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Full Length Research Paper

The Diagnostic Value of Hematological Indices in Ischemic Adnexal Torsion

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Abstract

Objective: To investigate the role of hematological indices, neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR), in the preoperative diagnosis of adnexal torsion (AT) and to examine the correlation between NLR and PLR levels to AT ischemic severity. Methods: A retrospective controlled study, assembled from 102 patients with surgically proven AT. Patients were divided into two groups based on the severity of the torsion, mild-moderate AT (MAT) and severe AT (SAT), using the Parelkar classification (gross appearance of the adnexa during surgery) and number of adnexal twists (>=3). Univariate analysis was performed, and the NLR and PLR levels were compared between the groups. A p-value of 0.05 was considered significant. Results: 35/102 patients had SAT (study group), and 67/102 had MAT (control group). Mean NLR of the study population was 5.05±3.37, not significantly higher in the study group 5.23±3.26, compared with the control group 4.95±3.44 (p =.69). PLR also was not significantly higher in the study group than in the control group (175±87.23 vs.161±78.39, p=.41). Conclusion: Although the difference in hematological biomarkers did not reach statistical significance, further study is warranted to determine the potential role of NLR and PLR in the presurgical diagnosis of AT.

Keywords: Adnexal torsion; Ovarian Torsion; Hematologic Inflammatory Markers; neutrophil-to-lymphocyte ratio (NLR); platelet-to-lymphocyte ratio (PLR); Ischemic Adnexa.

Synopsis: Higher values of serum inflammatory markers such as NLR and PLR might have a role in the presurgical diagnosis of Adnexal Torsion and its severity.

INTRODUCTION

Adnexal torsion (AT) is a gynecological surgical emergency that accounts for 2%-7% of surgical emergencies in women (Hibbard, 1985).While AT can occur at any age, it primarily affects women of reproductive age. ATis characterized by a partial or complete twist of the adnexa, ovary, or, more rarely, the tube alone, around a centerline consisting of the infundibulo-pelvic ligament and tubo-ovarian ligament (Graif et al., 1984). The adnexa can be twisted more than one rotation, and rarely, even three or more rotations that affect the severity of the adnexal condition. Delays in treatment have the potential to impede venous or lymphatic drainage resulting in congestion of the ovarian parenchyma and reduction or cessation of arterial perfusion,

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which may lead to ischemia, infarction, hemorrhagic necrosis, and gangrene (Oelsner et al., 2003).

The clinical presentation of AT may be varied and nonspecific. Common symptoms include the sudden onset of severe pelvic pain that may or may not be accompanied by a palpable adnexal mass. Additionally, symptoms of nausea, vomiting, and pyrexia may be present in some cases (Huchon and Fauconnier, 2010).

The ultrasonographical features of AT may include unilateral ovarian enlargement, ovarian edema, abnormal adnexal position, andthe presence free fluid in the Douglas pouch. The use of Doppler ultrasound, can reveal a decrease or absence of blood flow to the affected ovary and the appearance of a whirlpool sign (Chang et al., 2008; Peña et al., 2000; Mashiach et al., 2011). However, it should be noted that Doppler ultrasound can only depict arterial flow but not venous flow disturbances, which often precede arterial interruptions. In fact, normal Doppler ultrasound findings have been reported in 45%-61% of AT cases (Hasson et al., 2010). Additionally, the presence of abnormal adnexal sonographic images is not pathognomonic of torsion and are shared with other adnexal pathologies. To date, in routine clinical practice, there are no specific clinical, imaging or laboratory markers that confirm the preoperative diagnosis of AT or its severity, and a definitive diagnosis can only be achieved during surgery. Furthermore, uncertainty in the preoperative evaluation may result in delayed surgery and can negatively impact the female reproductive function. Therefore, improving the ability to diagnose AT can facilitate earlier surgery and may be important for future ovarian function (Ozler et al., 2013).

