Effect of Adjuvant Hyperbaric Oxygen Versus Routine Wound Care on Diabetic Foot Ulcer Healing: A comparative Study

Amel Saeid Mahmoud[1,2], Heba Ahmed Mohammed[3]

[1,3]Assistant prof. of Medical-Surgical Nursing Department, Faculty of Nursing, Cairo University

[2] Assistant prof. of Medical-Surgical Nursing Department, College of Nursing, King Saud bin Abdulaziz University for Health Sciences, Al-Ahsa, Saudi Arabia. /King Abdullah International Medical Research Center, Al-Ahsa, Saudi Arabia.

Corresponding author: Heba Ahmed Mohammed

Email: Heba.ahmed 2222@yahoo.com

Abstract

Background: A diabetic foot ulcer is a challenging complication of diabetes that has become a global health problem. The treatment process is troublesome for the patient and healthcare team, especially in advanced cases. Hyperbaric Oxygen therapy (HBOT) in combination with standard methods of diabetic foot ulcers management appears to be more effective than standard methods alone. **Aim:** To compare the effect of adjuvant hyperbaric oxygen therapy versus routine wound on diabetic foot ulcer healing. **Subjects and Method: Design:** A prospective non-experimental comparative study. **Setting**: at the medical, surgical and vascular surgery departments, outpatient clinics and hyperbaric oxygen therapy unit at Nasser Institute for Research and Treatment Cairo-Egypt. **Subjects:** sixty adult male and female patients with diabetic foot ulcer divided into two groups 30 patients in each of (the HBOT with standard wound management and standard wound management alone group) who met the inclusion criteria. **Tools**: I: Patient's assessment data include: demographic and clinical background information form, II: Wagner classification system, III: Numeric Pain scale and IV: MUNGS tool. **Results:** There was statistically significant difference between the two groups regarding Wagner score at the end of two and three months (T= 2.193, P=0.032) (T= 2.163, P=0.035) respectively. There was significant difference regarding pain severity at the end of three months (T= 2.538, P=0.014). There was statistically significant difference between the two groups regarding MUNGS score at the end of three months follow-up (T= 2.298, P=0.025). **Conclusion:** HBOT in combination with standard methods of diabetic foot ulcers management appears to be more effective than standard methods alone.

Keywords: Diabetic foot ulcer, Hyperbaric oxygen therapy, Standard diabetic foot ulcer care

Introduction

One of the most destroying complexities of diabetes is diabetic foot ulcer (DFU), it is considered a major cause of non-traumatic amputations worldwide and affecting an estimated 6.4% of the global diabetic population **(Tao & Yuan, 2024; Shah et al., 2022)**. DFU has a high danger of contamination with morbidity rate of (40-80%), moreover (14-20%) of patients with DFU require amputation. likewise amputations in diabetic patients is up to twenty times **hi**gher compared with the individuals who are non-diabetic and around (70-80%) of all non-traumatic amputations happen in patients with diabetes **(Oley et al., 2020; Armstrong et al., 2017)**. More worryingly, DFU has been strongly associated with an elevated risk of mortality, which is likely to be more than twofold that of patients with diabetes without this complication, what's more survival is reduced by 60% in 5 years for patients with DFU **(Alshmimry et al., 2021)**. In addition, in Egypt diabetes mellitus is prevalent where approximately 15.2 % of the Egyptian population has diabetes mellitus **(Abouzid et al., 2022)**.

Management of DFU is complex and perplexing as they are hard to treat, many stay asymptomatic for long periods of time, they are often infected, they have slow healing despite regular and intensive treatment, and they request long and meticulous treatment **(Laopoulou et al., 2020)**. Nevertheless, standard wound care of diabetic foot ulcer includes protection and relief of the ulcer, educate the patients to restrict standing and strolling, reclamation of foot perfusion, urgent vascular imaging and revascularization ought to be thought of. Furthermore, treatment of disease could be cleansing, debridement of necrotic tissue and encompassing callus as well as empirical oral antibiotic treatment. Moreover, metabolic control and treatment of comorbidity as glycemic control ought to be enhanced **(Vinkel et al., 2020)**. Alternative care modalities of diabetic foot ulcer include growth factors, bioengineered tissues, electrical stimulation, ultrasound therapy, hyperbaric oxygen therapy (HBOT) and negative pressure wound therapy **(Shukla et al., 2020)**.

Hyperbaric Oxygen Therapy consists of breathing 100% oxygen (FiO_2=1.0) under elevated pressure, and it is defined as a minimum of 1.4 atmosphere absolute (141.86 kPa) in a pressure chamber **(Vinkel et al., 2020)**. Hence increases tissue oxygen tensions, promotes healing by boosting revascularization and immune responses, limits edema and destroys certain anaerobic bacteria **(Sari & Fawzy, 2024; Shukla et al., 2020)**. HBOT Committee has recommended certain indications for which in vitro and in vivo pre-clinical research findings in addition to profound clinical experience have been convincing, one of them is DFU and wound healing **(Yisak & Kiwanuka, 2019)**.

In recent years international guidelines for adjuvant hyperbaric oxygen therapy of diabetic foot ulcers have been published; these guidelines recommend that patients with diabetic foot ulcers with Wagner grade 3 or higher, that have not shown significant improvement after 30 days of standard wound care, or who have newly received a surgical debridement of an infected foot, could be treated with hyperbaric oxygen therapy in addition to standard care **(Chen et al., 2024)**. A frequently used treatment regimen in many hyperbaric centers is the administration of hyperbaric oxygen therapy five times a week for 90 min per session. The total number of sessions varies based on the response of the wound to treatment and may comprise 40 or more sessions in total **(Vinkel et al., 2020)**.

Hyperbaric oxygen therapy is a safe treatment modality with few serious adverse effects and contraindications. Most adverse effects are minor and reversible. The most serious contraindication to HBOT is an unrecognized pneumothorax, which would worsen under chamber pressure. Relative contraindications to HBOT include febrile illness, which lowers the central nervous system seizure toxicity threshold, poorly controlled seizure disorder, hyperthyroidism, congestive heart failure, chronic obstructive pulmonary disease, and severe claustrophobia **(Lam et al., 2017)**.

