The diagnostic role of hemogram parameters in pregnant appendicitis

Erkan SomuncuACDE, İnanç Şamil SarıcıACDE, Emre BozdagCD, Adem ÖzcanB, Cenk ÖzkanB, Ceren BaşaranB

Department of General Surgery, University of Health Sciences, Kanuni Sultan Suleyman Training and Research Hospital, Istanbul, Turkey

ABSTRACT:
Introduction: Acute appendicitis is the most frequently encountered non-obstetric disease requiring surgical intervention during pregnancy. Early diagnosis reduces maternal and foetal morbidity/mortality rates.

Aim: This study aims to investigate haemogram parameters in the diagnosis of acute appendicitis in pregnant women.

Materials and methods: A retrospective case-controlled study was conducted in three groups. Thirty-nine pregnant patients with acute appendicitis (Group A), 39 fertile, non-pregnant patients with acute appendicitis (Group B) and 39 healthy pregnant women (Group C) were included in the study. The WBC, neutrophil and lymphocyte counts and NLR, PLR, MPV and RDW values were compared.

Results: The mean NLR values in Groups A, B and C were 7.39 (1.58–46.6), 5.66 (1–20) and 4.23 (1.54–10.77), respectively, and there was a significant difference in NLR values between the groups (P = 0.002). The mean PLR values in Groups A, B and C were 159.09 (69.1–574), 134.28 (21.5–360) and 120 (68.7–334), respectively, and the difference was statistically significant (P = 0.019). The cut-off value for WBC count was 14 155 106/μL (51.3% sensitivity; 82.1% specificity), for neutrophil count it was 10 955 106/μL (53.8% sensitivity; 84.6% specificity), for NLR it was 9.23 (46.2% sensitivity; 92.3% specificity) and for PLR it was 157.6 (51.3% sensitivity; 82.1% specificity). NLR had the largest area under the curve, with 0.667 NLR.

Conclusion: Neutrophil and WBC counts and PLR were found to be the most valuable inflammatory parameters. However, RDW, lymphocyte count and MPV levels were not found to be valuable markers in terms of sensitivity and specificity in the diagnosis of acute appendicitis in pregnant patients.

KEYWORDS: appendicitis, haemogram, NLR, pregnancy

ABBREVIATIONS
AA – acute appendicitis
USG – ultrasonography
CT – computed tomography
MRI – magnetic resonance imaging
WBC – white blood cells
NLR – neutrophil-lymphocyte ratio
MPV – mean platelet volume
RDW – red blood cell distribution width
PLR – platelet-to-lymphocyte ratio
ROC – receiver operating characteristic

INTRODUCTION

Acute appendicitis (AA) is a common cause of surgical abdomen [1, 2]. It has been reported that the incidence of perforation is approximately 7%, while the probability of perforation is between 17% and 20% [3, 4]. The mortality risk in the general population is less than 1%, but that rate may increase to 50% in elderly patients [5, 6]. The prevalence of AA in pregnancy is 1:1250 and 1:1500 [7]. Fertility is high at the age of 20–30 years [8–10]. Negative laparotomy in suspected appendicitis is 15%–35% in general surgery cases and 25%–50% in obstetric series [11–13].

Computed tomography (CT) is considerably superior to ultrasonography (USG) in the diagnosis of AA [14–16]. Magnetic resonance imaging (MRI) has recently gained momentum, especially in pregnant women, because it does not require contrast material and can effectively show inflammation [17]. Due to symptoms such as nausea, vomiting and loss of appetite overlapping, it is very difficult for clinicians to diagnose AA in pregnant women [18]. Inflammatory parameters on a haemogram can provide early diagnosis of AA, especially in suspicious cases. These parameters are critical to prevent unnecessary surgeries and possible complications for the mother and/or foetus in pregnant women [19, 20]. We aimed to investigate whether these inflammatory parameters have statistical significance in pregnant patients diagnosed with AA in our clinic.

