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Conservative Management of Diabetic Foot Infections: Real-world Outcomes

Diyabetik Ayak Enfeksiyonlarında Konservatif Tedavi: Gerçek Yaşam Sonuçları

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Abstract

Introduction: Diabetic foot infections (DFIs) remain a significant clinical problem despite advances in the treatment of diabetes mellitus. This study aims to contribute to the body of knowledge in this field by evaluating the epidemiological characteristics, treatment processes, and outcomes of patients diagnosed with DFIs.

Materials and Methods: We retrospectively analyzed the characteristics, treatments, and outcomes of patients with DFIs who were admitted between October 2020 and November 2023. All data were analyzed using Statistical Package for the Social Sciences version 22.0, and statistical significance was set at $p < 0.05$.

Results: The mean age of the 129 patients included in the study was 61.27 ± 9.75 years, and 74.4% were male. Overall, 90.7% of diabetic foot ulcers were classified as perfusion, extent/size, depth/tissue loss, infection, and sensation (PEDIS) grades 3 and 4. *Staphylococcus aureus* was the most frequently detected pathogen among patients with positive culture results. Osteomyelitis was detected in 85.3% of the patients, and 55.8% of the cases were treated with antibiotic therapy and/or debridement without amputation. The rate of piperacillin-tazobactam use was higher among patients with osteomyelitis who underwent surgical treatment. A higher rate of surgical treatment was observed in patients with higher PEDIS scores ($p = 0.004$).

Conclusion: The results of our study indicate that most patients recovered with antibiotic therapy and/or debridement without amputation.

Keywords: Amputation, diabetic foot infection, osteomyelitis, treatment

Öz

Giriş: Diyabetik ayak enfeksiyonları (DAE), diyabetes mellitus tedavisindeki ilerlemelere rağmen önemli bir klinik sorun olmaya devam etmektedir. Bu çalışmada, DAE tanılı hastaların epidemiyolojik özellikleri, tedavi süreçleri ve sonuçlarını değerlendirerek bu alandaki bilgi birikimine katkı sağlanması amaçlanmıştır.

Gereç ve Yöntem: Bu retrospektif çalışmada, Ekim 2020-Kasım 2023 tarihleri arasında kliniğimizde DAE tanısıyla yatırılarak takip ve tedavi edilen hastaların demografik, klinik ve laboratuvar verileri, tedavi yöntemleri ve sonuçları kaydedildi. Tüm veriler SPSS 22.0 programı kullanılarak analiz edildi ve istatistiksel anlamlılık düzeyi $p < 0,05$ olarak kabul edildi.

Bulgular: Çalışmaya dahil edilen 129 hastanın yaş ortalaması 61,27 ± 9,75 yıl olup %74,4'ü erkekti. Diyabetik ayak ülserlerinin %90,7'si perfüzyon, yaygınlık, derinlik, enfeksiyon ve duyu (PEDIS) 3 ve 4 idi. Yara yüzeyel sürüntü/derin doku kültür üremesi olan hastalarda en sık *Staphylococcus aureus*

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saptandı. Hastaların %85,3'ünde osteomiyelit saptandı ve olguların %55,8'inin amputasyon uygulanmaksızın antibiyotik tedavisi ve/veya debritman ile tedavi edildiği belirlendi. Cerrahi tedavi uygulanan osteomiyelit hastalarında piperasilin-tazobaktam kullanım oranı anlamlı düzeyde daha yüksekti. PEDIS skoru yüksek olan hastalarda daha yüksek oranda cerrahi tedavi uygulandığı bulundu (p = 0,004).

Sonuç: Çalışmamızın en dikkat çekici sonucu, hastaların çoğunun amputasyon uygulanmadan antibiyotik tedavisi ve/veya debritman ile iyileşmiş olmasıdır. Bu bulgular, ağır DAE ve osteomiyeliti olan hastalarda tedavi stratejilerinin iyileştirilmesine katkıda bulunabilir.

