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Assessment of Peripheral Blood Indices in Patients with Papillary Thyroid Carcinoma

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Abstract

Background: The most prevalent thyroid cancer is papillary thyroid carcinoma (PTC), frequently has an optimistic prognosis. However, the need for basic and credible biomarkers to assist in distinguish between benign and malignant thyroid nodules is highlighted by concerns for overdiagnosis and overtreatment. Complete blood count (CBC)-derived peripheral blood cell indices have become promising markers of tumour behaviour and systemic inflammation.

Method: There were 63 participants in this case-control study: 10 healthy controls, 37 patients with benign thyroid nodules, and 16 patients with histopathologically confirmed PTC. Inflammatory and platelet-related indices, as well as the lymphocyte-to-monocyte ratio (LMR), were among the clinical, demographic, and CBC parameters that were examined. One-way ANOVA and chi-square tests were used for statistical comparisons; $p < 0.05$ was deemed statistically significant.

Result: Patients with PTC had a significantly higher frequency of lymph node metastases ($p = 0.042$). When compared to benign cases, patients with PTC had a significantly lower LMR and a significantly higher granulocyte percentage ($p < 0.05$). While the platelet-large cell ratio (P-LCR) did not significantly differ between groups, several CBC parameters, such as white blood cell subtypes and platelet indices, did.

Conclusion: Granulocyte percentage, platelet parameters, and LMR are among the peripheral blood cell indices that are correlated with papillary thyroid carcinoma and may be useful supplementary biomarkers for distinguishing benign from malignant thyroid nodules. To validate their clinical applicability, more prospective research is required.

Keywords: Papillary Thyroid Carcinoma, LMR, P-LCR.

Abbreviation

LMR: the ratio of lymphocytes to monocytes; P-LCR: platelet-large cell rate.

Introduction

Thyroid gland malignancy is one of the most common cancers., and its incidence has increased over recent decades with incidence rate 6.6 per 100,000 caes. This is reflecting a rising public health burden associated with thyroid malignancies in 2020 [1]. Papillary thyroid carcinoma (PTC) is the predominant subtype (nearly 85% of cases). Papillary thyroid carcinoma is a differentiated carcinoma arising from the follicular epithelial cells of the thyroid and is most frequently detected as a painless thyroid nodule or a mass, although incidental detection is also common with the increased use of imaging methods [2]. PTC is early tendency to spread through the lymphatic system. Lymph node metastasis is observed in up to 50% of cases at the time of primary diagnosis, whereas distant metastases, particularly to the lungs, are less common. Despite this metastatic potential, PTC generally has slow biological behavior and associates with an excellent prognosis in most patients [3]. The proper diagnosis of PTC relies on a set of characteristic nuclear features, irregardless of the constructing growth pattern [4]. Guidelines of treatment strategies typically include thyroid hormone suppression therapy, radioactive iodine ablation, and thyroidectomy, which collectively participate to favorable survival outcomes [5]. Approximately 5–20% of PTC patients experience local recurrences or distant metastasis after therapeutic interventions, and these make disease progression remain clinical concerns [6]. Furthermore, raising recognition of postoperative hypothyroidism conditions following thyroidectomy illustrate the danger of overtreatment [7]. These problems emphasize the importance of accurate risk stratification to optimize treatment strategies and avoid useless interventions that may improve clinical decision-making. [8].

Peripheral blood cell indices that called complete blood count (CBC) represent quantitative hematological parameters that reflect the size, distribution, principally erythrocytes. The indices are generated by automated haematology analysers [9]. Peripheral blood indices have been increasingly studied as potential tumor-associated biomarkers across various cancers. In PTC, evidence from recent studies suggests that blood indices such as the lymphocyte to monocyte ratio (LMR), and platelets related parameters may associate with tumor behavior, metastasis, and progression but there remains a lack of systematic evaluation and standardized interpretation in PTC due to methodological variability in research designs [10,11]. However, the present study aims to investigate the association between peripheral blood cell indices and thyroid cancer in order to assess their potential role as supplementary biomarkers for disease characterization and risk assessment.

