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Clinical and Microbiological Characteristics of Diabetes-Related Foot Infections According to the Presence of Osteomyelitis

ORIGINAL ARTICLE

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ABSTRACT

Objective: This study aimed to compare clinical characteristics, classification scores, microbiological pathogen distribution, and antimicrobial resistance profiles among patients with diabetes-related foot infection according to the presence of osteomyelitis.

Materials and Methods: This retrospective study included adult patients diagnosed with diabetes-related foot infection at a secondary-care hospital between April 15, 2025, and April 15, 2026. Patients were divided into two groups: those with diabetes-related foot infection with concomitant osteomyelitis and those without concomitant osteomyelitis. Demographic data, clinical risk factors, laboratory findings, Site, Ischemia, Neuropathy, Bacterial infection, Area, and Depth (SINBAD) and Wound, Ischemia, and foot Infection (WIfI)/International Working Group on the Diabetic Foot (IWGDF) classification parameters, microbiological growth patterns, and antimicrobial resistance profiles were compared between groups.

Results: A total of 95 patients were included; 49 had osteomyelitis, and 46 did not have osteomyelitis. Recurrent foot infection, previous osteomyelitis, previous peripheral vascular intervention, antibiotic use within the previous month, neuropathy, and isolation of resistant microorganisms were significantly more frequent in the osteomyelitis group, whereas C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR) levels were significantly higher in this group ($p < 0.05$). Antimicrobial resistance was also more frequent in patients with osteomyelitis (59.2% vs. 34.8%, $p < 0.05$). Among culture-positive patients, polymicrobial growth was more common in the osteomyelitis group than in the non-osteomyelitis group (34.7% vs. 16.1%). *Staphylococcus aureus* was the most frequently isolated pathogen in both groups. Multidrug-resistant (MDR) Gram-negative isolates and methicillin-resistant *S. aureus* (MRSA) were numerically more frequent in the osteomyelitis group; however, these differences did not reach statistical significance.

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Conclusion: Osteomyelitis in diabetes-related foot infection was associated with recurrent infection, previous osteomyelitis, peripheral vascular intervention, neuropathy, recent antibiotic exposure, elevated inflammatory markers including CRP and ESR, polymicrobial growth, and increased antimicrobial resistance. These findings support individualized, empirically based treatment decisions informed by prior antibiotic exposure, healthcare-related risk factors, and local microbiological resistance patterns.

Keywords: Diabetic foot, osteomyelitis, antimicrobial resistance

INTRODUCTION

With the increasing prevalence of diabetes, diabetic foot ulcers are being encountered more frequently. It has been reported that infection develops in more than half of patients with diabetes-related foot ulcers, and that amputation is required in approximately 20% of moderate to severe cases (1). Diabetic foot infections most commonly arise in the setting of these ulcers and encompass a broad clinical spectrum, ranging from superficial soft tissue infections to deep tissue infections, osteomyelitis, and necrotizing infections. Due to the wide clinical spectrum, accurate patient assessment and determination of infection severity are critical for planning appropriate treatment strategies. Bone involvement during diabetes-related foot infection is a serious complication associated with an increased risk of amputation, prolonged antibiotic therapy, and hospitalization. Current clinical guidelines recommend systematic classification of infection severity to provide a standardized approach to the management of diabetic foot infections (2–4).

Diabetes-related foot infections are often polymicrobial, and the duration of treatment varies depending on patient-specific factors (5). Complications such as osteomyelitis frequently require prolonged and broad-spectrum antibiotic therapy; however, this approach may contribute to the development of antimicrobial resistance. In addition, patient-specific risk factors may influence the diversity of microbiological pathogens, which limits the suitability of a single empirical treatment approach for all cases (6).

Studies evaluating the relationship between the presence of osteomyelitis and clinical findings, classification systems, and microbiological characteristics in combination are limited in the literature. In particular, the literature needs to better characterize the clinical and microbiological features associated with osteomyelitis. Therefore, in this study, clinical characteristics, risk factors, antimicrobial resistance profiles, and Site, Ischemia, Neuropathy, Bacterial infection, Area, and Depth (SINBAD) and Wound, Ischemia, and foot Infection (WIfI) classification parameters were compared according to the presence of osteomyelitis in patients with diabetes-related foot infection.

MATERIALS AND METHODS

Study Design and Patient Selection

This retrospective study included patients who presented to the outpatient clinic or were hospitalized with a diagnosis of diabetes-related foot infection at a secondary-care hospital between April 15, 2025, and April 15, 2026. Patients with clinically diagnosed diabetes and an infected foot lesion from whom at least one microbiological sample was obtained during the evaluation process were included in the study. Patients were divided into two groups according to the presence of concomitant osteomyelitis: those with diabetes-related foot infection with osteomyelitis and those without concomitant osteomyelitis. Thereafter, these groups were referred to as the osteomyelitis and non-osteomyelitis groups, respectively. The groups were compared in terms of demographic characteristics, clinical risk factors, wound classification parameters, laboratory findings, microbiological pathogen distribution, and antimicrobial resistance profiles.