A range of studies have examined the efficacy of HBOT for improving wound healing and reducing amputation rates in patients with diabetic ulcers. Earlier study done by **Lam et al., (2017)** reported very favorable results, that in diabetic patients HBOT significantly improved chances of wound healing (OR, 9.992; 95% CI, 3.972–25.123) and reduced chances of amputation (OR, 0.242; 95% CI, 0.137–0.428). The Nursing role for the patient admitted to the hyperbaric chamber involves various steps, these include: preparation of the session, intra-session monitoring, and evaluation of evolution of the wound, while preparing a patient for the HBOT session, the nurse is responsible for educating the patient and family on HBOT, indications and explanation on the duration of the session. Prior to the session, it is also important to assess for claustrophobia and other discomforts of being put in a closed chamber **(Yisak & Kiwanuka, 2019)**.

Specific Nursing interventions of a patient include assessment for any attached medical device, medication history. Due to the nature of the hyperbaric environment, certain materials are not allowed inside the hyperbaric chamber as all flammable materials. In addition, the nurses should educate the patient on products that may produce harmful vapors in the chamber such as body oils, perfumes, lotions, nail polish and deodorants. Other materials that should be avoided during an HBOT session include hearing aids, metal framed eyeglasses, contact lenses, jewelry, watches, dentures and other devices. Noteworthy, both nicotine and caffeine containing products should be avoided. Other nursing concerns include follow-up care and monitoring for adverse effects of HBOT **(Yisak et al., 2019)**.

Currently, the outcome of the standard or traditional treatment of DFU is not satisfactory, this motivates a search for methods that can stimulate the acceleration of wound healing; one of these methods is the use of hyperbaric oxygen therapy **(Oley et al., 2020)**. Therefore, this study will be conducted to assess wound healing by using adjuvant hyperbaric oxygen therapy versus using routine wound care for patients with diabetic foot ulcer.

Significance of study

Diabetes is one of the main non-communicable chronic diseases in Egypt with a prevalence rate 15.1% among adults. DFU is one of the common complications of diabetes that affects the person's quality of life and represents a high burden on health care services **(Hassan, 2020)**. According to the International Diabetes Federation (IDF), diabetes is now one of the largest global health emergencies of the 21st century. There are now an estimated 537 million adults aged 20–79 with diabetes worldwide, these include an estimated undiagnosed 193 million. The number of people with diabetes may increase to 643 million in 2030 and 783 million by 2045. if no efforts are undertaken to halt this rise. 3 in 4 adults with diabetes live in low- and middle-income countries **(International Diabetes Federation [IDF], 2021)**.

Diabetic foot ulcers (DFUs) remain a common complication of diabetes mellitus and continue to be a highly relevant topic of clinical care and research due to substantial morbidity and mortality. Specifically, mortality rates are estimated to be 5% in the first 12 months from the development of a DFU and increase to be 42% within 5 years. These types of ulcers are associated with high health care expenditures, 33% of diabetes-related costs are linked to DFUs, the majority of which are related to hospital admissions, and up to 17% result in amputation **(Laopoulou et al., 2020)**.

From the researcher's clinical observation, DFU is a serious complication of diabetes which worsens the patient's condition even as having significant bio psychosocial and economic impact that adds burdens on the health care professionals. Hyperbaric oxygen therapy is considered one of the most advanced treatment modalities of DFU nowadays that has a great effect when used as adjunctive therapy with routine treatment, however there is few nursing research tackled this promising treatment modality. It is a noninvasive, safe and cost-effective treatment.

Although HBOT is increasingly popular and theoretically advantageous, its clinical efficacy remains contentious. While some studies suggest that HBOT can facilitate wound healing and reduce amputation rates in DFUs, others argue that the differences in healing rates are not statistically significant **(Tao & Yuan, 2024)**.

Moreover, hyperbaric therapy could be helpful to healthcare professionals and could decrease great effort during routine treatment, and can be applied clinically, hence, it is hoped that current study can provide evidence-based data to promote nursing practice and improve the quality of patients care in this field.

Additionally, this study might increase nurses' awareness and their ability to identify the "foot at risk," along with new modalities of proper DFU care that may prevent DFU deterioration and thus reduce the risk of amputation. Also, it could generate attention and motivation especially among nurses for future investigation to promote diabetic patient's health. Therefore, this comparative study conducted to compare the effect of adjuvant hyperbaric oxygen therapy versus routine wound care for patients with diabetic foot ulcer.

Aim of the study

The aim of this comparative study is to compare the effect of adjuvant hyperbaric oxygen therapy versus routine wound care for patients with diabetic foot ulcer.

Research hypothesis:

To fulfill the aim of the current study, the following research hypothesis will be postulated:

H1- There will be a difference in the total mean of Wagner foot ulcer scores between patients with DFU who will receive routine DFU management and those who will receive adjuvant HBOT.

H2- There will be a difference in the total mean of pain scores between patients with DFU who will receive routine DFU management and those who will receive adjuvant HBOT.

H3- There will be a difference in the total mean of MUNGS scores between patients with DFU who will receive routine DFU management and those who will receive adjuvant HBOT.

Operational definitions

- **Diabetic Foot Ulcer**; For the purpose of this study DFU will be a full-thickness wound below the ankle for duration at least ≥ one month (grade 2 or more on Wagner Ulcer Classification System). Patients with diabetes type ½.
- **Routine care of DFU**; In the current study, it includes but not limited to surgical debridement, antibiotics, and topical daily moist saline dressing with antiseptic were used or any other conventional care provided for this target of patients in the corresponding clinical setting.
- **Adjuvant Hyperbaric Oxygen Therapy;** Adjuvant HBOT is an adjunctive therapy with routine treatment, HBOT is breathing 100% oxygen (FiO_2=1.0) under elevated pressure once daily session for 5 days a week with 2 days off, for a total number of 20 to 40 sessions as per standard practice and according to the ulcer response. The session began with a gradual pressure increase to the designated treatment pressure of approximately 2.5 ATA over about 10 to 15 minutes in a 100% oxygen environment (compression phase). The treatment period "at pressure" lasted for 1 hour. Then, gradual decompression over about 10 to 15 minutes was made.

Subjects and Method

Research Design:

In the current study the researchers will use the prospective non-experimental comparative study. This design examines the relationships among different variables in which the independent variable has already occurred, thus observational rather than experimental. This type of comparative research is characterized by being started with the causes and determined to analyze the effects of a given condition **(Paul et al., 2017)**. For the current study this design used to compare two study groups to find out whether the independent variable (hyperbaric oxygen therapy and routine wound management) affected the outcome of the dependent variable (diabetic foot ulcer healing).

