



DRUG USE PATTERN AND USAGE OF ANTIMICROBIALS IN PATIENTS WITH DIABETIC FOOT ULCER IN A TERTIARY CARE TEACHING HOSPITAL

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Abstract

Introduction: One of the most dreaded effects of Diabetes Mellitus (DM) are diabetic foot ulcer (DFUs), which frequently become infected and result in problems like osteomyelitis, amputations, and septicemia. There are few accounts of information about the costs and patterns of antibacterial therapy for DFUs.

Objective: The objective of this study is to analyze the pattern of drug use in patients with diabetic foot ulcer in a tertiary care teaching hospital, in Chennai.

Methods: A prospective observational study was carried out in the department of General surgery at a tertiary care teaching hospital, Chennai. Demographic details and treatment data of 50 patients were collected in a specially designed data collection form, and the data were analyzed using Microsoft Excel.

Results: According to Wagner's classification, patients admitted with DFUs predominantly belonged to grade 3 category (50%), followed by grade 2 (28%) and grade 4 (22%) categories. A total of 50 organisms were obtained from the specimens. The most common isolates were *Staphylococcus aureus* (66%) and *Pseudomonas aeruginosa* (18%) followed by *E. coli* (10%). Cefotaxime was the most commonly prescribed empirical antibiotic (48%), followed by piperacillin-tazobactam (42%).

Conclusion: The majority of the organisms that were isolated from DFUs were resistant to various medicines. Piperacillin+ Tazobactam and linezolid were mainly effective against Gram-negative organisms, while cefotaxime and metronidazole were more effective against Gram-positive organisms. It's crucial to heal wounds locally. It highlights the importance of early detection, appropriate wound care, appropriate antibiotic therapy, and optimal glycemic control in the prevention and management of this complex condition.

Key words: Diabetic foot ulcer, Wagner's classification, antibacterial, Bacterial profiles.

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1. Introduction

Millions of individuals throughout the world are afflicted by the persistent and painful diabetic foot ulcers (DFU). By 2040, the World Health Organization predicts that 642 million individuals will have diabetes, up from an estimated 422 million now [Saeedi et al.2019]. Up to 25% of persons with diabetes are predicted to get a foot ulcer at some point in their lives, making DFU one of the most prevalent consequences of the disease [Yazdanpanah et al. 2018]. Because of the high expense of therapy and elevated risk of amputation, DFU places a substantial financial strain on healthcare systems in addition to the enormous physical and emotional stress it places on patients [Crocker et al. 2021]. Consequently, proper DFU treatment is essential for lowering morbidity, mortality, and healthcare costs. Many conditions, such as neuropathy, vascular disease, and immunological dysfunction, can lead to DFU, and all of them can harm the tissue and impede the healing of wounds [Ramirez-Acuña et al. 2019]. Foot ulcers were indeed estimated to affect 9.1 million to 26.1 million diabetics worldwide each year [Armstrong et al. 2017]. The use of medications to control pain and other symptoms in DFU patients is widespread, despite the fact that a variety of therapeutic alternatives, including as wound care, surgical intervention, and antibiotics, are also available. A single diabetic ulcer is estimated to cost nearly \$50,000, and chronic wounds in general cost the medical system and over \$25 billion per year, with the number of patients affected increasing yearly from 6.5 million, given the increasing prevalence of diabetes and other chronic diseases that may affect wound healing [Han et al.2017]. DFU-related pain can be excruciating and incapacitating, and it can negatively impact the patient's quality of life [Mariam et al. 2017]. As a result, pain control is crucial to the treatment of DFU. A multidisciplinary strategy is necessary for the therapy of diabetic foot ulcers, which includes meticulous wound care, glucose control, and treating underlying risk factors such as peripheral neuropathy and peripheral vascular disease. To stop problems from arising, early detection and action are also necessary [Woldemariam et al. 2020]. The findings of this study will provide valuable insights into the optimal management of DFU patients and help improve

their quality of life. The study's results can also help healthcare providers make informed decisions regarding drug use in DFU patients, ultimately leading to better treatment outcomes and reduced healthcare costs.

