Journal of Advances in Microbiology Research

E-ISSN: 2709-944X
P-ISSN: 2709-9431
JRM 2022; 3(1): 12-14
© 2022 JRM
www.microbiojournal.com
Received: 07-11-2021
Accepted: 15-12-2021

Dr. Krishna Kumar Patel
Assistant Professor,
Department of Microbiology
Govt. T. C. L. P. G. College,
Janjgir, Chhattisgarh, India

Dr. Sarita Patel
Assistant Professor,
Department of Zoology, Govt.
Naveen College, Sakari,
Bilaspur, Chhattisgarh, India

Correspondence
Dr. Krishna Kumar Patel
Assistant Professor
Department of Microbiology
Govt. T. C. L. P. G. College,
Janjgir, Chhattisgarh, India

Risk factors of diabetic foot ulcer with multidrug-resistant organism infection

Dr. Krishna Kumar Patel and Dr. Sarita Patel

Abstract
In recent years, the emergence of antibiotic resistant pathogens made increasingly difficult to establish appropriate empiric antimicrobial therapy protocols for acute diabetic foot infection (DFI) treatment. Early recognition of the population at risk for multidrug-resistant (MDR) bacterial infection is of paramount importance in order to decrease large-spectrum antibiotic over use. This study used retrospective cohort study in a diabetic foot unit. Patients with severe diabetic foot infection were included and divided according to their infection resistance profile (susceptible vs MDR bacteria). Data regarding their co-morbidities and length of hospital stay were collected. The primary endpoint was to determine the risk factors for MDR infections and to evaluate if these were associated with an increased length of stay (LOS). A total of 112 microbial isolates were included. Predominance of Gram-positive bacteria was observed and 22.3% of isolated bacteria were MDR. Previous hospitalization was associated with a higher likelihood of MDR infection. MDR bacterial infection was also associated with an increased LOS Our study showed a high incidence of MDR bacteria in patients with a diabetic foot infection, especially in those who had a recent hospitalization. MDR infections were associated with a prolonged LOS and represent a global public health issue for which emergent measures are needed.

Keywords: Bacterial infection, diabetic foot, drug resistance

Introduction
Diabetic foot infection (DFI) is the most common cause of non-traumatic amputation, hospitalization, and reduction of quality of life in people with diabetes [1]. Most moderate and severe Diabetic foot infections require systemic antibiotic therapy. Initial drug choice is usually empirical and based on the available clinical and epidemiologic data [2] showing the importance of local population studies. In recent years, the emergence of antibiotic resistant pathogens made increasingly difficult to select appropriate empirical antibiotic coverage for Diabetic foot infection treatment [3]. Based on our local findings, Neves *et al*. [4] suggested piperacillin/tazobactam as the best first-line empirical antibiotic option to treat moderate to severe Diabetic foot infection in our Diabetic foot referral inpatient centre, with an additional Methicillin-resistant Staphylococcus aureus (MRSA) coverage in high-risk patients.
However, considering the dynamic environment of the microbiological flora in diabetic foot infection, continuous monitoring of the bacterial prevalence in each diabetic foot centre is required. As such, this study aimed to analyze the micro-biological profile of patients admitted to our institute during January 2021 to January 2022. Our purpose was also to identify the risk factors for the development of a multidrug-resistant (MDR) infection and to determine if this type of infection was associated with an increase length of stay (LOS).

Materials and Method
A total of 103 hospitalization episodes from 96 patients. Seven patients were readmitted to our centre during the study period and each admission was analyzed separately as a new case of pus swabs, both from outdoor and indoor patients of different wards were aseptically collected during January 2021 to January 2022 submitted to Dept. of Microbiology, Chhattisgarh Institute of Medical Sciences, and identified on the basis of colony morphology according to Bergey's Manual of Determinative Bacteriology, 8th edition. Antimicrobial susceptibility testing was carried out by disk diffusion method of Bauer *et al*. (1966). Antibiotic susceptibility testing for each bacterial isolate was done on Muller Hinton agar in a 90 mm sterile Petri dish and incubated at 37ºC for 18hrs. The panel of antimicrobials tested were ampicillin (10µg), amikacin (30 µg), amoxycillin (25µg), cefotaxime (30 µg), cefuroxime (30 µg), cefoperazone (75 µg), ciprofloxacin (5 µg), gentamycin (10 µg), imipenem (10 µg), piperacillin (100 µg) and Tetracycline (30 µg) (HiMedia).

