A Prospective Study on Clinico-Bacteriological Study of Diabetic Foot and the Efficacy of Antibiotic Therapy in a Tertiary Care Hospital in Tirupati

Nannam Venkata Ramanaiah[1], Gandikota Venkata Prakash[2], Kumbha Roja Ramani[3], Shaik Heena[4], Dintyala Venkata S.S. Mythri[5], Udayagiri Shanmukha Srinivasulu[6]

[1, 2, 3, 4, 5, 6] Department of General Surgery, Sri Venkateswara Medical College, Sri Venkateswara Ram Narayana Ruia Hospital, Tirupati, Andhra Pradesh, India.

ABSTRACT

BACKGROUND

Diabetic foot is the most common and most feared complication of diabetes and is more significant than nephropathy, retinopathy, heart attack, and stroke combined. Diabetes-associated problems are the second common cause of lower-limb amputations in India. Foot disorders like ulcerations, infection, Gangrene are the leading causes of hospitalization in patients with diabetes mellitus in India.[1]

METHODS

A prospective study, carried out on 100 diabetic patients with foot ulcers over a period of one year from April 2019 to March 2020 at Sri Venkateswara Medical College hospital. The extent of foot infection was assessed based on Wagner's classification and were studied based on the culture and sensitivity obtained and the efficacy of the antibiotic used.

RESULTS

The data analysis of 100 patients has given the following results. 70 % (70 patients) of them were culture positive, and 30 % (30 patients) were culture negative. Culture positive patients were divided into two groups with 35 patients each. Group A started on empirical therapy, Group B on sensitive antibiotic therapy. Repeat swab taken on day 7 from the previously culture-positive patients (70 patients), it was found that 30 out of 35 patients of group-A (empirical therapy) were still culture positive with a similar or newer organism, only 5 patients were culture negative, whereas in 35 patients of Group-B (sensitive antibiotic therapy) only 5 patients were culture positive with a similar or newer organism, remaining 30 patients were culture negative. Sensitive antibiotic therapy was found to be effective than empirical therapy in treatment of diabetic foot ulcers.

CONCLUSIONS

Culture and sensitivity from the wounds play a critical role in prescribing appropriate antibiotic at the time of admission itself rather than starting the empirical treatment.

KEYWORDS

Diabetic Foot, Culture and Sensitivity, Empirical Antibiotic Therapy

Corresponding Author:
Dr. Shaik Heena,
 # 4/177, Beside Police Station,
Yerraguntla, Cuddapah - 516309,
Andhra Pradesh, India.
E-mail: heenasunyn@gmail.com

DOI: 10.18410/jebmh/2021/572

How to Cite This Article:
Ramanaiah NV, Prakash GV, Ramani KR, et al. A prospective study on clinico-bacteriological study of diabetic foot and the efficacy of antibiotic therapy in a tertiary care hospital in Tirupati. J Evid Based Med Healthc 2021;8(33):3145-3149. DOI: 10.18410/jebmh/2021/572

Submission 16-05-2021,
Peer Review 26-05-2021,
Acceptance 28-06-2021,
Published 16-08-2021.

BACKGROUND

Worldwide diabetes has affected more than 190 million people, and it is expected to reach 330 million by 2025. India is considered the world's diabetic capital.[2] due to the highest number of diabetic patients. Out of 62 million diabetics in India, 25 percent of people develop diabetic foot ulcers, out of which 50 % get infected, require hospitalization, and 20 % need an amputation. Diabetic foot ulcers contribute up to 80 % to non-traumatic amputations in India every year. Amputation, the end result of diabetic foot disease, is associated with significant morbidity and mortality.[3] It has immense social, psychological & financial (heavy medical expenditure) consequences for the patient and the family.[4] So identifying those who are at increased risk of diabetic foot complications is essential. There are multiple contributing factors in the pathogenesis of diabetic foot but the two main underlying risk factors are:

- Peripheral neuropathy
- Ischemia.

