The Role of Systemic Immune Inflammation Index in Predicting Treatment Success in Tuboovarian Abscesses

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Abstract

Purpose

The aim of this study was to determine the predictability of the systemic immune inflammation index (SII) on the response to medical treatment in tubo-ovarian abscess (TOA).

Methods

296 patients with TOA in a tertiary center were enrolled in the study. Patients were divided into two groups: Group1 (n = 165) included patients in whom medical treatment was successful, and Group2 (n = 131) included patients in whom surgery was required. Demographic, sonographic and laboratory findings were compared between groups. SII was calculated using peripheral blood parameters [SII= (platelets*neutrophils)/lymphocytes].

Results

Age, BMI, gravida, parity, smoking and menopausal status, CRP levels of patients were similar in both groups (p > 0.05). Mass size (4.398 ± 0.306 vs 7.683 ± 0.689, p < 0.001), white blood cell (WBC) (8685.08 ± 3981.98 vs 9994.35 ± 4468.024, p = 0.008), Hb (12.18 ± 1.65 vs 11.68 ± 1.65, p = 0.010), platelet to lymphocyte ratio (PLR) (151.26 ± 74.83 vs 230.77 ± 140.25, p < 0.001), neutrophil to lymphocyte ratio (NLR) (4.21 ± 3.27 vs 6.07 ± 6.6, p = 0.003), monocyte to lymphocyte ratio (MLR) (0.300 ± 0.177 vs 0.346 ± 0.203, p = 0.041) and SII (1014.18 ± 781.71 vs 2094.088 ± 2117.58, p < 0.001) were statistically higher in group 2. ROC Analysis was used to determine the predictability of the variables and PLR (AUC = 0.718, p < 0.001), NLR (AUC = 0.593, p = 0.593), MLR (AUC = 0.576, p = 0.024), SII (AUC = 0.723, p < 0.001) and size of mass (AUC = 0.670, p < 0.001) were found to be significant. The SII, size of mass and bilateral involvement of adnexa were found to be the strongest prognostic factors for surgical intervention (OR:1.004 (1.002–1.005), OR:1.018 (1.010–1.027), OR:3.397 (1.338–8.627); p < 0.001, p < 0.001, p = 0.010 respectively).

Conclusion

SII, size of mass and bilaterality can be used to predict medical treatment success in patients with TOA.

Introduction

Tubo-ovarian abscess (TOA) is one of the most common conditions in pelvic inflammatory disease (PID). It is an inflammation of the uterus, fallopian tubes, ovaries and adjacent pelvic organs that occurs in 34% of PID patients. Abdominal and pelvic pain, adnexal mass, fever and elevated inflammatory markers are
the classic symptoms of TOA. If the rupture results in an abscess, it can lead to sepsis and life-threatening conditions (1–3).

Ascending infection of cervix or vagina reaches first to the uterus and then into the fallopian tubes, leading to peritonitis and abscess formation in the pelvis (4). Ultrasonography is the first choice of imaging for TOA. Broad-spectrum antibiotics are used for medical treatment and surgical procedures (abscess drainage, salpingectomy or hysterectomy) can be performed. 30% of the cases require surgery due to the antibiotic therapy fails. In patients who have TOA, predicting failure of medical treatment can identify patients requiring surgical treatment early (5, 6).

Nonspecific inflammatory markers such as white blood cell (WBC) count and CRP can be used in the identification of TOA (7, 8). However, these parameters may also be within the normal range. The systemic immune inflammation index (SII), based on peripheral lymphocyte, neutrophil, and platelet counts, is a cheap and simple method for identifying inflammation (9). The SII has been confirmed in a variety of diseases and malignancies. However, the relationship between the SII and the success of medical treatment has not been investigated in TOA patients.

The aim of this study was to determine the predictability of the SII on the response to medical treatment in TOA.

**Methods**

The study includes patients in a tertiary center with a diagnosis of PID who were hospitalized between January 2017 and January 2022 and experienced TOA. 306 of 424 PID patients had been complicated with TOA. Patients' medical records were retrospectively reviewed, and 10 patients who were malignant at final diagnosis were excluded. Data were collected from 296 patients who met the inclusion criteria. The flow chart of the study was shown in Fig. 1.

PID diagnosis was based on uterine, cervical, and adnexal sensitivity. Vaginal discharge, fever, and elevated serum inflammatory markers were accepted as unremarkable findings. TOA diagnosis was made based on the ultrasound image of a unilateral or bilateral adnexal mass. Ultrasonography is used to visualize TOA formation.