Anahtar Kelimeler: Amputasyon, diyabetik ayak enfeksiyonu, osteomiyelit, tedavi

Introduction

Diabetes affects 828 million adults worldwide, and its age-standardized global prevalence among adults is estimated to be approximately 14%[1]. The prevalence of diabetes mellitus (DM) in Türkiye is rapidly increasing. While the prevalence among individuals older than 20 years was 7.8% in the TURDEP-I study conducted in 2000, it increased to 14–16% in studies conducted in 2009 and 2010[2]. According to the latest data, Türkiye has the second-highest prevalence of diabetes among upper-middle-income countries[3].

Diabetic foot infection (DFI) is one of the major complications of DM. The pathogenesis of DFI is a complex process resulting from the interaction of neuropathy, vasculopathy, immune dysfunction, and secondary infections[4]. According to estimates, 15% of patients with diabetes develop diabetic neuropathy and DFI, a complication of diabetes, at least once during their lifetime[5]. DFI increases the risk of hospitalization by 50-fold compared with that in individuals without diabetes[6]. In 2016, DFI led to more than 130,000 lower-extremity surgeries in the United States. The 5-year mortality rate after amputation is approximately 50%, and the first few years after surgery are considered the period with the highest mortality risk[7,8].

The management of DFI is complex and requires a multidisciplinary approach. Treatment varies depending on whether the infection is limited to soft tissue or whether osteomyelitis is present. Antibiotic therapy and surgical debridement form the cornerstone of treatment in patients with severe infections, and patients often require several weeks of antibiotic therapy along with long-term wound care[9].

The aim of this study is to contribute to the body of knowledge in this field by evaluating the epidemiological characteristics, treatment processes, and outcomes of patients diagnosed with DFI.

Materials and Methods

This retrospective study included patients aged 18 years and older who were hospitalized and received follow-up and treatment for DFI between October 2020 and November 2023. Patients younger than 18 years, pregnant women, patients with wounds caused by other inflammatory conditions, such as trauma, fracture, or thrombosis, and patients with missing data were excluded from the study. Approval for the study was obtained from Necmettin Erbakan University's Ethics Committee (date: 03.11.2023; decision no: 2023/4622). The requirement for obtaining informed consent from individual participants was waived by the Ethics Committee due to the retrospective nature of the study. The patients' age, sex, comorbidities, presence of DM-related complications, medical history, physical examination findings, clinical characteristics, and laboratory findings, including leukocyte count, erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), glycated hemoglobin A1c (HbA1c) levels measured at hospital admission, superficial wound swab/deep tissue culture results, treatment methods, and outcomes, were recorded using a data collection form developed by the researcher based on the literature.

Ulcerative lesions were defined as cellulitis-type infections in which the infection was limited to the skin and subcutaneous tissue, the muscle tissue remained intact, and there were no signs of systemic toxicity or ischemia. Osteomyelitis was diagnosed based on clinical, radiological, and microbiological findings. Plain radiography and/or magnetic resonance imaging were used for radiological evaluation. Acute osteomyelitis was diagnosed based on increasing pain at the base of the ulcer, erythema, increased local warmth, and a sausage toe appearance, whereas chronic osteomyelitis was diagnosed based on persistent or recurrent discharge, a sinus tract, minimal systemic symptoms, and typically mild to moderate pain, along with findings such as cellulitis and lymphangitis[9].

DFIs were classified according to the perfusion, extent/size, depth/tissue loss, infection, and sensation (PEDIS) classification, which is based on five basic features (PEDIS) and has been widely used in recent years[9].

