

A Current Overview of Chronic Wounds Presenting to a Plastic Surgery Unit in Central India

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Purpose: To analyze the demographic, clinical, and microbiological profile of patients presenting to our unit with chronic wounds of various etiologies with an intent to give a current overview of chronic wounds.

Patients and Methods: We performed a prospective observational study of patients presenting with chronic wounds from October 2018 to September 2019. The study was conducted at the Department of Burns and Plastic Surgery of a tertiary care institute in a non-metropolitan city in Central India. A total of 103 patients were included in the study. Data collected from the patients included demographic details, history, clinical features, and relevant laboratory reports. Wound swabs obtained by Levine's technique were sent for culture and sensitivity studies. Treatment was instituted according to the clinical picture and modified if necessary. Progress was monitored until the wound healed, either by conservative management or by surgical intervention. Patients were followed up for six months thereafter.

Results: Most of the patients presented with lower limb wounds (n=81, 78.64%). Swab specimens from 103 wounds were cultured. Among the isolates, gram-negative organisms were more common than gram-positive organisms. *Staphylococcus aureus* was the most common species isolated, followed by *Pseudomonas aeruginosa*. The frequency of infections caused by other gram-negative organisms like *Klebsiella pneumoniae*, *Escherichia coli*, and *Proteus mirabilis* was on the rise. There were significant differences in the patterns of antimicrobial resistance in our patients. Sharp debridements were required in almost all cases for wound preparation. Most of the patients (n=74, 71.84%) underwent surgical intervention for achieving wound closure. Split-thickness skin grafting (STSG) was the most common surgical intervention performed (n=45, 43.68% patients), followed by local and distant flaps.

Conclusion: Our study gives a current overview of the causes, clinical presentation, prevalent microbial flora, and their antibiotic susceptibilities prevalent in chronic wounds presenting to our unit. Treatments administered are discussed with emphasis on the different reconstructions performed.

Keywords: anti-bacterial agents, biofilms, drug resistance, multiple bacterial, *Pseudomonas aeruginosa*, *Staphylococcus aureus*, wound healing

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Introduction

Chronic wounds are often painful, debilitating and profoundly impair the quality of life of the affected individuals.¹ They impose an enormous economic burden on the patients and healthcare systems around the world. A study estimated that there were 2.2 million patients in the United Kingdom with a wound, equating to 4.5% of the

adult population. This led to 3.4 million hospital outpatient visits annually and a cost of £5.3 billion for managing these wounds and the associated comorbidities.² According to some estimates, chronic wounds of the lower extremity affected 2.4–4.5 million people in the United States.^{3,4} Chronic wound infections caused approximately 85% of all non-traumatic lower-limb amputations and 7–8% of fatalities in spinal cord injury victims.^{1,5,6}

Wound healing involves a cascade of complex and dynamic processes that can be affected by various factors such as elderly age, underlying diseases (venous incompetence, diabetes, and arterial insufficiency), obesity, medications, poor nutrition, and infection resulting in a chronic wound.⁷ Several factors affect the wound's ability to progress from the inflammatory phase to the proliferation phase.⁸ These include the underlying pathology, presence of non-viable tissue, and abnormal immune cell activity, which results in an excessive release of MMPs (matrix metalloproteinases). This process perpetuates the cycle of wound chronicity and extracellular matrix destruction.⁹ Chronic wounds are also characterized by senescent cells which have decreased proliferative and secretory capacities and decreased responsiveness to the wound healing signals.^{10–13}

All chronic wounds naturally contain microorganisms. Microbial involvement of a wound can be described in the terms of the wound infection continuum: contamination, colonization, local infection, spreading infection, and systemic infection.¹⁴ Clinically, a chronic wound infection can present with impaired healing, unhealthy granulation tissue, putrid odor, increased exudate, erythema >1–2 cm, warmth around the wound, and necrotic tissue.¹⁵ The majority of chronic wounds have been reported to consist of a predominantly polymicrobial flora composed of aerobes and anaerobes, although, delayed wound healing with or without clinical signs of infection was more commonly associated with aerobic or facultative pathogens. *Staphylococcus aureus*, *Pseudomonas aeruginosa*, and beta-hemolytic Streptococci were reported as the most common pathogens causing chronic wound infections in some earlier studies.¹⁶

