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**Original Research Article**

# Role of hyperbaric oxygen therapy in the treatment of chronic ulcers of the foot in patients with type II diabetes mellitus

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## ABSTRACT

**Background:** The aim of this study is to evaluate the effect of hyperbaric oxygen therapy (HBOT) in healing of chronic foot ulcers in patients with type II diabetes mellitus.
**Methods:** A case control study included 40 type II diabetic patients with chronic foot ulcers not healing for more than 4 weeks. It has been conducted at Naser Institute for Research and Treatment and Menoufia University Hospital during the period between April 2017 and September 2018. Patients with non-healing diabetic foot ulcers were referred by physicians and were also identified through a number of wound care clinics in various hospitals.
**Results:** Most ulcers were observed in the sole and heel in both groups A and B (n=14 and 9 respectively), while the rest of ulcers were distributed in other areas of the foot, namely the medial and lateral malleoli, dorsum and toes. On comparing the wound related complications developing during the treatment period, no statistically significant difference was found between both groups (p=0.147). As regards Wagner's grade, 7 patients (17.5%) had grade 4 ulcers, 18 patients (45%) had grade 3 ulcers and 15 patients (37.5%) had grade 2 ulcers, showing no statistically significant difference between both groups before treatment (p=0.259).
**Conclusions:** HBOT is a useful adjunct in the treatment of non-healing diabetic foot ulcers, and that the cost of HBOT itself will be reduced as it becomes more widely available in the clinical setting, and as further knowledge of its other advantages, such as limited side effects and relative safety, become more widely appreciated.

**Keywords:** Chronic ulcers, Hyperbaric oxygen therapy, Type II diabetes mellitus

## INTRODUCTION

Diabetes mellitus (DM) is a chronic disease characterized by an increase in blood sugar that can lead to many medical disorders. The prevalence of DM is difficult to estimate, because some people who have the condition are undiagnosed or may not be captured through data that reflect access to the health care system.[1] However, in the year 2000, it was estimated that the prevalence of diabetes would rise from 2.8% to 4.4% by 2030.[2] This is an alarming prediction in light of the high number of complications that are associated with this disease. The US Health and Nutrition Survey further demonstrated that 28.5% of those with diabetes develop peripheral neuropathy, 9.5% develop signs of peripheral arterial disease, and 7.7% develop foot ulcers; approximately three times the frequency observed in non-diabetic individuals.[3] Because of the neuropathy, a foot injury and subsequent infection cannot be felt, and since circulation is also affected, wound healing is compromised and causes the original ulcer to become chronic and may eventually require amputation.[4] Non-healing foot ulcers and their sequelae are a major source of morbidity.[5] At centers of excellence, 19-35% of ulcers are reported as non-healing.[6]

As a result of these complications, there were approximately 29,000 diabetics admitted to U.S. hospitals with a diagnosis of cellulitis or infected ulcers, 84000 admitted for abscesses of the foot, 217000 admitted for ulcerations of the lower extremity, 66000 admitted for osteomyelitis, 134000 admitted for chronic non-healing ulcers, and 79000 admitted for lower limb atherosclerosis with ulcers or gangrene in 2002.[7]

A staggering percentage of these individuals undergo surgical intervention while in the hospital. Even more are treated as outpatients for less complex problems as well as elective procedures. These numbers do not include the thousands of patients with diabetes admitted for Charcot reconstructions, and other conditions not included in the preceding statistics. Among patients who develop ulcerations, it was found that 24% required surgery in the form of an amputation at some level, costing an average of $44.790 (for surgery and hospitalization).[8]

Ultimately, when you combine all of the different diabetes-specific complications as well as the non-diabetes-related reasons that people with diabetes may need surgery, it represents millions of cases in the United States alone.[9]

The standard of care includes the maintenance of optimal blood glucose levels; use of debridement, frequent dressings; administration of antibiotics to control infection; adequate nutrition; pressure relief in the areas of the foot that are most subject to weight bearing; and amputation.[10] The rate of lower extremity amputation (LEA) has been measured to range between 6% and 23.5%.[11]