The unit of analysis for demographic, clinical, laboratory, and classification variables was the individual patient.

In cases where the same patient had multiple hospitalizations or infection episodes, each episode was considered an independent infection, provided that clinical recovery had been achieved after the previous infection and at least 30 days had elapsed, or that a new focus of infection had developed. Previous antibiotic exposure was defined as systemic antibiotic use within one month before admission for the current diabetes-related foot infection episode. Demographic and clinical data were obtained from electronic medical records.

The study was approved by the Non-Interventional Clinical Research Ethics Committee of Aydın Adnan Menderes University Faculty of Medicine on June 18, 2026, with decision no. 2026/240.

Inclusion Criteria

1. Age ≥18 years.
2. Admission to our hospital with a diagnosis of diabetes-related foot infection between April 15, 2025, and April 15, 2026.
3. Having been diagnosed with a diabetic foot infection according to the International Working Group on the Diabetic Foot (IWGDF) criteria and having had the severity of infection graded.
4. Diagnosis of osteomyelitis established in accordance with IWGDF recommendations based on clinical findings, imaging methods (plain radiography or magnetic resonance imaging), and, when necessary, surgical findings or histopathological evaluation results.
5. Availability of an aspiration, deep tissue, or bone sample obtained from the wound for microbiological examination.
6. Availability of sufficient clinical and laboratory data for analysis in electronic medical records.

Exclusion Criteria

1. Age <18 years
2. Absence of an aspiration, deep tissue, or bone sample obtained from the wound site
3. Microorganism isolates considered contaminants or not clinically significant
4. Repeated culture samples from the same infection episode
5. Patients with missing or incorrect clinical or laboratory data
6. Patients presenting with infections or foot lesions other than diabetes-related foot infection
7. Individuals experiencing homelessness
8. Patients with immunodeficiency
9. Patients diagnosed with vasculitis

Diagnosis of Osteomyelitis and Wound Classification

In patients with diabetic foot infection, **wound and infection classifications** were used to evaluate the clinical characteristics and severity of the lesion, as recommended by the International Working Group on the Diabetic Foot/Infectious Diseases Society of America (IWGDF/IDSA) guidelines. Osteomyelitis was diagnosed in accordance with the same guidelines through the combined evaluation of clinical, laboratory, and radiological findings (4,7). Scores were calculated based on the clinical assessment at the time of initial admission.

Surgical Sampling Procedure

Microbiological samples were obtained intraoperatively or at the bedside, depending on the patient's clinical status. Under sterile conditions, any necrotic tissue present in the wound area was debrided using appropriate surgical techniques. Following debridement, deep tissue, aspirate, or bone specimens were collected from the clinically infected area using sterile instruments. Superficial swab cultures were excluded from the analysis. The specimens were transported to the microbiology laboratory under sterile conditions for further analysis.

Microbiological Analysis

From the prepared fluid suspension of the specimen, 0.05 mL was inoculated onto 5% sheep blood agar and MacConkey agar plates using a sterile loop under aseptic conditions. The inoculated plates were incubated aerobically at 35°C and examined for microbial growth after 24 hours. If no growth was observed, the plates were re-incubated and reassessed at 48 hours post-inoculation.

Bacterial identification was performed using conventional biochemical methods. Upon detection of microbial growth, isolates were initially evaluated by Gram staining. Gram-negative organisms were identified based on standard biochemical characteristics, including glucose, sucrose, and lactose fermentation; citrate utilization; motility; urease and indole production; ornithine decarboxylase activity; and oxidase reaction. Gram-positive organisms were identified according to catalase activity, hemolytic patterns, coagulase production, susceptibility to optochin, bacitracin, and trimethoprim-sulfamethoxazole, as well as growth on bile esculin agar and in media containing 6.5% sodium chloride. Anaerobic cultures could not be performed.

Microbiological pathogen distribution and antimicrobial resistance profiles were evaluated on an isolate basis. Because more than one microorganism could be isolated from patients with polymicrobial growth, the number of isolates exceeded the number of patients.

Antibiotic Susceptibility Testing

Bacterial identification was performed using conventional biochemical methods. Antimicrobial susceptibility testing was performed and interpreted according to European Committee on Antimicrobial Susceptibility Testing (EUCAST) guidelines. Methicillin-resistant *Staphylococcus aureus* (MRSA) was identified using the cefoxitin disk diffusion method in accordance

with EUCAST criteria. Ampicillin-resistant enterococci were identified according to EUCAST breakpoints (8).