Evidence suggests that biofilms are present in over 90% of chronic wounds.¹⁷ During the inflammatory response to wound infection, leukocytes attach to the biofilm and release enzymes that propagate the inflammatory response and affects the healing processes, leading to the persistence of chronic wound.^{18–23} Biofilms exhibit the ability to mutate and alter their sensitivity to antibacterial agents. Planktonic bacteria are released from the biofilm

onto the wound bed forming new colonies that can lead to local infection or weakening of the collagen matrix.^{24,25}

Over the years, increasing resistance to commonly used antibiotics has been seen in chronic wounds.³ The increasing prevalence of multidrug-resistant organisms has complicated the choice of selecting an appropriate antibiotic for treating chronic wound infections. An understanding of the challenges in the management of chronic wounds and effectively addressing them will lead to a better outcome in terms of improved quality of life of the patients, reduced morbidity, mortality, and decreased healthcare costs. Figure 1 shows the various types of chronic wounds that are usually treated at our unit.

The objective of this study was to analyze the demographic, clinical, and microbiological profiles of patients presenting to our unit with chronic wounds of various etiologies. We intend to present a current overview of chronic wounds with regards to causes, clinical features, organisms isolated, antibiotic sensitivity profiles, treatments administered, and their outcomes.

Patients and Methods

Study Design

We performed a prospective observational study of patients presenting to us with chronic wounds over a period of one year, from October 2018 to September 2019. The study was conducted at the Department of Burns and Plastic Surgery of a tertiary care institute in a non-metropolitan city in Central India.

Inclusion Criteria

Patients who presented to us with chronic wounds (≥ 3 weeks duration) of any etiology and were willing to participate in the study.

Exclusion Criteria

None.

Method

Permission for conducting the study was obtained from the Institutional Human Ethics Committee (no. IHEC-LOP/2018/IM0194). The study protocol conformed to the ethical guidelines of the 1975 Declaration of Helsinki. Written informed consent was obtained from all the participants before their inclusion in the study. Data collected from the patients included demographic details, history, clinical features, and relevant laboratory reports.



Figure 1 Spectrum of chronic wounds presenting to our unit. (A) Long-standing post-traumatic chronic wound over leg region. (B) Chronic wound on the leg following cellulitis. (C) Trochanteric pressure sore. (D) Venous ulcer in the gaiter area. (E) Diabetic foot ulcer. (F) Chronic wound following a thermal burn.

After assessment and photographic documentation, a sample was taken from the wound for culture and sensitivity studies. When a patient presented with multiple wounds, the largest wound was selected for sampling and analysis. An area near the center of the wound free of necrotic tissue and debris was pre-cleaned with non-bacteriostatic saline. Then, the end of a culture swab was rotated over a 1 cm² area for 5 seconds with sufficient pressure to extract fluid from within the wound tissue (Levine's technique).²⁶ All specimens were appropriately labeled and dispatched together with patient information sheets for aerobic culture and antibiotic sensitivity studies. All the specimens were analyzed by the same microbiological laboratory. Standard antibiotic susceptibility testing was performed for the most commonly used antibiotics.

Empirical treatment was instituted if needed, according to the clinical picture and severity at presentation. Once culture and sensitivity reports were available, treatment was instituted or modified, as necessary. Local wound

treatment was performed with sharp/mechanical debridements followed by dressings with different agents. The progress was monitored until the wound healed, either by conservative management or by surgical intervention. STSG (Split-thickness skin grafts), local and distant flaps were the various surgical interventions performed. Patients were followed-up for six months after the wound healed.

Statistical Analysis

All the patient and wound data were entered in a spreadsheet created in Microsoft Excel™ software 2013 version (©Microsoft Corporation, Redmond, Washington, United States). Data analysis was carried out using Epi Info software version 7.2 (Epi Info™, Centers for Disease Control and Prevention, Atlanta, Georgia). Nominal variables were statistically described with frequencies and percentages. Continuous variables were described with means and standard deviations. Ordinal variables were also presented in the form of frequencies and percentages.