MATERIALS AND METHODS

Our study included 39 pregnant and 39 non-pregnant fertile women who were operated on for appendicitis in our general surgery clinic between May 2014 and 2019, and 39 randomly selected pregnant women who came to our obstetrics clinic for their routine check-ups on these dates. The haemogram parameters of the patients and the histopathological results of appendectomies were reviewed retrospectively from the medical records of the patients. All appendectomies reported as focal, suppurrative, perforated and gangrenous by histopathology were included in the study.

Pregnant patients who were operated on for AA were defined as Group A. The women of fertile age who were not pregnant were...
Laboratory analysis

The haemogram values obtained before the appendectomies and during the routine follow-ups were examined. MPV and RDW values and WBC, neutrophil, lymphocyte and platelet counts were analysed. The NLR and PLR values were calculated by dividing the neutrophil and platelet counts, respectively, by the lymphocyte count. Haematological parameters were measured by an automated haematology analyser (Sysmex XN-2000, Sysmex Corporation, Japan). The upper limits of the reference intervals were as follows: leukocyte counts (WBC): 4490–12,680 /µL; platelets: 150–400 × 10³/µL; neutrophils: 2.1–8.89 × 10³/µL; lymphocytes: 1.26–3.35 × 10³/µL; MPV: 9.3–12.1 fl; and RDW: 12%–13.6%.

Statistical analysis

Data analysis was performed using SPSS 22.0 (IBM Corporation, Armonk, NY, USA). The Shapiro-Wilk test was used to determine the data’s compliance to a normal distribution; Levene’s test was used to assess the homogeneity of variances among the groups. The independent sample T-test with bootstrap results was used to compare two separate groups, whereas the Mann-Whitney U test was used with the Monte Carlo simulation technique. One-way analysis of variance (robust test: Browne-Forsythe) was used together with bootstrap results to compare more than two groups with other groups. The Kruskal-Wallis H test, least significant differences and Games-Howell tests were used for post hoc analysis.

The correlation between the patient groups classified by the cut-off values was calculated according to the variables, and the real rating was expressed by an examination of sensitivity and specificity using the receiver operating characteristic (ROC) curve analysis. Quantitative data are expressed as mean ± standard deviation, median-interquartile range or median and range (maximum-minimum). The categorical data are expressed as n (number) or percentage (%) and analysed by Fisher’s exact test.

RESULTS

In Group A, 13 (33.3%) pregnant women were in the first trimester, 18 (46.1%) were in the second trimester and 8 (20.6%) were in the third trimester. Histopathological diagnosis was confirmed as AA in all appendectomies. In Group C, 6 (15.3%) healthy, pregnant women were in the first trimester, 13 (33.3%) were in the second trimester and 20 (51.4%) were in the third trimester. There was no significant difference between Groups A and C in terms of gestational age (P > 0.05). AA could not be diagnosed by USG in 15 (38.5%) of the 78 patients who underwent appendectomy, and there was no significant difference between the groups in terms of the success of USG. All pregnant and non-pregnant women diagnosed with AA underwent laparoscopy and laparotomy. There was no significant difference between the groups in terms of length of hospital stay (P > 0.28).

Morbidity and mortality were not observed in all cases. When Groups A and C were compared, higher WBC and neutrophil counts were detected in Group A. While the mean neutrophil count was statistically high, the mean lymphocyte count was statistically lower (P < 0.05). Mean NLR and PLR values were found to be statistically high (P = 0.002 and P = 0.019, respectively). When Group A was compared with other groups, the mean lymphocyte count, RDW and MPV were found to be statistically lower in Group A (P < 0.05) (Tab. I.). ROC curve analysis was performed to evaluate the ability of haemogram parameters to diagnose AA in pregnant women. The sensitivity and specificity were estimated based on the selected cut-off values (Fig. 1.).

