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Review Article

Relation Of Diabetic Ulcer Severity and Microorganism Resistance with The Level of Hba1c and Duration of Diabetes

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Abstract

Introduction: Diabetes mellitus (DM) is a chronic metabolic disorder associated with significant morbidity and mortality, primarily due to its long-term complications. The development of DFUs is multifactorial, involving peripheral neuropathy, peripheral vascular disease, immune dysfunction, and chronic hyperglycemia, all of which impair wound healing and increase susceptibility to infection. **Aims:** To evaluate the relationship between diabetic foot ulcer severity (Wagner grade) and antimicrobial resistance of isolated pathogens with patients' HbA1c levels and duration of diabetes. The study also aims to identify factors associated with higher ulcer grades and resistant infections to guide optimal management. **Materials & Methods:** This study was a cross-sectional observational study conducted at KPC Medical College & Hospital, Kolkata, over a period of one year from 1st February 2023 to 31st January 2024. A total of 100 patients with diabetic foot ulcers were included in the study. **Result:** In this study, Wagner's classification revealed that longer diabetes duration correlated with greater ulcer severity ($p = 0.035$). Patients with <10 years of diabetes mostly had Grade 1–2 ulcers, while those with ≥ 10 years exhibited more severe Grade 3–4 ulcers, indicating a clear association between disease duration and ulcer progression. **Conclusion:** We concluded that male gender and longer diabetes duration (≥ 10 years) were substantially linked with higher Wagner grades in this study of 100 individuals with diabetic foot ulcers, suggesting that chronic hyperglycemia leads to ulcer severity.

Keywords: Diabetic foot ulcer, Wagner's classification, HbA1c levels, Antimicrobial resistance, Duration of diabetes.

Introduction:

Diabetes mellitus (DM) is a chronic metabolic disorder associated with significant morbidity and mortality, primarily due to its long-term complications. Among these, diabetic foot ulcers (DFUs) represent one of the most serious complications, often leading to infection, prolonged hospitalization, and even lower limb amputation [1,2]. The development of DFUs is multifactorial, involving peripheral neuropathy, peripheral vascular disease, immune dysfunction, and chronic hyperglycemia, all of which impair wound healing and increase susceptibility to infection [3,4]. Glycosylated hemoglobin (HbA1c) is a widely accepted marker for long-term glycemic control and has been linked to both the incidence and severity of DFUs. Elevated HbA1c levels have been shown to impair leukocyte function, reduce chemotaxis, and compromise innate immunity, thereby increasing susceptibility to infection and delaying wound healing [5,6]. Several studies have reported a positive correlation between higher HbA1c levels and increased severity of DFUs, as measured by the Wagner or University of Texas classification systems [7]. Poor glycemic control not only predisposes patients to ulcer formation but also

influences the microbial environment of the wound, often resulting in more severe infections and colonization by resistant organisms. In addition to glycemic control, the duration of diabetes is an important determinant of DFU risk and severity. Chronic hyperglycemia over years leads to cumulative vascular and neuropathic damage, which increases both the likelihood and depth of ulcer formation. Studies have demonstrated that patients with a longer duration of diabetes are more likely to present with higher-grade ulcers and complex infections requiring prolonged medical management. Microbial colonization of DFUs is a critical factor in clinical outcomes. Gram-positive organisms, particularly *Staphylococcus aureus*, including methicillin-resistant strains (MRSA), are frequently isolated, along with Gram-negative organisms such as *Pseudomonas aeruginosa* and *Escherichia coli*. The prevalence of multidrug-resistant organisms (MDROs) in DFUs is rising, complicating treatment and increasing the risk of poor outcomes. Severity of the ulcer, poor glycemic control, and longer duration of diabetes have all been associated with a higher likelihood of infection by resistant pathogens.

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MATERIALS AND METHODS

Type of Study: A Cross-sectional observational study

Place of Study: KPC Medical College & Hospital, Kolkata

Study Duration: 1 year (From 1st February 2023 to 31st January 2024.)

Sample Size: 100 patients with diabetic foot ulcers

Inclusion Criteria:

- Patients diagnosed with Type 1 or Type 2 diabetes mellitus.

- Patients presenting with foot ulcers of any Wagner grade.
- Age ≥ 18 years.
- Patients willing to provide informed consent.

Exclusion Criteria:

- Non-diabetic foot ulcers (traumatic, vascular, or infectious not related to diabetes).
- Patients on immunosuppressive therapy or with known immunodeficiency.

- Patients with malignancy or chronic systemic infection.
- Pregnant or lactating women.
- Patients who do not consent to participate.