Results

A total of 103 patients were included in the study (Table 1). There were 79 (76.69%) males and 24 (23.3%) females, with a male to female ratio of 3.29:1. The age of the patients ranged from 3 to 86 years with a mean age and standard deviation of 40.96 years and 16.307, respectively. Trauma and infection were the most frequent causes of chronic wounds in the study. Majority of the patients presented with lower limb wounds (n=81, 78.64%). The size of the index wound ranged from 1.57 cm² to 675 cm² at presentation.

Swab specimens from 103 wounds were cultured and 99 pathogenic organisms belonging to 17 different species were isolated (Table 2). Seventy-five wounds (72.81%) had growth of a single organism from the wound. Among the isolates, gram-negative organisms were more common compared to gram-positive organisms (62 and 37 isolates, respectively). *Staphylococcus aureus* was the most common species isolated with 30 isolates (30 of 99, 30.30%). There were 20 (20.20%) isolates of *Pseudomonas aeruginosa*.

Antibiotic sensitivity profiles of the isolates to commonly used antibiotics were analyzed. Among the MSSA (methicillin-sensitive *Staphylococcus aureus*) strains, 77.77% (14 of 18) isolates were either sensitive or had intermediate sensitivity to Co-trimoxazole; 88.88% isolates were either sensitive or had intermediate sensitivity to Tetracycline and Clindamycin. Around 61.11% MSSA isolates showed resistance to Levofloxacin, 77.77% isolates showed resistance to Ciprofloxacin, and 55.55% isolates showed resistance to Erythromycin.

In MRSA (methicillin-resistant *Staphylococcus aureus*) isolates, 91.66% (11 of 12) isolates were sensitive to Clindamycin, 66.66% isolates were either sensitive or had intermediate sensitivity to Erythromycin, and all isolates were sensitive to Vancomycin. Around 91.66% MRSA isolates were resistant to Penicillin, Ciprofloxacin, and Levofloxacin; 58.33% isolates were resistant to Co-trimoxazole.

Among *Pseudomonas aeruginosa* strains isolated, 95% (19 of 20) were either sensitive or had intermediate sensitivity to Piperacillin+Tazobactam, 85% isolates were either sensitive or had intermediate sensitivity to Gentamycin, 80% isolates were sensitive to Ciprofloxacin, and 60% isolates were sensitive to Cefepime. Thirty percent isolates of *Pseudomonas*

Table 1 Demographic and Clinical Characteristics of the Patients

Characteristics	No. of patients n (%)
1. Sex	
Males	79 (76.69)
Females	24 (23.3)
Male:Female ratio	3.29:1
2. Age in years: mean (SD)	40.96 (16.307); age range: 3-86 years
3. Duration of wound in weeks category	
≤12 weeks	60 (58.25)
>12 to 24 weeks	14 (13.59)
>24 to 52 weeks	14 (13.59)
>52 to 104 weeks	12 (11.65)
>104 to 156 weeks	3 (2.91)
4. Etiology	
Trauma	29 (28.15)
Infection	25 (24.27)
Burns	14 (13.59)
a) Scald	7 (6.79)
b) Thermal	3 (2.91)
c) Electrical	3 (2.91)
d) Chemical	1 (0.97)
Venous incompetence	11 (10.67)
Diabetic foot	9 (8.73)
Pressure sore	7 (6.79)
Unstable scar	5 (4.85)
Hansen's	2 (1.94)
Marjolin's ulcer	1 (0.97)
5. Number of wounds at presentation	
One	89 (86.4)
Two	11 (10.67)
Three or more	3 (2.91)
6. Site	
Head and Neck	5 (4.85)
Upper Limb	9 (8.73)
Trunk	8 (7.76)
Lower Limb	81 (78.64)
7. Wound size in cm² categories	
1-10	30 (29.12)
10.1-20	13 (12.62)
20.1-50	17 (16.5)
50.1-100	21 (20.38)
100.1-200	17 (16.5)
200.1-500	3 (2.91)
>500	2 (1.94)

Abbreviation: SD, standard deviation.

