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Diabetic foot amputations in patients at the Peltier hospital in Djibouti

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ABSTRACT
Diabetes is a chronic (lifelong) condition that arises when the pancreas does not secrete adequate insulin or when the body does not utilize the produced insulin. Diabetes can cause serious health complications such as diabetic foot infections. This study aimed to investigate the problem of diabetic foot amputations and to evaluate the prevalence of pathogenic bacteria that cause diabetic foot infections. A retrospective study was conducted on hospitalized patients over a period of three years from 2020 to 2022. We analyzed 254 (34 %) patients who satisfied the study inclusion criteria. The average age of the patients was 59 years ± 6 years. The study focused on diabetic patients with foot ulcers that had at least two local clinical signs of infection. In our study, we reported 68 amputation cases in 254 diabetic patients with a foot wound, representing 27 % prevalence. The main causative organisms of diabetic foot infections were *Staphylococcus aureus* (35 %), *Staphylococcus sp.* (19 %), *Streptococcus sp.* (16 %), *Klebsiella pneumoniae* (14 %), *Pseudomonas aeruginosa* (12 %) and *Escherichia coli* (4 %). Methicillin-resistant *Staphylococcus aureus* (MRSA) strains were resistant to gentamicin and ciprofloxacin (38 %). Linezolid was the most effective anti-MRSA chemical.
The incidences of diabetic foot become a growing public health issue. A gram-positive coccus was the main pathogen responsible for diabetic foot infections with *Staphylococcus* predominating. The isolated bacteria were resistant to first-line antibiotics posing a substantial therapeutic challenge.

1. Introduction:

Diabetes is a chronic non-communicable pathology, that is a source of many complications and is difficult and expensive to manage. It is a chronic metabolic endocrine pathology characterized by hyperglycaemia. It is the consequence of either a defect in insulin secretion or of a reduction in its action on target tissues or both, under the influence of genetic and/or environmental factors **[1-2]**. Silent and painless, its progression is always towards metabolic and especially degenerative complications. Diabetes mellitus increases the incidence of mortality and morbidity. It is a major public health problem worldwide. It increases the prevalence of ulceration and amputation. Many complications can arise: cardiovascular, renal, neurological, and eye problems. It can also cause complications in the feet, which are the most common and feared **[1-2]**. The feet of diabetic patients are at high risk of developing serious trophic disorders.

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The risk is increased by the combination of neurological, arterial, and infectious complications. Lesions are often secondary to micro-traumas. The incidence of foot lesions in diabetic patients is very high. Neuropathy, arteriopathy, and foot deformities alone or in combination are risk factors for the development of foot lesions in diabetic patients **[3]**. Infection can occur with any of these processes and is an aggravating factor. The diagnosis of an infected diabetic foot is based on the presence of at least two of the following local signs: induration or thickening, perilesional erythema, tenderness or pain, warmth, and purulent discharge. Diabetic foot infection consists of bacterial invasion of tissue, accompanied by multiplication with or without an inflammatory response **[4-6]**. This infection acts as a complicating factor and increases the risk of amputation **[3-4]**. The International Diabetic Foot Consensus confirms that 80 % of non-traumatic amputations occur in diabetic patients **[1-4]**. The risk of amputation is 10 to 30 times higher in people with diabetes than in the general population **[5]**.

This study was initiated to investigate the problem of diabetic foot amputations and to determine the prevalence of pathogenic bacteria responsible for diabetic foot infections. The results will make it possible to consider probabilistic antibiotic therapy based on a more objective bacteriological profile. Antibiotic therapy in conjunction with surgical treatment remains good medical care.

2. Materials and methods:

This is a retrospective study conducted at the polyvalent medicine service of the Peltier Hospital in Djibouti. The study was carried out on hospitalized patients over a period of three years, between January 1, 2020, and December 31, 2022. Among 750 patients hospitalized during the study period, 197 patients (26 %) were aged 60 or older. After eliminating contaminants, duplicates, and missing data, we analyzed 254 (34 %) patients who satisfied the study inclusion criteria.

