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ORIGINAL ARTICLE

A Comparison of Pathogens in Skin and Soft-Tissue Infections and Pedal Osteomyelitis in Puncture Wound Injuries Affecting the Foot

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Objective: To compare pathogens involved in skin and soft tissue infection (SSTI) and pedal osteomyelitis (OM) in patients with and without diabetes with puncture wounds to the foot.

Methods: We evaluated 113 consecutive patients between June 2011 and March 2019 with foot infection (SSTI and OM) from a puncture injury sustained to the foot. Eighty-three patients had diabetes (DM) and 30 did not (NDM). We evaluated the bacterial pathogens in patients with skin and soft tissue infections (SSTI) and pedal osteomyelitis (OM).

Results: Polymicrobial infection were more common in patients with diabetes mellitus (83.1% vs 53.3%, *p*=.001). The most common pathogen for SSTI and OM in DM was *s. aureus* (SSTI 50.7%, OM 32.3%), whereas in NDM patients it was *Pseudomonas* (25%) for SSTI. Anaerobes (9.4%) and fungal (3.1%) infection were uncommon. *Pseudomonas aeruginosa* was only identified in 5.8% of people with diabetes.

Conclusions : The most common bacterial pathogen in both SSTIs and pedal OM was *staphylococcus aureus* in patients with DM. *Pseudomonas spp.,* was the most common pathogen in people without diabetes with SSTIs.

Foot infections are one of the most common underlying causes of lower extremity amputation and are usually the result of ulcerations in the feet of people with diabetes. Infections of the feet can involve the skin and soft tissue envelope, bone and joint or both. Breaks in the protective skin envelope via trauma or ulceration are commonly associated with sensory neuropathy with loss of protective sensation, which is present in up to 80% of people with

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diabetic foot disease.[1] Therefore, ulceration and foot infections in people without diabetes are less common. This may explain the scant published evidence that directly comparing the pathogens of infection or outcome data of foot infections in people with and without diabetes. Puncture injury is a non-selective, traumatic injury that occurs in both patients with and without diabetes. It has been associated with deep infections with complicated courses of treatment.[2-7] Most of the published work regarding infected puncture wounds involves pediatric osteomyelitis[8-19], which demonstrates a very high rate of osteomyelitis caused by Pseudomonas species. There are only a few studies that have evaluated and compared the pathogens of infection in puncture wounds in patients with and without out diabetes.[20-22] These studies reported a low rate of Pseudomonas infection.

In the current study, patients admitted to hospital for an infected puncture injury to the foot were identified from hospital records and placed into cohorts dependent on the presence or absence of diabetes mellitus and by the type of infection, skin and soft tissue infection (SSTIs) or pedal osteomyelitis (OM). Conventional culture results relating to the pathogens of infection from infected puncture wounds (SSTIs or OM) were compared against patients with and with diabetes.

METHODS

In this retrospective review, patients aged over 18 years of age that were admitted to hospital between June 2011 and March 2019 for treatment with a puncture wound injury to the foot were included (n=113). The diagnosis of diabetes mellitus was based on American Diabetes

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Association criteria.[23] A broad range of demographic and clinical parameters were collected; age, gender, shod or unshod at the time of injury, medical history, wound characteristics, laboratory (white blood cell, erythrocyte sedimentation rate, C-reactive protein, glycated Hemoglobin, albumin, estimated glomerular filtration rate), conventional culture (microbiology, culture and sensitivities, histopathology), medical history for peripheral vascular disease, peripheral sensory neuropathy, foot ulceration, and amputation and clinical outcomes.[24-25] Peripheral vascular disease was defined as an ankle to arm systolic blood pressure ratio of <0.90, >1.30, or non-compressible. Sensory neuropathy was defined as abnormal vibration sensation or abnormal sensation with 10-gram Semmes-Weinstein monofilament.[26-28] Leukocytosis was defined as white blood count (WBC) >11.0 x 10^9/L. SSTI were determined using Infectious Disease Society of America (IDSA) foot infection criteria (local swelling or induration, erythema, local tenderness or pain, local warmth, and/or purulent discharge).[29] OM was diagnosis via confirmation on histopathology and/or positive microbiology culture. All bone biopsies were either obtained intra-operatively with direct visualization or percutaneously using a bone marrow biopsy needle. All bone cultures were sent for aerobic, anaerobic, fungal, and acid-fast bacillus testing at the hospital pathology department. All bone biopsies were obtained within 24 hours of admission via percutaneous needle bone biopsy or intra-operatively – no antibiotic therapy was administered prior to bone biopsy.

