The Role of Neutrophil/Lymphocyte Ratio in Ovarian Torsions

Musa BÜYÜK [1], Nagihan KARACAR BÜYÜK [1], Kamuran SUMAN [1], Ebru GÖK [2],
Murat SUMAN [3], Havva KUŞCU [4]

ABSTRACT

Aim: Ovarian torsion is among the gynecological emergencies. Laboratory and imaging methods are used for diagnosis. Symptoms are generally nonspecific, making it difficult to differentiate from other acute abdominal emergencies. This study aims to investigate the diagnostic value of neutrophil-lymphocyte ratio (NLR) in addition to imaging methods for the diagnosis of ovarian torsion.

Material and Methods: A total of 120 patients were included in the study. The study was planned retrospectively. The patients included in the study were analyzed in three different groups. Those with follicular cysts were in Group 1, those with simple cysts were in Group 2, and those with ovarian torsion were in Group 3. The groups were compared in terms of laboratory parameters and demographic characteristics.

Results: When the groups were compared in terms of mean age, it was found that the mean age of Group 3 was significantly lower than Group 1 ($p<0.05$). When the WBC and NLR levels between the groups were compared, it was observed that the WBC and NLR levels of Group 3 were significantly higher than those of Group 1 and Group 2 ($p<0.05$). The sensitivity of NLR was found to be 91.00% and the specificity was 86,00%. The sensitivity of WBC was 86.00% and the specificity was 78.40%.

Conclusion: We believe that NLR can be used as an easy and cost-effective diagnostic method in emergencies. We also believe that it could be a valuable parameter in addition to imaging in diagnosing ovarian torsion.

Keywords: Neutrophil-lymphocyte ratio; ovarian torsion; ultrasonography.

Nötrofil/Lenfosit Oranının Over Torsiyonlarındaki Yeri

ÖZ

Amaç: Over torsiyonu, jinekolojik bir aciller arasında yer alır. Tanıda laboratuar ve görüntüleme yöntemlerine başvurulur. Semptomları genelde nonspesifikdir. Bu yüzden akut batın yapan diğer acillerden ayırıcı tanısı oldukça zordur. Çalışmamız, over torsiyonunun tanısında görüntüleme yöntemine artı olarak nötrofil-lenfosit oranının (NLR) tanısal değerini araştırmayı amaçlamaktadır.

Gereç ve Yöntemler: Çalışmaya 120 hasta dahil edildi. Çalışma retrospektif olarak planlandı. Çalışmaya dahil edilen hastalar folikül kisti olan, basit kisti olan ve over torsiyonu olan hastalar olarak 3 farklı grup halinde incelendi. Folikül kisti olanlar Grup1, basit kisti olanlar Grup 2 ve over torsiyonu olan hastalar Grup 3 olarak belirlendi. Gruplar laboratuvar parametreleri ve demografik özellikleri açısından karşılaştırıldı.

Bulgular: Gruplar yaş ortalaması açısından karşılaştırıldığında Grup 3'ün ortalamasının Grup 1'e göre anlamlı olarak daha düşük olduğu görülmüştür ($p<0,05$). Gruplar arası NLR ve WBC oranlarına bakıldığında Grup 3 WBC ve NLR düzeyleri Grup 1 ve Grup 2 ye göre daha yüksek olduğu izlenmiştir ($p<0,05$). NLR'nin sensitivitesi %91,00, spesifisitesi %86,00 olarak bulunmuştur. WBC nin ise sensitivitesi %86,00 ve spesifisitesi %78,40 olarak tespit edilmiştir.

Sonuç: NLR'nin, acil durumlarda kolay ve ekonomik bir tanı yöntemi olarak kullanılabilir olduğunu düşünmekteyiz. Jinekolojik bir acil olan over torsiyonu tanısını koymada görüntülemeye ek olarak bakılabilecek bir değer olacağı kanısındayız.

Anahtar Kelimeler: Nötrofil-lenfosit oranı; over torsiyonu; ultrason.