Setting:

The current study will be carried out in the medical, surgical and vascular surgery departments as well as outpatient clinics which provide routine treatment for patients with DFU, also in the hyperbaric oxygen therapy unit at Nasser Institute for Research and Treatment Cairo-Egypt. This unit contains a hyperbaric oxygen chamber, which is equipped with cameras to monitor patients and a communication system to communicate with the nurse and patients inside the capsule. There are also LED screens, sound system, and a system for dealing with emergencies and fires in the event of leakage of oxygen gas and the occurrence of a fire.

Subjects:

A purposive sample of 60 adult male and female patients enrolled in this study. The study sample were two groups (30 patients each). The first group those who was planned to receive routine hospital DFU care and the second group those who was planned to receive hyperbaric oxygen therapy as adjunct to routine treatment at diabetes foot clinic. The inclusion criteria: age ≥18 years old; type 1 or 2 diabetes, as recommended by literature review, they have DFU for at least ≥ one month (grade 2 or more Wagner Ulcer Classification System). Patients having foot infection were included. Exclusion criteria will include contraindications for hyperbaric treatment (severe obstructive pulmonary disease, upper respiratory tract infection, congestive heart failure, history of optic surgery, history of idiopathic convulsion, hypoglycemia, malignancy, claustrophobia and untreated thyrotoxicosis), current drug or alcohol misuse, vascular surgery in the lower limbs within the previous two months.

Data collection tools:

Data pertinent to the current study will be collected using the following tools:

I- Patient's demographic and Clinical Background Information Form, was developed by the researchers and it consists of questions regarding gender, age, marital status, level of education, smoking history, medical history, type of diabetes, ulcer duration, treatment,..etc

II- Wagner classification system: The Wagner system (Tool II) was developed by Meggitt in 1976 and expanded in 1981 by William Wagner to define a framework. Wagner wound classification scale is commonly used to grade the severity of diabetic foot ulcers. The Wagner Scale divides wound severity into six degrees based on depth and extent (G0-G5). It was used by researchers to determine one of the eligibility criteria and also to determine the severity of foot ulcers before and after intervention of routine wound care or hyperbaric oxygen therapy. Wagner foot ulcer classification scale. Grade Feature (0 = no ulcer, 1 = Superficial ulcer, 2= Deep ulcer, 3= Ulcer with bone involvement. 4= Forefoot gangrene, 5 = Full foot gangrene. The inter-rater reliability a κ-value is 0·415 (95% CI 0·413–0·418) **(Santema et al., 2016)**.

III- Numeric Pain scale; levels were evaluated for all patients at baseline, and during follow up. Levels scored on a 10-cm visual analogue scale from 0-'No pain to 10 -'sever pain'.

IV-The MUNGS tool; It is an assessment tool for evaluating wound healing progression developed by **(Suriadi et al., 2021)**. The MUNGS tool takes into account maceration, undermining/tunnelling, necrotic, granulation and wound-related signs or symptoms thus the acronym MUNGS and it was developed based on the authors' clinical observations of diabetic ulcer patients. These five aspects were graded as follows First; Maceration (None = 0, thin at the edge and/or maceration ≤2 cm from the wound edge = 1, > 2 cm from the wound edge and/or expanded = 2). Second; Undermining/tunnelling/sinus (None 0, ≤3 cm 1, >3 cm 2) this will be measured using a disposable paper ruler. Third; Necrotic tissue type {black, white, yellow, grey, brown, green} (None = 0, Soft slough and with ≥ 1 color = 1, Necrotic; with spongy, soft and colored skin = 2, Necrotic; hard, spongy or moist tissue and skin with ≥ 1 color = 3, Necrotic; dry, hard, black and/or brownish = 4). Fourth; Granulation tissue (Skin intact =0, Full granulation (100%) = 1, Granulation of 50 % to <100%= 2, Granulation of <50% = 3, No granulation = 4). Fifth; Other main four wound-related signs or symptoms (S&S) which are (wound edge: wound infection or inflammation: around the skin wound: granulation) and these consequently divided into sub items the score will be (None of these S&S = 0, One or two = 1, Three to five= 2 More than five = 3).

The total MUNGS score for each wound is calculated by summing the scores assigned to each of the five domains. Thus, the range of possible total MUNGS scores is between 0 and 15, with 0 representing a completely healed ulcer, and higher scores indicating poor wound healing progress. The inter-rater reliability of this tool which done by wound care nurses and expressed in terms of Cohen's kappa coefficient was 0.81.

Ethical considerations

An official approval was obtained from Research Ethics Committee- Faculty of Nursing, Cairo University

(IRB 0006883). In addition, an official permission was obtained from the director of medical, surgical and vascular surgery departments as well as outpatient clinics and also the director of hyperbaric oxygen therapy unit at Nasser Institute to conduct the current study. They also were given the chance to ask questions about the research; and were completely guaranteed that they could extract from the study at any time without any negative consequences. Participant informed consent was obtained prior to commencement of data collection. Anonymity and confidentiality of the collected data was assured through coding as well as keeping the documents in a safe locked place.

Procedure:

Once official permission was granted to proceed with the study, the researchers identified the potential subjects who meet the study inclusion criteria. Data was collected from May 2023 to Jun 2024 through three phases as follows:

First phase; Assessment phase, the researchers explained the nature, purpose of the study and confirming the whole ethical considerations for the participants. For the purpose of screening for and confirmation of eligibility, DFU was graded/scored by the Meggitt-Wagner system tool (II) to include those with G2 or more and the other mentioned inclusion criteria, willing participants provided informed written consent prior to enrolment. Then the demographic and clinical data were completed by the researchers using tool (I). At this time, the researchers established a base line assessment for the group (1) who received the routine DFU care either in the hospital wards or in the clinic and group (2) who received the hyperbaric oxygen therapy in addition to routine DFU care using Meggitt-Wagner system tool, Pain analogue scale, and the MUNGS tools.

Second phase; The intervention phase, the study was undertaken during the participants' routine clinical visits or staying at the hospital if required. The usual routine of care was maintained throughout the study under qualified nursing supervision. There was no alteration to the routine clinical care provided to the participants for the duration of the study for both group (1) and (2). Routine of care included but not limited to surgical debridement, antibiotic, and topical moist saline dressing with antiseptic and glycemic control. Group (2) who was planned to be treated with HBOT as decided by their physician, patients received once daily session for 5 days a week with 2 days off, for a total number of 20 to 40 sessions as per standard practice and according to the ulcer response. The session began with a gradual pressure increase to the designated treatment pressure of approximately 2.5 ATA over about 10 to 15 minutes in a 100% oxygen environment (compression phase). The treatment period "at pressure" lasted for 1 hour. Then, gradual decompression over about 10 to 15 minutes included all the sessions for all the patients performed by well-trained expert nurse.

