Mean Platelet Volume Index for Differentiation of Benign and Malignant Thyroid Disorders: Evaluation of a Possible Diagnostic Biomarker

Alireza Rastgoo Haghi,¹ Rashed Bawand,² Mohammad Farzad Nazari² and Mohammad Ali Seyf Rabiee³

Abstract

Background: Thyroid cancers are the most prevalent cancers of the endocrine system and platelets are effective components in the progression of thyroid tumors and can be affected by some products of tumor cells.

Objective: To measure the changes of mean platelet volume (MPV) index in patients with benign and malignant thyroid disorders compared to healthy individuals.

Materials and Methods: Patients who had undergone thyroidectomy were divided into two groups of benign and malignant thyroid disorders. There was also a healthy control group with normal thyroid function. All participants were compared for MPV.

Results: This study assessed 190 participants, including 44 males (23.2%) and 146 females (76.8%). The age range of the participants spanned from 9 to 90 years, with an average age of 43.2 years and a standard deviation of 16.3 years. The number of euthyroid volunteers was 101 (53.2%), while 39 individuals (20.5%, five men and 34 women) had malignant thyroid disorders and the other 50 cases (26.3%, one man and 49 women) had benign thyroid disorders. The difference in MPV between patients with benign and malignant thyroid disorders and normal subjects—in the form of binary comparisons—was significant. Multinodular goiter and papillary thyroid carcinoma were the most prevalent benign and malignant thyroid disorders, respectively and had significantly different MPVs. Furthermore, the MPV value enabled differentiation between normal individuals and patients with papillary thyroid carcinoma, patients with Hashimoto’s thyroiditis, and those with multinodular goiter. However, the MPV index did not enable other subgroups of malignant and benign thyroid disorders to be differentiated. Lymphatic invasions were also unable to be detected by measuring MPV changes.

Conclusion: Platelet volume measurement can be used as a complementary method for the differentiation of malignant and benign disorders of the thyroid gland.

Keywords: Mean platelet volume, thyroid, malignancy risk, benign, diagnostic biomarker

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INTRODUCTION

The thyroid gland plays an important role in regulating the body’s metabolism by producing and secreting thyroid hormones [1], and so thyroid disorders can greatly affect both quality of life and life expectancy [2, 3]. Thyroid cancers are the most prevalent endocrine malignancies and the fifth most frequent cancers among women [3–5]. As such, they play a prominent role in endangering a community’s health [6] and place a heavy financial burden on its health systems [3]. Although early diagnosis can prevent or mitigate most such consequences [3, 7], the main challenge with early detection of malignant thyroid disorders—and their differentiation from benign and less important lesions—is the lack of specific clinical and laboratory symptoms in the early stages [8].

An essential aspect of thyroid tumor progression is inflammation [9], in which platelets have an important role [10, 11]. There is also evidence indicating that some types of malignant cells can be affected by growth factors released by platelets, such as vascular endothelial growth factor (VEGF), platelet-derived growth factor (PDGF), and interleukins [12]. Malignant cells also produce some factors that can increase platelet production [12]. Younger platelets are also larger, more reactive, and able to produce more factors [13]. As a result, the measurement of mean platelet volume (MPV), as an early index of platelet activation [5], could potentially be used in the early diagnosis of thyroid tumors. MPV measurement is cheap, simple, and widely available. For these reasons, the main aim of the present study was to evaluate changes in the laboratory index of MPV in patients with benign and malignant thyroid disorders and compare them with the normal population.

MATERIALS AND METHODS

General principles: The study was conducted by census sampling. Ethics Committee approval was obtained from the Hamadan University of Medical Sciences. Informed consent according to the Helsinki Declaration was obtained from all participants. Non-participation in the study did not affect the diagnostic or therapeutic process. Data were collected without names and personal details except for age and sex, and the results were not provided to a specific person or organization.

