DIABETIC FOOT INFECTION IN SPAIN

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ABSTRACT

Introduction*: The associated complications of diabetes mellitus significantly impair the quality of life of affected patients. The disease leads to a wide variety of complications; among them foot ulcers are common being the most frequent cause of hospitalization of diabetic patients. Moreover, foot ulcers predict disability, morbidity, and mortality in diabetic patients in addition to incurring considerable healthcare costs. We investigate the bacteria involved in diabetic foot ulcers infection and record the evolution and epidemiological data of a group of patients.*

Materials and methods*: The study population consisted of prospectively enrolled diabetic patients who attended two hospitals in Barcelona: one specializing in foot care (Hospital Podologic of the University of Barcelona) and the other a tertiary referral hospital (Hospital de Sant Pau). A comparison of microbiological results and their dependence on the sampling method (swab or punch) was done.*

Results*: Diabetic Foot Syndrome was more prevalent in males than in females and more prevalent in patients with type 2 than type 1 diabetes. It becomes apparent that individuals living alone (singles, widowers and widows, etc.) tend to request medical assistance later or perhaps they take less attention to their feet, thus percentage of singles increased with the severity. Relatives and nursing care seem to play a relevant role in the evolution and prognosis of diabetic foot ulcers.*

Conclusion*: Relatives and nursing care seem to play a crucial role in the evolution and prognosis of diabetic foot ulcers. Pseudomonas and Staphylococcus were the most frequent bacteria infecting ulcers. The use of ciprofloxacin should be discouraged since resistance accounted up to a 40%.*

Keywords*: Diabetic foot, Nursing cares, Staphylococcus, Pseudomonas, antibiotic treatment.*

DOI: 10.19193/0393-6384_2018_3_100

Received *November 30, 2017;* ***Accepted*** *January 20, 2018*

Introduction

Diabetes mellitus (DM) is a metabolic disease characterized clinically by chronic hyperglycemia as well as disturbances in lipid and protein metabolism. The associated complications of DM significantly impair the quality of life of affected patients. Foot ulcers are one of the most common complication and the most frequent cause of hospitalization of diabetic patients. Foot ulcers predict disability, morbidity, and mortality in diabetic patients in addition to incurring considerable healthcare costs. DM-related foot complications are collectively referred to as diabetic foot syndrome (DFS), defined by the World Health Organization as "ulceration of the foot (distally from the ankle including it) associated with neuropathy and different grades of ischemia and infection"[(1)]. The vascular complications of DFS often lead to lower-extremity amputations. In fact, in developed countries, roughly 80% of amputations are performed in patients with foot ulcers.

The pathogenesis of foot ulcers is complex and multifactorial. The well-known triggers include

peripheral neuropathy, foot deformity, abnormal foot pressure, abnormal joint mobility, trauma, and peripheral artery disease. Of these, peripheral neuropathy is the most relevant cause of foot ulceration in diabetic patients. By impairing nerve activity, diabetic peripheral neuropathy impairs autonomic, sensory, and motor functions[2]. The loss of sensation makes the foot vulnerable to mechanical injury, thermal damage, or excess pressure by shoes. Thus, sensory neuropathy is the most important cause of foot ulceration in diabetic patients.

Infections of the ulcerated diabetic foot are an extremely serious complication of diabetes as they drastically increase the risk of amputation. Frequently these infections affect not only soft tissues but extend to the bone. Cellulitis as well as osteomyelitis are in many cases polymicrobial, with gram-positive cocci and gram-negative rods (fermentative, non-fermentative and anaerobes) commonly detected. Infection is assumed when "there is purulent drainage and/or the presence of two or more signs of inflammation"[3].

The care of diabetic foot ulcers requires both appropriate antimicrobial treatment and surgical intervention. Antimicrobial therapy should be established on the basis of microbiological culture, which in Spain and other countries is not routinely performed in DM patients.

Our study focuses on foot infections in DM patients with foot ulcerations treated at two hospitals in Barcelona and serving a total population of 2,800 diabetic patients/year. Epidemiological and microbiological data are reported and the roles of nursing and lifestyle are evaluated. The use of care services by patients, the role of relatives living together with them as well as the eventual role of nursing care were evaluated in relation with the prognosis and evolution of foot ulcers.

Materials and methods

The study population consisted of prospectively enrolled diabetic patients who attended two hospitals in Barcelona: one specializing in foot care (*Hospital Podologic* of the University of Barcelona) and the other a tertiary referral hospital (*Hospital de Sant Pau*). Patients had clinically diagnosed DM type 1 or 2 and were seen at either hospital for the treatment of foot ulceration. All of the enrolled patients provided informed consent to participate in the study. Patients with foot ulcers lacking signs of infection were excluded.

