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Diabetic foot ulcer, the effect of resource-poor environments on healing time and direct cost: A cohort study during Syrian crisis

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Abstract

Diabetic foot ulcer (DFU) is one of the slowest healing wounds that hurt the human body. Many studies from developed countries are concerned about materials, procedures, and equipment that accelerate the healing time. In Sweden, the diabetic foot management costs around 24965 $/patient. In this review, we would evaluate the healing time of DFUs during what is considered one of the worst humanitarian crisis of the 21st century. 1747 DFUs were studied from the main diabetic foot clinic in Damascus (2014-2019). We predicted many variables that could prolong the healing time. The cost according to these variables was also reported. The SINBAD Classification was performed to grade the severity of ulcers. We noticed that the median healing time for DFUs was 8 weeks. Almost half of these ulcers healed between 3 and 12 weeks. The time of healing for men was significantly longer than that for women. While the presence of infection doubled the median time of healing, the presence of peripheral artery disease doubled the mean of the direct health care cost. The location of the ulcer acted as another independent risk factor. In conclusion, DFUs face many barriers to heal during a crisis.The environment with resource-poor settings should be added to the traditional risk factors that delay the healing of DFUs for months or even years. More studies from disaster are as are needed to evaluate low-cost materials that could be cost effective in applying standard care of the diabetic foot.

KEYWORDS
diabetic foot infections, diabetic foot outcome, diabetic foot ulcers, healing time, peripheral artery disease, plantar ulcer

Key Messages
- DFUs faced many barriers against the healing during the disaster
- the environment with resource-poor settings is the main barrier
- the healing time for DFUs in crisis areas is affected by many factors
- SINBAD score is an easy clinical classification to detect ulcer severity
- by this trial; predicting healing time becomes easier in (very) low-economic countries

1 | INTRODUCTION

Foot ulcers are defined as lesions involving a skin break with loss of epithelium: they can extend into the dermis and deeper layers, sometimes involving bone and muscle.[1] Up to one-third of the half billion people with diabetes worldwide will develop a diabetic foot ulcer (DFU) over the course of their lifetime. Over half of DFUs will develop an infection. Of these, 17% will require an amputation.[2]

Adopting standard care to diabetic foot patient could not be always affordable, especially in the crisis area. Performing training programmes for health care workers, providing healthy environments to protect DFUs from injuries, fighting the infectious agents, and reducing the amputation rates would be hard challenges in the third world countries.[3]

Furthermore, the financial burden of the complete healing of the ulcer holds economic and social consequences, and that is what many peer-reviewed studies focus on. They worked on detecting variable factors that accelerate/prolong the healing time in every nation.[4,5] From Arab nation countries, the PubMed Library has not included studies that concern about the healing time of DFUs, the affecting factors, and the direct medical cost of this process.

Clinical trials from Syria could play an important role to clear the reality of how the societies during the disasters could face a big health issue like a DFU. Syria has a two-tier health care: a national health system that is applied by the government, which assumes fiscal and administrative responsibility for the health care of all its citizens, and a parallel system of private clinics and hospitals offers services with extra amenities. At this point, the financial burden of diabetic foot care and management is taken over by the government, patients, and (occasionally) the charitable organizations.

In the last decade, the whole Syrian health care system was severely harmed; the diabetic foot patients (in particular) often could not able to be admitted in the public hospital as inpatients. Alternatively, we applied in our clinic a regional anaesthesia for all aggressive debridement and minor amputation and the patient then completed his/her management by scheduled appointments as an outpatient. Moreover, the lack of sources led us to provide low-cost materials for dressing, footwear, and offloading. Here, we will also evaluate if these materials are useful and not wasting the time of the healing.

2 | MATERIAL AND METHODS

This retrospective cohort study is based on electronic medical record data from the Diabetic Foot Clinic in Damascus Teaching hospital; the main hospital in Damascus, the capital of Syria. It is considered the only tertiary referral diabetic foot clinic over the country. Orthopaedists, diabetologists, vascular and general surgeons used to refer diabetic foot patients for consultation, radiological investigations, labs, and advanced interventions that could be required.