Patients: The sample was comprised of 89 patients who had undergone thyroidectomy at Besat Hospital in Hamadan in 2020, and 101 healthy euthyroid volunteers. The patients were subdivided into benign and malignant categories based on pathological light microscopic diagnosis. The categories of benign disorders included: follicular adenoma, multinodular goiter, and Hashimoto’s thyroiditis (HT). The categories of malignant disorders included: papillary thyroid carcinoma (PTC), papillary carcinoma plus Hashimoto’s thyroiditis (PTC+HT), and other thyroid malignancies (including follicular, medullary, Hurthle cell, and anaplastic carcinomas).

Exclusion criteria: Patients were excluded for diabetes mellitus, hypertension, non-thyroid related chronic autoimmune and inflammatory disorders, acute and chronic infections, congestive heart failure, myeloproliferative disorders, history of chronic hepatic or renal disorders, anticoagulant consumption, and non-thyroidal diagnosed malignancies. The control subjects were required to have normal free T4 and TSH (thyroid stimulating hormone) levels and normal thyroid ultrasonography.

MPV measurement: Blood samples were taken from all patients (preoperative) and controls to enable a complete blood count (CBC) and measurement of MPV index, using the Sysmex® kx21 cell counter in the hematology section of the laboratory of the Besat Hospital in Hamadan.

Statistical Analysis: All data were entered into SPSS-20 and STATA-17. Quantitative values are presented as mean (M) and standard deviation (SD) scores, while qualitative variables are given as ratios and percentages. Then important data was illustrated in tables and figures. Given the non-normal distribution of MPV values, we utilized the non-parametric Kolmogorov-Smirnov test to compare these values across the control, benign, and malignant groups. Following this, to assess significant
differences identified by the Kolmogorov-Smirnov test, we conducted pairwise comparisons between all the subgroups using the Mann-Whitney U test. All related tests were two-tailed, with a p-value of <0.05 being considered statistically significant. In this study, the receiver operating characteristic curve was used for better evaluation of the sensitivity and specificity of the MPV index.

RESULTS

Demographic distribution: In this study, 190 individuals were evaluated, of which 44 (23.2%) were male and 146 (76.8%) were females. Thyroid disorders, regardless of type, were more prevalent among the females (83 women = 93%). The age range of the studied population was 9–90 years old (M ± SD = 43.2 ± 16.3). The mean ages of patients with malignant thyroid disorders, benign thyroid disorders, and healthy participants were 40.1 ± 16.7, 45 ± 12.3, and 43.6 ± 17.9 years old, respectively.

Pathological distribution: As shown in Figure 1, the number of healthy euthyroid volunteers was 101 (53.2%). 39 individuals (20.5%, five men and 34 women) had malignant thyroid disorders and the remaining 50 cases (26.3%, one man and 49 women) had benign disorders. The most prevalent malignant and benign disorders were papillary carcinoma (n = 22) and multinodular goiter (n = 35), respectively.

![Figure 1. Frequency of different kinds of thyroid disorders](image)

**MPV analysis:** As presented in Table 1, the mean ± SD of MPV value in the normal studied subjects was 8.74 ± 0.568 femtoliter (fL). The maximum MPV values belonged to the group with other thyroid malignancies, while the minimum MPV values in the patients’ group were for patients with multinodular goiter (Table 1 & Figure 2).
Table 1. Mean and standard deviation of the MPV values