Neutrophil to lymphocyte ratio (NLR) and Platelet to lymphocyte ratio (PLR) are hematological indices that represent systemic inflammatory response and are accepted as inflammatory markers. They are inexpensive, easy to obtain, and widely available in emergency settings. We aimed to investigate the roles of NLR and PLR in the preoperative evaluation of AT, and to compare the levels of these markers in patients with MAT and SAT.

MATERIALS AND METHODS

This retrospective cohort study was conducted at the Soroka University Medical Center (SUMC), a large tertiary teaching hospital serving over a million people, from January 2010 to December 2021. Institutional ethical review board approval (17/11/2020, Approval # 0444-20-SOR) was obtained prior to data collection from medical records of patients who underwent surgery for AT.

Inclusion criteria included patients with surgically proven AT (torsion of the ovary, salpinx, or both), age > 18 years at the time of data collection, with or without an ovarian cyst, and pregnant or non-pregnant women. Exclusion criteria included ovarian cancer, hematological conditions affecting blood counts (TTP, ITP), and steroid treatment within four weeks prior to surgery.

Demographic and clinical characteristics, preoperative sonographic features, laboratory results, and surgical macroscopic adnexal findings were retrieved from the patient's computerized medical records and surgical reports. Adnexal mass size was determined by preoperative ultrasound records and/or surgical findings. The ultrasound findings that were recorded included size, presence of edema, presence of an ovarian cyst, presence of free fluid, and presence or absence of ovarian blood flow.

Based on the Parelkar classification (Parelkar et al., 2014) and the number of adnexal twists (>=3) and according to the severity of the adnexal gross appearance during surgery, patients were divided into two groups: mild-moderate AT (MAT) and severe AT (SAT). Patients with a black-bluish adnexal discoloration, adnexal engorgement, edema, distinct hemorrhagic foci and/or adnexal torsion≥3 times were defined as having SAT (study group). The comparison group (MAT) included patients with normal to rose adnexal color, no engorgement, no edema, no distinct hemorrhagic foci and adnexal torsion=<2 times.

The preoperative complete blood count (CBC) results were recorded, and the CBC was carried out during the 24 hours prior to surgery. The following parameters were recorded: white blood count (WBC), hemoglobin levels (Hb), neutrophil counts, lymphocyte counts, platelets counts and NLR and PLR for both the study and comparison groups. These parameters were compared between the groups to explore any potential differences.

Statistical analysis was performed using SPSS version 17 (SPSS inc., Chicago, Illinois, USA). The initial analysis was performed using descriptive statistics (mean, SD, graphs) and advanced analytical statistics using parametric and non-parametric tests. Continuous variables with normal distribution are presented as mean ± SD and compared between the study groups using the t-test. Continuous variables that are not normally distributed are presented as median with inter-quartile range and their statistical analysis was performed using the Mann-Whitney test. Categorical variables are presented in counts and percentages and their statistical analyses were performed using the Chi-Square or Fisher Exact test when appropriate. All analyses with a two-sided p-value of <0.05 were considered significant.

Overall performance of the different hematological markers was compared by performing the receiver operating characteristic (ROC) curve and calculating the area under the curve (AUC) for each marker. The AUC of the NLR and PLR were compared in order to determine which of the markers had the best diagnostic performance in determining ischemic adnexal torsion.

RESULTS

This study includes one hundred and two women who underwent surgery for AT. Of these patients, thirty-five patients had SAT (study group), and sixty-seven patients had MAT (control group). We found that 20% were pregnant in the study group, whereas for the control group, 37.3% were pregnant. The difference was notable, although not statistically significant (P=0.19). The incidence of previous AT was similar in both groups (17.1%, 16.4%).

We found no correlation between disease severity and age, with women in both groups were mostly in the reproductive age, and no significant difference between the groups was noted (mean age 31.8±8.4 and 32.11±7.35 years, respectively) (Table 1).