Third phase; Follow-up phase was undertaken at the end of one, two and three months after the beginning of both the routine care or the HBOT where the diabetic foot ulcer will be assessed again using Meggitt-Wagner system tool (II), pain assessment analogue scale (tool III) and MUNGS tool (IV).

Statistical Analysis:

The collected data was tabulated, computed, and analyzed using the new version of Statistical Package for Social Science (SPSS) version 20 (Social Science, IBM, USA, 2020). Data was presented using descriptive statistics in the form of frequencies, percentage, etc. As well inferential t-test and ANOVA tests were utilized. Statistical significance was considered at P-value $\leq$ *0.05*.

Results

Statistical results of the present study are offered as follows:

Describes patient's demographic and clinical background information Form of the study (1) and study (2) groups (Tables 1-2). Delineates hypothesis testing for being supported or not (Figures 1-2 and Tables 3-5). Clarifying other additional findings as the correlation between Wagner classification score, pain score, and MUNGS score with selected demographic characteristics and medical data among study (1) and study (2) groups (Table 6).

Table (1) clarifies that (66.7% and 76.7% respectively) of the study (1) and study (2) groups' ages ranged between 50 to less than 60 years old with mean of (53.23±5.722) for the study (1) group, and (54.03 ± 5.340) for the study (2) group. Male gender represents (73.3%, and 80.0% respectively) of both the study (1) and study (2) groups. In relation to marital status (66.6%, and 73.3% respectively) of both the study (1) and study (2) groups were married. According to education level (50.0%, and 53.3%) of both the study (1) and study (2) groups had secondary school. As regards place of residence (56.7%, and 63.3%respectively) of both groups had lived in rural areas. With reference to occupation, (33.3%, and 40.0% respectively) of both the study (1) and study (2) groups were farmer. In relation to smoking (70.0%, and 63.3% respectively) of both the study (1) and study (2) groups were smokers. There were no statistically significant differences between the study (1) and study (2) groups in relation to personal demographic characteristics.

Table (2) shows that (56.7%, 53.3% respectively) of both study (1) and study (2) groups had type 2 diabetes mellitus with mean of its duration by years (9.23 ± 2.67) for the study (1) group, and (8.00 ± 2.72) for the study (2) group. (68.2%, 63.2% respectively) of both study (1) and study (2) groups had hypertension as a chronic disease. (40.0%, and 50.0 % respectively) of both study (1) and study (2) groups had foot ulcer in the toes. Mean of foot ulcer duration by month was (6.23± 2.775) for study (1) group and (5.80 ± 2.010) for study (2) group. (53.3%, and 56.7% respectively) of both study (1) and study (2) groups had a family history of foot ulcer. (90.0%) of both study (1) and (2) had pulse in their feet.

In relation to medical management of DM, (50.0%, and 40.0% respectively) of both study (1) and study (2) groups received diabetic, antihypertensive, and vascular medications. According to surgical management (60.0%, 56.7% respectively) of both study (1) and study (2) groups received daily dressing and debridement. Regarding amputation (10.0%, and 13.3%) of both groups had amputation. (66.7%, and 75.0% respectively) of them had amputation in their forefeet. Mean of amputation duration by months was (16 ± 6.928) for study (1) group and (13.50±6.550) for study (2) group. In addition, there was no statistically significant difference between both groups regarding clinical background information.

Table (3) represents that (76.7%, and 70.0%respectively) of the study (1) and study (2) groups had deep foot ulcer before intervention. At the end of one month after intervention (50.0%, and 56.7% respectively) of the study (1) and study (2) groups had also deep foot ulcer. At the end of 2 months after intervention (76.6%, and 50.0% respectively) of the study (1) and study (2) groups had superficial foot ulcer. While, at the end of 3 months after intervention (73.3%, and 46.7% respectively) of the study (1) and study (2) groups had also superficial foot ulcer. There was no statistically significant difference between study (1) and (2) groups before intervention and at the end of one month after intervention. While there was statistically significant difference between study (1) and (2) groups at the end of two months as χ^2 =4.593, p=0.032and also at the end of three months as χ^2 =6.685, p=0.035.

Figure (1) shows that mean and standard deviation of Wagner scores **before intervention** was (2.03± 0.669) for study (1) group, and (1.97± 0.718) for study (2) group. T- test and P. value before intervention were (T= 0.372, P=0.711). Mean and standard deviation of Wagner scores **at the end of one month after intervention** was (1.70± 0.651) for study (1) group, and (1.77± 0.626) for study (2) group. T-test and P. value were (T= 0.404, P=0.688). Mean and standard deviation of Wagner scores **at the end of two months after intervention** was (1.23± 0.430) for study (1) group, and (1.50± 0.509) for study (2) group. There was statistical significance difference between study (1) and (2) at the end of two months. T- test and P. value were (T= 2.193, P=0.032). While, mean and standard deviation of Wagner scores **at the end of three months after intervention** was (1.00± 0.525) for study (1) group, and (1.33± 0.661) for study (2) group. There was statistical significance difference between study (1) and (2) at the end of three months, T- test and P. value were (T= 2.163, P=0.035). ANOVA value was F (df: 1.923) = 404.904 P value was 0.000. P-value≤ 0.05 is significant at two tailed.

Table (4) indicates that (46.7%, and 50.0% respectively) of the study (1) and study (2) groups had severe pain before intervention. At the end of one month after intervention (40.0%, and 46.7% respectively) of the study (1) and study (2) groups had moderate level of pain. At the end of 2 months after intervention (60.0%) of study (1) group had mild pain, while (56.7%) of the study (2) groups had moderate pain. At the end of 3 months after intervention (96.7%, and 80.0% respectively) of the study (1) and study (2) groups had no pain. There was no statistically significant difference between study (1) and (2) groups before intervention, at the end of one and two months after intervention. While there was statistically significant difference between study (1) and (2) groups at the end of three months as χ^2 =4.043, p=0.044.

Figure (2) shows that mean and standard deviation of pain scores **before intervention** was (6.30± 1.745) for study (1) group, and (6.37± 1.732) for study (2) group. T- test and P. value before intervention were (T= 0.149, P=0.882). Mean and standard deviation of pain scores **at the end of one month after intervention** was (5.37± 1.732) for study (1) group, and (5.50± 1.614) for study (2) group. T-test and P. value were (T= 0.309, P=0.759). Mean and standard deviation of pain scores **at the end of two months after intervention** was (3.63± 1.377) for study (1) group, and (3.90± 1.296) for study (2) group. T-test and P. value were (T= 0.773, P=0.443). While, mean and standard deviation of pain scores **at the end of three months after intervention** was (2.07± 0.907) for study (1) group, and (2.70± 1.022) for study (2) group. There was statistical significance difference between study (1) and (2) at =3.398, p- value=0.001). On top, total Mean score and standard deviation of the end of three months, T- test and P. value were (T= 2.538, P=0.014). ANOVA value was F (df: 2.080) = 269.424 P value was 0.000. P-value≤ 0.05 is significant at two tailed.

