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# Successful treatment of type II diabetes mellitus with infected diabetic foot ulcer caused by ESBL producing Klebsiella pneumonia with cefepime plus sulbactam (Supime): A case report

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## Abstract

Diabetic patients are at significant risk of developing neuropathy, leading to a diabetic foot injury. Complications of diabetic foot injury may lead to gangrene and non-traumatic lower extremity amputations. Diabetic patients with diabetic foot ulcers are more prone to bacterial infections and are associated with high chances of amputation. The diabetic patient flora provides an ideal environment for Gram-positive and Gram-negative bacterial growth, leading to increased morbidity and mortality. The antimicrobial-resistant Gram-negative bacterial infections in diabetic patients have a higher probability of amputation. Here we discuss a case of a 70-year male diabetic patient successfully treated with Supime (cefepime plus sulbactam) who had undergone an amputation of the right great toe and infected left foot ulcer due to ESBL producing *K. Pneumonia.*

**Keywords:** Diabetic Foot; ESBL; *K Pneumonia*; Supime; Cefepime plus sulbactam

## 1. Introduction

Uncontrolled diabetes is one of the leading causes of morbidity and mortality, leading to exponential health care expenditure [1]. The prevalence of DM in the general population is as high as 8.3%. The incidence of DM increases with age. The percentage of the undiagnosed population is also high, especially in the developing and underdeveloped countries where health testing facilities are limited. It is estimated that the proportion of the undiagnosed population may have increased in the last decade [2, 3].

Diabetic foot infection admission in India accounts for up to 20% of hospital admission [4,5]. Multifactor are responsible for diabetic foot infections, namely neuropathy, peripheral disease, and susceptibility to infection, whenever there is direct injury to the foot [6, 7]. Uncontrolled diabetes could lead to peripheral neuropathy, a serious complication seen in diabetic patients. Peripheral neuropathy occurs in 60-70% of the diabetic population, with the most serious complications like diabetic foot ulcers, diabetic retinopathy, kidney failure and non-traumatic knee amputation [8,9].

Diabetic foot injury is usually a polymicrobial infection involving aerobes and anaerobes. Many researchers present evidence of aerobic and anaerobic bacteria. The common aerobic organisms are *E. coli, Klebsiella, Pseudomonas aeruginosa, Acinetobacter baumannii, Staphylococcus aureus, S. saprophytic, and S. epidermis Streptococcus pyrogens, S. mutants*. The anaerobic bacteria include *Streptococcus species, anaerobic Streptococci, Bacteroides fragilis and Clostridium species [*10]. Similarly, in a study conducted in Kolkata, India, in 2016, Pal and Gupta reported that diabetic patients with grade 4-foot ulcers were commonly infected with a mixed variety of bacteria, including ESBL *Klebsiella*

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*species*, MRSA, and so on [11, 12]. Management of these pathogens requires proper antimicrobial therapy. Beta-lactam antibiotics are commonly preferred to treat gram-negative bacterial infections, though clinicians prefer to use treatment based on their hospital antibiogram and susceptibility results. The growing drug resistance to the beta-lactam class creates a significant threat in treating infections and pathogens that produce various resistant mechanisms, especially ESBLs [13].

In an inpatient with diabetic foot ulcers, neuropathy plays a significant role in diabetic ulceration. Neuropathy leads to a lack of protective sensation followed by unaccommodated foot deformities, which exposes patients to undue sudden or repetitive stress, leading to ulceration formation with the risk of infections and possible amputation [14]. In diabetic foot ulcers, the conditions can be avoided by maintaining good hygiene in and around the foot ulcer and covering purulent lesions with a waterproof dressing [10]. Diabetic foot infections are usually inadequately managed because of poor knowledge of the microbial agents associated with the ulcers. There is a need to investigate the pathogens infecting these ulcers and their susceptibility pattern, which may improve the patient's management and reduce the frequency of amputation. Considering the paucity of data in treating ESBL producing pathogens, this case study shows the effectiveness of Supime (cefepime plus sulbactam) in treating ESBL K. pneumonia infection in patients undergoing gangrene toe amputation with infected bacterial foot ulceration.

## 2. Clinical Case

A 70-year male patient with a history of uncontrolled type 2 Diabetes Mellitus with irregular medical treatment was brought to our emergency department for a private nursing home. The patient had undergone amputation of the right great toe for gangrene in the past ten days and was under treatment for left diabetic foot ulcers. The patient had foul-smelling discharge from the left foot. The overall general condition of the patient was poor.

For the last four years, the patient presented with a foot ulcer in the left metatarsophalangeal area. The ulcer had never healed during the period. He had been admitted several times due to recurrent infections and had needed debridement and IV antibiotics on multiple occasions.

On examination, the patient was restless with the general condition was poor. His pulse was 108/minute, temperature $102^0$ F; BP was 128/82mmHg. Physical examination of his feet, right great toe, and left feet revealed a 3 x 3 cms wide ulcer in the metatarsophalangeal area. Hyperkeratosis, with swollen borders and exudation, was observed with foul-smelling discharge. Dorsal pedal and posterior tibial pulses on both the foot were present. He presents dermatitis on the toe's base with no external signs of varicose veins. The patient can perform his daily activities independently.