More than 60 % of diabetic patients foot ulcers are primarily due to underlying neuropathy. The most commonly described mechanism of action is the Polyol pathway. Additional nerve dysfunction is from glycosylation of nerve cell proteins. Ischemia of the endoneurial microvascular circulation induced by metabolic abnormalities from hyperglycemia is also believed to be the underlying nerve deterioration mechanism.

Assessment of Diabetic Foot Ulcers

American Diabetes Association (ADA) 2008 specified that Providers should take history regarding:

- Previous ulceration or amputation
- Any neuropathic symptoms, symptoms of peripheral vascular disease.
- Complications of diabetes, including vision impairment suggestive of retinopathy and nephropathy, especially dialysis or renal transplantation.
- Smoking because smoking is linked to the development of neuropathic and vascular disease.

In an examination of the foot, visual inspection of the barefoot should be performed in a well-lit room.

The Examination Should Include

- An assessment of the shoes; inappropriate footwear can contribute to the development of foot ulceration.
- Should check between the toes for the presence of ulceration or signs of infection.
- The presence of callus or nail abnormalities should be noted.
- Temperature difference between feet is suggestive of vascular disease.
- The foot should be examined for deformities. Hyperextension of the metatarsal-phalangeal joints with interphalangeal or distal phalangeal joint flexion leads to hammertoe and claw toe deformities.
- The Charcot arthropathy was another commonly mentioned deformity found in some affected diabetic patients. It was the result of a combination of motor, autonomic, and sensory neuropathies. Here, muscle and joint laxity have to lead to changes in the arches of the foot. Further, autonomic denervation leads to the demineralization of bone via impairment of vascular smooth muscle, which lead to an increase in blood flow to the bone with significant osteolysis.
- The Dorsalis Pedis artery and Posterior Tibial artery pulses should be palpated and characterized as present or absent. Loss of hair, claudication, and the presence of pale, shiny, thin, or cool skin are physical findings suggestive of potential ischemia. Measuring the Ankle-Brachial pressure Index (ABPI) for determining the extent of vascular disease.

Classification of Diabetic Foot Ulcers

Wagner's Grading was the most widely accepted classification used in diabetic foot ulcers. The lesions were graded by Wagner (1983) based on the depth of lesion and its extent.

Grade 0 - No ulcer but high-risk foot
Grade1 - Superficial ulcer (most simple site is head of 1st metatarsal).
Grade 2 - Deep ulcer with no bony involvement
Grade 3 - Abscess with skeletal involvement
Grade 4 - Localized gangrene
Grade 5 - Gangrene of whole foot

Debridement, regular dressings, appropriate antibiotic therapy and treatment of causative factors formulate the management of diabetic foot.

Objectives

1. To study the clinical characteristics of diabetic foot infections and their outcome at the end of the hospital stay.
2. To study the occurrence and susceptibility profile of isolated bacteria in diabetic foot infections and antibiotic therapy's efficacy in it.

METHODS

This is a prospective study conducted among 100 patients presenting with diabetic foot with ulcer above 18 years of age, who came to the Department of General Surgery, Sri Venkateshwara Ramanaraian Ruia Government General Hospital, Tirupati, over a period of one year after obtaining approval from the ethical and scientific committee. Severely ill, patients with comorbidities and diabetic foot patients without ulcers (Wagner grading 0) were excluded from the study.

Culture swab was taken from the ulcer immediately after the dressing is opened and sent to the lab. Results were analysed and those with culture positive were divided randomly into two groups A (treated with antibiotics based on culture sensitivity) and B (treated with empirical group of

antibiotics). Repeat swab as taken on day and the results were analysed.

Study Methods

Data was collected in standardized proforma from all the Patients presenting to department of General Surgery, S.V.R.R.G.G.H. Tirupati. Patients fulfilling the inclusion and exclusion criteria are selected. Informed written consent would be taken from patients included in the study.