Of the total estimated diabetic population of 15,000 patients, approximately 10% were treated at the two hospitals for an infected diabetic foot (95% confidence level, Z=1.96). The initial study population consisted of 176 patients. After the exclusion of those whose microbiological cultures were positive for more than five different bacterial species isolates, 146 patients were included in the study. *The Comité de Bioética de la Universidad de Barcelona* evaluated and approved the study (RB00003099). Study participants were interviewed face-to-face with one of the authors (CP), during which time data were collected by means of a standardized questionnaire. The following information was obtained: demographic characteristics, duration of DM, symptoms of neuropathy, quality of life, and medical history.

Two specimens were taken from each ulcer, the first one using swabs and the second by means of a 3-mm diameter trocar (punch). Both samples were immediately transported to the laboratory (<20 min) and processed. Primary cultures were obtained by direct inoculation from the swab onto plates of blood-agar, chocolate-agar, mannitol hypersaline, CAN (colistin nalidixic agar) agar, McConkey agar fastidious anaerobe agar, and Sabouraud agar supplemented with chloramphenicol. Samples harvested by punch were placed in 1 ml of Ringer ¼ solution and homogenized using a stomacher apparatus. One hundred μl of the homogenate was spread on the surface of the plates, which were then incubated at 37°C in air (blood agar, hypersaline Mannitol and McConkey), 5% CO2 (chocolate agar and CAN agar), an anoxic chamber (Whitley DG 250 Anaerobic workstation: fastidious anaerobe agar), or at 30°C in air (Sabouraud agar). The incubation periods were 48 h for cultures incubated under aerobic and microaerophilic conditions, 7 days for anaerobic cultures, and up to 15 days for fungi. All media were purchased from Scharlau (Barcelona, Spain), except fastidious anaerobe agar, which was purchased from LabM Ltd. (Lancashire, UK). Microbial identification was accomplished by microscopic examination, biochemical tests, and growth on selective medium. Isolates were stored frozen in skim milk at -80°C.

Susceptibility to the antimicrobials amoxicillin, amoxicillin plus clavulanate, cefoxitime, penicillin, erythromycin, tobramycin, mupirocin, gentamycin, tigecycline, vancomycin, cloxacillin, ciprofloxacin, cotrimozaxole, clindamycin, fusidic

acid, and amikacin was determined first by Kirby-Bauer disc diffusion assays (4). Minimal inhibitory concentrations (MIC) were determined by the microdilution method according to the Clinical & Laboratory Standards Institute (CLSI).

Results

Fungi were rare in foot ulcers as they were detected in only 3.9% of the samples. The most frequent species was Candida parapsilosis. The distribution of bacterial infections in our patients is shown in Table 1.

Microorganism (% of affected patients)	Species	N	Percentage
Fungi (3.9%)	*Cryptococcus spp.*	1	0.2
	Rhodotorula spp.	2	0.4
	Candida albicans	4	0.9
	Candida parapsilosis	11	2.4
Gram-negative bacteria (45.6%)	*Acinetobacter calcoaceticus*	5	1.1
	Pseudomonas spp.	86	18.9
	Escherichia coli	10	2.2
	Proteus spp.	32	7
	Other Enterobacteriaceae	75	16.4
Gram-positive bacteria (50.3%)	*Staphylococcus aureus*	97	21.2
	Coagulase-negative Staphylococcus	35	7.7
	Micrococcus spp.	8	1.8
	Streptococcus viridans	7	1.5
	Streptococcus pyogenes	25	5.4
	Enterococcus	26	5.7
	Other cocci	10	2.2
	Corynebacterium spp.	22	4.8

Table 1: Isolates from the clinical specimens included fungi (being *Candida parasilopsis* the most frequent), Gram positive bacteria (being *Staphylococcus aureus* the most prevalent) and Gram negative bacteria (*Pseudomonas* was the most frequent genus).

Among the gram-negative bacteria, *Pseudomonas* was the most frequently detected, followed by *Escherichia coli*. Gram-positive bacteria were also present in a significant number of the ulcers (Table 1).

The results of the antimicrobial susceptibility testing of the isolates are shown in Figure 1. Resistance to penicillin, amoxicillin, amoxicillin plus clavulanic acid (augmentine), and ciprofloxacin was frequently detected. More than 40% of the isolates were resistant to ciprofloxacin. The epidemiological data and some other characteristics of the patients are summarized in Table 2.