<table>
<thead>
<tr>
<th>Groups</th>
<th>M ± SD of MPV (fL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Malignant</td>
<td>9.4 ± 0.697</td>
</tr>
<tr>
<td>Benign</td>
<td>9.02 ± 0.577</td>
</tr>
<tr>
<td>Normal</td>
<td>8.74 ± 0.568</td>
</tr>
<tr>
<td>Papillary carcinoma</td>
<td>9.45 ± 0.82</td>
</tr>
<tr>
<td>PTC + HT*</td>
<td>9.17 ± 0.328</td>
</tr>
<tr>
<td>Other malignancies</td>
<td>9.53 ± 0.634</td>
</tr>
<tr>
<td>Multinodular goiter</td>
<td>8.9 ± 0.413</td>
</tr>
<tr>
<td>Follicular adenoma</td>
<td>9.24 ± 0.546</td>
</tr>
<tr>
<td>Hashimoto’s thyroiditis</td>
<td>9.34 ± 0.932</td>
</tr>
<tr>
<td>Papillary carcinoma + Hashimoto’s thyroiditis</td>
<td></td>
</tr>
</tbody>
</table>

Figure 2. Range of changes in MPV index

PTC = papillary thyroid carcinoma; PTC + HT = papillary thyroid carcinoma + Hashimoto’s thyroiditis

The binary comparisons of MPV differences between patients with benign thyroid disorders, thyroid malignancies, and individuals with normal euthyroid, were all significant (Table 2). Despite this, MPV variations between different types of thyroid malignancies were not significant, and nor were those between different kinds of benign thyroid disorders. Therefore, this value could not be used to distinguish different subgroups of malignant and benign thyroid disorders (Table 2).
Table 2. Evaluation of MPV difference signification

<table>
<thead>
<tr>
<th>Pairing</th>
<th>p-value</th>
<th>MPV difference signification</th>
</tr>
</thead>
<tbody>
<tr>
<td>Malignant &amp; benign</td>
<td>0.001</td>
<td>Yes</td>
</tr>
<tr>
<td>Malignant &amp; normal</td>
<td>0.000</td>
<td>Yes</td>
</tr>
<tr>
<td>Benign &amp; normal</td>
<td>0.004</td>
<td>Yes</td>
</tr>
<tr>
<td>Papillary carcinoma &amp; PTC + HT*</td>
<td>0.088</td>
<td>No</td>
</tr>
<tr>
<td>Papillary carcinoma &amp; other malignancies</td>
<td>1.00</td>
<td>No</td>
</tr>
<tr>
<td>PTC + HT &amp; other malignancies</td>
<td>0.285</td>
<td>No</td>
</tr>
<tr>
<td>Papillary carcinoma &amp; normal</td>
<td>0.000</td>
<td>Yes</td>
</tr>
<tr>
<td>Multinodular goiter &amp; Hashimoto’s thyroiditis</td>
<td>0.70</td>
<td>No</td>
</tr>
<tr>
<td>Multinodular goiter &amp; follicular adenoma</td>
<td>0.276</td>
<td>No</td>
</tr>
<tr>
<td>Hashimoto’s thyroiditis &amp; follicular adenoma</td>
<td>0.853</td>
<td>No</td>
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<tr>
<td>Multinodular goiter &amp; normal</td>
<td>0.051</td>
<td>No</td>
</tr>
<tr>
<td>Hashimoto’s thyroiditis &amp; normal</td>
<td>0.033</td>
<td>Yes</td>
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<tr>
<td>Multinodular goiter &amp; papillary carcinoma</td>
<td>0.000</td>
<td>Yes</td>
</tr>
<tr>
<td>Hashimoto’s thyroiditis &amp; PTC + HT</td>
<td>0.562</td>
<td>No</td>
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<tr>
<td>Hashimoto’s thyroiditis &amp; papillary carcinoma</td>
<td>0.500</td>
<td>No</td>
</tr>
<tr>
<td>Follicular adenoma &amp; papillary carcinoma</td>
<td>0.301</td>
<td>No</td>
</tr>
</tbody>
</table>

*PTC + HT = Papillary carcinoma + Hashimoto’s

The MPV value enabled the differentiation of normal subjects and patients with PTC, as well as patients with Hashimoto’s thyroiditis. In addition, the MPV difference between patients with PTC and multinodular goiter (in this study, the most prevalent benign and malignant thyroid disorders, respectively) was significant. However, the MPV difference between patients with multinodular goiter and normal subjects was approaching significance (p-value = 0.051). All other measured MPV differences, as shown in Table 2, were not significant.

