Risk Factors for Treatment Resistant Postoperative Surgical Site Infections

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Abstract

Aim: Surgical site infection (SSI) is the most common complication seen after surgery. The aim of this study was to determine the risk factors that cause resistance to antibiotic treatment for SSI.

Methods: All patients' records who underwent elective gynecologic surgery between 2021-2023 at the Department of Obstetrics and Gynecology, Kocaeli University were scanned. Patients who had positive surgical site culture were enrolled in the study. Control culture data taken after antibiotic therapy were recorded. The demographic, obstetric and perioperative characteristics were compared between culture negative (control group) and culture positive (study group) patients.

Results: Patients with positive cultures were included in the study. There was a significant difference in terms of chronic medication between the two groups(p=0.002). The duration of hospitalization before SSI development was also significantly higher in the study group(p=0.017). A significant difference was found between the 2 groups in terms of the number of antibiotics used for the treatment of SSI(p=0.027). The use of multi-antibiotic regimens was more common in the study group.

Conclusion: The use of oral antidiabetic drugs and prednisolone was higher and the duration of hospital stay was longer in patients that developed treatment-resistant SSI. The need for multi-antibiotic regimens based on initial culture results was more common in the study group. In order to reduce the incidence of treatment-resistant SSI in patients undergoing planned surgery, a throughout evaluation of the patient is essential. Clinicians should take into consideration the risk of treatment-resistant infection in SSI patients with chronic medication use, long hospital stay, and infections requiring multi-drug regimens.

***Keywords**: Gynecological surgery; surgical site infection; surgical site culture; resistance to antibiotic therapy*

1. Introduction

Every surgeon tries to perform surgery in the best way possible without causing any complications or harm to the patient. However, despite all possible efforts, perioperative or postoperative complications that increase patient morbidity may occur in any surgery. Surgical site infections (SSI) are just one of these complications[1]. SSI is the most common complication after gynecologic surgeries[2] and it has been shown that SSI develops at a rate of 2.7% after hysterectomy[3]. SSIs are superficial or deep infections that occur in the surgical area within one-month postoperatively[4]. Thus, predictors of post-operative SSI after gynecological surgery are of clinical benefit. This will also help when preparing guidelines for future reference[1].

Although defining risk factors for SSI is complex and difficult, there are numerous published studies concerning the risk factors[1,2,5,7]. However, the number of studies examining predictive factors for SSIs resistant to treatment in gynecologic surgery is quite low. When looking at the literature, modifiable factors, such as preoperative anemia, malnutrition, smoking, obesity, hypertension (HT), type 2 diabetes mellitus (DM) and unmodifiable predisposing factors such as age and malignancy have been identified for SSI[4]. If these factors are controlled as well as possible in the preoperative period, the risk of SSI may be reduced. If anemia is present, iron supplementation (or blood transfusion if time is limited), identifying and resolving the cause of malnutrition and applying total parenteral nutrition pre- and postoperatively if necessary, reducing or smoking cessation, ensuring weight loss if body mass index (BMI) is high, controlling HT and DM, using prophylactic antibiotics, and ensuring tissue oxygenation and normothermia in the intraoperative period have been shown to reduce the occurrence rate of SSI[4,8]. In obese patients, it is also recommended not to leave subcutaneous dead space and, if necessary, to use a negative pressure drain in this area[9].

The resistance of SSIs to antibiotics has been less well investigated, Therefore, we aimed to examine and identify the risk factors for patients who develop resistance to treatment which results in

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higher morbidity and mortality rates compared to patients who respond to treatment. If it is known which reasons cause resistance to treatment in patients who develop SSI, the success of the treatment can be achieved by correcting the modifiable factors or increasing attention in the presence of these factors.

2. Materials and Methods

This study was approved by the Kocaeli University non-invasive ethics committee (KU GOKAEK-2024/277). All patients between the ages of 18 and 90 years who underwent elective surgery for benign or malignant gynecological reasons between January 2021 and December 2023 in the Department of Obstetrics and Gynecology, Kocaeli University Hospital, Türkiye, were retrospectively screened for the presence of SSI. Patients who underwent wound culture after developing SSI findings and only those in whom growth was detected were included in the study. In our clinic, 1 g of cefamezin is routinely given to all patients preoperatively and control cultures are routinely taken from patients who are given appropriate antibiotic therapy after SSI. Demographic, obstetric and perioperative data of patients with positive control culture (study group) and patients with negative control culture (control group) were compared.

