ENT Updates

ORIGINAL ARTICLE

ENT UPDATES 11(2):115-119
DOI: 10.5152/entupdates.2021.846919

Relationship Between Parathormone and Inflammatory Markers on Complete Blood Count in Parathyroid Adenoma Patients

ABSTRACT

Objective: To investigate the effects of surgical treatment on blood parameters in patients with parathyroid adenoma.

Methods: Patients with a diagnosis of parathyroid adenoma, who underwent surgery between November 2011 and April 2016, were investigated retrospectively. These patients were evaluated according to white blood cell, lymphocyte, neutrophil, and platelet counts, hematocrit, mean platelet volume (MPV), neutrophil/lymphocyte ratio (NLR), platelet/lymphocyte ratio (PLR), and calcium and parathormone (PTH) levels before and after the surgery.

Results: The study included 103 patients. The number of male patients was 22 (21.4%), and the number of female patients was 81 (78.6%). The age of the patients ranged between 7 and 87, and the mean age was 54.7 ± 14.3. Preoperative and postoperative changes in lymphocyte, platelet, hematocrit, MPV, calcium and PTH levels were found to be statistically significant in our study, but the changes in NLR and PLR were not.

Conclusion: Hyperparathyroidism is a reason for chronic inflammation and may affect blood inflammation parameters. However, the correlation between NLR, PLR, and serum PTH levels was not statistically significant. This can be explained by the fact that surgery causes a significant change in the number of both platelets and lymphocytes. We found a positive correlation between lymphocyte, neutrophil, and platelet counts, hematocrit, MPV, and serum PTH levels.

Keywords: Parathormone, neutrophil, neutrophil/lymphocyte ratio, lymphocyte/platelet ratio, mean platelet volume

INTRODUCTION

Primary hyperparathyroidism (PHPT) occurs when one or more of the parathyroid glands secrete excessive amounts of parathormone (PTH). The negative feedback function that controls PTH release is impaired. The uncontrolled secretion of PTH results in hypercalcemia. Hypercalcemia usually occurs with calcium mobilization from the bones.[1,2] The causes of PHPT include parathyroid adenoma (85%), parathyroid hyperplasia (15%), and parathyroid cancer (1%).[3] The cure rate of PHPT after surgery is 90-95%.[4]

There are a few studies that suggest increasing systemic inflammation and inflammatory markers due to PHPT.[4-6] However, the effect of surgery on inflammation is conflicting. Some studies show that parathyroidectomy has no effect on inflammatory markers,[6,7] while others show a reversal of the inflammation.[8,9]

There are many biochemical and hematological markers to evaluate the systemic inflammatory process. In recent years, the relationship between inflammation and biomarkers reflecting inflammatory status has been investigated for many diseases. Since the physiological response of leukocytes to stress causes an increase in the neutrophil count and a decrease in the lymphocyte count, the ratio of these 2 subgroups to each other is used as an indicator of inflammation.[10] During the inflammatory response, changes occur in the rates of circulating leukocytes. The neutrophil/lymphocyte ratio (NLR) has been proposed as a simple marker of inflammatory response.[10] Platelets are another blood cell with a certain role in the coagulation and atherosclerotic processes.[11] The platelet/lymphocyte

Mehmet Furkan Çırakoğlu[1],
Ömer Bayır[2],
Volkan Yücel[3],
Muhammed Erkam Sencar[4],
İlknur Öztürk Ünsal[4],
Güleser Saylam[2],
Mehmet Hakan Korkmaz[2]

[1]Mehmet Furkan Çırakoğlu, Otorhinolaryngology Department, Ömer Halisdemir University Training and Research Hospital, Niğde, Turkey
[2]Otorhinolaryngology Department, Dışkapı Yıldırım Beyazıt Training and Research Hospital, Ankara, Turkey
[3]Otorhinolaryngology Department, Yüksek İhtisas University School of Medicine, Liv Hospital, Ankara, Turkey
[4]Department of Endocrinology and Matabolism Diseases, Dışkapı Yıldırım Beyazıt Training and Research Hospital, Ankara, Turkey

Cite this article as: Çırakoğlu MF, Bayır Ö, Yücel V, et al. Relationship between parathormone and inflammatory markers on complete blood count in parathyroid adenoma patients. *ENT Updates*. 2021; 11(2): 115-119.