Table (5) clarifies that the total mean scores of wound healing progression MUNGS **before intervention** was (10.67± 2.758) for study (1) and (11.20± 2.340) for study (2) groups where (T= 0.808, P=0.423). The mean and standard deviation of total MUNGS scores **at the end of one month after intervention** was (8.70± 3.239) for study (1), and (9.33± 2.758) for study (2) groups with (T= 0.815, P=0.418).

There was a statistically significant difference between the study (1) and study (2) groups at the end of 2 months after intervention in relation to maceration (T test =2.164, p-value=0.035). while the total mean and standard deviation of MUNGS scores **at the end of two months after intervention** was (5.77± 3.191) for study (1), and (6.87± 2.776) for study (2) groups respectively with (T= 1.424, P=0.160).

Also, there was a statistically significant difference between the study (1) and study (2) groups at the end of 3 months after intervention in relation to undermining/tunnelling/sinus of wound healing progression (T test =2.896, p- value=0.005) and granulation tissue (T test =2.054, p-value=0.045) and also wound-related signs or symptoms with (T test

MUNGS was (4.50± 1.138) for study (1), and (6.30± 2.926) for study (2) groups respectively. There was statistical significance difference between two groups where (T= 2.298, P=0.025). ANOVA value was F (df: 1.923) = 404.904 P- value was 0.000. **Table (6)** illustrates that there was a positive correlation between Wagner score and total MUNGS score with age, duration of diabetes mellitus, and duration of foot ulcer. Moreover, there was a positive correlation between pain score and duration of foot ulcer.

Table (1): Percentage distribution of patient's demographic characteristics of study (1) and study (2) groups (n= 60)

Variables	**Study (1)** Hyperbaric oxygen therapy group (30)		**Study (2)** Routine wound care group (30)		χ^2	P-value
	No.	**%**	**No.**	**%**		
Age / Yrs: - 20 < 30 years - 30 < 40 years - 40 < 50 years - 50 ≤ 60 years	0 0 10 20	0% 0% 33.3% 66.7%	0 0 7 23	0% 0% 23.3% 76.7%	0.739	0.390
Mean ± SD	53.23 ±5.722		54.03±5.340			
Gender: - Male - Female	22 8	73.3% 26.7%	24 6	80.0% 20.0%	0.373	0.542
Marital status - Married - Single - Divorced - Widow	20 0 2 8	66.6% 0.0% 6.7% 26.7%	22 0 2 6	73.3% 0.0% 6.7% 20.0%	0.381	0.827
Education Level: - Can read & write - Secondary - University	9 15 6	30.0% 50.0% 20.0%	10 16 4	33.3% 53.3% 13.4%	0.485	0.785
Place of Residence: - Urban - Rural	13 17	43.3% 56.7%	11 19	36.7% 63.3%	0.278	0.598
Occupation: - Worker - Farmer - Employee - House wife - Not working	5 10 8 6 1	16.7% 33.3% 26.7% 20.0% 3.3%	5 12 7 4 2	16.7% 40.0% 23.3% 13.3% 6.7%	0.982	0.913

Smoking: - Yes - No	21 9	70.0% 30.0%	19 11	63.3% 36.7%	0.300	0.584

**P-value≤ 0.05 is significant at two tailed.*

Table (2): Percentage distribution of patient's clinical background information of both study (1) and study (2) groups (n= 60)

Variables	Study (1) Hyperbaric oxygen therapy group (30)		Study (2) Routine wound care group (30)		χ^2	P-value
	No.	%	No.	%		
Type of Diabetes Mellitus: - Type 1 DM - Type 2 DM	13 17	43.3% 56.7%	14 16	46.7% 53.3%	0.601	0.438
Duration of diabetes mellitus: Mean ± SD	9.23 ± 2.67		8.00 ± 2.72			
Presence of chronic diseases: - Yes - No	22 8	73.3% 26.7%	19 11	63.3% 36.7%	0.693	0.405
Chronic diseases: - Hypertension - Hypertension and cardiac dis. - Hypertension, cardiac and renal disease.	15 6 1	68.2% 27.3% 4.5%	12 5 2	63.2% 26.3% 10.5%	0.541	0.763
Foot Ulcer location: - Toe - Forefoot - Middle Foot - Heel - Leg	12 5 6 6 1	40.0% 16.7% 20.0% 20.0% 3.3%	15 4 4 7 0	50.0% 13.3% 13.3% 23.4% 0.0%	1.921	0.750
Foot Ulcer Duration: - Mean ± SD	6.23± 2.775		5.80 ± 2.010			
Family history of foot ulcer: - Yes - No	16 14	53.3% 46.7%	17 13	56.7% 43.3%	0.601	0.438
Presence of pulse in the foot: - Yes - No	27 3	90.0% 10.0%	27 3	90.0% 10.0%	0.000	1.000
Medical Management of DM: - Diabetic, Vascular medications	8	26.7%	11	36.7%	1.231	0.746
	15	50.0%	12	40.0%		

- Diabetic, antihypertensive, and vascular medications. - Diabetic, antihypertensive, cardiac and vascular medications. - Diabetic, antihypertensive, cardiac, renal and vascular medications.	6 1	20.0% 3.3%	5 2	16.6% 6.7%		
Surgical Management of DM: - Daily dressing - Daily dressing, debridement (once) - Daily dressing, debridement (once) and incision. - Daily dressing, debridement (once) and amputation	 2 18 7 3	 6.7% 60.0% 23.3% 10.0%	 3 17 6 4	 10.0% 56.7% 20.0% 13.3%	0.448	0.930
Presence of amputation: - Yes - No	 3 27	 10.0% 90.0%	 4 26	 13.3% 86.7%	0.162	0.688
Site of amputation: - Toe - Forefoot	 1 2	 33.3% 66.7%	 1 3	 25.0% 75.0%	0.058	0.809
Duration of amputation Mean ± SD	16 ± 6.928		13.50±6.550			