Table 1

Demographic, obstetric and perioperative data of all patients

	Study Population (n=144)
Age, median (IQR)	53 (40-65)
BMI, median (IQR)	34.75 (29.85-41.45)
Gravidity, median (IQR)	3 (2-4)
Parity, median (IQR)	2 (1-3)
Abortion, median (IQR)	0 (0-0.75)
Number of living child, median (IQR)	2 (1-3)
Postmenopause, n (%)	81 (%56.3)
Hypertension (HT), n (%)	75 (%52.1)
Diabetes mellitus (DM), n (%)	62 (%43.1)
Oral antidiabetic, n (%)	37 (%58.9)
Insulin, n (%)	9 (% 12.5)
Prednisolone, n (%)	3 (%5.1)
Malignancy, n (%)	67 (%46.5)
Use of LMWH, n (%)	117 (%81.3)
Operation time (minutes), median (IQR)	95 (75-133.75)
Blood transfusion, n (%)	18 (%12.5)
First culture growth, n (%)	144 (%100)
Second culture growth, n (%)	49 (%34)

BMI: Body mass index; LMWH: low-molecular-weight heparins; $p<0.05$ is significant.

Patients who had local or systemic infectious symptoms, such as redness, increased temperature, and itching in the area where surgery would be performed before the operation, patients who had a culture taken because of infection in the wound area in the postoperative period but were using antibiotics at the time, and patients who were found to have developed SSI but no positive cultures were found were not included in the study.

The patients' age, BMI, indications for surgery, obstetric and gynecological history, menopause status, comorbidities, medications used, surgical approach types (Pfannenstiel, lower midline incision, midline incision, vaginal and laparoscopic approach), whether postoperative low molecular weight heparin (LMWH) was administered, surgery duration, amount of blood transfusion if administered, whether pathology results were benign or malignant, number of days of hospitalization, wound culture results, and whether secondary suture was required were recorded.

According to the culture results, single, double, triple or quadruple antibiotic combinations were selected according to their antibiograms and based on indicated sensitivities and were used in all patients.

Statistical evaluation was performed using IBM SPSS, version 29.0 (IBM Corp., Armonk, NY, USA). The normal distribution test was evaluated using Shapiro-Wilk and Kolmogorov-Smirnov tests. Numerical variables are given as Mean ± standard deviation, median (25th-75th percentile) and frequency (percentages). Differences between groups/materials were compared using Student's t test, One-way analysis of variance and Tukey's multiple comparison test for numerical variables with normal distribution and Mann Whitney U Test, Kruskal Wallis test and Dunn's multiple comparison test for numerical variables without normal distribution. Fisher's exact chi-square test, Yates' chi-square test and Monte Carlo chi-square test were used for categorical variables to evaluate the differences between groups. The relationship between numerical variables was evaluated using Spearman or Pearson correlation analysis, as appropriate. Logistic regression analysis was performed to determine risk factors for treatment-resistant wound infections. A $p<0.05$ was considered sufficient for statistical significance in two-sided tests.

Table 2

The growth percentages of the agents in the wound culture of all patients are given.

Bacterial Agents	n (%)
Escherichia coli	39 (%22.8)
Enterococcus faecalis	35 (%20.5)
Klebsiella pneumonia	20 (%11.7)
Staphylococcus aureus	13 (%7.6)
Pseudomonas aeruginosa	13 (%7.6)
Enterobacter cloacae	8 (%4.7)
Other Staphylococcus species	22 (%12.8)
Others*	21 (%12.3)

** Other agents included Proteus mirabilis, Morganella morgagni, Streptococcus agalactiae, Serratia marcescens, Klebsiella aeroginosa.*

3. Results

Demographic, obstetric and perioperative data of the patients are given in **Table 1**. A total of 144 patients who developed postoperative SSI and had positive wound cultures were identified. The median (range) age of the patients was 53 (40-65) years, ranging from 22-89 years old. The median BMI was 34.75 (29.85-41.45) kg/m^2 and 105 (72.9%) of the patients were obese (BMI ≥30 kg/m^2). More than half were postmenopausal (n=81, 56.3%). The number of patients with both cultures positive was 49 (34%). **Table 2** shows the percentage of growth of the agents in the wound culture of the patients.

