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Evaluation of inflammatuar response in hysterectomies: a retrospective study in Kocaeli, Turkey

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ABSTRACT

Objectives: The authors aimed to detect the inflammatory marker changes in laparoscopic hysterectomy (LH) and abdominal hysterectomy (AH) and to determine whether oophorectomy affected the results.

Material and methods: The patients who underwent LH and AH with or without oophorectomy between 2018 and 2019 were identified as two groups. The records of patients were reviewed retrospectively. Preoperative and postoperative in the first 24 hours hematocrit (HCT), hemoglobin (HB), white blood cell (WBC), platelet-lymphocyte ratio (PLR), and neutrophil-lymphocyte ratio (NLR) values were compared.

Results: WBC, NLR, and PLR were statistically increased, and HB and HCT were decreased in all groups in the postoperative period. However, all changes were more prominent in the AH group than in the LH group. In other words, in the postoperative period, there were fewer changes in the inflammatory markers WBC, NLR, and NLR in the LH group. Oophorectomy did not affect these results.

Conclusions: LH, as in other laparoscopic operations, was associated with lower inflammatory response. The addition of oophorectomy did not increase inflammation in either AH or LH. Clinical Trials registration number is NCT04184765.

Key words: hysterectomies; inflammation mediators; lymphocyte activation; neutrophil activation; platelet activation

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INTRODUCTION

Surgery suppresses postoperative inflammatory response [1–3]. Systemic leukocytic alterations, such as leukocytosis, neutrophilia, and lymphopenia, occur in response to operations because of the effects of various hormones and cytokines [4, 5]. Laparoscopic surgery should cause less immune impairment, as it is associated with less tissue damage than abdominal surgery is [6–8]. The measurement of leukocytic changes, including neutrophil (NLR) and platelet-lymphocyte (PLR) ratios could be a useful method for assessing the postoperative inflammatory response.

Although the role of systemic leukocytic changes in the inflammatory response is uncertain, white blood cell (WBC), neutrophil, platelet, and lymphocyte counts as well as NLR and PLR have been well studied in many diseases, such as diabetes, coronary artery disease, ulcerative colitis, surgeries, and various cancers [8–12]. Reich et al. first described laparoscopic hysterectomy [13]. However, there is not enough information in the literature about how these values change in laparoscopic hysterectomies (LH) with or without oophorectomy, which is frequently used in gynecological practice. Moreover, oophorectomy may change the inflammatory response by altering cytokines and the microenvironment. Animal studies showed that oophorectomy led to changes in inflammatory response and neutrophil count [14, 15].

In the present study, we aimed to investigate the value of alterations in WBC, NLR, and PLR in patients with and without oophorectomy for LH or abdominal hysterectomy (AH).

Although NLR and PLR levels, as preoperative and postoperative markers, have been the subject of many studies, to the best of our knowledge, this study is the first to evaluate their association with LH and AH with or without oophorectomy.

Objectives

Laparoscopic hysterectomy revealed less postoperative inflammation than abdominal hysterectomy. The addition

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of oophorectomy did not change this result. To the best of our knowledge, this study is the first to evaluate their association with LH and AH with or without oophorectomy.

MATERIAL AND METHODS

This study was conducted in the reference obstetrics and gynecology clinic. Informed consent was obtained from each patient in our hospital. The patients who underwent LH and AH with or without oophorectomy between 2018 and 2019 were identified as two groups. The records of patients were reviewed retrospectively. Preoperative and postoperative in the first 24 hours hematocrit (HCT), hemoglobin (HB), WBC, PLR, and NLR values were compared.

We determine the type of surgery according to the clinical condition of the patient, the gynecological examination, and the patient's request. In cases where there is no clinical suspicion, oophorectomy is performed according to the patients' wishes. In benign cases, the preferred type of hysterectomy is type 1 extra facial hysterectomy. We usually perform total laparoscopic hysterectomy, so the vaginal cuff is sutured laparoscopically.

Patients with chronic diseases, the presence of active infection, corticosteroid use, acetylsalicylic acid, and anticoagulant use were not included in the study. Bladder and bowel injuries, blood transfusion requirements, wound infection and hematoma, postoperative respiratory system complications were evaluated as surgical complications. Patients whose data could not be accessed were excluded.

Blood tests

Maternal venous blood samples were taken into hemogram tubes. The calibrations of the device were completed and analyzed using the Pentra DF Nexus Hematology System® (Horiba Healthcare, Japan). PLR and NLR were calculated by dividing platelet and neutrophil counts, respectively, by the lymphocyte count.

Statistical analysis

The Number Cruncher Statistical System (NCSS) 2007 (Kaysville, Utah, USA) was used for the statistical analysis. The normal distribution of the quantitative data was tested using the Shapiro–Wilk test and graphical analysis. The Student's t-test and the Mann–Whitney U test were used to compare the normal and the non-normal distributed quantitative variables, respectively. The paired sample t-test was used for the preoperative and postoperative comparisons of the variables with normal distribution. The Wilcoxon signed-rank test was used for the preoperative and postoperative comparisons of the variables with normal distribution. Pearson's chi-square test and Fisher's exact test were used to compare the qualitative data. Statistical significance was accepted at $p < 0.05$.