Table 2 Organisms Isolated

Characteristics	Result
1. No. of isolates per wound	No. of patients n (%)
One	75 (72.81)
Two	11 (10.67)
Three or more	8 (7.76)
No Growth	9 (8.73)
2. Gram staining of the isolates	No. of isolates n (%)
Total no. of isolates	99
Gram-positive organisms	37 (37.37)
Gram-negative organisms	62 (62.62)
3. Organism	No. of isolates n
<i>Staphylococcus aureus</i>	30
a) MSSA	18
b) MRSA	12
<i>Pseudomonas aeruginosa</i>	20
<i>Klebsiella pneumoniae</i>	12
<i>Escherichia coli</i>	10
<i>Proteus mirabilis</i>	8
<i>Enterobacter</i> species	4
<i>Acinetobacter baumannii</i>	3
<i>Streptococcus pyogenes</i>	2
<i>Enterococcus</i> species	2
<i>Proteus vulgaris</i> , <i>Proteus hauseri</i>	1 each
<i>Providencia stuartii</i> , <i>Citrobacter</i> species, Methicillin-resistant coagulase negative <i>Staphylococcus</i> , <i>Klebsiella oxytoca</i> , Methicillin-resistant <i>Staphylococcus</i> <i>haemolyticus</i> , <i>Staphylococcus lugdunensis</i>	

Abbreviations: MSSA, Methicillin-sensitive *Staphylococcus aureus*; MRSA, Methicillin-resistant *Staphylococcus aureus*.

aeruginosa were resistant to Ticarcillin+Clavulanate, Tobramycin, and Meropenem.

Table 3 presents the treatments used in the study subjects and complications. Most of the patients (n=74, 71.84%) needed surgical intervention for achieving wound closure. Among these, split-thickness skin grafting (STSG) was the most common surgical intervention performed, accounting for 43.68% (n=45) patients. Other procedures that were performed include random pattern local flaps, perforator-based local flaps, muscle flaps, free flaps, and a cross-leg flap. Figures 2 and 3 show the pre-operative and post-operative pictures of the cases in which a surgical intervention (skin graft or flap) was performed. Twenty-nine (28.15%) patients were treated conservatively.

Wound closure was achieved in most of the patients, except for four. One patient who presented with a long-standing previously undiagnosed Marjolin's ulcer of the

Table 3 Treatments and Complications

Treatment Modality	No. of Patients n (%)
1. Conservative Management	29 (28.15)
2. Surgical intervention	74 (71.84)
a) STSG	45 (43.68)
b) Random pattern local flaps	5 (4.85)
Transposition flap	1
Rotation flap	1
Limberg flap	1
V-Y advancement flap	1
Bilateral V-Y advancement flap	1
c) Perforator based local flaps	18 (17.47)
Sural artery flap	13
Posterior tibial artery perforator based fascio-cutaneous peninsular flap	2
Pedicled ALT flap	1
Superior gluteal artery perforator based pedicled islanded flap	1
FDMA flap	1
d) Muscle flaps	2 (1.94)
Hemi-soleus flap	1
Tensor fascia lata rotation advancement flap	1
e) Free flaps	2 (1.94)
Free ALT flap	2
f) Cross-leg flap	1 (0.97)
g) Above knee amputation	1 (0.97)
Complications	
Early	No. of patients n
1. Small areas of graft loss treated conservatively	11
2. Partial graft loss requiring re-grafting	6
3. Venous congestion in Sural artery flap	2
4. Superficial necrosis in distal part of FDMA flap	1
5. Total flap loss in free ALT flap	1
Long term	
Wounding in the skin grafts	9

Abbreviations: STSG, split-thickness skin grafting; ALT flap, anterolateral thigh flap; FDMA flap, first dorsal metatarsal artery flap.

leg region underwent an above-knee amputation. Three other patients who were kept on conservative management on an outpatient basis and had initial improvement in their wounds were lost to follow up.

Discussion

Trauma and infection accounted for causing the majority (52.42%) of the chronic wounds in our study population. This finding can be correlated with the male preponderance (76.69%), as males are more susceptible to occupational and



Figure 2 (A) Patient presenting with a post-thermal burn chronic wound over the posterior aspect of the leg. (B) Four weeks following split-thickness skin grafting with a well-settled graft.

