

ARE THERE ANY VARIATION IN NEUTROPHIL LYMPHOCYTE RATIO, MEAN PLATELET VOLUME AND PLATELET COUNT BETWEEN PAPILLARY THYROID CANCER AND BENIGN NODULAR THYROID DISEASES

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Abstract: Objective: Neutrophil lymphocyte ratio (N/L) and mean platelet (Plt) volume (MPV), the markers of systemic inflammatory response, has been investigated in many cancers, but data for the head and neck cancers and thyroid carcinoma are limited. It had been purposed to study N/L, MPV, and Plt levels in papillary thyroid carcinoma (PTC) as a diagnostic marker. **Material and Methods:** A total of 104 patients, had undergone ultrasonography guided fine needle aspiration (FNA) and thyroidectomy, for the indicated cases, between April 2010 and August 2013, were enrolled in the study. The laboratory tests, regarding N/L, MPV, and Plt, of the cases had been collected retrospectively. **Results:** No difference was found between PTC and benign nodular thyroid diseases (BNTD) in terms of age, gender, size of the nodule, N/L, MPV, and Plt ($p > 0.05$). **Conclusion:** The preoperative inflammatory hematological parameters, in terms of N/L, MPV, and Plt, may not be useful as a predictive diagnostic marker of the thyroid malignancy, PTC.

Key words: Thyroid neoplasms, Papillary thyroid cancer (PTC), Ultrasonography (US), Ultrasonography guided fine needle aspiration (US-g-FNA), Bethesda, Neutrophils, Lymphocytes, Neutrophil lymphocyte ratio, Mean platelet volume (MPV), Blood platelets.

INTRODUCTION

Thyroid cancer, the most common endocrine cancer, that has the dramatically increased incidence worldwide in terms of new diagnosis and mortality with the significant change in the papillary histotype (1-5). The shortage of the clinically proven markers in the diag-

nosis of thyroid cancers like the other head and neck cancers still sustains the adversity in absolute and definitive preoperative diagnosis in the field of Neck-Endocrine Surgery. Many studies established the augmentation of neutrophil lymphocyte ratio (N/L) and mean platelet (Plt) volume (MPV), the markers of systemic inflammatory response, being related with the progression and survival of the certain types of cancers (6, 7).

In the present study, the laboratory tests of the patients that have thyroid nodules have been evaluated retrospectively and the relationship between papillary thyroid cancer (PTC) and the inflammatory hematological parameters including N/L, MPV, and Plt had been investigated.

MATERIAL AND METHODS

A retrospective analysis comprised of the patients that possess the nodular thyroid disease, who had undergone one-endocrine surgeon performed ultrasonography (US) guided fine needle aspiration (FNA) between April 2010 and August 2013. The documents were consisting the complete blood counts and US guided FNA (US-g-FNA) cytologies (FNACs) which had been reported according to the guidance of The Bethesda System for Reporting Thyroid Cytopathology (TBSRTC), a 6-diagnostic-category system which was constituted through multidisciplinary formulation, which was proposed at the National Cancer Institute (NCI) Thyroid Fine Needle Aspiration State of the Art and Science Conference held in Bethesda, Maryland, 2007. TBSRTC is at present the most used and accepted reporting system

for reporting FNA cytology worldwide (8). The use of TBSRTC has also been endorsed by 2015 American Thyroid Association (ATA) management guidelines (9) as 2009 ATA guidelines (10) which is a revision of 2006 ATA guidelines (11). However, a special 2½-hour symposium entitled 'The Bethesda System for reporting thyroid cytopathology: past, present', future was moderated by Ali and Vielh at The 19th International Congress of Cytology (ICC) in Pacifico Yokohama, Japan, on 28 May–01 June, 2016 (12, 13). Pusztaszeri et al (14). Ali et al (12, 13) also discussed briefly the consensus of panel, recommendations, proposed modifications and updates for the second edition, TBSRTC II (12) by anticipating the second edition of TBSRTC, TBSRTC II, in early 2018.

As a result, cases were divided into two groups, benign nodular thyroid diseases (BNTD), diagnosed by the current TBSRTC I Class II as Group 1 and PTC whose diagnoses also had been verified histopathologically as Group 2. They were taken into account if the age, gender, size of the tumor had been correlated to the inflammatory hematological parameters regarding N/L, MPV, and Plt.

The Criteria for Incorporation into the Study

The screening outcome revealed the 104 cases in conformity with the criteria for being incorporated into the study. 95 cases with BNTD and 9 cases with PTC had been enrolled the present study between April 2010 and August 2013 by excluding the hematologic disorders, cardiac disorders, autoimmune diseases, inflammatory or infective diseases, endocrinologic diseases and diabetes, the patients with the elevated thyroid antibodies or impaired thyroid function tests, liver diseases, renal failure, recurrent diseases, previous or accompanying other malignancies, as well as those who had medical records as to the usage of steroids, anticoagulants, and alcohol along with those with a medical history of hepatitis.