Corresponding author:
Volkan Yücel
Email: *volkanvucel58@amail.com*
Received: *December 25, 2020*
Accepted: *March 18, 2021*

ratio (PLR) is another hematologic marker of systemic inflammation. PLR has been recently shown to be a better marker than NLR in indicating mortality and inflammation in end stage renal disease.[12]

The mean platelet volume (MPV) is a hematologic marker and an indicator of platelet function and activation.[13] Considering the role of platelets in many pathological conditions, it is thought that MPV can be used as a marker for inflammation.[14] There are also some studies showing a positive correlation between MPV and serum PTH levels.[3,15]

Secondary hyperparathyroidism is one of the causes of anemia in patients with chronic kidney disease.[16] In past studies, it was observed that the synthesis of endogenous erythropoietin, the formation of erythroid progenitors, and the survival of red cells were reduced by a high PTH.[17] There is also a study showing a relationship between PHPT and anemia.[18] Therefore, we wanted to investigate the relationship between serum PTH levels and hematocrit.

The aim of this study was to evaluate NLR, PLR, MPV, and other blood parameters in patients with parathyroid adenoma, to compare preoperative and postoperative values, and to investigate the effects of surgical treatment on blood parameters in patients with parathyroid adenoma.

METHODS

Patients who were operated for parathyroid adenoma in the Dışkapı Yıldırım Beyazıt Education and Research Hospital Otorhinolaryngology Clinic between November 2011 and April 2016 were included in the study. The data of the patients were retrospectively documented, and preoperative and postoperative data were compared.

For this study, the ethics committee approval was obtained from the Ethical Committee of Dışkapı Yıldırım Beyazıt Education and Research Hospital (20.07.2020 92/06) and the study was performed in accordance with the ethical standards of the 1964 Declaration of Helsinki. Informed consent was obtained from all individual participants included in the study.

All patients had high levels of calcium and PTH. The presence of parathyroid adenomas was assessed and localized by using neck ultrasonography and technetium-99m-MIBI scintigraphy. All patients underwent minimally invasive parathyroid surgery. True parathyroid adenoma excision was verified by perioperative frozen section. All patients were evaluated for serum calcium (normal range 8.5-10.5 mg/dL) and PTH (15-65 pg/dL) levels, and complete preoperative and postoperative blood counts.

As a routine for blood count analyses, samples were obtained after overnight fasting and between 8:00 AM and 9:00 AM. Preoperative data were obtained from the preoperative routine blood tests results 1 week before surgery. Postoperative blood sample controls were performed 1 month after surgery, in order to exclude the effect of surgery on inflammation. NLR and PLR were calculated as the neutrophil and platelet count divided by the lymphocyte count, both obtained from the same blood sample. All analyses were performed in the same laboratory, at the Dışkapı Yıldırım Beyazıt Education and Research Hospital.

The patients with suspected parathyroid hyperplasia or multiple endocrine neoplasia syndrome, malignancy, solid organ tumor, inflammatory disease, myeloproliferative disorders, diabetes mellitus, hypertension, infection, heart failure, hepatic or renal disorders, abnormal TSH level, recurrent or permanent hyperparathyroidism, and those who were taking anticoagulant medication, were excluded from the study.

