

## Research Article

# Determination of Risk Factors for Community-acquired Skin and Soft Tissue Infections and Comparison of Antibiotics Commonly Used in the Treatment

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## Abstract

**Objectives:** It was aimed to determine the risk factors for the development of skin and soft-tissue infections (SSTI), to compare duration of therapy of mostly used antibiotics and to compare laboratory parameters of complicated and uncomplicated SSTI.

**Methods:** In this study; patients with community-acquired SSTI who were hospitalized and treated in our clinic between November 2010 and October 2014 were evaluated retrospectively. Clinical and laboratory parameters of the patients, and the risk factors predisposing to SSTI were investigated. The patients were grouped into three according to the antibiotic used in treatment (Ampicillin-sulbactam, tigecycline and piperacillin-tazobactam) were the three most commonly used antibiotics in our clinic). Those three antibiotic therapy groups were also compared according to clinical features, laboratory parameters of the patients.

**Results:** In a total of 192 patients, presence of obesity, diabetes mellitus, peripheral vascular disease, saphenectomy, trauma, and tinea pedis were determined as the most common risk factors predisposing to SSTI. In complicated SSTI, the lesions were more deeply located, erythrocyte sedimentation rate and hemoglobin a1c levels were found to be higher, and hemoglobin levels were lower. The duration of hospital stay in patients who were treated with ampicillin/sulbactam was significantly lower than those who received tigecycline and piperacillin/tazobactam. Also, the duration of hospital stay in patients who were treated with tigecycline was significantly lower than those who received piperacillin/tazobactam. The patients with complicated SSTI had significantly higher use of piperacillin/tazobactam compared to tigecycline, which was used more frequently than ampicillin/sulbactam in those patients.

**Conclusion:** Determination of risk factors for the development of SSTI and the risk factors that would cause them to be more complicated are important in both implementation of necessary precautions before their development and initiation of the most appropriate antibiotic treatment in order to decrease morbidity and mortality.

**Keywords:** Complicated, community acquired, risk factors, skin and soft tissue infections, treatment

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Skin and soft tissue infections (SSTIs) can cause severe conditions ranging from limited, localized inflammation in the body to rapidly progressive and life-threatening

necrosis with severe systemic toxicity. In these cases, the clinician should carefully approach the clinical signs and symptoms that may help distinguish inflammatory events

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that are infectious emergencies, require rapid antimicrobial therapy, and require urgent surgical intervention.<sup>[1]</sup>

The first-line approach to evaluating a patient with SSTIs requires careful and detailed anamnesis. In the patient's medical history, whether the patient has recently been exposed to trauma or surgery, drugs used, diabetes mellitus (DM), peripheral vascular diseases, underlying immunosuppressive disease [Human Immunodeficiency Virus (HIV) infection, malignancy, etc.], corticosteroid or other immunosuppressive drug use predisposing factors such as should be questioned.<sup>[2]</sup>

This study analyzed patients diagnosed with SSTIs who were hospitalized and treated in the Infectious Diseases and Clinical Microbiology service between October 2010 and November 2014. This study aimed to compare the demographic characteristics of patients with STI and their clinical features, to identify risk factors that may predispose them to infection, to compare the effects of the most commonly used antibiotics in clinical practice on hospitalization, and to compare the clinical features and laboratory findings of complicated and non-complicated SSTI.

## Methods

This study retrospectively examined the files and epicrisis reports of 192 patients who were followed up and treated at the Infectious Diseases Clinic with the diagnosis of community-acquired SSTIs between 30 November 2010 and 15 October 2014. The patients included in the study were selected among those who were started on ampicillin/sulbactam, tigecycline, and piperacillin/tazobactam treatments, which are the most commonly used parenteral treatments for SSTI in clinical practice. Diagnoses of SSTI, diabetic foot infection (DAE), complicated SSTI, and uncomplicated SSTI were made following the guidelines and literature recommendations.<sup>[3,4]</sup> Patients younger than 18 years of age, pregnant women, concomitant septic arthritis and osteomyelitis, patients with SSTI in the head and neck region, and patients with hospital-acquired SSTI were the exclusion criteria of the study.

