ORIGINAL RESEARCH

Is it possible to predict Surgical Site Infection?

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Abstract

Introduction

Surgical site infection (SSI) is a widely seen postoperative complication that causes a decrease in life quality and an economic burden. In this study, we aim to find the predictive values of preoperative and postoperative neutrophile lymphocyte ratio (NLR) and platelet lymphocyte ratio (PLR) values for SSI.

Methods

In this retrospective study, 698 patients who had total abdominal hysterectomy operations with benign indications and confirmed histopathological results were accessed. In this study, the correlation of preoperative NLR, preoperative PLR, postoperative NLR, and postoperative PLR, with the occurrence of postoperative surgical site infection complications were examined.

Results

The overall SSI rate was 9.46% (n = 66) with 30 days follow-up postoperatively. Preoperative NLR and PLR values of the patients who had SSIs were significantly lower than the control group ($p < 0.05$). Postoperative NLR and PLR values of the patients who had SSIs were significantly higher than control group ($p < 0.05$). In the patients who had postoperative SSIs, the increase of the values of postoperative NLR and PLR were significantly higher than the control group ($p < 0.05$).

Conclusions

In our study, hematological markers of NLR and PLR were found to be independent and significant predictive markers for SSI.

Key words: Hematological Marker, Lymphocyte, Neutrophile, Platelet, Surgical Site Infections.

Introduction

Surgical site infections(SSIs) are the main cause of nosocomial infections with an incidence of 3-20%[1]. SSIs are the leading cause of nosocomial infection among operated patients and the third cause(14.2%) among all hospitalized patients[2]. SSIs are any incisional infection or any organ/space infection occurring within 30 days of the operation and within 1 year of operation if an implant or prosthetic material was used[2]. Risk factors for SSIs are categorized into two main categories patient-based and operation based. Age, nutritional state, diabetes mellitus, smoking, obesity, spontaneous infection presence, impaired immune system, and preoperative hospital stay length are the patient-based factors whereas operation-based factors are skin antisepsis, preoperative shaving method, preoperative skin preparation, operation duration, antimicrobial prophylaxis, operation room ventilation, nonproper sterilization of surgical instruments, foreign body presence in the surgical sites, drainage usage, and weak surgical techniques.

In our two tertiary medical centers based study, medical records of 698 abdominally hysterectomised patients with benign indications and phannenstiel incisions were evaluated retrospectively. The complication of SSI is still feared and despite the progress in terms of surgical techniques and prevention strategies; their incidence remains high. That is why predictive markers and preventive strategies for SSIs are urgent to find. The aim of the study is to maintain appropriate operation time with the help of preoperative hematological markers and by the help of postoperative hematological markers, to get early diagnosis and early management for SSIs.

Methods

In this study, 698 abdominal hysterectomised patients' medical data collected from 2 different tertiary medical centers between the dates of January 2017 to December 2019 and evaluated retrospectively. The inclusion criteria for the study were to have benign indications, to have pfannestiel incision for the operation, and to have an age above 18 years old. The exclusion criteria for the study were to be a pediatric patient, had a medical history of chemotherapy, radiotherapy, or immunosuppressive therapy, have a supracervical hysterectomy operation, to have an oncological indication, have a blood transfusion during the operation, and to have a mid-line incision.

The demographical features of the patients which are also risk factors for SSIs were evaluated: the patients were evaluated and categorized by the features of age, diabetes mellitus, being a current smoker, body mass index, spontaneous infection, parity number, with the number of previous abdominal operations, education level of the patient, chronic disease presence, preoperative hospital stay length, operation duration, and the presence of surgical drainage. Patients were parted into two main categories to have postoperative SSIs and to not have any. Patients who have not SSIs defined as control group. In our study, SSI was defined as having culture test positivity which was taken from the surgical site within 30 days after the operation and 66 of 698 patients had postoperative SSIs(9.46%). In this study, preoperative and postoperative hematological markers of NLR and PLR were evaluated from the blood tests in the preoperative 30

https://dx.doi.org/10.4314/mmj.v35i3.9

days and postoperative 6th hour respectively.

