Impact of Thyroid Autoantibody Positivity on Inflammation and Platelet Indices among Hemodialysis Patients

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Abstract

Aim: The frequency of inflammation and autoimmune diseases is increased in hemodialysis patients. Autoimmune thyroid disease (AITD), characterized by inflammation of the thyroid gland due to immune reactivity to thyroid antigens, is common in this population. This study investigates the relationship between thyroid autoantibody positivity (TAAP), platelet function, and other inflammatory markers in hemodialysis patients.

Methods: This cross-sectional study recruited 154 hemodialysis patients, categorized into TAAP (n=22) and thyroid autoantibody negative (TAAN, n=132) groups. Patients, on thrice-weekly dialysis for at least 3 months, were not receiving levothyroxine. Data were obtained from routine monthly tests and hospital records. Exclusion criteria included active malignancy, recent chemotherapy, infections, liver cirrhosis, thalassemia, iron deficiency, hemolysis, and recent major surgery. Patients were analyzed for demographic data, metabolic parameters, platelet indices, including mean platelet volume (MPV) and platelet count (PLT), and other inflammatory markers.

Results: Patients with TAAP showed significantly higher MPV/PLT ratio (0.06/0.04, p=0.005) and lower PLT (163.05±46.67 vs 200.73±67.30, p=0.013) and platelet crit (PCT) (0.15±0.04 vs 0.18±0.06, p=0.046) compared to TAAN patients. No significant differences were observed between groups for metabolic parameters or for other inflammatory markers.

Conclusions: Our study revealed significant differences in platelet and inflammatory indices between hemodialysis patients with thyroid autoantibody positivity (TAAP) and those without (TAAN). Specifically, TAAP patients exhibited higher mean platelet volume (MPV), alongside lower platelet count (PLT) and platelet crit (PCT) levels. These findings suggest a potential association between TAAP and alterations in platelet function and activation among hemodialysis patients.

Keywords: *Hemodialysis, Autoimmune thyroid disease, Inflammatory markers,*

1. Introduction

The development of AITD occurs due to loss of immune tolerance and reactivity to thyroid autoantigens such as thyroid peroxidase (TPO), thyroglobulin (TG) and thyroid stimulating hormone receptor (TSHR). And it is known that inflammation can trigger thyroid tissue destruction by the discharge of cytokines.[1] AITD, characterized by inflammation of the thyroid gland, is prevalent among patients undergoing hemodialysis.[2] Similarly, hemodialysis patients often exhibit heightened inflammation due to various factors inherent in renal failure and dialysis treatment.[3]

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Platelets have been implicated in the pathogenesis of autoimmune disorders through interactions with immune cells and the release of pro-inflammatory factors.[4] Platelets, known for their dual role in inflammation and hemostasis, play a crucial role in modulating immune responses and maintaining vascular integrity.[5] MPV, an indicator of platelet function and activation, has emerged as a potential biomarker for assessing inflammatory states and immune dysregulation.[6] It is also known that AITD can cause changes in platelet-related indices including MPV.[7] Understanding the implications of AITD on platelet function in hemodialysis patients holds clinical relevance.[8] Identifying markers of platelet activation and inflammation could aid in risk stratification and therapeutic decision-making in this vulnerable population.[9]

This cross-sectional study aims to examine the relationship between autoantibody positivity and platelet function in hemodialysis patients. By comparing platelet and inflammatory indices between euthyroid patients with TAAP and TAAN patients, this research

seeks to elucidate potential alterations in platelet activity associated with autoantibody positivity in the hemodialysis population. Moreover, unraveling the underlying mechanisms linking autoantibody positivity and platelet dysfunction may pave the way for targeted interventions to mitigate cardiovascular complications and improve outcomes in hemodialysis patients.

2. Materials and methods

2.1. Study design and participants

This study employed a cross-sectional design to investigate the association between thyroid autoantibody positivity and platelet function in hemodialysis patients. A total of 154 hemodialysis patients were recruited for this study. Patients were categorized into two groups based on thyroid autoantibody positivity: TAAP (n=22) and TAAN patients (n=132). No patients were receiving levothyroxine treatment. Patients who had undergone hemodialysis for at least 3 months were eligible for inclusion. Patients received hemodialysis three times a week. Their laboratory results were obtained from routine monthly dialysis tests and hospital records. Exclusion criteria comprised active malignancy, history of chemotherapy, acute or chronic infection, liver cirrhosis, thalassemia, iron deficiency, hemolysis, and major surgery within the last 6 months. Patients were not receiving antithyroid therapy and had not undergone radioactive iodine or thyroid surgery. This study received approval from the Ethics Committee of Adana Şehir Training and Research Hospital in June 2024, under decision number 40, and informed consent was obtained from all participating patients.