TABLE 1 SINBAD classification system and score

Category	Definition	Score
Site	Forefoot	0
	Midfoot and hindfoot	1
Ischaemia	Pedal blood flow intact: at least one palpable pulse	0
	Clinical evidence of reduced pedal flow	1
Neuropathy	Protective sensation intact	0
	Protective sensation lost	1
Bacterial infection	None	0
	Present	1
Area	Ulcer <1 cm^2	0
	Ulcer ≥1 cm^2	1
Depth	Ulcer confined to skin and subcutaneous tissue	0
	Ulcer reaching muscle, tendon or deeper	1
Total possible score		6

Data were collected for the following variables: Age (which was defined as the age at first consultation at the outpatient clinic), gender, DFU presentation date and healing date (if applicable), infection, peripheral artery disease (PAD), DFU location, and the severity of the DFU at the presentation according to SINBAD classification system. This classification system and the scoring are given in[6] Table 1.

In our systematic practice, the patient used to underwent full neurological and peripheral vascular evaluation. The 10-gmonofilament test is used to evaluate the protective senses. The ankle brachial index was performed as a measure for detecting the presence of PAD. The infection is detected mostly clinically and treated by antimicrobial agents. The ulcers were monitored by an experienced team every day, three times a week, or once a week depending on the severity of the ulcer. The diameter (mm) and depth (mm) of each ulcer were a part of monitoring and performed by a scale. The initial size of the ulcer was taken after the primary debridement. Proper footwear, diabetic shoes, insoles, felted foam technique, and total contact dressing were applied as required.

This processing of diabetic foot care was divided into units for financial purposes (Table 2). We could recognise a wide range between public and private services. The prescription also had a variable cost and could not be standard for every case. Lastly, we could note that the economic collapse in Syria has a heavy effect on the medical staff wage in the consultant and procedures units. The materials in the dressing and footwear prescription sections adjusted the low-economic status, while the relatively high cost of the imaging and interventional radiology was a reason to restrict their roles in the plan of the management.

Retrospectively, we reviewed 2653 neuropathic/neuroischaemic DFUs in the charts of 1724 diabetic patients who visited our clinic between January 2014 and December 2019. Of 2653 ulcers, we detected 2187 primary/recurrent ulcers and 466 non-healing wounds within 1 month after a minor amputation (amputation limited to the foot), which were also identified as new ulcers. We excluded 92 and 538 DFUs that needed a major or minor amputation, respectively. Two hundred ten ulcer patients were not able to be followed-up till complete healing because of either non-compliant patients (N = 202) or death by other medical problems (N = 8).

Data of simultaneous DFUs in one patient were also removed (66 cases). The number of residual studied ulcers was 1747. The ulcer was defined as "healed" when a complete epithelialization was performed without discharge, and there was no recurrence of the ulcer within 4 weeks following the registered date of healing.

2.1 | Statistical analysis

Statistical analysis was performed using IBM Statistical Package for the Social Sciences version 25 data analysis software.[7] The data were explored for its completeness, missing values, and outliers before the actual data analysis was performed. Descriptive statistical analysis was performed for variables including demographic characteristics and ulcer characteristics.

Descriptive statistics for the study population at baseline were calculated as median, mean, SDs, counts, and percentages. Non-parametric test was performed for the continuous outcomes. The outcome of the time to healing and categorical variables (Gender, age, SINBAD Classification, infection, PAD, deformity, and location) was examined with the use of the Mann-Whitney U test and Kruskal-Wallis one-way analysis of variance (ANOVA). Mann-Whitney U test was used for independent variables

TABLE 2 Estimated unit costs (US $)

