Diabetic Versus Non Diabetic Foot Ulcers, Comparative Cross Sectional Study

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Abstract

Background: Diabetic foot infection (DFI) remains one of the most serious complications of diabetes mellitus and a main reason of non-traumatic amputation of lower limb. Identifying risk factors and microbiological patterns is crucial for targeted therapy and improved outcomes.
The aim of the current research was to detect the risk factors for diabetic foot infections and detection of their microbiological Characteristics and antibiotics sensitivity for these infections.
Subjects and Methods: Cross-sectional comparative research has been carried out on 74 cases recruited from outpatient clinics of internal medicine and general surgery departments of Minia university hospital from April 2021 to April 2022. 54 patients had diabetes (Group I) and 20 were non-diabetic (Group II). Clinical evaluation, laboratory investigations, and cultures from infected sites were performed.
Results: There are multiple risk factors that have rules in pathogenesis of (DFI) and ulceration as age, gender, smoking and presence of hypertension. Staph aureus was the most often organism isolated from diabetic foot ulcer.
Conclusion: Gram (+) bacteria is the most common organism isolated from diabetic foot ulcer. Vancomycin, Amikacin and imipenem have broad spectrum activity against Gram (-) and gram- (+) organisms.

Key Words: Diabetic foot ulcer (DFU); Diabetic foot infection; Non-diabetic foot ulcer; Gram-positive organisms.

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Introduction:

The International Diabetes Federation forecasts that 537 million individuals have diabetes in 2021, constituting ten percent of the worldwide population, which has risen by 1.2% over the preceding five years. This number is predicated to rise to 783 million by 2045 (IDF et al 2017). Diabetic foot ulcers (DFUs) are a complication of diabetes, affecting an estimated 9.1–26.1 million individuals yearly, with a worldwide occurrence of 6.3% (Zhang et al., 2017). Malaysian research indicated a diabetic foot ulcer infection rate of 41.5% (Kee et al., 2019), whereas an Australian investigation found a comparable rate of 40.1% (Jia et al., 2017). Wound infection in individuals with DFU is a significant predictor of lower limb amputation (Acar et al., 2017), with over one million diabetic cases suffering lower limb loss each year due to ineffective therapeutic interventions for DFI (Ndosi et al., 2018). The 3-year death rate following the initial amputation ranges from twenty percent to fifty percent (Apelqvist and Larsson, 2000). Besides evident physical morbidity and mortality, diabetic foot ulcers provide considerable psychological issues for cases, encompassing melancholy, emotional distress, and anxiety disorders (Polikandrioti et al., 2020).

Diabetic foot infection is the predominant reason of hospitalization in individuals with diabetes, & the complexity of its treatment might lead to prolonged hospitalizations and, thus, elevated health care costs. Consequently, to achieve improved therapeutic results for cases, it is essential to efficiently control and manage these infections (Richard, et al., 2011).

Diabetes-related peripheral neuropathy affects the distal nerves of the extremities, leading to diminished pain perception and progressive numbness. Consequently, DFU might develop and progress undetected after relatively modest external traumas. Shear stress on the foot and Irregular plantar pressure, related to diminished foot mobility and abnormal structural characteristics like Charcot deformity and hammer toe, may facilitate development of ulcer (Fernando, et al., 2013). Upon infection of a diabetic foot ulcer, the primary determinant of clinical result is peripheral arterial disease (PAD), distinguished by the partial or total occlusion of one or more arteries due to atherosclerotic illness. The rate of PAD is two to four times greater in those with diabetes (Creager et al., 2008).

Peripheral artery disease-related vascular complications in diabetes lead to perfusion deficits that diminish flow of blood to diseased tissues, thereby significantly impairing the clearance of infected ulcers through restricting the supply of immune mediators and cells to diabetic foot infections. Moreover, acute hyperglycemia in diabetes impairs the responses of innate immune that often protect against infection. Numerous deficiencies in neutrophil function have been demonstrated in diabetic animal models and human research, involving diminished respiratory burst (Perner et al., 2003), restricted phagocytic activity, & reduction of toll-like receptors for identifying pathogen (Jialal et al., 2013).

