

# Diabetic Foot Infections with Pseudomonas: Jabir Abueliz Diabetic Center Khartoum Experience

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## Abstract

**Background:** The isolation of *Pseudomonas* organism in diabetic foot infection (DFI), is notorious of being multidrug resistant. The objective of this study is to report on the incidence, antibiotic sensitivity, treatment and outcome of pseudomonas infection.

**Patients and methods:** This is a prospective observational analytic hospital based study in which all diabetic patients with *Pseudomonas aeruginosa* infected wounds seen in JADC during 18 months period were included.

**Results:** Pseudomonas was grown in 302 out of 3620 cultures (8.3%) of whom 70 cultures were true pathogenic (1.9%). 41.4% of patients infected with pseudomonas were clinically septic when first seen in the clinic of whom 92.9% were febrile at presentation and 67.1% had chills. Ceftriaxone and ciprofloxacin were the most commonly used antibiotics. Amikacin was the most sensitive antibiotics in 77.1%. All patients took antibiotics >21 days after the isolation of *pseudomonas* to complete the eradication in combination of daily sharp excision of all coloured infected tissues. Forty six patients (66%) needed amputation, 30 had minor toes (43%) and 16 had transtibial amputation, (23%).

**Conclusion:** Diabetic foot infected with pseudomonas carries a higher risk for toe or lower limb amputation. For complete medical eradication of *P. aeruginosa*; antibiotics should be used for at least 21 days combined with daily sharp excision of infected discoloured tissues.

**Keywords:** Diabetic foot infection; Pseudomonas; Antibiotic sensitivity

## Introduction

*Pseudomonas aeruginosa* is an important human opportunistic bacterium in the diabetic foot. It is a gram-negative aerobic, rod-shaped non-fermenting bacterium with unipolar motility [1]. *P. aeruginosa* is often preliminarily identified by its pearlescent appearance and grape-like [2] or tortilla-like odour in vitro. It can be responsible for a spectrum of presentations from superficial colonization of ulcers to extensive tissue damage, including osteomyelitis, septic arthritis and bacteraemia [3]. Definitive clinical identification of *P. aeruginosa* often includes identifying the production of pyocyanin and fluorescein, as well as its ability to grow at 42°C [4,5].

*P. aeruginosa* and *Staphylococcus aureus* are the most commonly isolated organism from diabetic ulcer [6]. In study from Malaysia culture of 86 diabetic septic foot patients revealed *S. aureus* (38.4%), *P. aeruginosa* (17.5%) [7] Dhanasekaran et al. reported the prevalence of *Pseudomonas* species to be 18.79% from a diabetic centre in Chennai [8]. Fidelis Mbunda et al. stated that *P. aeruginosa* (25.5%) was the most frequent gram negative bacteria isolated, whereas gram positive bacteria commonly isolated was *S. aureus* (13.7%) [9]. Similar bacterial profile was reported by Lim et al. [10].

*P. aeruginosa* is commonly resistant to antibiotics, and because of this it is a dangerous and dreaded pathogen [11]. 44% of *P. aeruginosa* are multi drug resistant [6]. In the Mueller Hinton agar-based antibiogram-resistogram pattern study of *P. aeruginosa* isolated from foot ulcers of diabetes patients, multidrug resistance for about 8 to 11 antibiotics was observed among 55.5% of the strains. No single antibiotic showed 100% sensitivity to all *P. aeruginosa* strains. Resistance was least with cefotaxime (16.6%), followed by an intermediate resistance of 66.7%

observed for ciprofloxacin. Ciprofloxacin and cefotaxime were found to be better choices for diabetes patients with foot ulcers in this part of the region when compared to gentamicin, imipenem, piperacillin, and other third-generation cephalosporins [11].

In a Tanzanian university teaching hospital experience, the majority of isolates were sensitive to meropenem (100%), imipenem (100%), vancomycin (81.8%), clindamycin (55.6%) and Ciprofloxacin (53.6%) [12]. Nevertheless, imipenem resistant *Pseudomonas* appears as a new challenging problem especially in hospitalized patient [13]. Imipenem resistance was observed in (61.2%) of the isolates in Brazil [14].

The objective of this study is to report on the incidence, clinical presentation, antibiotic sensitivity, treatment and outcome of pseudomonas infection in patients with Diabetic Foot Infection (DFI) presenting to Jabir Abu Eliz Diabetic Centre Khartoum (JADC).