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This study was approved by the Institutional Review Board at the sites were the study was conducted. Data was compiled using Microsoft Excel (Microsoft Corporation, Redmond, WA). Continuous Data are given as mean, median, 95% confidence intervals (CI) and standard deviation (±). A chi square test was used to compare dichotomous variables. A one-way Analysis of Variance (ANOVA) was used to evaluate continuous variables, and the Mann-Whitney U Test was used for non-parametric data. For all comparisons and modelling, the level of significance was set at $p<.05$. Data were analyzed using programs on www.socscistatistics.com.

RESULTS

Broad demographic and clinical variables are described in Table 1. Briefly, 113 patients with foot infections related to a puncture wound were included for review. Most patients had diabetes (DM = 83, 73% vs non-DM = 30, 27%). At presentation, patients with DM had significantly higher WBC (CI 10.5-12.2, $p<.05$), ESR (CI 51.5-65.7, $p<.001$), and CRP (CI 7.3-10.7, $p<.001$) (Table 1). Patients with DM also had lower albumin (CI 3.4-3.6, $p<.001$) and pre-albumin (CI 2.3-16.1, $p<.001$) (Table 1).

All patients presented with a puncture wound with acute sign of infection. However, only 75% soft tissue culture yielded positive pathogens (n=85, 75%). Conversely, 32 of 113 (28%) patients developed pedal OM, of which only one (3.1%) patient did not have diabetes (NDM). Of the 83 DM patients with a puncture wound, 69 (83.1%) soft tissue culture yielded positive pathogens and 31 (37.3%) presented with pedal osteomyelitis. Conversely, of the 30 patients with NDM

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and a puncture wound, 16 (53.3%) soft tissue culture yielded positive pathogens. DM SSTIs were 5.3 times more likely to have polymicrobial infections compared to patients with NDM (CI 0.06-0.64, p<.005) (Table 1). The likelihood of a DM patient with a puncture wound developing pedal OM was 17.3 times higher than a non-DM patient (CI 0.01-0.45, p<.001).

Microbiology evaluation of all patient deep tissue cultures yielded 34 different pathogens of infection (Fig. 1): 11 (32.4%) Gram-positive bacteria, 17 (50%) Gram-negative bacteria, 6 (17.6%) anaerobes, and 1 (2.9%) fungi (Fig. 1). Overall, the most common pathogens for SSTIs were aerobic Gram-positive cocci; *Staphylococcus aureus* (42.4%) and *Staphylococcus epidermis* (31.8%) (Fig. 1). The most common pathogens of infection in SSTIs in non-DM patients were *Pseudomonas aeruginosa* (4 of 16 isolates, 25%)*, and Staphylococcus epidermis* (3 of 16 isolates, 18.8%); however, *Pseudomonas aeruginosa* was uncommon in patients with DM (4 of 69 isolates, 5.8%). The most common in DM patients were *Staphylococcus aureus* (35 of 69 isolates, 50.7%), and *Staphylococcus epidermis* (24 of 69 isolates, 34.8%)

Microbiology evaluation of all bone cultures yielded 20 different pathogens of infection. Eight (40%) Gram-positive bacteria, 8 (40%) Gram-negative bacteria, 3 (15%) anaerobes, and 1 (5%) fungi (Fig. 2). The most common pathogen of infection in DM patients with pedal OM were aerobic Gram-positive cocci; *Staphylococcus aureus* (10 of 31 isolates, 32.3%)*,* followed by *Staphylococcus epidermidis* (8 of 31 isolates, 25.8%) and *Enterobacter cloacae* (8 of 31, 25.8%).

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Pseudomonas aeruginosa as a pathogen of infection in DM patients with pedal OM was uncommon (3 of 31 isolates, 9.7%).

Discussion

Most of the available data regarding puncture wounds to the foot have been described primarily in context to pediatrics *Pseudomonas* osteomyelitis.[30-37] It has been 26 years since there was a large-scale study that evaluated pathogens of infection in foot puncture wound injuries in patients with diabetes.[20] This study highlights differences in clinical presentation, rates of SSTI and pedal OM, and the bacterial pathogen of infection of puncture wound infections in patients with and without diabetes.

