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MULTIDRUG RESISTANCE IN DIABETIC FOOT WOUNDS IN RURAL POPULATION OF SOUTH INDIA -A PROSPECTIVE STUDY

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A B S T R A C T

Background: Multidrug-resistant organisms (MDROs) are increasingly implicated in diabetic foot infections, particularly in rural populations, where limited healthcare resources may exacerbate the issue. This study aimed to evaluate the prevalence of MDROs in diabetic foot ulcers and assess factors influencing wound healing in a rural South Indian setting.

Methods: A prospective, hospital-based observational study was conducted at Karpaga Vinayaka Institute of Medical Sciences, Tamil Nadu, from July 2024 to January 2025. A total of 85 diabetic patients with foot ulcers were enrolled. Clinical evaluations included history, physical examination, and laboratory investigations such as blood tests, chest X-ray, ECG, and wound culture and sensitivity. Patients were categorized based on the presence of MDROs and wound healing outcomes.

Results: Of the 85 patients, 64.7% harbored at least one MDRO. The most common MDROs included *Staphylococcus aureus*, *Escherichia coli*, *Pseudomonas aeruginosa*, and *Proteus mirabilis*. Poor glycemic control (HbA1c > 8%) was significantly associated with the presence of MDROs ($p = 0.031$). Peripheral neuropathy was a significant predictor of non-healing ulcers ($p = 0.007$). Among patients with MDRO infections, wound healing was slower compared to those without MDROs.

Conclusion: The high prevalence of MDROs in diabetic foot ulcers in rural South India highlights the need for stringent glycemic control, early intervention for neuropathy, and culture-based antibiotic therapy. These measures are crucial for improving wound healing and reducing the risk of amputation in diabetic foot patients.

Keywords: Multidrug-resistant organisms (MDROs), diabetic foot ulcers, rural population, glycemic control, wound healing, neuropathy, *Staphylococcus aureus*, *Escherichia coli*

INTRODUCTION

Diabetic foot ulcers (DFUs) represent a serious and common complication of diabetes mellitus, affecting approximately 15–25% of diabetic patients during their lifetime and often leading to infection, hospitalization, and amputation [1]. The risk of lower extremity amputation in individuals with DFUs is up to 40 times greater than in non-diabetic populations, and the mortality rate after amputation approaches 50% within five years [2]. Chronic hyperglycemia impairs leukocyte function, microvascular perfusion, and wound healing, creating a favorable environment for bacterial colonization and infection [3].

In recent years, the emergence and spread of multidrug-resistant organisms (MDROs) in DFUs has compounded the clinical challenge. Studies have reported that up to 50–60% of DFU infections harbor MDROs, including methicillin-resistant *Staphylococcus aureus* (MRSA), extended-spectrum β-lactamase (ESBL)-producing Gram-negative bacilli, and carbapenem-resistant *Pseudomonas aeruginosa* [4]. These resistant pathogens are associated with longer hospital stays, higher healthcare costs, and increased risk of amputation and mortality [5].

Rural populations often face additional barriers to optimal diabetic foot care, including limited access to healthcare facilities, lack of specialized wound care services, and delayed presentation due to socioeconomic constraints [6]. In South India, where the prevalence of type 2 diabetes mellitus is among the highest globally, data on the microbiological profile and antibiotic resistance patterns in rural DFUs remain scarce [7]. Understanding the local epidemiology of MDROs is essential for guiding empirical antibiotic therapy, formulating antimicrobial stewardship policies, and improving patient outcomes.

Accordingly, this prospective study was undertaken in the Department of General Surgery at Karpaga Vinayaka Institute of Medical Sciences and Research Centre, Chengalpattu, Tamil Nadu, to evaluate the prevalence of MDROs in diabetic foot wounds, identify associated risk factors, and assess their impact on ulcer healing in a rural South Indian population.

MATERIALS AND METHODS

Study Design and Setting

This prospective, hospital-based observational study was conducted in the Department of General Surgery at Karpaga Vinayaka Institute of Medical Sciences and Research Centre, Chengalpattu, Tamil Nadu. The study duration was from July 2024 to January 2025.

Study Population

The study included patients admitted with diabetic foot ulcers in the General Surgery Department during the study period.

Sampling Method and Sample Size

A purposive sampling method was used. A total of 85 patients who met the inclusion criteria and consented to participate were enrolled in the study.

Inclusion Criteria

- All diabetic patients presenting with foot lesions.