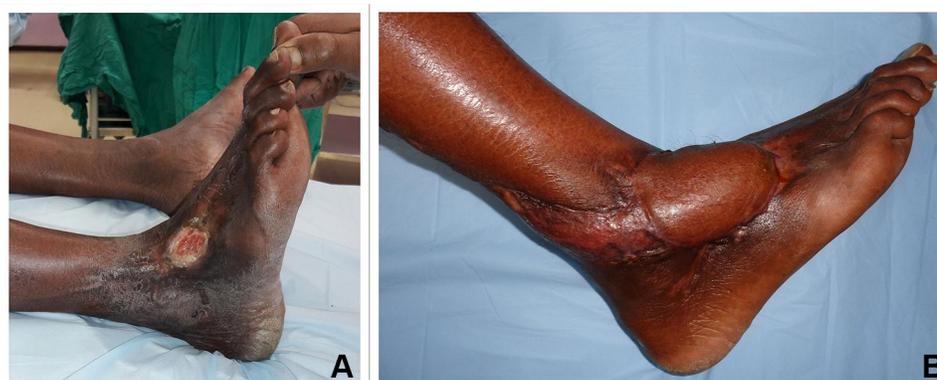


Figure 3 (A) Patient presenting with a long-standing post-traumatic chronic wound over the dorsum of the foot. (B) Two months following excision of the wound and reconstruction with islanded Sural artery flap.

accidental trauma. Burns, venous disease, diabetic foot, and pressure injuries were some of the other important causes. Gupta et al conducted a community-based cross-sectional study on the epidemiology of wounds and reported that untreated trauma, diabetes, and leprosy were the common causes of chronic wounds in their study population.²⁷ This profile is different from that of western literature in which the majority of the chronic wounds are caused by venous disease followed by arterial disease.

In our study, most of the chronic wounds were located in the lower limbs (78.64%). The vulnerability of the lower limbs for wounding has been consistently reported in many of the earlier studies.^{1,27-31} Most of the patients presented with a single wound. But 14 (13.58%) patients had two or more wounds at presentation.

Identification of the causative organisms by microbial cultures and specific anti-microbial therapy are important

measures in the management of chronic wound infections that are unresponsive to standard treatment. Many chronic wounds are indiscriminately treated with antibiotics because of the belief that high wound bioburden contributes to delayed healing.²⁶ In the present study, we have used wound swabs obtained by Levine's technique for cultures. These swabs improve the ability to verify which of the chronic wounds really have high bioburden, thus decreasing the number of patients receiving unnecessary antibiotic treatment. The Levine method samples both the surface biofilm and from beneath the surface,^{24,26} and the culture results are comparable to those obtained by tissue biopsy.^{26,32,33} An international consensus update on wound infection published in 2016 also recommended Levine's technique as it was more effective than Z-swab technique for microbial cultures.¹⁴

Previous studies have shown that chronic wounds mostly have a polymicrobial flora.²⁴ In our study, the

majority (n=75, 72.81%) of the wounds had only one organism isolated from the wound in aerobic cultures. There were only 10.67% wounds with 2 species isolated from the wound and 7.76% wounds with 3 or more species isolated from the wound. No pathogenic organism was isolated in 8.73% wounds. Overall, there were more gram-negative organisms isolated than gram-positive organisms. We believe that these findings should be carefully considered when selecting empirical antibiotic therapy in patients presenting with severe infections. Empirical antibiotic therapy should also include coverage for MSSA or MRSA in patients at risk of these infections.

Angel et al reported that *Staphylococcus aureus* and *Pseudomonas aeruginosa* are the most commonly isolated pathogens in chronic wounds.²⁴ Our study revealed similar findings. Staphylococcal species comprised 33.3% of all isolates recovered; 90.9% of these isolates comprised *Staphylococcus aureus*. *Pseudomonas aeruginosa* was the second most common species isolated comprising 20.20% isolates.

The emergence of community-acquired MRSA has been previously studied.^{34,35} In our study, cultures of specimens from 12 (11.65%) patients had grown MRSA. We found that 91.66% MRSA isolates were susceptible to Clindamycin and 100% isolates were susceptible to Vancomycin. Vancomycin should be considered as the drug of choice for treating MRSA infections caused by multi-drug resistant strains. Clindamycin can be considered as an alternative in less severe cases. We have also found that 91.66% of MRSA strains were resistant to Ciprofloxacin and Levofloxacin. Some earlier studies also reported 80% quinolone resistance in MRSA.³⁶ Hence, quinolones should not be considered as an option for empirical therapy, in cases where MRSA is suspected. Even in cases of MSSA, we do not recommend therapy with Quinolones considering the degree of resistance among the isolates (77.77% isolates resistant to Ciprofloxacin and 61.11% resistant to Levofloxacin).