The types of operations performed on the patients are shown in **Table 3**. The most common operation was hysterectomy ± unilateral/bilateral salpingooophorectomy ± bilateral pelvic paraaortic lymph node dissection (BPPALND) ± omentectomy due to malignancy. Histopathological reports confirmed that 67 (46.5%) of the patients were operated on for malignant causes. The median operation time was 95 (75-133.75) minutes.

Table 3

Types of operations performed on patients in both groups.

Operations	n (%)
Hysterectomy ± unilateral/bilateral salpingo-oophorectomy ± BPPLND ± omentectomy (Malignant cause)	68 (%47.2)
Hysterectomy ± unilateral/bilateral salpingo-oophorectomy (Benign cause)	36 (%25.0)
Myomectomy	11 (%7.6)
Oophorectomy (unilateral/bilateral)	5 (%3.5)
Salpingectomy (unilateral/bilateral)	3 (%2.1)
Ovarian cyst excision	8 (%5.6)
Vulvectomy (malignant)	7 (%4.8)
Vaginal hysterectomy ± unilateral/bilateral salpingo-oophorectomy	3 (%2.1)
Other vaginal procedures	3 (%2.1)

BPPLND: bilateral pelvic and paraaortic lymph node dissection.

Table 4

Comparison of demographic, obstetric and medical history data of the patients between the two groups.

		Control group (n=95)	Study group (n=49)	p
Second culture growth, n (%)		0 (%0)	49 (%100)	<0.001
Age, median (IQR)		52 (41-65)	54 (37.5-64.5)	0.835
BMI, median (IQR)		35 (29.4-41)	33.3 (30.2-42.2)	0.647
Obesity, n (%)		67 (%70.5)	38 (%77.6)	0.483
Gravidity. median (IQR)		3 (2-5)	2 (1.5-3)	0.152
Parity, median (IQR)		2 (1-4)	2 (1-3)	0.172
Abortion, median (IQR)		0 (0-1)	0 (0-0.5)	0.973
Number of living child, median (IQR)		2 (1-3)	2 (1-3)	0.189
Postmenopause, n (%)		52 (%54.7)	29 (%59.2)	0.740
Hypertension (HT), n (%)		44 (%46.3)	31 (%63.3)	0.080
Diabetes mellitus (DM), n (%)		36 (%37.9)	26 (%53.1)	0.118
Drugs, n (%)	OAD	17 (%18.0)	20 (%40.9)	0.002
	Insulin	6 (% 6.4)	3 (%6.1)	
	Prednisolone	1 (%1.1)	2 (%4.0)	

OAD: Oral antidiabetics; BMI: Body mass index; p<0.05 is significant.

Demographic, obstetric and history data of the patients are compared between the two groups in **Table 4**. While the number of patients with growth in only the first culture was 95 (66%), the number of patients with growth in both cultures was 49 (34%). No significant difference was found in terms of age, BMI, obstetric data, presence of menopause, HT and DM diagnoses between these two groups. However, there was a significant difference between the groups in terms of chronic drug use (p=0.002).

Table 5 compares the data of the groups in the preoperative and postoperative follow-ups. No significant difference was found in terms of surgical approach. No significant difference was found in terms of being operated on due to malignancy, operation times, blood transfusion requirements and postoperative LMWH use. The median hospital stay before the development of SSI was significantly longer in the study group (p=0.017). A significant difference was found in the number of antibiotics used in the treatment of SSI between the two groups (p=0.027). The use of triple and quadruple antibiotic regimens was more common in the study group. No significant difference was found in terms of the need for secondary sutures.

Table 5

Comparison of peroperative and postoperative follow-up data between the two groups.