The files of 192 patients included in the study were scanned retrospectively. The patients' age, weight, comorbid conditions that may facilitate the development of SSTI, history of hospitalization in the last three months, antibiotic use in the previous month, length of hospitalization, and treatment applied were recorded. The obtained data were recorded in a computer environment. SSTI clinical features, involved area, wound depth, presence of bulla and necrosis, fever, and laboratory parameters [white blood cell (WBC), hemoglobin (Hb), C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), HbA1c] saved to excel form.

The BMIs of the patients were calculated according to the formula  $\text{weight (kg)} / \text{height}^2 (\text{m}^2)$ . Those below  $18.5 \text{ kg} / \text{m}^2$  were underweight, those between  $18.5\text{-}24.9 \text{ kg} / \text{m}^2$  were average weight, those between  $25\text{-}29.9 \text{ kg} / \text{m}^2$  were overweight, those between  $30\text{-}39.9 \text{ kg} / \text{m}^2$  were defined as obese, those over  $40 \text{ kg} / \text{m}^2$  were defined as severely obese (morbidly obese).<sup>[5]</sup>

Suppose the culture was taken from the patients, whether there was reproduction, whether debridement was performed, and the clinical results were recorded. When a clinical and laboratory response was received, patients were discharged with consecutive oral antibiotherapy to reduce hospitalization and associated complications.

## Results

A total of 192 cases, including 102 (53.1%) males and 90 (46.9%) females, were included in the study. The ages of the patients ranged from 18 to 93 years, and the average was  $56.70 \pm 14.99$  Dec. The mean duration of hospitalization was  $9.06 \pm 9.36$  (range: 2-10) days. The distribution of the demographic characteristics of the patients is shown in Table 1.

When the underlying diseases of the patients included in the study were evaluated; 94 (49%) were obese and morbidly obese, 74 (38.5%) had DM, 71 (37%) had hypertension, 33 (17.2%) had coronary artery disease, 16 (8.3%) had CRD, 82 (42.7%) had PAH, 32 (16.7%) had tinea pedis, and immunosuppression was observed in 14 (7.3%) of them. Lymphedema was detected in 10 (11.2%) of the patients participating in the study, a trauma in 16 (18%), saphenectomy in 16 (18%), and congestive heart failure in 8 (9%) of them.

When the wound depth was examined, severe cellulitis was detected in 120 (62.5%), DAE in 41 (21.4%), superficial cellulitis in 29 (15.1%), and abscess in 2 (1%) of the cases. Of the patients, 29 (15.1%) were diagnosed with uncomplicated SSTI, and 163 (84.9%) were diagnosed with complicated SSSTI (Table 2).

Cultures could be taken before antimicrobial treatment in 38 (19.8%) cases. Of the cultured cases, 10 (26.3%) Gram-positive, 10 (26.3%) Gram-negative, and 3 (7.9%) mixed bacterial growths were observed. There was no reproduction in 15 (39.5%) of them.

ESR values of patients with complicated SSTI were statistically significantly higher than those with uncomplicated SSTI ( $p=0.042$ ). Hemoglobin values of patients with complicated SSTIs were statistically significantly lower than those with uncomplicated SSTIs ( $p=0.002$ ). In the complex SSTI group, the HbA1c value was statistically significantly higher than in the uncomplicated SSTI group ( $p=0.001$ ).

**Table 1.** Distribution of demographic characteristics of patients

	Min-Max	Mean±SD		n	%
Age	18-93	56.70±14.99	tinea pedis	32	16.7
Weight (kg)	40-190	85.53±20.48	malignancy	13	6.8
Length (m)	1.50-1.90	1.65±0.08	breast ca	7	53.8
BMI (kg/m <sup>2</sup> )	13.84-57.78	31.49±7.38	endometrium ca	2	15.4
Hospitalization time (days) (Median)	2-10 (7)	9.06±9.36	prostate ca	1	7.7
	n	%	Hematological malignancy	1	7.7
Gender			Lung ca	1	7.7
Male	102	53.1	Other	1	7.7
Female	90	46.9	Another focus of infection	9	4.7
Age groups			lymphangitis	1	11.1
<65 age	129	67.2	Abscess	2	22.2
≥65 age	63	32.8	The respiratory system	3	33.3
BMI			UTI	1	11.1
Underweight	4	2.1	Other	2	22.2
Normal weight	15	7.8	Immunosuppression	14	7.3
Overweight	79	41.1	lymphedema	10	11.2
Obese	72	37.5	COPD	15	16.9
Morbid obese	22	11.5	Trauma	16	18
Underlying disease			previous saphenectomy	16	18
DM	74	38.5	CHF	8	9
Insulin	64	86.5	past operation	4	4.5
OAD	10	13.5	skin disease	4	4.5
Hypertension	71	37	past amputation	6	6.7
CAD	33	17.2	animal bite	1	1.1
CRF	16	8.3	Other	9	10.1
PAD	82	42.7	Hospitalization in the last three months	21	10.9
			Antibiotic use in the last one month	115	59.9

