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Orijinal Araştırma / Original Article

The Effects of Thyroid-Stimulating Hormone, Free Thyroxine Levels, and Thyroid Antibodies on Mean Platelet Volume: Original Research

Tiroid Uyarıcı Hormon, Serbest Tiroksin Seviyeleri ve Tiroid Antikorlarının Ortalama Trombosit Hacmi Üzerindeki Etkileri: Orijinal Araştırma

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Abstract

Background: Coagulation abnormalities have been reported in patients with impaired metabolism of thyroid hormones. Platelets play an important role in coagulation and Mean Platelet Volume (MPV) has been considered as an inflammatory biomarker in multiple diseases.

Objectives: The aim of this study was to investigate whether any relationship exists between the values of thyroid-stimulating hormone (TSH), free thyroxine,(FT4) anti-thyroid peroxidase (Anti TPO), anti-thyroglobulin (Anti TG) and those of the MPV.

Material and Method: Patients who were admitted to the Endocrinology outpatient clinic between October 2013 and July 2019 with a pre-diagnosis of thyroid disease were included in the study. The data were analyzed with IBM SPSS V23. Compatibility with normal distribution was examined with the Shapiro Wilk test. The relation between the variables was evaluated with Spearman rank correlation.

Results: Records of 1098 patients were examined. There is a very weak positive relationship between TSH and MPV (r: 0,07), there is no significant relationship between FT4, Anti TPO, Anti TG and MPV.

Conclusion: Patients have high TSH values display a increased MPV should hence be acknowledged in risk prediction of thrombotic events.

Keywords: Thyroid hormones, mean platelet volüme, thyroid diseases

Öz

Giriş: Tiroid hormonlarının metabolizması bozulmuş hastalarda pıhtılaşma anormallikleri bildirilmiştir. Trombositler pıhtılaşmada önemli bir rol oynar ve Ortalama Trombosit Hacmi (MPV), birçok hastalıkta inflamatuar bir biyobelirteç olarak kabul edilir.

Amaç: Bu çalışmanın amacı, tiroid uyarıcı hormon (TSH), serbest tiroksin, anti-tiroid peroksidaz (Anti TPO) ve anti-tiroglobulin (Anti TG) değerleri ile MPV değerleri arasında herhangi bir ilişki olup olmadığını araştırmaktı.

Gereç ve Yöntem: Endokrinoloji polikliniğine Ekim 2013 - Temmuz 2019 tarihleri arasında tiroid hastalığı ön tanısıyla başvuran hastalar dahil edildi. Veriler IBM SPSS V23 ile analiz edildi. Normal dağılıma uyumluluk Shapiro Wilk testi ile incelendi. Değişkenler arasındaki ilişki Spearman sıra korelasyonu ile değerlendirildi.

Bulgular: 1098 hastanın kayıtları incelendi. TSH ile MPV arasında çok zayıf bir pozitif ilişki vardı (r: 0,07), ST4, Anti TPO, Anti TG ve MPV arasında anlamlı bir ilişki yoktu.

Sonuç: Yüksek TSH değerlerine sahip hastalarda yüksek MPV değerleri görülmekte olup trombotik olayların risk tahmini yapılabilir.

Anahtar Kelimeler: Tiroid hormonları, ortalama trombosit hacmi, tiroid hastalığı

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INTRODUCTİON

Platelets play a significant role in the pathogenesis of cardiovascular diseases by promoting the complication of an injured atherosclerotic lesion into thrombus. The rupture of an atherosclerotic plaque cause release of a variety of prothrombotic factors in the bloodstream and exposes the subendothelial matrix to the contact with blood elements. This leads to platelet activation, adhesion and aggregation and hence thrombus formation initiates.[1,2]

Platelet activation typically represented by shape change from discoid to spherical and volume increase.[3] This phenomenon can be easily identified with modern hemocytometers and shown with the increase of the mean platelet volume (MPV).[4]

MPV is a machine-calculated measurement of the average size of platelet found in blood and is typically included in blood test as part of the complete blood count. Since the average platelet size is larger when the body is producing increased numbers of platelets, the MPV test results can be used to make inferences about platelet production in bone narrow or platelet destruction problems.[5]

In the literatüre, coagulation abnormalities has been reported in patients with impaired metabolism of thyroid hormones. These typically range from mild laboratory anomalies[6-8] to clinically relevant thrombotic episodes like cardiovascular disease and venous thrombosis.[9]

Also hypothyroidism results in the decrease of cardiac output and cardiac contractility. Studies suggested that accelerated atherosclerosis and thrombosis are the causes of cardiovascular morbidity in hypothyroidism patients.[10,11]

The study of MPV can provide important information on the course and prognosis in many inflammatory conditions.[12]