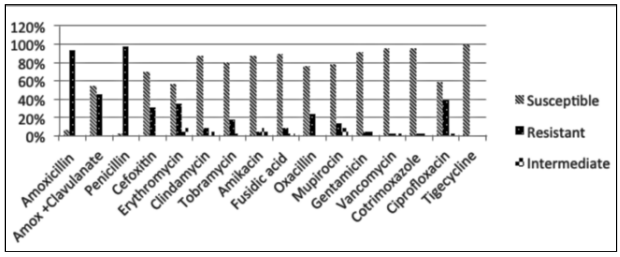

Fig. 1: Frequencies of high, moderate, and susceptible isolates to antimicrobials tested, including all antibiotic families used in clinics. As much as 40 % of isolates were resistant to ciprofloxacin whose use in the treatment of infecte3d foot ulcers is extended in Spain.

Of the 176 patients, 130 (73.9 %) were male and 46 (26.1%) were female.

The most frequent reasons for hospital admission in our patients were: chronic complications of diabetes (42.1%), hyperglycemia (26.4%), and infection (15.7%).

Among our 143 patients affected by type 2 diabetes mellitus (type 2 DM), 110 were males and 33 were females whereas a total of 20 males and 13 females were previously diagnosed of type 1 diabetes mellitus (type 1 DM).

Ulcers were mostly localized in the forefoot (49.4 %) and most of these were of neuropathic etiology; 33.9% of the ulcers were localized to the toes and were mostly vasculopathic in origin; the remaining 16.7% were in the hind foot. In many of our patients, diabetic foot was concomitant with one or several other diabetic complications, especially nephropathy (54.5%), retinopathy (75.3%), and cardiopathy (55.7%) (Table 3).

Results concerning lifestyle were surprising since it seems crucial when predicting the evolution of diabetic foot (Table 4). Among the study patients with grade 2 ulcerations (deep ulcer affecting the skin, adipose tissue, and ligaments and in some cases including slight infection), 74.6% lived with someone else whereas 25.4% lived alone. By contrast, among patients with grade 3 ulcerations (deep ulcer, abscess, articular sepsis, and moderate infection), 56.3% lived with someone else and 43.8% lived alone.

Data		N	Percentage
Sex	Female	46	26.1
	Male	130	73.9
Diabetes type	1	33	18.7
	2	143	81.2
Duration	0–5 years	11	6.3
	6–10 years	10	5.7
	11–15 years	42	23.9
	16–20 years	36	20.5
	21–25 years	34	19.3
	26–30 years	18	10.2
	31–35 years	12	6.8
	36–40 years	7	4
	41–45 years	4	2.3
	61–65 years	1	0.6
	>65 years	1	0.6
Lifestyle	Alone	54	30.6
	With relatives	122	69.3
Age	31–40	34	19.3
	41–50	35	19.9
	51–60	47	26.7
	61–70	41	23.3
	71–80	18	10.2
	>81	1	0.6
Degree of ulceration	2	126	71.6
	3	46	27.3
	4	2	1.1
Ulcer site	Forefoot	86	49.4
	Toes	59	33.9
	Heel	29	16.7
Vasculopathy/Neuropathy	Neuropathy	86	49
	Vasculopathy	5	3
	Both	83	48
Number of complications diagnosed (see Table 3)	1	44	25
	2	55	31.3
	3	42	23.9
	4	19	10.8
	5	16	9.1

Table 2: Epidemiological data of the study population.

The number of patients with grade 4 ulcers was too small to obtain some conclusion.

Finally, one can see in figure 2 that the number of different bacterial isolates obtained in the swab and punch cultures are shown. Cultures initiated from swabs yielded a significantly greater diversity of isolates. In addition to microbial pathogens, several normal skin inhabitants were harvested.

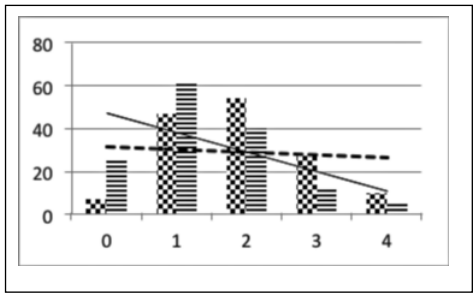

Fig. 2: Comparison of the number of bacterial isolates from samples depending on the method for sampling: swab and punch

Yes	26.10%	44.30%	17.00%	29.50%	11.40%	14.80%
No	73.90%	55.70%	83.00%	70.50%	88.60%	85.20%
Total	100.00%	100.00%	100.00%	100.00%	100.00%	100.00%

Table 3: Frequent complications (nephropathy (Nephro), retinopathy (Retino), cardiopathy (Cardio)) of diabetes mellitus in the population requiring nursing care for diabetic foot syndrome in the population studied.