BMI: body mass index, DM: Diabetes mellitus, CAD: Coronary Artery Disease, CRF: Chronic Renal Failure, PAH: Peripheral Arterial Disease, UTI: Urinary tract infection, COPD: Chronic Obstructive Pulmonary Disease, CHF: Congestive Heart Failure, ca: cancer.

(Table 3). When compared in terms of hospitalization times, it was found to be statistically significantly higher in the complicated DYDE group than in the uncomplicated group ( $p=0.009$ ).

Ampicillin/sulbactam was administered to 48 (25%) of the patients, tigecycline to 109 (56.8%), and piperacillin/tazobactam to 35 (18.2%) of the patients. Wound debridement was performed in 15 (7.8%) of the cases. A statistically significant difference was found between the hospitalization times of the subjects according to the type of antibiotic used ( $p=0.001$ ). According to the Tukey HSD test results to determine the difference, The duration of hospitalization of the cases using ampicillin/sulbactam was significantly lower than those using tigecycline and piperacillin/tazobactam ( $p<0.01$  for each). The duration of hospitalization of the cases using tigecycline was also significantly lower than those using piperacillin/tazobactam ( $p=0.005$ ).

## Discussion

The clinical spectrum of SSTIs is wide, ranging from simple impetigo to necrotizing SSTIs accompanied by tissue and organ loss. A folliculitis caused by the same agent may cause a fully localized infection in one patient, while it may cause sepsis in another patient with DM, PAD or immunosuppression. Therefore, when evaluating the patients, a detailed anamnesis should be taken, other accompanying diseases should be questioned, a complete systemic examination should be performed, and parenteral antibiotic therapy should be initiated by hospitalization in case of clinical necessity. In the literature, DM, peripheral vascular disease, CRF, immunosuppression, malignancy, obesity, and trauma have been reported to be the most common risk factors that facilitate the occurrence of SSTI.<sup>[3,4]</sup> In our study, the most common risk factors were obesity, peripheral vascular disease, DM, CKD, and immunosuppression,

**Table 2.** Clinical features of patients with skin and soft tissue infections

	n	%
Wound area		
Cruris	101	52.6
Ankle and Foot	54	28.1
Femoral Region	9	4.7
Upper Extremity	13	6.8
Body	3	1.6
Femoral+Cruris	12	6.3
Wound Classification		
Complicated SSTI (Severe Cellulite)	120	62.5
Uncomplicated SSTI (Superficial Cellulite)	29	15.1
Complicated SSTI (DAE)	41	21.4
Complicated SSTI (Abscess)	2	1.0
Bullous	21	10.9
Necrosis	16	8.3
Complicated SSTI	163	84.9
Antibiotics used in the treatment		
Ampicillin/sulbactam	48	25.0
tigecycline	109	56.8
Piperacillin/tazobactam	35	18.2

which are compatible with the literature.

Obesity describes the weight gain per square meter with the effect of environmental and genetic factors and is a risk factor for many diseases, especially cardiovascular diseases.<sup>[6-8]</sup> The incidence of SSTI (especially dermatophyte infections, intertrigo, infective cellulitis, folliculitis, and other fungal and bacterial infections) is higher in obesity. The excess skin folds of obese patients and the contact of these folds with each other, their humidity, and lack of air cause fungal and bacterial infections.<sup>[9]</sup> Stasis in the venous and lymphatic circulation in the lower extremities also causes the development of recurrent cellulitis and SSTI. In the study of Karpelin et al.; lower extremity edema, disruption of skin barriers, and obesity have been reported as essential risk factors for recurrent cellulitis and SSTI.<sup>[10]</sup> Approximately half of the patients in our study had obesity and morbid obesity, and the most common disease associated with SSTI was obesity.