	Control group (n=95)	Study group (n=49)	p
Surgical approach, n (%)			
Pfannenstiel incision	19 (%20.0)	12 (%24.5)	
Lower midline incision	23 (%24.2)	11 (%22.4)	0.796
Midline incision	37 (%38.9)	18 (%36.7)	
Vaginal intervention	10 (%10.5)	3 (%6.1)	
Laparoscopic intervention	6 (%6.3)	5 (%10.2)	
Presence of malignancy, n (%)	43 (%45.3)	24 (%49.0)	0.805
Operation time (minutes), median (IQR)	95 (75-130)	100 (75-145)	0.499
Blood transfusion, n (%)			
·1 Unit	6 (%6.3)	4 (%8.2)	
·2 Unit	3 (%3.2)	0 (%0)	
·3 Unit	2 (% 2.1)	0(%0)	0.446
·4 Unit	1 (% 1.1)	1 (%2.0)	
·5 Unit	0(%0)	1 (%2.0)	
Use of LMWH (postoperative), n (%)	75 (%78.9)	42 (%85.7)	0.447
Length of stay (days), median (IQR)	5 (4-9)	8 (4-18.5)	0.017
Antibiotic treatment given according to the first culture, n (%)			
·Single	72 (%75.8)	34 (%69.4)	0.027
·Double combination	18 (% 18.9)	6 (% 12.2)	
·Triple combination	5 (% 5.3)	6 (% 12.2)	
·Quadruple combination	0 (% 0)	3 (% 6.1)	
Secondary suture requirement, n (%)	7 (%7.4)	7 (%14.3)	0.236

LMWH: Low-molecular-weight heparins; p<0.05 is significant.

4. Discussion

SSI, which affects surgical treatment outcomes, is the most common hospital-acquired infection[2]. The incidence of SSI after obstetric and gynecologic surgery is between 4.6% and 10.3%[1,2]. However, defining risk factors for SSI is complex and difficult. Current findings in the literature on risk factors are generally limited due to small sample sizes and poor statistical power[2].

In the present study, and unlike in other studies examining infection risk factors, all patients who had already had growth were included, but the risk factors of patients who had growth in the sec-

ond culture despite appropriate treatment according to identified antibacterial sensitivities were investigated. In a meta-analysis including 13 articles for SSI in gynecology, BMI ≥24, malignant lesions, ≥60 minutes of surgery, ≥300 mL of intraoperative bleeding, urinary catheter retention time and ≥3 vaginal digital examinations were reported as independent risk factors for SSI in obstetric and gynecological surgery[2]. Our findings support these data with nearly three-quarters of our cohort being obese, more than half were operated for malignant reasons and the median surgery time was longer than one hour. However, only 18 (12.5%) patients required blood transfusion. In a study including 206 Caesarean section operations, controlling BMI, shortening the operation time, good bleeding control, and reducing the duration of urinary catheterization were found to be beneficial in preventing SSI[5].

In gynecological operations, incisions are usually applied to the skin, vulva, vagina, umbilical region and other areas where many microorganisms are found. These incisional surgical approaches are significant in terms of infection[2]. The operations with the lowest SSI rate are laparoscopy and sterilization (tubal ligation) surgeries. The highest infection rate was seen in radical and extended hysterectomies. In addition, it has been suggested that vaginal hysterectomy (1%) has a lower SSI incidence than abdominal surgery (5.7%)[10]. Abdominal distension frequently occurs in the early postoperative period and therefore the wound layers are subjected to significant tension. From this perspective, it has been suggested that more frequent use of transverse incisions will greatly reduce the incidence of both hernia and wound infection complications[10]. We also added the types of abdominal incisions applied to the patients and the vaginal approach rates to the study for comparison. However, we found that these differences were not a risk factor in terms of the development of resistance to treatment in SSIs.