Table 1

Demographic data of the patients.

Variables	n/ Min/Max	% / Mean±Std
Gender		
• Female	77	50
• Male	77	50
Dialysis Access		
• Av Fistula	106	68,8
• Catheter	48	31,2
Primary Disease		
• Diabetes Mellitus	40	26,0
• Hypertension	53	34,4
• Glomerulonephritis	3	1,9
• Kidney Stone	4	2,6
• Drug associated	2	1,3
• Neurogenic Bladder	2	1,3
• Polycystic Kidney Disease	2	1,3
• idiopathic	48	31,2
Age	21/92	52,62±15,35
Height (m)	1,43/2	1,64±0,09
Weight (kg)	33/130	68,87±18,15
Body Mass Index	11,69/48,93	25,36±5,80
Dialysis vintage (months)	3/252	54,09±53,49
Kt/V	1,25/2,65	1,72±0,31
URR	66/96	73,05±7,87

URR: urea reduction rate

2.2. Statistical Analysis:

Statistical analysis was performed using SPSS 18.0 software. Descriptive statistics were utilized to summarize data, presenting categorical variables as numbers and percentages, and numerical variables as mean and standard deviation. Student's t-test was employed for normally distributed numerical variables, while the Mann-Whitney U test was used for non-normally distributed variables. Chi-square and Fisher exact tests were utilized for categorical variables. Significance was set at $p<0.05$.

3. Results

In the entire cohort, 77 (50%) patients were female, while 14 out of 22 patients (63.6%) with AITD were female. The mean Kt/V was 1,720.31, and Urea reduction rate (URR) was 737.8 (Table 1). Demographic data of the patients is shown in Table 1.

Table 2

Comparison of hemodialysis patients with and without thyroid antibody positivity in terms of demographic and laboratory parameters

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Variables	Thyroid Autoantibody Positivity		p
	Yes (Mean±Std) n:22	None (Mean±Std) n: 132	
Gender (Female/Male)	14(%18,2)/8 (%10,4)	63(%81,8)/69(%89,6)	0,167
Age	60,27±15,81	51,15±15,02	0,010
Dialysis vintage	48,35±49,51	55,05±54,26	0,606*
Glucose	123	106	0,319**
Calcium-Phosphorus Index	43,53±12,79	43,51±15,10	0,995*
Parathormone	682	475	0,599**
Total Cholesterol	157,19±36,45	165,99±41,76	0,428*
Ldl Cholesterol	99,19±24,66	103,15±31,12	0,629*
Hdl Cholesterol	34,25±7,95	38,31±8,95	0,090*
Triglycerides	187	147	0,287**
Hemoglobin	10,65±1,89	11,10±1,90	0,306
Transferrin saturation (median)	0,52	0,44	0,186
Ferritin (median)	639,25	655,40	0,720
Free T3, Ref. (2,6 - 4,37 ng/L)	2,40	2,50	0,508
Free T4, Ref. (0,61-1,38ng/dL)	0,75	0,78	0,383
TSH Ref. (0,54-5,6 IU/mL)	2,22	1,76	0,085
Antithyroglobulin Antibody Ref. (0-4 IU/mL)	13	0,90	0,001
Antithyroid peroxidase Antibody Ref. (0-9 IU/mL)	15,85	0,70	0,001

*free T3: triiodothyronin, free T4: thyroxin, TSH: thyroid stimulating hormone. *The distribution was homogeneous, Student T test was used for comparison. ** The distribution was not homogeneous, Mann Whitney -U test was used for comparison in these parameters. *** Chi-square test was applied.*

There were no significant differences between patients with TAAP and TAAN patients in terms of metabolic parameters, parathormone, calcium-phosphorus product, hemoglobin, iron status (including transferrin saturation and ferritin), dialysis duration, gender, age and inflammatory parameters (Table 2). Table 2 also pre-

sents a comparison of free T3(triiodothyronin), free T4 (thyroxin), thyroid stimulating hormone (TSH), antithyroglobulin, and antithyroid peroxidase (antiTPO) levels between the two groups.