Statistical analysis was performed using Statistical Package for the Social Sciences (SPSS) version 22.0 (IBM SPSS Corp.; Armonk, NY, USA). Numerical variables were summarized with mean ± standard deviation (SD) and median (minimum-maximum) values. Categorical variables were represented by numbers and percentages. The Kolmogorov–Smirnov test was used to determine whether the numerical variables were normally distributed, while the homogeneity of the variances was examined by Levene's test. The Wilcoxon test was used to determine whether there was a difference between preoperative and postoperative values in terms of numerical variables. The significance level was accepted as $P < .05$.

RESULTS

The study included 103 patients, of whom 22 (21.4%) were male and 81 (78.6%) were female. The patients were aged between 7 and 87, and the mean age was 54.7 ± 14.3.

All of the patients were operated for PHPT and all of the postoperative pathology results were reported as parathyroid adenoma. The preoperative and postoperative blood parameters of the patients were evaluated.

The mean preoperative PTH value was 280.1 ± 314.2 pg/dL and the mean postoperative PTH value was 44.9 ± 61.0 pg/dL. The decrease in PTH levels after surgery was significant ($P < .001$). The mean preoperative Ca value was 10.9 ± 0.8 mg/dL, while the postoperative mean value was 9.9 ± 4.5 mg/dL. The decrease in Ca level after surgery was significant ($P < .001$).

We evaluated the hematocrit, mean white blood cell (WBC) count, neutrophil count, lymphocyte count, platelet count, MPV value, NLR value, and PLR value between the preoperative and postoperative blood samples. There was no significant effect of surgery on WBC count or neutrophil count. The decrease in lymphocyte count and platelet count after surgery was statistically significant ($P = .006$ and $P = .035$). Also, the decrease in hematocrit value after surgery was statistically significant ($P < .001$). There was no statistically significant effect of surgery on NLR and PLR values (Table 1).

DISCUSSION

PHPT is a common endocrine disorder characterized by elevated serum PTH and Ca levels. The main treatment for PHPT is surgery, and it has been used successfully for many years. The cure

Table 1. Preoperative and Postoperative Laboratory Parameters of the Patients

	Preoperative Values		Postoperative Values		
	Mean ± SD	**Median [25-75 Percentiles]**	**Mean ± SD**	**Median [25-75 Percentiles]**	***P***
WBC (×10³/mm³)	7.57 ± 2.08	7.2 [5.9-9.0]	7.39 ± 1.95	7 [6.1-8.7]	.104
Neutrophil (×10³/mm³)	4.57 ± 1.62	4.4 [3.6-5.3]	4.53 ± 1.83	4.2 [3.4-5.4]	.548
Lymphocyte (×10³/mm³)	2.27 ± 0.87	2.2 [1.73-2.74]	2.07 ± 0.73	2.1 [1.67-2.48]	.006
Platelet (×10³/mm³)	255.8 ± 69.6	250 [210-293]	247.1 ± 73.6	244 [197-297]	.035
Hematocrit (%)	41.2 ± 4.6	40.8 [37.8-44.3]	38.8 ± 4.8	38.8 [35.8-42.2]	<.001
MPV (fL)	8.95 ± 1.05	8.9 [8.2-9.7]	8.82 ± 1.04	8.8 [8.0-9.5]	<.001
NLR	2.26 ± 1.17	2.05 [1.43-2.84]	2.66 ± 2.52	1.92 [1.51-2.77]	.073
PLR	126.8 ± 66.3	119.5 [93.4-146.3]	134.4 ± 73.5	117.5 [95.4-153.5]	.147
PTH (pg/dL)	280.1 ± 314.2	177.7 [121.5-276.3]	44.9 ± 61.0	18.7 [7.3-61.9]	<.001
Ca (mg/dL)	10.9 ± 0.8	10.8 [10.4-11.3]	9.9 ± 4.5	9.7 [9.1-10.3]	<.001

rate of PHPT after surgery is 90-95%.[4] In our study, 103 operations on patients with parathyroid adenoma were successful, and there was a significant decrease in PTH and Ca levels.