Exclusion Criteria

- Diabetic patients with pure venous ulcers.
- Patients with neurological disorders or neuropathies not related to diabetes.
- Patients unwilling to provide informed consent.

Data Collection Tools and Clinical Assessment

Each participant underwent a thorough clinical evaluation, including detailed history taking, physical examination, and the following investigations:

- Basic blood investigations
- Chest X-ray
- Electrocardiogram (ECG)
- Pus/swab culture and sensitivity testing from the ulcer site

Classification and Diagnostic Tools:

- Foot ulcers were graded using the Meggitt-Wagner classification system (Grades I–V).
- Peripheral neuropathy was assessed using a 128 Hz tuning fork and a 10 g Semmes-Weinstein monofilament. Peripheral neuropathy was diagnosed according to the International Consensus on the Diabetic Foot.
- Retinopathy was evaluated by an ophthalmologist through fundus examination.
- Peripheral vascular disease (PVD) was diagnosed in patients with absent dorsalis pedis pulses and/or ankle-brachial index (ABI) < 0.9.

Microbiological Assessment and Antibiotic Management

Wound swabs were collected before initiating empirical antibiotic therapy. Specimens were processed for direct microscopy and aerobic bacterial culture using standard microbiological techniques. The antimicrobial susceptibility profile of each isolate was recorded.

- For mild infections, oral Amoxicillin-Clavulanic acid was administered.

- For necrotic or severe wounds, intravenous antibiotics (including Clindamycin or Metronidazole for gram-negative coverage) were used.
- Antibiotic therapy was later tailored based on culture sensitivity reports.

Surgical Management and Follow-up

Patients with unhealthy ulcers underwent appropriate surgical interventions such as debridement or amputation. Regular dressings were carried out, and therapy was modified as per the culture results. All patients were followed up for 12 weeks post-treatment, either in person or via telephonic communication, to assess wound healing status.

Grouping for Analysis

- Patients were categorized into two groups: those harboring at least one multidrug-resistant organism (MDRO) and those without MDRO.
- To evaluate wound healing, patients were classified as healed (complete resolution or significant reduction in ulcer size) or unhealed (no significant change or worsening of ulcer).

Data Entry and Statistical Analysis

Data were entered into Microsoft Excel (2007) and analyzed using SPSS software version 20.0.

- Descriptive Statistics: Categorical variables were presented as frequencies and percentages; continuous variables were summarized using mean ± standard deviation (SD).
- Inferential Statistics:
  - The Chi-square test was used to compare categorical variables.
  - The Student's t-test was used for continuous variables.
  - A p-value < 0.05 was considered statistically significant.

RESULTS AND OBSERVATIONS;

Table 1: Distribution of Study Subjects According to Age and Gender (N = 85)

Age Group (years)	Male (n)	Female (n)	Total (n)	Percentage (%)
< 40	2	1	3	3.5%
41–50	9	5	14	16.5%
51–60	17	11	28	32.9%
61–70	20	13	33	38.8%
71–80	3	3	6	7.1%
81–90	1	0	1	1.2%
Total	52	33	85	100%

Table 2: Distribution of Study Subjects According to Duration of Diabetes and HbA1C Levels (N = 85)

Duration of Diabetes	No. of Subjects	Percentage (%)	HbA1C Category	No. of Subjects	Percentage (%)
< 5 years	20	23.5%	6%–7% (Good Control)	18	21.2%
5 – 10 years	39	45.8%	7%–8% (Fair Control)	28	32.9%
10 – 15 years	18	21.2%	> 8% (Poor Control)	39	45.9%
15 – 20 years	6	7.1%			
> 20 years	2	2.3%			
Total	85	100%	Total	85	100%

Table 3: Diabetic foot Ulcer grade

The majority of the patients had Wagner's ulcers of grades II and III. It was noteworthy that there weren't many ulcers in Wagner's grade IV and V patients

Grade	**No. of subjects**	**Percentage**
1	**13**	**15.3%**
2	**36**	**42.3%**
3	**27**	**31.7%**
4	**7**	**8.2%**
5	**2**	**2.3%**
Total	**85**	**100%**
Variable	**Number**	**Percentage**

Table 4: Distribution of Study Subjects According to Recurrence of Ulcer and Osteomyelitis (N = 85)

Recurrence of Ulcer	**No. of Subjects**	**Percentage (%)**	**Osteomyelitis**	**No. of Subjects**	**Percentage (%)**

No (New Ulcer)	34	40.0%	Absent	53	62.3%
Yes (Recurrent Ulcer)	51	60.0%	Present	32	37.7%
Total	**85**	**100%**	**Total**	**85**	**100%**