1 Afyonkarahisar State Hospital, Afyon, Türkiye
2 Erciyes University, Faculty of Medicine, Kayseri, Türkiye
3 Afyon Cay State Hospital, Afyon, Turkey
4 Süleyman Demirel University, Isparta, Turkiye

INTRODUCTION

Ovarian torsion is a gynecological emergency that occurs when the ovarian pedicle twists around itself, either incompletely or completely, leading to impaired circulation. This results in vascular pathologies such as ovarian enlargement, interstitial hemorrhage, edema, and decreased venous return(1). Subsequently, arterial flow disturbances occur and partial rupture, ischemia, and necrosis may be observed in the ovary. However, these clinical symptoms are non-specific, which can lead to delays in diagnosis and treatment (1).

Several methods are used to diagnose of ovarian torsion, including inflammatory markers, grayscale ultrasonography, Doppler ultrasonography, and tomography (2). However, making an accurate diagnosis is often difficult because non-specific symptoms can be present. Therefore, many markers such as ischemia-modified albumin, interleukin-6, and TNF-alpha have been used for diagnostic purposes (3). An increase in white blood cell (WBC) count is the first and most commonly used marker to show inflammation in clinical practice (4). Studies have also shown an increase in WBC count in cases of ovarian torsion. In addition, many inflammation-based scoring systems such as thrombocyte-lymphocyte ratio, prognostic nutrition index, and neutrophil-lymphocyte ratio (NLR) have been used to predict the prognosis of inflammatory diseases (5). NLR is a non-invasive method that can be easily detected in peripheral blood without requiring additional costs (6). This study aims to determine the diagnostic accuracy of NLR in cases of suspected ovarian torsion in emergency gynecological patients.

MATERIAL AND METHODS

This study was conducted at a state hospital's Women's and Obstetrics Clinic after obtaining approval from the local ethics committee (2030-EK-2). The study included patients who had been treated and followed up for ovarian cysts between February 2016 and December 2021. The data was obtained from patient files and computer records. We excluded patients with hyperthyroidism, tubal ovarian abscess, malignancy and patients who had incomplete laboratory data, especially blood count values (1). Group 1 included patients with simple follicular cysts smaller than 4 cm, while Group 2 included patients with simple cysts larger than 4 cm (7). Group 3 included patients who underwent surgical treatment due to torsion. Patient recruitment was stopped after reaching a sufficient number of 40 patients in each group. The sample size was determined using the minitab 16 statistical program. A minimum of 39 subjects in each group must be included in the study in order to show that the standard deviation of the difference between the measurements in terms of the variable examined with 95.00% confidence interval, 5.00% type 1 error and 90.00% power is 1.90 and the difference between the means is 1.56 units as meaningful. One-way ANOVA was used for power analysis. The patients' demographic data and complete blood count results, including age, white blood cell count, hemoglobin level, red cell distribution width, mean platelet volume, and neutrophil/lymphocyte ratio, were recorded and compared between the groups.

Statistical Analysis

The data analysis was conducted using the IBM SPSS v.19.0 (Statistical Package for Social Science) software package. The normal distribution of numerical data obtained by measurement was evaluated using the Shapiro-Wilk test. Descriptive analyses were presented as mean ± standard deviation for continuous variables. Differences between patient groups for continuous variables were assessed using One-Way ANOVA or Kruskal Wallis variance analysis. Levene test was used to assess the homogenity of the variances. An overall p-value of less than 0,05 was considered to show a statistically significant result. When an overall significance was observed, pairwise post-hoc tests were performed using Tukey's test. Mann-Whitney U test was performed to test the significance of pairwise differences using Bonferroni correction to adjust for multiple comparisons. An overall 5.00% type-I error level was used to infer statistical significance. Receiver Operating Characteristics (ROC) analysis was performed to determine the accuracy rates of the diagnostic parameters. When a significant cut-off values vas observed, the sensitivity, specificity, positive predictive value (PPV), and negative predictive values (NPV) are presented. While evaluating the area under the curve, a 5.00% type-I error level was used to accept a statistically significant predictive value of the test variables.