According to some studies, an elevated serum PTH level increases systemic inflammation and inflammatory markers.[4-6] However, the effect of surgery on inflammation is conflicting. Some studies show that parathyroidectomy has no effect on inflammatory markers,[6,7] while others show a reversal of the inflammation.[8,9]

Neutrophils, lymphocytes, and platelets are important blood elements involved in the inflammation process. The numbers and ratios of these cells to each other can be used as a marker of systemic inflammation. Neutrophils are the most common cell types among leukocytes. These cells are produced from the stem cells in the bone marrow and released into the circulation. Neutrophils are phagocytic cells that play an important role in acute infections, inflammations, and some cancers.[19,20] Neutrophils of patients with elevated PTH levels present impaired ability of migration,[21] phagocytosis,[22] bactericidal activity,[23] and chemotaxis.[24] In our study, the number of preoperative WBCs decreased from 7.57 ± 2.08 × 10^3/mm^3 to 7.39 ± 1.95 × 10^3/mm^3, and the number of neutrophils decreased from 4.57 ± 1.62 × 10^3/mm^3 to 4.53 ± 1.83 × 10^3/mm^3 postoperatively, but these decreases were not statistically significant.

Lymphocytes are the main component of the adaptive immune system. They play a role in the recognition of foreign antigens, the response to these antigens, the elimination of pathogens and pathogen-infected cells, and the development of immune memory against these pathogens. Lymphocytes inhibit the proliferation and metastatic activity of tumor cells by causing cytotoxic cell death and cytokine production. Lymphopenia has been shown to produce an immune-tolerant microenvironment around the tumor, and therefore has a poor prognostic effect.[25] A study conducted by Ownby et al.[26] showed that the increased number of peripheral lymphocytes has a positive effect on the prognosis of breast cancer and patient survival. Lewin et al.[27] demonstrated the PTH-dependent proliferation of T-cells in uremic rats.Also, Klinger et al.[28] showed that PTH increases the number of T-cells in a dose-dependent manner. Shasha et al.[29] examined T-cell function in PHPT both before and 1 month after parathyroidectomy. Before the surgery, the total T-cell count was low, with a decreased ability to become activated. All of these abnormalities were restored following parathyroidectomy. Alexiewicz et al.[30] found that PTH caused dose-dependent inhibition of B-cell proliferation. In our study, the preoperative mean value of lymphocytes was 2.27 ± 0.87 × 10^3/mm^3 and the mean postoperative value was 2.07 ± 0.73 × 10^3/mm^3. The decrease in lymphocyte count was statistically significant after surgery. This is because, as Klinger et al.[28] have demonstrated, there is a relationship between increased PTH and increased lymphocyte count and the proinflammatory process, and our study confirms this.

In past studies, NLR has been suggested as an excellent biomarker for different inflammatory conditions.[31] NLR is also a marker of inflammatory status for neoplastic diseases. NLR increases due to the increase in the number of neutrophils or the decrease in the number of lymphocytes, and this balance shifts in favor of the pro-tumoral inflammatory state, while the increase in the number of lymphocytes or decrease in neutrophils turns this balance in favor of the anti-tumoral immune state.[32] Therefore, the increase in NLR is a sign of poor prognosis, whereas the decrease in NLR is a sign of good prognosis. Liu et al.[33] reported that increased NLR values correlate with tumor size in differentiated thyroid cancers, and in addition, higher NLR values carry a higher risk for recurrence. In a study by Zeren et al.,[34] the size of the parathyroid adenoma was also correlated with NLR rates. In our study, the mean NLR was 2.26 ± 1.17 preoperatively and 2.66 ± 2.52 postoperatively, and the difference was not statistically significant (0.073). This result can be explained by the effect of surgery on both neutrophil and lymphocyte counts. Moreover, PLR is an inexpensive and cost-effective inflammatory marker indicating chronic inflammation, like NLR. It has been emphasized that PLR is more valuable than NLR as an inflammation marker in patients with ESRD.[12] In various chronic diseases, PLR has been used as an inflammatory marker and has been shown to be effective in monitoring prognosis.[35] In a recent study, it has been shown that parathyroidectomy reduced the PLR values in patients with secondary hyperparathyroidism.[8] In our study, the mean PLR was calculated as 126.8 ± 66.3 preoperatively and 134.4 ± 73.5 postoperatively, and this decrease was not statistically significant. It can be shown that the reason for this was that surgery caused a significant change in both platelet and lymphocyte values.