The most common clinical presentations were acute abdominal pain (98.5% and 100%, respectively) and tender adnexa (91.4% and 95.5%, respectively), with fever being a rare occurrence (0, 3%) (Table 2).

Sonographic finding showed that ovarian cysts were common in both groups (71.4% and 80.6%, respectively). However, the Whirlpool sign was observed in only 16 women (15.6%) from the entire study population, with no statistically significant difference between the groups (Table 3).

We observed a lateral predisposition, with the left ovary being twisted more often than the right one, although this difference was not statistically significant (54.3% vs. 45.7% in the study group and 60.6% vs. 39.4% in the control group). Adnexal torsion was more common than only a tubal torsion or an isolated ovarian torsion (65.7%, 59.1%) (table 4).

Regarding the hematological indices NLR and PLR, we found no significant difference in their mean values between the study and control groups. The mean NLR of the study population was 5.05 ± 3.37, with a higher mean NLR in the study group, 5.23 ± 3.26, than in the control group, 4.95 ±3.44 (P=0.69). The PLR showed the same trend and was 175 ±87.23 for the study group and 161±78.39 for the control group (P=0.41) (Table 5).

DISCUSSION

NLR and PLR are hematological biomarkers that previously have been suggested as predictors for various obstetric and gynecological conditions. These conditions include among the rest the prediction of pre-eclampsia among women at high risk during prenatal follow-up (Gogoi et al., 2018),an early predictor of small-for-gestational-age neonates (Levy et al., 2020), an indication of the stage of cervical cancer (Prabawa et al., 2019), presurgical diagnosis of endometriosis (Yang et al., 2013) and as early predictors of post-cesarean infection (Rotem et al., 2020).

Additionally, NLR and PLR have been suggested as novel serum indices that may facilitate the presurgical diagnosis of AT specifically (Ercan et al., 2015; Kinay et al., 2021; Yilmaz et al., 2015; Soysal and Baki, 2018; Zangene et al., 2017; Gu et al., 2018; Bakacak et al., 2015). Nevertheless, these studies were confined by a limited number of patients (ranging from 24 to 67 patients) and did not focus specifically on the ischemic subtype of AT.

This study investigated the correlation between NLR, PLR, and AT. The NLR values observed in the study group were 5.23±3.26, whereas those in the control group were 4.95±3.44. These values exceeded the cut-off values of 3,as previously identified by Ercan et al.(2015) as indicative of the presence of AT. Therefore, our findings further support the potential role of NLR in the preoperative diagnosis of AT.

Similarly, we examined the correlation between PLR and AT. The values for the study group were 175±87.23, and those for the control group were 161±78.39. Once again, these values surpassed the optimal cut-off value of 154.4, as Kinay et al. (2021) reported for AT detection.

We undertook this study to explore factors that may facilitate clinical decision-making and assist in a presurgical diagnosis of AT. As of now, a definitive diagnosis of AT can solely be attained during surgery. Nevertheless, NLR and PLR measurements may present accessible and cost-effective means of predicting AT at an earlier stage. Moreover, AT is predominantly prevalent in women of reproductive age. In this study, 102 women treated for AT at the SUMC exhibited average ages of 31.89±8.26 and 32.11±7.35 in the study and comparison groups, respectively. AT may have a detrimental effect on the ovary, ovarian reserve, and future reproductive outcomes. Therefore, early diagnosis can facilitate timely surgical intervention, which is imperative for preserving future ovarian function and reserve (Ozler et al., 2013). Early treatment of AT has demonstrated favorable long-term effects on ovarian appearance and function (Oelsner et al., 2003). In our study, the adnexa was preserved in all patients except for one that had a black-bluish appearing ischemic mucinous cystadenoma.

The current study not only explored the correlation between hematological indices (NLR and PLR) and AT but also scrutinized the correlation with the degree of ischemia of the adnexa. To the best of our knowledge, this is the first study that has addressed the clinical severity of the damage. Furthermore, compared to previous studies, our research involved the largest cohort of patients (n=102) surgically diagnosed with AT.