1. Objective

The objective of this study is to analyze the pattern of drug use in patients with diabetic foot ulcer in tertiary care teaching hospital, Chennai.

2. Study Site

A Prospective observational study was conducted in Department of Surgery, which is 1350bedded tertiary care teaching hospital, Chennai.

2.1. Inclusion Criteria

- i) Patients admitted to the hospital with diabetes, diabetic foot ulcer from both genders.
- ii) Patients who are taking antidiabetics, antibiotics and other drugs related to this study.

2.2. Exclusion Criteria

- i) Patients with pregnancy.
- ii) Patients with drug abuse or addict.
- iii) Patients who are not willing to participate or cooperate.
- iv) Patients with mentally ill.

The patient information forms have been prepared to inform the patient or patient caretakers about the purpose and necessity of the study. The patient information form includes the details of the patient regarding age, gender, height, weight, patient IP number, reason for admission, Patient past medical and medication history, family and personal history, vital signs, blood sugar, blood pressure, drug chart details as well as trade name and generic name of the drugs and their prescribed dosage, frequency, route of administration, medications chart along with clinical diagnosis.

2.3. Sample Size Determination

The total number of samples included in this study will be 50 patients using 95% confidence interval, Formula to derive sample size

$$N = \frac{Z^2 P (100 - P)}{E^2}$$

2. Results

Table.1. Demographic variables

Variables	No.of. Patients	Percentage
Gender		

Male	33	66%
Female	17	34%
Age		
30-40	3	6%
40-50	9	18%
50-60	24	48%
60-70	9	18%
70-80	5	10%
Social habits		
Smoker	9	18%
Alcoholic	7	14%
Both	15	30%
None	19	38%
Length of stay		
10-20 Days	15	30%
20-30 Days	23	46%
30-40 Days	12	24%

Out of the total patients, 66% were males, and 34% were females. This suggests that males are more likely to develop diabetic foot ulcers than females. The majority of the patients were in the age group of 50-60 years (48%), followed by the age group of 40-50 years (18%). This indicates that middle-aged and elderly people are more susceptible to diabetic foot ulcers. Among the patients who have social habits, 38% did not have any social habits, while 30% had a history of both smoking and alcohol consumption. This implies that social habits like smoking and

alcohol consumption can increase the risk of diabetic foot ulcers. The majority of the patients (46%) had a length of stay of 20-30 days, followed by 30% with a length of stay of 10-20 days. This indicates that treating diabetic foot ulcers can be a lengthy process and may require a significant amount of hospitalization. The inferences can be used to identify potential risk factors and develop strategies for the prevention and management of diabetic foot ulcers.

Table.2. comorbid wise distribution

Conditions		No. of Patients	% Patients
Diabetes	Type 1	15	30%
	Type 2	35	70%
Hypertension		24	48%
Dyslipidaemia		8	16%
Coronary Heart Disease		13	26%

The above table provides a summary of the medical conditions of a group of patients. Among the patients, 30% were diagnosed with type 1 diabetes, while 70% had type 2 diabetes. Hypertension was found in 48% of patients, while 16% had dyslipidemia. Additionally, 26% of patients had coronary heart disease. In addition to the conditions listed above, 12% of patients also had diabetic foot ulcers. This is a complication of diabetes that occurs

when high blood sugar levels damage the nerves and blood vessels in the feet, leading to ulcers and infections. Diabetic foot ulcers can be challenging to manage, and patients require ongoing care and monitoring to prevent further complications. Therefore, it is crucial for patients with diabetes to receive regular medical check-ups and follow a healthy lifestyle to manage their condition effectively.

