The Egyptian Journal of Hospital Medicine (October 2023) Vol. 93, Page 7286- 7290

Identifying Potential Risk Factors and Evaluating the Microbiological Profile of Infections in Diabetic Feet

Ghada Mohammed Elsagheer[1], Hanan Mohamed Elsotouhy[2], Eman Hussein Khalil[*1], Mohamed Mamdouh Sedik[1], Eman M. Fahmy[3]

[1]Department of Internal Medicine, Faculty of Medicine, Minia University, Egypt
[2]Department of Internal Medicine, Faculty of Medicine, Mansoura University, Egypt
[3]Department of Endocrinology, Helwan Faculty of Medicine, Helwan University, Egypt
***Corresponding author:** Eman M. Fahmy, **Mobile:** (+20) 01000539149, **E-mail:** eman.fahmy@helwan.med.edu.eg

ABSTRACT

Background: Diabetic foot ulcers (DFU) account for about 20% of hospitalisations for diabetes-related reasons. These wounds may cause patients to develop fatal infections or possibly organ damage. As a result, it is crucial to have antibiotic therapy to reduce these consequences.

Objective: The current study set out to identify the risk factors for DFU infection, the most typical organism that was isolated from DFU, and the antibiotics' susceptibility to infection.

Patients and methods: This study was conducted on 74 patients divided into 2 groups: Control group who were not diabetic and presented with foot ulcers and a diabetic group of 54 Diabetic patients attending the clinic for the first time with DFU (30 females and 24 males).

Results: Gram-positive organism was isolated from 61.1% of DFU while 33.3% were gram-negative. Isolates were Staph aureus in 19 (35.2%), 14.8% was coagulase-negative staph, 11.1% for streptococci, pseudomonas, and klebsiella (MDRO) and 5.6% for klebsiella (ESBL) and E-coli, while negative culture was in 3%. Among non-diabetics, the isolates were 60% staph aureus, and 10% for each of pseudomonas, klebsiella (ESBL), and E-coli. While 5.6% of diabetics and 10% of non-diabetics were negative cultures. There was no significant difference between the two groups. Staph aureus was the most common organism isolated from DFU.

Conclusion: The most typical organism identified from DFU was a gram-positive bacterium. Broad-spectrum action against both Gram-positive and Gram-negative organisms was seen by vancomycin, imipenem and amikacin.

Keyword: Type2 DM, Foot ulcer, Gram-positive.

INTRODUCTION

Around the world, 425 million people have diabetes, according to figures from 2017. This progressive chronic metabolic illness is spreading quickly across the globe compared to 2013 and 1980, which recorded 382 million ands108 million cases respectively [(1)]. Microvascular and macrovascular problems, which are caused by the deposition and buildup of glucose and associated metabolites in the arteries and result in a persistent reduction in blood flow and tissue damage, are the main side effects of this condition [(2)]. Diabetes causes an inadequate blood supply, which leads to diabetic ulcer development. The foot is where diabetic ulcers occur most frequently. Neglecting this area of the body, the shape of the arch and toes, and the colonisation of bacteria and fungi between the toes due to the sweating of the foot in the socks are all causes of this complication, which is primarily in the toes [(2)]. Other areas of the body are susceptible to such ulcers for various reasons, including neuropathy as the main aetiology [(3)].

The most common kind of classic DFUs are tiny, mid-punctured, persistent sores that typically develop on the plantar surface of malformed metatarsals and Charcot's joints [(4)].

The International Diabetes Federation has focused on the prevalence of diabetic foot disease worldwide as of 2021. A lower limb may be lost due to diabetes worldwide every 30 seconds, with the lifetime chance of getting a foot ulcer in a diabetic patient reaching up to 25% [(5)].

It is not unusual for DFU to receive inadequate care. This is particularly since there are few facilities that specialise in treating DFU. Use of antibiotics without sensitivity in culture, the use of medications that have no effect on the species recovered from the wound site, and improper treatment duration are only a few examples of mistreatments that can result in DFU. At least in Western nations, aerobic Gram-positive cocci, particularly Staphylococcus aureus, are the major cause of most acute infections in individuals who have not received antibiotic treatment. Gram-positive aerobic cocci typically develop in polymicrobial infections that are persistent or have a prior history of antibiotic therapy [(5)].