Resource use in outpatient clinic:		Estimated unit cost
Clinic attendance (including nurse or consultant visit) (per week)		7$ (in average)
Angiogram	One of these investigations *per ulcer with PAD* when the cost is affordable.	115$
Computed tomography angiography		100$
Surgical procedures: Wide/Debridement (per ulcer)		Mini = 5$/Max = 150$
Dressings and other consumables (per week)		18$
Prescribing: (antibiotics, opioids, supplements, etc.) (per week)		Mini = 4$/Max = 400$
Footwear prescription:		
Felted foam (for temporary offloading) (per plantar ulcer)		10$
Shoes/± soles (per ulcer)		20$

TABLE 3 Association between categorical variables with healing time of neuropathic diabetic foot ulcers

Variables	Frequency	(%)	Healing time (weeks)				P value[*]
			Median	Mean	SD	Mean rank	
Gender							
Male	964	55.2	8.00	11.47	11.624	921.42	.000
Female	783	44.8	6.00	9.80	11.032	815.61	
Age (years)							
≥50	1505	86.8	8.00	10.82	11.499	870.02	.518
<50	228	13.2	8.00	10.08	10.681	847.09	
SINBAD Classification							
SINBAD score ≥3	768	44.0	14.00	16.34	13.714	1159.35	.000
SINBAD score ≤2	979	56.0	4.00	6.31	6.316	650.15	
Presence of infection							
Yes	553	31.7	12.00	14.78	12.863	1090.06	.000
No	1194	68.3	6.00	8.84	10.104	773.93	
Presence PAD							
With PAD	251	14.4	14.00	18.40	16.571	1191.03	.000
Without PAD	1496	85.6	6.00	9.43	9.696	820.81	
Presence of deformity							
Yes	130	7.4	12.00	13.70	10.507	1064.81	.000
No	1617	95.6	8.00	10.50	11.432	858.66	
Location of wound							
Plantar	581	34	10.00	13.56	13.094	977.39	.000
Non-plantar	1126	66	6.00	9.48	10.229	790.33	

Note: Mann-Whitney *U* test.

Abbreviation: PAD, peripheral artery disease.

[*]Statistically significant, *P* < .05.

with two groups while Kruskal-Wallis one-way ANOVA was used to compare three or more independent variables. It was considered to have a statistically significant difference with *P* < .05.

3 | OUTCOME

The mean healing time for patients with a neuropathic DFU was 10.72 weeks while the median healing time was 8.00 weeks. Among all DFUs, 49.5% (n = 864) healed within 3 to 12 weeks and 12.2% (n = 214) of them took >20 weeks to be healed. In Table 3, we could find the following results.

3.1 | Demographic characteristics

This study involved 1410 patients (>18 years old) with neuropathic DFUs. Of the patients, 55.2% (n = 946) were male and 44.8% (n = 783) were female, with an overall mean age

of 60.3 ± 11.1 years old. The mean age of every gender was, female: 61.0 ± 11.4 years old; male: 59.7 ± 10.9 years old. Mann-Whitney *U* test indicated that the healing time of male (mean rank: 921.42; n = 946) was significantly longer than female (mean rank: 815.61; n = 783), *U* = 331 688.500, z = −4.374, *P* = .000, two-tailed.

3.2 | SINBAD classification

We classified the 1747 DFUs according to SINBAD classification system: Score 1: 28% (N = 489); score 2: 28% (N = 490); score 3: 17.4% (N = 304); score 4: 17.7% (N = 309); score 5: 7.7% (N = 135); score 6: 1.1% (N = 20). It is clear that 44.0% of the sample sits within SINBAD score ≥ 3, and longer healing time was significantly observed for DFU with SINBAD score ≥ 3 (mean rank: 1159.35; n = 768) compared with DFU with SINBAD score <3 (mean rank: 650.15; n = 979) *U* = 156 787.500, z = −21.010, *P* = .000, two-tailed.

3.3 | Infected ulcers vs non-infected ulcers

The incidence of the infection would be higher in an unhealthy environment, which is more common in the low socio-economic status, camps, and crisis areas such as many of Syrian towns. We recorded DFUs as a DFI when the infection occurred in any stage of treatment: from the presentation till the healing. The study named 553 ulcers (31.7%) as an infected ulcer with healing time (mean rank: 1090.06; n = 553) significantly longer than those with non-infected ulcer (mean rank: 773.93; n = 1194) $U = 210\,661$, z = −12.223, $P = .000$.