Table 5: MDROS among the subjects

Multi-Drug Resistant Organisms	Number of patients	Percentage
MDRO	55	64.7%
NON- MDRO	30	35.3%

Table 6: Frequency Distribution of Organisms and Multidrug Resistant Organisms (MDROs) in Ulcers (N = 264)

Organism	N (%)	MDRO N (%)	Ulcers with MDRO (%)	Specific MDRO Type
GRAM-POSITIVE COCCI				
Staphylococcus aureus	46 (17.6%)	25 (55%)	18%	MRSA (16), MRCONS (9)
Enterococcus faecalis	18 (6.8%)	9 (47.36%)	6%	MDR Enterococcus faecalis
Enterococcus avium	1 (0.4%)	1 (100%)	0.66%	MDR Enterococcus avium
Enterococcus faecium	4 (1.4%)	1 (25%)	0.66%	MDR Enterococcus faecium
Granulicatella adiacens	2 (0.7%)	-	-	-
Group C Streptococci	1 (0.4%)	-	-	-
Group G Streptococci	1 (0.4%)	-	-	-
Streptococcus pyogenes	4 (1.4%)	-	-	-
Streptococcus viridans	2 (0.7%)	-	-	-
GRAM-NEGATIVE RODS				
Escherichia coli	47 (17.9%)	37 (78%)	26%	ESBL (32), ESBL+AMPC (5)
Pseudomonas aeruginosa	43 (16.5%)	32 (74%)	22.6%	MDR Pseudomonas aeruginosa
Proteus mirabilis	19 (7.3%)	13 (70%)	9.3%	ESBL (12), AMPC (1)
Klebsiella pneumonia	22 (8.6%)	9 (41.66%)	6.6%	ESBL
Acinetobacter baumannii	13 (4.7%)	8 (61.53%)	5.3%	MDR Acinetobacter baumannii
Enterobacter aerogenes	8 (2.9%)	3 (37.5%)	2%	AMPC
Citrobacter diversus	8 (3.2%)	3 (33.33%)	2%	MDR Citrobacter diversus
Morganella morganii	4 (1.4%)	2 (50%)	1.3%	MDR Morganella morganii
Providencia species	2 (0.7%)	2 (100%)	1.3%	MDR Providencia species
Citrobacter species	2 (0.7%)	-	-	-
Enterobacter cloacae	1 (0.4%)	-	-	-
Enterobacter species	3 (1.1%)	-	-	-
Proteus vulgaris	3 (1.1%)	-	-	-
Pseudomonas fluorescens	1 (0.4%)	-	-	-
GRAM-NEGATIVE COCCI	1 (0.4%)	-	-	-
OTHERS	8 (3.2%)	-	-	-
TOTAL	**264 (100%)**	**145 (55%)**	-	

Table 7: Association between MDRO and Duration of Diabetes

	MDRO			
Duration	**No**	**YES**	**X2**	**'p' value**

			Value	
<5YEARS	5(16.7%)	15(27.3%)		
5-10 YEARS	16(53.3%)	23(41.8%)		
10-15 YEARS	4(13.3%)	14(25.4%)		
15-20 YEARS	4(13.3%)	2(3.6%)		
>20 YEARS	1(3.3%)	1(1.8%)	5.6111	0.230
Total	30(100%)	55(100%)		

Table 8: Association between Glycemic Control and MDRO

HbA1C	MDRO		X2 value	'p' value
	No	Yes		
1(6%-7%)Good	14(46.7%)	12(21.8%)		
2(7%-8%)Fair	8(26.7%)	14(25.5%)		
3(>8%)poor	8(26.6%)	29(52.7%)		
Total	30(100%)	55(100%)	6.9581	0.031*

Table 9: Association of Clinical Factors with Healing Among Subjects (N = 85)

Clinical Condition	Healing Status	Absent N (%)	Present N (%)	Total (N = 85)	Chi-Square (X^2)	p-value	Significance
Retinopathy	No Healing	45 (91.8%)	4 (8.2%)	49	0.7186	0.397	Not significant
	Healing	31 (86.1%)	5 (13.9%)	36			
Osteomyelitis	No Healing	31 (63.3%)	18 (36.7%)	49	0.0410	0.839	Not significant
	Healing	22 (61.1%)	14 (38.9%)	36			
Arteriopathy	No Healing	27 (55.1%)	22 (44.9%)	49	0.6615	0.416	Not significant
	Healing	23 (63.9%)	13 (36.1%)	36			
Neuropathy	No Healing	13 (26.5%)	36 (73.5%)	49	7.3611	0.007*	**Significant**
	Healing	20 (55.6%)	16 (44.4%)	36			
Hypertension (HTN)	No Healing	25 (51.0%)	24 (49.0%)	49	2.0808	0.149	Not significant
	Healing	24 (66.7%)	12 (33.3%)	36			