Major LEAs are amputations of the leg above or below the knee, whereas minor LEAs involve amputation of the toes or the forefoot. Not surprisingly, quality of life is significantly reduced in patients with ulcers and after major amputations.[12] Systemic hyperbaric oxygen therapy (HBOT) has been proposed as an adjunctive treatment for diabetic foot ulcers.[13] The technology includes enclosing the patient entirely in a pressurized chamber, breathing 100% pure oxygen at a pressure more than 1 atmospheric air pressure, either in a monoplace or a multiplace decompression chamber. Advocates have suggested that the experimentally demonstrated effects of HBOT on improving wound tissue hypoxia, enhancing perfusion, reducing edema, down regulating inflammatory cytokines, promoting fibroblast proliferation, collagen production, and angiogenesis make it a useful adjunct in clinical practice for "problem wounds", such as diabetic foot ulcers.[14]

HBOT is also touted for eradicating difficult to treat soft tissue and bone infections by mechanisms that include killing microorganisms, improving leukocyte and macrophage function, and enhancing the effect of antimicrobials.[15] Noted complications are rare but may include claustrophobia; ear or sinus trauma due to pressure; temporary worsening of short sightedness; and central oxygen poisoning. Careful monitoring during the treatment sessions and follow-up by a trained health care provider is recommended.[1] Thus, theoretically, HBOT could improve the healing of ischemic foot ulcers in patients with diabetes, and it has been suggested that its use will decrease the risk of LEA.[16]

The aim of this study is to evaluate the effect of HBOT in healing of chronic foot ulcers in patients with type II DM.

## METHODS

A case control study included 40 type II diabetic patients with chronic foot ulcers not healing for more than 4 weeks. It has been conducted at Naser Institute for Research and Treatment and Menoufia University Hospital during the period between April 2017 and September 2018. Patients with non-healing diabetic foot ulcers were referred by physicians and were also identified through a number of wound care clinics in various hospitals.

### *Inclusion criteria*

Inclusion criteria were age ≥18 years, type II DM and Wagner grading of foot lesions 2, 3 or 4 not healing for at least 4 weeks.

### *Exclusion criteria*

Patients in need for urgent amputation due to ongoing exacerbated infection, patients with critical occlusion of major blood vessels of the lower limb, any of the following medical conditions which preclude safe treatment in a monoplace chamber: neuropsychiatric problems: claustrophobia; or seizure disorder, chest problems: chronic obstructive pulmonary disease; thoracic surgery within the preceding 3 months; previous spontaneous or trauma induced pneumothorax. ENT problems: chronic sinusitis; chronic or acute otitis media or major ear drum trauma, Participation in another investigative drug or device trial within 30 days before the study and Women who were pregnant, breast feeding, or women of childbearing potential who were not taking adequate birth control.

### *Study design*

In the study 40 patients meeting the inclusion criteria were divided into 2 equal groups as follow: group (A): chronic foot ulcers were treated by standard wound care alone and group (B): chronic foot ulcers were treated by HBOT in combination with standard wound care.

### *Patient assessment*

Upon arrival, patients of both groups were assessed for: demographic data: age, sex, residence and occupation, diabetic history, medications and other medical risk factors as hypertension, liver or renal impairment and

smoking, general examination, local examination of the affected limb, including: vascular examination: peripheral pulses, pallor, cyanosis, capillary refilling time, trophic changes, nails and temperature, neurological examination: sensory and motor examination,

***Wound assessment***

Wounds were assessed according to the following criteria, ulcer duration in weeks, site, size in $cm^2$, depth, type and percentage of tissue covering the ulcer floor, type of wound discharge. The collected data was used to classify the wounds according to Wagner's classification system, and Bates-Jensen wound assessment tool.