All patients received medical treatment after blood count, biochemical parameters, CRP, urine samples were checked. The medical treatment protocol was determined according to CDC guidelines. Gentamicin loading dose IV or IM (2mg/kg body weight) followed by maintenance dose (1.5 mg/kg body weight) every 8 hours with clindamycin 900 mg IV every 8 hours. Response to medical treatment was assessed on days 2, 4 and 6 by checking the blood count, CRP level, fever and ultrasonography. Medical treatment was continued intravenously until clinical improvement occurred, then doxycycline 500 mg + metronidazole 500 mg orally every 12 hours continued for 14 days. Medical treatment is considered unsuccessful if, after 72 hours of antibiotic therapy, there is new onset or persistent fever, abdominal and pelvic pain, elevation of CRP and white blood cells, increase in mass size, or signs of sepsis. If necessary
surgical intervention was done. This included abscess drainage, salpingectomy, hysterectomy and bilateral salpingectomy with/or oophorectomy, depending on the patient's desire of fertility.

Patients excluded from the study because they were taking immunosuppressive drugs, were malignant, had a different medical treatment protocol and required urgent surgery.

Neutrophil, lymphocyte, and platelet levels estimated from blood samples were used for calculation of neutrophil to lymphocyte ratio (NLR), platelet to lymphocyte (PLR) and SII indices. When total neutrophil or platelet count divided by total lymphocyte count NLR and PLR were calculated. SII was calculated by multiplication of platelet and neutrophil count and it is divided by lymphocyte count. Formula of SII = (P × N)/L.

Statistical analysis was performed with SPSS v.26 software (SPSS Inc, Chicago, IL, USA). Descriptive statistics were presented as mean ± standard deviations. For nominal variables, independent samples t-test was used, and for ordinal variables, the X² test was used for comparisons. Fisher's exact test was used for categorical variables with small samples. Binary logistic regression was performed to determine the medical treatment failure in patients. Significance was assumed at 95% confidence interval (CI) and p value of < 0.05. Cut-off values, sensitivity, specificity of clinical characteristics for surgical intervention and the area under the curve (AUC) was determined by The Receiver Operating Characteristic (ROC) curve. For prediction of surgical intervention, odds ratio of significant variables was calculated.

Results

The number of patients diagnosed with PID during the study period was 424. 296 of whom had complications at final diagnosis with TOA. All patients received medical treatment. Patients were divided into two groups according to their response to medical treatment. 131 patients did not respond to medical treatment and required surgical intervention. 165 patients treated with medical treatment. Group1 included patients whom medical treatment was successful and Group2 included patients in who required surgery.

Age, BMI, gravida, parity, smoking status and menopausal status of patients were similar in both groups (p > 0.05). WBC, Hb, PLR, NLR, MLR, and SII of the two groups were statistically different (p < 0.005) (Table 1). No difference was observed in CRP between the groups. The size of the adnexal mass was compared between the groups. In Gr1, the size of the mass was smaller than in Gr2 (4.398 ± 0.306 cm3 and 7.683 ± 0.689 cm3, respectively). This difference proved to be statistically significant (p < 0.001). The incidence of bilateral adnexal mass was higher in the Gr2 than in the Gr1 (17.6%-9.1%) (p = 0.036).
Table 1
Characteristics and Laboratory values of the patients

<table>
<thead>
<tr>
<th></th>
<th>Group 1 (n = 165)</th>
<th>Group 2 (n = 131)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (y)</td>
<td>39.89 + 9.51</td>
<td>41.28 + 8.66</td>
<td>0.195</td>
</tr>
<tr>
<td>BMI (kg/m2)</td>
<td>29.047 + 5.75</td>
<td>30.034 + 6.35</td>
<td>0.163</td>
</tr>
<tr>
<td>Gravida</td>
<td>2.06 + 1.07</td>
<td>2.35 + 1.11</td>
<td>0.120</td>
</tr>
<tr>
<td>Parity</td>
<td>1.76 + 0.9</td>
<td>1.96 + 1.07</td>
<td>0.087</td>
</tr>
<tr>
<td>Smoking status</td>
<td></td>
<td></td>
<td>0.798</td>
</tr>
<tr>
<td>Yes</td>
<td>84 (50.9)</td>
<td>47 (49)</td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>81 (49.1)</td>
<td>49 (51)</td>
<td></td>
</tr>
<tr>
<td>Menopause status</td>
<td></td>
<td></td>
<td>0.557</td>
</tr>
<tr>
<td>Premenopause</td>
<td>147 (89.1)</td>
<td>120 (91.6)</td>
<td></td>
</tr>
<tr>
<td>Postmenopause</td>
<td>18 (10.9)</td>
<td>11 (8.4)</td>
<td></td>
</tr>
<tr>
<td>Mass location</td>
<td></td>
<td></td>
<td>0.036</td>
</tr>
<tr>
<td>Unilateral</td>
<td>150 (90.9)</td>
<td>108 (82.4)</td>
<td></td>
</tr>
<tr>
<td>Bilateral</td>
<td>15 (9.1)</td>
<td>23 (17.6)</td>
<td></td>
</tr>
<tr>
<td>WBC (u/l)</td>
<td>8685.08 + 3981.98</td>
<td>9994.35 + 4468.024</td>
<td>0.008</td>
</tr>
<tr>
<td>Hb (mg/dl)</td>
<td>12.18 + 1.65</td>
<td>11.68 + 1.65</td>
<td>0.010</td>
</tr>
<tr>
<td>CRP (mg/l)</td>
<td>38.28 + 5.95</td>
<td>54.83 + 8.61</td>
<td>0.062</td>
</tr>
<tr>
<td>SII</td>
<td>1014.18 + 781.71</td>
<td>2094.088 + 2117.58</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>NLR</td>
<td>4.21 + 3.27</td>
<td>6.07 + 6.6</td>
<td>0.003</td>
</tr>
<tr>
<td>MLR</td>
<td>0.300 + 0.177</td>
<td>0.346 + 0.203</td>
<td>0.041</td>
</tr>
<tr>
<td>PLR</td>
<td>151.26 + 74.83</td>
<td>230.77 + 140.25</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Mass size (cm3)</td>
<td>4.398 + 0.306</td>
<td>7.683 + 0.689</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Day of surgery</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4th day</td>
<td>-</td>
<td>56 (42.7)</td>
<td></td>
</tr>
<tr>
<td>6th day</td>
<td>-</td>
<td>75 (57.3)</td>
<td></td>
</tr>
</tbody>
</table>