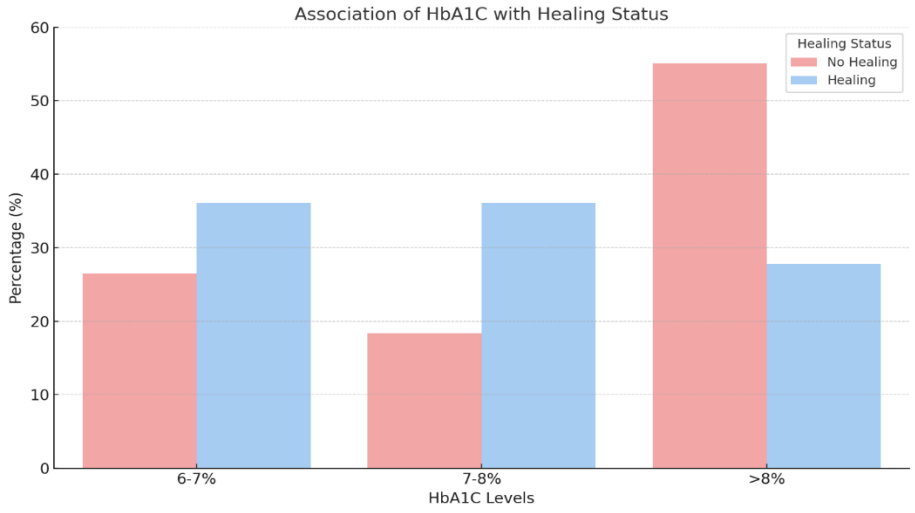

Figure 1: HbA1C and its association with HEALING among the subjects

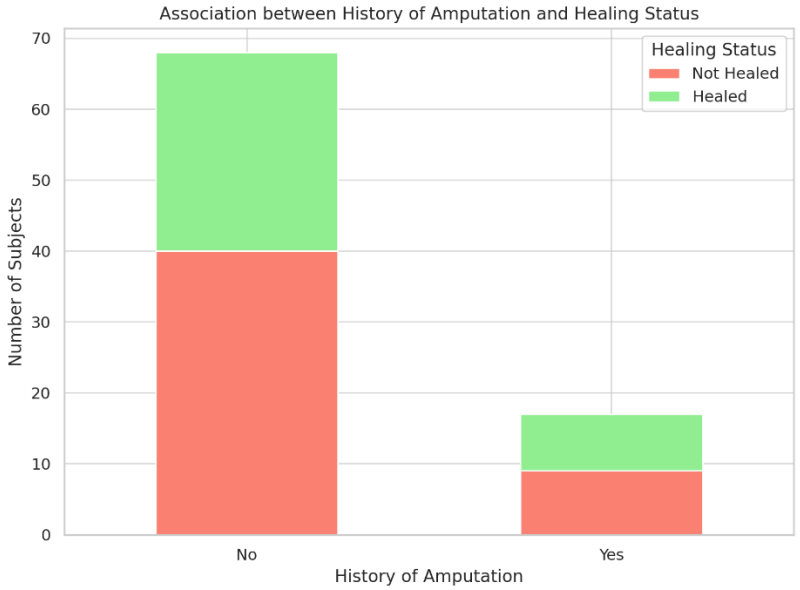

Figure 2: History of Amputation - association with HEALING among the subjects

DISCUSSION

The findings of this study underscore the significant impact of multidrug-resistant organisms (MDROs) on the outcomes of diabetic foot ulcers in the rural population of South India. The prevalence of MDROs in diabetic foot ulcers was notably high, with 64.7% of the patients harboring at least one resistant pathogen. This finding is consistent with previous studies that highlight the growing concern of MDROs in diabetic foot infections, particularly in low-resource settings where surveillance and antimicrobial stewardship programs may be less robust. Several studies have reported that infections caused by MDROs lead to prolonged hospital stays, increased treatment costs, and worse clinical outcomes, including higher amputation rates and mortality [1][2].