**P-value* ≤ *0.05 is significant at two tailed*

Table (3) Frequency and categorical distribution of Wagner Classification System of foot ulcer among study (1) and study (2) groups (n=60)

Wagner Classification system of foot ulcer	**Study (1)** Hyperbaric oxygen therapy group (30)		**Study (2)** Routine wound care group (30)		χ^2	**P-value**
	No.	**%**	**No.**	**%**		
Before intervention:						
- No open ulcer, high risk	**0**	**0.0%**	**0**	**0.0%**		
- Superficial ulcer	**4**	**13.3%**	**6**	**20.0%**	**0.491**	**0.921**
- Deep ulcer	**23**	**76.7%**	**21**	**70.0%**		
- Ulcer with bone involvement	**1**	**3.3%**	**1**	**3.3%**		
- Forefoot gangrene	**2**	**6.7%**	**2**	**6.7%**		
At the end of one month after intervention:						
- No open ulcer, high risk	**0**	**0.0%**	**0**	**0.0%**		
- Superficial ulcer	**12**	**40.0%**	**10**	**33.3%**	**0.307**	**0.858**
- Deep ulcer	**15**	**50.0%**	**17**	**56.7%**		
- Ulcer with bone involvement	**3**	**10.0%**	**3**	**10.0%**		
- Forefoot gangrene	**0**	**0.0%**	**0**	**0.0%**		
At the end of two months after intervention:						
- No open ulcer, high risk	**0**	**0.0%**	**0**	**0.0%**		
- Superficial ulcer	**23**	**76.6%**	**15**	**50.0%**	**4.593**	**0.032***
- Deep ulcer	**7**	**23.3%**	**15**	**50.0%**		
- Ulcer with bone involvemen	**0**	**0.0%**	**0**	**0.0%**		
- Forefoot gangrene	**0**	**0.0%**	**0**	**0.0%**		
At the end of three months after intervention:						
- No open ulcer, high risk	**4**	**13.3%**	**3**	**10.0%**		
- Superficial ulcer	**22**	**73.3%**	**14**	**46.7%**	**6.685**	**0.035***
- Deep ulcer	**4**	**13.4%**	**13**	**43.3%**		
- Ulcer with bone involvement	**0**	**0.0%**	**0**	**0.0%**		
- Forefoot gangrene	**0**	**0.0%**	**0**	**0.0%**		

**P-value≤ 0.05 is significant at two tailed*

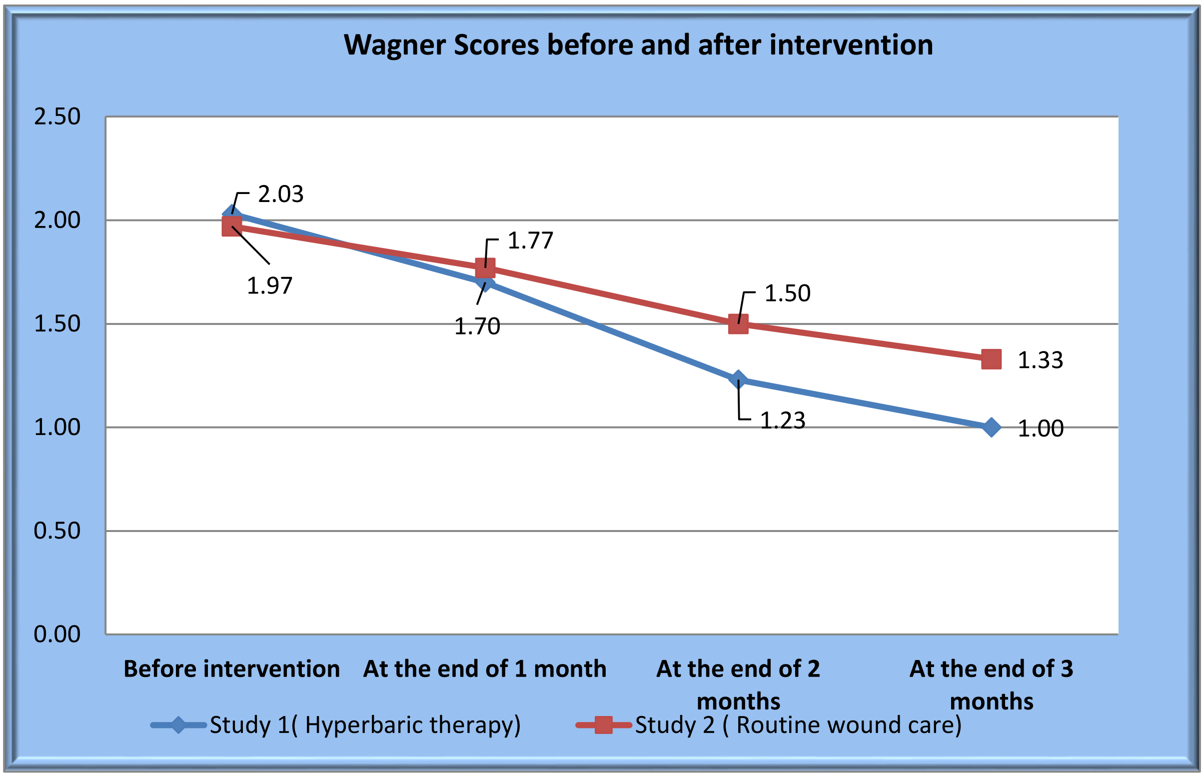

Figure (1) Comparison of mean scores of Wagner Classification of foot ulcer among study (1) and study (2) groups (n=60)

Table (4) Frequency and categorical distribution of pain scale among study (1) and study (2) groups (n=60)

Pain Scale	**Study (1)** Hyperbaric oxygen therapy group (30)		**Study (2)** Routine wound care group (30)		χ^2	**P-value**
	No.	**%**	**No.**	**%**		
Pain scale before intervention:						
- Non	**0**	**0.0%**	**0**	**0.0%**	**0.072**	**0.965**
- Mild	**2**	**6.6%**	**2**	**6.6%**		
- Moderate	**14**	**46.7%**	**13**	**43.4%**		
- Severe	**14**	**46.7%**	**15**	**50.0%**		
Pain scale at the end of one month after intervention:	**0**	**0.0%**	**0**	**0.0%**		
- Non	**7**	**23.3%**	**5**	**16.6%**	**0.487**	**0.784**
- Mild	**12**	**40.0%**	**14**	**46.7%**		
- Moderate	**11**	**36.7%**	**11**	**36.7%**		
- Severe						