1. Routine and Specific Investigations
2. Collection of specimens
3. Specimen processing
4. Identification of pathogens
5. Antimicrobial susceptibility testing
6. Detection of MRSA
7. Detection of ESBL
8. Repeat swab taken after one week, two weeks

RESULTS

Grade 1, 2, 3 and 4 had distribution of 14%, 43% and 23%, 18% respectively. While Grade 5 is 2%. It was noted that out of the 100 patients studied wound swab was taken from all of them. 70% of them were culture positive, and 30% were culture negative**.**

Grade1	14 %
Grade2	43 %
Grade3	23 %
Grade4	18 %
Grade5	2 %
Total	**100 %**

Table 1. Wagner Grading of Wound

Sl. No.	Culture	Percentage
1.	Positive	70.0
2.	Negative	30.0
Total		**100.0**

Table 2. Distribution Based on Culture Reports Taken on Day One

Type	Organism	Percentage
Gram positive	Staphylococci	42.0
	Streptococci	18.0
	Enterococci	8.0
Gram negative	Pseudomonas	16.0
	E – coli	10.0
	Klebsiella	4.0
	Proteus	2.0

Table 3. Distribution Based on the Type of Organisms Isolated

Sl. No.	Type of Organism	Sensitivity
1.	Staphylococcus	Ceftriaxone, Co Trimoxizole, Amoxyclav, Vancomycin, Ofloxacin.
2.	Streptococcus	Ampicilin, Amoxicillin and Cefoperazone Sulbactum
3.	Enetrococci	Gentamycin, Vancomycin, Linezolid
4.	Pseudomonas	Amikacin, Cefaperazone-Sulbactam, Imipenem, Meropenem
5.	E. Coli	Levofloxacin, AMIKACIN and Cefoperazone Sulbactum
6.	Klebsiella	Pipaeracailin Tazobactum, Imipenem and MEROPENEM
7.	Proteus	Ceftriaxone, Imipenem, Meropenem, Piperacillin, Cef-Sulbactam

Table 4. Distribution of Organisms Based on the Sensitivity

Among the gram-positive microorganisms, it was noted that Staph aureus is the most common bacteria isolated, representing 42.0%, Streptococcus (18.0 %), Enterococcus (8.0 %). Among the gram-negative organisms, it was noted that Pseudomonas is the most common organism isolated (16.0 %), E- Coli (10.0 %), Klebsiella (4.0 %), Proteus (2.0 %).

Antibiotic susceptibility testing is done for isolated organisms, which showed that Staphylococcus was commonly sensitive to ceftriaxone, co cotrimoxazole, amoxiclav, vancomycin, ofloxacin. Streptococcus was sensitive to Ampicillin, cefoperazone sulbactam, and Amoxicillin. Enterococci were found to be susceptible to gentamycin, vancomycin, linezolid. Pseudomonas was sensitive to Amikacin, cefoperazone-sulbactam, imipenem, meropenem. E. Coli was sensitive to, Levofloxacin, Amikacin, and cefoperazone sulbactam. Klebsiella species were exposed to piperacillin-tazobactam, Imipenem, and Meropenem. Proteus bacteria were susceptible to ceftriaxone, imipenem, meropenem, piperacillin, cefoperazone-sulbactam**.**

Sl. No.	Culture Report on Day 7	Group-A (Empirical Therapy)	Group-B (Sensitive Antibiotic)	Total No. of Patients
1	Positive	30 (17.5) [8.93]	5 (17.5) [8.93]	35
2	Negative	5 (17.5) [8.93]	30 (17.5) [8.93]	35
		Total		**70**

Table 5. Distribution Based on Culture Report of Repeat Swab on Day 7

From the results obtained in the repeat swab taken on day seven from the previously culture-positive patients (70.0 %), it was found that 30 out of 35 patients of group-A were still culture positive with either similar or newer organism, only 5 patients were culture negative, whereas in 35 patients of Group-B only 5 patients were culture positive with either matching or newer organism, remaining 30 patients were culture negative.

The p-value is calculated based on the chi-square test and is found to be significant. The chi-square statistic is 35.7143. The P -Value is <0.00001. Significant at P-<.05. The chi-square statistic with Yates correction is 32.9143. The P-value is <0.00001. Significant at p-<.05.