Extended-spectrum beta-lactamase (ESBL)-producing isolates were defined, in accordance with EUCAST recommendations, as isolates showing reduced susceptibility to third-generation cephalosporins and, when necessary, confirmed phenotypically. The presence of inducible beta-lactamase (IBL), including AmpC beta-lactamase, was evaluated according to EUCAST expert rules and susceptibility patterns (8).

Multidrug-resistant (MDR) microorganisms were defined as isolates resistant to at least three different antimicrobial classes, in accordance with the criteria recommended by the European Centre for Disease Prevention and Control (ECDC) and the Centers for Disease Control and Prevention (CDC) (9,10).

Statistical Analysis

The assumption of normal distribution for quantitative variables was assessed using the Kolmogorov-Smirnov test. Descriptive statistics were presented as mean ± standard deviation for normally distributed quantitative variables, median (25th–75th percentile) for non-normally distributed variables, and frequency (%) for categorical variables. For independent group comparisons, the independent samples t-test was used for normally distributed variables, and the Mann-Whitney U test was used for non-normally distributed variables. Associations between categorical variables were evaluated using the chi-square test. A p value of < 0.05 was considered statistically significant.

RESULTS

Osteomyelitis was detected in 49 of the 95 patients included in the study, while 46 patients had no evidence of osteomyelitis. Patients were divided into two groups according to the presence of osteomyelitis and analyzed accordingly.

When categorical variables were examined, the rate of recurrent foot infection in the osteomyelitis group (77.6%) was significantly higher than that in the non-osteomyelitis group (52.2%) (p = 0.009). The proportion of patients with a previous history of osteomyelitis was significantly higher in the osteomyelitis group (53.1%) than in the non-osteomyelitis group (13.0%) (p < 0.001). In addition, the rate of previous peripheral vascular intervention was significantly higher in the osteomyelitis group (69.4%) than in the non-osteomyelitis group (28.3%) (p < 0.001). The rate of antibiotic use within the previous month was also significantly higher in the osteomyelitis group (91.8%) than in the non-osteomyelitis group (76.1%) (p = 0.035). Detailed data for all variables are presented in Table 1.

The neuropathy rate was significantly higher in the osteomyelitis group (85.7%) than in the non-osteomyelitis group (61.4%) (p = 0.07). The rate of antimicrobial resistance was also significantly higher in the osteomyelitis group (59.2%) than in the non-osteomyelitis group (34.8%) (p = 0.017). When laboratory

Table 1. Demographic and clinical characteristics of patients with diabetes-related foot infection according to the presence of osteomyelitis.

	Without osteomyelitis	With osteomyelitis	*p*	Achieved power (1–β)
Age	66.15 ± 9.90	62.43 ± 10.87	0.085	-
Sex				
Male	31 (67.4)	37 (75.5)	0.381	-
Female	15 (32.6)	12 (24.5)		
Type of diabetes				
Type 1	1 (2.2)	5 (10.2)	0.205	-
Type 2	45 (97.8)	44 (89.8)		
Smoking				
Absent	36 (78.3)	38 (86.4)	0.315	-
Present	10 (21.7)	6 (13.6)		
Duration of diabetes	20.00 (10.75 – 27.50)	18.00 (12.00 – 25.00)	0.372	-

Table 1. Demographic and clinical characteristics of patients with diabetes-related foot infection according to the presence of osteomyelitis. (*Continued.*)

	Without osteomyelitis	With osteomyelitis	*p*	Achieved power (1–β)
HbA1c	7.40 (6.25 – 8.35)	7.80 (6.53 – 9.15)	0.295	-
Duration of diabetic foot	35.00 (25.00 – 75.00)	55.00 (30.00 – 90.00)	0.217	-
Comorbidity				
Absent	18 (39.1)	19 (38.8)	0.972	-
Present	28 (60.9)	30 (61.2)		
Previous hospitalization				
Present	27 (58.7)	36 (73.5)	0.128	-
Absent	19 (41.3)	13 (26.5)		
Recurrent foot infection				
Present	24 (52.2)	38 (77.6)	**0.009**	0.782
Absent	22 (47.8)	11 (22.4)		
Previous osteomyelitis				
Present	6 (13.0)	26 (53.1)	**<0.001**	0.985
Absent	40 (87.0)	23 (46.9)		
Previous debridement				
Present	10 (21.7)	10 (20.4)	0.874	-
Absent	36 (78.3)	39 (79.6)		
Previous amputation				
Present	6 (13.0)	10 (20.4)	0.338	-
Absent	40 (87.0)	39 (79.6)		
Previous peripheral vascular intervention				
Present	13 (28.3)	34 (69.4)	**<0.001**	0.980
Absent	33 (71.7)	15 (30.6)		
Renal failure				
Present	8 (17.4)	13 (26.5)	0.283	-
Absent	38 (82.6)	36 (73.5)		
Dialysis				
Present	2 (4.3)	4 (8.2)	0.678	-
Absent	44 (95.7)	45 (91.8)		
Antibiotic use within the previous month				
Present	35 (76.1)	45 (91.8)	**0.035**	0.578
Absent	11 (23.9)	4 (8.2)		