***Wagner scale***

The foot ulcer classification system used in this study was described and popularized by Wagner. In the Wagner system, the natural history of dysvascular foot breakdown is divided into six grades ranging from Grade 0 (pre-ulcer) to Grade 5 (amputation required). The system is similar to an ordinal scale denoting ranked order, allowing for nonparametric data analysis. Grade is determined based on depth of the skin lesion and the presence or absence of infection and gangrene. [17]

***Bates-Jensen wound assessment tool***

The Bates-Jensen wound assessment tool (Barbara Bates-Jensen © 2001), is a validated wound assessment tool that evaluates 13 wound characteristics with each item scored on a 1-5 scale. A total score is obtained by adding all individual scores and the results are plotted on the Wound Status Continuum. Higher total scores indicate a more severe wound status.[18]

***Interventions***

*Duplex scanning*

Selected patients of both groups were subjected to duplex scanning of both lower limbs, to exclude the presence of critical occlusion of a major blood vessel which would impair healing and require further surgical intervention.

*Dressing changes*

Based on the characteristics of the wound, dressings were changed as required (at a minimum of 2 dressing changes per day). Wound care was standardized throughout the entire study to a single dressing type (i.e. wash by regular saline 0.9%, povidone iodine, saline and applying cream containing collagenase clostridiopeptidase and protease enzymes).

*Antibiotic therapy*

Clinical signs of infection were noted, swabs obtained and antibiotic therapy was initiated as required according to culture and sensitivity results.

***Local wound debridement***

Referral for debridement of the wound occurred when necessary.

***Hyperbaric oxygen therapy***

Each patient was observed in the hyperbaric medicine consult prior to treatment. Treatment issues were discussed with the patient and a written informed consent was obtained once contraindications were excluded.

During the procedure, the selected patients were placed in a compression chamber with increased pressure between 2.0 and 2.5 atmospheres absolute for 60 to 90 minutes, once daily. In the chamber, the patients inhaled 100% oxygen. Hyperbaric oxygen was administered 6 days a week. Any in-chamber adverse reactions were noted. Unless hospitalization was required due to a diabetic foot complication with indication for intravenous antibiotics or amputation, or any other medical comorbidity, HBOT was administered in an ambulatory setting

***Data collection***

Data to evaluate the efficacy of HBOT were collected at screening, baseline, and weekly throughout the treatment phase. At the end of the treatment phase, each patient's wound was evaluated. If the patient's wound has not healed, the wound care physician, in consultation with the vascular surgeon decided if further HBOT or other treatment was indicated. Data were collected via interview and physical measurements.

***Statistical methods***

Data was recorded in a database sheet which was verified before data entry. SPSS program version 17 was used for data analysis. P value: to find significant relation between two or more percentages for qualitative data: Statistical significance if $p<0.05$, statistical high significance if $p<0.01$, statistical not significant if $p>0.05$.

## RESULTS

The demographic characteristics of the studied groups (n=40) demonstrated that the age of patients ranged between 49-65 years in group A with a mean age of 58.1 years, compared to 43-63 years in group B with a mean age of 56.05 years. The number of males in group A was higher than females, with male to female ratio 13:7. On the contrary, the number of females was higher than males in group B, with male to female ratio 8:12. However, there was no statistically significant difference between both groups regarding sex (p=0.113). The number of smokers in group A was higher than that of group B (n=11 and 7 respectively), showing no statistically significant difference between both groups (p=0.204), (Table 1).

**Table 1: Comparison between the two studied groups regarding age, sex and smoking.**

| | Type of treatment | | | | T-test | |
|---|---|---|---|---|---|---|
| | Standard wound care | | HBOT | | T | P value |
| | N | % | N | % | | |
| **Age (in years)** | | | | | | |
| Range | 49-65 | | 43-63 | | 1.221 | 0.230 |
| Mean±SD | 58.100±5.310 | | 56.050±5.306 | | | |
| **Sex** | | | | | $X^2$ | |
| Male | 13 | 65.00 | 8 | 40.00 | 2.506 | 0.113 |
| Female | 7 | 35.00 | 12 | 60.00 | | |
| **Smoking** | | | | | | |
| Non-smoker | 9 | 45.00 | 13 | 65.00 | 1.616 | 0.204 |
| Smoker | 11 | 55.00 | 7 | 35.00 | | |

T: T-test, $X^2$: Chi-square, p value is significant if p<0.05.