In the study of Hook et al., it was concluded that blood culture, needle aspiration culture, or skin biopsy is not necessary in mild cellulitis cases without systemic toxicity findings.<sup>[11]</sup> Since 77.6% of the patients included in our study were diagnosed with cellulitis, wound cultures were not taken from them. Instead, cultures were obtained from 19.8% of the remaining 22.4% of non-cellulite patients. A complex flora consisting of Enterococci, Enterobacteriaceae, obligate anaerobes, *Pseudomonas aeruginosa*, and sometimes other

gram-negative non-fermentative bacteria can develop in chronic wounds, and these factors may be causative in SSTI.<sup>[12]</sup> Our study detected gram-positive and gram-negative microorganisms equally in the cultures taken.

SSTI is one of the most common infectious diseases in the community and the most frequent use of antibiotics. In the study of Miller et al., the incidence of SSTI was found to be 47.9% in outpatient and hospitalized patients.<sup>[13]</sup> For treating mild skin and soft tissue infections, penicillin, first or second-generation cephalosporins, macrolides or clindamycin should be used. However, increasing methicillin resistance in community-acquired staphylococcal infections poses a severe threat to our country.<sup>[14]</sup> In a study by Lipsky et al. involving 1033 patients diagnosed with complicated SSTI, the most common risk factors were reported as hospitalization in the last three months and antibiotic use in the previous one month.<sup>[15]</sup> In our study, the rate of patients with a history of hospitalization in the last three months was 10.9%, while the rate of patients using antibiotics during the previous one month was 59.9%. Most patients were treated with tigecycline, which has higher efficacy against methicillin-resistant staphylococcus aureus (MRSA). In our study, piperacillin/tazobactam treatment with high anti-pseudomonal efficacy was initiated significantly more frequently in patients diagnosed with complicated SSTI and diabetic foot. The fact that the HbA1c values of the patients receiving piperacillin/tazobactam treatment were significantly higher than the other patients supports the fact that piperacillin/tazobactam treatment was started more frequently in patients with diabetic foot infection. In our study, it was observed that the hospitalization period of the patients who were started on piperacillin/tazobactam treatment was the longest with an average of 12 days, and the shortest hospitalization period in the patients who were started on ampicillin/sulbactam treatment. This finding supports the initiation of ampicillin/sulbactam therapy in more superficial and uncomplicated patients and piperacillin/tazobactam therapy in complicated patients.

Since the wound depth and the severity of the infection increased in patients with complicated SSTI, the ESR value in our study was significantly higher than in patients with uncomplicated SSTI, as expected. Another result of our research was that the hemoglobin value in complicated SSTI cases was significantly lower than in uncomplicated cases. We think that the reason for this is that comorbid conditions are more common in complicated cases. Because comorbid conditions may be associated with an increased incidence of chronic disease anemia. In the study conducted by Özen G in 237 patients diagnosed with SSTI, the hemoglobin value was found to be low in 54.5% of the patients and high in 82.1% of the ESR patients.<sup>[16]</sup>