Antibiotic prophylaxis was applied to the patients in the same procedure: 2 grams of cefazolin sodium in the operation room. If the duration of the operation continues more than 3 hours, second dose was applied. Surgical site skin antisepsis among the patients were standarized. If the patients had diabetes mellitus; they were consulted to nutritionist to have appropriate nutritional status and to have controlled blood sugar levels for the operation.

The patients that had blood transfusion during the operation excluded from the study since it increases infection risk and may cause change in the values of the hematological markers. Supraservical hysterectomies have no contamination with vaginal space so it changes the operation category that is why they were excluded from the study.

All the operations were done with same operational techniques. The number of the practitioners in the operation rooms were same for all the operations and also the sterilization techniques that are used by the stuff were same. The surgical equipment was sterilised using the same procedures for all the operations. Postoperative procedures were also standardised.

University local ethical commitee approval was taken(protocol 2089, 06 December 2019)

Statistics

IBM Statistical Package for Social Sciences (SPSS) Statistics for Windows, version 26 (IBM Corp., Armonk, N.Y., USA) was used for statistical analysis. Data are presented as mean ± standart deviation, frequency and percentage. The normality of data was tested by Kolmogorov–Smirnov test. Comparisons between groups were performed using Mann–Whitney U or Chi-Square tests, and Wilcoxon tests depending on the data distribution. $p < 0.05$ considered statistically significant. ROC curve analysis was performed for calculation of the cut-off value.

Results

The mean age of the patients was 48.6±4.1 (min 20 and max 83 years old) and the mean BMI was 29.3±5.6. An increase in body mass index, operating length, and preoperative hospital stay have a positive correlation with SSI rate (p=0.126, p=0.358, and p=0.951 respectively) although not statistically significant. SSI incidence has a negative correlation with education level of the patients(p=0.064).

Table 1: Impact of Demographical Findings on Surgical Site Infections

		Surgical site infection(+)			Surgical site infection(-)			p
		Avg ±ss /n-%		Median	Avg±ss /n-%		Median	
Age		49.8 ± 7.1		48.0	48.5 ± 7.2		47.0	0.219 m
BMI		30.3 ± 6.2		30.0	29.0 ± 5.6		28.7	0.126 m
Education level	illiterate	17	26.6%		177	27.9%		0.064 x²
	primary school graduate	43	67.2%		364	57.4%		
	high school	4	6.3%		76	12.0%		
	University	0	0.0%		16	2.5%		
	Post graduate	0	0.0%		1	0.2%		
Parity		1.9 ± 1.6		2.0	2.2 ± 1.7		2.0	0.367 m
Current smoker	(+)	26	40.6%		189	29.8%		0.074 x²
	(-)	38	59.4%		445	70.2%		
Comorbidity Presence	(+)	27	42.2%		236	37.2%		0.518 x²
	(-)	37	57.8%		398	62.8%		
Diabetes Mellitus	(+)	10	15.6%		68	10.7%		0.236 x²
	(-)	54	84.4%		566	89.3%		
Secondary Infection Presence	(+)	0	0.0%		2	0.3%		1.000 x²
	(-)	64	100.0%		632	99.7%		
Drainage Presence	(+)	25	39.1%		174	27.4%		0.050 x²
	(-)	39	60.9%		460	72.6%		
Operation History	(+)	21	32.8%		213	33.6%		0.899 x²
	(-)	43	67.2%		421	66.4%		
Operation number		0.5 ± 0.7		0.0	0.5 ± 0.9		0.0	0.662 m
Operation length		165.2 ± 56.4		152.5	156.1 ± 45.0		150.0	0.358 m
Preop hospitalisaton length		1.9 ± 2.4		1.0	1.6 ± 1.5		1.0	0.951 m