DISCUSSION

In our study, 86 % of subjects were with age > 45years, while 35 %,30 %,21 % was the age distribution observed with ranges of 56 - 65 years, 46 - 55years and >65 years of age. Microangiopathy is the principal cause in the pathogenesis of complications related to Diabetes which can be manifested as nephropathy, retinopathy and neuropathy. In our study the rate of occurrence of these complications in Diabetic foot patients were 14 %, 11 % and 26 % respectively at the time of admission.

Diabetic foot can be classified based on the depth of the wound as Wagner grading which was most widely accepted one. In our study, Wagner Grade 1, 2, 3 and 4 had distribution of 14 %, 43 % and 23 %, 18 % respectively. While Grade 5 is 2 % showing predominant grade 2 presentation, which is comparable with the study by Catherine et al.,[5] where Wagner grade 2(30 %) and grade 4(36 %) were the observations. In our study, it was noted

that out of the 100 patients studied wound swab was taken from all of them. 70 % of them were culture positive, and 30 % were culture negative. Out of the culture positives, 84.0 % had isolated single bacteria, and 16.0 % had isolated polymicrobial growth.

Out of the culture positives, it was noted that 68 % of the organisms were Gram-positive, and the remaining 32 % are Gram-negative. Among the gram-positive organisms, it was noted that Staph aureus is the most common bacteria isolated representing 42.0 %, Streptococcus (18.0 %), Enterococcus (8.0 %). Among the gram-negative organisms, it was noted that Pseudomonas is the most common organism isolated (16.0 %), E- coli (10.0 %), Klebsiella (4.0 %), Proteus (2.0 %) which is not comparable with the study done by Rahul Naresh wasnik et al.[6]

Antibiotic susceptibility testing is done for isolated organisms, which showed that Staphylococcus was commonly sensitive to ceftriaxone, co cotrimoxazole, amoxiclav, vancomycin, ofloxacin. Streptococcus was sensitive to Ampicillin, cefoperazone sulbactam, and Amoxicillin. Enterococci were found to be susceptible to gentamycin, vancomycin, linezolid. Pseudomonas was sensitive to Amikacin, cefoperazone-sulbactam, imipenem, meropenem. E. Coli was sensitive to, Levofloxacin, Amikacin, and cefoperazone sulbactam. Klebsiella species were sensitive to piperacillin-tazobactam, Imipenem, and Meropenem. Proteus bacteria were susceptible to ceftriaxone, imipenem, meropenem, piperacillin, cefoperazone-sulbactam.

Out of 70 % of culture-positive patients (70 patients),50 % of patients (35 patients) were treated with empirical antibiotics, taken as Group-A, and the remaining 50 % of patients (35 patients) were treated with sensitive antibiotic based on culture sensitivity reports, taken as Group-B and swab repeated on day 7 and results were analyzed.

From the results obtained in the repeat swab taken on day 7 from the previously culture-positive patients (70.0 %), it was found that 30 out of 35 patients of group-A were still culture positive with a similar or newer organism, only 5 patients were culture negative, whereas in 35 patients of Group-B only 5 patients were culture positive with a similar or newer organism, remaining 30 patients were culture negative.

Rahul Naresh wasnik et al.,[6] in their study "Evaluation of antimicrobial therapy and patient adherence in diabetic foot infections" of 150 patients, showed the response of the isolated microbes is better when they are treated with susceptible antibiotics based on the culture and sensitivity when compared to those treated with empirical treatment that is followed based on the most common organism and antibiotic susceptibility of it which is prevalent in our area.

In their study, on evaluation of 150 subjects regarding the timing of culture test, timing and drug selection of empirical and definitive therapy they found that empirical therapy prescribed was not in accordance with hospital policies where the research was done. Righteousness of drug dose, route, timing along with appropriate drug improves the clinical outcome in these cases.

Irma Susanti et al,[7] studied the relationship between antibiotic usage and the rate of healing in wounds and concluded that the relationship between suitability and efficacy of definitive antibiotics to wound improvement was not significant because were factors other than antibiotics related to wound improvement. The most related element to the wound improvement was debridement in the operation room.