According to the ROC analysis, the sensitivity and specificity values for WBC was 14 155 cells/ml (51.3% sensitivity; 82.1% specificity), for neutrophil count it was 10 955 cells/ml (53.8% sensitivity; 84.6% specificity), for NLR 9.23 (46.2% sensitivity; 92.3% specificity) and for PLR 157.6 (51.3% sensitivity; 82.1% specificity). NLR had the largest area under the curve (Tab. II., Fig. 1.).

DISCUSSION

The diagnosis of AA in pregnant women evaluated by abdominal pain is incredibly difficult due to the anatomical and physiological changes brought about by pregnancy. Physiological conditions such as anorexia, nausea and vomiting, which we frequently see during pregnancy, may mask the symptoms of AA. The appendix is displaced in pregnant women. This occurs when the uterus expands and shifts from the pelvis into the abdomen and the tonus in the abdominal muscles decreases [21]. USG is the first choice in all patients with abdominal pain who are admitted with the suspicion of appendicitis, whether they are pregnant or not. The use of CT, which is more valuable in the gastrointestinal system, is limited in pregnant women in order to protect the foetus. MRI is not always easily accessible [18, 22, 23]. The uterus begins to compress the surrounding organs starting in the 12th week of pregnancy. From the 12th week of pregnancy, the uterus gradually begins to push the
surrounding organs. The sensitivity of USG used in the diagnosis of appendicitis during pregnancy has been reported to be between 7% and 96%. This variability may be due to trimester, obesity, anatomical variations and the radiologist [24]. In our study, there was no significant difference between Groups A (61%) and B (77%) in terms of the adequacy of USG in diagnosing appendicitis.

Therefore, physical examination and history are very valuable in diagnosing AA in pregnant women. However, this may not be easy for the clinician. Delays in diagnosis and uncertainty for surgery raise the risk of appendix perforation. If the appendix is perforated, intra-abdominal sepsis can develop and morbidity and mortality for both mother and foetus increase [21, 25, 26]. Pregnant women should be evaluated promptly for a correct diagnosis of AA, and unnecessary operations should also be avoided. In the literature, negative appendectomy rates during pregnancy vary between 3% and 23% [11, 27]. Histopathological diagnosis was compatible with AA in all patients operated on in our study group.

A haemogram is a quick and valuable diagnostic test that is available almost everywhere in the emergency department. It plays a vital role in the diagnosis of AA. In addition, inflammatory markers such as WBC, neutrophil and lymphocyte counts and values such as NLR, PLR, MPV and CRP are very valuable. The growing body of studies about these parameters in the literature are increasingly important and noteworthy in terms of AA [2, 28, 29]. CRP, an acute phase reactant, is a very useful critical marker for the diagnosis and monitoring of acute and chronic inflammatory conditions. In pregnant women, it is not specific for the diagnosis of AA, but may be helpful to support the diagnosis [30]. CRP levels were significantly higher in all of our appendectomies.

Leukocytosis is common in patients with AA during pregnancy, when the leukocyte count can reach as high as 18 000–30 000 mm3 in the period close to delivery [21]. The mean WBC count in all of our patients with AA was 14 525 ± 4895 mm3, and a significant difference was found between this group and healthy pregnant women (P<0.019).

The sensitivity and specificity values for WBC with cut-off values of more than 14 155 were 51.3% and 82.1%, respectively. Therefore, we can recommend the use of leukocyte count in combination with NLR, PLR and other haemogram parameters in the diagnosis of acute appendicitis in pregnant women because it provides higher sensitivity and specificity. In nearly all inflammatory diseases, the normal metabolic response of circulating leukocytes is an elevated neutrophil level and a lower lymphocyte count [31]. As a result, higher neutrophil counts and lower lymphocyte counts are inevitable in AA. Similarly, when we compared the pregnant women who underwent appendectomy with the healthy pregnant women, we found the same results with a statistically significant difference (P < 0.05).