RESULTS

Hysterectomy was performed in 234 patients, 92 of which were abdominal and 142 were laparoscopic. Nine patients in the first group and eight patients in the second group did not meet our inclusion criteria. Three patients in the first group and two patients in the second group were excluded from the study because they could not be contacted. Finally, data on 80 patients in the AH group and 132 patients in the LH group were evaluated. Oophorectomy was added to 16 patients in the AH group and 23 patients in the LH group.

The demographic features and inflammatory markers are shown in Tables 1 and 2. Preoperative and postoperative changes in NLR and PLR between the oophorectomy group and the non-oophorectomy group are shown in Table 3. The average age is lower in the AH group. Except this, there were no significant differences between the groups in terms of the demographic data. The most common indication in the LH group was uterine descensus, whereas the most common indication in the AH group was fibroids. Although no difference in complications was observed, the length of hospital stay was lower in the LH group. Regardless of the procedure, WBC, NLR, and PLR were statistically increased, and HB and HCT were decreased in all groups in the postoperative period. However, all changes were more prominent in the AH group. In other words, in the postoperative period, the inflammatory markers WBC, NLR, and NLR changed less in the LH group. Oophorectomy did not affect these results.

DISCUSSION

The main findings of our study are as follows:

1. The preoperative and postoperative HB and HCT values did not change significantly in both the AH and the LH groups; however, the NLR and PLR values changed significantly. Moreover, the changes were more prominent in the AH group. This result was not surprising because it was consistent with the literature. The inflammatory response was also less in the LH group, where less tissue damage was expected.
2. In both the AH and the LH groups, oophorectomy did not change these results. The inflammatory responses in the laparoscopy and the open surgery have been evaluated in many previous studies, which showed that the immune response was suppressed by adjusting the cytokines level and cellular components of the immune system after open surgery [16–18]. Less tissue trauma in laparoscopic surgery may be associated with the lower response to systemic inflammation [19]. In many previous studies, the total leukocyte count was increased after open surgery, but it did not increase after laparoscopic surgery [20, 21]. The potential advantages of laparoscopy over laparotomy include shorter op-

Table 1. Evaluation of descriptive characteristics by type of operation

	Abdominal hysterectomy (n = 80)	Laparoscopic hysterectomy (n = 132)	p value
Age [years]	46.91 ± 5.26	50.63 ± 8.06	[a]0.001**
Gravida	2.94 ± 2.00	3.40 ± 1.63	[a]0.067
Systemic disease	7 (8.8)	23 (17.4)	[b]0.079
Number of previous operations	26 (32.5)	44 (33.3)	[b]0.900
Indication			
Dysfunctional uterine bleeding	15 (18.8)	31 (23.5)	**[b]0.418**
Symptomatic fibroids	52 (65.0)	30 (22.7)	[b]0.001**
Postmenopausal bleeding	3 (3.8)	8 (6.1)	[c]0.292
Adnexal mass	7 (8.8)	16 (12.1)	[b]0.444
Desensus uteri	1 (1.3)	22 (16.7)	[b]0.001**
Endometrial hyperplasia	2 (2.5)	21 (15.9)	[b]0.002**
Mole pregnancy	0 (0)	1 (0.8)	[c]1.000
Cervical intraepithelial hyperplasia	0 (0)	3 (2.3)	[c]0.292
Patients without oophorectomy	64 (80.0)	109 (82.6)	[a]0.639
Complications	3 (3.8)	8 (6.1)	[c]0.540
Duration of hospital stay [days]	2.58 ± 0.90	2.28 ± 0.68	[d]0.002**

[a]Student t Test; [b]Pearson χ^2 Test; [c]Fisher's Exact Test; [d]Mann-Whitney U Test; **Indicates statistical significance; Data are expressed as number (%) or mean ± standard deviation

Table 2. Evaluation of WBC, HGB, HCT, PLT, and NLR measurements by operation type