Methods

Case-control study including 63 samples were included in this research. 16 samples from patients with PTC, 37 samples from benign thyroid nodules cases, and 10 samples from healthy controls. Individuals with non-specific thyroid conditions or other subtypes of thyroid malignancies were excluded. The surgical procedure was performed on all cases, and they were diagnosed based upon pathological examination.

The research was carried out between December 2024 and July 2025. Thyroidectomy cases for various causes were examined in terms of age, sex, and the kind of thyroid pathology whether benign or malignant at Al-Kafeel Hospital and Safeer Imam Hussain Surgical Hospital and in Kerbala, Iraq. An organized questionnaire was created specially to gather data that aids in the selection of participants based on the study's selection criteria. Each patient's medicinal & social data was collected by a questionnaire which including age, gender, smoking state, family history of disease, laboratory investigations was measured for patient’s complete blood count (CBC).

The statistical analysis for our study was performed by using the The jamovi (2025) Version 2.6. Descriptive statistics were analysed for each group. The normality was checked using the Shapiro-Wilk test as a numerical means. The differences between study groups were calculated by one-way ANOVA test with p-value < 0.05 for significant differences.

Ethical Approval

The hospital ethics committee approved the study plan, and all patients or their relatives were informed. The Ethical Committee at Kerbala University- College of Medicine, gave their approval to study plan. Verbal approval was taken from all patients included in the study.

Results

Age and BMI of participants with PTC, participants with benign thyroid nodules, and healthy controls are shown in Table 1. There was no statistically significant age and body mass index (BMI) difference between the groups (p-value= 0.713, 0.562; respectively).

Table 1. Age and BMI of participants with PTC, participants with benign thyroid nodules, and healthy controls (Benign=37; Malignant=16; Control=10)

Variables	Benign Mean (SD)	Malignant Mean (SD)	Control Mean (SD)	*p*-Value
Age (year)	43.1 (13.3)	44.8 (10.3)	40.5 (15.6)	0.713
BMI (kg/m2)	27.7 (5.3)	26.5 (4.4)	28.4 (2.7)	0.562

The demographic and clinical features of individuals with PTC, individuals with benign thyroid nodules, and healthy controls **Table 2**. There was no statistically significant sex, family history, and smoking differences between the groups (*p*-value= 0.262, 0.569, 0.343; respectively). Metastasis showed a statistically significant correlation with malignancy and was more common in PTC than in benign nodules (*p*-value= 0.042). The significance of lymph node metastasis as a measure of aggressive disease behavior was further demonstrated by its association with malignant group (*p*-value= 0.042). Regarding patient outcomes, there was not statistically significant difference was observed between benign and malignant groups in cure versus prognosis status (*p*-value= 0.089).

Table 2. The demographic and clinical features of individuals with PTC and individuals with benign thyroid nodules (Benign=37; Malignant=16).

Variables		Benign	Malignant	X^2	*p*-Value
Sex	Male	3	3	1.26	0.262
	Female	34	13		
Family History	Yes	20	10	0.324	0.569
	No	17	10		
Smoking	Yes	2	0	0.899	0.343
	No	35	16		
Metastasis	Yes	1	3	4.12	0.042*
	No	36	13		
LN Metastasis	Yes	1	3	4.12	0.042*
	No	36	13		
Fate of Patient	Cure	6	6	2.89	0.089
	Prognosis	31	10		

Differences between the ratio of peripheral blood cell count in study groups were shown in **Table 3**. A number of hematological and inflammatory markers specifically, granulocyte percentage, platelet parameters, LMR, and lymphocyte-related indices were differed significantly between study groups, suggesting their potential role as biomarkers in PTC.

Table 3. Differences between the ratio of peripheral blood cell count in study groups (Benign=37; Malignant=16; Control=10).

