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Research

The Effect of a Checklist for Perioperative Hyperglycemia Management on Surgical Site Infections: A Randomized Controlled Trial

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Keywords:
stress hyperglycemia
surgical site infection
blood glucose level control
normoglycemia

A B S T R A C T

Purpose: This study was conducted to evaluate the effect of managing perioperative normoglycemia using a structured and standardized normoglycemia checklist on surgical site infection (SSI).
Design: The study is a prospective randomized controlled experimental case-control study.
Methods: A normoglycemia checklist was applied to the patients selected for the experimental group preoperatively, intraoperatively, and postoperatively (continuous insulin infusion applied to keep the blood glucose level within the range of 80 to 150 mg/dl until 48 hours postoperative) according to their blood glucose levels. The routine practice available in the clinic was applied to the control group.
Findings: The rate of SSI development in the control group (27.5%) was significantly higher than in the experimental group (2.5%) ($P < .05$). The culture was examined only in patients with deep incisional SSI, and *E. Coli* and Gram (-) Bacillus were the most prolific microorganisms. The risk of re-hospitalization of the control group patients was 2 times higher than the experimental group ($P < .05$).
Conclusions: This study reports the prevalence, diagnosis, and pathophysiology of perioperative hyperglycemia in patients undergoing cholecystectomy and provides a practical method for the management of blood glucose levels in surgery patients diagnosed with diabetes mellitus and developing stress hyperglycemia.

Healthcare-associated infections (HAIs) are acquired by patients when receiving care and are the most common problem affecting patient safety and the quality of healthcare worldwide. Surgical site infection (SSI) is one of the most common HAIs affecting up to one-third of patients who undergo a surgical procedure.[1,2] Although the global burden remains unknown because of the difficulty to gather reliable data, it is estimated that hundreds of millions of patients are affected by HAIs each year, leading to significant mortality and financial losses for health systems.[2,3] The rates of SSIs are much higher in abdominal surgery than in other types of surgery, with several prospective studies[4,5] indicating an incidence of 15% to 25% depending on the level of contamination. Moreover, the endemic burden of SSI is estimated to be significantly (at least 2 to 3 times) higher in low- and middle-income countries than in high-income nations.[2] According to the Infection Control Unit data of the hospital where this study was conducted, there was no SSI rate for the patients who underwent cholecystectomy. However, there was a total of general HAI rates (bloodstream infection, catheter-associated urinary tract infection, ventilator-associated pneumonia) in a 1-year general surgery clinic in 2018 (76%). The prevention of SSI is increasingly important as the number of surgical procedures performed worldwide rises.[6] In recent years it has been estimated that 40% to 60% of SSIs are preventable by the application of evidence-based strategies.[7] Perioperative hyperglycemia is strongly a risk factor for SSI. Therefore, the importance of hyperglycemia management in the prevention of SSI in the perioperative period is emphasized.[6,8,9]

Hyperglycemia due to Diabetes Mellitus (DM) in the perioperative period is considered a stand-alone risk factor for SSI.[8] However, it was determined that stress hyperglycemia occurring in surgical patients without DM is a much more important risk factor for SSI.[9] It is a transient increase in blood glucose level that occurs as a result of normal physiological responses triggered by surgical tissue trauma in patients without DM.[10] The causes of stress hyperglycemia in the perioperative period are high levels of anti-insulin hormones (glucagon, adrenaline, cortisol, and growth hormone) and decreased insulin secretion due to the neuroendocrine response to surgical stress.[11] The reason for the decrease in insulin secretion is that proinflammatory cytokines (TNF-α, IL-1, IL-6) synergistically induce the disruption of insulin signaling, transient insulin resistance, and termination of anabolic processes, and promote increased catabolic activity.[12] In addition, prolonged fasting before surgery may exacerbate the

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condition. Studies[13,14] show that as the perioperative fasting time increases, the catabolic response and insulin resistance increase as well. Furthermore, it was found that mitochondrial protein synthesis, mitochondrial enzyme activity, and oxidative phosphorylation were all stimulated by insulin.[15]

A high blood glucose level reduces the immune response by reducing the chemotaxis of polymorphonuclear leukocytes to the wound site and causing impairment in phagocytic activity.[16,17] Due to increased catabolism, oxidative stress, and inflammatory cytokine release in the body, granulation tissue is impaired, and the formation of SSI is accelerated.[18] In a previous study,[19] it was reported that hyperglycemia (>200 mg/dl), which occurred especially in the preoperative and postoperative 48 hours, increased the formation of SSI.

In the perioperative period, the evidence-based guidelines emphasize the prevention of SSI by controlling hyperglycemia with continuous insulin infusion and the prevention of insulin resistance by keeping the fasting period short.[2,20,21,22] However, the recommendations in the guidelines are often not applied in routine practice.[13]

Team collaboration is needed for the management of hyperglycemia, which is an important parameter in preventing SSI. The nurse in this team plays an important role in perioperative care and the prevention of complications regardless of the nature and type of surgery. Nurses take an active role in the control of blood glucose levels and the management of normoglycemia. The importance of pathways or protocols, which have been created in line with evidence-based guidelines for unity and continuity of practice, enabling nurses who play important roles in such processes to make quick decisions during their applications, is obvious because blood glucose appropriate insulin dose calculation creates an excessive burden on nurses. Therefore, practical glucose management protocols are needed to improve nursing efficiency and productivity.[23] Studies[24,25] have emphasized the importance of developing normoglycemia pathways or protocols as the guidelines not only for nurses but also for all healthcare professionals, helping to make quick decisions in a short time and increasing the quality of patient care. However, there is no applicable perioperative normoglycemia protocol with proven efficacy in individuals with a diagnosis of DM and developing stress hyperglycemia. The purpose of the study was conduct to evaluate the effect of managing perioperative normoglycemia using a structured and standardized normoglycemia checklist on surgical site infection (SSI).