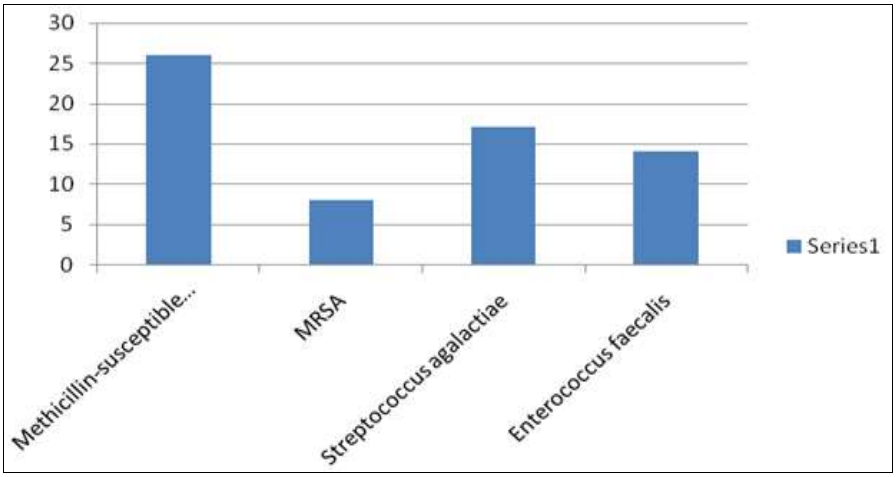
P. aeruginosa (ATCC27853) was used as the control strain. After incubation, plates were examined for zones of inhibition and categorized to sensitive, intermediate and resistant according to National Committee for Control Laboratory Standards (NCCLS, 1993).

Double disc diffusion method was used to detect the extended spectrum beta lactamases (ESBL). A disk of co-amoxicillin (20 µg amoxicillin/10 µg clavulanic acid) was placed in the center of the agar surface. The discs of cefotaxime, ceftriaxone, ceftazidime and aztreonam (30 µg) were arranged in such a way that the distance between the central disc and surrounding discs was 20 mm. The plates were incubated at 37°C for 24 h. If the inhibition zone around one or more cephalosporins discs was extended on the side nearest to the co- amoxiclav disc, the organism is an ESBL - producer.

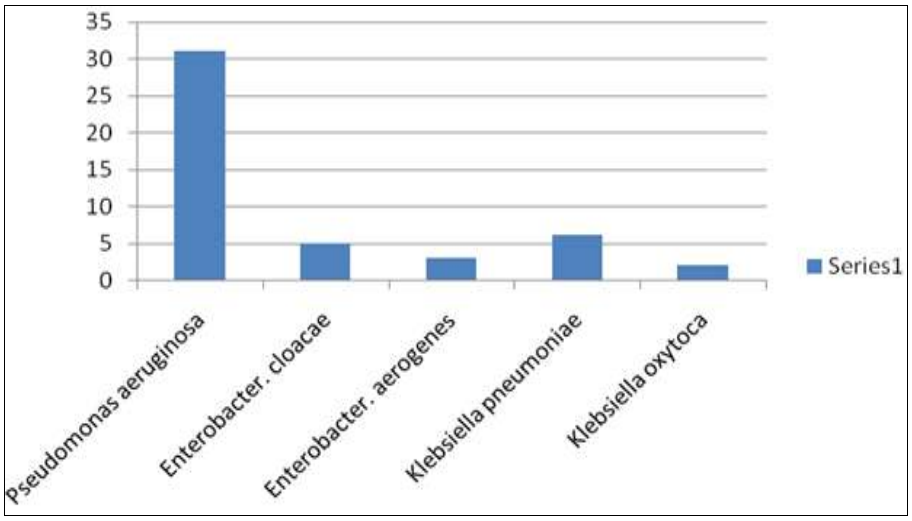
The first microbiological sample of every patient was analysed. Contaminated samples (n = 12), negative microbial results (n = 5), and samples collected after ant biotherapy initiation (n = 3) were excluded. Thirty samples had more than one isolate. A total of 112 bacteria isolates were included in our study (Table 1). A Gram-positive bacteria predominance was observed (58.1% of microbial isolates; 1.38/1 Gram-positive/Gram-negative ratio). S. aureus (SA) was the most common Gram-positive bacteria (n = 34), followed by Streptococcus spp (n = 34) and Enterococcus spp (n = 14). Gram-negative isolates included Pseudomonas spp (n = 31), Enterobacter spp. (n = 8), and Klebsiella spp. (n = 8. The overall resistance for piperacillin-tazobactam in non-SA infections (n = 79) was 26.5% (n = 21). Ertapenem resistance was 12% (n = 3) in the MDR group (excluding MRSA). Overall resistance to Ertapenem was 36.7% in the non-SA group (n = 29).