## Patients and Methods

This is a prospective observational analytic hospital based study in

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**Received** October 21, 2013; **Accepted** December 26, 2013; **Published** December 31, 2013

**Citation:** Wahab WFA, Bakhiet MA, Mahadi SEIDI, Mahmoud SM, Widataal AH, et al. (2013) Diabetic Foot Infections with Pseudomonas: Jabir Abueliz Diabetic Center Khartoum Experience. Clin Res Foot Ankle S3: 001. doi: [10.4172/2329-910X.S3-001](http://dx.doi.org/10.4172/2329-910X.S3-001)

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which all diabetic patients with *P. aeruginosa* infected wounds seen in JADC during an 18 months study period.

Patients were offered regular daily sharp debridement of all necrotic and stained tissues until clean granulation tissue was achieved. Tissues or bone were taken from the deepest part of the ulcer and were dipped immediately in a transport media (Stewart transport media) and sent for culture and sensitivity after overnight incubation at 37°C on (Mac Conkey agar). Cultures growing pseudomonas are sub-cultured in (Maller Henton agar).

Antibiotic sensitivity testing used the standard (Kirby-Bauer) disc diffusion test. The results were obtained in three days period. A second culture was done one or two weeks later depending on the clinical response.

## Results

A total of 2210 patients with DFI where seen in JADC and 47,505 dressing were done during the study period. There were 3620 bacteriological cultures for those patients of which 302 (8.3%) grew Pseudomonas of which 70 were pathogenic (Table 1), (1.9%). Thirty seven patients (52.9%) presented to JADC already infected with pseudomonas infection while 33 patients (47.1%) acquired the infection while treated in the centre.

Twenty nine patients (41.4%) were clinically septic when first seen in the clinic. 92.9% of the patients were febrile at presentation and 67.1% had chills (Table 2). In 51.4% the ulcer had fruity odour and in 27.1% it had a foul smell. 78.8% of the ulcer was found to be yellow green, blue green, frothy green or red brown in colour.

Daily meticulous focused excision of all coloured tissues was done along with application of silver sulphadiazine ointment in 61 patients (87.1%) and every other day in 6 patients 8.6%. Tap water was standard for wound dressing in 51 patients (72.9%), tests of significance showed that the dressing material did not affect the rate of amputation (p value 0.736).

Organism isolated	Number	Percentage
No growth	1955	54%
<i>E. coli</i>	673	18.6%
Staph. Aureus	373	10.8%
Pseudomonas	302	8.3%
Klebsiella	272	7.5%
Staph. epidermidis	20	0.05%
Proteus	19	0.05%
Candida	4	0.01%
Yeast	2	0.005%
Strep. Fecalis	None	None
Total	3620	100%

Table 1: Results of cultures done to all patients in JADC during the study period.

Symptom	Yes
Fever	92.9%
Chills	67.1%
Tiredness	55.7%
Muscle and joint pain	37.1%
Swelling	18.6%
Dehydration	2.9%

Table 2: Symptoms of diabetic patients with foot ulcer infected with pseudomonas n (70).

Antibiotic	Sensitivity
Amikacin	77.1%
Gentamycin	60.0%
Ceftaxone	60.0%
Ciprofloxacin	52.9%
Ceftazidime	8.6%
Ceftizoxime	5.7%

Table 3: Sensitivity of pseudomonas to different antibiotics (n=70).

The initial culture showed Pseudomonas (alone) in 54 patients (77.1%) while it was polymicrobial in the rest of the study group. In the second bacteriological culture 41.4% (n=29) had no growth detected.

Amikacin was the most effective antibiotics to pseudomonas bacteria in 77.1% (n=54), (Table 3). Ceftriaxone and ciprofloxacin were the most commonly used antibiotics after the second culture 31.4% (n=22) and 28.6% (n=20) respectively. All patients took antibiotics for more than 21 days after the isolation of pseudomonas to completely eradicate the infection. Forty six patients (66%) needed amputation, 30 had minor toes (43%) and 16 had transtibial amputation, (23%).

## Discussion

The identification of the causative organism by bacteriological culture in DFI is an important step in treating sepsis. Polymicrobial infections predominate in severe DFI.