Platelets are discoid, anucleate cellular fragments originating from the cytoplasm of megakaryocytes, and they are the main cells of primary hemostasis. Platelet activation and aggregation increase with inflammation. The simplest parameters measurable for platelet activation are platelet count and MPV. MPV is the platelet activity marker that is most commonly used to evaluate inflammatory processes and malignancies. It is known that platelet count and MPV increase in many diseases with inflammation and hypoxia in their pathophysiology.[13,14] In many studies, it has been shown that MPV values were correlated with PTH levels.[3,15] The data in our study also support these studies. The preoperative mean MPV value was 8.95 ± 1.05 fL, while the postoperative mean MPV value decreased to 8.82 ± 1.04 fL, and this change was statistically significant. This can be explained by the decrease in both platelet and lymphocyte values due to the suppression of inflammation caused by the decreased PTH values after surgery.

Another interesting finding in the present study was a positive correlation between hematocrit and PTH levels. In past studies, it has been shown that hyperparathyroidism can cause bone marrow fibrosis and anemia.[17,18] Moreover, Adhikary et al. showed reverse correlation between the level of serum parathyroid hormone and the hematocrit level.[16] Contrary to this study, in our study, the mean hematocrit value was calculated as 41.2 ± 4.6% preoperatively and 38.8 ± 4.8% postoperatively, and this decrease was statistically significant.

The study was limited by the relatively small number of patients, and more accurate results can be achieved in a wider patient population. In addition, this is a retrospective study and the data were collected from the past control results of the patients. This is the reason why we calculated NLR and PLR using neutrophil and lymphocyte counts obtained from a single hemogram. Despite these limitations, this study gives us valuable information about the hematologic markers of the PHPT patients.

CONCLUSION

The hemogram is an international standard blood test for many diseases that does not require additional equipment, and is easy to reach and perform. By using many biomarkers such as neutrophils, lymphocytes, platelets, NLR, PLR, and MPV, which can be detected by a hemogram, the inflammatory process can be followed cost-effectively. Although there are changes in post-surgical blood parameters in PHPT, we think that the benefit of these parameters in daily use will be limited, since the change of PTH levels is effective on multiple parameters.

Ethics Committee Approval: The ethics committee approval received from the Ethical Committee of Dışkapı Yıldırım Beyazıt Training and Research Hospital, Ankara, Turkey (July 20, 2020 and 92/06).

Informed Consent: Informed consent was obtained from all participants who participated in this study.

Peer Review: Externally peer-reviewed.

Author Contributions: Concept- M.F.Ç.; Design - Ö.B.; Supervision - M.H.K., G.S., Ö.B.; Funding - Materials - M.F.Ç., V.Y.; Data Collection and/or Processing -M.F.Ç., M.E.S., İ.Ö.Ü.; Analysis and/or Interpretation - M.F.Ç.; Literature Review - M.F.Ç., V.Y.; Writing - V.Y.; Critical Review - M.H.K., G.S.

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

Financial Disclosure: The authors declared that this study has received no financial support.