Study Variables:

- Age
- Gender
- Duration of diabetes
- Type of diabetes (Type 1 / Type 2)
- Wagner grade of foot ulcer
- Presence of comorbidities
- HbA1c level
- Fasting and postprandial blood glucose

Statistical Analysis:

Data were entered into Excel and subsequently analyzed using SPSS and GraphPad Prism. Continuous variables were summarized as means with standard deviations, while categorical variables were presented as counts and percentages. Comparisons between independent groups were performed using two-sample t-tests, and paired t-tests were applied for correlated (paired) data. Categorical data were compared using chi-square tests, with Fisher's exact test applied when expected cell counts were small. A p-value of ≤ 0.05 was considered statistically significant.

RESULTS**Table 1: Demographic Distribution of Study Participants**

Parameter	Number of Patients	Percentage (%)	p-value
Male	60	60%	0.00466
Female	40	40%	
Age <50 years	45	45%	0.34
Age $\geq$ 50 years	55	55%	
Duration of diabetes <10 years	52	52%	0.62
Duration of diabetes $\geq$ 10 years	48	48%	

Table 2: Distribution of Diabetic Ulcer Severity (Wagner's Classification)

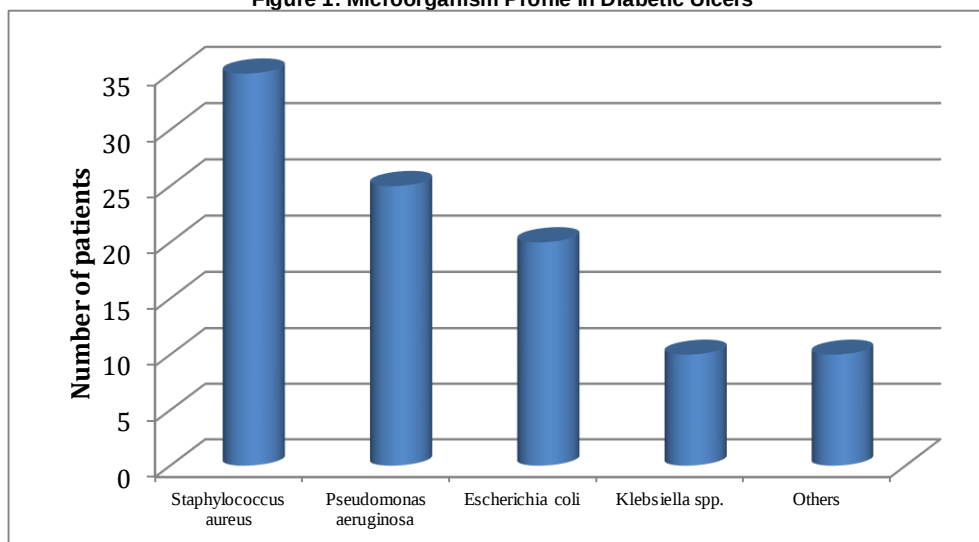
Wagner Grade	Duration <10 years.	Duration $\geq$ 10 years	p-value
Grade 1	20 (38.5%)	10 (20.8%)	0.035
Grade 2	18 (34.6%)	15 (31.3%)	
Grade 3	10 (19.2%)	15 (31.3%)	
Grade 4	4 (7.7%)	8 (16.6%)	

Table 3: Microorganism Profile in Diabetic Ulcers

Organism	Number of patients	Percentage (%)	p-value
Staphylococcus aureus	35	35%	0.12
Pseudomonas aeruginosa	25	25%	
Escherichia coli	20	20%	
Klebsiella spp.	10	10%	
Others	10	10%	

Table 4: Antibiotic Resistance Pattern of Major Isolates

Organism	Resistant to $\geq$ 1 Antibiotic	Percentage (%)	p-value
Staphylococcus aureus	20	57.10%	0.041
Pseudomonas aeruginosa	18	72%	
Escherichia coli	12	60%	
Klebsiella spp.	7	70%	

Figure 1: Microorganism Profile in Diabetic Ulcers

In this study of 100 patients, 60 were male and 40 were female, and this difference was statistically significant ($p = 0.00466$). Regarding age, 45 patients were younger than 50 years, while 55 patients were 50 years or older, with no significant difference between the groups ($p = 0.34$).