The immune system is generally at risk in patients with malignant tumors and SSIs are frequently seen in these patients[2]. However, in the present study, malignancy was not found to be a risk factor for resistance to treatment. It has been reported that HT is not a risk factor for SSI[1,6]. Our results support this as HT was not a risk factor for resistance to treatment. While DM is considered a risk factor for SSI in many studies[11-15], such a finding was not reported others[1,2,6,7,16]. Our findings also suggest that that DM was not a risk factor for SSIs in the study group. When we compared the BMIs and the number of obese patients between the two groups, there was no significant difference and that SSIs were not a risk factor for resistance to treatment. Other studies have also found that high BMI was not a risk factor for SSI[16]. However, the meta-analysis of SSI in gynecological surgery reported that BMI ≥24 kg/m2 conferred a 2.5 greater risk of SSI, BMI >28 a 16-fold increase in risk and and BMI >30 a 7-fold increase in risk[2]. In addition to its anti-inflammatory and hyperglycemic effects, single-dose dexamethasone administration did not increase the risk of SSI (p=0.19)[18]. However, in our study, it was found that chronic prednisolone and oral antidiabetic use was significantly more common in the group that developed treatment-resistant SSI.

The duration of surgery (>1 hour or >1.5 hours) has been identified as a risk factor for SSI in several studies (1,2,5,10). In the present study, the median duration of surgery was calculated as around 1.5 hours. However, when we evaluated the resistance to treatment in SSI by comparing the two groups, no significant difference was found. The hemoglobin value of all patients who underwent surgery was above 10 mg/dL. However, it was observed that some patients had to be transfused with erythrocyte suspension, varying from 1-5 units, in the postoperative period. When the two groups were compared, no significant difference was found in terms of transfusion requirement. When the literature was examined, the need for blood transfusion was given as a risk factor for SSI[1,2], and the need for blood transfusion is common in women with SSI (23.75%)[10]. However, another study stated that the need for blood transfusion was not a risk factor for SSI[16].

Infection is associated with increased hospital stay and therefore increased healthcare costs[2]. Studies have shown that a longer duration of hospitalization is associated with SSI that occurs later[19,20]. Our findings support this in the group that developed treatment-resistant SSI. It has been reported that the proportion of patients who required secondary sutures after SSI was high at 87.7%[4]. In the present study, secondary sutures were needed in only 14 patients and no significant difference was detected between the two groups for this procedure. This suggests that the presence of resistant SSI does not predict the need for secondary sutures.

5. Conclusion

In the present study, chronic drug use, multiple antibiotic treatment and long hospital stay before the development of SSI were evaluated as risk factors for treatment-resistant SSI. Clinicians should consider the possible risk of treatment-resistant infection in SSI patients who have a history of chronic drug use, especially steroids and oral anti-diabetic therapies, having long-term hospital stay pre-operatively and/or with a history of multiple antibiotic treatment regimens

Statement of ethics

This study was approved by the Ethics Committee of Kocaeli University non-invasive ethics committee (KU GOKAEK-2024/277)The study was performed according to the Declaration of Helsinki.

Source of Finance

The authors declare that they have received no financial support for this study

Conflict of interest statement

The authors declare that they have no conflict of interest.

Availability of data and materials

The data supporting the conclusion of this article will be available by the authors without undue reservation.

Author contributions

All authors contributed to the article.

References

1.Bahadur A, Mundhra R, Kashibhatla J, et al. Intraoperative and Postoperative Complications in Gynaecological Surgery: A Retrospective Analysis. Cureus. 2021 May;13(5):e14885. https://doi.org/10.7759/cureus.14885

2.Yang Z, Wang D, Yang M, et al. Risk factors for surgical site infection in Patients undergoing obstetrics and gynecology surgeries: A meta-analysis of observational studies. PLoS ONE. 2024;19(3): e0296193. https://doi.org/10.1371/journal.pone.0296193

3.Lake AG, McPencow AM, Dick-Biascoechea MA, et al. Surgical site infection after hysterectomy. Am J Obstet Gynecol. 2013;209(5):490.e1-9. https://doi.org/10.1016/j.ajog.2013.06.018

4.Uslu Yuvacı H, Aslan MM, Köse E, et al. Obstetrik ve Jinekolojik Operasyonlarda Cerrahi Alan Enfeksiyonları İle İlgili Risk Faktörlerinin Değerlendirilmesi. Online Türk Sağlık Bilimleri Dergisi. 2020;5(1):41-8. https://doi.org/10.26453/otjhs.600815