Table 3

Comparison of hemodialysis patients with and without thyroid antibody positivity in terms of inflammatory and thrombolytics parameters

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Variables	Thyroid Autoantibody Positivity		p
	Yes (Mean±Std) n:22	None (Mean±Std) n: 132	
C reactive protein	7,55	8,85	0,861**
Lymphocyte/monocytes	3,00	2,53	0,171**
Neutrophils/lymphocytes	3,01	3,36	0,517**
Neutrophils	4472,72± 1894,15	4597,73± 1730,66	0,757**
Lymphocytes	1381,82± 477,73	1424,43± 573,53	0,742**
Monocytes (median)	450	500	0,105**
PLT	163,05±46,67	200,73±67,30	0,013**
PDW (median)	17,2	17	0,327**
MPV	9,32±1,16	8,84±1,11	0,066**
PCT	0,15±0,04	0,18±0,06	0,046**
PLT/Lymphocytes	0,12	0,14	0,128**
Systemic immune inflammatory index	451,45	630,00	0,133**
MPV/PLT	0,06	0,04	0,005**
MPV/PDW	0,54	0,52	0,189**

*PLT: Platelet, PDW: Platelet derivation weal, MPV: Mean Platelet Volume, PCT: plateletcrit (MPVxPLT/1000), Systemic immune inflammatory index formula: Neutrophils X Monocytes/ Lymphocytes) ** Since the distribution was not homogeneous, Mann Whitney -U test was used for comparison of these parameters.*

4. Discussion

The findings of our cross-sectional study highlight the significant interplay between autoimmune thyroid diseases and platelet function in hemodialysis patients, underscoring the role of inflammation in modulating platelet activity and its potential implications for cardiovascular risk.

One of the notable observations from our study is the elevation in mean platelet volume MPV among euthyroid patients with TAAP compared to TAAN counterparts. These findings align with existing literature associating higher MPV levels with AITD, even in euthyroid individuals, indicative of potential platelet activation and altered hematological profiles in this context.[10] Previous research indicates that MPV tends to be elevated in patients with Hashimoto's thyroiditis, even in a euthyroid state.[11] Although MPV levels were higher in patients with autoimmune thyroiditis in our study, the difference did not reach statistical significance. However, we observed a higher MPV/PLT ratio and lower platelet counts in patients with TAAP. A meta-analysis by Cao et al. demonstrated significantly increased PLT and MPV values in patients with AITD. Interestingly, subgroup analysis revealed that elevated PLT levels were specifically associated with Hashimoto's disease and overt hypothyroidism, while MPV elevation was observed in patients with Graves' disease, hyperthyroidism, and euthyroid autoimmune thyroid disease. Conversely, patients with Hashimoto's disease and hypothyroidism exhibited lower MPV compared to healthy controls.[6]

Importantly, the elevation in MPV among hemodialysis patients with TAAP warrants attention due to its potential clinical implications, particularly in the context of cardiovascular risk. Elevated MPV levels have been linked to an increased risk of atherothrombotic complications, which is of particular concern in hemodialysis patients who already face a heightened risk of cardiovascular events.[11] In this context, elevated MPV levels may serve as a valuable indicator of increased cardiovascular risk among hemodialysis patients, reflecting its association with inflammation-related mechanisms.

Inflammatory activity in the body may influence the risk of thyroid disease, with obesity playing a significant role in this risk. Xin Yu Hu et al.'s study suggested that controlling inflammation levels could be essential for maintaining normal thyroid function.[12] In our study, the lack of significant difference in the systemic inflammatory index between the two groups highlights the potential importance of MPV as an inflammatory marker in this context.

Furthermore, our study revealed lower platelet counts and PCT levels among TAAP patients compared to TAAN patients. While the precise mechanisms underlying these differences remain to be elucidated, it is plausible that alterations in platelet production or clearance pathways may contribute to autoimmune processe.[13] The lower PCT levels observed in autoantibody-positive patients may be attributed to their lower platelet counts, highlighting the interplay between platelet indices in the context of AITD.

It is important to acknowledge the limitations of our study, including its cross-sectional design and relatively small sample size. Longitudinal studies with larger cohorts are needed to validate our findings and elucidate the temporal relationship between AITD and alterations in platelet function and hematological parameters among hemodialysis patients.

5. Conclusion

In conclusion, our study reveals a relationship between thyroid autoantibody positivity and platelet function in hemodialysis patients. Elevated MPV in TAAP patients suggests potential platelet activation, aligning with existing literature. The higher MPV/PLT ratio and lower platelet counts highlight the interplay between platelet indices and autoimmune processes. Future longitudinal studies with larger cohorts are needed to validate these findings and explore their clinical implications further.

Conflict of interest statement

The author declares that he has no financial interests related to the content of this report.

Statement of ethics

This study was conducted in accordance with the ethical principles of the Declaration of Helsinki and was approved *Adana City Training and Research Hospital Ethics Commitee for this study (Decision No: 2024-40)*

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Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

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