Table 1: Microbiologic profile in Diabetic foot

A	**Gram-positive bacteria**	**65**
1	Staphylococcus aureus	34
	Methicillin-susceptible Staphylococcus aureus	26
	MRSA	8
2	Streptococcus spp	17
	Streptococcus agalactiae	17
3	Enterococcus spp	14
	Enterococcus faecalis	14
B	**Gram-negative bacteria**	**47**
1	Pseudomonas spp	31
	Pseudomonas aeruginosa	31
2	Enterobacter spp	8
	Enterobacter. cloacae	5
	Enterobacter. aerogenes	3
3	Klebsiella spp	8
	Klebsiella pneumoniae	6
	Klebsiella oxytoca	2



Graph 1: Gram-positive bacteria



Graph 2: Gram-negative bacteria

Discussion

Diabetic foot infection (DFI) process causes a vicious cycle of extensive decomposition in glucose metabolism, as hyperglycemia further increases the severity of the infection itself [5-7]. As such, proper antibiotic coverage is a key element in early stabilization of these patients and should be based on known potential etiologic agents. In Portugal, few studies have been performed to characterize the local causative pathogens of DFIs. An apparent Gram-positive predominance has been initially suggested [4, 8-10]. But some authors had recently described a shift towards Gram-negative isolates, possibly in relation with the rising prevalence of neuro ischemic infected ulcers [11]. Our results do not corroborate these latest findings but we acknowledge that they should be properly confirmed by further larger studies. Regarding MDR infections, a high incidence has been ubiquitously described [4, 8-11] and our study also highlights that these infections correlate with an increased LOS. Despite controversy regarding the association of MDR infections with a worse outcome in DFIs [12-14] our data are a surrogate marker for a poor overall prognosis. Some authors suggested that previous hospitalization [14, 15]. Long standing diabetes [16], recent antibiotherapy [15], retinopathy [17] ulcer size [15, 16] and the presence of osteomyelitis [14, 15] were associated with an increased risk of an MDR infection. In our study, we were able to show that hospitalization during the previous year is a statistically significant risk factor for the occurrence of DFI by MDR bacteria.

Our study shows an alarming resistance of these agents to a recently optimized empirical anti-biotherapy regimen, suggesting that we are running off of proper antibiotics for DFI [18-21]. Currently in our unit we are facing a huge dilemma: should we use piperacillin-tazobactam, prioritizing a better overall coverage but knowing that we are delaying proper care for the severe MDR infections, linked to poorer outcomes? Or must we be focused on these MDR agents, favoring Ertapenem usage and acknowledging that we are allowing more non-MDR to be mistreated? In our view, the solution relies on multiple empiric antibiotic regimens that are guided by the patient risk factors for MDR infections. As such, we believe that future studies should be focused on the development of a reliable risk stratification tool, allowing proper antibiotic selection for both high and low-risk patients.