For the duration of diabetes, 52 patients had diabetes for less than 10 years and 48 patients for 10 years or more, which was not statistically significant ($p = 0.62$). The distribution of diabetic ulcer severity according to Wagner grading showed a significant association with the duration of diabetes ($p = 0.035$). Among patients with diabetes for less than 10 years, 20 patients (38.5%) had Grade 1 ulcers, 18 patients (34.6%) had Grade 2, 10 patients (19.2%) had Grade 3, and 4 patients (7.7%) had Grade 4. In contrast, among those with diabetes for 10 years or more, 10 patients (20.8%) had Grade 1, 15 patients (31.3%) had Grade 2, 15 patients (31.3%) had Grade 3, and 8 patients (16.6%) had Grade 4 ulcers. In the study, a total of 100 microbial isolates were identified from diabetic ulcers. *Staphylococcus aureus* was the most common organism, isolated in 35 patients (35%), followed by *Pseudomonas aeruginosa* in 25 patients (25%), *Escherichia coli* in 20 patients (20%), *Klebsiella* spp. in 10 patients (10%), and other organisms in 10 patients (10%). The association of organism distribution with the studied variable was not statistically significant ($p = 0.12$). Antibiotic resistance among the isolated organisms showed that *Staphylococcus aureus* was resistant to at least one antibiotic in 20 patients (57.1%), *Pseudomonas aeruginosa* in 18 patients (72%), *Escherichia coli* in 12 patients (60%), and *Klebsiella* spp. in 7 patients (70%). This distribution of resistance was statistically significant ($p = 0.041$).

DISCUSSION

We showed that in our study of 100 patients with diabetic foot ulcers, males were significantly more affected than females (60% vs. 40%, $p = 0.00466$), while age and duration of diabetes alone were not statistically different between groups. However, longer duration of diabetes (≥ 10 years) was significantly associated with higher Wagner grades, with 31.3% and 16.6% of patients presenting with Grade 3 and 4 ulcers, respectively, compared to 19.2% and 7.7% in those with diabetes < 10 years ($p = 0.035$), highlighting the role of chronic hyperglycemia in ulcer severity. Microbiologically, *Staphylococcus aureus* was the most common isolate (35%), followed by *Pseudomonas aeruginosa* (25%) and *Escherichia coli* (20%), although organism distribution was not significantly associated with the studied variables ($p = 0.12$). Antibiotic resistance was high, with 57.1% of *S. aureus*, 72% of *Pseudomonas*, 60% of *E. coli*, and 70% of *Klebsiella* showing resistance to at least one antibiotic ($p = 0.041$), emphasizing the need for culture-guided therapy. These findings indicate that male patients and those with longer diabetes duration are at higher risk for severe ulcers, and the high prevalence of resistant pathogens underscores the importance of targeted antimicrobial management to improve outcomes in diabetic foot infections. In similar study by Ahmad et al., who reported 80.1% male predominance and a significant correlation between longer diabetes duration and higher Wagner grades in 196 DFU patients [8], and with Malepati et al., who observed Wagner grade II–III ulcers in a cohort of 150 patients with mean diabetes duration of 10.5 years [9]. Microbiologically, *Staphylococcus aureus* was the most common isolate (35%), followed by *Pseudomonas aeruginosa* (25%) and *Escherichia coli* (20%), although organism distribution was not significantly associated with patient variables ($p = 0.12$); similar trends were reported by Arunagirinathan et al., who found *E. coli* and *S. aureus* as predominant pathogens with high resistance rates in 126 Indian DFU patients [10]. Zhang X et al. high antibiotic resistance in our cohort, including 57.1% of *S. aureus*, 72% of *Pseudomonas*, 60% of *E. coli*, and 70% of *Klebsiella* showing resistance to at least one antibiotic ($p = 0.041$), aligns with meta-analytic data indicating multidrug-resistant infections in ~50% of DFU cases, particularly among Gram-negative bacteria [11]. Collectively, these studies support our observation that male patients and those with longer diabetes duration are at higher risk for severe ulcers and underscore the importance of targeted, culture-guided antimicrobial therapy to improve outcomes in DFU.

Conclusion

We concluded that male gender and longer diabetes duration (≥ 10 years) were substantially linked with higher Wagner grades in this study of 100 individuals with diabetic foot ulcers, suggesting that chronic hyperglycemia leads to ulcer severity. While the distribution of pathogens like *Pseudomonas aeruginosa*, *Escherichia coli*, and *Staphylococcus aureus* did not significantly change with HbA1c levels or the length of diabetes, a significant percentage showed resistance to at least one antibiotic, especially *Pseudomonas* and *Klebsiella*, underscoring the growing problem of antimicrobial resistance. In order to maximize management, these results highlight the significance of early identification of high-risk patients and culture-guided therapy. To lower morbidity and enhance outcomes in diabetic foot infections, proactive glycemic control monitoring and focused antimicrobial approaches are crucial.

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