Descriptive statistics are presented as median (25th–75th percentile) or frequency (%). The Mann-Whitney U test was used for quantitative variables, the independent samples t-test was used for the age variable, and the chi-square/Fisher's exact test was used for categorical variables.
HbA1c: Glycated hemoglobin.

findings were evaluated, both C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR) levels were significantly higher in the osteomyelitis group than in the non-osteomyelitis group ($p = 0.007$ and $p = 0.003$, respectively). Detailed data are presented in Table 2.

Patients with positive cultures were additionally analyzed by dividing them into two groups according to antimicrobial resistance status. The mean age was significantly lower in the group with antimicrobial resistance (60.76 ± 10.23) than in the group without antimicrobial resistance (67.36 ± 9.87) ($p = 0.002$).

When categorical variables were evaluated, the rate of a previous history of osteomyelitis was significantly higher in the group with antimicrobial resistance (44.4%) than in the group without antimicrobial resistance (24.0%) ($p = 0.035$). No statistically significant differences were found between the groups with respect to other clinical characteristics ($p > 0.05$). Detailed data are presented in Table 3.

As shown in Table 4, the infection classification score was significantly higher in the group with antimicrobial resistance than in the group without antimicrobial resistance ($p = 0.003$). When laboratory findings were evaluated, CRP levels were significantly higher ($p = 0.018$), whereas hemoglobin (Hb) levels were significantly lower in the group with antimicrobial resistance ($p = 0.028$).

In the microbiological evaluation, microbial growth was detected in all patients in the osteomyelitis group, whereas no growth was observed in 15 of the 46 patients in the non-osteomyelitis group. Among patients with positive cultures, polymicrobial growth was more frequent in the osteomyelitis group (34.7%) than in the non-osteomyelitis group (16.1%).

Table 2. Wound classification, laboratory findings, and resistance status according to the presence of osteomyelitis.

	Without osteomyelitis	With osteomyelitis	*p*	Achieved power (1–β)
Wound classification (according to IWGDF)	2.00 (2.00 – 3.00)	3.00 (2.00 – 3.00)	0.255	-
Presence of ischemia				
Present	26 (60.5)	36 (76.6)	0.099	-
Absent	17 (39.5)	11 (23.4)		
SINBAD score	4.00 (3.00 – 5.00)	4.00 (4.00 – 5.00)	0.096	-
Infection classification (according to IWGDF)	3.00 (3.00 – 3.50)	3.00 (3.00 – 4.00)	**0.028**	0.607
Neuropathy				
Present	27 (61.4)	42 (85.7)	**0.007**	0.764
Absent	17 (38.6)	7 (14.3)		
Resistance status				
Absent	30 (65.2)	20 (40.8)	**0.017**	0.663
Present	16 (34.8)	29 (59.2)		
Leukocyte count	9.65 (7.98 – 12.80)	11.30 (8.45 – 13.30)	0.282	-
CRP	61.00 (20.50 – 118.75)	120.00 (55.25 – 198.75)	**0.007**	0.793
Hb	10.91 ± 1.95	10.28 ± 1.56	0.083	-
ESR	63.0 (42.3–92.0)	92.0 (73.0–110.0)	**0.003**	0.890

Descriptive statistics are presented as mean ± standard deviation, median (25th–75th percentile), or frequency (%). The independent samples t-test was used for normally distributed quantitative variables, the Mann-Whitney U test was used for non-normally distributed quantitative variables, and the chi-square test was used for categorical variables.
IWGDF: International Working Group on the Diabetic Foot, **SINBAD:** Site, Ischemia, Neuropathy, Bacterial infection, Area, and Depth, **CRP:** C-reactive protein, **ESR:** Erythrocyte sedimentation rate, **Hb:** Hemoglobin.

Table 3. Demographic and clinical characteristics according to antimicrobial resistance status.