m Mann-whitney u test/ x² Ki-kare test

Table 2:The predictive role of NLR- PLR on SSIs

	Surgical Site Infections (+)		Surgical Site Infections (-)		p
	Mean± SD/n-%	Median	Mean±SD/n-%	Median	
Neutrophile Number					
Preop	3.4 ± 1.3	3.0	4.5 ± 1.9	4.1	0.000 m
Postop	23.1± 5.1	23.0	13.3 ± 4.1	13.0	0.000 m
Preop/Postop Change	19.7± 5.2	19.5	8.9 ± 3.7	8.7	0.000 m
	0.000 w		0.000 w		
Platelet Number					
Preop	221.3 ± 54.2	217.0	292.8 ± 79.8	286.0	0.000 m
Postop	409.1± 84.1	413.0	263.4 ± 78.8	254.0	0.000 m
Preop/Postop Change	187.8 ± 95.6	188.5	-29.4 ± 50.4	-28.0	0.000 m
	0.000 w		0.000 w		
Lymphocyte Number					
Preop	2.7 ± 0.5	2.7	2.3 ± 0.7	2.2	0.000 m
Postop	0.6 ± 0.1	0.6	0.8 ± 0.5	0.7	0.000 m
Preop/Postop Change	-2.1± 0.5	-2.1	-1.4 ± 0.7	-1.4	0.000 m
	0.000 w		0.000 w		
NLR					
Preop	1.4 ± 0.9	1.2	2.1 ± 1.1	1.9	0.000 m
Postop	42.5 ± 12.2	40.9	20.4 ± 10.4	19.2	0.000 m
Preop/Postop Change	41.8 ± 19.0	40.5	18.3 ± 10.2	17.4	0.000 m
	0.000 w		0.000 w		
PLR					
Preop	83.7 ± 23.6	79.1	141.2 ± 55.0	130.8	0.000 m
Postop	778.6 ± 236.1	744.8	393.1 ± 194.4	355.9	0.000 m
Preop/Postop Change	694.9 ± 229.3	668.2	212.5 ± 989.5	220.1	0.000 m
	0.000 w		0.000 w		

m: Mann-Whitney u test / w: Wilcoxon test

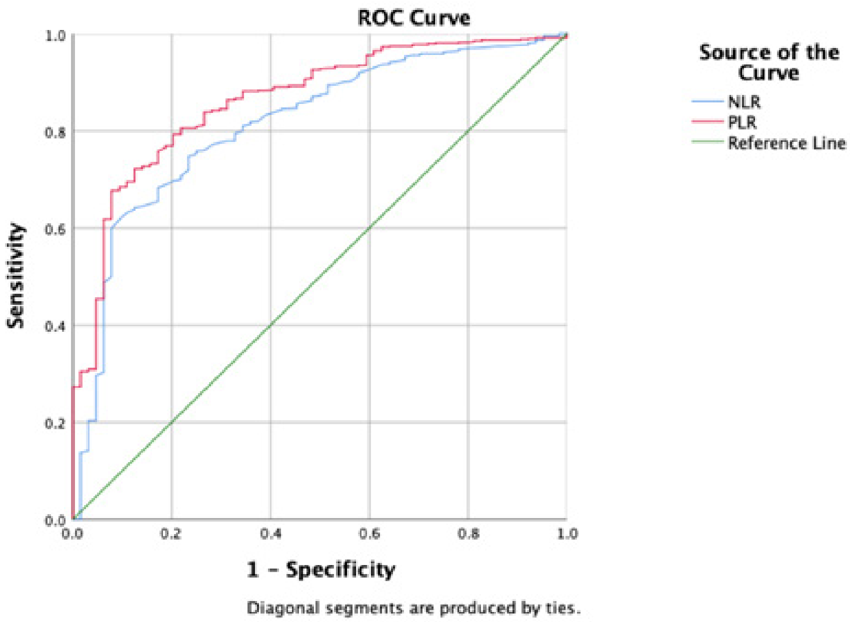

Figure 1. ROC curve for preoperative NLR and PLR to predict surgical site infections

