



ASSOCIATION OF HEMOSTATIC PARAMETERS WITH  
ENDOTHELIAL DYSFUNCTION MARKERS IN AUTOIMMUNE  
THYROIDITIS

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Autoimmune thyroiditis (AIT) at the hypothyroid stage is characterized by hypocoagulable changes and endothelial dysfunction. This study aimed to assess the correlations between hemostatic parameters and endothelial markers in AIT. These changes are clinically significant, as they may lead to an increased tendency for bleeding or, conversely, to elevated thrombotic risk.

To evaluate hemostatic alterations and endothelial dysfunction markers in patients with hypothyroid-stage AIT and to assess their correlations.

A total of 98 patients with AIT (euthyroid AIT, subclinical and overt hypothyroidism) and 20 healthy controls were examined. Hemostatic indices included activated partial thromboplastin time (APTT), prothrombin index (PTI), fibrinogen concentration, and von Willebrand factor (vWF). Endothelial dysfunction was assessed by serum endothelin-1 (ET-1) and soluble intercellular adhesion molecule-1 (sICAM-1).

Results demonstrated significant prolongation of APTT (26.0 → 46.1 s,  $p < 0.001$ ), reduction in PTI (103.5% → 90.2%,  $p < 0.001$ ), and decreased fibrinogen levels (3.4 → 2.2 g/L,  $p < 0.001$ ). vWF activity also declined (85.3 → 59.0 IU/dL,



$p < 0.001$ ). Conversely, endothelial markers were elevated: ET-1 increased from 2.1 → 5.9 pg/mL, and sICAM-1 from 6.1 → 9.7 ng/mL ( $p < 0.001$ ).

Correlation analysis revealed strong negative associations between PTI and endothelial markers (PTI vs. ET-1:  $r = -0.46$ ; PTI vs. sICAM-1:  $r = -0.44$ ), and between PTI and vWF ( $r = -0.49$ ). APTT showed positive correlations with ET-1 ( $r = +0.41$ ) and sICAM-1 ( $r = +0.38$ ). Fibrinogen also demonstrated a moderate inverse relationship with ET-1 ( $r = -0.33$ ). These findings confirm that hypocoagulable changes in AIT at the hypothyroid stage are tightly linked to endothelial dysfunction. The interplay of decreased fibrinogen and vWF with elevated ET-1 and sICAM-1 supports the concept of immune-mediated endothelial damage as a driver of vascular risk in hypothyroidism.

## INTRODUCTION

Autoimmune thyroiditis (Hashimoto's thyroiditis) is the most common autoimmune endocrine disorder and frequently evolves into hypothyroidism. While the hormonal and metabolic consequences of hypothyroidism are well established, increasing focus has been placed on hemostatic alterations and endothelial dysfunction accompanying AIT, which may contribute to cardiovascular morbidity [2,6,10].

Low plasma levels of thyroid hormone shift the hemostatic system toward a hypocoagulable and hyperfibrinolytic state, manifesting in prolongation of clotting times and reduction of procoagulant factors [1,7,11]. Untreated hypothyroidism is also associated with acquired von Willebrand syndrome, characterized by reduced von Willebrand factor (vWF) and factor VIII levels [7]. Simultaneously, endothelial dysfunction is marked by elevated circulating endothelin-1 (ET-1) and soluble intercellular adhesion molecule-1 (sICAM-1), as well as altered vWF release, reflecting endothelial activation or damage. Endothelial dysfunction plays a central role in vascular homeostasis, and its dysregulation contributes to inflammation, vasoconstriction, thrombosis, and atherosclerosis [5,9,14]



However, despite multiple independent descriptions of coagulation and endothelial abnormalities in hypothyroidism and AIT, the precise correlations between hemostatic parameters (e.g. APTT, PTI, fibrinogen, vWF) and endothelial markers (ET-1, sICAM-1) remain insufficiently studied. Clarifying such interrelationships is crucial, as it may explain the variability in bleeding versus thrombotic risk among patients, and suggest integrated biomarker approaches for vascular risk stratification [3,4,8].

Therefore, this study was designed to investigate the correlation between coagulation abnormalities and endothelial dysfunction in patients with hypothyroid-stage AIT. By analyzing clotting times, fibrinogen levels, vWF activity, platelet function, and endothelial markers (ET-1, sICAM-1), our goal is to better understand the nexus linking thyroid autoimmunity, hypocoagulation, and vascular injury [15,16].