BMI: Body mass index; WBC: White Blood Cell PLR: Platelet to Lymphocyte Ratio NLR: Neutrophil to Lymphocyte Ratio MLR: Monocyte to Lymphocyte Ratio SII: Systemic Immune Inflammation Index
ROC Analysis was used to determine the predictability of WBC, Hb, PLR, NLR, MLR, SII, and mass size for medical treatment failure. PLR, NLR, MLR, SII and mass size were found to be significant. Figure 2 shows the ROC curve of variables. Cut-off values, AUC, sensitivity and specificity of the variables were presented in Table 2. The AUC of SII was highest, followed by the size of the mass. The AUC of MLR was the lowest.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Cut value</th>
<th>AUC</th>
<th>p value</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>Lower Bound</th>
<th>Upper Bound</th>
</tr>
</thead>
<tbody>
<tr>
<td>SII</td>
<td>1102.405</td>
<td>0.723</td>
<td>&lt; 0.001</td>
<td>68.7%</td>
<td>68.5%</td>
<td>0.666</td>
<td>0.780</td>
</tr>
<tr>
<td>NLR</td>
<td>3.245</td>
<td>0.593</td>
<td>0.004</td>
<td>66.4%</td>
<td>50.3%</td>
<td>0.529</td>
<td>0.658</td>
</tr>
<tr>
<td>MLR</td>
<td>0.273</td>
<td>0.576</td>
<td>0.024</td>
<td>60.3%</td>
<td>60%</td>
<td>0.510</td>
<td>0.642</td>
</tr>
<tr>
<td>PLR</td>
<td>158.69</td>
<td>0.718</td>
<td>&lt; 0.001</td>
<td>67.2%</td>
<td>66.7%</td>
<td>0.659</td>
<td>0.777</td>
</tr>
<tr>
<td>Mass size</td>
<td>3.968</td>
<td>0.670</td>
<td>&lt; 0.001</td>
<td>66.4%</td>
<td>60%</td>
<td>0.607</td>
<td>0.733</td>
</tr>
</tbody>
</table>

PLR: Platelet to Lymphocyte Ratio  NLR: Neutrophil to Lymphocyte Ratio  MLR: Monocyte to Lymphocyte Ratio  SII: Systemic Immune Inflammation Index

Binary logistic regression analysis was performed on the variables that were significant in the univariate analysis. SII, NLR, MLR, size of mass, and bilateral adnexal mass were the main prognostic factors determining surgical intervention (Table 3). Bilateral adnexal mass formation was the strongest predictor of medical failure with OR: 3.397, SII and mass size follows it.
Table 3
Multiple logistic regression analysis for surgical intervention

<table>
<thead>
<tr>
<th></th>
<th>Odds Ratio (95% CI)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>SII</td>
<td>1.004 (1.002–1.005)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>NLR</td>
<td>0.546 (.428-.696)</td>
<td>0.000</td>
</tr>
<tr>
<td>MLR</td>
<td>0.015 (.001-.271)</td>
<td>0.004</td>
</tr>
<tr>
<td>PLR</td>
<td>0.997 (.991-1.003)</td>
<td>0.258</td>
</tr>
<tr>
<td>Mass size</td>
<td>1.018 (1.010–1.027)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Bilateral mass</td>
<td>3.397 (1.338–8.627)</td>
<td>0.010</td>
</tr>
</tbody>
</table>

PLR: Platelet to Lymphocyte Ratio NLR: Neutrophil to Lymphocyte Ratio MLR: Monocyte to Lymphocyte Ratio SII: Systemic Immune Inflammation Index

Discussion

TOA is the most common complication of PID and if not treated, can lead to life-threatening conditions. It is important to distinguish patients who require invasive procedures to treat the TOA. There were no susceptible markers for deciding surgical intervention. The parameters of the complete blood count are easy to obtain, inexpensive, and universal. By using these parameters, the SII can be calculated easily. It can be used in prediction of surgical intervention.