The presence of microbial growth in superficial wound swabs or deep tissue cultures, the type of microorganisms isolated, the antibiotics used for medical treatment and their duration, and the treatment methods applied (vacuum-assisted wound closure, major surgery, or minor surgery) were recorded. Lower-extremity amputations were categorized as minor (at or below the ankle) or major (above the ankle). Microbiological examinations (Gram staining and culture) were performed on debridement or aspiration specimens obtained from the lesions. Clinical samples were cultured on blood agar and eosin methylene blue agar plates. Identification of microorganisms

and antimicrobial susceptibility testing were performed using the VITEK-2 Compact, Phoenix BD100, and M50 automated systems.

Clinical success was defined as improvement in clinical and radiological findings along with laboratory parameters at the end of treatment.

Statistical Analysis

The obtained data were analyzed using IBM SPSS Statistics for Windows, Version 22.0 (IBM Corp., Armonk, NY, USA). In the descriptive analyses, categorical data were presented as frequencies (n) and percentages (%), whereas continuous data were presented as the mean ± standard deviation (SD) and median (minimum–maximum).

The Pearson chi-square (χ^2) test and Fisher's exact test were used to compare categorical variables. The normality of the distribution of continuous data was assessed using the Kolmogorov–Smirnov and Shapiro–Wilk tests. For comparisons of continuous data between two independent groups, the independent-samples t-test was used for parametric data, whereas the Mann–Whitney U test was used for non-parametric data. For comparisons among more than two independent groups, one-way analysis of variance was used for parametric data, whereas the Kruskal–Wallis test was used for non-parametric data. Variables showing statistically significant differences in the Kruskal–Wallis test were evaluated using post-hoc pairwise comparisons with the Mann–Whitney U test, and the Dunn–Bonferroni correction was applied. Results were evaluated at a 95% confidence interval, with statistical significance set at $p < 0.05$.

Results

A total of 129 patients diagnosed with DFI were included in the study. The mean age of the patients was 61.27 ± 9.75 years, and 74.4% (n = 96) were male. Overall, 55.0% (n = 71) of the patients had additional comorbidities and/or at least one diabetes-related complication in addition to DM (Table 1).

Table 1. Demographic and clinical characteristics of the patients.

	Mean ± SD	**Median (min–max)**
Age (years)	61.27 ± 9.75	60 (37–86)
	Number (n)	**Percent (%)**
Gender		
Female	33	25.6
Male	96	74.4
Comorbidity or DM complication*	71	55
Retinopathy	29	22.5
Chronic renal disease	20	15.5
Hypertension	21	16.3
Coronary heart disease	13	10.1
Hyperlipidemia	-	7.5
Cerebrovascular diseases	7	5.4
Presence of an infected ulcer		
No ulcer or sausage finger	15	11.6
0–2 cm open wound + discharge	44	34.1
≥2 cm open wound + discharge	70	54.3
Presence of osteomyelitis		
Ulcered infected lesion	19	14.7
Phalangeal bone osteomyelitis	58	45
Tarsal bone osteomyelitis	52	40.3
PEDIS score		
2	12	9.3
3	60	46.5
4	57	44.2

*, some patients had multiple comorbidities and/or diabetes-related complications; DM, diabetes mellitus, PEDIS, perfusion, extent/size, depth/tissue loss, infection, and sensation; SD, standard deviation; min, minimum; max, maximum.

The most frequent physical examination finding was an open wound measuring ≥2 cm with discharge, which was observed in 54.3% (n = 70) of the patients. When diabetic foot ulcers (DFUs) were classified according to the PEDIS classification, 46.5% of the patients were classified as PEDIS grade 3 and 44.2% as PEDIS grade 4 (Table 1).

Among patients with positive superficial wound swab/deep tissue culture results, *Staphylococcus aureus* was the most frequently isolated microorganism (n = 21, 16.3%) (Table 2). Osteomyelitis was detected in the phalangeal bones in 45.0% (n = 58) of the patients and in the tarsal bones in 40.3% (n = 52). Overall, 55.8% (n = 72) of the patients were treated with antibiotic therapy and/or debridement without amputation. The most frequently used antibiotics were fluoroquinolones, which were prescribed in 72.9% of the cases. The mean duration of antibiotic therapy was 33.6 ± 21.6 days (Table 2).