In this study, *E. coli* was found to be the most common isolate (18.6%). Staph aureus (10.8%), followed by pseudomonas (8.3%). In a previous study from JADC Staph aureus was isolated in 48.46% of cultures, *Pseudomonas aeruginosa* (16%) and *Klebsiella* (13.85%) [15]. Other authors reported staphylococcus aureus in 38.4% of cultures from diabetic ulcers, pseudomonas aeruginosa in 17.5% and proteus mirabilis in 14% [16]. In a study from India *E. coli* was isolated in 27.7%, proteus in 16.9%, *Klebsiella* in 13.6%, Staph aureus in 13.6% and pseudomonas spp in 11.3% [17]. Fidelis Mbunda et al. [9] and Lim et al. [10] reported similar results. Priyadarshini Shanmugam, Jeya M, and Linda Susan S stated that the commonest isolate was *Pseudomonas spp* (16%) [18]. These findings also correlate well with those of Pappu K et al. [19], who reported that 76% of the organisms which were isolated were gram negative bacilli, Pseudomonas being the predominant pathogen (23%), followed by *Staphylococcus aureus* (21%). Zubair et al. [20] reported *Escherichia coli* (26.6%) and *Pseudomonas aeruginosa* (10.6%) as the predominant gram negative isolates. The difference in pattern and type of isolates in different series of studies was within the difference noticed in literature.

More than half of the patients already had pseudomonas infection when they presented for the first time and the rest acquired the infection in the center. This may be attributed to cross infection during the initial assessment of the wound in the main dressing room.

The effective treatment of DFU infected by *P. aeruginosa* depends on administration of appropriate antibacterial agents. No single protocol is agreed upon worldwide for Pseudomonas infection in diabetic wounds.

In this study amikacin was found to be very effective, (77.1%) of the Pseudomonas were sensitive to it, Ceftriaxone and ciprofloxacin were the most commonly used antibiotics after the second culture. However, in Spain a new resistant strain to amikacin that causes high-level of resistance was found [21]. A bacteriological study from India showed sensitivity of pseudomonas to different antibiotics as follows, 68% to amikacin, 56% to gentamicin, 56% to imipenem and 100% to meropenem. The combination therapy significantly reduces the

mortality from pseudomonas [22]. Tamil Selvi Sivanmaliappan and Murugan Sevanan; stated that Ciprofloxacin and cefotaxime were found to be better choices for diabetes patients with foot ulcers in Coimbatore, India when compared to gentamicin, imipenem, piperacillin, and other third-generation cephalosporins [11]. Michael Edmonds reported that Pseudomonas may be sensitive to ciprofloxacin as an oral agent. Otherwise parenteral therapy is necessary and includes ceftazidime, aminoglycosides, meropenem, piperacillin/tazobactam, and ticarcillin/clavulanate [9]. Resistance to Imipenem was noted [14].

Meropenem was used empirically in some patient in this study and was found to be very effective in controlling sepsis. This correlate well with the Tanzanian university teaching hospital experience [12].

In this study the coupling of antibiotics with daily sharp and precise removal of all coloured tissues is a cornerstone of eradication. All the wounds were cleaned using clean tap water [23]. The notorious behaviour of pseudomonas to grow on daily basis after being completely excised was very noticeable and hence meticulous sharp dissection of affected tissues was essential.

The integrated management for patients with ulcer infected with pseudomonas needed more than 21 days in all patients to eradicate the organism without the need for amputation.

The rate of minor amputation was 43% and major amputation 23%. This could be attributed to several factors, namely the severity of sepsis, late presentation and resistant bacteria. Even higher rates of amputation were reported [24,25]. Eighty-five percent of amputations are preceded by an ulcer. The main reason for this is that foot ulcers are highly susceptible to infection, Pecoraro RE reported [25]. In conclusion, most cultures of pseudomonas were found to be sensitive to amikacin and ceftriaxone. For complete medical eradication; antibiotics should be used for at least 21 days with daily dressing pattern.

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**Citation:** Wahab WFA, Bakhiet MA, Mahadi SEIDI, Mahmoud SM, Widataal AH, et al. (2013) Diabetic Foot Infections with Pseudomonas: Jabir Abueliz Diabetic Center Khartoum Experience. Clin Res Foot Ankle S3: 001. doi: [10.4172/2329-910X.S3-001](https://doi.org/10.4172/2329-910X.S3-001)

This article was originally published in a special issue, **Diabetic Foot Infections: Treatment & Cure** handled by Editor(s), Prof. José Luis Lázaro Martínez, University of Madrid, Spain, Dr. Jake P. Heiney, University of California, USA