Several studies in the literature in recent years have suggested that an increased NLR or PLR may be better markers for AA than CRP, WBC or neutrophil count [2, 33]. Yazar et al. [2] reported 78.6% sensitivity and 80% specificity for NLR and 100% sensitivity and 42.9% specificity for PLR in their study on pregnant women, in whom they diagnosed AA with 90.5% accuracy. According to our cut-off values, 46.2% sensitivity and 92.3% specificity were found for NLR and 100% sensitivity and 42.9% specificity for PLR. Based on these results, we hypothesise that NLR is more valuable in the diagnosis of AA in pregnant women.

MPV, which is known to show the functional state of platelets, can also reflect the inflammatory state. There are some studies in the literature addressing this issue: in the diagnosis of AA, Narci et al. [34] detected high MPV values; however, Albayarak et al. [35] found significantly lower MPV values in patients with AA compared to the control group. On the other hand, Yazar et al. [2] and Çınar et al. [20] did not find a significant difference between the groups when they compared MPV values in their studies. The MPV values of pregnant women with AA were statistically lower than the control group (P < 0.05), but we could not demonstrate a cut-off value of MPV.

The RDW, which we use in the differential diagnosis of anaemia, is a measure of the distribution of circulating red blood cells.
It is valuable for distinguishing microcytic anaemia of iron deficiency from hemoglobinopathies and thalassemia. Although the diagnostic value of RDW for AA is not often mentioned in the literature, Narci et al. [36] found the RDW to be significantly lower in patients with appendicitis. Similar to most studies in the literature, we did not find RDW to have predictive value.

The main limitations of this study are its small sample size, due to the relatively low incidence of AA in pregnancy, and its retrospective design.

CONCLUSIONS

Our study shows that parameters such as neutrophil or WBC count, neutrophil-to-lymphocyte ratio and platelet-to-lymphocyte ratio are better inflammatory markers in the diagnosis of AA in pregnancy. On the other hand, no statistically significant results were found for some other parameters, including lymphocyte count and RDW and MPV values. We believe that prospective studies with large samples are needed to reveal more specific, reliable biomarkers in the diagnosis of AA in pregnant women.

REFERENCES

15. Acar E., Ozcan Ö., Deliktas H. et al.: Laboratory markers has many valuable parameters, including lymphocyte count and RDW and MPV values. We believe that prospective studies with large samples are needed to reveal more specific, reliable biomarkers in the diagnosis of AA in pregnant women.

Tab. II. Sensitivity and specificity of diagnostic haematological variables and cut-off values to diagnose acute appendicitis in pregnancy, based on the area under the receiver operating characteristic curve.

<table>
<thead>
<tr>
<th>HAEMOGLOBIN PARAMETERS (CUT-OFF VALUES)</th>
<th>SENSITIVITY (%)</th>
<th>SPECIFICITY (%)</th>
<th>AUC ± SE</th>
</tr>
</thead>
<tbody>
<tr>
<td>White blood cells (cells/mL) &gt;14155</td>
<td>51.3</td>
<td>82.1</td>
<td>0.599 ± 0.058</td>
</tr>
<tr>
<td>Neutrophil count (cells/mL) &gt;10955</td>
<td>53.8</td>
<td>84.6</td>
<td>0.619 ± 0.056</td>
</tr>
<tr>
<td>Neutrophil-to-lymphocyte ratio &gt; 23</td>
<td>46.2</td>
<td>92.3</td>
<td>0.667 ± 0.055</td>
</tr>
<tr>
<td>Platelet-to-lymphocyte ratio &gt;157.6</td>
<td>51.3</td>
<td>82.1</td>
<td>0.606 ± 0.056</td>
</tr>
</tbody>
</table>

ROC curve analysis (Youden's index) [1-Honley and McNell].

AA – Acute appendicitis, AUC – Area under the receiver operating characteristic curve, SE – Standard error.