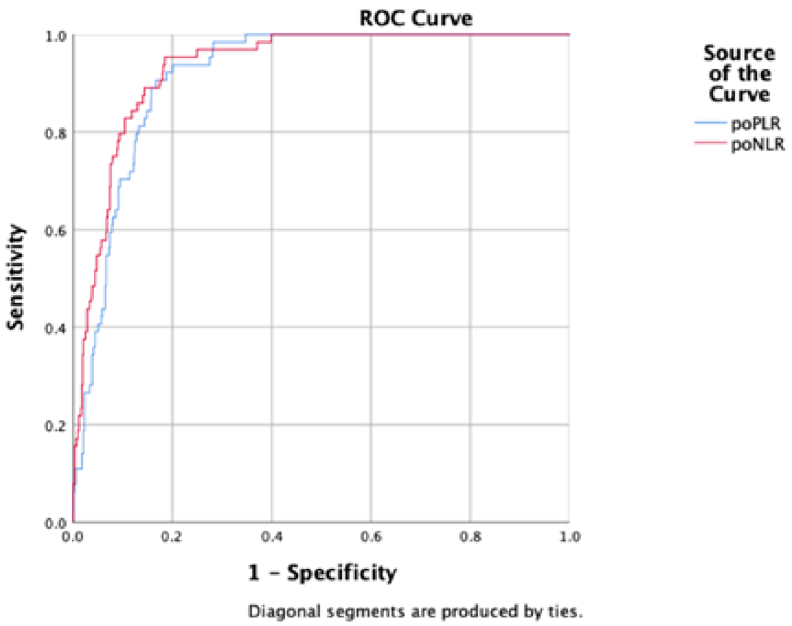

Figure 2. ROC curve for postoperative NLR and PLR to predict surgical site infections

Being a current smoker, the presence of Diabetes Mellitus and drainage presence also have a positive correlation with the occurrence of SSIs (p=0.074,p= 0.236, p=0.050 respectively). No difference was observed in demographic features in terms of SSIs (Table 1)(p>0.05). When the indications of operations were overviewed: it is found that 53% of the hysterectomised patients had the indication of myoma uteri(n=370) followed by medical treatment-resistant vaginal bleeding with a ratio of 24,3%(n=170). Other indications were benign adnexial mass(n=82), endometrial hyperplasia without atypia(n=44), endometrial polyp(n=7), endometrioma(n=8), uterine prolapses(n=4), prophylactic surgery for gene mutations(n=4), dermoid cyst(n=1), hematometry(n=1), HGSIL(n=1), ovarian cyst(n=1), plasenta percreata(n=1), uterine rupture(n=1), overian torsion(n=1), transsexualism(n=1), virilization(n=1).

In our study, 9.46% (n = 66) of the patients were complicated with SSIs postoperatively. 57.58% of these complicated patients were hospitalized (n=38); whereas 42.42% of the patients were treated as outpatient (n=28). The patients that are hospitalized due to SSI were 5.4% of total hysterectomised patients. Preoperative NLR and PLR values of the patients who had SSI were significantly lower than the control group (p<0.001). The mean preoperative NLR of SSI patients was 1.4±0.9 and the mean preoperative PLR of SSI patients was 83.7±23.6. Postoperative NLR and PLR values of the patients who had SSIs were significantly higher than the control group (p < 0.001). The mean postoperative NLR of SSI patients was 42.5±12.2; whereas the mean postoperative PLR of SSI patients was 778.6 ± 236.1. In the patients who had postoperative SSIs, the increase of the values of postoperative NLR and PLR were significantly higher than the control group (p < 0.001) (shown in Table 2).

It is found that there is a reverse association between preoperative NLR and PLR values and SSI; and the optimal cut-offs of preoperative NLR and PLR to predict SSI were 1.645 and 110.170 respectively(NLR AUC=0.814, sensitivity=87.5%, specificity=64.2%; PLR AUC=0.864, sensitivity=85.9%, spesificity=72.7%) (Figure 1).

Calculated NLR and PLR values from the postoperative total blood count evaluated with ROC curve analysis for diagnostic values in terms of prediction of SSI(sensitivity, spesifity, area under the curve). The optimal cut-offs of postoperative NLR and PLR to predict SSI were 28.785 and 527.890 respectively (NLR AUC=0.916, sensitivity=90.6%, specificity=82.3%; PLR AUC=0.933, sensitivity=93.8%, spesificity=80.0%) (Figure 2).

The health system of many countries confronts refugee health problems nowadays. Refugees have fewer economic opportunities and have low hygienic status due to their life standards which make them have high risk for SSIs. There were also hysterectomysed Syrian refugees in this study who had postoperative SSI. Overall the number of operated refugees were 34,7 % of all hysterectomised patients(n=242). 20,24% of these operated refugees had SSI(n=49). When we compare the incidence of postoperative SSI rate between two ethnicity we see more than 2 fold increase in Syrian refugees which may be due to low life qualities(20,24% vs 8,16).