	Abdominal hysterectomy (n = 80)	Laparoscopic hysterectomy (n = 132)	p value
Preop WBC [$\times 10^3/mm^3$]	6.63 ± 1.96	6.95 ± 1.94	[a]0.254
Postop WBC [$\times 10^3/mm^3$]	11.17 ± 371	9.80 ± 2.97	[a]0.004**
[c]p-value	0.001**	0.001**	
Difference (Postop-Preop)	4.54 ± 3.40	2.85 ± 2.70	[a]0.001**
Preop HB [g/dL]	12.23 ± 1.73	12.45 ± 1.40	[a]0.341
Postop HB [g/dL]	10.66 ± 1.46	10.65 ± 1.32	[a]0.942
[c]p value	0.001**	0.001**	
Difference (Postop-Preop)	–1.57 ± 1.00	–1.80 ± 0.79	[a]0.080
Preop HCT	37.07 ± 4.44	37.57 ± 3.40	[a]0.387
Postop HCT	32.93 ± 3.98	32.62 ± 3.28	[a]0.531
[d]p-value	0.001**	0.001**	
Difference (Postop-Preop)	–4.14 ± 3.02	–4.96 ± 2.30	[a]0.027*
Preop PLR	9.36 ± 5.37	9.86 ± 5.57	[b]0.291
Postop PLR	23.65 ± 16.84	17.24 ± 10.25	[b]0.007**
[d]p-value	0.001**	0.001**	
Difference (Postop-Preop)	14.29 ± 15.28	7.38 ± 10.73	[b]0.001**
Preop NLR	2.72 ± 5.20	2.16 ± 1.60	[b]0.838
Postop NLR	8.67 ± 8.38	6.41 ± 6.35	[b]0.005**
[f]p-value	0.001**	0.001**	
Difference (Postop-Preop)	5.96 ± 9.64	4.25 ± 6.45	[b]0.002**

[a]Student's t-Test; [b]Mann–Whitney U Test; [c]Paired Samples t-Test; [d]Wilcoxon Signed-Rank Test; *$p < 0.05$; **$p < 0.01$; Data are expressed as mean ± standard deviation; HB — hemoglobin; HCT — hematocrit; NLR — neutrophil-lymphocyte ratio; PLR — platelet-lymphocyte ratio; Postop — postoperative value; Preop — preoperative value; WBC — white blood cell

Table 3. Evaluation of PLR and NLR measurements according to oophorectomy in the AH and LH groups

	Oophorectomy (+)	Oophorectomy (–)	[a]p
AH (n = 80)	n = 16	n = 64	
PLR difference (Postop-Preop)	16.93 ± 12.35	13.62 ± 15.95	0.163
NLR difference (Postop-Preop)	6.94 ± 4.60	5.71 ± 10.55	0.207
LH (n = 132)	n = 23	n = 109	
PLR difference (Postop-Preop)	10.46 ± 14.37	6.73 ± 9.75	0.575
NLR difference (Postop-Preop)	4.92 ± 5.72	4.11 ± 6.61	0.789

[a]Mann–Whitney U Test; Data are expressed as mean ± standard deviation; AH — abdominal hysterectomy; LH — laparoscopic hysterectomy; NLR — neutrophil-lymphocyte ratio; PLR — platelet-lymphocyte ratio; Postop — postoperative value; Preop — preoperative value

eration time, smaller surgical scarring, faster recovery time, fewer adhesions, and lower cost [22, 23]. The lower systemic inflammatory response may be the reason for the advantages of laparoscopy [2].

It is reasonable to assume that there is a lower inflammation response in LH. However, no previous study has investigated the response to inflammation in LH. Although NLR and PLR have been studied in many diseases, such as various cancers, inflammatory diseases, and preeclampsia, they have not been evaluated in LH. Our study groups consisted of patients who did not have any disease, did not use medication, and underwent hysterectomy for benign reasons. Therefore, it was crucial to demonstrate WBC, NLR, and PLR changes in these patients.

Animal studies have shown that oophorectomy changed the leukocyte count by altering the cytokine response. Souza et al. reported an increased neutrophil count in the bronchoalveolar lavage fluid in ovariectomized mice [14]. To the best of our knowledge, no similar human study has been conducted. In the present study, the authors found that removal of the ovaries did not affect the changesin inflammatory markers after surgery.

NLR and PLR measurement, unlike other immune mediators such as interleukins, are inexpensive and simple tests in routine practice. Changes in total leukocyte counts (*e.g.*, neutrophilia, lymphopenia, and increased NLR) have been shown to increase mortality and morbidity in cancer patients, cardiovascular diseases, and chronic renal disease [9, 12, 24, 25]. We believe that these values are predictors of postoperative morbidity and mortality. Because morbidity was low in both groups, no difference was found in this respect. It could also be expected that the energy modality used in LH would affect inflammation. Bipolar energy was used in all patients in both groups.

The limitations of our study include its retrospective design. Patients whose data could not be accessed were excluded from the study. Moreover, the number of cases was too small to compare morbidity. Another important point is that in the present study, the LHs were performed by experienced gynecologists, each of whom had more than five years' of experience in this surgical procedure. However, the AH were performed by less experienced gynecologists. This difference in surgical experience could have biased the results of our study. However, the strength of this study is that it is the first in the literature to evaluate the inflammation marker in LH and determine whether oophorectomy affected the results.

CONCLUSIONS

Laparoscopic hysterectomy revealed less postoperative inflammation than AH. This result is demonstrated by inexpensive and straightforward tests in daily practice. The addition of oophorectomy does not increase inflammation in either AH or LH.

Conflict of interest

The authors report no declarations of interest.

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