## **MATERIALS AND METHODS**

The study comprised 98 patients with autoimmune thyroiditis (AIT) at the hypothyroid stage (euthyroid ait – 28 patients, subclinical hypothyroidism – 33 patients, overt hypothyroidism – 37 patients) and 20 healthy controls matched for age and sex. Diagnosis was established based on elevated anti-thyroid peroxidase antibodies (AT-TPO), thyroid hormone profile (TSH, fT4, fT3), and ultrasound findings. Hematological indices (Hb, Er, Ht, Tr, WBC) were measured on a Mindray BC-5000 hematology analyzer (China) with Human GmbH reagents. Coagulation parameters (PT, PTI, INR, fibrinogen, APTT) were determined using a COAX 2 Biosystems coagulometer (Spain). Platelet aggregation and adhesion were assessed on a BIOLA ALAT-2 220LA aggregometer (Russia) with ADP-induced assays. Endothelial markers (vWF, ET-1, sICAM-1) were quantified by ELISA on a Mindray CL-1000i system. Thyroid hormones (TSH, fT4, fT3) were also analyzed by chemiluminescent immunoassay on the same platform.

Statistical analysis was conducted using SPSS 26.0. Data are expressed as mean  $\pm$  SD; group differences were tested with Student's *t*-test or Mann–Whitney U test, and correlations evaluated with Pearson's coefficient (*r*). Significance was set at  $p < 0.05$ .

## RESULTS

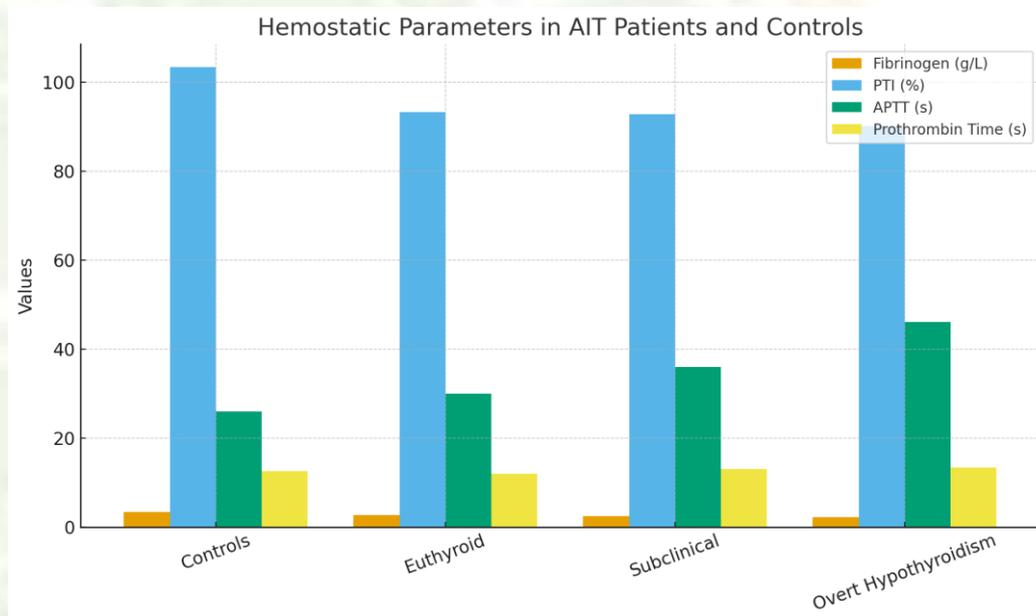
The study enrolled 98 AIT patients (28 euthyroid, 33 subclinical, 37 overt hypothyroidism) and 20 healthy controls.

**Hematology.** All AIT groups showed reduced hemoglobin, erythrocytes, and hematocrit ( $p < 0.05$ ), with platelet counts lower in overt hypothyroidism.

**Coagulation.** A hypocoagulable pattern was observed: fibrinogen decreased ( $3.4 \pm 0.18$  vs.  $2.2\text{--}2.6$  g/L,  $p < 0.001$ ), PTI reduced ( $103.5 \pm 2.0\%$  vs.  $90.2\text{--}93.3\%$ ,  $p < 0.001$ ), prothrombin time prolonged ( $13.4 \pm 0.29$  vs.  $12.5 \pm 0.38$  s), and APTT markedly extended ( $26.0 \rightarrow 46.1$  s). INR was slightly elevated ( $1.0\text{--}1.1$  vs.  $0.95$ ).