**Table 3.** Evaluation of descriptive characteristics and laboratory results in complicated SSTI and uncomplicated SSTI

	uncomplicated SSTI (n=29) Mean±SD (Median)	complicated SSTI (n=163) Mean±SD (Median)	p
Fever (°C)	36.96±1.10 (36.7)	36.92±0.93 (36.6)	<sup>d</sup> 0.853
WBC (/mm <sup>3</sup> )	12262.14±6654.85 (9850)	11609.67±5607.12 (10200)	<sup>e</sup> 0.863
CRP (mg/L)	111.31±97.36 (97)	118.54±91.84 (102)	<sup>e</sup> 0.551
ESR (mm/h)	57.60±28.14 (57)	74.63±29.37 (76)	<sup>e</sup> 0.042*
Hemoglobin (g/dl)	12.90±1.43 (12.9)	11.73±1.81 (11,8)	<sup>d</sup> 0.002**
HbA1c (%)	6.04±0.82 (5.8)	7.30±2.10 (6,4)	<sup>d</sup> 0.001**
Hospitalization (days)	6.62±2.76 (6)	9.49±10.05 (7)	<sup>e</sup> 0.009**
	<b>n (%)</b>	<b>n (%)</b>	
Gender			
Woman	9 (31.0)	81 (49.7)	<sup>c</sup> 0.098
Male	20 (69.0)	82 (50.3)	
Wound Depth			
Cellulite	29 (100)	98 (60.1)	<sup>f</sup> 0.001**
Ulcer Wound	0 (0)	22 (13.5)	
DFE	0 (0)	41 (25.2)	
Abscess	0 (0)	2 (1.2)	
BMI			
Underweight	0 (0)	4 (2.5)	<sup>f</sup> 0.001**
Normal weight	6 (20.7)	9 (5.5)	
Overweight	23 (79.3)	56 (34.4)	
Obese	0 (0)	72 (44.2)	
Extremely Obese	0 (0)	22 (13.5)	
DM	0 (0)	74 (45.4)	<sup>c</sup> 0.001**
HT	8 (27.6)	63 (38.7)	<sup>c</sup> 0.353
CAD	5 (17.2)	28 (17.2)	<sup>b</sup> 1.000
CRF	0 (0)	16 (9.8)	<sup>b</sup> 0.137
PAD	9 (31)	73 (44.8)	<sup>c</sup> 0.240
tinea pedis	8 (27.6)	24 (14.7)	<sup>b</sup> 0.105
malignancy	0 (0)	13 (8)	<sup>b</sup> 0.223
immunosuppression	0 (0)	14 (8.6)	<sup>b</sup> 0.134
COPD	1 (3.4)	14 (8.6)	<sup>b</sup> 0.476
lymphedema	0 (0)	10 (6.1)	<sup>b</sup> 0.364
Trauma	0 (0)	16 (9.8)	<sup>b</sup> 0.137
Prior Saphenectomy	1 (3.4)	15 (9.2)	<sup>b</sup> 0.474
CHF	2 (6.9)	6 (3.7)	<sup>b</sup> 0.347
Bullosa	0 (0)	21 (13)	<sup>b</sup> 0.048*
Hospitalization in the last 3 months	3 (10.3)	18 (11)	<sup>b</sup> 1.000
Ab. use in the last 1 month	18 (62.1)	97 (59.5)	<sup>c</sup> 0.957

<sup>b</sup>Fisher's Exact Test, <sup>c</sup>Yates' Continuity Correction Test, <sup>f</sup>Fisher-Freeman-Halton Test, <sup>d</sup>Student t Test, <sup>e</sup>Mann Whitney U Test, \*p<0.05, \*\*p<0.01; DM: Diabetes mellitus, DFE: Diabetic foot infection, CAD: Coronary Artery Disease, CRF: Chronic Renal Failure, PAD: Peripheral Artery Disease, COPD: Chronic Obstructive Pulmonary Disease, CHF: Congestive Heart Failure.

As a result, It is essential to determine the risk factors in skin and soft tissue infections, which we frequently encounter in clinical practice, to take the necessary precautions to prevent the disease before it occurs and to implement life-

style changes. For example, the regulation of blood glucose and foot care in patients with diabetes, weight loss in overweight patients, and raising awareness of foot care by treating patients with tinea pedis are among these measures

after the disease develops, it should be evaluated whether hospitalization is required by making an early diagnosis, and the patients who have been decided to be hospitalized should also be assessed by evaluating the risk factors and starting the most appropriate antibiotic therapy.

## Limitations

Our study is a retrospective study; only hospitalized patients were included. Of the 192 patients in our study, 29 were diagnosed with uncomplicated SSTI. Antibiotics selected for complicated SSTIs have a broader spectrum of action and a longer hospitalization duration. Therefore, we think multicentric and prospective studies should be carried out on this issue.

## Disclosures

**Ethics Committee Approval:** The local ethics committee obtained ethical approval numbered 89513307/1009/441.

**Peer-review:** Externally peer-reviewed.

**Conflict of Interest:** None declared.

**Authorship Contributions:** Concept – N.A.; Design – N.A.; Supervision – A.B.; Materials – N.A.; Data collection and/or processing – N.A.; Analysis and/or interpretation – N.A., A.B.; Literature search – N.A., A.B.; Writing – N.A.; Critical review – A.B.

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