The bone test was performed to determine communication between the surface of the ulcer and the joints, and it was negative. Blood samples were taken to test for blood glucose levels. The Pain Visual Analogue Scale (VAS) was 7, predominately during the daytime. Culture of the wound from the left foot and amputated site were sent to the lab. Blood sugar levels varied between fasting 162mg% to 180 mg% and postprandial up to 243 mg%. The patient's wound debridement and the dressing were done. Considering the condition of the patient and the hospital antibiogram policy, the patient was put on Supime (cefepime plus sulbactam) 3gm BD dose with 30 minutes of infusion and on oral diabetic drugs. The culture report from the left foot ulcer showed gram-negative pathogen *Klebsiella Pneumonia* sensitive to Supime. Thus, considering the response and culture sensitivity report, Supime therapy was continued for nine days and supportive care and treatment. The patient was continued with a diabetic diet and oral hypoglycaemic agent. The patient diabetic blood levels were controlled, and his overall condition improved. The patient was discharged from the hospital with the advice of regular wound dressing.

## 3. Discussion

Diabetes is one of the critical factors in causing peripheral neuropathy, which causes damage to the nerves in the feet, and neuropathy can manifest in various forms, including local/multifocal and autonomic neuropathies. Such patients have reduced or no sensations in the feet, which could cause injury or damage to the foot, as the pain sensation is diminished, and the patient will not be aware of the harm caused to the feet by ill-fitting footwear or object which injures his foot. Such patients miss the causative factors and may continue to walk, which further damages the foot tissues and makes them more prone to infections. Such foot injuries and ulcerations because of diabetic neuropathy lead to 80% of the amputation [15]. Many more issues and concerns are attributed to peripheral neuropathy like hammertoes, the collapse of the mid-foot, and blisters. These may appear on numb areas of the foot as the patient is unaware of the pressure or injury. (Diabetic Neuropathies). The untreated bacterial and fungal infections in the foot ulcers can lead to amputations [16, 17].

Infections by ESBL producing pathogens further increase the challenge of treating the patient, especially when ESBL resistance bugs are more prevalent in India. A study on 645 clinical isolates conducted in India across four centres (PGIMER, Chandigarh, AIIMS New Delhi, CMC Vellore and JIPMER Puducherry) showed 42 per cent (102/245) pathogens as *K. pneumonia* ESBL producers [18]. Similarly, a study on 44 consecutive patients with open diabetic foot infections had wound swabs taken for culture, and sensitivity testing observed 14% of the cases as *Klebsiella pneumonia* [19]. The emergence of antimicrobial resistance against BL-BLI and carbapenem drugs is due to numerous elements which assist the scattering of resistance among clinical pathogens, including the production of MBL enzymes, biofilm formation, and overexpression of efflux pumps and antibiotic accumulation [20]. Currently, there is a paucity of data on the prevalence of ESBLs in diabetic foot infections. In a study, Shobha et al. have reported 27.3% *K. pneumonia*, 25.2% *E. coli*, 21.42% *Pseudomonas spp,* 25% *Enterobacter spp*. and 17% *Acinetobacter spp*. to be ESBL producer in wound samples collected from patients suffering from a diabetic foot injury [21].

The main goal of diabetic foot care should involve a combination of methodologies and preventive strategies, including patient education, involvement, and adherence to physician recommendations, maintaining tight glycaemic control, and performing routine skin, foot, and nail inspections [22,23]. The patients must follow better medication adherence, as it will help improve DM control and decrease the strain on the healthcare system [24, 25]. Chronic diabetic foot wounds don't heal with dressing only and epithelize once the cause is solved. Few publications mention that up to 49 to 85% of all diabetic foot complications are editable and can be achieved through approaches like proper wound care, interdisciplinary strategies and specific health education and empowerment of the patients and caretakers.

This case demonstrates the complications of DM and the infection of *K. pneumonia* in the diabetic foot due to non-adherence to treatment. Due to neuropathy, the patient was unaware of the pain associated with the foot ulcer and thus neglected the wound. As the ulcer was treated timely, the patient developed serious health problems, which led to the amputation of the right great toe. Adherence to the treatment and broad-spectrum antibiotic treatment like Supime followed by proper foot care helped the patient slow down the disease progression and recovered faster.

## 4. Conclusion

Non-adherence to diabetes treatment complicates the management modality of infected diabetic foot ulcers. Thus, effectively treating patients with infected ulcerated diabetic feet with appropriate broad-spectrum antibiotic coverage and supportive therapy is warranted. In our case, an infected diabetic foot ulcer patient was successfully treated for ESBL producing *K. pneumonia* with a broad spectrum antibiotic Supime (cefepime plus sulbactam). Supime can be considered a safe and effective therapy in treating infected diabetic foot ulcers based on the positive patient outcome.

## Compliance with ethical standards

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### *Disclosure of conflict of interest*

There is no conflict of interest between the authors.

### *Statement of ethical approval*

Since the current case is a retrospective study data with no identifying patient information disclosed, the ethics approval was waived off.

### *Statement of informed consent*

Informed consent from the patient was taken to publish his case without disclosing his personal information.

### *Authors Contribution*

Conceptualisation, writing -original draft and preparation by Dr Vijay and Dr Ayush, writing review and editing by Dr Pankaj Mandale. All authors have read and agreed to the published version of the manuscript.

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