PATIENTS AND METHODS

This prospective case-controlled-hospital-based study was carried out on 400 diabetic patients who attended the DF Unit at Mansoura University Hospital in the period between February 2011 and April 2022. A total of 74 patients with foot ulcers were selected and then were divvied into two groups: 54 patients were diabetic, and 20 patients were non-diabetic.

Inclusion criteria: Patients with type 1 or type 2 diabetes who had diabetic foot ulcer attending to the Diabetic Clinic.

Exclusion criteria: Grade 0 ulcer, pre- or post-ulcerative lesion that has healed. Patients already on

Received: 16/04/2023
Accepted: 13/06/2023

anti-microbial treatment and patients with osteomyelitis who were excluded by doing X-ray.

All patients included in the study underwent the following procedures: Full clinical history, including smoking status and diabetes history, full clinical exam., including general and systemic checks, and lab analysis for ulcers including CBC, HbA1c, RFT, ESR, CRP, FBS, PPBS, and A/C ratio. Culture and sensitivity from the DFU.

All participants completed a thorough form that included questions on their age, sex, unusual behaviours, length of diabetes' duration, type of diabetes, and diabetes medication. We assessed the subject's height and weight, and then we computed the BMI in kg/m^2. After 5 minutes of rest, arterial blood pressure was assessed.

Ethical approval:

Mansoura & Minia Faculties of Medicine Medical Ethics Committees gave their approval to this study. All participants gave written consents after receiving all information. The Helsinki Declaration was followed throughout the study's conduction.

Statistical analysis

SPSS V. 23 was used by an IBM computer to analyse the data. Quantitative variables were described as mean ± SD, median, and IQR. Qualitative variables were described using percentages and numbers. To compare quantitative variables in parametric data (SD<50% mean), independent sample t-test was utilised. Comparing quantitative variables in nonparametric data (SD > 50% mean) was done using the Mann-Whitney U test. To compare two groups with reference to qualitative factors, the chi-square test was performed. In terms of quantitative data, the analysis of variance test (ANOVA) was employed to compare multinominal factors. P value ≤ 0.05 for statistical significance and ≤ 0.001 for highly significant result.

RESULTS

Out of 400 diabetic patients 74 patients with foot ulcers were included in this study; 54 patients were diabetic, and 20 patients were non-diabetics foot ulcers. Demographic and clinical data of the studied groups revealed that more than half of diabetic patients were males 34 (63%) while in non-diabetic patients, the male: female ratio was 1:1. 25. 9% of the diabetic group had hypertension, 11 (20.4%), and 38% were smokers Table (1), among the diabetic patient group.

Eleven patients (20.4%) had type I diabetes mellitus and 43 (79.6%) had type II diabetes mellitus. The mean duration of diabetes was 12.8 years. More than half of diabetic patients (61.1 %) were on insulin while 27.8% were taking oral hypoglycemic. This table shows the vital signs of participants. Systolic blood pressure was higher in diabetics (126.5 mmHg) compared to non-diabetics (15 mmHg) (p= 0.012).

Table (1): Demographic and clinical data of studied groups

		Case (n=54)	Control (n=20)	P value
Age (years)	Mean±SD (Range)	55.8±16.1 (27-85)	55.8±16.1 (27-85)	
Sex	Male Female	34 (63.0%) 20 (37.0%)	10 (50.0%) 10 (50.0%)	0.313
HTN	**Yes** **No**	14 (25.9%) 40 (74.1%)	0 (0.0%) 20 (100.0%)	0.008
Smoking	**Yes** **No**	21 (38.9%) 33 (61.1%)	4 (20.0%) 16 (80.0%)	0.127
Type of DM	Type I Type II	11 (20.4%) 43 (79.6%)		
TTT	Oral Insulin Insulin plus oral	15 (27.8%) 33 (61.1%) 6 (11.1%)		
Duration of DM(ys)	Mean±SD (Range)	12.8±6.2 (5-30)		
SBP	Mean±SD (Range)	126.5±17.9 (100-170)	115±14 (100-140)	**0.012 ***
DBP	Mean±SD (Range)	77.8±10.3 (60-100)	73±10.3 (60-90)	0.079
Heart rate	Mean±SD (Range)	89.3±12.9 (62-120)	83.7±29.5 (8-115)	0.258