Hypotheses

H_0: The normoglycemia checklist developed has no effect on SSI prevention.

H_1: The normoglycemia checklist developed has an impact on SSI prevention.

Methods

Design

This was a prospective randomized controlled experimental type case-control study. SSI rates vary according to the operation area and size. To control this situation, only patients who underwent cholecystectomy were included in the study. Data were collected from 80 patients having cholecystectomy in the General Surgery Clinic and Operating Room of a university hospital in a city located in Turkey between October 3, 2019 and August 1, 2020.

Study Participants and Sampling

Study inclusion criteria were; (a) patients with a diagnosis of DM or developing stress hyperglycemia (preoperative fasting blood glucose level above 100 mg/dl), (b) patients who underwent elective cholecystectomy only, (c) age of 18 years and over, (d) hospitalization for at least 48 hours in the postoperative period, (e) American Society of Anesthesiologists' (ASA) physical status classification I-III, (f) being conscious, and being a volunteer to participate in the study. Exclusion criteria were; patients with cholecystitis, fasting blood glucose level below 100 mg/dl or exceeding 350 mg/dl at the first measurement, fasting blood glucose level exceeding 350 mg/dl despite the intervention, patients whose fasting blood glucose level could not be kept within the desired range (80 to 150 mg/dl) despite infusion, pregnancy or suspicion of pregnancy, those with liver and kidney failure, those who had a disease that would affect the stomach and intestinal emptying, those with an infection identified preoperatively.

Intravenous blood glucose levels were measured preoperatively (during preoperative anesthesia preparation) in patients who were admitted to the clinic for cholecystectomy. Patients with DM or fasting blood glucose levels above 100 mg/dl in this measurement (stress hyperglycemia) and meeting the inclusion criteria were enrolled in the study. The patients were stratified according to age and surgery type, Body Mass Index (BMI), gender, ASA classification, and the cause of hyperglycemia. Next, the participants were assigned randomly to either the experimental group or the control group using 1:1 block randomization. The assignment was made to the control and experimental groups by someone who was blinded to the study. To verify the homogeneity of the groups after the randomization, the experimental and control groups were compared using the Chi-Square Test according to age and Body Mass Index scores. It was determined that there was no statistically significant difference between the groups and the groups were homogeneous (Table 1).

The required sample size was estimated using G*Power software. Given the study a power of 0.90, it was calculated that at least 30 participants were required in each group. Considering the potential for participant withdrawals during the study, 40 participants were assigned to each group and no individual left the study. The control group received routine clinical care (Figure 1).

Interventions were applied to the patients in the experimental group by the normoglycemia checklist and blood glucose level was kept within the target range (80 to 150 mg/dl). The experimental and control groups were followed up prospectively in terms of SSI by telephone and face-to-face interviews at regular intervals for 30 days postoperatively. Wound assessment was done with the Centers for Disease Control and Prevention[20] definition of SSI.

Interventions

Experimental Group

In the patients assigned to the experimental group, the blood glucose level was followed up using a glucose meter starting from the morning of the surgery according to the blood glucose level measurement scheme (Figure 2). In the experimental group, interventions were applied to the patients preoperatively, intraoperatively, and at the 48th hour postoperatively in the clinic, in line with the normoglycemia checklist (Appendix 1). In patients with a blood glucose level above 100 mg/dl, a continuous insulin infusion was initiated (in cooperation with the physician). The blood glucose level was kept within the target range (80 to 150 mg/dl). To prevent insulin resistance, the fasting period was planned to be between 6 to 8 hours for solid foods and 2 to 4 hours for clear liquids preoperatively, but this practice could not be realized due to institutional problems. In patients diagnosed with DM, oral antidiabetic medication or short-acting insulin preparations were stopped on the day of surgery, and the NPH (Neutral Protamine Hagedorn) dose was reduced by 50%.[26] Surgery was postponed in patients with a blood glucose level above 350 mg/dl. Infusion changes were made according to the normoglycemia checklist in patients using steroids. Only 3

Table 1
Comparison of Demographic Features of Patients in Experimental and Control Groups (N = 80)