This study has several interesting components. This is the second study of infected puncture wounds in adults with and without diabetes, the first published in 1994.[20] This study identified that pedal osteomyelitis was 17.3 times more likely to occur in infected puncture wounds in people with diabetes. The majority of pathogens in SSTI were polymicrobial (69.6%) and the most common pathogen was *Staphylococcus aureus* (42.4%). Overall, MRSA and *Pseudomonas* were uncommon in both SSTI (11.8%, 9.4%) and steomyelitis (3.1%, 9.4%). Anaerobic infections were only identified in subjects with diabetes (SSTI 13.0%, OM 9.7%). In contrast among NDM patients, the majority of the SSTI were monomicrobial (68.7%) with more Gram-negative pathogens, with *Pseudomonas* (25%) being the most common bacteria (Fig. 1). The most common OM pathogens were *S. aureus*, *S. epidermdis* and *E. clocae* (Fig. 2).

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Similar to what Lavery[21], Parks[38], MacDonald[39], and Citron[40] reported, we found that the most common pathogen in SSTIs was *staphylococcus aureus* (42.4%). They also all reported that anaerobes pathogens in diabetic foot infection were uncommon.[18,19,21,38-40] Our findings share the same insight; however, we found that the anaerobic infections only occurred In DM patients. The prevalence of anaerobes was 4.4% in patients with osteomyelitis and 10.8% in patients with SSTIs. This finding suggests that given anaerobes were uncommon, parenteral antibiotic treatment may not need to cover anaerobes, unless clinical suspicion is high (i.e. such as the presence of soft tissue gas on radiographs). One caveat to consider, however, is the potential limitation of conventional culture in identifying all pathogens of infection in OM. Recently, Johani et al. utilized molecular and microscopy approaches to demonstrate that microorganisms in diabetic foot osteomyelitis were predominantly bacterial biofilms.[18] Biofilms in clinical situations may be slow-growing (or at least contain slow-growing cells), which may account for potential negative culture results, particularly for more fastidious anaerobes. We further found that cultures identifying fungi were rare for both SSTI (1.2%) and pedal OM (3.1%), a consistent previous finding.[17,18]

There are several limitations to this study. This was a retrospective review, which inherently relies on the accuracy of patient charts. Measurement bias is also possible because other experienced physicians may use different operational definition of disease processes.

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Moreover, since this cohort of patients was treated at a safety net hospital, selection bias is a possibility because our hospital serves a low-income population with a large minority population. This was unlikely to change common bacterial pathogens, however.

Conclusions

This study highlights the pathogens present in both SSTI and pedal OM in puncture injuries effecting both patient with and without diabetes. Pseudomonas in both SSTI and pedal OM was not common. The most common pathogens in both SSTI and OM was *S. aureus* and *S. epidermidis*. Diabetes mellitus remains the biggest risk factor for developing polymicrobial infection and OM.

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Conflict of Interest: None reported.

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Table 1: Laboratory values, number of soft tissue and bone infection, and location of injury between DM to non-DM.

	DM	Non-DM	95% CI	OR	p-value
n (Total = 113)	83	30			
Age (Years)	52.1, 52 (10.2)	46.7, 51.5 (13.3)	45.6 – 52.8		.11
Male	66 (79.5)	20 (66.7)	0.2 – 1.3	1.94	.24
Shoe	49 (59)	19 (63.3)	0.51 – 2.84	0.83	.68
Labs					
White Blood Count	11.3, 12.2 (4.8)	9.1, 8.7 (2.7)	10.5 – 12.2		<.05
Erythrocyte Sedimentation Rate	65.5, 68.8 (34.8)	27.9, 18 (23.5)	51.5 – 65.7		<.00001
C-Reactive Protein	7.6, 10.8 (9.4)	3.9, 2.2 (4.7)	7.3 – 10.7		<.0001
Glycated Hemoglobin (%)	10.5, 10.5 (2.4)	5.5, 5.4 (0.3)	9.2 – 10.3		<.00001
Albumin	35, 3.4 (0.5)	4.0, 3.9 (0.5)	3.4 – 3.6		<.001
Pre-Albumin	12.7, 13.7 (6.6)	27.3, 27.3 (0.4)	12.3 – 16.1		<.001
Glomerular Filtration Rate <60	16 (19.3)	1 (3.3)	0.02 – 1.14	6.93	<.05
Peripheral Arterial Disease	14 (16.9)	0			
Location of Injury					
Forefoot	65 (78.3)	16 (53.3)	0.13 – 0.77	3.16	<.01
Midfoot	13 (15.7)	9 (30)	0.87 – 6.15	0.43	.09
Rearfoot	5 (6.0)	5 (16.7)	0.83 – 11.67	0.32	.08
Positive Soft Tissue Culture	69 (83.1)	16 (53.3)	0.09 – 0.58	4.31	.001
Monomicrobial	21 (30.4)	11 (68.7)	1.55 – 16.28	0.2	<.005
Polymicrobial	48 (69.6)	5 (31.3)	0.06 – 0.64	5.03	<.005
2 Pathogens	30 (62.5)	4 (80)	0.13 – 1.48	0.42	.17
3 Pathogens	12 (25)	1 (20)	0.04 – 2.63	1.33	.26