**Table 2: Comparison between the two studied groups regarding ulcer site.**

| Site | Type of treatment | | | | | | Chi-Square | |
|---|---|---|---|---|---|---|---|---|
| | Standard wound care | | HBOT | | Total | | | |
| | N | % | N | % | N | % | $X^2$ | P value |
| **Dorsum** | 2 | 10.00 | 1 | 5.00 | 3 | 7.50 | | |
| **Heel** | 5 | 25.00 | 1 | 5.00 | 6 | 15.00 | | |
| **Sole** | 9 | 45.00 | 8 | 40.00 | 17 | 42.50 | | |
| **Toes** | 2 | 10.00 | 7 | 35.00 | 9 | 22.50 | 8.170 | 0.147 |
| **Lateral malleolus** | 2 | 10.00 | 1 | 5.00 | 3 | 7.50 | | |
| **Medial malleolus** | 0 | 0.00 | 2 | 10.00 | 2 | 5.00 | | |
| **Total** | 20 | 100.00 | 20 | 100.00 | 40 | 100.00 | | |

$X^2$: Chi-square, p value is significant if p<0.05.

**Table 3: Comparison between the two studied groups regarding ulcer duration (in weeks) and wound related complications.**

| | Type of treatment | | | | T-test | |
|---|---|---|---|---|---|---|
| | Standard wound care | | HBOT | | T | P value |
| | N | % | N | % | | |
| **Ulcer duration (in weeks)** | | | | | | |
| Range | 4-16 | | 4-48 | | -1.480 | 0.147 |
| Mean±SD | 6.900±3.210 | | 10.300±9.761 | | | |
| **Wound related complications (local)** | | | | | $X^2$ | |
| No | 18 | 90.00 | 20 | 100.00 | 2.105 | 0.147 |
| Yes | 2 | 10.00 | 0 | 0.00 | | |

T: T-test, $X^2$: Chi-square, p value is significant if p<0.05.

Regarding ulcer site, there was no statistically significant difference between groups A and B (p=0.147). However, most ulcers were observed in the sole and heel in both groups A and B (n=14 and 9 respectively), while the rest of ulcers were distributed in other areas of the foot, namely the medial and lateral malleoli, dorsum and toes (Table 2).

The ulcer duration ranged between 4-16 weeks with a mean duration 6.9±3.2 weeks in group A, compared to 4-48 weeks with mean ulcer duration 10.3±9.761 weeks in group B. There was no statistically significant difference between groups A and B regarding ulcer duration (p=0.147). On comparing the wound related complications developing during the treatment period, no statistically significant difference was found between both groups (p=0.147). However, it was noteworthy that zero patients (0%) in group B developed wound related complications, in contrast to group A in which 2 patients (10%) developed severe infection and septicemia that lead to below knee amputations (Table 3).

**Table 4: Comparison between the two studied groups regarding ulcer margins, floor, discharge before and after treatment.**

| | | Type of treatment | | | | | | Chi-square | |
|---|---|---|---|---|---|---|---|---|---|
| | | Standard wound care | | HBOT | | Total | | | |
| | | N | % | N | % | N | % | $X^2$ | P value |
| **Ulcer margins** | | | | | | | | | |
| Before | Normal | 11 | 55.00 | 14 | 70.00 | 25 | 62.50 | 0.960 | 0.327 |
| | Inflamed | 9 | 45.00 | 6 | 30.00 | 15 | 37.50 | | |
| After | Normal | 13 | 72.22 | 19 | 95.00 | 32 | 84.21 | 3.697 | 0.055 |
| | Inflamed | 5 | 27.78 | 1 | 5.00 | 6 | 15.79 | | |
| P value | | 0.446 | | 0.096 | | | | | |
| **Ulcer floor** | | | | | | | | | |
| Before | Clean | 5 | 25.00 | 10 | 50.00 | 15 | 37.50 | 2.667 | 0.102 |
| | Necrotic | 15 | 75.00 | 10 | 50.00 | 25 | 62.50 | | |
| After | Clean | 12 | 66.67 | 18 | 90.00 | 30 | 78.95 | 3.103 | 0.078 |
| | Necrotic | 6 | 33.33 | 2 | 10.00 | 8 | 21.05 | | |
| P-value | | 0.024* | | 0.016* | | | | | |
| **Ulcer discharge** | | | | | | | | | |
| Before | None | 1 | 5.00 | 3 | 15.00 | 4 | 10.00 | 10.797 | 0.013* |
| | Serous | 4 | 20.00 | 2 | 10.00 | 6 | 15.00 | | |
| | Serosanguineous | 0 | 0.00 | 7 | 35.00 | 7 | 17.50 | | |
| | Purulent | 15 | 75.00 | 8 | 40.00 | 23 | 57.50 | | |
| After | None | 3 | 16.67 | 18 | 90.00 | 21 | 55.26 | 20.905 | <0.001* |
| | Serous | 5 | 27.78 | 1 | 5.00 | 6 | 15.79 | | |
| | Serosanguineous | 6 | 33.33 | 1 | 5.00 | 7 | 18.42 | | |
| | Purulent | 4 | 22.22 | 0 | 0.00 | 4 | 10.53 | | |
| P value | | 0.004* | | <0.001* | | | | | |

