

Relationship of the platelet distribution width/platelet count ratio with thyroid antibody levels in patients with Hashimoto's thyroiditis

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Abstract

Objective: I investigated whether the platelet distribution width/platelet count (PDW/PC) ratio, which is an inexpensive and simple test performed for almost all patients, is applicable in the follow-up of patients with Hashimoto's thyroiditis and examined the relationship of this ratio with thyroperoxidase and thyroglobulin antibody levels.

Materials and methods: The study groups consisted of 67 patients with Hashimoto's thyroiditis and 17 controls. All participants were aged 20 to 75 and treated the Internal Medicine outpatient clinic of my institution. The PDW/PC ratio and thyroid antibody levels were retrospectively evaluated in patients with normal liver and renal function and normal white blood cell counts, hemoglobin levels, and hematocrit levels.

Results: Thyroid antibody levels were significantly higher in patients with Hashimoto's thyroiditis than in controls. PC was higher in patients with Hashimoto's thyroiditis, whereas the PDW/PC ratio was lower. However, these differences were not statistically significant.

Conclusion: In this study, I did not find a statistically significant relationship between thyroid antibody levels and PDW/PC. However, a weak correlation between these variables was identified.

Keywords

Thyroperoxidase, thyroglobulin, Hashimoto's thyroiditis, platelet, platelet distribution width, platelet count, thyroid, autoimmune disease

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Introduction

Hashimoto's thyroiditis was named after Dr. Hakaru Hashimoto, who initially identified this disease.¹ This common autoimmune disease can occur concomitantly with other autoimmune diseases.² Autoimmune thyroiditis is a multifactorial disease that has some genetic predisposition (HLA-DR3, HLA-DR4, CD40, and PTPN-22), and it is also associated with environmental factors such as vitamin D or selenium deficiency; exposure to toxins, amiodarone, or lithium; age; and sex. In addition, autoimmune thyroiditis is linked to immunologic changes, high interleukin (IL)-6 levels, and high T lymphocyte counts.³ Thyroid follicular cells express Toll-like receptors (TLRs), which are key regulators of the innate immune response. Platelets similarly express TLRs on their surfaces.⁴⁻⁶

Autoimmune thyroid diseases are typified by elevated levels of pro-inflammatory cytokines such as IL-1 β , interferon- γ , and tumor necrosis factor- α .⁷ The role of anti-thyroid antibodies in Hashimoto's disease was first described in experimental thyroiditis in mice in 1990. In addition, anti-thyroid antibodies participate in complement fixation.⁸⁻¹⁰

Mononuclear cell accumulation occurs in the thyroid gland, leading to shrinkage of the gland and fibrosis.¹¹ This process can occur in a wide range of cases ranging from the primary type, in which the cause is not fully explained, to the secondary type attributable to the use of drugs such as interferon and cytotoxic T-lymphocyte antigen 4 inhibitors.^{12,13}

Platelets are anucleated cells with important roles in response to damage, and they participate in clotting and inflammation through their secreted immune mediators.¹⁴ These cells are basic components of hemostasis and thrombosis.¹⁵ They are the smallest cells in blood, having roles in tumor growth and angiogenesis.¹⁶ In addition to

their known function in hemostasis, they secrete various cytokines involved in inflammation. IL-1 β is released by active platelets, and its release leads to the release of IL-6 and IL-8, thereby triggering inflammation.^{17,18}

The platelet distribution width (PDW) is a parameter that indicates the variability in platelet volume. When platelets are activated, their size and shape change, leading to pseudopod formation. When platelet activation is increased, a parallel increase in PDW is anticipated.¹⁹ Inflammatory cytokines are released from activated platelets in inflammatory conditions such as Hashimoto's thyroiditis. Thus, the present study examined whether the PDW/platelet count (PC) ratio was correlated with thyroid antibody levels in patients with Hashimoto's thyroiditis.