RESULTS

The distribution of demographic and laboratory data for the groups is summarized in Table 1. According to the data, the mean age and Hb values of Group 3 were significantly lower than those of Group 1 (p=0.010 for age and p=0.018 for Hb). There was no significant difference between the groups in terms of RDW and MPV values (p=0.740 for RDW and p=0.125 for MPV). While WBC and NLR ratios were significantly higher in Group 3 than in the other groups (p=0.012), there was no significant difference between Group 1 and Group 2 (p=0.364 for WBC and p=0.595 for NLR).

According to the results of the overall accuracy rates for NLR and WBC values, a cut-off value of 2.65 was obtained for NLR, and the sensitivity, specificity, PPD, and NPD were found to be 91.00%, 86.00%, 79.20%, and 95.10%, respectively. The cut-off value for WBC was found to be 8.62, and the corresponding accuracy rates were 86.00%, 78.40%, 64.90%, and 92.30%, respectively. (Table 2, Figure 1,2)
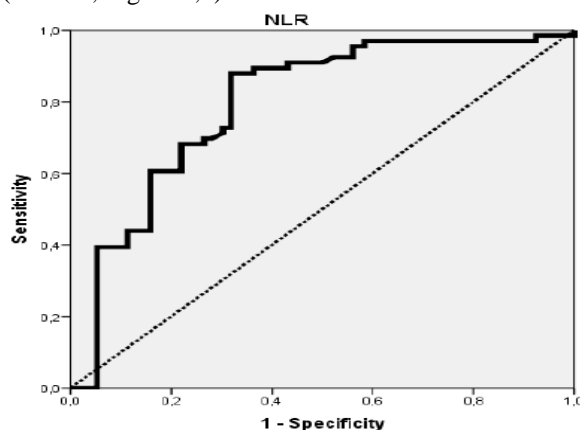

Figure 1. Roc curve analysis for nlr

Table 1. Distribution of data according to groups

	Grup 1 (n=40 patients) Mean ± SD	Grup 2 (n=40 patients) Mean ± SD	Grup 3 (n=40 patients) Mean ± SD	P_1	P_2	P_3
Age (years)	35.20 ± 1.12	28.95 ± 1.27	27.64 ± 1.22	0.010	0.870	0.625
WBC (x109/L)	8.30 ± 1.90	7.47 ± 1.68	10.96 ± 2.43	0.563	0.012	0.890
Hg (g/dL)	12.92 ± 1.15	11.66 ± 2.41	12.38 ± 1.22	0.018	0.668	0.560
RDW (%)	14.81 ± 1.40	15.12 ± 1.36	14.67 ± 2.14	0.642	0.705	0.740
MPV (fL)	7.68 ± 1.45	7.84 ± 1.60	8.33 ± 1.25	0.658	0.801	0.125
NLR	2.21 ± 0.56	2.65 ± 0.88	7.32 ± 1.41	0.805	0.012	0.710

P_1 Comparing the Group 3 with the Group 1, P_2 Comparing the Group 3 with the other Groups, P_3 Between all groups

Table 2. Diagnostic accuracy rates of WBC and NLR

	Sensitivity	Specificity	Cut-off value	AUC	PPD	NPD
WBC	%86.00	%78.40	8.62	%86.00	%64.90	%92.30
NLR	%91.00	%86.00	2.65	%92.50	%79.20	%95.10

(AUC: Area under the curve, PPD: Positive predictive value, NPD: Negative Predictive Value)
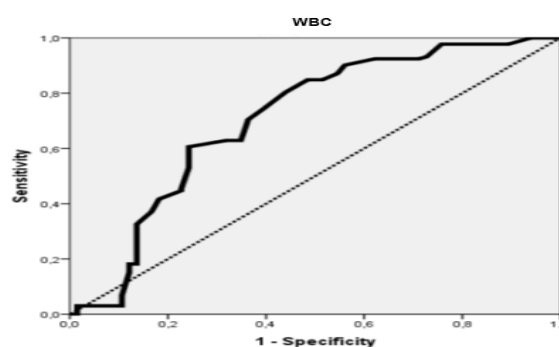
Figure 2. Roc curve analysis for wbc