$X^2$: Chi-square; p value is significant if p<0.05.

**Table 5: Comparison between the two studied groups regarding ulcer depth and size before and after treatment.**

| | | Type of treatment | | | | Chi-square | |
|---|---|---|---|---|---|---|---|
| | | Standard wound care | | HBOT | | | |
| | | N | % | N | % | $X^2$ | P value |
| **Depth** | | | | | | | |
| Before | Intact skin | 0 | 0.00 | 0 | 0.00 | 7.037 | 0.030* |
| | Partial thickness | 0 | 0.00 | 5 | 25.00 | | |
| | Full thickness | 14 | 70.00 | 13 | 65.00 | | |
| | Full thickness involving damage to muscles, tendons or bone | 6 | 30.00 | 2 | 10.00 | | |
| After | Intact skin | 0 | 0.00 | 5 | 25.00 | 20.046 | <0.001* |
| | Partial thickness | 0 | 0.00 | 9 | 45.00 | | |
| | Full thickness | 16 | 88.89 | 5 | 25.00 | | |
| | Full thickness involving damage to muscles, tendons or bone | 2 | 11.11 | 1 | 5.00 | | |
| P value | | 0.304 | | 0.018* | | | |
| **Ulcer size (in $cm^2$)** | | | | | | **T-test** | |
| | | | | | | **T** | **P value** |
| Before | Range | 4-84 | | 1-99 | | 0.409 | 0.685 |
| | Mean±SD | 22.750±19.379 | | 19.550±29.154 | | | |
| After | Range | 1-105 | | 0-81 | | 1.702 | 0.097 |
| | Mean±SD | 28.944±32.861 | | 12.960±24.828 | | | |
| Differences | Mean±SD | -4.778±23.794 | | 6.590±6.596 | | | |
| Paired test | P value | 0.406 | | <0.001* | | | |

T: T-test, $X^2$: Chi-square, p value is significant if p<0.05.

**Table 6: Comparison between the two studied groups regarding ulcer's Wagner grade before and after treatment.**

| Wagner's grade | | Type of treatment | | | | | | Chi-square | |
|---|---|---|---|---|---|---|---|---|---|
| | | Standard wound care | | HBOT | | Total | | | |
| | | N | % | N | % | N | % | $X^2$ | P value |
| Before | Grade 0 | 0 | 0.00 | 0 | 0.00 | 0 | 0.00 | 2.698 | 0.259 |
| | Grade 1 | 0 | 0.00 | 0 | 0.00 | 0 | 0.00 | | |
| | Grade 2 | 5 | 25.00 | 10 | 50.00 | 15 | 37.50 | | |
| | Grade 3 | 11 | 55.00 | 7 | 35.00 | 18 | 45.00 | | |
| | Grade 4 | 4 | 20.00 | 3 | 15.00 | 7 | 17.50 | | |
| After | Grade 0 | 0 | 0.00 | 5 | 25.00 | 5 | 13.16 | 21.956 | <0.001* |
| | Grade 1 | 0 | 0.00 | 9 | 45.00 | 9 | 23.68 | | |
| | Grade 2 | 12 | 66.67 | 6 | 30.00 | 18 | 47.37 | | |
| | Grade 3 | 6 | 33.33 | 0 | 0.00 | 6 | 15.79 | | |
| | Grade 4 | 0 | 0.00 | 0 | 0.00 | 0 | 0.00 | | |
| P value | | 0.016* | | <0.001* | | | | | |

$X^2$: Chi-square; p value is significant if p<0.05.