References

1. Boulton AJM, Vileikyte L, Ragnarson Tennvall G, Apelqvist J. The global burden of diabetic foot disease. Lancet. 2005 Nov; 366(9498):1719-1724.
2. Lipsky BA, Berendt AR, Cornia PB, *et al.*, infectious diseases society of America clinical practice guideline for the diagnosis and treatment of diabetic foot infections. J Am Podiatr Med. Assoc. 2013 Jan;103(1):2-7.
3. Olid AS, Sola I, Barajas-Nava LA, Gianneo OD, Cosp XB, Lipsky BA. Systemic antibiotics for treating diabetic foot infections. Cochrane Database Syst Rev. 2015;(9):CD009061. https://www.cochranelibrary.com/cdsr/doi/10.1002/14651858.CD009061. Pub2/abstract.
4. Neves JM, Duarte B, Pinto M, Formiga A, Neves J. Diabetic foot infection: causative pathogens and empiric antibiotherapy considerations the experience of a tertiary center. Int J Low Extrem Wounds. 2019;18(2):122-128.
5. Lipsky BA, Aragón-Sánchez J, Diggle M, *et al.* IWGDF guidance on the diagnosis and management of foot infections in persons with diabetes. Diabetes Metab Res Rev. 2016 Jan;32:(1):45-74.
6. Magiorakos AP, Srinivasan A, Carey RB, *et al.* Multidrug resistant, extensively drugresistant and pandrugresistant bacteria: an international expert proposal for interim standard definitions for acquired resistance. Clin. Microbiol Infect. 2012 Mar;18 (3):268-281.
7. Butranova OI, Razdrogina TN. Antibiotics for skin and soft tis-sues infections in type 2 diabetes mellitus. Int J Risk Saf. Med. 2015;27(1):S57-S58.
8. Cabete J, Martins de Carvalho F, Moniz L, Pinto M, Neves J, Pereira Alves C. Microbiological profile and antibiotic susceptibility patterns of organisms isolated from diabetic foot ulcers in a Portuguese hospital. Rev Port Cir Cardiotorac Vasc. 2011 Jan;18(1):53-60.
9. Mendes JJ, Marques-Costa A, Vilela C, *et al.* Clinical and bacteriological survey of diabetic foot infections in Lisbon. Diabetes Res Clin Pract. 2012 Jan;95(1):153-161.
10. Barbosa A, Carvalho R, Carvalho A. Evaluation of the efficacy of a diabetic foot infection empirical antibiotic therapy proto-col. A retrospective inpatient study. Revista Portuguesa de Diabetes. 2016 Mar 1;11:14-17.
11. Machado C, Teixeira S, Fonseca L. Evolutionary trends in bacteria isolated from moderate and severe diabetic foot infections in a Portuguese tertiary center. Diabetes Metab Syndr Clin Res Rev. 2020;14(3):205-209.
12. Richard JL, Lavigne JP, Got I, *et al.* Management of patients hospitalized for diabetic foot infection: results of the French OPIDIA study. Diabetes Metab. 2011 Jun;37(3):208-215.
13. Zenelaj B, Bouvet C, Lipsky BA, Uçkay I. Do diabetic foot infections with methicillin-resistant Staphylococcus aureus differ from those with other pathogens? Int J Low Extrem Wounds. 2014;13(4):263-272.
14. Hartemann Heurtier A, Robert J, Jacqueminet S, *et al.* Diabetic foot ulcer and multidrug-resistant organisms: risk factors and impact. Diabet Med. 2004 Jul;21(7): 710-715.15.
15. Ji X, Jin P, Chu Y, Feng S, Wang P. Clinical characteristics and risk factors of diabetic foot ulcer with multidrug-resistant organism infection. Int J Low Extrem Wounds. 2014;13:64-71. https://doi.org/10.1177/1534734614521236.
16. Mohi G, Datta P, Chander J, Gupta V, Attri A. Evaluation of various risk factors associated with multidrug-resistant organ-isms isolated from diabetic foot ulcer patients. Journal of Laboratory Physicians. 2019;11:58. https://doi.org/10.4103/jlp.jlp10618.
17. Richard JL, Sotto A, Jourdan N, *et al.* Risk factors and healing impact of multidrug-resistant bacteria in diabetic foot ulcers. Diabetes Metab. 2008 Sep;34(4) 1:363-369.
18. Lipsky BA. Diabetic foot infections: current treatment and delaying the “post-antibiotic era”. Diabetes Metab Res Rev. 2016 Jan;32(1):246-253.
19. Neu HC. The crisis in antibiotic resistance. Science. 1992;257(5073):1064-1073.
20. Alanis AJ. Resistance to antibiotics: are we in the post antibiotic era? Arch Med Res. 2005 Nov;36(6):697-705.
21. Blair JMA, Webber MA, Baylay AJ, Ogbolu DO, Piddock LJV. Molecular mechanisms of antibiotic resistance. Nat Rev Microbiol. 2015 Jan;13(1):42-51