DISCUSSION

In this study, NLR was determined to be a useful indicator for the diagnosis of ovarian torsion and suitable for clinical application. Ovarian torsion can lead to serious consequences if correct diagnosis and treatment are not performed (8). The utero-ovarian ligament, broad ligament, and infundibulopelvic ligament are among the supporting ligaments of the ovary. If the infundibulopelvic ligament rotates around itself, blood flow to the ovary can be blocked (9). In this case, edema may develop in the ovary and decreased arterial flow can be further reduced. Reduced arterial flow can cause ischemia and ultimately lead to necrosis, infarction, and local hemorrhage in the ovarian tissue. In this condition, the ovary loses its function (10).

Ovarian torsion can occur in different periods of women's lives, including prepubertal, pubertal, reproductive, perimenopausal, and menopausal periods (11). Some studies have indicated that ovarian torsion is less common in the premenarchal age group and postmenopausal group (17.20%) (12). For instance, in a study including 53 torsion patients, the most common age range for torsion was found to be 20-29 years (13). This finding also indicates that the mean age of the torsion group (Group 3) was lower than the other groups in our study, with an average age of 27.65. Clinical symptoms of ovarian torsion may vary depending on the severity of torsion. Abdominal pain, nausea-vomiting, and fever are resistant symptoms that do not respond to medical treatment. In complete torsions, peritonitis and acute abdominal symptoms may also occur due to delayed diagnosis. Since ovarian torsion shows a non-specific clinical course similar to other acute abdominal pathologies, diagnosis is not always easy (14). Delayed diagnosis can lead to ovarian loss, decreased

fertility, and serious complications, so early diagnosis is crucial.

Clinical, laboratory, and imaging methods are used in the diagnosis of ovarian torsion. As ovarian torsion is a pathology that causes acute abdomen, clinical symptoms such as abdominal pain, nausea/vomiting, and fever have limited diagnostic value. However, as ovarian torsion is an acute inflammatory condition, markers such as WBC, C-reactive protein (CRP), and D-dimer may increase in response to inflammation (15). An experimental study found that D-dimer levels were elevated in cases of ovarian torsion (16). CRP, an acute-phase reactant that rises in inflammatory events, has been emphasized to have diagnostic value in acute abdominal pain by Chi and colleagues (17). Mazouni et al. found that an increase in white blood cell (WBC) count was observed in 36.50%-64.00% of patients diagnosed with adnexal torsion (18). Another study reported an increase in WBC levels in patients with ovarian torsion (19). In our study, we found that WBC values were significantly higher in the ovarian torsion group than in other groups. The neutrophil-to-lymphocyte ratio (NLR) is used as a biomarker in many diseases, such as cardiovascular diseases, cancer, diabetes, hypertension, and autoimmune diseases (20). It is also commonly used in the diagnosis of gynecological and obstetric diseases. For example, it can be used in the diagnosis of diseases such as pelvic inflammatory disease, endometriosis, preterm labor, preeclampsia, gestational trophoblastic disease, endometrial hyperplasia, endometrial cancer and gestational diabetes (21).

Researchers have reported that NLR can be used in distinguishing between preoperative ovarian cysts and torsion, but it has no diagnostic value in differentiating

between ovarian cyst rupture and torsion (22). In a different study, it was found that the NLR ratio was high in patients with ovarian torsion (23). In another study, NLR was reported to be significantly high in patients with intestinal ischemia (24). In our study, we also found that NLR values were significantly higher in the group with ovarian torsion compared to other groups. These results are noteworthy as they are consistent with the literature.

Various studies have shown an increase in MPV and RDW levels in inflammatory conditions such as acute appendicitis. However, some studies have reported no relationship between MPV and adnexal torsion (25). In our study, we could not find a significant difference in RDW and MPV levels between the groups.

