncomplicated GD, potentially explain the absence of associations in our cohort.[8,20]

In our study, none of the evaluated inflammatory indices were independently associated with remission in multivariable analysis. This finding is consistent with studies reporting limited predictive value of these indices in hyperthyroid states.[9] The absence of a relationship between systemic inflammatory indices and remission may be attributed to the underlying pathophysiology of GD: Unlike systemic inflammatory conditions, GD is primarily driven by specific autoantibodies, particularly TRAb. Therefore, non-specific inflammatory markers derived from peripheral blood counts may not adequately reflect the underlying autoimmune mechanisms that determine disease course.

A notable finding in our study was the high prevalence of PTC among surgically treated patients (60%), which substantially exceeds the 1–5% rate typically reported in the general GD population.[21] This higher rate is most likely explained by the referral center bias inherent to our tertiary setting: we tend to receive patients with more complex disease, including those with coexisting thyroid nodules or suspicious ultrasonographic findings that prompted surgical referral. Importantly, all carcinomas were micropapillary (≤1 cm), discovered as incidental findings on pathological examination, with no preoperative nodules identified on ultrasonography, and all surgical referrals were based on ATD treatment failure rather than malignancy suspicion. Importantly, carcinoma can occur in GD patients without nodules, and the absence of nodules on ultrasonographic examination does not exclude the risk of malignancy.[21,22] The high rate of PTC in our surgical subgroup underscores the importance of careful ultrasonographic evaluation even in the context of GD, particularly in referral centers. This finding should be interpreted cautiously given the small number of surgically treated patients (n=10) in our cohort. A sensitivity analysis excluding surgically treated patients confirmed that the primary findings were not influenced by this subgroup (Suppl Table 1).

Our findings support the established prognostic relevance of TRAb in GD. Baseline and longitudinal TRAb measurements may contribute to individualized assessment of disease course alongside other clinical factors. Patients with high baseline TRAb levels may benefit from extended ATD courses (beyond 18 months) or earlier counseling regarding definitive therapy options. Current guidelines already incorporate TRAb as a factor guiding treatment duration; our data support its systematic use as a prognostic biomarker at the point of diagnosis. In clinical practice, patients with persistently elevated or rising TRAb during treatment should be closely monitored for treatment failure, and shared decision-making regarding definitive therapy should be initiated earlier in this subgroup. Conversely, early TRAb negativization during ATD therapy may serve as a positive prognostic indicator, supporting a trial of treatment discontinuation after the minimum recommended duration. However, the present findings do not establish a specific TRAb threshold for selecting treatment strategies, and treatment decisions should continue to be based on the overall clinical context and shared decision-making.

A notable strength of this work lies in its simultaneous assessment of multiple systemic inflammatory markers in relation to remission in GD, which has been rarely explored. Furthermore, the use of multivariate analysis allowed us to identify independent predictors, strengthening the validity of our findings.

Limitations

Nevertheless, certain limitations need to be considered. The retrospective design carries a risk of selection bias. The relatively small cohort and single-center setting may restrict the applicability of the findings. Indices were measured at only 1 time point, which may not adequately represent their fluctuations throughout the disease course. Several established predictors of remission were not evaluated in the present study, including thyroid volume on ultrasonography, presence and severity of Graves' orbitopathy, smoking status, family history of thyroid disease, and detailed ATD dose data throughout the treatment course. The absence of these variables represents a significant limitation and may have influenced the predictive models. A formal sample size

calculation was not performed before data collection; the final cohort of 78 patients may limit statistical power for detecting modest effect sizes. In addition, the small sample size and limited number of outcome events resulted in low precision for some regression estimates, as reflected by the very wide CIs observed for certain inflammatory indices, particularly MLR. Therefore, these effect estimates should be interpreted cautiously. The possibility that some patients currently classified as remission may relapse with extended follow-up cannot be excluded. Finally, referral center bias may affect the generalizability of our findings, particularly with respect to the high PTC rate in the surgical subgroup. Prospective multicenter studies with larger sample sizes incorporating these variables are warranted.

CONCLUSION

Baseline TRAb showed a consistent association with remission status and greater discriminatory ability than the hematological inflammatory indices examined in this cohort. In contrast, NLR, MLR, PLR, SII, SIRI, and AISI were not significantly associated with remission. Given the limited sample size and single-center design, these findings, including the exploratory TRAb cut-off, require confirmation in larger independent cohorts.

Disclosures

Ethics Committee Approval: The study protocol was approved by the University of Health Sciences, Prof. Dr. Cemil Tascioglu City Hospital Ethics Committee (No: 184, Date: 26/09/2023).

Informed Consent: Due to the retrospective nature of the study, informed consent was waived by the ethics committee.

Conflict of Interest: The authors declare that there is no conflict of interest.

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Supplementary Table 1. Sensitivity analysis – excluding surgical patients (n=68)

Model	Index	TRAb OR* (95% CI)	TRAb p-value	Index OR (95% CI)/p
1	NLR	1.261 (1.134–1.402)	<0.001	1.835 (0.502–6.707)/p=0.358
2	MLR	1.260 (1.133–1.402)	<0.001	0.463 (0.000–9364)/p=0.879
3	PLR	1.260 (1.133–1.401)	<0.001	1.000 (0.982–1.019)/p=0.974
4	SII	1.260 (1.133–1.400)	<0.001	1.001 (0.997–1.005)/p=0.683
5	SIRI	1.258 (1.132–1.398)	<0.001	1.237 (0.205–7.473)/p=0.817
6	AISI	1.260 (1.133–1.401)	<0.001	1.000 (0.995–1.005)/p=0.953

Sensitivity analysis excluding the 10 surgically treated patients. Remission n=35, non-remission n=33. All TRAb p<0.001. OR: Odds ratio; CI: Confidence interval; NLR: Neutrophil-to-lymphocyte ratio; MLR: Monocyte-to-lymphocyte ratio; PLR: Platelet-to-lymphocyte ratio; SII: Systemic immune-inflammation index; SIRI: Systemic inflammation response index; AISI: Aggregate index of systemic inflammation