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4 Pathogens	6 (12.5)	0			
Osteomyelitis	31 (37.3)	1 (3.3)	0.01 – 0.45	17.29	<.0005
Monomicrobial	16 (51.6)	0			
Polymicrobial	15 (48.4)	1 (100)			
2 Pathogens	13 (86.7)	1 (100)			
3 Pathogens	1 (6.7)	0			
4 pathogens	1 (6.7)	0			

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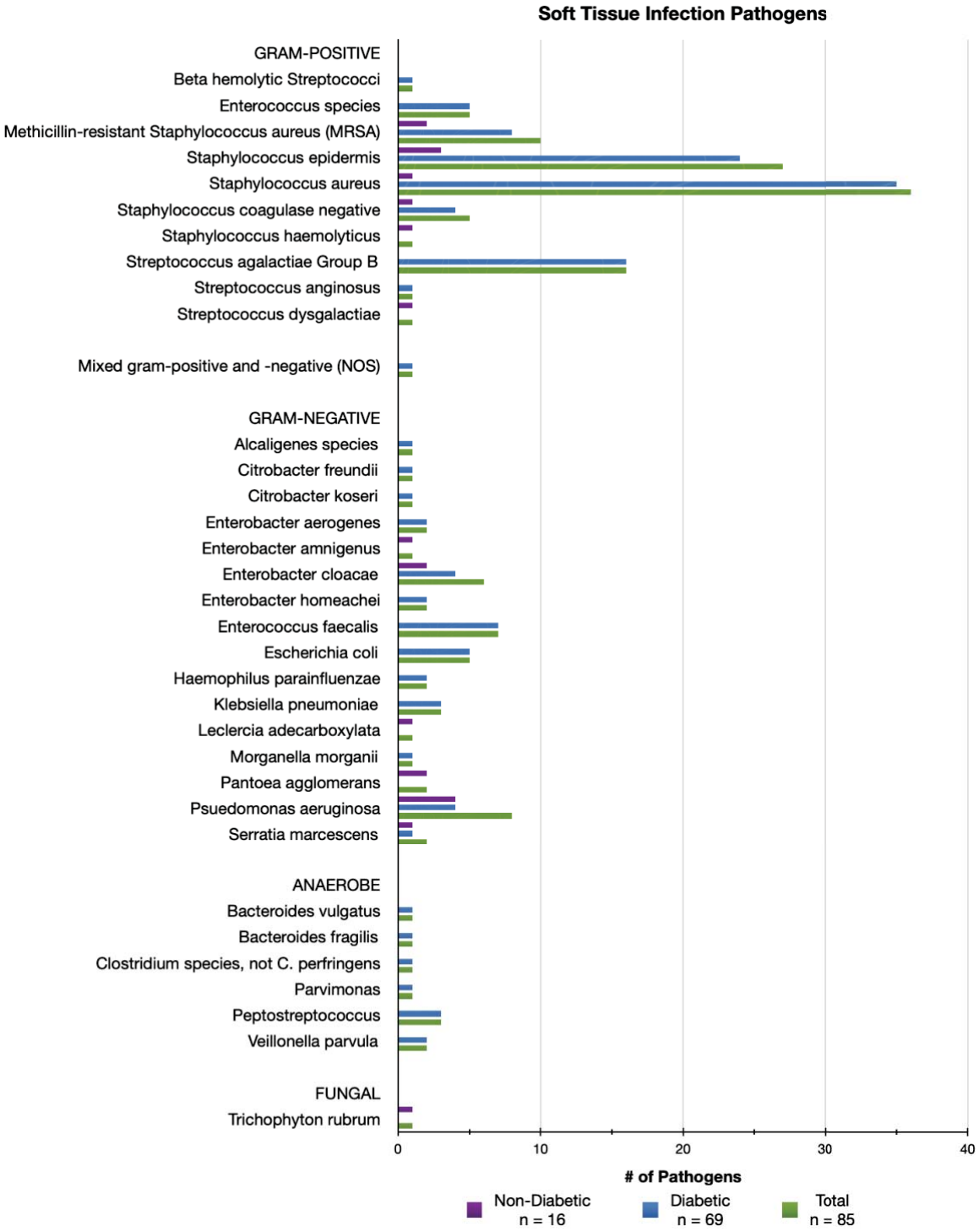

Fig. 1: Breakdown of soft tissue infection pathogens in patients with and without DM.