Gram-positive organism was isolated from 61.1% of diabetic foot ulcer while 33.3% were gram-negative. Isolates were Staph aurous in *19 (35.2%)*, 14.8% was coagulase-negative staph, 11.1% for streptococci, pseudomonas, and Klebsiella (MDRO); 5.6% for Klebsiella (ESBL) and E-coli, while negative culture was in 3%. Among non-diabetics, the isolates were 60% staph aureus, and 10% for each of pseudomonas, klebsiella (ESBL), and EE-coli. While 5.6% of diabetics and 10% of non-diabetics were negative cultures, there was no significant difference between the two groups. P value is significant (Table 2).

Table (2): Distribution of bacterial isolates from diabetic and non-diabetic patients with foot infection

	Case (n=54)	**Control (n=20)**	**p value**
Culture Organism			
Gram +ve	**33 (61.1%)**	**12 (60.0%)**	0.104
Staph aureus coagulase	*19 (35.2%)*	*12 (60.0%)*	
Negative staph	*8 (14.8%)*	*0 (0.0%)*	
Streptococci	*6 (11.1%)*	*0 (0.0%)*	
Gram -ve	**18 (33.3%)**	**6 (30.0%)**	
Pseudomonas	*6 (11.1%)*	*2 (10.0%)*	0.105
Klebsiella (MDRO)	*6 (11.1%)*	*0 (0.0%)*	0.101
Klebsiella (ESBL)	*3 (5.6%)*	*2 (10.0%)*	0.114
E-Coli	*3 (5.6%)*	*2 (10.0%)*	0.114
Negative culture	**3 (5.6%)**	**2 (10.0%)**	0.115

Staph aureus isolated from diabetic ulcers were sensitive to imipenem (100%), vancomycin (100%), Amikacin (94.7%), doxycycline, levofloxacin and Piperacillin /Tazobactam (84.2%). Coagulase-negative staphylococci (CoNS) were sensitive to Imipenem (100%), vancomycin (100%), Piperacillin/Tazobactam (100%), and Doxycycline (87.5%). Streptococci were sensitive to most antibiotics except nitrofurantoin, ceftazidime, ceftriaxone, and cefoxitin. All gram-positive isolates were susceptible to imipenem and vancomycin (100%). Amoxicillin resistance was found in 100% staph aureus (Table 3).

Table (3): Sensitivity pattern of gram-positive bacteria isolated from DFU infection.

	Staph aureus		**coagulase - negative staph**		**Streptococci**	
	(n=19)		**(n=8)**		**(n=6)**	
	S	R	S	R	S	R
Imipenem	19 (100%)	0 (0%)	8 (100%)	0 (0%)	6 (100%)	0 (0%)
Ciprofloxacin	14 (73.7%)	5 (26.3%)	1 (12.5%)	7 (87.5%)	6 (100%)	0 (0%)
Amikacin	18 (94.7%)	1 (5.3%)	6 (75%)	2 (25%)	6 (100%)	0 (0%)
Nitrofurantoin	2 (10.5%)	17 (89.5%)	0 (0%)	8 (100%)	0 (0%)	6 (100%)
Doxycycline	16 (84.2%)	3 (15.8%)	7 (87.5%)	1 (12.5%)	6 (100%)	0 (0%)
Ceftazidime	0 (0%)	19 (100%)	0 (0%)	8 (100%)	0 (0%)	6 (100%)
Amoxicillin	0 (0%)	19 (100%)	0 (0%)	8 (100%)	6 (100%)	0 (0%)
Levofloxacin	16 (84.2%)	3 (15.8%)	0 (0%)	8 (100%)	6 (100%)	0 (0%)
Vancomycin	19 (100%)	0 (0%)	8 (100%)	0 (0%)	6 (100%)	0 (0%)
Piperacillin/Tazobactam	16 (84.2%)	3 (15.8%)	8 (100%)	0 (0%)	6 (100%)	0 (0%)
Ceftriaxone	0 (0%)	19 (100%)	0 (0%)	8 (100%)	0 (0%)	6 (100%)
Cefotaxime	0 (0%)	19 (100%)	0 (0%)	8 (100%)	6 (100%)	0 (0%)
Cefoxitin	1 (5.3%)	18 (94.7%)	0 (0%)	8 (100%)	0 (0%)	6 (100%)