Demographic Features	Control Group (n = 40)			Experimental Group (n = 40)			χ^2/ t	P
	n	%	Odds	n	%	Odss		
Type of surgery								
Open	12	30.0	-	12	30.0	-	χ^2 = 0.00	1.000
Laparoscopic	28	70.0		28	70.0			
BMI (kg/m^2)								
Normal = 18-24	5	12.5	-	10	25.0	-	χ^2 = 8.13	.071
Overweight = 25-29	20	50.0		8	20.0			
Obesity = 30 and Above	15	37.5		22	55.0			
Gender								
Female	30	75.0	-	24	60.0	-	χ^2 = 2.05	.152
Male	10	25.0		16	40.0			
Smoking								
Yes	4	10.0	-	13	32.5	-	χ^2 = 6.05	**.014**
No	36	90.0		27	67.5			
Alcohol consumption								
Yes	3	7.5	-	1	2.5	-	χ^2 = 1.05	.305
No	37	92.5		39	97.5			
ASA classification								
ASA I	16	40.0	-	22	55.0	-	χ^2 = 3.33	.189
ASA II	21	52.5		13	32.5			
ASA III	3	7.5		5	12.5			
Cause of hyperglycemia								
DM	7	17.5	-	9	22.5	-	χ^2 = 1.39	.239
Stress hyperglycemia	33	82.5		31	77.5			
Insulin use (DM)								
Yes	5	83.3		4	44.4		χ^2 = 2.27	.132
No	1	16.7		5	55.6			
Albumin level (g/dl)								
Low	14	35.0	2.33	1	2.5	0.111	χ^2 = 13.9	**.000**
Normal	26	65.0		39	97.5			
Hemoglobin level (g/dl)								
Low	12	30	-	7	17.5	-	χ^2 = 1.726	.189
Normal	28	70		33	82.5			
		X ± SD			X ± SD			
Age (years)		58.53 ± 16.71			58.53 ± 16.71		t = 0.000	1.000

ASA, American Society of Anesthesiologists; BMI, body mass index; DM, diabetes mellitus.
Boldface indicates the *P* value is significant.

patients in the experimental group were using steroids and SSI did not develop in these patients. Oral intake was initiated as early as possible to prevent insulin resistance in patients whose bowel movements started by listening to the bowel sounds using a stethoscope postoperatively.

The major complication of insulin infusion is hypoglycemia. Hypoglycemia was accepted when the blood glucose level decreased below 80 mg/dl. During the infusion, patients were checked for symptoms of hypoglycemia (tremor, tachycardia, hypotension, resistance to inotropes, sweating, confusion, agitation, and loss of consciousness). Necessary measures were made in case of hypoglycemia. Another complication of insulin administration is a decrease in potassium (K^+) level. K^+ level was checked at least twice a day, and if there was an increase in the insulin infusion rate, the K^+ level was checked more frequently. If serum K^+ was below 3.5 mmol/l, 10 mEq K^+ IV infusion was performed within 1 hour.[27] There was no patient with low K^+ in the study. Since the insulin given in the infusion solution would lose its effectiveness after 4 hours, the insulin infusion fluid was prepared again every 4 hours. When the researcher was not in the clinic, the practices were continued by two nurses who had been trained before starting the study.

Control Group

No application other than routine clinical practice was performed in the control group preoperatively, intraoperatively, and at the 48th hour postoperatively.

Routine practice in the clinic: In patients diagnosed with DM, blood glucose levels are measured at 4-hour intervals. When the blood glucose level increases above 200 mg/dl in DM patients, insulin is administered subcutaneously. The insulin dose is calculated as 10 units (200-100)/10 = 10 units) for a blood glucose level of 200 mg/dl. If the blood glucose level is above 300 mg/dl, 20 units (300-100)/10 = 20 units) is given as an infusion. During the infusion, the blood glucose level is followed up hourly. There is no practice for determining the blood glucose level in patients without a diagnosis of DM and for treatment in those with high blood glucose levels. Oral intake is discontinued in all patients after midnight preoperatively. In the postoperative period, gas or defecation output is taken as a criterion for starting oral intake.

Data Collection Instruments

The questionnaire was prepared with 16 items for the experimental and control groups, including risk factors affecting the occurrence of SSI, comorbid diseases, and general information in the literature.[3,20]

The normoglycemia checklist was developed by the researchers in line with evidence-based guidelines.[20,21,28] The content of the checklist used in the study was approved by 4 university professors; two from general surgery, one from anesthesiology and reanimation, and one from surgical nursing. The insulin infusion dose was determined in conjunction with a professorial endocrinologist. The normoglycemia checklist (See Appendix 1) includes nursing interventions to prevent