REFERENCES

1. Han CH, Fry CH, Sharma P, Han TS. A clinical perspective of parathyroid hormone related hypercalcaemia. *Rev Endocr Metab Disord*. 2020;21(1):77-88. [CrossRef]
2. Silverberg SJ, Bilezikian JP. The diagnosis and management of asymptomatic primary hyperparathyroidism. *Nat Clin Pract Endocrinol Metab*. 2006;2(9):494-503. [CrossRef]
3. Arpaci D, Kuzu F, Emre AU, et al. Elevated mean platelet volume in patients with primary hyperparathyroidism. *Int J Clin Exp Med*. 2016;9:6330-6335.
4. Christensen MHE, Fenne IS, Nordbø Y, et al. Novel inflammatory biomarkers in primary hyperparathyroidism. *Eur J Endocrinol*. 2015;173(1):9-17. [CrossRef]
5. Chertok-Shacham E, Ishay A, Lavi I, Luboshitzky R. Biomarkers of hypercoagulability and inflammation in primary hyperparathyroidism. *Med Sci Monit*. 2008;14(12):CR628-CR632.
6. Almqvist EG, Bondeson AG, Bondeson L, Svensson J. Increased markers of inflammation and endothelial dysfunction in patients with mild primary hyperparathyroidism. *Scand J Clin Lab Investig Suppl*. 2011;71(2):139-144. [CrossRef]
7. Bollerslev J, Rosen T, Mollerup CL, et al. Effect of surgery on cardiovascular risk factors in mild primary hyperparathyroidism. *J Clin Endocrinol Metab*. 2009;94(7):2255-2261. [CrossRef]
8. Yang PS, Liu CL, Liu TP, et al. Parathyroidectomy decreases neutrophil-to-lymphocyte and platelet-to-lymphocyte ratios. *J Surg Res*. 2018;224:169-175. [CrossRef]
9. Christensen MHE, Pedersen EKR, Nordbø Y, et al. Vitamin B6 status and interferon-γ-mediated immune activation in primary hyperparathyroidism. *J Intern Med*. 2012;272(6):583-591. [CrossRef]
10. Zahorec R. Ratio of neutrophil to lymphocyte counts-rapid and simple parameter of systemic inflammation and stress in critically ill. *Bratisl Lek Listy*. 2001;102(1):5-14.
11. Butterworth RJ, Bath PMW. The relationship between mean platelet volume, stroke subtype and clinical outcome. *Platelets*. 1998;9(6):359-364. [CrossRef]
12. Yaprak M, Turan MN, Dayanan R, et al. Platelet-to-lymphocyte ratio predicts mortality better than neutrophil-to-lymphocyte ratio in hemodialysis patients. *Int Urol Nephrol*. 2016;48(8):1343-1348. [CrossRef]
13. Bath PMW, Butterworth RJ. Platelet size: measurement, physiology and vascular disease. *Blood Coagul Fibrinolysis*. 1996;7(2):157-161. [CrossRef]
14. Korniluk A, Koper-Lenkiewicz OM, Kamińska J, Kemona H, Dymicka-Piekarska V. Mean platelet volume (MPV): new perspectives for an old marker in the course and prognosis of inflammatory conditions. *Mediators Inflamm*. 2019;2019:9213074. [CrossRef]
15. Irkorucu O. Mean platelet volume and solitary parathyroid adenoma. *Int J Clin Exp Med*. 2016;9:14536-14541.
16. Adhikary LP, Pokhrel A, Yadava SK, Khadka D, Thakur R. Relation between serum intact parathyroid hormone level and hematocrit in chronic kidney disease patients. *Kathmandu Univ Med J (KUMJ)*. 2015;13(51):220-223. [CrossRef]
17. Meytes D, Bogin E, Ma A, Dukes PP, Massry SG. Effect of parathyroid hormone on erythropoiesis. *J Clin Invest*. 1981;67(5):1263-1269. [CrossRef]
18. Bhadada SK, Bhansali A, Ahluwalia J, et al. Anaemia and marrow fibrosis in patients with primary hyperparathyroidism before and after curative parathyroidectomy. *Clin Endocrinol (Oxf)*. 2009;70(4):527-532. [CrossRef]
19. Waugh DJJ, Wilson C. The interleukin-8 pathway in cancer. *Clin Cancer Res*. 2008;14(21):6735-6741. [CrossRef]