Variables	**Benign** **Mean (SD)**	**Malignant** **Mean (SD)**	**Control** **Mean (SD)**	***p*-Value**
WBC (10^3/l)	7.2 (2.1)	7.9 (1.9)	15.9 (14.7)	0.001 *
LYM (10^3/l)	2.5 (0.9)	2.3 (0.6)	3.9 (3.0)	0.029 *
LYM%	36.3 (9.0)	31.4 (8.9)	21.8 (15.5)	0.001 *
MID (10^9/l)	0.5 (0.5)	0.4 (0.2)	10.4 (15.0)	<0.001 *
MID%	5.8 (2.0)	5.6 (2.1)	4.2 (3.4)	0.196
GRA (10^9/l))	4.2 (1.7)	5.3 (1.7)	4.7 (1.6)	0.140
GRA%	56.1 (10.9)	64.2 (9.3)	44.7 (30.3)	0.023 *
RBC (10^12/l)	4.8 (0.4)	4.8 (0.6)	22.8 (29.4)	<0.001 *
HGB(g/dl)	13.0 (1.2)	13.0 (1.5)	10.7 (4.5)	0.012 *
PCV(HCT)%	39.1 (3.3)	39.0 (4.8)	53.1 (21.4)	<0.001 *
RDW"fL	52.2 (7.4)	54.2 (7.8)	51.7 (12.6)	0.703
RDW%	12.0 (1.8)	12.3 (1.8)	25.2 (21.4)	<0.001 *
PLT (10^9/l)	304.4 (78.5)	295.8 (75.0)	174.7 (129.5)	<0.001 *
MPV (fL)	9.6 (1.0)	9.2 (0.9)	70.4 (97.6)	<0.001 *
PDWa"fL	12.3 (1.8)	11.3 (1.2)	11.7 (2.3)	0.215
PDW%"	40.7 (1.7)	39.2 (8.0)	32.3 (15.2)	0.021 *
PCT"%	0.4 (0.4)	0.3 (0.1)	13.0 (20.6)	<0.001*
P-LCR"%	23.5 (7.0)	21.8 (6.6)	19.8 (15.7)	0.586
P-LCC"(10^9/l)	70.2 (27.4)	66.6 (26.7)	51.9 (20.0)	0.183
LMR	7.8 (3.4)	6.6 (2.9)	4.4 (3.9)	0.037 *

*Significant.

Discussion

The thyroid gland is a vital endocrine organ that is involved in many physiological processes, normal physiological activity, and the growth and development of the human body. As a result, the process behind the onset and progression of thyroid illness appears to be very intricate. PTC accounts for the majority of thyroid illness, which is becoming more common every year. The 5-year survival rate for thyroid cancer patients has increased to 99.4% due to increasingly standardised therapy; nonetheless, concerns regarding overdiagnosis and overtreatment remain. We must acknowledge that surgery is the main treatment for nearly every kind of thyroid cancer, including DTC. However, because of the incorrect diagnosis, we could do some needless procedures, which also entails some needless dangers, such as parathyroid damage or recurrent laryngeal nerve damage that might not be avoidable [12]. Considering that when patients visit the hospital for thyroid problems, the blood test and ultrasound are now routine tests. In an effort to identify a marker that may accurately and sensitively detect PTC without requiring patients to undergo further testing, this article lists possible markers found in the blood of PTC patients. We can prevent needless procedures by using biomarkers to distinguish between benign and malignant tumors [13].

Our findings emphasise the significance of systemic inflammation in cancer by showing a strong connection between peripheral blood cell indices and the pathological state of thyroid nodules. According to statistical analysis, the granulocyte percentage (GRA%) was significantly higher in the malignant group (64.2±9.3%) than in the benign group (56.1±10.9%) with a p-value of 0.023. Additionally, the LMR significantly decreased in the malignant cohort (6.6±2.9) compared to the benign cohort (7.8±3.4, *p*-value= 0.037). Additionally, significant differences were found in platelet-related measures, namely Platelet Count (PLT) and Mean Platelet Volume (MPV), both of which had high statistical significance (*p*-value < 0.001).