Ulceration	Patients living alone (%)	Patients living with someone
Grade 2 (deep ulcer, affecting skin, adipose tissue and ligaments , possibly with slight infection)	25.4	74.6
Grade 3 (Deep ulcer, abscess, articular sepsis, moderate infection)	56.3	43.8
Grade 4 (necrosis, severe infection)	50	50

Table 4: Relation of lifestyle (living alone or with someone) and grade of ulceration.

Discussion

The finding that *Candida parapsilosis* was the most frequent fungi is in agreement with the results of Missoni et al.[5], in their study of a Croatian population, in which the rate of fungal infection was 5% and *C. parapsilosis* was the most prevalent isolate, detected in 61.5% of the patients with fungal

infections. Results concerning bacterial infection resulted to be similar to those of Maksum et al[6], who reported *Pseudomonas* spp. infections in 16.9% of the samples, followed by *E. coli* (10.2%), *Enterobacter* spp. (7.0%; reported in our study as other Enterobacteriaceae), Proteus spp. (6.7%), and *Acinetobacter* spp. (3.2%).

Antimicrobial resistance is a relevant public health concern worldwide, particularly in patients at high risk of developing infections, such as diabetic patients. In our work resistance to penicillin, amoxicillin, amoxicillin plus clavulanic acid (augmentine), and ciprofloxacin was frequently detected. In Spain, ciprofloxacin is often prescribed for the treatment of infected foot ulcers, although in our patients >40% of the isolates were resistant. This finding highlights the importance of microbiological analysis prior to the prescription of antimicrobials in DM patients with foot infections.

Sex distribution of patients herein studied reflected that of the patients seen at the two hospitals for infected foot ulcers and was in contrast to that of other studies, in which there were no significant differences in the sex of patients seen for other diabetic complications[7, 8].

According to Lin et al.[9], among elderly diabetic patients, ketonuria, ketonemia, and diabetic ketoacidosis are more common in women, whereas diabetic nephropathy, neoplasms, and respiratory infections are more frequently found in men. Valizadeh et al.[10] reported that female sex, in combination with other characteristics, including age >60 years, lower education level, longer disease duration, and higher level of hemoglobin A1c, are associated with a higher risk of retinopathy. Kawamoto et al.[11] reported a higher incidence of coronary syndromes among diabetic women. It is worldwide assumed that while in healthy people the risk for cardiovascular diseases is higher among men, when looking at diabetics there is a complete reversed situation that is to say that women had greater incidence of cardiovascular complications[12]. Herrera-Rangel et al,[13] showed that sex influences postural stability in DM type 2 patients, with males being more vulnerable than females. Postural disorders are among the causes of foot ulcers, as they result in abnormal foot pressure.

In their recent meta-analysis, Al-Rubeaan et al.[14] concluded that Diabetic Foot Syndrome was more prevalent in males than in females and more prevalent in patients with type 2 than type 1 diabetes, as also determined in our study.

Data concerning lifestyle suggest that individuals living alone tend to delay seeking medical assistance or pay less attention to foot care, resulting in more severe ulceration at the time of hospital admission. A similar conclusion was reached by Fan et al.[15], who showed that educational intervention aimed at foot self-care is feasible, acceptable to adult patients with type 2 DM, and effective in reducing the occurrence of more severe ulcerations and related problems. Thus, increased efforts to encourage diabetes self-management and to educate and support patients and their relatives will likely improve outcome. An earlier study similarly demonstrated that the provision of coordinated care is negatively associated with amputation rates[16]. In conclusion, relatives and nursing care seem to play a relevant role in the evolution and prognosis of diabetic foot ulcers.

Finally, from the comparison of bacteriological results obtained from samples taken with swab or punch it should be stated that a punch should be used to sample deep diabetic ulcers. Moreover, because most neuropathy patients have severely impaired sensations in the affected area, minimal or no pain is invoked during sampling.

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Funding. This work was financed by the Fibrodress project. NSFA - Programa Nacional de Salud y Farmacia IPT-2012-0602-300000

Authors' Contribution: All authors significantly contributed to the paper. EC, EF and TV performed the experimental microbiology work. CP did the clinical work. MV conceived of the study, and MV and TV wrote the paper

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