Table 1 — The comparison of demographic features and hematological parameters between the patients with benign nodular thyroid disease and PTC

Parameters	Benign	PTC	p Value
MPV, femtoliters, fL	191 ± 262	172 ± 234	0,470
Plt, x10 ⁹ /L)	271 ± 56	280 ± 66	0,649
N/L	1,8 ± 0,8	1,4 ± 0,4	0,051
Age, year	50 ± 12	53 ± 9	0,565
Size, mm	18 ± 9	19 ± 10	0,728
Gender, male/female	15/80	0/9	0,351

PTC, papillary thyroid carcinoma; MPV, mean platelet volume; Plt, platelet; N/L; neutrophil lymphocyte ratio; Size, size of the nodule

Statistical Analysis

The statistical analysis were performed by using SPSS 23.0 computer program. The Fisher Exact Test was applied for gender parameter. The Mann Whitney U-tests were applied for MPV, N/L and size parameters due to the samples not being obtained from normal population according to Kolmogorov-Smirnov and Shapiro Wilk Normality tests. The Independent sample t-tests were used to detect difference among two groups for age and Plt parameters and p value less than 0.05 was considered as statistically significant.

RESULTS

9 (8.65%) out of 104 cases possessing thyroid nodules (male/female: 15/89, 10.41%/61.8%) had PTC, while 95 (91.35%) had BNTD. It had not been detected any statistically significant difference between the cases with BNTD, Group 1 and cases with PTC, Group 2 in terms of age, gender, size of the nodule, N/L, MPV, and Plt ($p > 0.05$) (Figure 1a-f). Therefore, according to the statistical test results, there was no difference between PTC and benign thyroid nodules for all the parameters (Table 1).