Improper treatment of diabetic foot ulcers isn't rare. This is mostly attributable to the absence of specialized management centers for diabetic foot ulcers. The improper management of diabetic foot ulcers may result from several factors, including the administration of antibiotics without culture sensitivity testing. Administer medications that don't affect the species obtained from the wound location or are of unsuitable therapy length. In untreated individuals, most acute infections are largely monobacterial and, particularly in Western countries, mostly involve aerobic Gram-positive cocci, notably Staphylococcus aureus. Chronic infections or those with a prior history of antibiotic therapy are commonly polymicrobial, typically involving Gram-positive aerobic cocci or obligate anaerobic Gram (-) bacilli (Sekhar, et al., 2014).

Aim of The Work

The goal of the research was to recognize the risk factors related to diabetic foot infections and to determine their microbiological characteristics and antibiotic susceptibility patterns, comparing findings between diabetic and non-diabetic cases with foot ulcers.

Materials and Methods

Study Design and Setting

Cross-sectional comparative research has been carried out on 74 patients recruited from outpatient clinic and internal medicine department in cooperation with general surgery department and outpatient clinic of Minia university hospital from April 2021 to April 2022. 54 patients had diabetes (Group I) and 20 were non-diabetic (Group II). Clinical evaluation, laboratory investigations, and wound cultures were performed. Data were analyzed utilizing SPSS version 20.

Participants

A total of 74 cases with foot infections and ulcerations have been enrolled. They were divided into:

Group I (Diabetic): 54 patients,11 (20.4%) had Type I, 43 (79.6%) with type II diabetes mellitus and clinically diagnosed foot infection.

Group II (Non-diabetic): 20 cases with foot infections but without diabetes.

Inclusion Criteria:

All known diabetic and non-diabetic cases suffering from infections, foot ulcers, and gangrene with Age ≥18 years.

Exclusion Criteria:

Immunocompromised cases other than diabetes

Patients on antibiotics within 48 hours prior to sample collection

Data Collection

Detailed history, including duration of diabetes, comorbidities, and risk factors, was recorded. Physical examination. Neuropathy was assessed using monofilament testing and vascularity by Doppler studies.

Sample Collection and Microbiological Analysis:

Pus or tissue samples were collected under aseptic conditions before starting antibiotics and cultured on blood agar, MacConkey, and nutrient agar. Organisms have been identified utilizing standard biochemical tests. Antibiotic susceptibility has been assessed by the Kirby–Bauer disk diffusion technique with regard to CLSI 2020 guidelines.

Ethical approval has been obtained from the ethical committee of Faculty of Medicine, Minia University.

Statistical Analysis

Information have been evaluated with SPSS version 20. Continuous variables have been expressed as mean ± SD, while categorical variables have been reported as percentages and frequencies. Chi-square tests and t-tests have been utilized. A p-value under 0.05 has been deemed statistically significant.

Results:

A total of seventy-four cases with foot ulcers have been included in this study; 54 cases were diabetic, and 20 patients were non-diabetic.

Table (1) Demographic & Clinical Characteristics of the studied groups:

	DFI patients (54)	Non-DFI patients (20	p-value
Age(years) Mean±SD	58.4 ± 9.8	46.2 ± 11.3	**<0.001**
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	 27 (50%) 27 (50%)	 2 (20%) 18 (80%)	0.001**
Occupation: Daily worker Business House Wife Farmer Service	 10 5 15 14 10	 5 2 8 5 0	0.98
Education: Illiterate Basic education Secondary High education	 28 (52%) 11 (20 %) 13 (24%) 2 (4 %)	 5 (25%) 6 (30%) 2 (0.4%) 7 (38%)	**< 0.001**
Residence: Rural Urban	 37 (70%) 17 (30%)	 18 (90%) 2 (10%)	0.06
Type of DM Type I Type II	 11 (20.4%) 43 (79.6%)		
Period of diabetes (years) < 10 10–20 > 20	 30 (55.6) 17 (31.5) 7 (3.78)		
TTT Oral only Insulin Insulin plus oral	 15 (27.8%) 33 (61.1%) 6 (11.1%)		
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
Peripheral neuropathy (%)	30 (56%)	2 (8%)	**0.002**
Peripheral vascular disease (%)	24 (44%)	3 (12%)	**0.01**