Table.3. Grade-wise classification

Grade	Severity Grade	No. of Patients	% Patients
I	Not Infected	0	0
II	Mild	14	28%
III	Moderate	25	50%
IV	Severe	11	22%
Procedure			
Grafting		13	26%
Amputation		10	20%
Osteotomy		9	18%
wound debridement		18	36%

Table.4. Grade-wise classification

Bacteria	Organisms	No.of. Patients	% Patients
Gram-Positive Bacteria	Streptococcus. Species	2	4%
	Pseudomonas	9	18%
	Staphylococcus aureus	32	66%
	Enterococcus sp.	2	4%
Gram-Negative Bacteria	Escherichia Coli	5	10%

The most common isolates in the present study were Staphylococcus aureus (66%) and Pseudomonas aeruginosa (18%) followed by E. coli (10%). Gram-

positive organisms dominated the gram-negative in the case of the number of organisms isolated in this study.

Table.5. Drug-wise distribution

Drug Class	Drugs	No. of Patients	% Patients
Antibiotics	Cefotaxime	24	48%
	Piperacillin+ Tazobactam	21	42%
	Amoxicillin	6	12%
	Tazobactam	3	6%
	Cefoperazone	12	24%
	Linezolid	9	18%
	Clindamycin	9	18%
	Ciprofloxacin	9	18%
	Metronidazole	23	46%
	Sulbactam+ Cefoperazone	6	12%
	Meropenem	3	6%
	Sulfametaxzole	5	10%
	Trimethoprim	5	10%
Anti Diabetics	Metformin	20	40%
	Glimepiride	11	22%
	Teneligliptin	2	4%
	vildagliptin	6	12%
	Metformin and Glimepiride	1	2%

Most of the patients (50%) with diabetic foot ulcers were classified as having a moderate grade, indicating that their ulcers were deeper and more severe than those in the mild category. 22% of patients had severe grade ulcers, which indicates that their ulcers had progressed to a critical stage that requires urgent attention and intervention. None of the patients had grade I ulcers, suggesting that all patients who presented with diabetic foot ulcers required medical intervention. The most common procedure performed on patients with diabetic foot ulcers was wound debridement (36%), followed by grafting (26%), osteotomy (18%), and amputation (20%). Wound debridement is a crucial procedure for removing infected and dead tissue from the wound bed, promoting the healing process, and preventing further complications. The fact that amputation was performed on 20% of patients

indicates that some diabetic foot ulcers may be so severe that they cannot be treated by other means, and amputation may be the only option

to prevent the further spread of infection and other complications. The data highlights the importance of early detection and treatment of diabetic foot ulcers to prevent the progression to severe stages and the need for more invasive procedures. Based on the data provided, the following inferences can be drawn: 96% of the patients with diabetic foot ulcers received antibiotics in this study. The most commonly prescribed antibiotics were Cefotaxime (48%) and Piperacillin (42%), followed by Metronidazole (46%), which are broad-spectrum antibiotics that are effective against a wide range of bacterial infections. The fact that Cefoperazone (24%), Linezolid (18%), Clindamycin (18%), and Ciprofloxacin (18%) were also prescribed suggests that different types of bacterial infections were present and required targeted treatment. It is worth noting that Tazobactam (6%), Meropenem (6%), Sulfamethoxazole (10%), and Trimethoprim (10%) were less commonly prescribed, indicating that they may have been reserved for specific cases or used as alternative treatments. Anti-diabetic drugs were administered to 48% of the patients with diabetic foot ulcers, indicating that glycaemic control is an essential aspect of diabetic foot ulcer management. Metformin (40%) was the most commonly prescribed anti-diabetic drug, followed by Glimepiride (22%) and Vildagliptin (12%). It is notable that one patient (2%) was prescribed both Metformin and Glimepiride, suggesting that combination therapy may be used in some cases to achieve optimal glycaemic control. The data highlights the importance of appropriate antibiotic treatment for infections in diabetic foot ulcers and the need for effective glycaemic control to prevent the development and worsening of ulcers.