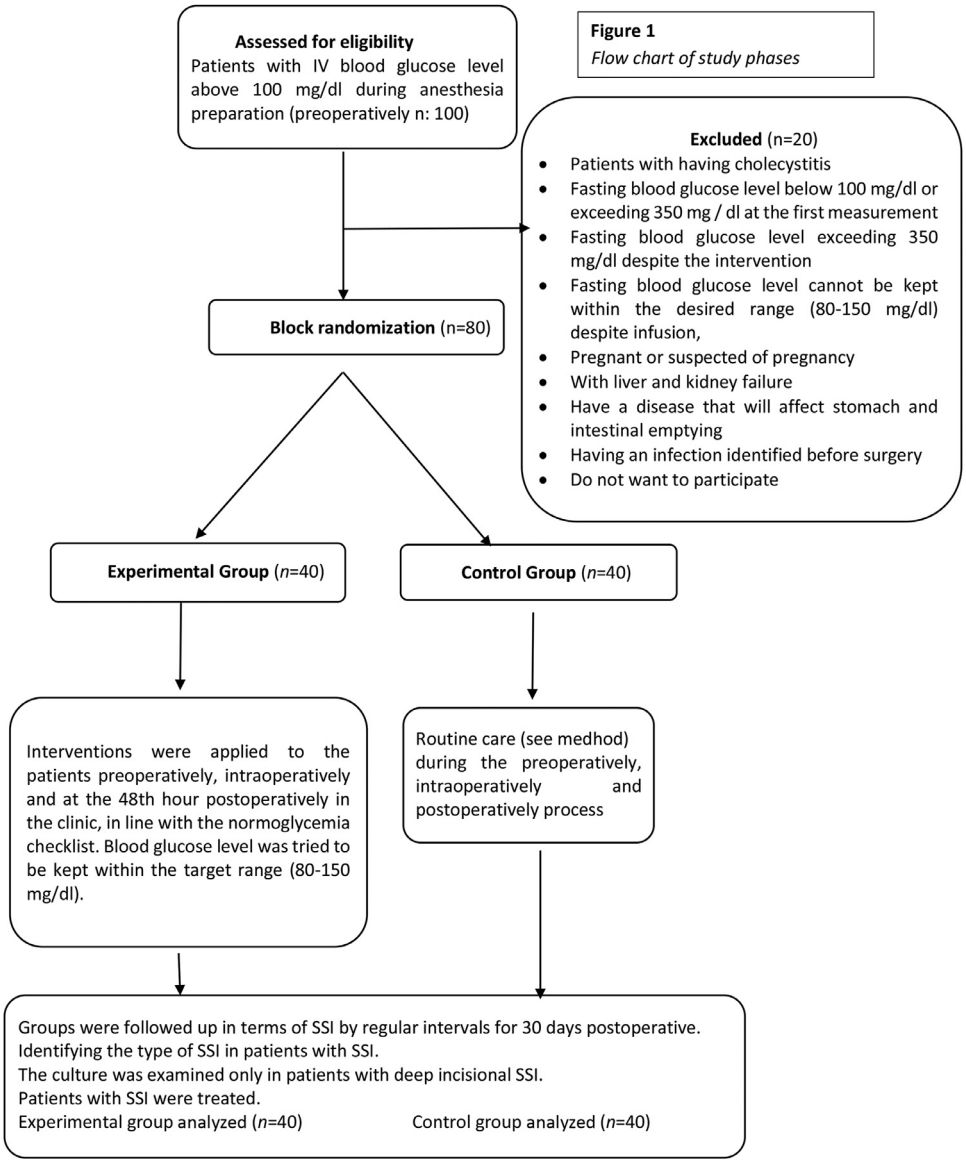

Figure 1. Flow chart of study phases. IV, intravenous; SSI surgical site infection.

hyperglycemia (80 to 150 mg/dl) and provide normoglycemia. Insulin infusion rates were previously evaluated in a study[29] and were shown to achieve the target blood glucose concentrations in more than 70% of patients (See Appendix 2).

Ethical Consideration

Approval was obtained from the Ethics Committee (2019-07/06) of the university located in the city where the study was conducted

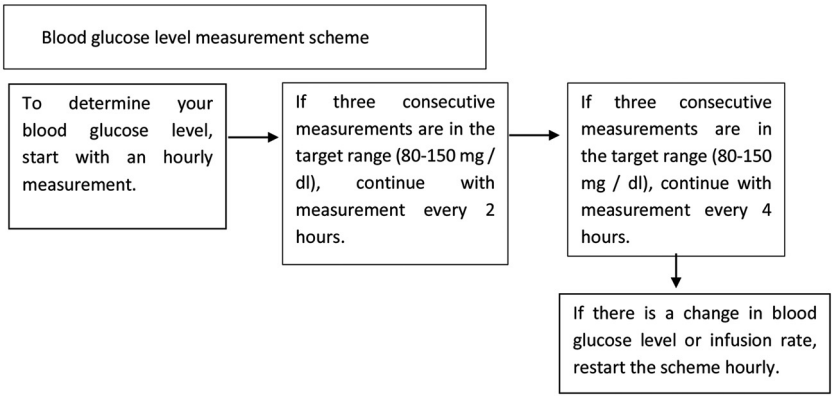

Figure 2. Blood glucose level measurement scheme.

Table 2
Comparison of Patients in the Experiment and Control Groups According to the Development of Surgical Site Infection and Characteristics (N = 80)

Development of SSI and Characteristics	Control Group (n = 40)			Experimental Group (n = 40)			χ^2/ U	*P*
	n	%	Odds	*n*	%	Odds		
SSI								
Development	11	27.5	14.8	1	2.5	2.15	χ^2 = 9.80	**.002**
Did not develop	29	72.5		39	97.5			
The first sign of infection								
Purulent discharge	8	72.7	-	1	100.0	-	χ^2 = 0.36	.546
Fever and discharge	3	27.3		0	0.0			
Types of SSI								
Superficial incisional	5	45.5	-	1	100.0	-	χ^2 = 1.09	.296
Deep incisional	6	54.5		0	0.0			
Organ/space	0	0		0	0			
The most prolific microorganisms								
E. Coli and Gram (-) Bacillus	5	83.3	-	0	0.0	-		_
Staphylococcus aureus	1	16.7		0	0.0			
Re-hospitalization								
Yes	5	12.5	2.14	0	0.0	-	χ^2 = 5.33	**.021**
No	35	87.5		40	100.0			
	X ± SD				X ± SD			
Which day SSI developed	12.73 ± 3.823			8.00 ± 0.000			*U* = 1.50	.333
Postoperative first oral intake (hour)	12.95 ± 1.584			6.45 ± 0.815			*U* = 23.1	**.000**

SSI, surgical site infection.
Boldface indicates the *P* value is significant.

and also from the hospital (93596471-010.99-E.30219). Every stage of the research was conducted according to ethical principles. The researcher fully explained the purpose of the research, the procedures, and the relevant risks and benefits of the intervention to all of the participants. After the participants provided their informed consent, a trained research assistant collected their basic data. Participants were free to withdraw from the study at any time during the study period.