MPV is a useful index to reflect platelet activation, and has been considered as an inflammatory biomarker in multiple diseases.[13]

Furthermore, increased MPV has been detected in a variety of malignancies.[14-16]

Bayhan et al. studied with patients who underwent total thyroidectomy because of benign or malignant diseases of the thyroid.MPV was significantly higher in patients with malignant thyroid diseases than in those with benign thyroid diseases.[17]

Since an increased MPV is broadly acknowledged as a risk marker for platelet function and activation[18] and fluctuations of thyroid hormones are frequently associated with thrombotic complication, we planned a retrospective study to find the effects of thyroid-stimulating hormone (TSH), free thyroxine (FT4), anti-thyroid peroxidase (Anti- TPO), anti-thyroglobulin (Anti-TG) on MPV values.

MATERIAL AND METHOD

Ethical approval with the number of 2019 /0024 was taken from the KTO Karatay University Faculty of Medicine date of October, 25, 2019. All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki.

The study was designed as a retrospective descriptive study. Patients who were admitted to the Endocrinology outpatient clinic between 1st of October 2013 and 31st July 2019 with a pre-diagnosis of thyroid disease and who underwent MPV test were included in the study.

We retrospectively reviewed the files of patients and recorded age, gender, TSH, FT4, Anti- TPO, Anti-TG and MPV values. Any patient who did not perform any of these tests with MPV was excluded from the study. The first laboratory results of patients were taken into account.

TSH, FT4, Anti-TPO, Anti-TG were measured on the ARCHITECT i2000SR immunoassay analyzer (Abbott Diagnostics).

MPV levels were measured in venous blood samples placed in EDTA-standard tubes using Abbott Cell-Dyn 3700 Hematology Analyzer with the flow cytometry method.

The data were analyzed with IBM SPSS V23. Compatibility with normal distribution was examined with the Shapiro Wilk test. The relation between the variables was evaluated with Spearman rank correlation. The significance level was taken as $p < 0.05$.

RESULTS

File records of 1098 patients were examined. 849 of them were women (77.30%) and 249 of them were men (22.70%). (**Table 1**).

Table 1. Frequency distribution of gender

	N	%
Gender		
Female	849	77.30
Male	249	22.70

N : number

The mean age was 47.10, standard deviation was 15.90 (minimum 15, maximum 93 years).

Through these patients 1092 had TSH results, 1084 had FT4 results. Anti TPO was analysed in 1016, anti TG was analysed in 1073 patients.

The laboratory reference ranges provided by the manufacturer used in this study were as follows: MPV: 7.50-12 fl, TSH 0.35–4.94 µIU/ml, FT4 0.7-1.4 ng/dl, TPOAb < 5.61 IU/ml, and TgAb < 4.11 IU/mL.

The mean value of TSH, FT4, Anti TPO, Anti TG and MPV were 2.80 µIU/ml, 1.30 ng/dl, 151.90 IU/ml, 70.50 IU/ml and 7.50 fl respectively. While the standart deviations were 24.30 for TSH, 1.80 for FT4, 357.50 for Anti TPO, 184.10 for Anti TG and 1.20 for MPV.

The median value of TSH, FT4, Anti TPO, Anti TG and MPV were 0.40 µIU /ml, 1.10 ng/dl, 1.10 IU/ml, 3.40 IU/ml and 7.30 fl respectively (**Table 2**).

Table 2. Descriptive statictics

	N	Mean	Std. Deviation	Median	Minimum	Maximum
Age	1098	47.10	15.90	45	15	93
TSH	1092	2.80	24.30	0.40	0	734
FT4	1084	1.30	1.80	1.10	0.10	57
Anti TPO	1016	151.90	357.50	1.10	0	6000
Anti TG	1073	70.50	184.10	3.40	0	1000
MPV 0	1098	7.50	1.20	7.30	0	16.10

N: number, Std. Deviation: Standard Deviation, TSH: Thyroid-stimulating hormone, FT4:Free thyroxine, Anti TPO: Anti thyroid peroxidase, Anti TG: Anti thyroglobulin, MPV: Mean platelet volüme

While there is a very weak positive relationship between TSH and MPV (r: 0.07), there is no significant relationship between ST4, Anti TPO, Anti TG and MPV (**Table 3**).