5.Li L, Cui H. The risk factors and care measures of surgical site infection after cesarean section in China: a retrospective analysis BMC Surg. 2021;21:248. https://doi.org/10.1186/s12893-021-01154-x

6.Shi L, Gu Q, Zhang F, et al. Predictive factors of surgical site infection after hysterectomy for endometrial carcinoma: a retrospective analysis. BMC Surg. 2021 Jun;21(1):292.
https://doi.org/10.1186/s12893-021-01264-6
7.Yang R, Wang L, Shui C. A meta-analysis of the risk factors of surgical site infection after hysterectomy for endometrial cancer. Int Wound J. 2023 Oct;21(2):e14420.
https://doi.org/10.1111/iwj.14420
8.Najjar PA, Smink DS. Prophylactic antibiotics and prevention of surgical site infections. Surg Clin North Am. 2015;95(2):269-83. https://doi.org/10.1016/j.suc.2014.11.006
9.Inotsume-Kojima Y, Uchida T, Abe M, et al. A combination of subcuticular sutures and a drain for skin closure reduces wound complications in obese women undergoing surgery using vertical incisions. J Hosp Infect. 2011;77(2):162-5.
https://doi.org/10.1016/j.jhin.2010.07.016
10.Tayade S, Gangane N, Kore J, et al. Surveillance of surgical site infections following gynecological surgeries in a rural setup – Lessons learnt.Indian Journal of Obstetrics and Gynecology Research, 2019;6(1):58-62.
11.Mortada H, Alwadai A, Bamakhrama B, et al. The impact of diabetes mellitus on breast reconstruction outcomes and complications: a systematic literature review and meta-analysis. Aesthetic Plast Surg. 2023;47(2):570-83.
12.Zhao D, Liang GH, Pan JK, et al. Risk factors for postoperative surgical site infections after anterior cruciate ligament reconstruction: a systematic review and meta-analysis. Br J Sports Med. 2023;57(2):118-28.
13.Xu Z, Qu H, Gong Z, et al. Risk factors for surgical site infection in patients undergoing colorectal surgery: A meta-analysis of observational studies. PLoS One. 2021;16(10):e0259107.
https://doi.org/10.1371/journal.pone.0259107
14.Tuomi T, Pasanen A, Leminen A, et al. Incidence of and risk factors for surgical site infections in women undergoing hysterectomy for endometrial carcinoma. Acta Obstet Gynecol Scand. 2016;95(4):480-5.
15.Inci A, Talmac M, lker V, et al. Risk factors influencing development of surgical site infection inpatients who were operated due to endometrial cancer. Disease and Molecular Medicine. 2016;4(2):13.
16.Löfgren M, Poromaa IS, Stjerndahl JH, et al. Postoperative infections and antibiotic prophylaxis for hysterectomy in Sweden: a study by the Swedish National Register for Gynecologic Surgery. Acta Obstet Gynecol Scand. 2004 Dec;83(12):1202-7.
https://doi.org/10.1111/j.0001-6349.2004.00609.x
17.Arakaki Y, Nakasone T, Kinjyo Y, et al. Surgical site infection in patients with endometrial cancer undergoing open surgery. European Journal of Gynaecological Oncology. 2019;40(4):599–602.
https://doi.org/10.12892/ejgo4501.2019
18. Sanders JC, Russell PK, Tubog TD. Use of Single-Dose Dexamethasone in Patients with Diabetes Undergoing Surgery: A Systematic Review and Meta-Analysis. AANA J. 2023 Jun;91(3):185-93.
19.Koch K, Varga PP, Ronai M, et al. Complication Pattern of Sacral Primary Tumor Resection: A Study on the Risk Factors of Surgical Site Infection and Bowel or Bladder Dysfunction and Their Associations with Length of Hospital Stay. Asian Spine J. 2023 Oct;17(5):851-61.
https://doi.org/10.31616/asj.2022.0404
20. Khan KI, Mahmood S, Akmal M, et al. Comparison of rate of surgical wound infection, length of hospital stay and patient convenience in complicated appendicitis between primary closure and delayed primary closure. J Pak Med Assoc. 2012 Jun;62(6):596-8.