Materials and methods

Data for patients with Hashimoto's thyroiditis who visited the Amasya University Research and Education Hospital Internal Medicine outpatient clinic (Amasya, Turkey) between April 1, 2019 and April 1, 2020 were retrospectively examined. The eligibility criteria were an age of 20 to 75 years and the absence of other chronic diseases. Patient data were accessed through a hospital database. Patients with a history of liver or kidney dysfunction, diabetes, cancers including thyroid cancer, infection, and any chronic disease were excluded. The use of acetylsalicylic acid and other drugs that affect platelet function was not permitted during the study. Individuals who had not previously been diagnosed with Hashimoto's thyroiditis and whose parenchyma was homogeneous on ultrasound were included in the control group. A diagnosis of Hashimoto's thyroiditis was based on positivity for thyroid peroxidase antibody (TPOAb) and thyroglobulin antibody (TgAb). On thyroid

ultrasound, disease-specific heterogeneity and/or pseudonodule formation were observed in the thyroid parenchyma structure. In my hospital, PDW and PC are measured using an XN-1000 hematology analyzer (Sysmex, Kobe, Japan). The normal values for the analyzed parameters are as follows: PDW, 9.7 to 15.1 fL; PC, $173 \times 10^9/L$ to $360 \times 10^9/L$; free triiodothyronine (FT3), 2.3 to 4.2 ng/L; free thyroxine (FT4), 0.84 to 1.76 ng/L; thyroid-stimulating hormone (TSH), 0.35 to 5.5 mIU/L; TPOAb, 0 to 60 U/mL; and TgAb, 0 to 60 U/mL. The aforementioned parameters were measured using an ADVIA Centaur® XP Immunoassay System (Siemens, Munich, Germany). Biochemical parameters were measured using a Cobas 8000 system (Roche, Basel, Switzerland). I retrospectively examined these values and compared them between the patient and control groups. This study was conducted under the approval of the Tokat Gaziosmanpaşa University Research Hospital ethical board (approval number: 20-KAEK-064; approval date: May 3, 2020). Because this was a retrospective study, the requirement for informed consent was waived.

The differences between the groups were determined using Student's *t*-test for continuous variables and the Mann-Whitney

U test for non-continuous variables. Significance was indicated by $P < 0.05$. Statistical analysis was performed using GraphPad Prism version 6.00 (GraphPad Software, San Diego, CA, USA, www.graphpad.com).

The reporting of this study conforms to the REMARK guidelines.²⁰

Results

Eighty-four participants were included in the study, including 67 patients diagnosed with Hashimoto's thyroiditis and 17 controls. The Hashimoto's thyroiditis cohort included 54 women and 9 men, whereas the control cohort included 13 women and 4 men. The descriptive statistical information of the groups is presented in Table 1.

PDW and PC were slightly but not significantly higher in the patient group than in the control group (Table 1). The PDW/PC ratio was lower in the patient group, albeit without significance. TgAb ($P < 0.0001$), TPOAb ($P < 0.0001$), and FT3 levels ($P = 0.0123$) were significantly higher in the patient group than in the control group.

In the correlation analysis, a negative correlation was observed between TPOAb and PDW ($r = -0.06155365$), and a weak correlation was detected between TPOAb

Table 1. Statistical parameters between the patient and control groups.

	Patient group	Control group	P
FT3 (ng/L)	3.393 ± 1.425	3.658 ± 0.6377	0.0123*
FT4 (ng/L)	1.330 ± 0.5993	1.334 ± 0.3346	0.6291
TSH (mIU/L)	3.401 ± 3.147	2.344 ± 1.500	0.4214
TPOAb (U/mL)	472.7 ± 559.5	37.32 ± 17.49	<0.0001*
TgAb (U/mL)	103.7 ± 120.3	19.03 ± 9.684	<0.0001*
PDW (fL)	12.54 ± 1.930	12.44 ± 2.335	0.7426
PC ($\times 10^9/L$)	264,456 ± 87,696	259,025 ± 91,975	0.9670
PDW/PC	0.001355 ± 0.007611	0.001413 ± 0.005625	0.9755

Statistical analysis was performed using Student's *t*-test or the Mann-Whitney U test.

FT3, free triiodothyronine; FT4; free thyroxine; TSH, thyroid-stimulating hormone; TPOAb, thyroperoxidase antibody; TgAb, thyroglobulin antibody; PDW, platelet distribution width; PC, platelet count.

and PC ($r=0.1885002$, Table 2). A weak correlation was observed between TgAb and PC ($r=0.1226639$), but no correlation was noted between TgAb and PDW ($r=-0.03254965$). The PDW/PC ratio also had weak correlations with TPOAb ($r=-0.1166246$) and TgAb ($r=-0.126331$).