DISCUSSION

In the current investigation, we discovered that all patients had diabetes for more than 4 years on average. Furthermore, 14% of diabetic individuals had already experienced foot lesions. The prevalence of prior ulcer history was higher in insulin-dependent diabetes mellitus (IDDM) patients (45%) compared to non-insulin-dependent diabetes mellitus (NIDDM) patients (18.6%). Additionally, 25.9% of our diabetic patients already had amputations. 25% of them had hypertension, 92.6% had neuropathy, 33.3% had nephropathy, and 29.6% had retinopathy. Similar findings were reported by **Banu *et al.*** [6] who discovered that 19.2% of DFIs were caring for trauma patients and 92.3% of patients had diabetes for more than a year. According to **Foster *et al.*** [7]**,** 76% of diabetics who were hospitalised had an RBS of at least 200 mg/dl. Furthermore, 13% of diabetic individuals had already undergone an amputation.

The prevalence of hypertension was 57%, of neuropathy was 62%, of nephropathy was 17%, and that of retinopathy was 30% in terms of diabetes-related comorbidities. **Tesfaye *et al.*** [8] reported 45% prevalence of hypertension and a 32% rate of retinopathy. According to **Li *et al.*** [9], 63% of diabetics developed neuropathy. **Saini *et al.*** [10] found 18% nephropathy rate. In our analysis, IDDM diabetes was more prevalent than NIDDM diabetes in terms of neuropathy, nephropathy, and retinopathy. The more common problems in people with IDDM may be explained by the longer duration of their diabetes.

Gram-positive organism was isolated from 61.1% of diabetic foot ulcer while 33.3% were gram-negative. Isolates were staph aureus, 14.8% coagulase-negative staph, 11.1% for each of streptococci, pseudomonas and klebsiella (MDRO) and 5.6% for klebsiella (ESBL) and E-coli. Among non-diabetics, the isolates were 60% staph aureus, and 10% for each of pseudomonas, klebsiella (ESBL), and E-coli. While, 5.6% of diabetics and 10% of non-diabetics were negative culture. Our results are supported by **Jneid *et al.*** [11] who reported that staphylococcus aureus sp. was the organism most frequently isolated from diabetic foot ulcer tissue, followed by enterococcus faecalis, enterobacter cloacae, staphylococcus lugdunensis, proteus mirabilis, staphylococcus epidermidis sp., and finegoldia magna. Common staphylococcus aureus colonisation been mentioned in more research as well. Staphylococcus aureus was shown to be the primary cause of diabetic foot infections in a study conducted in France that also examined the bacterial agents of DFU and infection [12]. According to **Iyanar *et al.*** [13]**,** staphylococcus aureus, enterococcus faecalis, and pseudomonas aeruginosa are the germs responsible for diabetic foot ulceration.

In contrast to our findings, a research by **Hadi *et al.*** [14] found that Gram-negative bacteria were more common in diabetic foot injury (DFI) than Gram-positive bacteria (71 versus 29%). However, in their investigation, pseudomonas aeruginosa was the most prevalent pathogen, followed by proteus mirabilis and klebsiella sp. Staphylococcus aureus and streptococcus sp. are the two most common bacteria found in gram-positive and gram-negative isolates, respectively.

Staph aureus isolated from diabetic ulcers were sensitive to imipenem (100%), vancomycin (100%), Amikacin (94.7%), doxycycline, levofloxacin and piperacillin/tazobactam (84.2%). Coagulase-negative staphylococci (CoNS) were sensitive to imipenem (100%), vancomycin (100%), piperacillin/tazobactam (100%), and doxycycline (87.5%). Streptococci was sensitive to most of antibiotics except nitrofurantoin, ceftazidime, ceftriaxone, and cefoxitin. All gram-positive isolates were susceptible to imipenem and vancomycin (100%).

Our study, which is supported by **Rastogi *et al.*** [15] research, found 100% sensitivity to vancomycin in the examination of Gram-positive bacteria, including enterococci sp. and staphylococcus aureus. Some extended the sensitivity of this common strain to ciprofloxacin [16].

CONCLUSION

The most typical organism identified from DFU was a gram-positive bacterium. Broad-spectrum action against both Gram-positive and Gram-negative organisms was seen by imipenem, vancomycin and amikacin.