	No resistance	Resistance present	*p*	Achieved power (1–β)
Age	67.36 ± 9.87	60.76 ± 10.23	**0.002**	0.936
Sex			0.204	-
Male	33 (66.0)	35 (77.8)		
Female	17 (34.0)	10 (22.2)		
Type of diabetes			0.418	-
Type 1	2 (4.0)	4 (8.9)		
Type 2	48 (96.0)	41 (91.1)		
Smoking				
Absent	41 (83.7)	33 (80.5)	0.694	-
Present	8 (16.3)	8 (19.5)		
Duration of diabetes	20.00 (13.50 – 30.00)	15.00 (10.00 – 25.00)	0.090	-
HbA1c	7.90 (6.80 – 8.70)	7.30 (6.10 – 8.70)	0.277	-
Duration of diabetic foot	30.00 (25.00 – 60.00)	60.00 (30.00 – 100.00)	0.054	-
Comorbidity				
Absent	16 (32.0)	21 (46.7)	0.143	-
Present	34 (68.0)	24 (53.3)		
Previous hospitalization				
Present	33 (66.0)	30 (66.7)	0.945	-
Absent	17 (34.0)	15 (33.3)		
Recurrent foot infection				
Present	33 (66.0)	29 (64.4)	0.874	-
Absent	17 (34.0)	16 (35.6)		
Previous osteomyelitis				
Present	12 (24.0)	20 (44.4)	**0.035**	0.558
Absent	38 (76.0)	25 (55.6)		
Previous debridement				
Present	8 (16.0)	12 (26.7)	0.203	-
Absent	42 (84.0)	33 (73.3)		
Previous amputation				
Present	5 (10.0)	11 (24.4)	0.060	-
Absent	45 (90.0)	34 (75.6)		
Previous peripheral vascular intervention				
Present	20 (40.0)	27 (60.0)	0.052	-
Absent	30 (60.0)	18 (40.0)		

Table 3. Demographic and clinical characteristics according to antimicrobial resistance status. (*Continued.*)

	No resistance	Resistance present	*p*	Achieved power (1–β)
Renal failure				
Present	10 (20.0)	11 (24.4)	0.602	-
Absent	40 (80.0)	34 (75.6)		
Dialysis				
Present	2 (4.0)	4 (8.9)	0.418	-
Absent	48 (96.0)	41 (91.1)		
Antibiotic use within the previous month				
Present	41 (82.0)	39 (86.7)	0.533	-
Absent	9 (18.0)	6 (13.3)		

Descriptive statistics were presented as median (25th–75th percentile) or frequency (%). The Mann-Whitney U test was used for quantitative variables, and the chi-square test or Fisher's exact test was used for categorical variables.
HbA1c: Glycated hemoglobin.

Table 4. Wound classification and laboratory findings according to antimicrobial resistance status.

	No resistance	Resistance present	*p*	Achieved power (1–β)
Wound classification (according to the IWGDF)	2.50 (2.00 – 3.00)	2.00 (2.00 – 3.00)	0.952	-
Presence of ischemia				
Present	31 (66.0)	31 (72.1)	0.775	-
Absent	16 (34.0)	12 (27.9)		
SINBAD score	4.00 (3.00 – 5.00)	4.00 (4.00 – 6.00)	0.063	-
Infection classification (according to IWGDF)	3.00 (3.00 – 3.00)	3.00 (3.00 – 4.00)	**0.003**	0.855
Neuropathy				
Present	36 (73.5)	33 (75.0)	0.983	-
Absent	13 (26.5)	11 (25.0)		
Leukocyte level	9.65 (8.08 – 12.60)	11.30 (8.15 – 14.55)	0.323	-
CRP	63.00 (20.50 – 144.50)	104.00 (56.50 – 214.75)	**0.018**	0.664
Hb	10.96 ± 1.91	10.15 ± 1.52	**0.028**	0.613
ESR	80.5 (44.0–97.0)	86.0 (60.0–108.0)	0.303	-

Descriptive statistics were presented as mean ± standard deviation, median (25th–75th percentile), or frequency (%). For quantitative variables with a normal distribution, the independent samples t-test was used; for quantitative variables without a normal distribution, the Mann-Whitney U test was used; and for categorical variables, the chi-square test was used.
IWGDF: International Working Group on the Diabetic Foot, **SINBAD:** Site, Ischemia, Neuropathy, Bacterial infection, Area, and Depth, **CRP:** C-reactive protein, **ESR:** Erythrocyte sedimentation rate, **Hb:** Hemoglobin.