Data on the predictive value of systemic inflammatory markers for thyroid cancer have been inconsistent [14, 15]. These conflicting and unclear results might be due to the significant variability in the differentiation of the thyroid tumours included in the earlier investigations. The anti-tumor activity of immune cells, such as activated T cells and natural killer cells, can be suppressed by systemic inflammatory responses [16]. Neutrophil, lymphocyte, and platelet counts, either by themselves or as their ratios, are surrogate markers for systemic inflammation., have been linked to prognosis for a number of malignancies, despite unclear underlying mechanisms [17,18]. Yokota et al. found that recurrence was linked to low lymphocyte-to-monocyte ratio (LMR), particularly in patients with advanced PTC [19].

Invasion and the inflammatory index have been linked in a number of earlier investigations, although the results have been mixed [20]. For the first time, it was discovered that LMR may predict capsular invasion (*p*-value= 0.017). As of right now, the precise mechanism is unknown. Among the potential causes include the development of circulating monocytes into myeloid-derived suppressor cells (MDSCs) and tumor-associated macrophages (TAMs) [21]. By speeding up the transition between epithelium and stroma, they aid in the growth, invasion, and metastasis of tumour cells, whereas lymphocytes may encourage the production of cytotoxins like perforin and the release of different inflammatory mediators that either directly or indirectly have antitumor effects [22]. As a result, LMR is probably a tumour marker in PTC patients and may somewhat represent the condition of the host immune system. This might be because the production of various inflammatory mediators may increase platelets [23].

In contrast to platelet quantity, it has been revealed in recent years that platelet volume is more strongly associated with platelet activation [24]. The average platelet size, which represents the platelet creation rate and stimulation, is shown by the MPV, or average platelet volume [25]. Larger platelets appear to have more metabolic and enzymatic activity than smaller ones, according to several studies [26]. As a result, the crucial significance of MPV in tumour assessment has received increasing attention. Osada [27] discovered that 20 healthy control participants had a lower MPV than patients with stomach cancer. In a similar vein, we found that the biggest LN size ≥ 1cm was predicted by greater MPV (*p*-value= 0.002).

Some research has shown that platelet size, not platelet count, is linked to platelet activation [28]. Two popular measures of platelet volume are MPV and PDW. MPV represents the average platelet size as well as the stimulation and rate of platelet formation [29]. Compared to smaller platelets, larger platelets have higher metabolic and enzymatic activity [30]. The intricate relationships between inflammatory elements in the tumour microenvironment are highlighted by this seemingly paradoxical result. Furthermore, DTC's laziness may also help to explain it. Higher values of the PDW, which measures the homogeneity of platelet volume, suggest the presence of unusually big and tiny platelets in the blood [31]. When assessing the causes of thrombocytopenia, PDW is more trustworthy than MPV [32].

Additionally, our analysis was the first to identify an LMR ≤4.7 (OR=4.790; 95% CI: 1.034-22.187; P=0.045) as a possible

independent risk factor for the advancement of postoperative Ctn. According to certain research, low LMR is also linked to a poor prognosis for anaplastic thyroid cancer and PTC [33]. This may be explained by the ability of circulating monocytes to change into tumor-associated macrophages and myeloid suppressor cells, which accelerate the epithelial-mesenchymal transition and contribute to tumour development, invasion, and metastasis [34].

There are many limitations to our study. There could have been some unidentified or undetected variables that could have affected our results even though individuals with conditions that could affect complete blood counts were eliminated. Our study had a very limited number of instances. To validate our findings, further extensive and prospective research is required.

Conclusion

Granulocyte percentage, platelet parameters, and LMR are among the peripheral blood cell indices that are correlated with papillary thyroid carcinoma and may be useful supplementary biomarkers for differentiating thyroid nodules that are benign from those that are cancerous. To validate their clinical applicability, more prospective research is required.

Funding:

Nil.

Conflict of Interest:

Nil.

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