There was a statistically significant association between an increased ulcer diameter and leukocyte count and the presence of osteomyelitis ($p = 0.043$ and $p < 0.001$, respectively).

Table 2. Distribution of superficial wound swab/deep tissue culture results, antibiotic therapies, laboratory parameters, and treatment durations.

	Number (n)	**Percent (%)**
Wound/deep tissue culture		
Culture not taken or no growth	23	17.8
Polymicrobial	20	15.5
Gram-positive bacteria	45	34.9
Staphylococcus aureus (7 MRSA/14 MSSA)	21	16.3
Coagulase-negative *staphylococci*	12	9.3
Streptococcus pyogenes/Streptococcus agalactiae	3	1.6
Other Gram-positives	9	7.0
Gram-negative bacteria	41	31.8
Enterobacter spp.	14	10.9
Escherichia coli	12	9.3
Pseudomonas aeruginosa	8	6.2
Proteus spp.	5	3.9
Klebsiella spp.	2	1.6
Antibiotic therapy*		
Fluoroquinolones	94	72.9
Teicoplanin	68	52.7
Piperacillin–tazobactam	38	29.5
Meropenem	17	13.2
Linezolid	13	10.1
Amoxicillin	5	3.9
Ceftriaxone	5	3.9
Tigecycline	3	2.3
Cefazolin	3	2.3
Other	11	8.5
Laboratory parameters	**Mean ± SD**	**Median (min–max)**
Leukocyte count ($10^3/\mu L$)	11.70 ± 5.28	10.65 (4–33.4)
Sedimentation rate (mm/h)	60.82 ± 32.11	57 (2–140)
CRP (mg/L)	103.65 ± 88	75 (2–341)
HbA1c (%)	9.61 ± 2.44	9.5 (5–16.7)
Treatment duration (days)	33.64 ± 21.6	28.5 (7–120)

*, multiple antibiotics were administered to many patients; CRP, C-reactive protein; HbA1c, glycated hemoglobin A1c; MRSA, methicillin-resistant *Staphylococcus aureus*; MSSA, methicillin-susceptible *Staphylococcus aureus*; n, number; min, minimum; max, maximum.

Table 3. Comparison of patient characteristics according to diabetic foot ulcer status.

	No ulcers or sausage fingers were present (n = 15)	0–2 cm open wound (n = 44)	≥2 cm open wound + discharge (n = 70)	p-value
Gender n (%)				
Female	3 (20)	10 (22.7)	20 (28.6)	0.683*
Male	12 (80)	34 (77.3)	50 (71.4)	
Age (years) median (min–max)	65 (51–80)	59.5 (37–86)	59.5 (45–85)	0.056**
Comorbidity and/or DM complications n (%)				
Absent	6 (40)	17 (38.6)	35 (50)	0.454*
Present	9 (60)	27 (61.4)	35 (50)	
Presence of osteomyelitis n (%)				
No osteomyelitis or ulcerated infected lesion	4 (26.7)	6 (13.6)	9 (12.9)	<0.001*
Phalangeal osteomyelitis	7 (46.7)	30 (68.2)	21 (30)	
Tarsal osteomyelitis	4 (26.7)	8 (18.2)	40 (57.1)	
Surgical treatment n (%)				-
Medical treatment or medical treatment + debridement	10 (66.7)	22 (50)	40 (57.1)	
Finger amputation	4 (26.7)	20 (45.5)	5 (7.1)	
Amputation including the metatarsal	0	1 (2.3)	5 (7.1)	
Foot amputation	1 (6.7)	0	2 (2.9)	
Below-knee amputation	0	1 (2.3)	18 (25.7)	
PEDIS score				
2	4 (26.7)	5 (11.4)	3 (4.3)	0.054*
3	6 (40)	23 (52.3)	31 (44.3)	
4	5 (33.3)	16 (36.4)	36 (51.4)	
Antibiotic therapy				
Fluoroquinolone	13 (86.7)	37 (84.1)	44 (62.9)	0.020*
Teicoplanin	9 (60)	20 (45.5)	39 (55.7)	0.472*
Piperacillin–tazobactam	3 (20)	7 (15.9)	28 (40.0)	0.016*
Meropenem	1 (6.7)	2 (4.5)	14 (20.0)	0.044*
Linezolid	2 (13.3)	3 (6.8)	8 (11.4)	-
Amoxicillin	1 (6.7)	2 (4.5)	2 (2.9)	-
Ceftriaxone	0 (0)	3 (6.8)	2 (2.9)	-
Tigecycline	0 (0)	0 (0)	3 (4.3)	-
Cefazolin	0 (0)	0 (0)	3 (4.3)	-
Other	1 (6.7)	4 (9.1)	6 (8.6)	-
Laboratory findings				
Leukocyte count ($10^3/\mu L$)	10.5 (6.05–23.0)	9 (4.7–18.03)	11.03 (4–33)	0.043**
Sedimentation rate (mm/h)	53.53 ± 33.79	57.63 ± 33.01	64.41 ± 31.17	0.368***
CRP (mg/L)	43 (4–244)	80 (2–253)	76 (5–341)	0.440**
HbA1c (mmol/mol) mean ± SD	9.44 ± 2.49	9.49 ± 2.20	9.71 ± 2.59	0.861***
Treatment duration (days) median (min–max)	29.0 (15–60)	30 (10–120)	22.0 (7–90)	0.751**