Pain scale at the end of two months after intervention:					**1.669**	**0.196**
- Non	**0**	**0.0%**	**0**	**0.0%**		
- Mild	**18**	**60.0%**	**13**	**43.3%**		
- Moderate	**12**	**40.0%**	**17**	**56.7%**		
- Severe	**0**	**0.0%**	**0**	**0.0%**		
Pain scale at the end of three months after intervention:					**4.043**	**0.044***
- Non	**0**	**0.0%**	**0**	**0.0%**		
- Mild	**29**	**96.7%**	**24**	**80.0%**		
- Moderate	**1**	**3.3%**	**6**	**20.0%**		
- Severe	**0**	**0.0%**	**0**	**0.0%**		

******P-value≤ 0.05 is significant at two tailed.***

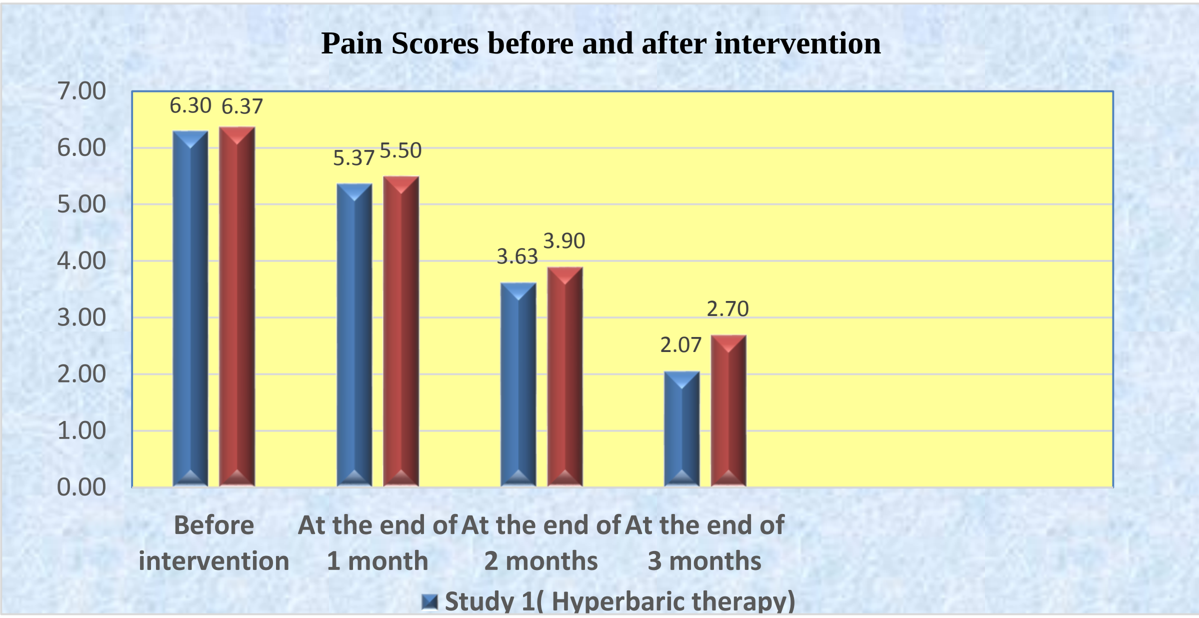

Figure (2) Comparison of mean pain scores among study (1) and study (2) groups (n=60)

Table (5) Comparison of mean scores of wound healing progression (MUNGS) among study (1) and study (2) groups (n=60)

Wound healing progression (MUNGS)	Study (1) Hyperbaric oxygen therapy group (30)	Study (2) Routine wound care group (30)	T-Test	P-value
	Mean ± SD	Mean ± SD		
Before intervention:				
- Maceration	1.60±0.498	1.80±0.407	1.703	0.094
- Undermining/tunnelling/sinus	1.13±0.776	1.30±0.750	0.846	0.401
- Necrotic tissue type	2.77±0.817	2.83±0.699	0.340	0.735
- Granulation tissue	2.77±0.679	2.83±0.648	0.389	0.699
- Other wound-related signs or symptoms as wound edge, wound infection or inflammation.	2.37±0.615	2.40±0.563	0.219	0.827
Total Score:	10.67±2.758	11.20±2.340	0.808	0.423
At the end of one month after intervention:				
- Maceration	1.40±0.563	1.63±0.490	1.712	0.092
- Undermining/tunnelling/sinus	0.93±0.785	1.07±0.785	0.658	0.513
- Necrotic tissue type	2.17±0.791	2.23±0.728	0.340	0.735
- Granulation tissue	2.17±0.950	2.30±0.837	0.577	0.566
- Other wound-related signs or symptoms.	2.10±0.607	2.17±0.531	0.453	0.652
Total Score:	8.70±3.239	9.33±2.758	0.815	0.418
At the end of two months after intervention:				
- Maceration	0.83±0.648	1.20±0.664	2.164	0.035*
- Undermining/tunnelling/sinus	0.43±0.568	0.70±0.651	1.691	0.096
- Necrotic tissue type	1.60±0.814	1.73±0.785	0.646	0.521
- Granulation tissue	1.47±0.973	1.70±0.837	0.996	0.323
- Other wound-related signs or symptoms.	1.37±0.615	1.57±0.568	1.308	0.196
Total Score	5.77±3.191	6.87±2.776	1.424	0.160
At the end of three months after intervention:				
- Maceration	0.57±0.568	0.80±0.610	1.533	0.131
- Undermining/tunnelling/sinus	0.30±0.266	0.70±0.596	2.896	0.005*
- Necrotic tissue type	1.33±0.802	1.60±0.814	1.278	0.206
- Granulation tissue	1.20±1.064	1.73±0.944	2.054	0.045*
- Other wound-related signs or symptoms.	1.17±0.592	1.67±0.547	3.398	0.001*
Total Score	4.50±1.138	6.30±2.926	2.298	0.025*
F **P- Value**	404.904 0.000*			

P-value≤ 0.05 is significant at two tailed.

Table (6): Correlation between Wagner classification score, pain score, and total MUNGS score and selected items of demographic and medical data (n= 60).

Variables	Wagner Score	Pain Score	Total MUNGS Score
Age	Correlation: 0.314 P-value: 0.015*	Correlation:0.111 P-value: 0.398	Correlation: 0.354 P-value: 0.006*
Duration of Diabetes Mellitus	Correlation: 0.389 P-value: 0.002*	Correlation:0.222 P-value: 0.089	Correlation: 0.416 P-value: 0.001*
Duration of foot ulcer	Correlation: 0.286 P-value: 0.027*	Correlation:0.283 P-value: 0.028*	Correlation: 0.250 P-value: 0.054*

*Correlation is significant at P-value≤ 0.05 (2 – tailed).