Kavitha VK et al,[8] in a study conducted by her regarding the choice of wound care in diabetic foot ulcers, concluded that successful management of diabetic foot wounds requires the multidisciplinary teamwork of specialists.

As noted everywhere, early diagnosis of complications, timely reassessment of wound status, appropriate treatment of wound with apt topical regime and treatment of wound related causes include the management of diabetic foot.

Only the low albumin levels remained significantly associated with poor wound healing upon the multivariate adjustment. Hypoalbuminemia could be secondary to the underlying malnutrition, which would also cause poor wound healing. Alternatively, an association of low albumin levels with wound healing may reflect the systemic inflammatory state in patients who go on to develop poor wound outcomes. Although there was insufficient data on ESR, CRP in this cohort could focus on analyzing the role of systemic inflammation on wound healing using these markers. In addition, future analyses with a larger sample size could help to reveal significant independent associations between hemoglobin levels or WBC levels with wound outcomes since limited sample sizes make it difficult to ascertain their role in wound healing in our study.

In addition to the lab biomarkers and clinical co-morbidities coexistent with skin ulcers, the secondary infection of these wounds and the need for systemic antibiotics were a significant prognostic factor of poor outcome. This emphasizes strongly that wound infection prevention is critical to avoid poor outcomes such as amputation. In this context, early or perhaps even the prophylactic antibiotic use among high-risk patients (for instance, those with Diabetes) may be warranted.[9-11]

Seyed Mohammad Alavi et al.[12] in their study, he concluded that staphylococcus aureus, Escherichia coli, Staphylococcus epidermidis, and Proteus Vulgaris were the most common causes of diabetic foot infections in the present study. And the antibiotic resistance rate was 65 % among the isolates. Due to polymicrobial illness and antibiotic resistance, surgical intervention must be concerned.

They could not find the significant differences between the variety of isolated organisms and the grade of ulcers, but the same organisms' load was higher in patients with stage 5. S. aureus was the commonest isolate, which was in agreement with our study and with studies of Tahaway[13] and Unachukwuet al.[14]

Anandi et al, in their study found both monomicrobial and polymicrobial infections and their sensitivity patterns. Polymicrobial infection was found in sixteen patients while monomicrobial infection was found in ten patients. S.aureus was isolated along with either E.coli, Klebsiella spp. or S. epidermidis in seven out of sixteen patients while in remaining nine patients E.coli was isolated along with S. aureus, S. epidermidis or other gram negative bacilli.

Monomicrobial infection was noted in ten pateints.[15] These results are in accordance with our study while 65 % resistance was noted in their study which doesn't correlate with our study.

In the study of Hartemann et al,[16] which yielded 18 % multidrug resistance S. aureus showed increased resistance to Cloxacillin (91 %), Amoxycillin (91 %), Ceftazidime (72 %), Vancomycin (63 %), and Clindamycin (54 %), the resistance was higher compared to the study of Pathare et al.,[17] as they reported 40 % resistance in this organism to similar antibiotics.

S.aureus showed good sensitivity to Ciprofloxacin as the similar results were reported previously by Tahawy[13] both of which are not comparable to our study, because in our study staph aureus is highly sensitive to cotrimoxazole, ceftriaxone, amoxiclav.

Anandi et al. found that the emergence of resistance to multiple drugs by the organisms was associated with history of previous hospitalization for the same wound. Type of the wound (either ischemic or neuropathic), duration of the wound, demographic factors like age, gender, the type of diabetes or the presence of associated complications were not found significant in the emergence of multidrug resistance.

The rate of resistance to used antibiotics was 100 % for all gram-negative isolates while it was 50% in proteus mirabilis. Ciprofloxacin sensitivity was noted for Klebsiella, proteus Vulgaris and pseudomonas aeruginosa isolates in their study[15] while this was not comparable with our study.