Prevalence of MDROs and Microbial Profile

The microbial profile of the diabetic foot ulcers in this study revealed a predominance of both Gram-positive cocci, such as *Staphylococcus aureus* and *Enterococcus faecalis*, and Gram-negative rods, including *Escherichia coli* and *Pseudomonas aeruginosa*. The high prevalence of *Staphylococcus aureus* (17.6%) and *Escherichia coli* (17.9%) is in agreement with the literature, as these organisms are commonly isolated from diabetic foot infections [3][4]. The study also demonstrated a considerable prevalence of methicillin-resistant *Staphylococcus aureus* (MRSA) and extended-spectrum beta-lactamase (ESBL)-producing *Escherichia coli*, reflecting the challenges in managing infections in this population.

Our results also indicated that *Pseudomonas aeruginosa* (16.5%) and *Proteus mirabilis* (7.3%) are among the major pathogens involved in multidrug resistance. The presence of these pathogens is particularly concerning, as they are often associated with chronic, non-healing wounds and are notorious for their ability to develop resistance to multiple classes of antibiotics [5]. The identification of these pathogens as MDROs suggests an urgent need for improved antimicrobial stewardship and targeted therapy based on culture sensitivity results.

Factors Influencing the Occurrence of MDROs

In this study, a significant association was found between poor glycemic control (HbA1c > 8%) and the presence of MDROs. This aligns with several studies that demonstrate that uncontrolled diabetes fosters an environment conducive to the growth of resistant pathogens. Hyperglycemia impairs immune function, decreases the ability of neutrophils to combat infections, and alters wound healing, making diabetic patients more susceptible to infections, including those caused by MDROs [6][7].

Furthermore, the study showed that peripheral neuropathy was significantly associated with healing outcomes. Neuropathy, a common complication of diabetes, is associated with loss of sensation, which increases the risk of trauma to the foot and delays seeking medical attention for wounds. This delayed intervention could lead to the development of infected, non-healing ulcers, which in turn increases the likelihood of MDRO colonization [8].

Duration of Diabetes and Its Impact

The duration of diabetes was also found to influence the occurrence of MDROs, though the association was not statistically significant. However, the trend observed, where longer duration of diabetes (particularly >10 years) was associated with a higher prevalence of MDROs, is consistent with previous research suggesting that prolonged

hyperglycemia and associated comorbidities, such as peripheral vascular disease and neuropathy, predispose to chronic infections and the emergence of resistant organisms [9][10].

Healing Outcomes and the Role of MDROs

The study also explored the impact of MDROs on wound healing. As expected, patients harboring MDROs had significantly worse healing outcomes. This highlights the challenges in managing diabetic foot ulcers in the presence of resistant organisms. Several studies have reported that infections caused by MDROs are harder to treat, leading to increased treatment failures and the need for more aggressive interventions, such as surgical debridement or amputation [11][12].

In this study, patients with associated neuropathy had significantly better healing outcomes, suggesting that early detection and treatment of neuropathic ulcers may lead to improved healing. This finding underscores the importance of comprehensive care for diabetic foot patients, including regular foot examinations, glycemic control, and appropriate antimicrobial therapy.

Limitations and Future Directions

This study has several limitations. Firstly, it was conducted in a single hospital, and the results may not be generalizable to other settings. Secondly, while microbiological culture and sensitivity testing were performed, the resistance mechanisms of the identified pathogens were not further explored. Future studies could focus on identifying the molecular mechanisms behind the resistance of common pathogens in diabetic foot ulcers, which could help inform more targeted therapeutic strategies. Additionally, larger multicenter studies are needed to validate these findings and explore the impact of novel antimicrobial agents in the management of MDROs in diabetic foot infections.

CONCLUSION

This prospective study in a rural South Indian tertiary care centre revealed a high prevalence (64.7%) of multidrug-resistant organisms (MDROs) in diabetic foot ulcers, with *Staphylococcus aureus*, *Escherichia coli*, *Pseudomonas aeruginosa*, and *Proteus mirabilis* being the most common pathogens. Poor glycaemic control (HbA1c > 8%) was significantly associated with MDRO colonization, and the presence of MDROs correlated with delayed ulcer healing. Peripheral neuropathy emerged as a key predictor of poor healing outcomes. These findings underscore the critical need for rigorous glycaemic management, early detection and treatment of neuropathy, and institution of targeted antibiotic therapy guided by culture and sensitivity results. Strengthening antimicrobial stewardship programs and enhancing access to specialized diabetic foot care, particularly in resource-limited rural settings, are essential to reduce MDRO burden, improve healing rates, and prevent amputations in this vulnerable population.

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