Several studies have discussed NLR cut-off value for predicting AT, with suggested values ranging from 2.44 to3.56 (sensitivity 62%-88.9%, specificity 70.7%-100%) (Ercan et al., 2015; Kinay et al., 2021; Yilmaz et al., 2015; Soysal and Baki, 2018; Lee et al., 2018; Wang et al., 2017).Our findings are consistent with these reports, as the majority of participants in our study had an NLR (mean NLR 5.05) exceeding 3, which was established as the cut-off value by Ercan et al. (2015). Furthermore, we

Table 1. Demographical characteristics of patients who underwent surgery for adnexal torsion stratified by severity.

	Severe AT (N=35)	Mild-moderate AT (N=67)	P Value
Age (Mean±SD)	31.89±8.26	32.11±7.35	0.98
Ethnicity N (%)			
Jewish	19 (54.3%)	49 (73.1%)	0.06
Arab	16 (45.7%)	18 (26.9%)	
Menstrual status N (%)			
Premenarchal	1 (2.9%)	1 (1.5%)	
Reproductive age	27 (77.1%)	41 (61.2%)	0.19
Pregnancy	7 (20.0%)	25 (37.3%)	
Gravidity (Median, IQR)	2 (0-3)	1 (0-2)	0.14
Parity (Median, IQR)	1 (0-3)	0 (0-1)	0.04
Ovulation induction N (%)	3 (8.6%)	14 (20.9%)	
Previous adnexal torsion N (%)	6 (17.1%)	11 (16.4%)	0.93
Previous pelvic surgery N (%)	12 (34.3%)	17 (25.4%)	0.34

AT - adnexal torsion, SD - standard deviation, IQR - Interquartile range.

Table 2 Clinical presentation of patients who underwent surgery for adnexal torsion stratified by severity.

	Severe AT (N=35)	Mild-moderate AT (N=67)	P Value
Acute abdominal pain N (%)	35 (100%)	66 (98.5%)	0.47
Tender adnexa N (%)	32 (91.4%)	63 (95.5%)	0.41
Nausea or vomiting N (%)	15 (42.9%)	36 (53.7%)	0.30
Fever > 37.8 N (%)	0 (0.0%)	2 (3.0%)	0.30
Diarrhea or Constipation N (%)	2 (5.7%)	8 (11.9%)	0.31

AT - adnexal torsion.

Table 3 Ultrasonographical features of patients who underwent surgery for adnexal torsion stratified by severity.

	Severe AT (N=35)	Mild-moderate AT (N=67)	P Value
Presence of ovarian cyst N (%)	25 (71.4%)	54 (80.6%)	0.29
US Doppler N (%)			
abnormal blood flow	34.3%	32.9%	
Decreased peripheral vascularity	4 (11.4%)	6 (9.0%)	0.76
Absence of blood flow	8 (22.9%)	16 (23.9%)	
Number of twists (Median, IQR)	3 (2-3)	2 (1-2)	<0.01
Number Twisted adnexal>=3	22	0	
Ovarian edema N (%)	18 (51.4%)	41 (61.2%)	0.34
Abnormal adnexal position N (%)	4 (11.4%)	4 (6.0%)	0.33
Free fluid in the Douglas pouch N (%)	20 (57.1%)	29 (43.3%)	0.18
Whirlpool sign N (%)	3 (8.6%)	13 (19.4%)	0.15

AT - adnexal torsion, IQR - Interquartile range.

observed higher values within the study group (5.23±3.26), comprised of patients with SAT, compared to the comparison group (4.95±3.44), consisting of patients with MAT.

Table 4. surgical characteristics of patients who underwent surgery for adnexal torsion stratified by severity.