Table (1): illustrates that more than fifty percent of diabetic cases were males 34 (63%) while in non-diabetic patients, male: female ratio was 1:1. 25.9% of cases diabetic group has hypertension, 50% were smoker, Among the diabetic patient group,11 patients (20.4%) had type I diabetes mellitus and 43(79.6%) had type II diabetes mellitus. More than half of diabetic patients (61.1 %) were on insulin while 27.8% were taking oral hypoglycemic. Also, it shows the vital signs of participants. Systolic blood pressure was higher in diabetics (Mean 126.5±17.9) compared to non-diabetics (Mean 115±14) (p= 0.012). a significant association among DFU frequency and smoking, SBP and the level of education. As regarding peripheral neuropathy and peripheral vascular disease, we found that there is a high incidence of these diseases in diabetic cases comparing to non-diabetic subjects, and it was statistically significant (P value 0.002, 0.01 respectively)

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

	Case	Control	P value
	(n=54)	(n=20)	
Culture Organism			
Gram +ve	33 (61.1%)	12 (60.0%)	
Staph aureus	19 (35.2%)	12 (60.0%)	
coagulase-negative staph	8 (14.8%)	0 (0.0%)	
Streptococci	6 (11.1%)	0 (0.0%)	
Gram-ve	18 (33.3%)	6 (30.0%)	0.104
Pseudomonas	6 (11.1%)	2 (10.0%)	
Klebsiella (MDRO)	6 (11.1%)	0 (0.0%)	
Klebsiella (ESBL)	3 (5.6%)	2 (10.0%)	
E-Coli	3 (5.6%)	2 (10.0%)	
Negative culture	5 (5.8%)	2 (12.0%)	

MDRO: Multi drug resistance to organisms.
ESBL: Extended spectrum beta lactam

Table (2): it shows that Gram positive organisms were isolated from 61.1% of diabetic foot ulcer while 33.3% were gram negative. Isolates were Staph aurous was in 19 cases (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 5%. Among non-diabetics the isolates were 60% staph aurous, 10% for each of pseudomonas, klebsiella (ESBL) and E-coli. While 5.8% of diabetics and 12% of non-diabetics were negative culture., there was insignificant variance among both groups. P value was insignificant

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%)

Table (3): It shows the sensitivity pattern of gram positive bacteria isolated from DFU infection and shows that 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 of antibiotics except to nitrofurantoin, ceftazidime, ceftriaxone and cefoxitin. All gram-positive isolates were prone to imipenem and vancomycin (100%). Amoxicillin resistance has been observed in 100% staph aureus and CoNS .

Discussion

Annually, some 18.6 million individuals globally are affected via diabetic foot ulcers (Lipsky et al., 2019), and the occurrence of diabetic foot infections is significant (Prompers et al., 2008). DFI is the primary etiological factor for amputating lower limb in cases with diabetic foot ulcers. The World Health Organization reports that the death rate post-amputation is surpassed only by that of lung tumor, making it the 2nd highest globally (Khodadadi, et al., 2019).

Our investigation demonstrates that cases with DFI predominantly comprise of middle-aged and older males with various comorbidities, agreeing with results from additional research (Wu, et al., 2016) - (Meganathan and Rejitha, 2019). This may correlate with men's requirement for increased outdoor labor, inadequate foot care, & lifestyle variance associated with gender. They frequently have poor control of blood glucose, consequently DFI can happen in a very short duration of time (DM under ten years).

Conversely, Al-Rubeaan et al. (2015) found no correlation among age & the onset of diabetic foot infections. Fawzy et al. (2019) demonstrated that older cases, with a mean age of sixty-five years, exhibited a higher susceptibility to DFU in Saudi Arabia.