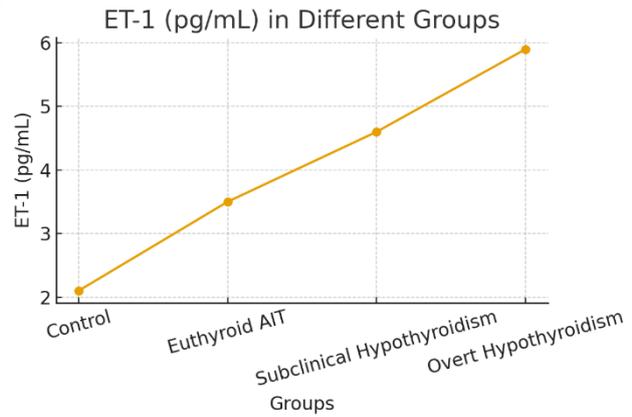
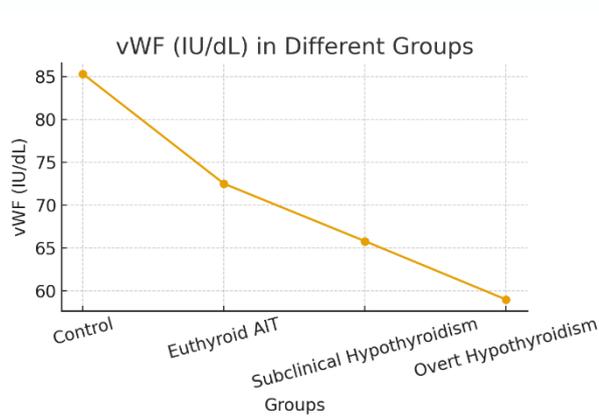
**Platelet function.** Adhesion and ADP-induced aggregation were significantly suppressed in subclinical and overt groups ( $p < 0.001$ ).

Figure 1.

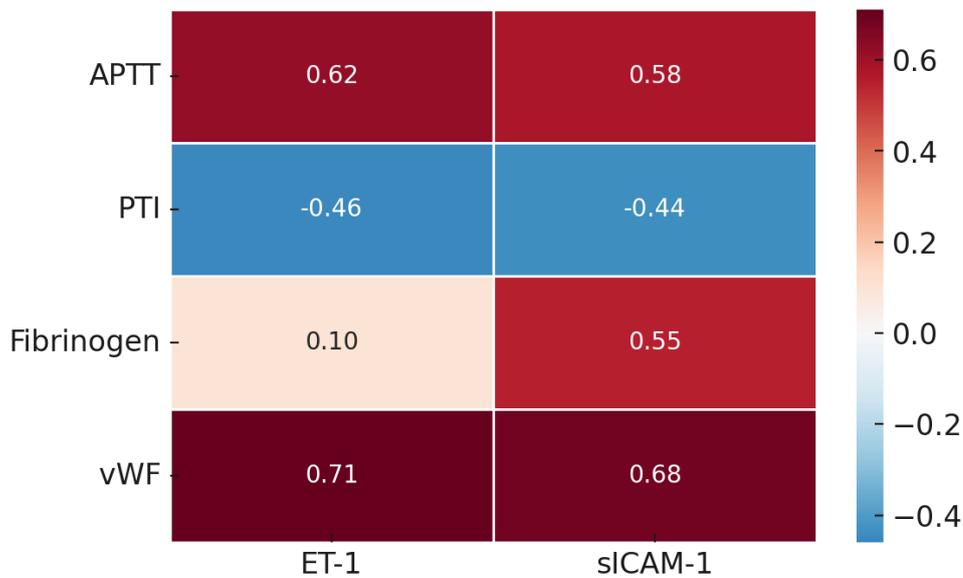


**Endothelial markers.** vWF was reduced ( $85.3 \pm 2.5$  vs.  $59.0\text{--}61.9$  IU/dL,  $p < 0.001$ ), while sICAM-1 ( $6.1 \pm 0.29 \rightarrow 8.4\text{--}9.7$  ng/mL) and ET-1 ( $2.1 \pm 0.07 \rightarrow 4.6\text{--}5.9$  pg/mL) were elevated ( $p < 0.001$ ).

Figure 2.



Correlation Heatmap: Hemostatic vs Endothelial Markers (AIT Hypothyroid stage)



**Correlation analysis.** Negative correlations were observed between PTI and endothelial markers (vWF  $r=-0.49$ ; ET-1  $r=-0.46$ ; sICAM-1  $r=-0.44$ ), while APTT showed a positive correlation with ET-1 and sICAM-1. Fibrinogen correlated positively with sICAM-1 ( $r=0.55$ ).

## CONCLUSION

1. Patients with autoimmune thyroiditis at the hypothyroid stage demonstrated a hypocoagulable profile, characterized by prolonged APTT, reduced PTI, decreased fibrinogen levels, and impaired platelet function.



2. Endothelial dysfunction was evident, with reduced vWF and elevated sICAM-1 and ET-1, indicating endothelial activation and vascular injury.
3. Significant correlations were identified between hemostatic parameters and endothelial markers: PTI and fibrinogen showed negative associations with sICAM-1 and ET-1, while APTT correlated positively. These findings confirm the combined development of hypocoagulation and endothelial dysfunction.

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