Data Analysis

Data were analyzed using SPSS Version 22.0 (IBM, Inc). Descriptive statistics were used to analyze frequency distributions, percentages, means, and standard deviations. Statistical significance was defined as $P < .05$. Chi-Square Analysis and *t*-test were used as the homogeneity test, the Kolmogorov-Smirnov test was used to determine whether the data were suitable for normal distribution to select the appropriate statistical analyses. The Chi-Square test and the Mann-Whitney U test were used to determine the SSI development status and SSI characteristics between the groups and determine the risk factors for SSI in the control group. Logistic Regression Analysis was used to determine the probabilities (risk coefficients) of the risk factors that might be effective in the occurrence of SSI. Pearson's Product-Moment Correlation Analysis was used to determine the relationship between SSI and blood glucose levels.

Results

During the study, there were no patients who left the experimental and control groups or died. Table 1 shows no difference between the patients in the experimental and control groups in terms of age, surgery type, cause of hyperglycemia, gender, BMI, ASA classification, insulin use, and alcohol consumption, which indicates intergroup homogeneity ($P > .05$). The smoking rate and albumin level in the control group were found to be significantly lower than the experimental group ($P < .05$).

SSI development status and SSI features are shown in Table 2. The rate of SSI development in the control group (27.5%) was significantly higher than in the experimental group (2.5%) ($P < .05$). Deep incisional SSI was higher in the control group, superficial incisional SSI was higher in the experimental group, and the first sign of infection in the groups was purulent discharge. The culture was examined only in patients with deep incisional SSI, and *E. Coli* and Gram (-) Bacillus were the most prolific microorganisms. The risk of re-hospitalization of the control group patients was 2 times higher than the experimental group ($P < .05$). Oral intake was started in a shorter time in the postoperative period in the experimental group, whose oral intake was initiated by listening to bowel sounds in line with the normoglycemia checklist, and no complications were experienced ($P < .05$).

Table 3 shows the comparison of the patients in the control group with and without SSI. Since SSI developed in only one patient in the experimental group, a statistical comparison could not be made. In the control group, it was determined that the majority of the patients who developed SSI underwent open surgery and had re-hospitalizations, did not smoke, had low albumin levels, high ASA classification, and significantly longer time of hospital discharge and suture removal ($P < .05$).

Table 4 shows the comparison of influencing factors with the albumin level of patients. There was a significant relationship between the patients' albumin levels and their high BMI scores. There was no significant relationship between the albumin levels of the patients and the ASA classification, and chronic disease and smoking status.

Table 5 shows the SSI development status according to the blood glucose levels of the experimental and control group patients. Preoperative, intraoperative, and postoperative blood glucose levels were significantly higher in patients who developed SSI in the control group compared to patients who did not. In both groups, the blood glucose level increased the most in the postoperative period, while it tended to decrease in the intraoperative period.

Discussion

In recent years, it has been emphasized that SSI development will increase in direct proportion to the increasing number of surgical operations and that SSI development can be prevented by controlling normoglycemia.[30] The number of studies that provide a better understanding of SSIs is increasing. However, the number of randomized controlled studies examining the effect of hyperglycemia management on SSI is insufficient.[31]

Table 3
Comparison of Postoperative Features of Patients in the Control Group With and Without Surgical Site Infection (n = 40)

Postoperative Features	Surgical Site Infection						χ^2/ U	*P*
	Development			Did not Develop				
	n	%	Odds	*n*	%	Odds		
Type of surgery								
Open	7	66.6	8.40	5	17.2		χ^2 = 8.17	**.004**
Laparoscopic	4	36.4		24	82.8			
Re-hospitalization								
Yes	5	45.5	5.83	0	0.0		χ^2 = 15.065	**.000**
No	6	54.5		29	100.0			
Albumin level (g/dl)								
Low	7	63.6	5.50	7	24.1	-	χ^2 = 5.469	**.019**
Normal	4	36.4		22	75.9			
Smoking								
Yes	2	18.2	-	2	6.9	-	χ^2 = 1.129	**.028**
No	9	81.8		27	93.1			
ASA classification								
ASA I	2	18.2		14	48.3		χ^2 = 9.727	**.008**
ASA II	6	54.5		15	51.7			
ASAIII	3	27.3		0	0.0			
		X ± SD			X ± SD			
Time of suture removal (day)	15.64 ± 5.482			8.69 ± 2.766			*U* = 48.000	**.001**
Time of hospital discharge (day)	4.45 ± 3.205			2.59 ±.733			*U* = 52.500	**.001**

ASA, American Society of Anesthesiologists.
Boldface indicates the *P* value is significant.