The current investigation reveals a distinction among both groups about sex in relation to the development of diabetic foot infections. Over half of the diabetes cases were male (34, 63%), whereas the male-to-female ratio in non-diabetic cases was 1:1. This aligns with the findings of Yazdanpanah et al. (2018), who found male gender as a risk factor for diabetic foot ulcers in Iran. Contrary to Galal et al. (2021), they indicated that gender was not correlated with the development of diabetic foot ulcers in Egypt. Likewise, Al Kafrawy et al. (2014) demonstrated that sex wasn't a risk factor for the development of diabetic foot ulcers. Fawzy et al. (2019) indicated that female cases in Saudi Arabia exhibited a higher susceptibility to diabetic foot ulcers than their male counterparts. This variance may be attributable to variations in the study participants and the methods applied.

This investigation revealed that illiteracy was significantly greater between cases with DFI (fifty-two percent) at (p-value under 0.001). Consequently, educated individuals are more inclined to ask medical advice, adhere to healthy lifestyles, & engage in preventive practices compared to those who are illiterate. Similarly, Galal et al. (2021) indicated that illiteracy constituted a substantial risk factor for diabetic foot infections. Cardoso et al. (2019) identified illiteracy as a risk factor between Brazilian cases.

In this research, the prevalence of countryside living is significantly elevated in the DFI group (seventy percent) compared to the other group (thirty percent) (p-value equal 0.06). This result aligns with Mariam et al. (2017), indicating that rural locations are correlated with the frequency of diabetic foot ulcers between Ethiopian diabetics. Salama & Zorin (2017) in Egypt & Tolossa et al. (2020) in Ethiopia observed similar findings. Moreover, Yimam et al. (2021) observed that rural diabetics were eightfold more susceptible to developing DFU compared to urban diabetics. The outcomes may indicate that residing in rural areas encourages inadequate foot care practices and walking barefoot.

In our research, the incidence of DFU in patients on insulin therapy represents (61.1%) compared to (27.8%) in cases treated with oral anti-diabetic medications.

Yazdanpanah et al. (2018) observed that cases utilizing insulin were more predisposed to developing foot ulcers compared to those treated utilizing oral anti-diabetic medications. Cases with diabetes might initiate insulin therapy when they have uncontrolled diabetes accompanied by complications. This outcome aligns with the studies conducted by Al-Rubeaan et al. (2015) in Saudi Arabia & Jiang et al. (2015) in China. In Egypt, Salama and Zorin (2017) discovered that 71.7 percent of cases with diabetic foot administered insulin, in contrast to 29.5 percent of those without diabetic foot. Nevertheless, Galal et al. (2021)

observed that management modalities in the form of insulin and oral hypoglycemic drugs are protective predictors of DFU.

In our study systolic blood pressure is statistically significant high in DFU in comparison with Non DFU patients. This outcome was supported by a study of Brennan, et al., 2018. In contrast, research by Khan, et al., 2018.as the outcomes of the research found that hypertension association with DFU was not statistically significant.

Smoking constitutes a notable risk factor in this research, with fifty percent of cases with diabetic foot ulcers being smokers, in contrast to twenty percent of those without DFUs (p-value equal 0.001). Consistent with our findings, Galal et al. (2021), Salama & Zorin (2017), & Al Kafrawy et al. (2014) demonstrated that smoking is a prognostic factor for DFU. In conclusion, smoking is a primary risk factor correlated with diabetic foot ulcers and peripheral vascular illness. Furthermore, Obaid & Eljed (2014) indicated that smoking elevates the chance of getting diabetic foot, even among former smokers.

In the present study, peripheral vascular disease found in (44%) of DFU in compared to (12%) in non-DFU patients. These results matched to the results of Brito et al. (2017), Cardoso et al. (2019), & Yazdanpanah et al. (2018).

Conversely, Refaat et al. (2019) reported that the absence of peripheral pulse wasn't found in any of their cases, regardless of the presence of diabetic feet, while evaluating diabetic foot risk factors between Egyptian cases.