	Severe AT (N=35)	**Mild-moderate AT (N=67)**	**P Value**
Side N (%)			
Right	16 (45.7%)	26 (39.4%)	0.54
Left	19 (54.3%)	41 (60.6%)	
Torsion organ N (%)			
Ovary	10 (28.6%)	24 (36.4%)	
Tube	2 (5.7%)	3 (4.5%)	0.73
Adnexa	23 (65.7%)	39 (59.1%)	
Parelkar classification N (%)			
1	1 (9.1%)	10 (25.6%)	
2	0 (0.0%)	5 (12.8%)	
3	8 (25.0%)	24 (61.5%)	
4	23 (71.9%)	0 (0.0%)	
	N=32/35	N=39/67	

AT - adnexal torsion.

Table 5 Hematological inflammatory markers of patients who underwent surgery for adnexal torsion stratified by severity.

	Severe AT (N=35)	**Mild-moderate AT (N=67)**	**P Value**
Hemoglobin (Mean)	12.28	12.50	0.448
Hematocrit (Mean)	37.17	37.46	0.703
WBC (Mean)	10.67	10.13	0.423
RDW (Mean)	14.14	13.56	0.176
Neutrophils (Mean)	7.98	7.53	0.491
Lymphocytes (Mean)	1.93	1.99	0.791
MCV (Mean)	83.35	84.54	0.433
PLT (Mean)	280.54	267.52	0.375
MPV (Mean)	10.42	10.36	0.785
NLR (Mean)	5.23	4.95	0.696
PLR (Mean)	175.88	161.40	0.396

PLR has also been studied extensively in various clinical settings (Yilmaz et al., 2015;Zhu et al., 2020; Gogoi et al., 2018), including testicular torsion and AT, and has demonstrated potential as a diagnostic tool for AT. Kinay et al. (2021) reported significantly higher PLR values in the AT group (210.5 ± 132.7), compared with patients with non-AT group (147.9 ± 48.7)($p<0.001$). Their study also identified a PLR cut-off value of154.4 (sensitivity 61%, specificity 64%), which is consistent with our findings, showing a mean PLR value of 166.37. Moreover, we observed higher PLR values in the study group than in the comparison group (175±87.23 vs. 161±78.39, in the SAT and MAT groups, respectively).

Our study hypothesized that presurgical serum inflammatory markers such as the NLR and PLR are associated with the diagnosis of AT and its severity. Unfortunately, our findings led us to reject this hypothesis. Despite observing higher levels of NLR and PLR in the severe AT group, this difference did not reach statistical significance. Additionally, we found the mean NLR levels in pregnant women were higher than the previously reported values in the literature (Kinay et al., 2021). It is possible that our sample size was underpowered to detect a significant difference between the groups, but exploring our hypothesis on a larger cohort would be worthwhile.

Our study possesses some limitations. Firstly it is a retrospective study, which may lead to potential biases due to missing data. There is also a possibility of the presence of confounding variables, which we haven't

accounted for. Secondly, the diagnosis of ischemic adnexa was based on the subjective judgment by surgeons during surgery (discoloration, presence of edema) and not on measurable criteria. To overcome this, we tried to quantify the degree of severity in a standardized manner by using the Parelkar classification (Parelkar et al., 2014) in addition to the number of twists. However, even these criteria might be susceptible to subjectivity. Given that AT treatment occurs in an emergency setting, we were unable to factor in the differences in the level of expertise of the US operator and the operating surgeon.

Finally, our research did not investigate the correlation between the hematological indices (NLR and PLR levels) and the long-term ovarian function post-detorsion (anti-mullerian hormone levels, antral follicle count, subsequent pregnancy rate etc.).

In conclusion, our study revealed elevated levels of NLR and PLR in patients with AT, including during pregnancy. However, we lack sufficient evidence to support their efficacy as presurgical markers of AT severity.. Laparoscopy remains the best method to diagnose AT, particularly among women of reproductive age, given the vital need to conserve ovarian function. Further studies are needed to assess the role of hematological biomarkers, NLR and PLR, in the presurgical diagnosis of AT.

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Declaration of Competing Interest: The authors report no conflict of interest.

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