There have been similar studies in the literature examining medical treatment failure at TOA (2, 10–16). Chan et al. found that when the mass size was > 7.5 cm and the BMI was > 25 kg/m2, the failure of medical treatment increased (10). Similar to Chan most of the studies showed that TOA size and age were the predictors of increased hospitalization, complications and surgical procedures (11–15). Fouk et al. created a scoring system including age, mass size, leukocyte count at admission and bilaterality that can mostly predict surgical intervention (2). Karaca et al. showed that age, mass size, CRP, WBC and procalcitonin levels were not associated with failure of medical treatment (16). In our study, mass size and bilateral involvement were found to be risk factors for treatment failure. Age, BMI, WBC and CRP were not found associated with surgical intervention.

Increased level of WBC, CRP and ESR was associated with TOA (8, 11, 17). Studies showed that inflammatory markers can predict the success of the medical treatment. Elevated levels of CRP and WBC were found related to the treatment failure (11). Similarly, Hwang et al. found association between age, ESR and medical treatment failure also (8). Inconsistent to this data Akkurt et al. found no relation between CRP and response to treatment (17). Our study found no relation between CRP level and surgical intervention also.
In recent years, there have been studies investigating the predictability of NLR and PLR in many diseases and the success of treatment in obstetrics and gynecology. In TOA cases; WBC and neutrophil levels were found elevated; lymphocyte levels were found decreased and this results with the increase NLR (18). Aydin et al. found that NLR can predict the response to medical treatment with a sensitivity of 71% and a specificity of 74%, and PLR with a sensitivity of 74% and a specificity of 65% (19). In another study it was shown that neutrophil levels were increased in the TOA patients who needed surgical treatment and NLR could be used as a predictor of surgical intervention (14). In contrast to these studies, Akselim et al. examined hematologic parameters such as WBC, platelets, CRP, NLR and PLR. They found that only CRP was a risk factor for treatment failure (20). In our study, CRP was not different in both groups. This may be due to the CRP is an acute inflammatory serologic marker and it rapidly increases after onset of inflammation. SII, PLR, NLR, and MLR were different between groups and SII, NLR, and PLR were found to be risk factors for treatment failure. SII increased the risk of surgical intervention 1.004 times (95% CI 1.002–1.005). This is the first time in the literature that SII and medical treatment failure have been studied in TOA. Even when inflammatory markers were within the normal range or similar between groups the index of systemic inflammation SII can be used to predict medical treatment success.

The retrospective data collection is a main limitation of the study. Although it is a retrospective study; the large number of patients, the constant treatment modalities in the gynecology clinic and the single-center study are the strengths of our study. Another strength is that it is the first study in the literature to investigate SII and TOA.

**Conclusion**

TOA is a common condition in women that needs to be treated, and if treatment fails, it can be life-threatening. The decision to have surgery can be tricky. SII, size of mass and bilaterality proved to be prognostic factors for failure of medical treatment. The SII can be easily calculated and used to predict the success of medical treatment. Studies with larger cases are needed to support our findings.

**Declarations**

**Authorship Contributions:**

Surgical and Medical Practices: C.K, B.K, V.K

Concept: V.K, Y.E.U

Design: V.K, Y.E.U

Data Collection or Processing: C.K, B.K

Analysis or Interpretation: C.K, V.K

Literature Search: C.K, B.K
Writing: C.K.

Conflict of Interest:
No conflict of interest is declared by the authors.

Financial Disclosure:
The authors declared that this study receive no financial support

Authorship Contributions:
All authors contributed to the study conception and design. Material preparation, data collection and analysis were performed by [CANER KOSE], [BUSRA KORPE]. The first draft of the manuscript was written by [CANER KOSE] and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

Consent to participate:
Written informed consent was obtained from all participants

Ethics:
Ethics committee approval: The study design was approved by the institutional research ethics committee (approval number: 06/11)

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Figures

Figure 1

Flow chart of the study
Figure 2

ROC analysis of SII (AUC = 0.723, p<0.001), PLR (AUC=0.718, p<0.001), NLR (AUC=0.593, p=0.593), MLR (AUC=0.576, p=0.024), mass size (AUC=0.670, p<0.001)