Discussion

In my study, thyroid antibody levels displayed no significant relationships with PDW or PC. PDW and PC were slightly elevated in the patient group, ultimately because of the autoimmune disease and presence of an inflammatory condition. The lack of significant differences may be attributable to the small size of this study. Similarly, there was no statistically significant relationship between thyroid antibody levels and the PDW/PC ratio. The results of this study revealed that PDW and PC increased because of inflammatory reactions, but I did not record statistically significant results. Prior studies identified low PDW as a negative acute phase reactant in patients with rheumatoid arthritis.²¹

Few studies have examined PDW and the mean platelet volume (MPV) in patients with thyroid conditions. Bilge *et al.*²² found that MPV and PDW were high in patients with Hashimoto's thyroiditis and noted that these changes may be associated with inflammation and malignancy. In a study conducted by Güvendi *et al.*,²³ PDW was elevated in patients with Hashimoto's thyroiditis. They suggested this indicated can be used for diagnosis and follow-up of the disease.²³ Findikli and Tutak²⁴ observed increases in PDW and MPV in 60 female patients with subclinical hyperthyroidism. Li *et al.*²⁵ investigated the diagnostic value of PDW and albumin levels in patients with thyroid nodules and malignancies. Similar to the results of other studies, they reported an increase in PDW in patients with malignancies. Onalan *et al.* studied the

Table 2. Correlations of the measured parameters in patients with Hashimoto's thyroiditis.

	FT3	FT4	TSH	TPOAb	TgAb	PDW	PC	PDW/PC
FT3								
FT4	0.899646							
TSH	-0.2636233	-0.3116611						
TPOAb	0.133547	0.1178527	0.2352145					
TgAb	-0.177477	0.1373785	0.1693726	0.3857874				
PDW	0.02660326	-0.07494333	0.1112569	-0.06155365	-0.03254965			
PC	-0.1598984	-0.2089642	-0.1370956	0.1885002	0.1226639	-0.347574		
PDW/PC	-0.09885885	-0.05747781	0.3158156	-0.1166246	-0.126331	-0.106961	-0.5233738	

FT3, free triiodothyronine; FT4; free thyroxine; TSH, thyroid-stimulating hormone; TPOAb, thyroperoxidase antibody; TgAb, thyroglobulin antibody; PDW, platelet distribution width; PC, platelet count. The correlation was categorized as weak ($r = 0.00-0.24$), moderate ($r = 0.25-0.49$), strong ($r = 0.50-0.74$), or very strong ($r = 0.75-1.00$). (-) denotes a negative correlation.

platelet/lymphocyte ratio (PLR) in 121 patients with hypothyroidism or subclinical hypothyroidism and determined that PLR may be useful in the course of inflammatory diseases.²⁶ Wen *et al.* reported the prognostic value of MPV and PDW in a study of 558 patients with papillary thyroid cancer. In patients with coexistent papillary thyroid cancer and Hashimoto's thyroiditis, the researchers suggested that decreased MPV and PDW may be prognostic.²⁷ Gorar and colleagues studied platelet function in 75 patients with Hashimoto's thyroiditis and 29 healthy controls. They reported a positive correlation between FT4 levels and PC. They suggested that platelet function is influenced by autoimmunity and thyroid hormone levels.²⁸

Atkas and co-workers examined MPV, PDW, red blood cell distribution width, and PC in patients with Hashimoto's thyroiditis. Among these parameters, only RDW differed between the patient and healthy control groups.²⁹ I also observed an increase in PDW in patients with Hashimoto's thyroiditis, but the difference was not significant. The increase in PC, albeit small, draws attention to the effect of inflammation on coagulation. The reasons for not finding a significant difference between the groups are that other conditions can affect PDW and that PDW is a negative acute phase reactant. In addition, this study was small because it did not include patients with chronic diseases, which makes my study valuable. However, the small number of patients and retrospective nature of the study represent limitations. Further studies with larger cohorts will provide additional insights.

Conclusion

Thyroid antibody levels were not significantly correlated with PDW, PC, or the PDW/PC ratio. However, weak correlations

between thyroid antibody levels and the PDW/PC ratio were observed.

Declaration of conflicting interest

The author declares that there is no conflict of interest.

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