The selection of the experimental and control groups and the applied interventions were applied exactly as described in the study protocol. In this study, SSI developed in only one patient in the experimental group, but the percentage of SSI development (27.5%) was found to be quite high in the control group. In the study, according to the risk coefficient, it was determined that the risk of developing SSI postoperatively was 15 times higher in the control group compared to the patients in the experimental group (Odds: 14.79). The practices performed in the experimental group in line with the normoglycemia checklist reduced the risk of developing SSI postoperatively from 27.5% to 2.5%, and the difference between the groups was statistically significant ($P < .05$). According to this result, the **H_1** Hypothesis indicating that "The normoglycemia checklist developed has no effect on SSI prevention" was confirmed. In one study, the incidence of SSI after cholecystectomy was 0.71%,[32] while it was 1.44%[33] in another study. In a study[34] in which postoperative blood glucose control was performed with colorectal surgery patients, it was determined that the SSI rate decreased from 29% to 14%, and it decreased from 14.6% to 5.7%[35] in patients undergoing gynecologic oncology surgery. In this study, it can be said that continuous insulin infusion was effective in preventing SSI for the control of normoglycemia. In another,[36] it was revealed that continuous insulin infusion effectively reduced the incidence of SSI and re-hospitalization compared to intermittent infusion and subcutaneous insulin injection in the control of blood glucose levels. In this study, low K+ levels due to insulin infusion did not develop in patients, and hypoglycemia did not develop except for two patients. According to the study results, we determined that the normoglycemia checklist developed is effective, safe, and usable in controlling blood glucose levels and preventing SSI without causing serious hypoglycemia during the perioperative period in patients with stress hyperglycemia and DM. Furthermore, the checklist can provide application convenience, reliability, and unity in practice by preventing dilemmas in the healthcare team.

Table 4
Comparison of Influencing Factors With Albumin Level of Patients (N = 80)

Preoperative Features	Albumin Level (g/dl)				χ^2/ U	*P*
	Low		Normal			
	n	%	*n*	%		
BMI (kg/m^2)						
Normal = 18-24	1	6.7	14	21.6	χ^2 = 8.48	**.005**
Overweight = 25-29	10	66.7	18	27.7		
Obesity = 30 and above	4	26.6	33	50.7		
Smoking						
Yes	3	20	14	21.5	χ^2 = 0.070	.793
No	12	80	51	78.5		
ASA classification						
ASA I	4	26.7	34	52.3	χ^2 = 2.277	.118
ASA II	9	60	25	38.5		
ASAIII	2	13.3	6	9.2		
Chronic diseases of patients						
None	5	33.3	39	60	χ^2 = 1.304	.257
DM	0	0	1	1.5		
HT	8	53.3	16	24.6		
Heart diseases	1	6.7	7	10.8		
Asthma	1	6.7	0	0		
COPD	0	0	2	3.1		

ASA, American Society of Anesthesiologists; BMI, body mass index; DM, diabetes mellitus; COPD, chronic obstructive pulmonary disease; HT, hypertension.
Boldface indicates the *P* value is significant.

In this study, the patients in the experimental group had a shorter first postoperative feeding period compared to the control group, and the difference between the groups was statistically significant ($P < .05$). In the significant decrease in SSI in the experimental group compared to the control group, the shortening of the postoperative fasting period may have been effective in addition to insulin infusion therapy. Likewise, in a study[37] conducted with patients with DM and undergoing lumbar surgery, it was stated that actively controlling blood glucose level changes and starting a normal diet as soon as possible postoperatively could effectively reduce the risk of SSI.

In this study, a positive correlation was revealed between increased perioperative blood glucose levels and SSI development in the control group patients. We determined that patients with stress hyperglycemia (72.7%) developed SSI at a higher rate than those diagnosed with DM (27.3%), and the difference between them was significant. Moreover, in this study, prediabetes was identified in 3 patients in the experimental group, and they were referred to the endocrine outpatient clinic for diagnosis. In other studies,[3,10,30] hyperglycemia increased the rate of SSI regardless of the diagnosis of DM. In this

Table 5
Comparison of Surgical Site Infection Development According to Blood Glucose Levels of Patients (N = 80)

Blood Glucose Levels (mg/dL)	Surgical Site Infection					
	Development	Did not Develop				
	X ± SD	X ± SD	*U*	*P*	*r*	*P*
Control group (n = 40)						
Preoperative blood glucose levels	171.82 ± 68.32	128.93 ± 22.70	*U* = 77.000	**.009**	+0.440	**.004**
Intraoperative blood glucose levels	137.73 ± 47.19	101.48 ± 20.62	*U* = 72.000	**.008**	+0.484	**.002**
Postoperative blood glucose levels	209.00 ± 53.37	150.31 ± 13.36	*U* = 33.500	**.000**	+0.671	**.000**
Experiment group (n = 40)						
Preoperative min blood glucose levels	130.00 ± 0.00	107.74 ± 8.81	*U* = 1.000	.108	+0.375	**.017**
Preoperative max blood glucose levels	155.00 ± 0.00	139.56 ± 20.19	*U* = 7.500	.297	+0.122	.455
Intraoperative min blood glucose levels	100.00 ± 0.00	83.03 ± 12.65	*U* = 4.500	.193	+0.210	.193
Intraoperative max blood glucose levels	112.00 ± 0.00	97.46 ± 18.36	*U* = 6.000	.242	+0.126	.439
Postoperative min blood glucose levels	135.00 ± 0.00	108.67 ± 13.31	*U* = 1.000	.108	+0.302	.058
Postoperative max blood glucose levels	180.00 ± 0.00	149.10 ± 20.42	*U* = 4.000	.179	+0.236	.143

Max, maximum; Min, minimum.
Boldface indicates the *P* value is significant.