Valencia et al reported in their study that more than half (56%) of the *Pseudomonas aeruginosa* isolates from leg ulcers were resistant to quinolones.³⁰ In contrast, we found out that in our study subjects, *Pseudomonas aeruginosa* isolates were largely sensitive to quinolones (80% isolates were sensitive to Ciprofloxacin and 75% isolates were sensitive to Levofloxacin). Therefore, we propose that quinolones can be considered as an option for the empirical treatment of suspected *Pseudomonas aeruginosa* infections of chronic wounds. We have also found that the

frequency of infections caused by other gram-negative organisms such as *Klebsiella pneumoniae*, *Escherichia coli*, and *Proteus mirabilis* are increasing.

In our study, apart from the anti-microbial therapy to treat wound infections, wound bed preparation was done with a combination of sharp/mechanical debridements followed by dressings with different agents ([Table S1, supplementary data](#)). Nanocrystalline silver gel was the most common dressing agent used in the study patients. Madhusudhan performed a prospective randomized controlled trial in pseudomonal wound infections and concluded that 1% acetic acid is a simple, safe and effective topical antiseptic that can be used in the elimination of *P. aeruginosa* from chronic-infected wounds.³⁷

Sharp/mechanical debridements were performed in almost all of our study patients. Attempts were made to perform debridement at every dressing until the wound was grossly free from slough. Necrotic tissue in the form of slough or eschar is very commonly found in chronic wounds.³⁸ It not only affects wound healing but also heightens the risk of infection.³⁹ Therefore, debridements are required to get rid of the non-viable tissue and disrupt the biofilms. Appropriate debridement helps accelerate the wound healing process, by removing the barrier of non-viable tissue.⁴⁰ It also helps to break down the defenses of the microbes, exposing them, and permitting more effective action of topical antimicrobials.⁴¹ The importance of surgical debridement in wound bed preparation and its role in disrupting biofilms has been highlighted in the recent international consensus studies.^{42,43} In our study, 28.15% of patients underwent conservative management alone, which consisted of debridements, dressings, and antimicrobials, when needed.

Around 71.84% patients underwent surgical intervention, in addition to conservative management. The coverage provided included split-thickness skin grafts, local and distant flaps. Langer et al performed a prospective study on the adjunctive role of NPWT (Negative-pressure wound therapy) in the healing of chronic wounds.⁴⁴ A significant observation from this study is that, in their study group of 60 patients, they identified that coverage in the form of a flap was required at presentation in 63.33% of patients with chronic wounds. Hence, we can infer that where available, early referral to reconstructive services may shorten the course and improve the outcome in chronic wounds. Further, in this study, after the institution of NPWT, 60% of the patients had wound healing by secondary intention, and 40% of patients required split-

thickness skin grafts.⁴⁴ In our study, STSG was performed in 43.68% of the patients.

Our study had some limitations. We did not employ methods to isolate anaerobic organisms and fungi because of some logistical constraints. Also, the small sample size in our study may not be enough to draw general conclusions applicable to all types of chronic wounds in different settings. Further studies with larger sample sizes are necessary.

Conclusion

Chronic wounds impose an enormous burden on the patients and healthcare systems around the world. Knowledge regarding the causative factors, prevalent organisms in chronic wound infections, antibiotic susceptibility patterns of the isolates, and treatment options is extremely useful to all the people involved in patient care, infection control, healthcare administration, and planning. Our study gives a current overview of the causes, clinical presentation, prevalent microbial flora, and their antibiotic susceptibilities in the chronic wounds presenting to our unit. Treatments administered are discussed with emphasis on the different reconstructions performed.

Abbreviations

ALT flap, anterolateral thigh flap; FDMA flap, first dorsal metatarsal artery flap; MMPs, matrix metalloproteinases; MRSA, methicillin-resistant *Staphylococcus aureus*; MSSA, methicillin-sensitive *Staphylococcus aureus*; NPWT, negative pressure wound therapy; SD, standard deviation; STSG, split-thickness skin grafting.

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