Limitations of the Study

1. Sample size was a limiting factor as the duration of the study was limited to twelve months. Hence a better application of the results can be made if the study was done in a broader spectrum of population.
2. This study is from a single centre. Hence a better application of the results can be made if the study was a multicentre one encompassing a broader spectrum of population.

CONCLUSIONS

- The common complications encountered were neuropathy, retinopathy, and nephropathy.
- The glycemic control in the majority of the patients is inferior, which in turn adds to the delayed wound healing and for the worsening of the wound/ gangrene.
- Culture and sensitivity from the wounds play a critical role in prescribing appropriate antibiotic at the time of admission itself rather than starting the empirical treatment.
- The multidisciplinary approach can be followed to treat the diabetic foot and related complications for better clinical outcomes.

Data sharing statement provided by the authors is available with the full text of this article at jebmh.com.
Financial or other competing interests: None.
Disclosure forms provided by the authors are available with the full text of this article at jebmh.com.

REFERENCES

[1] Sadikot SM. The diabetic foot: treatment (http://www.diabetesindia.com/diabetes/updates.htm#footproblem)
[2] Murugan S, Mani KR, Devi U. Prevalence of MRSA among diabetic patients with foot ulcers and their antimicrobial susceptibility pattern. Journal of Clinical and Diagnostic Research 2008;2:979-984.
[3] Singh N, Armstrong DG, Lipsky BA. Preventing foot ulcers in patients with diabetes. JAMA 2005;293(2):217-228.
[4] Frykberg GR. Diabetic foot ulcers: pathogenesis and management. Journal of American Academy of family Physicians 2002;66(9):1655-1662.
[5] Amalia CS, Colayco MD, Myrna T, et al. Microbiologic and clinical profile of anaerobic diabetic foot infections. Phil J Microbiol Infect Dis 2002;31(4):151-160.
[6] Wasnik RN, Marupuru S, Mohammed ZA, et al. Evaluation of antimicrobial therapy and patient adherence in diabetic foot infections. Clin Epidemiol and Global Health 2019;7(3):283-287.
[7] Susanti I, Arianto B, Purnamayanti A. Antibiotics efficacy analysis on diabetic foot ulcer inpatients. International Journal of Pharma Medicine and Biological Sciences 2016;5(4):232-236.
[8] Kavitha VK, Tiwari S, Purandare VB, et al. choice of wound care in diabetic foot ulcer: aa practical approach. World Journal of Diabetes 2014;5(4):546-556.
[9] Jonsson K, Jensen JA, Goodson WH, et al. Tissue oxygenation, anaemia and perfusion in relation to wound healing in surgical patients. Annals of Surgery 1991;214(5):605-613.
[10] Thomas M, Tsalamandris C, MacIsaac R, et al. Anaemia in diabetes: an emerging complication of microvascular disease. Current Diabetes Reviews 2005;1(1):107-126.
[11] Hunt TK, Twomey P, Zederfeldt B, et al. Respiratory gas tensions and pH in healing wounds. The American Journal of Surgery 1967;114(2):302-307.
[12] Alavi MS, Khosravi AD, Sarami A, et al. Bacteriologic study of diabetic foot ulcer. Pak J Med Sci 2007;23(5):681-684.
[13] El-Tahawy AT. Bacteriology of diabetic foot. Saudi Med J 2000;21(4):344-347.
[14] Unachukwu CN, Obunge OK, Odia OJ. The bacteriology of diabetic foot ulcers in Port Harcourt, Nigeria. Nigr J Med 2005;14(2):173-176.
[15] Anandi C, Alaguraja D, Natarajan V, et al. Bacteriology of diabetic foot lesions. Indian J Med Res 2004;22(3):175-178.
[16] Hartemann-Heurtier A, Robert J, Jacqueminet S, et al. Diabetic foot ulcer and multidrug-resistant organisms: risk factor and impact. Diabet Med 2004;21(7):710-715.
[17] Pathare NA, Sathe SR. Antibiotic combinations in polymicrobic diabetic foot infections. Indian J Med Sci 2001;55(12):655-662.