*, Pearson chi-square test; **, Kruskal–Wallis test; ***, One-way analysis of variance; CRP: C-reactive protein; n, number; DM, diabetes mellitus; HbA1c, glycated hemoglobin A1c; min, minimum; max, maximum.

The rate of fluoroquinolone use was lower among patients with open wounds measuring ≥2 cm than among the other groups, whereas the rates of piperacillin–tazobactam and meropenem use were significantly higher (p = 0.020, p = 0.016, and p = 0.044, respectively) (Table 3).

The rate of piperacillin–tazobactam use was significantly higher in patients with osteomyelitis (p = 0.012). No statistically significant differences were observed between the presence of osteomyelitis and treatment duration, leukocyte count, ESR, or CRP level (p > 0.05) (Table 4).

Surgical treatment was performed at a higher rate in patients with higher PEDIS scores (p = 0.004). In addition, the rate of piperacillin–tazobactam use and ESR values were significantly higher among patients who underwent surgery (p = 0.043 and p = 0.044, respectively). No statistically significant differences were observed in sex, age, comorbidities and/or DM-related complications, or HbA1c levels according to whether surgery was performed (p > 0.05).

Discussion

In the coming years, as the prevalence of DM increases, a substantial increase in the incidence of diabetes-related complications, such as DFI, is expected. Given that DFI treatment requires prolonged antibiotic use and considering the global

Table 4. Comparison of patient characteristics according to the presence of osteomyelitis.