3.4 | The effect of PAD in the healing time

The recorded data mentioned 273 (15.6%) ulcers that combined with a grade of PAD in the same lower extremity. Twenty-two of these cases underwent percutaneous trans-luminal angiography and stenting or bypass. The test indicated that the healing time for ulcers with PAD (mean rank: 1191.03; n = 251) was significantly higher than the ulcers without PAD (mean rank: 820.81; n = 1496) $U = 108\,173$, z = −10.795, $P = .000$, two-tailed.

3.5 | The effect of deformity in the healing time of DFUs

In this sample; there were 130 DFUs that were combined with variant types of foot deformity. Charcot foot was found in seven cases. The mean rank of healing time for these 130 DFUs was 1064.81. It is clearly higher than those 1617 DFUs without simultaneous deformity (mean rank: 858.66) $U = 80\,300$, z = −4.498, $P = .000$, two-tailed.

3.6 | The effect of DFU location in the healing time

3.6.1 | The healing time for plantar ulcer

The location of the wound ulcer was also found to have a statistically significant relationship with the healing time of the DFU. The test indicated that the healing time for patients with ulcers located at the plantar side of the foot (mean rank: 977.39; n = 581) was significantly higher than the patients whose ulcers were not located at the plantar side of the foot (mean rank: 790.33; n = 1126) $U = 255\,414.5$, z = −7.453, $P = .000$, two-tailed.

3.6.2 | The anatomical region of DFUs

Kruskal-Wallis ANOVA indicated that there were significant differences between the healing times of DFUs according to anatomical region of foot: forefoot vs midfoot or hindfoot. The median of healing time for forefoot was 6.00 while for midfoot or hindfoot was 12.00 for each of them (Table 4). Other variables studied in this analysis were not statistically significant.

3.7 | The direct health care cost to achieve DFU healing

We could expect the direct health care cost of the DFU in Syria (2014-2019) from the estimated unit costs (Table 3). This cost had two divisions: (a) the fixed one, which included the cost of vascular procedures, debridement cost, offloading, shoes, and soles. (b) The weekly cost, which depended on the duration of the healing time like antibiotics, dressing, and clinical attendance. The cost of achieving the complete healing of ulcer was studied in Table 5; the severity of the ulcer, PAD, infection, and

TABLE 4 Association between the wound anatomical region and healing time of diabetic foot ulcers

Variables Wound anatomical region:		Frequency	(%)	Healing time (weeks)			
				Median	Mean	Mean difference	*P* value[*]
Forefoot	Midfoot	1245	73.0	6.00	9.35	−5.035[*]	.000
	Hind foot					−6.751[*]	.000
Midfoot	Forefoot	240	14.1	12.00	14.38	5.035[*]	.000
	Hind foot					−1.717	.235
Hind foot	Forefoot	210	12.3	12.00	16.10	6.751[*]	.000
	Midfoot					1.717	.235

Note: Kruskal-Wallis one-way analysis of variance.

[*]Statistically significant, $P < .05$.

	Number	Mean of healing time (weeks)	Fixed cost	Weekly cost	Direct health care costs to achieve healing per ulcer			
					Mean	SD	Median	P value*
Severity of ulcer (SINBAD)								
SINBAD score ≥3	768	16.34	135	225	3810.59	3085.551	3285.00	.000
SINBAD score ≤2	979	6.31	60	50	375.73	315.812	260.00	
Infected ulcer:	553	14.78	135	325	4939.48	4180.563	4035.00	.000
No infected ulcer	1194	8.84	135	50	576.92	505.191	435.00	
Presence of PAD:	251	18.40	160	225	4299.64	3728.547	3310.00	.000
Without PAD	1496	9.43	60	225	2182.16	2181.604	1410.00	
Plantar ulcer	581	13.56	95	225	3145.86	2946.247	2345.00	.000
Non-plantar ulcer	1126	9.48	85	225	2219.10	2301.581	1435.00	

Abbreviation: PAD, peripheral artery disease.