Discussion

NLR and PLR are cheap and easily applicable inflammatory hematological markers. There are lots of studies for using these markers as diagnostical markers in different health areas in the literature, but studies for the usage of them on SSI of abdominal operations are limited. In the animal studies; it is found that neutrophile, platelet, and monocyte values had an important value in terms of wound repair[1].

In our study, we found that NLR and PLR values which are calculated from both preoperative and postoperative total blood counts are independent predictive markers for SSI. Abdominal operations are commonly used treatment options; therefore it is important to deal with the complications. Protective and predictive factors for these complications also have great importance. In fact, we believe that our study not only enlightens the gynecological cases but also all abdominal operations. Since SSI also causes an economic burden on the health economy, finding a predictive marker is substantial[4]. In these terms, there is a need for more extensive studies in this area. Due to the interpretation of our results(which is a new study in this field in terms of

https://dx.doi.org/10.4314/mmj.v35i3.9

its design and findings); in the future, we believe that there would be cut-off values of PLR and NLR for the prediction of the SSIs. If preoperative NLR and PLR values are under this limit values then perhaps the operation would be set for the future date and hematological status would be checked again in that future date. If postoperative NLR and PLR values are above these limit values; then the surgeon would be alerted and the treatment of the patient will start before SSI symptoms occurred.

Incidence shows geographical differences due to economic and social factors. In Sub-Saharan Africa, the prevalence of SSI in hospitals ranges from 6.8-26% whereas the estimated overall risk for SSI is 1.2% of operations in France[3,4]. The prevalence of nosocomial infections is significantly higher in developing countries compared with developed countries[5]. As it is mentioned in the results section; in our study when we compare the incidence of postoperative SSI rate between two ethnicity we see a more than 2-fold increase in Syrian refugees which may be due to low life qualities (20,54% vs 8,16).

In a study, Maruyama et al. evaluate NLR and PLR hematological markers' relation with wound repair on head and neck reconstruction operations[6]. In that retrospective study, the cases are autologous flap transferred patients and their indications were skull base tumors and esophagial cancers. Hematological markers may be changed due to reasons other than SSI since the cases were malign and the patients were immunosuppressive. Maruyama et al. evaluate all the wound impairment cases such as hematoma, wound dehiscence, skin necrosis, and abscess as wound impairment not just SSIs. In this study, 18 women and 59 men's medical data were evaluated and among these 77 patients; 34 patients had incisional dehiscence[6]. Although the study design is different; the end result of the study is similar: preoperative PLR and NLR had a predictive predisposing marker role in the wound impairment.

Platelets and lymphocytes develop from the same hematopoietic stem cells but the lifetime of platelets and lymphocytes are different. Platelets have 20 days length of life cycle; since lymphocytes have nearly 1 month. In the time of abnormal hematopoiesis PLR value would decrease since platelets have a shorter lifetime. There may be many reasons to affect hematopoiesis and one of them is SSI. Maruyama et al. underline abnormal hematopoiesis due to myelosuppression because of malignancy as the reason for the decrease in PLR level[6]. The decrease in thrombopoietin production from the liver is another cause of the decrease in PLR [7]. Another reason is the increase in coagulation due to tissue destruction[8]. Tissue destruction and an increase in coagulation are probably the reasons for the PLR decrease in our study. The decrease in the number or the quality of platelets directly affects wound impairment. That is why a decrease in preoperative PLR values may be an important predictive hematological marker for SSI.

Neutrophiles same as platelets reach to wound site with chemotaxis and leave proteolytic enzymes from the granules to start bactericidal action in an inflammatory period. Same to PLR values decrease in NLR values also impair wound healing[8]. Thus we believe that is the reason of low preoperative NLR values can be predictive in terms of SSIs. Maruyama et al., similar to our study, found that NLR values are significantly lower in the wound impairment group other than in the control cases. Our study had only female cases whereas Maruyama et al deals with both genders. Our study was designed more efficiently way since the effects of gender differences, malignancy, and the state of immunsuppresiveness were eliminated.