	Without osteomyelitis (n = 19)	With osteomyelitis (n = 110)	p-value
Gender n (%)			
Female	8 (42.1)	25 (22.7)	0.090*
Male	11 (57.9)	85 (77.3)	
Age (years) median (min–max)	61 (47–77)	60 (37–86)	0.561**
Comorbidity and/or DM complications n (%)			
None	6 (31.6)	52 (47.3)	0.204***
Yes	13 (68.4)	58 (52.7)	
Surgical treatment n (%)			
Medical treatment or medical treatment + debridement	19 (100)	53 (48.2)	
Finger amputation	-	29 (26.4)	-
Amputation including the metatarsal	-	6 (5.5)	
Foot amputation	-	3 (2.7)	
Below-knee amputation	-	19 (17.3)	
Antibiotic therapy			
Fluoroquinolone	15 (78.9)	79 (71.8)	0.519***
Teicoplanin	9 (47.4)	59 (53.6)	0.613***
Piperacillin–tazobactam	1 (5.3)	37 (33.6)	**0.012***
Meropenem	3 (15.8)	14 (12.7)	0.716*
Linezolid	0	13 (11.8)	0.213*
Amoxicillin	0	5 (4.5)	1.000*
Ceftriaxone	0	5 (4.5)	1.000*
Tigecycline	0	3 (2.7)	1.000*
Cefazolin	0	3 (2.7)	1.000*
Other	0	11 (10)	0.367*
Laboratory findings			
Leukocyte count ($10^3/\mu L$)	8.9 (4–21.3)	10.70 (4.7–33.4)	0.182**
Sedimentation rate (mm/hour)	50.27 ± 34.35	62.63 ± 31.52	0.132****
CRP (mg/L)	65 (4–340)	78 (2–341)	0.396**
HbA1c (mmol/mol)	9.30 (5.7–16.4)	9.60 (5–16.7)	0.218**
Treatment duration (days) median (min–max)	24 (10–53)	29 (7–120)	0.399**

*, Fisher's exact test; **, Mann–Whitney U test; ***, Pearson chi-square test; ****, independent-samples t-test; CRP, C-reactive protein; n, number; DM, diabetes mellitus; HbA1c, glycated hemoglobin A1c; min, minimum; max, maximum.

increase in antibiotic resistance, comprehensive and up-to-date research is needed on the etiology, prognostic factors, and response rates to different antibiotic regimens for DFI.

Being older than 65 years is a known risk factor for the development of DFUs[10]. A global study reported the mean age of patients with DFUs as 61.86 ± 12.10 years[11]. Similarly, an international meta-analysis reported the mean age of patients with DFUs as 61.7 ± 3.7 years[12]. Studies from Türkiye also support this demographic profile. While one study reported the mean age of patients with DFI as 71.5 ± 12 years[13], another multicenter study reported a median age of 61 years[14]. The mean age observed in our study (61.27 ± 9.75 years) is consistent with the published literature, reflecting the global demographic profile of our patient population and supporting the generalizability of our findings.

Studies on DFI consistently show a predominance of male patients. In the study by Lynar et al.[15], the proportion of male patients was reported as 61.3%, whereas another study reported a rate of 76.7%[16]. In our study, 74.4% of the patients were male. These findings support the hypothesis that male sex is a predisposing factor for the development of DFI. This may be explained by greater exposure to outdoor working conditions, poorer adherence to foot care practices, and sex-related lifestyle differences.

Approximately 40–60% of patients with DFUs have chronic kidney disease (CKD). CKD is an established risk factor for the development and recurrence of DFUs and is a significant predictor of adverse outcomes, such as poor healing, amputation, and death[17]. In our study, 15.5% of the patients had CKD.

Significant coronary artery disease (CAD) is observed in approximately 60% of patients with neuroischemic DFUs, and CAD is the leading cause of death in patients with DFUs[17]. Previous studies have also reported that the prevalence of diabetic retinopathy ranges from 22.5% to 95.6% among patients with DFI[18,19]. In our study, retinopathy was detected in 22.5% of the patients, whereas CAD was identified in 10.1%. The finding that 55% of the patients had DM-related complications and/or comorbidities indicates that DFI management involves a complex clinical scenario in which multiple factors can influence treatment outcomes. Therefore, in patients with DFI, the treatment plan should be determined using a multidisciplinary approach that also considers accompanying comorbidities and complications.

Osteomyelitis is present at the time of admission in approximately 20% of outpatients and 40–60% of hospitalized patients with DFI. Therefore, patients with moderate-to-severe infections should be hospitalized, at least initially[20]. In our study, 62.8% (n = 81) of the patients were hospitalized, and osteomyelitis was detected in 85.3% of these patients. Because osteomyelitis is a common and serious complication of DFI, its presence should always be considered in this patient population and evaluated using appropriate diagnostic methods.