3. Discussion

The data presented in this study provides valuable insights into the characteristics, risk factors, and management of diabetic foot ulcers. One of the key findings is that males are more likely to develop diabetic foot ulcers than females, suggesting that gender may play a role in the development of this condition. This result is similar to another study it shows male patients are more prone to get DFU [Navarro-Peternella et al. 2016]. In addition, the majority of patients were middle-aged or elderly, indicating that age is a significant risk factor for diabetic foot ulcers. This highlights the need for targeted screening and prevention strategies for these populations, this result is similar to another study it shows that elder patients are more prone to affect with DFU [M. Sue Kirkman et al. 2012]. This study also suggests that social habits such as smoking and alcohol consumption can increase the risk of diabetic foot ulcers and also another study

shows similar results that smoking increases the risk of DFU. This finding underscores the importance of lifestyle modifications and cessation of these habits to reduce the risk of developing diabetic foot ulcers. Another important finding is that diabetic foot ulcers can be a lengthy and complicated condition to manage. Patients with severe-grade ulcers required amputation, indicating the severity of the condition and the need for early intervention. Additionally, wound debridement was the most commonly performed procedure, emphasizing the importance of removing infected and dead tissue to promote healing and prevent further complications [Yazdanpanah et al. 2015]. Antibiotic therapy was administered to almost all patients with diabetic foot ulcers, highlighting the high prevalence of infections in this population. The use of broad-spectrum antibiotics such as Cefotaxime and Piperacillin, along with targeted therapy with other antibiotics, emphasizes the need for appropriate treatment of infections in diabetic foot ulcers. This result is similar to other studies it shows that cefotaxime is used highly in diabetic foot ulcer patients [Singh, A.k, et al. 2020]. Parenteral antibiotics were given to DFU patients who had mild to severe clinical symptoms of infection. Due to the predominance of gram-negative organisms isolated, ceftriaxone and piperacillin-tazobactam were the most frequently prescribed empirical antibacterial agents in the current research. The present study also shows the changing trend in the organisms causing diabetic foot infections,

with gram-negative bacteria replacing gram-positive bacteria as the commonest agents. Similar to a study done [by Turhan, V et al. 2013] *Staphylococcus aureus* 66% was the commonest organism isolated on pus culture in the present study. In contrast, *Pseudomonas* and *E. coli* were the most common bacterial isolates in the study. The medications are frequently mixed with anti-anaerobic medications like metronidazole or ornidazole and clindamycin in cases where the infected DFUs smelled bad. When there is severe soft tissue necrosis or when a more functional foot is required, bone resection and amputation are frequently essential in similar study [Dumville, J. C et al 2017]. Finally, the use of anti-diabetic drugs to manage glycemic control was found to be essential in the treatment of diabetic foot ulcers. The most commonly prescribed drug was Metformin, followed by Glimperide and Vildagliptin. Combination therapy was also used in some cases to achieve optimal glycemic control also another study shows a similar result [Halimi, S et al.2008].

4. Conclusion

In conclusion, the present study provides valuable insights into the characteristics, risk factors, and management of diabetic foot ulcers. The prevalence of diabetic foot ulcer was found to be high in this study. Excess weight was the major factor that leads to cause diabetes and in this study, we reported that obesity plays a crucial role in developing diabetes and thus causes lengthy stay in the hospital. This research revealed that Gram-negative bacilli predominated and that both Gram-positive cocci and Gram-negative bacilli contributed to diabetic foot infections. But the most frequent organism identified from the lesions was *Staphylococcus aureus*. The variation in the numerous studies on the microbial pattern of diabetic foot infection demonstrates that the empirical therapy should be chosen for each case taking into account the most prevalent specific pathogen of the area and its susceptibility to antibiotics. It highlights the importance of early detection, appropriate wound care, appropriate antibiotic therapy, and optimal glycemic control in the prevention and management of this complex condition. Further research is needed to develop effective prevention strategies and improve the management of diabetic foot ulcers.