The study focused on diabetic patients with foot ulceration with at least two local clinical signs of infection (induration, redness, pain, heat, or suppuration) who were admitted to the unit. All diabetic patients who underwent lower limb amputation as a result of diabetes complications during the study period and who gave their consent were included. Free and informed verbal consent was obtained from the patients before their inclusion in the study. After collecting epidemiological and clinical data; taking biological samples and performing radiological examinations; first-line antibiotic therapy was started, pending bacteriological results. An arteriopathy of the lower limbs is sought: ischemic necrosis of the extremities of the toes in the form of blackening of the toes, the sensation or absence of the peripheral arterial pulses of the lower limbs, and cold extremities. Neuropathy is sought: deformity, callus, gangrene, and Charcot's foot. The paraclinical examination collected a recent history of less than 3 months: blood glucose, complete blood count (CBC), erythrocyte sedimentation rate (ERS), glycated hemoglobin (good balance [6.5-7.5 %], and poor balance > 7.5 %), standard X-ray of the foot, arterial Doppler ultrasound of the lower extremities and pus swab from the wound. The affected foot was graded according to the University of Texas classification. This classification has 4 grades based on the depth of the lesion and 4 stages according to the presence or absence of infection and/or arterial disease. It allows the percentage of amputation of the foot to be determined. Patients with an infected diabetic foot had samples taken from the lesion by aspiration of pus through healthy skin, curettage swab of the base of the ulceration, or tissue biopsy for bacteriological study. The samples were taken to the laboratory for microscopic examination, culture, and bacterial identification followed by an antibiogram. Bacterial susceptibility to antibiotics was determined by the Kirby-Bauer method. This study was carried out on samples for diagnostic purposes. The identification of isolated bacteria was based on the morphological, cultural, and biochemical characteristics using the API20E®, APINE®, API STAPH® strips (BioMérieux, France), VITEK® cards (BioMérieux, France), and the coagulase test.

The antibiogram was performed by the diffusion method in solid medium, on Mueller-Hinton agar (MH) for non-fastidious bacteria, and on MH supplemented with 5 % sheep blood (MH-S) and MH supplemented with 5 % horse blood and 20 mg/l β-NAD (MH-F) for fastidious bacteria. BioMerieux Analytical Profile Index panels were used for microbial identification **[7-8]**. Methicillin-resistant *Staphylococcus aureus* or MRSA was detected by the Oxacillin disc diffusion method **[8]**. Isolates were considered methicillin-resistant if the inhibition zone was less than 10 mm.

3. Results and discussion:

Among the 750 patients hospitalized during the study period, 197 patients (26 %) were aged 60 years and over. After eliminating contaminations, duplicates, and missing data, we analyzed 254 (34 %) patients who met the study inclusion criteria (infected foot lesion).

We observed 136 males (53.5 %) and 118 females (46.5 %), giving a sex ratio of 1.37. The average age of the patients was 59 years ± 6 years (average ± SD) with extremes ranging from 39 years to 74 years. The average duration of the lesion development was 38 days. The lesions were spontaneous in 183 patients (72 %). They were necrotic in 196 patients (77 %) and osteitis in 162 patients (64 %). Infection was at stage 2 in 39 (15 %), stage 3 in 165 (65 %), and stage 4 in 50 (20 %) patients. One hundred and thirty-nine (139) patients had received antibiotic therapy prior to hospitalization. 254 pus samples

were taken: 218 (86 %) cultures were positive including 203 monomicrobial (93 %) and 15 bimicrobial (7 %). 233 bacteria were isolated. The average number of bacteria isolated per positive culture was 1.07 (233/218).
The table 1 shows the distribution of the different bacteria isolated. There was no statistically significant relationship between the bacterial genus or species found on the lesions and the following factors: time to treatment, site of the lesion on the foot, stage of severity of the lesion, presence of osteitis, and pre-hospital antibiotic therapy.

Table 1. Frequency of bacteria isolated from diabetic foot infections in hospitalized patients at the Peltier Hospital (n = 233).