Before treatment, 9 patients (45%) had inflamed margins around the ulcers in group A, and 6 patients (30%) in group B, showing no statistically significant difference between both groups (p=0.327). After treatment, 5 patients (27.78%) still had inflamed ulcer margins in group A (p=0.446), compared to 1 patient (5%) in group B (p=0.096) denoting better response to treatment in the group that received standard wound care plus HBOT than standard wound care alone. However, there was no statistically significant difference between both groups after treatment (p=0.055). 15 patients (75%) in group A had necrotic ulcer floors before treatment, in contrast to 10 patients (50%) in group B, showing no statistically significant difference between both groups (p=0.102). After treatment, 6 patients (33.33%) in group A still had necrotic ulcer floors, compared to 2 patients (10%) in group B, denoting good response to treatment in both groups (p=0.024 and 0.016 for respectively). However, no statistically significant difference was noted between both groups after treatment (p=0.078). Before treatment, 19 patients in group A (95%) had ulcer discharge, compared to 17 patients (85%) in group B, ranging between serous, serosanguineous and purulent discharges. After treatment, 15 patients (75%) still had ulcer discharge in group A, in contrast to only 2 patients (10%) in group B, showing a statistically significant difference between both groups (p<0.001), (Table 4).

In group A, 0 patients (0%) achieved full ulcer closure, and 6 patients (30%) showed improvement in their ulcer depth. In group B, 5 patients (25%) achieved complete ulcer closure and 10 patients (50%) showed improvement in their ulcer depth, showing a statistically significant difference between both groups after treatment (p≤0.001). Before treatment, the mean size of ulcers was 22.75 for group A and 19.55 for group B, showing no statistically significant difference between both groups by using T-test (p=0.685). At the end of treatment, an increase in the mean size of ulcers was noted in patients of the placebo group (mean=28.944) compared to patients of the HBOT group who showed a decrease in their mean ulcer size (mean =12.96), (Table 5).

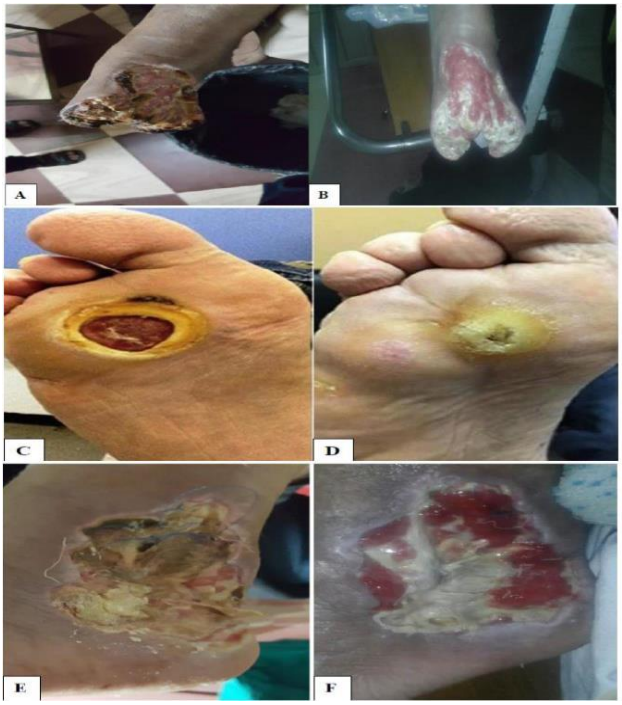


**Figure 1: (A) Male patient 55 years old, with diabetic ulcer involving the left foot, not healed for 2 months, previous amputation for all toes was done; necrotic tissue, foot and leg edema and purulent discharge are noted; (B) diabetic foot ulcer after 3 weeks' treatment with HBOT, ulcer floor is covered with granulation tissue, with disappearance of necrotic tissue and purulent discharge; (C) female patient 50 years old with diabetic neuropathic ulcer involving the right sole, ulcer not healed for 2 months; (D) completely healed ulcer after 3 weeks' treatment with HBOT; (E) male patient 58 years old with diabetic ulcer involving the right ankle, ulcer floor is covered by necrotic tissue, and purulent discharge was noted on daily dressing; (F) diabetic ulcer after 3 weeks' treatment with HBOT, floor is covered with granulation tissue, with less necrotic tissue and disappearance of purulent discharge.**