5. References

- Saeedi, Pouya, et al. 2019. 'Global and Regional Diabetes Prevalence Estimates for 2019 and Projections for 2030 and 2045: Results from the International Diabetes Federation Diabetes Atlas, 9(Th) Edition.' *Diabetes research and clinical practice* 157: 107843
- Yazdanpanah, Leila et al. 2018. 'Incidence and Risk Factors of Diabetic Foot Ulcer: A Population-Based Diabetic Foot Cohort (ADFC Study)-Two-Year Follow-Up Study.' *International journal of endocrinology* 2018: 7631659
- Crocker, Rebecca M, Kelly N B Palmer, David G Marrero, and Tze-Woei Tan. 2021. 'Patient Perspectives on the Physical, Psycho-Social, and Financial Impacts of Diabetic Foot Ulceration and Amputation.' *Journal of diabetes and its complications* 35(8): 107960
- Ramirez-Acuña, Jesus Manuel et al. 2019. 'Diabetic Foot Ulcers: Current Advances in Antimicrobial Therapies and Emerging Treatments.' *Antibiotics (Basel, Switzerland)* 8(4)
- Armstrong, David G., Andrew J.M. Boulton, and Sicco A. Bus. 2017. 'Diabetic Foot Ulcers and Their Recurrence'. *New England Journal of Medicine* 376(24): 2367–75.
- Han, George, and Roger Ceilley. 2017. 'Chronic Wound Healing: A Review of Current Management and Treatments'. *Advances in Therapy* 34(3): 599–610
- Mariam, Tesfamichael G et al. 2017. 'Prevalence of Diabetic Foot Ulcer and Associated Factors among Adult Diabetic Patients Who Attend the Diabetic Follow-Up Clinic at the University of Gondar Referral Hospital, North West Ethiopia, 2016: Institutional-Based Cross-Sectional Study' ed. Andrea Scaramuzza. *Journal of Diabetes Research* 2017: 2879249
- Woldemariam, Guesh Teklu et al. 2020. 'Determinants of Diabetic Foot Ulcer among Adult Patients with Diabetes Attending the Diabetic Clinic in Tikur Anbessa Specialized Hospital, Addis Ababa, Ethiopia: Unmatched Case-Control Study'. *Diabetes, Metabolic Syndrome and Obesity: Targets and Therapy* 13: 3739–47
- Navarro-Peternella, F. M., Lopes, A. P. A. T., de Arruda, G. O., Teston, E. F., & Marcon, S. S. (2016). Differences between genders in relation to factors associated with risk of diabetic foot in elderly persons: A cross-sectional trial. *Journal of clinical & translational endocrinology*, 6, 30–36.
- M. Sue Kirkman, Vanessa Jones Briscoe, Nathaniel Clark, Hermes Florez, Linda B. Haas, Jeffrey B. Halter, Elbert S. Huang, Mary T. Korytkowski, Medha N. Munshi, Peggy Soule Odegard, Richard E. Pratley, Carrie S. Swift; Diabetes in Older Adults. *Diabetes Care* 1 December 2012; 35 (12): 2650–2664
- Xia, N., Morteza, A., Yang, F., Cao, H., & Wang, A. (2019). Review of the role of cigarette smoking in the diabetic foot. *Journal of diabetes investigation*, 10(2), 202–215.
- Yazdanpanah, L., Nasiri, M., & Adarvishi, S.

- (2015). Literature review on the management of diabetic foot ulcer. *World journal of diabetes*, 6(1), 37–53.
- Singh, A. K., Yeola, M., Singh, N., & Damke, S. (2020). A study on diabetic foot ulcers in Central rural India to formulate empiric antimicrobial therapy. *Journal of family medicine and primary care*, 9(8), 4216–4222.
- Turhan, V., Mutluoglu, M., Acar, A., Hatipoğlu, M., Önem, Y., Uzun, G., Ay, H., Öncül, O., & Görenek, L. (2013). Increasing incidence of Gram-negative organisms in bacterial agents isolated from diabetic foot ulcers. *Journal of infection in developing countries*, 7(10), 707–712.
- Dumville, J. C., Lipsky, B. A., Hoey, C., Cruciani, M., Fison, M., & Xia, J. (2017). Topical antimicrobial agents for treating foot ulcers in people with diabetes. *The Cochrane database of systematic reviews*, 6(6), CD011038.
- Halimi, S., Schweizer, A., Minic, B., Foley, J., & Dejager, S. (2008). Combination treatment in the management of type 2 diabetes: focus on vildagliptin and metformin as a single tablet. *Vascular health and risk management*, 4(3), 481–492.