The loss of the monofilament ten grams' test represents an additional critical risk factor for diabetic foot ulcer. in the present investigation fifty-six percent of cases with diabetic foot ulcers failed the Monofilament 10g test, in contrast to eight percent of non-DFU cases. The present data corroborates the results of Abdissa et al. (2020), which indicated that DFU were 11.2 times more prevalent among those with peripheral neuropathy. Similarly, Cardoso et al. (2019) revealed that over fifty percent of the individuals in their research exhibited subpar results on the monofilament examination. Assaad Khalil et al. (2014) identified monofilament insensitivity as a significantly significant risk factor for complications of diabetic foot.

In the present study Gram positive organisms have been isolated from (61.1%) of diabetic foot ulcer while (33.3%) were gram negative. Isolates revealed that, Staph aurous was in (35.2%), coagulase-negative staph was in (14.8%), (11.1%) for streptococci, pseudomonas and Klebsiella (MDRO); (5.6%) for Klebsiella (ESBL) and E-coli, while negative culture found in (5%). Among non-diabetics the isolates were (60%) staph aurous, (10%) for each of pseudomonas, klebsiella (ESBL) and E-coli. While (5.8%) of diabetics and (12%) of non-diabetics were negative culture. there was insignificant variance among both groups.

Our findings, corroborated by the research of Jneid et al. (2018), indicate that the predominant organism extracted from DFU tissues was Staphylococcus aureus, followed by Enterococcus faecalis, Staphylococcus lugdunensis, Enterobacter cloacae, Staphylococcus epidermidis, Finegoldia magna, and Proteus mirabilis. The research determined that, following a 1-month monitoring, the only factor associated with wound enhancement was the existence of E. Faecalis, in contrast to cases exhibiting no wound enhancement.

Research conducted in France assessed the bacterial agents responsible for DFU and infections, identifying Staphylococcus aureus as the predominant cause of DFI. (R. R. Yotsu. Et al., 2014)

Research by Pitocco et al. 2019 identified the microorganisms responsible for diabetic foot ulcers as Enterococcus faecalis, Staphylococcus aureus, and Pseudomonas aeruginosa (D. Pitocco, et al., 2019).

Research by Rampal et al. (2019) demonstrated that Gram (-) bacteria predominated in diabetic foot infections in comparison with Gram-positive bacteria (seventy-one percent against twenty-nine percent); notably, the most commen bacteria was Pseudomonas aeruginosa, followed by Klebsiella species & Proteus mirabilis. Gram-positive isolates & Gram- negative isolates include Staphylococcus aureus, followed by Streptococcus species.

India, & Turkey that noted outcomes observations where Gram-negative bacteria commen in DFI (Raja, et al., 2007).

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 of antibiotics except to nitrofurantoin, ceftazidime, ceftriaxone and cefoxitin. All gram-positive isolates were susceptible to imipenem and vancomycin (100%).

Our research supported by, In the research of Rastogi et al. described one hundred percent sensitivity to vancomycin in the assessment of Gram (+), like Staphylococcus aureus as well as Enterococci sp. (Rastogi, et al., 2017)

Al Benwan et al. stated the greatest Gram-negative responses to amikacin, imipenem, & piperacillin-tazobactam. (Al Benwan, et al., 2012)

Research conducted by Sekhar et al. indicated that the most significant therapeutic reaction in Gram-negative strains has been noted for amikacin, meropenem, and cefoperazone-sulbactam. Additionally, a one hundred percent susceptibility of Staphylococcus aureus to cotrimoxazole & a one hundred percent resistance to ciprofloxacin were reported. Nonetheless, more investigations have demonstrated, to a certain degree, the susceptibility of this prevalent strain to ciprofloxacin. (Sekhar, et al., 2014)

Conclusion:

Diabetic foot infections were significantly related to modifiable risk factors like smoking, hypertension, and neuropathy. Staphylococcus aureus was the predominant pathogen, showing full sensitivity to imipenem and vancomycin. Early detection and targeted antibiotic therapy are crucial to improving outcomes and reducing amputation risk.

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