study, the blood glucose level was higher in the experimental and control groups during the postoperative period compared to the preoperative and intraoperative periods. Stress hyperglycemia is evident on the first day after surgery, especially due to postoperative pain and prolonged total fasting time. The observations in our study show that the need for insulin infusion increases postoperatively, especially in the first hours when pain is intense, and this situation gradually returns to normal with the initiation of oral feeding. In a similar study,[38] the blood glucose level was found to be the highest within 24 hours postoperatively. SSI development in patients with stress hyperglycemia at a higher rate may be due to individuals experiencing severe stress to reach the same blood glucose level as the DM patient. However, the routine follow-up of blood glucose levels is not performed in surgery patients, except for patients diagnosed with DM. Therefore, the control and management of blood glucose levels are very important in preventing SSI in all patients during the perioperative period, not focusing only on DM. Furthermore, the follow-up of blood glucose levels during the perioperative period in patients may allow the early recognition of important health problems such as dysglycemia or prediabetes and the application of the necessary treatment.

In this study, preoperative albumin levels were lower in the control group compared to the experimental group patients (<35 g/l). In addition, 63.6% of the patients in the control group who developed SSI had a low preoperative albumin level, and the albumin level <35 g/l created 6 times more risk for SSI development. Likewise, Alkaaki and others[5] found the preoperative albumin level was 36 g/l on average in the group without SSI and 31 g/l in the group with SSI. Peng et al[37] detected a relationship between low albumin levels and SSI in the postoperative period. In this study, low albumin levels had no significant relationship with ASA classification, smoking, and chronic diseases of the patients. However, the albumin level was significantly lower in those with high BMI. Determining and controlling modifiable risk factors that affect SSI formation provide primary prevention for patients. Provision of albumin support preoperatively and postoperatively (secondary prevention) to patients with an albumin level <35g/l determined by primary prevention is important in preventing SSI development. In this study, SSI developed more in patients undergoing open surgery in the control group compared to laparoscopic surgery patients, and the difference was statistically significant ($P < .05$). According to the risk coefficient, it was found that patients undergoing open surgery developed 8.4 times more SSI compared to laparoscopic surgery patients. In the annual report of various countries published by the European Centre for Disease Prevention and Control[36] (ECDC) the rate of SSI development was reported to be 1.5% (0.4 to 3.1) after laparoscopic cholecystectomy and 3.9% (1.1 to 10.9) after open cholecystectomy. Likewise, in studies[5,30] conducted on this subject, open surgery increased the risk of SSI compared to laparoscopic surgery. However, in the report of ECDC,[39] a statistically significant increase was stated in the incidence of SSI after laparoscopic cholecystectomy in recent years. Therefore, it can be said that applying the normoglycemia protocol to patients regardless of the surgery type can be effective in reducing the incidence of SSI.

In this study, only one patient in the experimental group developed superficial incisional SSI, while in the control group, 5 patients (45.5%) developed superficial incisional SSI, and 6 patients (54.5%) developed deep incisional SSI. Similarly, Telli-Dizman[40] and others found that the deep incisional SSI rate (50%) was higher than the superficial incision rate (27%). In other studies,[30,37] on the contrary, the superficial incisional SSI rate was higher than other SSI types. In the report of ECDC,[39] the deep incisional SSI rate was found to be higher in open surgery compared to laparoscopic surgery. Similarly, the rate of SSI was higher in patients who underwent open surgery in our study. In this study, the first sign of infection in patients with SSI was purulent discharge (72.7%), and the most common microorganism at the surgical site was *E. Coli* and Gram (-) Bacillus (83.3%). In other studies[5,30,39] these two microorganisms reproduced at a higher rate after cholecystectomy and abdominal surgery. We found that the suture removal time and discharge time were prolonged, and the risk of re-hospitalization was 6 times higher in the control group patients (15.64 ± 5.482) who developed SSI compared to patients who did not (8.69 ± 2.766). According to the normoglycemia checklist, it can be said that the faster wound healing of the experimental group patients, whose blood glucose level was maintained, shortened the suture removal time, and discharge time. In other studies,[36,41] SSI increased re-hospitalization twice, and keeping the blood glucose level within normal limits decreased re-hospitalization. Perioperative blood glucose control can reduce healthcare costs by preventing SSI.

In the literature, the need for a standard treatment protocol for perioperative hyperglycemia is emphasized.[42] In this study, the effectiveness of the normoglycemia checklist developed for the management of blood glucose levels in patients diagnosed with DM and developing stress hyperglycemia was evaluated. In conclusion, it can be said that this study reports the prevalence, diagnosis, and pathophysiology of perioperative hyperglycemia in patients undergoing cholecystectomy and provides a practical outline for the management of blood glucose levels in surgery patients diagnosed with DM and developing stress hyperglycemia.

Study Limitations and Suggestions

The study's limitations were that the study was conducted on patients hospitalized only in one hospital and undergoing cholecystectomy, the study was completed with a limited number of patients due to the COVID-19 pandemic, and the data collection process was carried out between certain dates. Another limitation was that the HbA1C level of patients without DM was not followed in the routine practice of the hospital. Therefore, an evaluation in terms of HbA1C levels could not be made in the study. Randomized controlled studies with a higher number of patients in different sample groups should be repeated using the normoglycemia checklist. In many countries worldwide, the routine follow-up of blood glucose levels is not performed in surgery patients, except for patients diagnosed with DM; therefore, patients who develop stress hyperglycemia cannot be identified. Rather than focusing only on patients diagnosed with DM, our recommendation is to follow up glucose levels in all patients during the perioperative period, with or without DM diagnosis (stress hyperglycemia), and this should be put into standard practice as a part of the safe surgical checklist.