Several studies have reported ulcer size and depth as independent risk factors for the development of osteomyelitis, with larger and deeper ulcers being more likely to progress to osteomyelitis[21]. In our study, a statistically significant association was observed between ulcer size and the presence of osteomyelitis ($p < 0.001$). Based on these findings, patients with ulcers measuring ≥2 cm should be evaluated more thoroughly for osteomyelitis.

One study reported that parameters such as ulceration and perfusion, which are included in the PEDIS classification, were significantly associated with amputation and that all patients who underwent major or minor amputation had high PEDIS scores[22]. Similarly, in our study, the rate of surgical intervention was higher among patients with higher PEDIS scores. These findings demonstrate that the PEDIS classification is an important tool for determining the treatment needs of patients with DFI and that high-risk patients should be monitored more closely.

HbA1c levels are closely associated with diabetic complications. Elevated HbA1c levels reflect poor glycemic control and are associated with an increased risk of developing vasculopathy and neuropathy. In the meta-analysis by Tang et al.[23], HbA1c level was reported to be one of the factors predicting the development of DFUs. In our study, HbA1c values >9 measured at the time of DFI diagnosis suggest that patients may be at an increased risk of developing moderate-to-severe DFI.

CRP and ESR are important laboratory parameters used to detect infection and inflammation. CRP is an acute-phase reactant synthesized by the liver, whereas ESR is a non-specific marker of inflammation. Both parameters are widely used in clinical practice for the diagnosis, follow-up, and evaluation of treatment response in various diseases. In one study, the mean CRP values were significantly higher in patients who underwent major or minor amputation than in those who did not undergo amputation[24]. Another study reported that ESR has the highest sensitivity for the diagnosis of DFI and that low ESR values can be used to rule out the diagnosis[25]. In our study, CRP and ESR values were significantly higher in patients who underwent surgery ($p = 0.043$). These results suggest that CRP and ESR may be clinically valuable in predicting the need for surgery in patients with DFI.

In a study conducted at a tertiary care center involving patients with DFI, the most frequently isolated pathogen was *Staphylococcus aureus*; 57% of the isolates were identified as methicillin-susceptible *Staphylococcus aureus* (MSSA) and

43% as methicillin-resistant *Staphylococcus aureus* (MRSA)[26]. Similarly, in our study, *Staphylococcus aureus* was the most frequently isolated microorganism from wound and deep tissue cultures (16.3%), with 66.7% of the isolates identified as MSSA and 33.3% as MRSA. Consistent with data from developed countries, the predominance of Gram-positive bacteria as causative agents in previously untreated patients with DFI may reflect improvements in hygiene standards, foot care practices, and healthcare services in our country. Studies conducted in our country have shown that Gram-negative bacteria generally predominate in the etiology of DFI; however, Gram-positive microorganisms, particularly *Staphylococcus aureus*, also account for a substantial proportion of cases[27]. In our study, *Staphylococcus aureus*, polymicrobial pathogens, *Enterobacter* spp., and coagulase-negative *staphylococci* were identified in descending order of frequency. These findings are consistent with previous reports and support the frequent occurrence of polymicrobial infections in chronic wounds[28,29].

Although amputation has traditionally been the standard approach for moderate-to-severe DFI and osteomyelitis, current evidence supports the effectiveness of antibiotic therapy. Recent randomized controlled trials have demonstrated similar success rates for medical and surgical treatment. In the study by Lázaro-Martínez et al.[30], patients were randomized to an antibiotic group [(AG), n = 24] or a surgical group [(SG), n = 22]. The AG received antibiotic therapy alone, whereas the SG received antibiotic therapy for 10 days following conservative surgery. The primary cure rates were 75.0% in the AG and 86.3% in the SG ($p = 0.33$)[30]. In our study, 55.8% of the patients diagnosed with osteomyelitis achieved clinical success without amputation following antibiotic therapy combined with debridement and/or vacuum-assisted closure therapy.