As regards Wagner's grade, 7 patients (17.5%) had grade 4 ulcers, 18 patients (45%) had grade 3 ulcers and 15 patients (37.5%) had grade 2 ulcers, showing no statistically significant difference between both groups before treatment (p=0.259). At the end of treatment, no patients (0%) in group A reached grade 0 or 1 ulcers, compared to 14 patients (70%) in group B, showing a statistically significant difference between both groups (p<0.001), (Table 6).

## DISCUSSION

Our study has been conducted on 40 type 2 DM patients, with foot ulcers not healing for more than four weeks. Due to randomization, there was no statistically significant difference between both groups in their demographic characteristics. However, it was noteworthy that among the studied sample (n=40), there was nearly an equal distribution of foot ulcers between males and females (n=21 and 19). This disagrees with Duzgun et al who showed a higher incidence of foot ulcers in males in their studied sample (males=64%, females=36%).[19] Also this disagrees with Londahl et al whose study showed a further more rise of foot ulcers in males (males=81%, females= 19%).[20] The above mentioned disagreement can be explained by the equal physical effort exerted outside home by both genders in our society, and consequently the equal exposure to risk of trauma and occurrence of foot ulceration.

In this study, the mean age of patients was 58.1 in group A, and 56.05 in group B. This agrees with the study conducted by Viswanathan et al which showed a mean age of foot ulceration of 55.6 and 61 in the studied groups.[21] Also this agrees with Markova and Mostow whose studied sample (n=36) showed a mean patient age of 60.08.[22] Still, this finding contradicts with Londahl et al whose study showed a higher age of patients (mean age=69 and 68 for the studied groups).[20] This can be explained that in their study conducted in Sweden, there is a higher level of awareness among the population about the disease of DM and its complications, and the importance of proper blood sugar control, self-hygiene and avoidance of foot trauma. This differs from the fore mentioned studies which were conducted in Egypt, India and China, where the level of awareness, blood sugar control and self-care decreases.

In this study, most ulcers were observed in soles and heels of the patients, representing 57.5% of the studied sample (n=40). This agrees with the study performed by Londahl et al.[20] In their study conducted on 94 diabetic patients with chronic foot ulcers, it has been noted that 35 patients (37.2%) showed plantar forefoot and heel ulcers, while the other patients had ulcers distributed in other areas of the foot. This can be attributed to the fore mentioned pathophysiology, which states that peripheral neuropathy and ischemia are the two main factors responsible for the development of diabetic foot ulcers (both of which are more notable in the sole), leading to ulceration due to trauma or excessive pressure during walking on a deformed foot that lacks protective sensation. However, the above mentioned result disagrees with the study performed by Viswanathan et al.[21] Their study conducted on 6 patients with type 2 DM showed equal distribution of foot ulcers among the patients (33.3% in heel, 33.3% in dorsum and 33.3% in toes). This result can be attributed to the smaller sample of patients than in the fore mentioned studies.

In our study, there was no statistically significant difference between both groups as regards the improvement in ulcer floor (p=0.078) or inflamed margins around the ulcers (p=0.055). However, statistically significant results were obtained regarding the reduction in ulcer size (p≤0.005), type and amount of discharge (p≤0.001), and ulcer depth (p≤0.001). Notably, complete ulcer closure occurred in 5 patients (25%) of the HBOT group, and furthermore 10 patients (50%) showed improvement in their ulcer depth, with a total of 15 patients (75%) showing good response to treatment with HBOT. This is compared to zero patients achieving full ulcer closure in the placebo group, and only 6 patients (30%) showing improvement in their ulcer depth category. This matches with the results obtained by Duzgun et al.[19] In his unblended, randomized study, the effect of HBOT was compared with standard therapy in 100 patients with foot ulcer duration of at least four weeks. Treatment was administered as 2 sessions per day, followed by 1 session on the following day, alternating throughout the course of therapy, which typically extended for a period of 20 to 30 days. During a mean follow-up period of 92 weeks, primary healing was achieved in 66% of patients receiving HBOT compared with 0% following standard therapy.