Conclusion

In conclusion, it can be said that this study reports the prevalence, diagnosis, and pathophysiology of perioperative hyperglycemia in patients undergoing cholecystectomy and provides a practical outline for the management of blood glucose levels in surgery patients diagnosed with DM and developing stress hyperglycemia.

Appendix 1

Normoglycemia Checklist

Normoglycemia Checklist

Preoperative

Blood glucose level measurement scheme
- The blood glucose level is determined hourly.
- If three consecutive measurements are in the target range (80-150 mg/dl), continue with a measurement every 2 hours.
- If three consecutive measurements are in the target range (80-15mg/dl), continue with a measurement every 4 hours.
- If there is a change in blood glucose level or infusion rate, restart the scheme hourly.
- If the blood glucose level is in the critical range (80 mg/dl less or 350 mg/dl more), evaluate it at 30-minute intervals.
- Continue the above scheme in the same way up to 48 hours postoperatively.

Record Measurement time:
Blood glucose level:

-Is the blood glucose level above 100 mg/dl? Yes ☐ No ☐
If yes
-Start a continuous insulin infusion
-If blood glucose is above 350 mg/dl despite infusion, surgery should be postponed.
-K^+ level was checked at least twice a day (Intra- pre and postoperative 48 hr)
-If serum K^+ was below 3.5 mmol/l, 10 mEq K^+ iv infusion was performed within 1 hr

-Was solid food discontinued 6-8 hours before surgery? Yes ☐ No ☐
-Was the fluid discontinued 2-4 hours before surgery? Yes ☐ No ☐
-Does the patient have cancer? Yes ☐ No ☐
-Does the patient take steroid medication? Yes ☐ No ☐

Intraoperative

-Is the blood glucose level above 100 mg/dl? **Yes** ☐ Start continuous insulin infusion or continue existing infusion
Record: Measurement time: **No** ☐ Stop infusion if in the range of 80-100 mg/dl.
Blood glucose level: **No**, If below 65 mg/dl, apply hypoglycemia treatment.
-Is the blood glucose level in the range of 80 Yes ☐ Start anesthesia
-150 mg/dl? No, Adjust your insulin infusion rate before giving anesthesia.
Wound Classification
Clean ☐
Clean-Contaminated ☐
Contaminated ☐
Dirty ☐

Postoperative

-Monitor blood glucose level for the first 48 hours **Yes** ☐ Start continuous insulin infusion or continue existing infusion
-Is the blood glucose level above 100 mg/dl? **No** ☐ Stop infusion if in the range of 80-100 mg/dl.
Record: Measurement time: **No**, If below 65 mg/dl, apply hypoglycemia treatment.
Blood glucose level:
Listen to bowel sounds with a stethoscope, have a bowel movements started? Yes ☐ Start oral intake
Oral intake start time: Post-operative hour No, Keep listening to bowel sounds

Follow-up for 30 Days After Surgery

Are there any signs of surgical site infection? Yes ☐, What is the symptom:
Local pain-tenderness, swelling, redness, warmth No ☐
Discharge at the wound site,
Positive culture result etc.
If yes (What is the type of surgical site infection)
Superficial Incisional ☐
Deep Incisional ☐
Organ / space ☐

Appendix 2

Insulin Infusion Rates for Blood Glucose between 80-150 mg/dl

Blood glucose level mg/dl	1–3 units/hr	> 3 units/hr
<80	Discontinue infusion; Blood glucose level evaluate in 30-minute intervals, * 50 ml dextrose, 50%, IV push; recheck blood glucose in 30 min; inform physician; if blood glucose < 65 mg/dl, * Restart insulin infusion if blood glucose > 150 mg/dl	
80 - 100	Discontinue infusion; recheck blood glucose in 1 hr; if blood glucose > 100 mg/dl, go to the appropriate box below	
101 - 125	If 1-3 units/ hr is applied: Decrease by 2 units/hr from previous insulin infusion rates	If more than 3 units/hr is applied: Decrease the rate to 50% from previous insulin infusion rates
126 - 150	If 1-3 units/hour is applied: Decrease by 1 unit/hr from previous insulin infusion rates	If more than 3 units/hr is applied: Decrease by 2 units/hr from previous insulin infusion rates

Notes. If the patient has a history of diabetes or is currently on steroids when the blood glucose is in the range of 101–150 mg/dl, maintain the same insulin infusion rate. IV: intravenous.[29]

Insulin Infusion Rates for Blood Glucose above 150 mg/dl

Blood glucose level mg/dl	Regular Insulin, Bolus	Regular Insulin, Infusion
151 - 200	No bolus	2 units/h intravenously If necessary increase 1-2 units/ hr
201 - 250	3 units intravenously If necessary increase 1 unit/hr	2 units/h intravenously If necessary increase 2 units/ hr
251 - 300	6 units intravenously If necessary increase 1units /hr	3 units/h intravenously If necessary increase 2 units/ hr
301 - 350	9 units/h intravenously If necessary increase 1 unit/hr	3 units/h intravenously If necessary increase 2 units/ hr

Notes. If restarting insulin infusion drip for blood glucose of 151–200 mg/dl, start at 1 unit/hr.[29]

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