Moxifloxacin is a broad-spectrum fluoroquinolone indicated for the treatment of complicated skin and soft tissue infections and can be administered intravenously (IV) or orally. In a clinical study evaluating the efficacy of moxifloxacin for the treatment of moderate-to-severe DFI, it was found to be as effective as sequential therapy with amoxicillin-clavulanate followed by IV piperacillin–tazobactam[31]. Currently, because of the availability of orally administered antibiotics with high bioavailability, such as fluoroquinolones, co-trimoxazole, and linezolid, many patients with DFI can be managed on an outpatient basis[9]. In our study, fluoroquinolones, most commonly moxifloxacin, were the most frequently prescribed antibiotics for the treatment of DFI, accounting for 72.9% of cases.

The frequency of resistant pathogens, such as *Staphylococcus aureuss* and *Pseudomonas aeruginosa*, is increasing in DFIs[32,33]. The IWGDF/IDSA recommends the use of oral, narrow-spectrum agents for mild superficial infections and IV broad-spectrum regimens covering Gram-negative and anaerobic microorganisms for moderate-to-severe infections. In deep and/or very large ulcers, the use of IV piperacillin–tazobactam or broad-spectrum agents such as carbapenems is recommended in patients at risk of multidrug-resistant infections[9]. In our study, fluoroquinolones (72.9%), teicoplanin (52.7%), piperacillin–tazobactam (29.5%), and meropenem (13.2%) were the most frequently prescribed antibiotics. However, fluoroquinolone use was lower in patients with ulcers measuring ≥2 cm, whereas the use of piperacillin–tazobactam and meropenem was significantly higher. Similarly, piperacillin–tazobactam use was higher in patients with osteomyelitis who underwent surgical treatment ($p = 0.012$ and $p = 0.043$, respectively). The significantly higher use of piperacillin–tazobactam suggests that broad-spectrum antipseudomonal antibiotic therapy may be particularly beneficial for patients with osteomyelitis requiring major surgery. In patients with moderate-to-severe DFI, because osteomyelitis is more frequently encountered, treatment should be initiated with IV broad-spectrum agents, followed by de-escalation based on culture results.

The recommended treatment duration for osteomyelitis developing after DFI is 4–6 weeks[9], and the mean treatment duration in our study (33.6 ± 21.6 days) appears to be consistent with these recommendations.

Study Limitations

Our study was a single-center, retrospective study. Its retrospective design resulted in some missing or incomplete data.

Conclusion

The most notable finding of our study is that most patients achieved clinical success with antibiotic therapy and/or debridement without undergoing amputation. Although our study contributes to the current epidemiological understanding of DFI, it also provides insights for improving treatment strategies and antimicrobial selection in patients with severe DFI and osteomyelitis.

The prevalence of diabetes is expected to increase in the coming years, and consequently, the incidence of complications such as DFI is also likely to increase. Long-term antibiotic therapy is required for the treatment of DFI. Given the increasing prevalence of antibiotic resistance and the resulting reduction in available treatment options, comprehensive and up-to-date studies are needed on the etiology, prognosis, and response to various antibiotic therapies for DFI.

Ethics

Ethics Committee Approval: Approval for the study was obtained from Necmettin Erbakan University's Ethics Committee (date: 03.11.2023; decision no: 2023/4622).

Informed Consent: The requirement for obtaining informed consent from individual participants was waived by the Ethics Committee due to the retrospective nature of the study.

Footnotes

Authorship Contributions

Surgical and Medical Practices: R.Ç.K., B.K., R.B., İ.E., Concept: B.K., Design: B.K., Data Collection or Processing: R.Ç.K., Analysis or Interpretation: R.Ç.K., B.K., R.B., Literature Search: R.Ç.K., B.K., R.B., Writing: R.Ç.K., B.K., R.B., İ.E.

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