The isolate-based microorganism distribution and antimicrobial resistance rates according to the presence of osteomyelitis are presented in Table 5. In the isolate-based evaluation, Gram-negative bacteria accounted for 56.8% of isolates and Gram-positive bacteria for 43.2% in the non-osteomyelitis group. The most frequently isolated pathogens in this group were *S. aureus* (18.9%), *Klebsiella pneumoniae* (13.5%), and *Pseudomonas aeruginosa* (13.5%). In the osteomyelitis group, Gram-negative bacteria accounted for 56.7% of isolates and Gram-positive bacteria for 43.3%. The most frequently isolated pathogens in this group were *S. aureus* (22.4%), *Escherichia coli* (11.9%), and *P. aeruginosa* (10.4%). No statistically significant difference was found between the groups in terms of the overall distribution of Gram-positive and Gram-negative bacteria. Among the individual microorganisms, only *Acinetobacter* spp. was significantly more frequent in the non-osteomyelitis group than in the osteomyelitis group ($p = 0.043$). No statistically significant differences were detected between the groups for the other microorganisms or antimicrobial resistance patterns.

When resistance profiles were evaluated, the MDR rate among Gram-negative isolates was 33.3% in the non-osteomyelitis group and 44.7% in the osteomyelitis group. Extended-spectrum beta-lactamase production was observed only in the non-osteomyelitis group (9.5%), whereas IBL production was detected only in the osteomyelitis group (5.3%). Among Gram-positive pathogens, the MRSA rate among *S. aureus* isolates was numerically higher in the osteomyelitis group than in the non-osteomyelitis group (66.7% vs. 42.9%). Similarly, methicillin resistance among coagulase-negative staphylococcal isolates was numerically higher in the osteomyelitis group than in the non-osteomyelitis group (75.0% vs. 50.0%). Among *Enterococcus* spp. isolates, ampicillin resistance was detected only in the non-osteomyelitis group (25.0%). However, these differences in antimicrobial resistance patterns were not statistically significant.

DISCUSSION

In this study, the relationship between the presence of osteomyelitis and clinical characteristics, as well as microbiological resistance profiles, and clinical classification scores was evaluated in patients with diabetes-related foot infections. Our findings showed that osteomyelitis was associated with recurrent foot infection, a history of previous osteomyelitis, previous peripheral vascular intervention, neuropathy, and antibiotic use within the previous month.

In our study, a history of peripheral vascular intervention was more frequent in the osteomyelitis group. In diabetes-related foot infection with osteomyelitis, inadequate local circulation due to peripheral vascular disorders may hinder the achievement of sufficient antibiotic concentrations at the site of infection, thereby making the control of infection more difficult (11). This condition may contribute to the chronicity of infection and predispose patients to the development of osteomyelitis through recurrent infections. In addition, neuropathy was more frequent in the osteomyelitis group. Diabetic neuropathy facilitates the development of recurrent trauma and ulceration by causing the loss of protective sensation, and this process predisposes patients to the development of osteomyelitis through the spread of infection to deeper tissues (12). This finding suggests that neuropathy may play an important role not only in the development of ulcers but also in the progression of infection to bone involvement.

The literature indicates that inflammatory markers such as CRP have limited sensitivity and specificity for the diagnosis of osteomyelitis and that these markers are more useful in distinguishing infectious from non-infectious foot pathologies (13). In our study, both CRP and ESR levels were significantly higher in patients with osteomyelitis than in those without osteomyelitis. This finding suggests that patients with bone involvement had a greater systemic inflammatory burden. In the literature, ESR has been reported to be more closely associated with diabetic foot osteomyelitis than CRP (14). However, inflammatory markers alone are insufficient to establish the diagnosis of osteomyelitis, and current recommendations emphasize their interpretation alongside clinical findings, probe-to-bone test results, imaging, and microbiological or histopathological evidence, when available (4). Therefore, the elevated ESR and CRP levels observed in our study should be interpreted as supportive group-level findings rather than independent diagnostic markers for osteomyelitis.

In the microbiological evaluation, polymicrobial growth was more frequent in the osteomyelitis group than in the non-osteomyelitis group. This finding is consistent with studies reporting that infection in diabetes-related foot infections with concomitant osteomyelitis may be associated with complex microbial communities rather than a single pathogen. A study in which bone samples from cases of diabetes-related foot infection with osteomyelitis were examined using molecular and microscopic methods demonstrated that polymicrobial communities and biofilm structures can frequently be observed in these cases. Therefore, the more frequent detection of polymicrobial growth in the osteomyelitis group in our study may reflect the deeper, more chronic, and more complicated nature of bone infection (15).

The finding that *S. aureus* was the most frequently isolated pathogen in both groups is consistent with the literature

Table 5. Isolate-based microbiological pathogen distribution and antimicrobial resistance profiles according to the presence of osteomyelitis.