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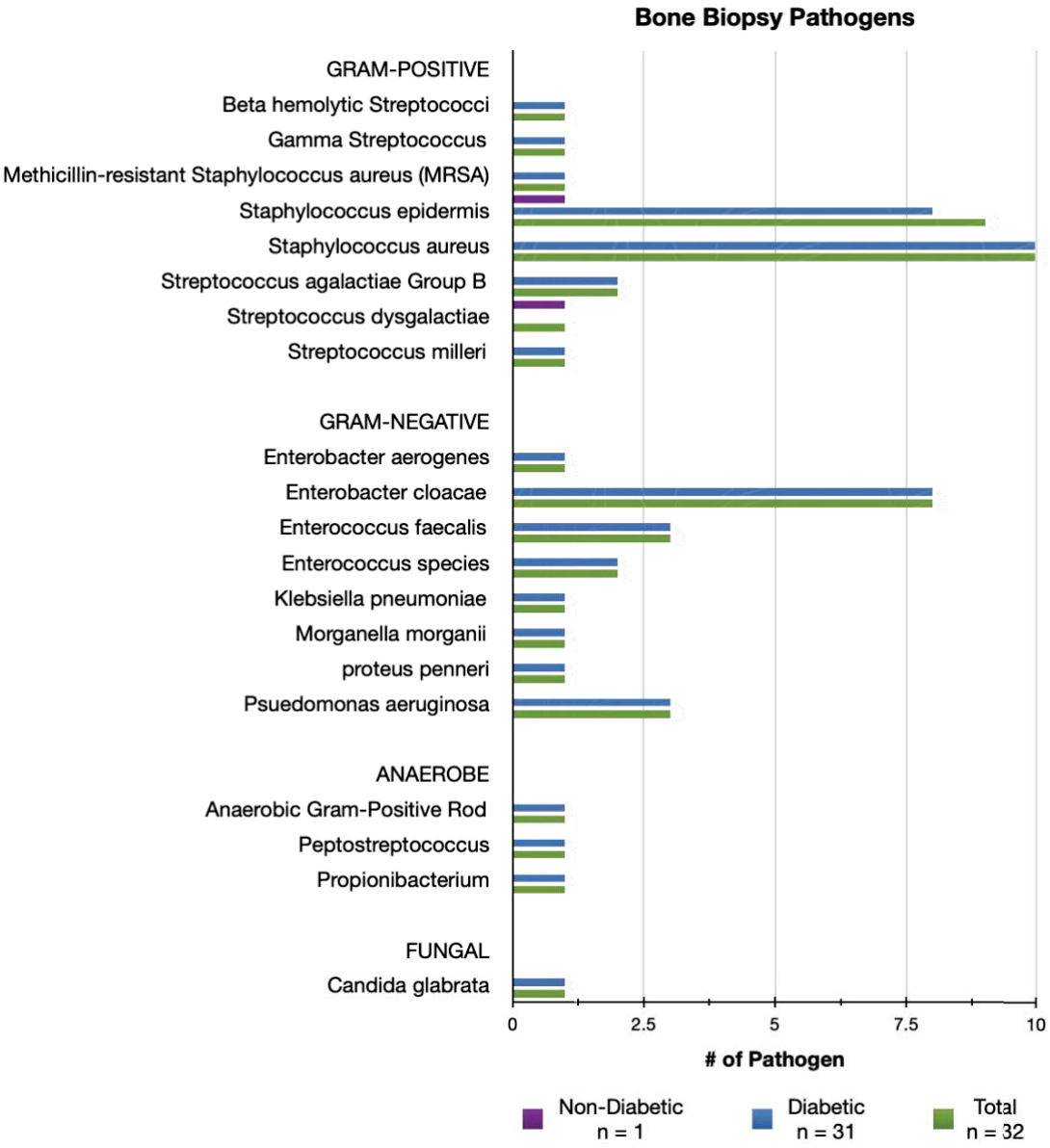

Fig. 2: Breakdown of osteomyelitis pathogens in patients with and without diabetes mellitus. (Non-diabetic pathogens were part of a polymicrobial infection.)