*Statistically significant, $P < .05$/Mann-Whitney U test.

plantar position of ulcer played significant roles in increasing the economic burden of DFUs.

4 | DISCUSSION

The wide variation of the diabetic foot cost between different countries was recorded in many published articles.[4] While the expenses incurred as a total cost for healing DFUs in Sweden was estimated around US$24965/patient without amputation, the economic burden of DFUs in India showed expenses of US$1960 for the treatment.[8] These differences between the developed countries and low-income countries (especially those that suffer from disaster and crisis) could be explained by many factors. Firstly, the pay differentials among health care workers between the two categories of countries. Secondly, the developed countries usually use the costly advanced equipment more frequently in diagnosis, monitoring, and supporting the DFUs management (eg, laboratories, MRI, nuclear bone scan, angiogram, vascular procedures, revascularization, etc.).[9] Also, materials that were used in the dressing, offloading, and footwear are definitely not the same in the two categories of countries. Even though our trial did not reach the diabetic foot *inpatients*, there is no doubt that offering the full management care at the clinic succeeded in preserving hospital resources for other emergency fields in crisis situation.

On the other hand, we noticed that shoes, soles, and their materials we have obtained in Syria for a long time do not achieve the complete healing in the time and increase the rate of early recurrence of neuropathic DFUs (within 4 weeks). We could say that the cost of these materials would not be effective and the medical society should provide high-quality shoes/soles to prevent incomplete healing and early recurrence.

One of the limitations on studying the economic burden of DFUs in low-income societies is the difficulty of predicting the *indirect* cost, especially during a disaster or crisis.

The guidelines of IWGDF 2019 estimate the SINBAD scoring system a simple and quick classification to use; it has been validated for healing in diverse DFU populations, and has been shown to be acceptable to clinicians.[10] This classification has been *validated* for both ulcer healing and amputation prediction, presenting good results, and has good reliability.[11]

Diabetic foot complications may be disabling or even life-threatening, no doubt that the diabetic ulcer infections (DFI) are the major complications and play a main role in slowing the healing.[12] In our trial, DFI doubled the median of the healing time.

PAD is present in approximately one-half of all patients with foot ulcers.[13] Although every diabetic foot classification involves PAD as a predicting factor that combined by others to determine the risk of amputation and the chance of healing, many studies suggest that PAD is considered as an independent risk factor and DFUs with or without concomitant PAD should be defined as two separate disease states.[14] The mild severity of PAD and the costly procedures for revascularization were the main causes of lower numbers of PAD patients (N = 22) who had been performed for revascularization procedures.

The significantly prolonged time and high cost for the healing of plantar ulcer are an index for the necessity of improving materials that support accelerating the healing. The cost-effective approach of using inexpensive materials did not encourage us to recommend it as ideal materials.

5 | CONCLUSION

DFUs face many barriers against healing during a crisis. The environment with resource-poor settings should be added to the traditional risk factors that delay the healing of DFUs for months or even years.

In addition, this clinical trial adds another proof that SINBAD Classification predicts the outcome of DFUs. More studies from disaster areas are needed to evaluate and suggest more affordable materials that are helpful in applying standard care and management in the diabetic foot field.

CONFLICT OF INTEREST

The authors report no commercial or other association that might pose a conflict of interest with respect to this clinical trial.

AUTHOR CONTRIBUTIONS

Mhd Belal Alsabek: Attending Surgeon at Al-Mouwassat University Hospital, corresponding author, collected the data, wrote the manuscript, and analysed the data statistically. **Abdul Razzak Abdul Aziz:** General and diabetic foot surgeon. The head of diabetic foot clinic in Damascus Teaching Hospital. D-Foot National Representative-Syria. He supervised the management of the patients in the sample during the 5 years of the trial, offered the plan of the treatment, supervised the clinical trial, and reviewed the manuscript. All the authors made an equal contribution to the creation of the presented clinical trial.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author.

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