According to Wagner's grade, more patients in the HBOT group reached grade 0 and 1 ulcers (n=5 and 9 respectively) in contrast to zero patients in the placebo group, resulting in a statistically significant difference between both groups (p≤0.001). Moreover, the Bates-Jensen Wound Assessment Tool (BWAT) showed more decrease in ulcer severity in the HBOT group than the control group (p≤0.001). These results denote better healing rates in the group that received adjuvant HBOT in their ulcer treatment, than the group that received standard wound care alone. Our findings are in agreement with those reported in the previous randomized studies focused on ulcer healing by Kalani et al included 38 patients with ischemic ulcers without full-thickness gangrene.[10] After three years, 76% of the 17 patients receiving HBOT had healed their ulcers to intact skin compared with 48% of those given conventional treatment. In the randomized trial by Kessler et al, the effect of two daily 90-min sessions of HBOT five days a week for two weeks was compared with regular treatment in 28 hospitalized patients with neuropathic Wagner grade 1 to 3 ulcers.[23] After two weeks of treatment, the reduction in ulcer area was doubled in the HBOT group (p=0.037). This improvement disappeared during the next two weeks of follow-up. However, this disagrees with

Abidia et al.[16] In that study of 18 patients, a non-significant improvement of healing rate following HBOT was seen after six weeks. This can be explained that he evaluated the effect of HBOT compared with hyperbaric air in ischemic Wagner grade 1 and 2 ulcers. Still, the results reached statistical significance at 1-year follow-up.

On comparing the wound related complications developing during the treatment period, no statistically significant difference was found between both groups (p=0.147). However, it was noteworthy that zero patients in the HBOT group developed wound related complications, in contrast to the control group that showed 2 patients developing severe infection that lead to below knee amputation. This agrees with Duzgun et al.[19] He reported that in regard to distal (distal to the MTPJ level) versus proximal (proximal to the MTPJ level) amputation, 24 (48%) of those in the ST group underwent distal amputation whereas 17 (34%) of them required proximal amputation. In the group receiving HBOT, 4 (8%) underwent distal amputation, and zero (0%) required proximal amputation. However, this disagrees with Londahl et al who reported that within the 1st year of treatment, the number of major (above ankle) amputations was higher in the HBOT group than the placebo group (n=3 and 1 respectively).[20] This can be explained by the longer duration of study, as in the HBOT group, two of the three amputations were done 2 months after inclusion, while the third amputation was done at 191 days. The amputation in the placebo group was performed 98 days after inclusion.

Our study also revealed decreased need for debridement in the HBOT group than the ST group. Out of 20 patients in the ST group, 13 patients (65%) underwent wound debridement, either bedside or in the operating room. This is compared to only 4 patients (20%) that needed debridement in the HBOT group. This is concomitant with Duzgun et al who reported that 50 patients (100%) of those in the ST group required either operative debridement in the operating room, an amputation, or the use of a flap or skin graft; whereas 8 (16%) of those in the group receiving HBOT required these forms of surgical management.[19]

The limitation to this study is that the time taken for complete healing of some diabetic foot ulcers was not studied. It may also be cost-effective when measured against outcomes such as amputations, repeated debridement, hospital stay and psychological disability. Still, our study has proven that HBOT is a useful adjunct in the treatment of diabetic foot ulcers, and the cost itself will be reduced as it becomes more widely available in the clinical settings.

## CONCLUSION

HBOT is a useful adjunct in the treatment of non-healing diabetic foot ulcers, and that the cost of HBOT itself will be reduced as it becomes more widely available in the clinical setting, and as further knowledge of its other advantages, such as limited side effects and relative safety, become more widely appreciated.

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