Table 3. Correlation analysis results

		TSH	ST4	Anti TPO	Anti TG	MPV 0
TSH	r					
	p	---				
ST4	r	-0.567				
	p	0.000	---			
Anti TPO	r	0.103	0.000			
	p	0.001	0.990	---		
Anti TG	r	0.038	0.044	0.672		
	p	0.209	0.151	0.000	---	
MPV 0	r	0.075	-0.045	0.006	-0.013	
	p	0.013	0.137	0.843	0.664	---

r: Spearman rank correlation, N: number, Std. Deviation: Standard Deviation, TSH: Thyroid-stimulating hormone, FT4:Free thyroxine, Anti TPO: Anti thyroid peroxidase, Anti TG: Anti thyroglobulin, MPV: Mean platelet volüme

DISCUSSION

Strengths of the study: Our study covers a period of 6 years and the data of 1098 people have been reached. This is a very good number if we compare with the literature.

Limitations of the study: Data loss is one of our limitations. For example the MPV value of 1098 people has been studied but 6 people with MPV values could not have been compared with other values. Our analyses is limited. We have performed only one analysis according to our aim of the study.

MPV is a precise measurement of their dimension, calculated by hematological analyzers on the basis of volume distribution during routine blood morphology test. MPV ranges between 7.50 and 12 fl, whereas the percentage of large platelets should amount to 0.20-5% of the whole platelet population. In physiological conditions, MPV is inversely proportional to the platelet count, which is associated with hemostasis maintenance and preservation of constant platelet mass.[12]

MPV can be affected by multiple factors. The study of MPV can provide important information on the course and prognosis in many inflammatory conditions. Increased MPV was observed in cardiovascular diseases, peripheral diseases, cerebral stroke, respiratory diseases, chronic renal failure, intestine diseases, rheumatoid diseases, diabetes and various cancers. Decreased MPV was noted in tuberculosis during disease exacerbation, ulcerative colitis, SLE in adult, and different neoplastic diseases.[12,19] Because of these factors MPV should be assessed in parallel with other inflammatory markers.

The results of the present study demonstrated a very weak positive relationship the TSH level and MPV. In our study patients were not questioned for other chronic diseases. So it may be argued that an elevated MPV is secondary to other factors that are affected with the MPV.

But the number of samples in the study is quite high since 6-year patient data is scanned.

In the literature there were studies investigating the association between MPV and thyroid diseases.

In the study of Lippi et al. a significant association was found between MPV and TSH values in both simple ($r = 0.12$; $p < 0.001$) and multivariable regression analysis (beta coefficient, 0.07; $p < 0.001$.[20]

Erikci et al. studied patients with subclinical hypothyroidism and euthyroidic healthy control group, and reported that the MPV values were significantly higher in cases than in controls.[21]

Carlioglu et al found significantly higher MPV values in patients with euthyroid Hashimoto thyroiditis than in healthy controls. And there was also positive correlation between anti-TPO, anti-tiroglobulin and MPV levels.[22]

Kim et al. retrospectively studied 6893 asymptomatic Korean adults who were 20 years of age or older and who underwent voluntary regular health check-ups. They found that MPV was positively correlated with the TSH level.[23]

Our study is compatible with the literature. But it seems reasonable to suggest that MPV plays a role in the thrombotic process and that elevated TSH levels are not only a causal factor.

Although in hypothyroidism patients atherosclerosis and thrombosis are accelerated and this results in increase in MPV levels[10-11], there are studies that showed increase in MPV levels with hyperthyroidism.

Platelet changes, such as lower platelet count increased MPV together with the shortened platelet lifespan, were observed in Graves disease previously.[24] Bagir et al. compared recurrent Graves disease with remission and found MPV significantly higher in the recurrent group and attributed this state to hypermetabolism.[25]

In the study of Erem et al. a significant association was only found between MPV and anti-thyroid peroxidase (TPO) antibodies in patients with Graves disease.[26]

In our study, we found a very weak positive relationship significant relationship between TSH and MPV. The results of this study may have some clinical implications. Regardless of the fact that an increased MPV may be considered as a risk factor or a simple marker of thrombosis.[27,28]

As such, it seems reasonable to suggest that platelet activation, as reflected by an increased MPV, may be an important mediator of thrombotic complications in patients with fluctuations of thyroid hormones.[29]

CONCLUSION

The observation that patients have high TSH values display a increased MPV should hence be acknowledged in risk prediction of thrombotic events and also in the clinical management or antithrombotic prophylaxis of subjects in the euthyroid state. But still further and comprehensive studies are needed. The other factors that affect MPV levels can be questioned thus the relationship between MPV and TSH levels can be specifically evaluated.

ETHICAL DECLARATIONS

Ethics Committee Approval: Ethical approval with the number of 2019 /0024 was taken from the KTO Karatay University Faculty of Medicine date of October,25,2019.

Informed Consent: Because the study was designed retrospectively, no written informed consent form was obtained from patients.

Referee Evaluation Process: Externally peer-reviewed.

Conflict of Interest Statement: The authors have no conflicts of interest to declare.

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Author Contributions: All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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