Ultrasonography is a commonly used method for the diagnosis of ovarian torsion. Ultrasonography findings include abnormal position of the ovary, enlargement of the ovary, presence of a cyst, and accumulation of fluid in the cul-de-sac. Doppler ultrasonography is used to determine the presence or absence of blood flow, and the absence of both venous and arterial blood flow primarily indicates torsion. However, ultrasonography still has some limitations in diagnosis. For example, in 60.00% of cases with ovarian torsion, blood flow can be detected both venously and arterially (26). Ultrasonography was a diagnostic method we used to determine the groups and assist in making surgical decisions in our study.

CONCLUSION

In conclusion, NLR appears to be a useful parameter in the diagnosis of ovarian torsion. It provides an easy and inexpensive diagnostic option, especially in emergencies situations, and prevents potentially fatal outcomes such as delayed diagnosis leading to ovarian loss and severe peritonitis. Therefore, the use of NLR in the diagnosis of ovarian torsion is recommended. We believe that our study will contribute to larger and more comprehensive studies in the future.

Authors's Contributions: Idea/Concept: M.B., K.S., H.K.; Design: N.K.B., E.G.; Data Collection and/or Processing: M.B., K.S, M.S.; Analysis and/or Interpretation: M.S., E.G., N.K.B.; Literature Review: M.B., K.S., H.K.; Writing the Article: M.B., K.S.; Critical Review: M.S.

REFERENCES

1. Öksüzoğlu A. The role of neutrophil/lymphocyte ratio and mean platelet volume in diagnosis of ovarian torsion. Jinekoloji-Obstetrik ve Neonatoloji Tıp Derg. 2021; 18(3): 867-72.

2. Khanzadeh S, Tahernia H, Hernandez J, Sarcone C, Lucke-Wold B, Salimi A, et al. Predictive Role of Neutrophil to Lymphocyte Ratio in Adnexal Torsion: A Systematic Review and Meta-Analysis. Mediators of Inflammation. 2022; 2022. https://doi.org/10.1155/2022/9680591

3. Ghimire A, Ghimire S, Shrestha A, Pant SR, Subedi N, Pant PR. Preoperative neutrophil lymphocyte ratio in prediction of adnexal mass torsion. Obstetrics and Gynecology International. 2023; 2023. https://doi.org/10.1155/2023/3585189

4. Nissen M, Sander V, Rogge P, Alrefai M, Tröbs R-B. Neutrophil to lymphocyte ratio and platelet to lymphocyte ratio might predict pediatric ovarian torsion: a single-institution experience and review of the literature. Journal of Pediatric and Adolescent Gynecology. 2021; 34(3): 334-40.

5. Lee J, Park J, Lee HJ, Kim MJ, Lee YH, Chong GO, et al. Original articles preoperative hematological parameters for predicting ovarian torsion in patients with mature cystic teratoma. International Journal of Women's Health. 2021; 13; 317-26.

6. Nori W, Ali AI, Hamed RM. The utility of platelets indices and other blood parameters in gynecological diseases. Al-Anbar Medical Journal. 2021; 17(1). http://doi.org/10.33091/AMJ.1201712021

7. Kavak SB, Kavak E, Kurkut B, İlhan R, Başpınar M. The importance of clinical, radiologic and laboratory parameters in the diagnosis of ovarian torsion: retrospective study.. İstanbul Kanuni Sultan Süleyman Tıp Derg. 2014; 6(1): 20-2.

8. Kaplanoglu D, Bulbul M, Odemis G, Kaplanoglu M. Can various complete blood count parameters helpful in preoperative diagnosis of adnexal torsion? Revista da Associação Médica Brasileira. 2021; 67: 873-7.

9. Guile SL, Mathai JK. Ovarian Torsion. In: StatPearls. StatPearls Publishing, Treasure Island (FL); 2023. PMID: 32809510.

10. Chen H, Wang F, Hu X, Dai X, Wang Y. Preoperative clinical characteristics for differentiating malignant transformation from torsion of mature cystic teratoma. Journal of Obstetrics and Gynaecology. 2023; 43(1): 2151357.