The hypothesis of our study is that: there could be the perfect time for every human body to have the operation and that time could be found by preoperative hematological markers: PLR and NLR. It is an easy and cheap way to find if the body is in ideal condition for having an operation. Postoperative PLR and NLR would also give an early prediction about SSIs and will give the chance for early treatment to the clinician before the clinical symptoms arise.

Another study in the literature is done by Rotem et al on cesarean cases between 2012-2016 years in Soroka University Medical Faculty retrospectively[10]. The study included all infections that happened in 6 weeks after the operation; not just SSI. Those infections included endometritis, SSI, mastitis, urinary system infections, sepsis, pneumonia, and infected hematoma. Since the postpartum period is also a complicated period in terms of the immune system and infections; this study has a complex design. Although there could be other factors that could affect the result of the study, at last, it is found that postoperative NLR and PLR are significantly higher in the infected group compared with the control group(11.14 vs. 7.76, 176.52 vs. 149.90, $p < 0.01$)[10]. In our study same with Rotem et al. postoperative NLR and PLR are significantly higher in the surgical site infection group compared with the control group(42.5 vs 20.4, 778.6 vs 393.1, $p<0.05$). In another retrospective case-control study on cesarean delivery by Aktoz et al it is found that WBC; neutrophil count, and NLR levels increased while PLT, and lymphocyte count levels were decreased after cesarean delivery in both SSI and control groups. It is also found that PLR increased after cesarean delivery in the SSI group while remain stable in control group but predictive value is not statistically significant[11].

Another study focuses on predictive values of inflammation markers to predict SSIs following mesh repair of groin hernia. Zhuo et al considers 39 SSIs among the 1177 patients within 1 year postoperatively. ROC curve analysis showed that preoperative NEU, NLR and PLR levels could remarkly predict SSI. The optimal cut-offs of NLR and PLR to predict SSI were 2.44 and 125.42 respectively(NLR AUC=0.875, sensitivity=97.44%, specificity=70.3%; PLR AUC=0.723, sensitivity=74.36%, spesificity=64.24%)[12].

In other studies in the literature; using the hematological markers as predictors was always a dilemma. In a study, NLR was evaluated as a marker for tuba ovarian abscess (TOA) and it is found that NLR could be used as a marker in the prediction of medical treatment failure in TOA patients[13]. In another study, the relation of thrombocytosis between stage and grade in patients with endometrial cancer is evaluated and it is found that there is no correlation between[14], and in a study by Bacanakgil et al it is found that NLR can be used as a potential hematological marker for endometrial malignancy[15].

In the literature, the infected group is limited by just the data of hospitalized patients whereas in our study we included all the outpatient and hospitalized surgical site infected patients' data. In this study, preoperative and postoperative NLR and PLR levels from the same patients were calculated and their predictive values were compared. The patients of the study were chosen by immune stable patients and the indications

https://dx.doi.org/10.4314/mmj.v35i3.9

of the operations were benign. The cases were selected as female to exclude differences in hematological markers due to gender. We believe that this study could be improved by adding more centers(the cases from 2 tertiary centers were included) to the study and by increasing the number of the cases. There should be more studies in this field to have cut-off references. In fact, our study is the first study in the literature that compares preoperative and postoperative NLR and PLR values on the prediction of SSI development and that enlightens the way to predict SSI early and the way to find the individual based right time for the operations.

Conclusion

SSI; other than being a health problem, is also an economic burden. It is important to have a predictive marker to find the right time to operate the patients. It is also important to predict the development of SSI before the clinical signs and to get alerted.

In our study, the aim is to get predictive strength of preoperatively & postoperatively calculated NLR and PLR levels in terms of SSIs independent from other comorbidities and demographical factors. At last it is found that NLR and PLR levels either calculated preoperatively or postoperatively are valuable, remarkable and independent predictive hematological markers for SSI development. These hematological markers are significant to prevent SSI by choosing right operation time and diagnosing SSI earlier among operated patients. For common use; the cut-off levels for these hematological markers should be calculated by making wider multiple center-based studies.

Conflict of Interest

There isn't any conflict of interest by the authors.

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