- **Acknowledgement:** The authors would like to thank our skillful specialists, assistant lectures, and laboratory technicians for their indispensable technical assistance.
- **Sponsoring financially:** Nil.
- **Competing interests:** Nil.

REFERENCES

1. **Global Burden of Disease Collaborative Network (2020):** Global Burden of Disease Study 2019. Results. Institute for Health Metrics and Evaluation. https://vizhub.healthdata.org/gbd-results.
2. **Romeo G, Lee J, Shoelson S (2012):** Metabolic syndrome, insulin resistance, and roles of inflammation- mechanisms and therapeutic targets. Arterioscler Thromb Vasc Biol., 32 (8): 1771-6.
3. **Boulton A and Whitehouse R (2022):** The diabetic foot. In: Endotext. South Dartmouth (MA): MDText.com. https://pubmed.ncbi.nlm.nih.gov/28121117/
4. **Simonik M, Wilczek J, LaPorta G *et al.* (2018):** Biomechanical Comparison of Intramedullary Beaming and Plantar Plating Methods for Stabilizing the Medial Column of the Foot: An In Vitro Study. Journal of Foot and Ankle Surgery, 57 (6): 1073-1079.
5. **IDF (2021):** International Diabetes Federation IDF Diabetes Atlas, 10th ed. Vol. 102, Diabetes Research and Clinical Practice. https://diabetesatlas.org/idfawp/resource-files/2021/0/IDF_ Atlas_10th_Edition_2021.pdf

6. **Banu A, Noorul Hassan M, Rajkumar J *et al.* (2015):** Spectrum of bacteria associated with diabetic foot ulcer and biofilm formation: A prospective study. Australasian Medical Journal, 8 (9): 280-5.
7. **Foster Z, Bruce G, Parry C *et al.* (2013):** A root cause analysis of amputations in patients with diabetes in Plymouth 2012. Diabetic Medicine, 30: 116-20.
8. **Tesfaye S, Gill G (2011):** Chronic diabetic complications in Africa Epidemiological studies from Europe and North. African Journal of Diabetes Medicine, 19: 1-5.
9. **Li C, Wang W, Ji Q *et al.* (2023):** Prevalence of painful diabetic peripheral neuropathy in type 2 diabetes mellitus and diabetic peripheral neuropathy: A nationwide cross-sectional study in mainland China. Diabetes Res Clin Pract., 198: 110602. doi: 10.1016/j.diabres.2023.110602.
10. **Saini D, Kochar A, Poonia R (2021):** Clinical correlation of diabetic retinopathy with nephropathy and neuropathy. Indian J Ophthalmol., 69 (11): 3364-3368.
11. **Jneid J, Cassir N, Schuldiner S *et al.* (2018):** Exploring the microbiota of diabetic foot infections with culturomics. Front Cell Infect Microbiol., 8: 282. doi: 10.3389/fcimb.2018.00282
12. **Kadhim F, Mohammed S (2021):** Microbiological profile, antibiogram, and risk factors of patients with diabetic foot infections: A systemic meta-analysis. Biomedical and Biotechnology Research Journal, 5 (3): 235-44.
13. **Iyanar K, Premavathy R, Cecilia S *et al.* (2014):** Isolation and antibiotic susceptibility of bacteria from foot infections in the patients with diabetes mellitus type I and type II in the district of Kancheepuram, Tamil Nadu, India. Int J Res Med Sci., 2 (2): 457–461.
14. **Hadi P, Rampal S, Neela V *et al.* (2023):** Distribution of Causative Microorganisms in Diabetic Foot Infections: A Ten-Year Retrospective Study in a Tertiary Care Hospital in Central Malaysia. Antibiotics, 12 (4): 687. https://doi.org/10.3390/antibiotics12040687
15. **Acharya Y, Dhanda G, Sarkar P *et al.* (2022):** Pursuit of next-generation glycopeptides: A journey with vancomycin. Chemical Communications, 58 (12): 1881-97.
16. **Sharma D, Patel R, Zaidi S *et al.* (2017):** Interplay of the quality of ciprofloxacin and antibiotic resistance in developing countries. Front Pharmacol., 8: 546. doi: 10.3389/fphar. 2017.00546.