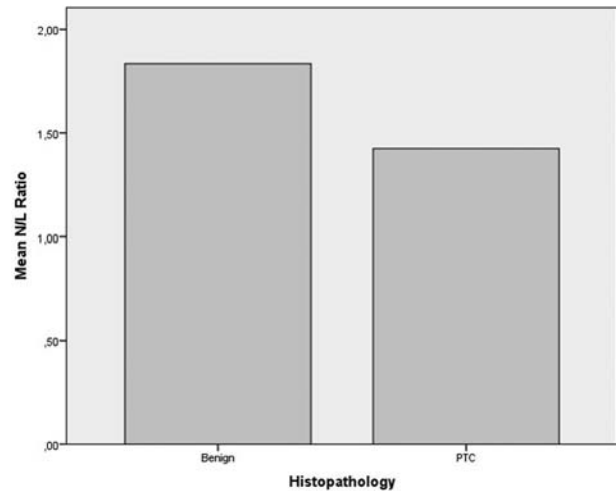


Figure 1a: The median N/L from PTC and Control group

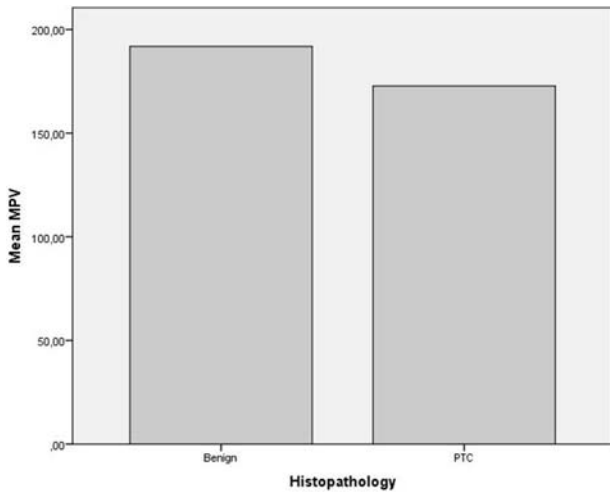


Figure 1b — The median MPV from PTC and Control group

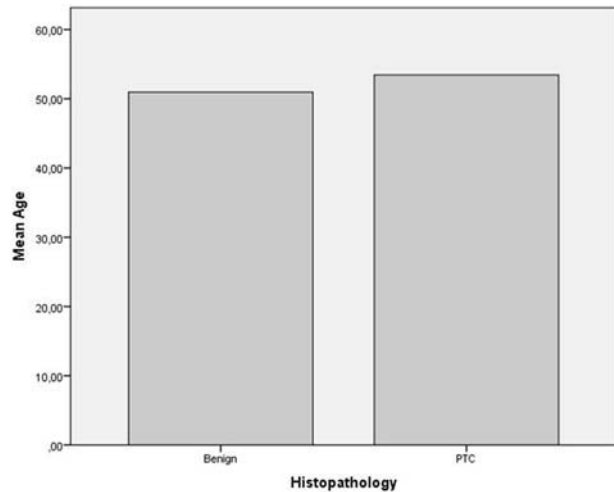


Figure 1d — The median age from PTC and Control group

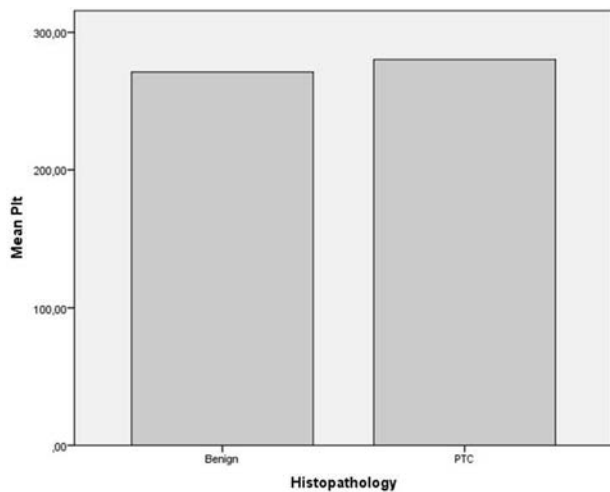


Figure 1c — The median Plt from PTC and Control group

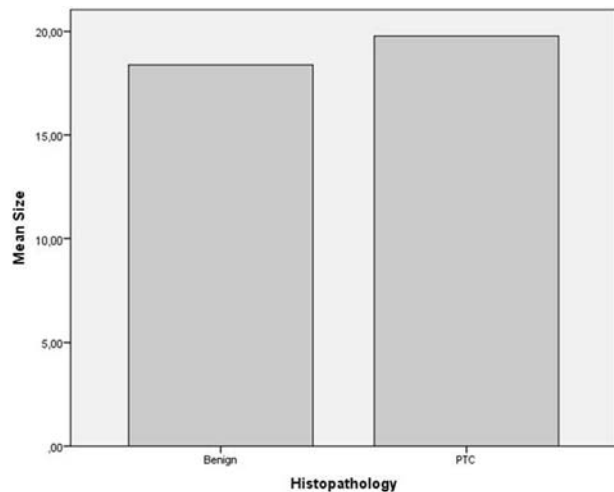


Figure 1e — The median size of the nodule from PTC and Control group

DISCUSSION

As a common clinical problem, the thyroid nodules, reveal the prevalence of approximately 5% in women and 1% in man living in iodine-sufficient areas of the world epidemiologically in palpation, whereas 19%-68% is the detection rate in high resolution US, with higher frequencies in women and elderly (9). The thyroid nodules are important clinically as long as eliminating the thyroid cancer comprising 7%-15% of the cases being based on age, sex, radiation exposure history to head and neck and thorax, particularly during first two decades, family history, and the other factors (15, 16).

Differentiated thyroid cancer (DTC), consisting PTC, follicular thyroid carcinoma (FTC), and Hurthle cell carcinoma (HCC), constitutes vast majority, > 90%, of the thyroid cancers (17). In the United States, the yearly incidence of thyroid cancer has nearly tripled from 4.9 per 100,000 in 1975 to 14.3 per 100,000 in

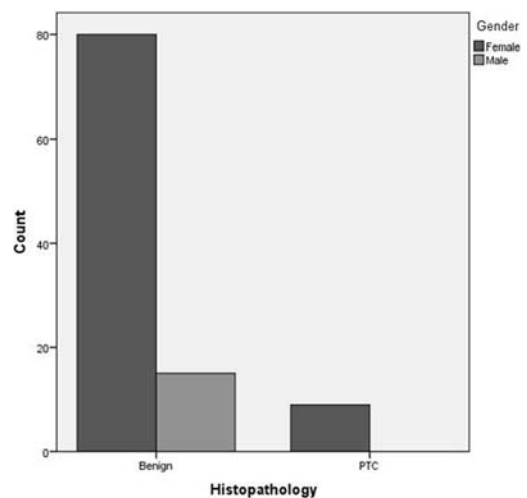


Figure 1f — The numerical value of gender from PTC and Control group

2009 and virtually the entire change has been attributed to an increase in the incidence of papillary thyroid cancer (18, 19). One study estimates PTC will be

become the third most common cancer in women at a cost of \$19–21 billion in the United States (20).