The receiver operating characteristic (ROC) curves were used for the evaluation of the sensitivity and specificity of the MPV index, to distinguish disorders (Figure 3) (the gold standard is pathological light microscopy). The area under the ROC curve is greater than 0.5 in all three graphs. In addition, the area in which MPV enabled the differentiation of normal samples from patients with malignant thyroid lesions is greater than 0.8, which is a relatively show good efficiency.
In this study, 16 patients with papillary thyroid carcinoma and PTC+HT had lymphatic invasions (MPV = 9.42 ± 0.559) but 15 cases did not (MPV = 9.31 ± 0.875). There was no significant difference in the MPV value of these two groups (p-value = 0.075).

**Ultra-sonographic analysis:** There was a very close agreement (95.5%) between the preoperative thyroid ultrasound results and the final diagnosis of the patients (through staining and examination of pathology slides via light microscopy); in 85 cases out of 89, the final diagnosis was consistent with the diagnosis made through ultrasound imaging. The three patients whose final diagnosis were inconsistent with ultrasound diagnosis were all from the other thyroid malignancies category. This indicates the lower accuracy of this diagnostic method in these types of lesions; however, this small group of patients had the highest MPV rates, which may indicate the efficiency of this index in the non-invasive diagnosis of these patients.

**DISCUSSION**

In the present study, the most prevalent benign and malignant disorders of the thyroid gland were multinodular goiter and PTC, respectively. Both benign and malignant thyroid disorders were more prevalent among the females. According to previous studies, the prevalence of thyroid cancer has been increasing, especially since 2002 [14]. The prevalence of thyroid cancer in 1990 was 0.0–0.25 per 100,000 people but by 2010 it had increased to 4.2–13.7 per 100,000 people [14].
Most of this increase can be attributed to the rising incidence of PTC as the most prevalent malignant thyroid disorder [15]. However, Lawal et al. [16] found follicular cancer to be the dominant thyroid malignancy in areas with dietary iodine deficiency.

Similar to our results, other studies have found that most thyroid disorders are more prevalent among women [14, 17, 18], with even the increased prevalence of thyroid malignancies being 2.5 times higher in women than men [14]. Benign thyroid disorders have also been found to prevail among women in previous studies [15, 19].

In our study, the MPV value of patients with malignant thyroid disorders was significantly higher than patients with benign disorders, and it was also higher than normal samples; likewise, the MPV value of patients with benign thyroid disorders was significantly higher than normal individuals. However, there was no significant MPV difference between types of malignant disorders or different benign disorders of the thyroid gland. Similarly, Bayhan et al. [13] sampled 146 patients who had undergone thyroidectomy (99 with benign disorders and 45 with malignant), finding that the MPV index in the malignant group was significantly higher than in the benign. In the same way, Carlioglu et al. [20] studied 47 patients with advanced papillary thyroid cancer, 47 patients with micropapillary thyroid cancer, and 62 healthy individuals and found that MPV levels in patients with advanced papillary thyroid cancer and micropapillary thyroid cancer were significantly higher than the healthy control. Nevertheless, in the study of Yu et al. [5], 280 patients with thyroid cancer and 280 control subjects were compared for MPV and PDW (Platelet Distribution Width) values. The patients with thyroid cancer had lower MPV, which contrasts with the results of the present study.

In our study, the MPV index enabled differentiation between normal subjects and patients with PTC + HT. In addition, the difference in MPV between patients with PTC and patients with multinodular goiter was significant. However, MPV did not enable the differentiation of other evaluated thyroid disorders or detect lymphatic invasions. In the same way, Baldane et al. [21] found that MPV levels in patients with PTC were significantly higher than in patients with benign goiter and healthy controls, consistent with our results. In contrast, Dincel et al. [22] found no significant differences in the MPV of different groups. In this work, 160 patients were divided into three groups: PTC, multi-nodular goiter, and healthy subjects. Platelet-related indices, including MPV, were compared between these groups.