	With osteomyelitis n/N(%)	Without osteomyelitis n/N(%)	Total n/N (%)	*p*
Gram-positive	29/67 (43.3)	16/37 (43.2)	45/104 (43.3)	0.997
Staphylococcus aureus	15/67 (22.4)	7/37 (18.9)	22/104 (21.2)	0.678
Methicillin-sensitive	5/15 (33.3)	4/7 (57.1)	9/22 (40.9)	0.376
Methicillin-resistant	10/15 (66.7)	3/7 (42.9)	13/22 (59.1)	0.376
Coagulase-negative staphylococcus	4/67 (6.0)	4/37 (10.8)	8/104 (7.7)	0.451
Methicillin-sensitive	1/4 (25.0)	2/4 (50.0)	3/8 (37.5)	1.000
Methicillin-resistant	3/4 (75.0)	2/4 (50.0)	5/8 (62.5)	1.000
Enterococcus spp.	6/67 (9.0)	4/37 (10.8)	10/104 (9.6)	0.741
Ampicillin-resistant	0/6 (0.0)	1/4 (25.0)	1/10 (10.0)	0.400
Streptococcus spp.	4/67 (6.0)	1/37 (2.7)	5/104 (4.8)	0.653
Gram-positive resistant bacteria	13/67 (19.4)	6/37 (16.2)	19/104 (18.3)	0.687
Gram-negative	38/67 (56.7)	21/37 (56.8)	59/104 (56.7)	0.997
Klebsiella spp.	9/67 (13.4)	5/37 (13.5)	14/104 (13.5)	1.000
Klebsiella pneumoniae	4/67 (6.0)	5/37 (13.5)	9/104 (8.7)	0.275
Klebsiella oxytoca	4/67 (6.0)	0/37 (0.0)	4/104 (3.8)	0.294
Klebsiella spp.	1/67 (1.5)	0/37 (0.0)	1/104 (1.0)	1.000
Pseudomonas aeruginosa	7/67 (10.4)	5/37 (13.5)	12/104 (11.5)	0.751
Proteus spp.	5/67 (7.5)	4/37 (10.8)	9/104 (8.7)	0.718
Proteus mirabilis	1/67 (1.5)	4/37 (10.8)	5/104 (4.8)	0.053
Proteus vulgaris	4/67 (6.0)	0/37 (0.0)	4/104 (3.8)	0.294
Escherichia coli	8/67 (11.9)	1/37 (2.7)	9/104 (8.7)	0.153
Enterobacter spp.	2/67 (3.0)	0/37 (0.0)	2/104 (1.9)	0.537
Citrobacter spp.	1/67 (1.5)	1/37 (2.7)	2/104 (1.9)	1.000
Serratia marcescens	2/67 (3.0)	1/37 (2.7)	3/104 (2.9)	1.000
Morganella morganii	4/67 (6.0)	1/37 (2.7)	5/104 (4.8)	0.653
Stenotrophomonas maltophilia	0/67 (0.0)	0/37 (0.0)	0/104 (0.0)	-
Acinetobacter spp.	0/67 (0.0)	3/37 (8.1)	3/104 (2.9)	**0.043**
Gram-negative MDR bacteria	17/38 (44.7)	7/21 (33.3)	24/59 (40.7)	0.393
ESBL-producing Gram-negative bacteria	0/38 (0.0)	2/21 (9.5)	2/59 (3.4)	0.123
IBL-producing Gram-negative bacteria	2/38 (5.3)	0/21 (0.0)	2/59 (3.4)	0.534
Total MDR bacteria	32/67 (47.8)	15/37 (40.5)	47/104 (45.2)	0.479

MDR: Multidrug-resistant, ESBL: Extended-spectrum beta-lactamase, IBL: Inducible beta-lactamase, MRSA: Methicillin-resistant *Staphylococcus aureus*.

reporting this microorganism as one of the principal pathogens in diabetes-related foot infections and with recent multicenter data on diabetic foot osteomyelitis (16). While the MRSA rate among *S. aureus* isolates was reported as 20.8% in that study, the higher MRSA rate observed in the osteomyelitis group in our study may be related to center-specific resistance characteristics and antibiotic use within the previous month. One study reported that, in addition to *S. aureus* being frequently isolated in diabetic foot infections, it can persist in the chronic wound environment and may undergo genomic changes over time (17). This finding supports the view that, particularly in chronic and complicated cases, *S. aureus* is not only a common pathogen but also an important microorganism in terms of patient follow-up and treatment.