Bacteria isolated	**Numbers**	**Percentage (%)**
Staphylococcus aureus	81	35
Staphylococcus sp.	44	19
Streptococcus sp.	37	16
Klebsiella pneumoniae	33	14
Pseudomonas aeruginosa	28	12
Escherichia coli	10	4
Total	**233**	**100**

The main causative organisms of diabetic foot infections are *Staphylococcus aureus* (35 %), *Staphylococcus sp.* (19 %), *Streptococcus sp.* (16 %), *Klebsiella pneumoniae* (14 %), *Pseudomonas aeruginosa* (12 %) and *Escherichia coli* (4 %).
In our study, gram-positive cocci were the most common pathogens found to be responsible for diabetic foot infections with a predominance of *Staphylococcus* (54 %).
Methicillin resistance was observed in *Staphylococcus aureus* isolates (31 %). Methicillin-resistant *Staphylococcus aureus* (MRSA) has several virulence factors that help destroy host cells, increasing the risk of infection. In our study, MRSA strains were resistant to gentamicin and ciprofloxacin (38 %). Linezolid was the most active molecule against MRSA. Regular monitoring of antimicrobial resistance in *Staphylococcus aureus* strains, implementation of hygiene measures, and education of healthcare workers, especially on the washing of hands, are helping to reduce the rate of MRSA **[8]**.
Augmentin, ceftriaxone, linezolid, and vancomycin were the drugs of choice for treating diabetic foot infections at the Peltier Hospital, in doses adapted to renal failure. The parenteral route remains the most common way of administering an anti-infective drug in the hospital.
The infected diabetic foot was diagnosed in 34 % of hospitalized diabetic patients. The infection was monomicrobial (93 %) and caused by *Staphylococcus aureus* (35 %). No factor studied was associated with the type of bacteria found on the lesions.
A prevalence of 8.8 to 35 % has been reported in Africa **[5]**, making diabetic foot the first infectious complication of diabetes in hospitalized patients.

In our study, neither the time to treatment, pre-hospital antibiotic therapy, the stage of lesion severity, the location of the lesions on neither the foot, nor the condition of the underlying bone determined the type of bacteria identified.
Out of 254 diabetic patients with a foot wound, we recorded 68 cases of amputation, at a frequency of 27 %. We did not find a statistically significant relationship between the duration of diabetes progression and the components of the foot ($p=0.82$); or between the duration of wound development and the components of the foot ($p=0.81$). The high number of amputations due to diabetes could be explained by the long delay of patients before consulting at the hospital. A history of lower limb amputation represented 12 % of cases. Diabetes had been developing for more than 10 years in 54 % of our patients. Glycated haemoglobin was ≥ 8 % in 80 % of our patients, indicating an imbalance of diabetes. The duration of wound development before treatment was less than 1 month in 64 % of cases. According to the University of Texas classification, 38 % of patients had a 100 % risk of amputation: Grade 3 stage D and Grade 3 stage C **[3-5].**
Hypertension accounted for 56 % of the modifiable cardiovascular risk factors. This hypertension could be part of the macroangiopathic complications of diabetes.
Overweight and obesity were present in 59 % of our patients: BMI ≥ 25 Kg/m². The being overweight is very common in type 2 diabetics according to the literature **[2]**. The foot lesion occurred spontaneously in 68 % of cases. This result is not surprising, since the foot is the predilection site for diabetic arteriopathy and neuropathy in addition to being one of the parts of the limbs most exposed to various attacks; combined with the various chronic complications of diabetes (arteriopathies and neuropathies) and infections, favour lesions which, if not treated or poorly treated, can progress unfavourably **[5]**.
Late treatment is the first factor in amputation in diabetic patients with a wound. Glycaemic imbalance is the second factor in the amputation of diabetic wounds. Delayed healing represented 41 % of our patients with a hospital stay ≥ 30 days. The older the diabetes, the more its component is neurological and vascular without there being a statistically significant relationship ($p=0.83$). The more the foot is mixed (neurological and vascular components), the higher the risk of amputation,

with no statistically significant relationship (p=0.60). The problem of amputation is secondary to the late treatment of patients, poor glycaemic control, and the component (neurological and vascular) of the foot. Some medicinal plants can be used for these infections **[9-18]**.

4. Conclusion

The incidence of diabetic foot continues to rise and represents a growing public health challenge. Resistance of isolated bacteria to first-line antibiotics poses a serious therapeutic challenge. Infectious diabetic foot disease is mono-bacterial with a predominance of Gram-positive bacteria, especially *Staphylococcus*. Prevention (foot care, surveillance, daily hygiene, good glycaemic control, etc.) remains essential, especially for those at risk.

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