11. Mazza MG, Lucchi S, Rossetti A, Clerici M. Neutrophil-lymphocyte ratio, monocyte-lymphocyte ratio and platelet-lymphocyte ratio in non-affective psychosis: a meta-analysis and systematic review. The World Journal of Biological Psychiatry. 2020; 21(5): 326-38.

12. Coşkun B, Timur B, Coşkun B, KINCI F, Şimşir C. Clinical and pathologic evaluation of adnexal torsion patients in adolescence, reproductive and postmenopausal periods. Middle Black Sea Journal of Health Science. 2019; 5(2): 85-92.

13. Sahlu Z, Negash S, Yusuf L. Adnexal torsion a five-years retrospective review in two hospitals. Ethiop Med J. 2014; 52(4): 155-64.

14. Güngör ND, Yurci A, Güçlü M. Retrospective analysis of ovarian torsion incidence in 5186 women undergoing controlled ovarian hyperstimulation. Journal of Health Sciences and Medicine. 2021; 4(5): 630-3.

15. Tobiume T, Shiota M, Umemoto M, Kotani Y, Hoshiai H. Predictive factors for ovarian necrosis in torsion of ovarian tumor. The Tohoku journal of experimental medicine. 2011; 225(3): 211-4.

16. Jammal MP, Martins Filho A, Bandeira GH, Murta BMT, Murta EFC, Nomelini RS. Laboratory predictors of survival in ovarian cancer. Revista da Associação Médica Brasileira. 2020; 66: 61-6.

17. Chi C-H, Shiesh S-C, Chen K-W, Wu M-H, Lin X-Z. C-reactive protein for the evaluation of acute abdominal pain. The American journal of emergency medicine. 1996; 14(3): 254-6.

18. Mazouni C, Bretelle F, Menard J, Blanc B, Gamerre M. Diagnosis of adnexal torsion and predictive

factors of adnexal necrosis. Gynecologie, obstetrique & fertilite. 2005; 33(3): 102-6.

19. Sivapragasam V, Gopinath KR, Manjappa AA, Menon M. Adnexal Torsion in adolescents: a case series. Journal of South Asian Federation of Obstetrics and Gynaecology. 2023; 14(6): 639-43.

20. Adu-Bredu TK, Arkorful J, Appiah-Denkyira K, Wiafe YA. Diagnostic value of the sonographic whirlpool sign in the diagnosis of ovarian torsion: A systematic review and meta-analysis. Journal of Clinical Ultrasound. 2021; 49(7): 746-53.

21. Bridwell RE, Koyfman A, Long B. High risk and low prevalence diseases: Ovarian torsion. The American Journal of Emergency Medicine. 2022; 56: 145-50.

22. Mandelbaum R, Smith M, Violette C, Matsuzaki S, Matsushima K, Klar M, et al. Conservative surgery for ovarian torsion in young women: perioperative complications and national trends. BJOG: An International Journal of Obstetrics & Gynaecology. 2020; 127(8): 957-65.

23. Otjen JP, Stanescu AL, Alessio AM, Parisi MT. Ovarian torsion: developing a machine-learned algorithm for diagnosis. Pediatric Radiology. 2020; 50: 706-14.

24. Yatsenko O, Vlachou PA, Glanc P. Predictive value of single or combined ultrasound signs in the diagnosis of ovarian torsion. Journal of Ultrasound in Medicine. 2021; 40(6): 1163-72.

25. Hartman SJ, Prieto JM, Naheedy JH, Ignacio RC, Bickler SW, Kling KM, et al. Ovarian volume ratio is a reliable predictor of ovarian torsion in girls without an adnexal mass. Journal of pediatric surgery. 2021; 56(1): 180-2.

26. Barghi B, Shokoohi M, Khaki AA, Khaki A, Moghimian M, Soltani M. Eugenol improves tissue damage and oxidative stress in adult female rats after ovarian torsion/detorsion. Journal of Obstetrics and Gynaecology. 2021; 41(6): 933-8.