N/L, known as marker of systemic inflammatory response, have been associated with progression and survival in most kind of cancers (6, 7). Chang et al (21) found N/L, Hb, and Plt count beneficial for predicting long-term mortality in cases with nasopharyngeal carcinoma. N/L estimated as a negative indicator for oral cancer (22), breast cancer (23), and pancreatic adenocarcinoma (24). Feng et al (25) reported in a pilot study the elevated levels of N/L in cases with papillary thyroid microcarcinoma (PTmC) and PTC. Hower, N/L was not statistically different the patients with BNTD and PTC, in the present study. Similiar to the present study, Liu et al (26) reported a metanalysis on December 2016 to be able to clarify the undecided association between N/L and DTC. They conducted a systematic meta-analysis based on 7 prospective cohort studies published between 2013 and 2015, to investigate a potential association between N/L and DTC comprising 7349 patients. It was not detected any significant difference in N/R between the patients with benign nodules and PTC aged < 45 years and those aged ≥ 45 years, similar to our study.

Larger platelets are more metabolically and enzymatically active than the smaller ones. MPV reflects platelet activity indicating being an important biological variable (26). In a Turkish study, MPV was suggested as a possible biomarker in the diagnosis of PTC and estimator for therapeutic effectiveness in PTC in terms of its attenuated postoperative levels (27). However, we haven't detected significant difference between the groups, BNTD and PTC, in terms of MCV and Plt.

CONCLUSION

The present study lasted approximately three and a half years. However, a retrospective design, a relatively low sample count, not analyzing postoperative values of hematologic parameters and not comparing them with the preoperative ones were the limitations of the present study.

In conclusion, preoperative N/L, MPV, and Plt levels may not be useful as a predictive diagnostic marker of thyroid malignancy, PTC, in contrast to the rela-

ted investigation. However, further studies with larger groups in multidisciplinary and multicentric studies may reveal the different results in the future.

Conflict of interest

No any conflict of interest relevant to this article was declared.

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It has not been used any funding for the present work. DS had contributed in constituting the notion and hypothesis, intellectual planning and management of the study, collecting the data, performing the statistical analysis, writing the whole manuscript, its linguistic and academical revisions. IS had contributed in examining the patients and performing US-guided-FNA for each indicated thyroid nodule, collecting the data, academical revision of the manuscript. All the authors finally approved the submitted and proof versions without any conflict of interest.

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Abbreviations

N/L — Neutrophil lymphocyte ratio

MPV — Mean platelet volume

Plt — Platelet

PTC — Papillary thyroid cancer

BNTD — Benign nodular thyroid diseases

DTC — Differentiated thyroid cancer

FTC — Follicular thyroid carcinoma

HCC — Hurthle cell carcinoma

US — Ultrasonography

FNA — Fine needle aspiration

US-g-FNA — US guided FNA

FNAC — FNA cytology

TBSRT — The Bethesda System for Reporting Thyroid Cytopathology

ATA — American Thyroid Association

Sažetak

DA LI POSTOJE VARIJACIJE U ODNOSU NEUTROFILA I LIMFOCITA, SREDNJEG VOLUMENA TROMBOCITA I BROJA TROMBOCITA IZMEĐU PAPILARNOG TIROIDNOG KARCINOMA I BENIGNOG NODULARNOG POREMEĆAJA ŠTITNE ŽLEZDE?

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Uvod: Odnos neutrofila i limfocita (N/L) i srednjeg volumena trombocita (MPV), markeri sistemskog inflamatornog odgovora, istraživani su u mnogim karcinoma, ali podaci o karcinomima glave i vrata i tiroidnom karcinomu su ograničeni. Cilj ove studije bio je da se izuči povezanost N/L, MPV, Plt niova u papilarnom karcinomu tireoidne žlezde (PTC) kao dijagnostičkog markera.

Materijal i metode: Ukupno 104 pacijenta koja su bila podvrgnuta ultrasonografski vođenoj biopsiji pomoću tanke igle (FNA) i tireoidektomiji za slučajeve kod kojih je to indikovano uključeni su u studiju u periodu između aprila 2010. i avgusta 2013. godine. Podaci o laboratorijskim analizama, koje uključuju N/L odnos, MPV, Plt bili su sakupljeni retrospektivno.

Rezultati: Nije postojala statistički značajna razlika između PTC i benignog nodularnog poremećaja štitaste žlezde u pogledu godina, pola, veličine nodula, N/L, MPV i Plt ($p > 0.05$).

Zaključak: Preoperativni inflamatorni hematološki parametri, kao što su N/L, MPV i Plt nisu upotrebljivi kao prediktivni dijagnostički markeri tireoidnog maligniteta, PTC.

Ključne reči: tireoidna neoplazma, papilarni tireoidni karcinom (PTC), ultrasonografija, ultrasonografski vođena biopsija tankom iglom, bethesda, neutrofil, limfociti, odnos neutrofila i limfocita, srednja vrednost volumena trombocita, trombociti.

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