One of the notable findings of this study was that both antimicrobial resistance and antibiotic use within the previous month were significantly higher in the osteomyelitis group. The literature indicates that previous antibiotic use and the presence of osteomyelitis may be associated with multidrug-resistant microorganisms; in addition, discordance between soft tissue and bone cultures in diabetes-related foot infections with concomitant osteomyelitis has been reported to contribute to the development of resistance by increasing the use of broad-spectrum antibiotics (18,19). In a prospective multicenter study conducted in Türkiye, resistant bacterial growth was detected in 43% of diabetes-related foot infection cases; antibiotic use within the previous 30 days was identified as an independent risk factor for resistant bacterial growth, and resistant bacterial growth was found to be associated with treatment failure and increased antibiotic costs (20). Similarly, another study from Türkiye reported an MDR rate of 47.9% in diabetes-related foot infection and demonstrated that MDR growth was associated with polymicrobial growth and a history of hospitalization (21). Recent cohort data have also emphasized that antimicrobial-resistant pathogens complicate the management of diabetes-related foot infection and may be associated with poor clinical outcomes (22). These findings support the possibility that the high resistance rates observed in the osteomyelitis group in our study may be related to previous antibiotic exposure, the polymicrobial nature of the infection, and complicated clinical characteristics. Although the higher rate of resistant microorganism isolation in the younger age group was a notable finding in our study, this observation does not fully align with the classical risk factors described in the literature. A meta-analysis found no significant association between age and multidrug-resistant organism (MDRO) infection; however, previous hospitalization, antibiotic use, osteomyelitis, ulcer size, vascular disease, and a history of surgical intervention were identified as more consistent risk factors (23). Therefore, the high resistance rates observed in younger patients and the elevated prevalence of MDROs in our study are consistent with the literature when considered in the context of recent antibiotic use and healthcare exposure rather than as a direct effect of age.

Although bone biopsy (histology and culture) is considered the gold standard for the diagnosis of osteomyelitis, the diagnostic process generally begins with clinical evaluation. Accurate identification of the causative microorganism is critical for treatment. However, studies evaluating the diagnostic value of clinical and laboratory findings remain limited (24).

In the evaluation of clinical classification systems, no significant association was found between osteomyelitis and either the SINBAD score or the IWGDF wound classification. Although the literature has shown that the SINBAD score is associated with adverse clinical outcomes such as amputation, hospitalization, and secondary infection, its role in predicting deep infections such as osteomyelitis remains unclear (25). In contrast, the WIfI classification was developed primarily to predict limb prognosis because it simultaneously evaluates wound, ischemia, and infection components, and therefore has the potential to reflect outcomes related to the depth of infection (4). However, studies directly evaluating the performance of these classification systems in predicting the presence of osteomyelitis remain limited in the current literature.

Our study has several limitations. First, anaerobic cultures could not be performed. Therefore, we were unable to determine the role of anaerobic microorganisms in diabetes-related foot infections. In addition, the limited number of patients and the small number of isolates in some subgroups made the interpretation of subgroup analyses, particularly those involving MRSA, ESBL, AmpC/IBL, and enterococcal resistance, more challenging. Because the microbiological analyses presented in Table 5 were performed on an isolate basis, multiple isolates obtained from the same patient or infection episode could be included in the analysis. Therefore, these observations may not have been statistically independent, and within-patient or within-episode clustering may have affected the variance estimates and p values. Accordingly, the statistical comparisons presented in Table 5 should be interpreted with caution. Another limitation is that comorbidities were evaluated as an overall variable rather than being analyzed separately according to individual conditions or secondary infection foci.

Nevertheless, our study also has several strengths. These include the comparison of diabetes-related foot infections with and without osteomyelitis not only in terms of clinical

characteristics but also with respect to microbiological pathogen distribution, antimicrobial resistance profiles, laboratory findings, and classification systems. Furthermore, the separate analysis of patients according to the presence of resistant microorganism growth contributed to the identification of clinical characteristics associated with antimicrobial resistance. The use of real-world data and the reflection of secondary care hospital practice enhance the relevance of our findings for everyday clinical practice.

In conclusion, in patients with diabetes-related foot infection, concomitant osteomyelitis was associated with recurrent foot infection, a history of previous osteomyelitis, previous peripheral vascular intervention, neuropathy, antibiotic use within the previous month, elevated CRP and ESR levels, and resistant microorganism growth. Microbiologically, *S. aureus* was the most frequently isolated pathogen, while polymicrobial growth, the rate of Gram-negative MDR organisms, and the MRSA rate appeared to be higher in the osteomyelitis group. These findings support the need for individualized empirical treatment decisions in diabetes-related foot infections with concomitant osteomyelitis, taking into account the patient's previous antibiotic use, healthcare exposure, risk of antimicrobial resistance, and local microbiological data.

Ethical Approval: The study was approved by the Non-Interventional Clinical Research Ethics Committee of Aydın Adnan Menderes University Faculty of Medicine on June 18, 2026, with decision no. 2026/240.

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