20. De Larco JE, Wuertz BRK, Furcht LT. The potential role of neutrophils in promoting the metastatic phenotype of tumors releasing interleukin-8. *Clin Cancer Res*. 2004;10(15):4895-4900. [CrossRef]
21. Doherty CC, Labelle P, Collins JF, Brautbar N, Massry SG. Effect of parathyroid hormone on random migration of human polymorphonuclear leukocytes. *Am J Nephrol*. 1988;8(3):212-219. [CrossRef]
22. Alexiewicz JM, Smogorzewski M, Fadda GZ, Massry SG. Impaired phagocytosis in dialysis patients: studies on mechanisms. *Am J Nephrol*. 1991;11(2):102-111. [CrossRef]
23. Salant DJ, Glover AM, Anderson R, et al. Polymorphonuclear leucocyte function in chronic renal failure and after renal transplantation. *Proc Eur Dial Transplant Assoc*. 1976;12:370-379.
24. Khan F, Khan AJ, Papagaroufalis C, et al. Reversible defect of neutrophil chemotaxis and random migration in primary hyperparathyroidism. *J Clin Endocrinol Metab*. 1979;48(4):582-584. [CrossRef]
25. Ray-Coquard I, Cropet C, Van Glabbeke M, et al. Lymphopenia as a prognostic factor for overall survival in advanced carcinomas, sarcomas, and lymphomas. *Cancer Res*. 2009;69(13):5383-5391. [CrossRef]
26. Ownby HE, Roi LD, Isenberg RR, Brennan MJ. Peripheral lymphocyte and eosinophil counts as indicators of prognosis in primary breast cancer. *Cancer*. 1983;52(1):126-130. [CrossRef]
27. Lewin E, Ladefoged J, Brandi L, Olgaard K. Parathyroid hormone dependent T cell proliferation in uremic rats. *Kidney Int*. 1993;44(2):379-384. [CrossRef]
28. Klinger M, Alexiewicz JM, Linker-Israeli M, et al. Effect of parathyroid hormone on human T cell activation. *Kidney Int*. 1990;37(6):1543-1551. [CrossRef]
29. Shasha SM, Kristal B, Steinberg O, Shkolnik T. Effect of parathyroidectomy on T cell functions in patients with primary hyperparathyroidism. *Am J Nephrol*. 1989;9(1):25-29. [CrossRef]
30. Alexiewicz JM, Klinger M, Pitts TO, et al. Parathyroid hormone inhibits B cell proliferation: implications in chronic renal failure. *J Am Soc Nephrol*. 1990;1(3):236-244. [CrossRef]
31. Imtiaz F, Shafique K, Mirza SS, et al. Neutrophil lymphocyte ratio as a measure of systemic inflammation in prevalent chronic diseases in Asian population. *Int Arch Med*. 2012;5(1):2. [CrossRef]
32. Mallappa S, Sinha A, Gupta S, Chadwick SJD. Preoperative neutrophil to lymphocyte ratio >5 is a prognostic factor for recurrent colorectal cancer. *Colorectal Dis*. 2013;15(3):323-328. [CrossRef]
33. Liu CL, Lee JJ, Liu TP, et al. Blood neutrophil-to-lymphocyte ratio correlates with tumor size in patients with differentiated thyroid cancer. *J Surg Oncol*. 2013;107(5):493-497. [CrossRef]
34. Zeren S, Yaylak F, Ozbay I, Bayhan Z. Relationship between the neutrophil to lymphocyte ratio and parathyroid adenoma size in patients with primary hyperparathyroidism. *Int Surg*. 2015;100(7-8):1185-1189. [CrossRef]
35. Kucuk H, Tecer D, Goker B, et al. Platelet/lymphocyte ratio and mean platelet volume in patients with granulomatosis with polyangiitis. *Adv Rheumatol*. 2019;60(1):4. [CrossRef]