**CONCLUSION**

In conclusion, this study suggests MPV evaluation as a laboratory, low-cost, simple, and attainable auxiliary method for the differentiation between normal individuals, patients with benign, and patients with malignant disorders of the thyroid gland. However, this index is not accurate for determining the exact type of disorders.

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

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**Data Availability Statement:** The data that support the findings of this study are available from the corresponding author upon reasonable request.

**Ethics:** The study followed ethical guidelines, including adherence to national legal requirements. Ethics Committee and Institutional Review Board (IRB) approvals for the study were obtained from the Hamadan University of Medical Sciences.
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M託سط حجم الصفائح الدموية للتمايزة بين اضطرابات الغدة الدرقية الحميدة والأخيبة: تقييم العلامات الحيوية التشخيصية المحتملة

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الملخص

خلفية والأهداف: سرطانات الغدة الدرقية هي أكثر أنواع السرطان شيوعًا في الجهاز الصماوي، وتعتبر الصفائح الدموية مكونات فعالة في تقدم أورام الغدة الدرقية ويمكن أن تتأثر ببعض المنتجات الصادرة عن خلايا الورم. هدفنا إلى قياس التغيرات في مؤشر حجم الصفائح الدموية المتوسط (MPV) لدى المرضى الذين يعانون من اضطرابات الغدة الدرقية المحميدة والأخيبة مقارنة بالأفراد الأصحاء.

منهجية البحث:

تم تقسيم المرضى الذين خضعوا لاستئصال الغدة الدرقية إلى مجموعتين: مجموعة تعاني من اضطرابات الغدة الدرقية الحميدة ومجموعة تعاني من اضطرابات الغدة الدرقية الخبيثة. كما كان هناك مجموعة ضابطة صحية ذات وظيفة درقية طبيعية، أو الأفراد الأصحاء.

النتائج:

شملت هذه الدراسة 190 مشاركًا، منهم 44 ذكرًا (23.2%) و146 أنثى (76.8%). تراوحت أعمار المشاركين من 9 إلى 90 عامًا، بمتوسط عمر 43.2 عامًا وانحراف معياري 16.3 عامًا. بلغ عدد المتطوعين الذين لديهم وظيفة درقية طبيعية (الغدة الدرقية السليمة) 101 شخصًا (53.2%)، بينما كان لدى 39 فردًا (20.5%)، خمسة رجال و34 امرأة اضطرابات درقية. كان الفرق في MPV بين المرضى المصابين بالإصابة بالاضطرابات الدرقية الحميدة والأخيبة والأشخاص الطبيعيين، فيما كان في الغدة الدرقية المتعددة العقيدات وسرطان الغدة الدرقية الحليمي أكثر الاضطرابات الدرقية الحميدة والأخيبة ملحوظًا. كانت الاضطرابات fantasia MPV مختلفة بشكل ملحوظ. كذلك، سمحت قيمة MPV بالتمييز بين الأفراد الطبيعيين والمصابين بسرطان الغدة الدرقية الحليمي، والمرضى المصابين بتضخم الغدة الدرقية هاشيموتو، وأولئك المصابين بالغدة الدرقية المتعددة العقيدات. ومع ذلك، لم يسمح مؤشر MPV بتمييز الأنواع الفرعية الأخرى من الاضطرابات الدرقية الحميدة والأخيبة في MPV. الاستنتاج:

يمكن استخدام قياس حجم الصفائح الدموية كطريقة تشخيصية لمتايزة الاضطرابات الحميدة والأخيبة في الغدة الدرقية.

الكلمات الدالة: متوسط حجم الصفائح الدموية؛ غدة درقية؛ خبيثة؛ حميدة؛ العلامات الحيوية التشخيصية.