Discussion

The prevalence of diabetic foot ulcers is increasing by 9% annually worldwide. Diabetic foot ulcers are difficult to treat and usually are treated sub-optimally with general wound care strategies so it takes a longer time to heal and care is enormously variable **(Mousa et al., 2020).**

The results of the current study delineate that around two-thirds of the study sample's ages ranged from fifty to less than sixty, with a mean of 53.63 years old. The study sample was predominantly male, with more than two-thirds married and almost half of the participants having completed secondary education. This finding could be justified by men often do not prioritize foot care to the same extent as women, and they tend to delay seeking medical attention for foot-related issues. In terms of residency, more than half of the study participants lived in rural areas, with approximately one-third of them being farmers. Over two-thirds of the study sample were smokers. Regarding demographic parameters, there was no statistically significant difference between the two study groups; this may rule out any extraneous variables that could have an impact on the groups' different outcomes.

Tong et al., (2020) supported the former findings and reported that DFU is relatively common in middle-aged (54 to less than 64 years old) males patients with diabetes and history of current smoking. **Xia et al., (2019)** highlighted the fact that smoking can exacerbate diabetic peripheral sensory, autonomic and motor neuropathy, which are important reasons for the occurrence of foot ulcerations. Unsurprisingly, **Tasman et al., (2024)** shows that DFU patients living in a rural or economically distressed community are at risk of greater overall disease burden and wound severity. Additionally, rural patients were more likely to present with DFU with a grade 3 wound. This provides quantification for the impact of rural and economically distressed countries.

Based on the clinical data of the study sample, the findings of the current study revealed that more than half and two-thirds of the study sample had type 2 diabetes mellitus with a mean duration of 8.01 years, and hypertension as a chronic disease respectively. While around fifty percent developed DFU in the toes with a mean duration of 6.01± 2.775 months, this relatively long duration of DFU may be justified in the light of the current study findings that most of the study sample were working as farmers and lived in rural regions where the access to medical services could be limited. Furthermore, above half of the study sample reported a family history of foot ulcers. The majority of the participants exhibited palpable feet pulses. In terms of surgical management, more than half of the participants underwent daily dressing pulse one time debridement procedures. With respect to amputations, a minority of the study sample underwent this procedure, with more than two-thirds of the amputations taking place in the forefoot. The mean duration of amputation was recorded at 14.75 months. Furthermore, no statistically significant differences were observed between the two study groups in relation to clinical data of the study sample which again confirm the homogeneity of the studied sample.

It is noteworthy that, **Doğruel et al., (2022); Tong et al., (2020)** pointed out that, the prevalence of DFU being more common in type 2 than type 1 DM with the mean duration of diabetes was 9.7 ± 7.7 years, and the mean duration of DFU was 57.6 ± 78.6 days. the current study findings are aligned with **Tai et al., (2021); Tang et al., (2024)** who concluded that most patients (73.7%) had comorbidity of DM2 at least 1 year before the DFU diagnosis, followed by hypertension (55.4%). Post-digital amputation wounds made up (60%) of the wound.

In the context of DFU healing in terms of the total mean score of Wagner Classification as well as wound healing progression MUNGS, the current study findings revealed that prior to intervention, a substantial proportion of the study participants presented with deep foot ulcers as classified by the Wagner scale. Following one month of intervention, this percentage was observed to decrease by approximately half. Consistent with prior studies, the present study findings, indicating that Wagner Grade 3 diabetic foot ulcers are prevalent among patients with diabetes mellitus. However, studies conducted in Ethiopia and India reporting a higher incidence of Wagner Grade 2 DFU. These findings underscore the importance of early intervention for DFU to prevent the progression to severe stages and associated complications **(Vahwere et al., 2023; Mariam et al., 2017;Ambegoda et al., 2015)**.

No statistically significant differences were detected in the mean scores of Wagner Classification of foot ulcer or wound healing progression MUNGS among the study participants when comparing pre-intervention and one-month post-intervention data. These findings suggest a relatively homogenous sample throughout this initial phase of the study. On the other hand, a statistically significant difference was observed between the two study groups in the mean scores of Wagner Classification after both two and three-months follow-up. Additionally, the hyperbaric study group demonstrated significantly higher mean scores for wound healing progression MUNGS at the three-month follow-up. These findings provide support for the first and third research hypotheses. In this regard recent advances in DFU pathophysiology have demonstrated that impaired angiogenesis plays a pivotal role in the progression of DFU, thereafter, enhancing tissue oxygenation emerges as a critical therapeutic strategy **(Tao & Yuan, 2024)**.

Additionally, **Putri et al., (2024)** indicated that the partial pressure of oxygen (pO2) is a major determinant in wound healing. Thus, the results of the current study could be attributed to the fact that hyperbaric oxygen therapy causes a rise in the oxygen partial pressure in the blood, to support the hypoxic tissue. Furthermore, **Vinkel et al., (2020)** clarified that a sustainable effect of hyperbaric oxygen therapy on tissue oxygenation is obtained by neovascularization. The oxygen tension remains above baseline for a few hours following the hyperbaric treatment session. However, it is assumed that the intermittent period of hypoxia and hyperoxia in wounds initiates a cascade reaction that stimulates neovascularization through an increase in vascular endothelial growth factor. An explanation for this effect may be that diabetes is strongly associated with reduced microcapillary tissue perfusion; tissue hypoxia and neuronal dysfunction, all of which are improved by microcapillary angiogenesis as induced by systemic hyperbaric oxygen therapy.

The findings of a recent systematic review and metanalysis congruent with the current study findings which concluded that there is a notable enhancement in complete ulcer healing rates in patients subjected to HBOT compared to those receiving standard care **(Tao & Yuan, 2024)**. Similarly, another systematic review and meta-analysis indicated that HBOT yielded a significant benefit for treating DFU. The HBOT group exhibited a higher rate of complete healing of DFU (62%) and lower major amputation rates (24%) **(Swaminathan et al., 2024)**.

Conversely, **Sari and Fawzy, (2024)** mentioned that research shows conflicting results on the efficacy of HBOT for wound healing, dictating its usage alongside other modalities. Consideration of indications, costs, and resources is crucial. In sync, the evidence-based guideline 2023 established by the International Working Group on the Diabetic Foot (IWGDF) regarding wound healing interventions for DFUs recommends that HBOT exhibits moderate beneficial effects compared to standard care alone. This therapy has been shown to enhance overall wound healing and decrease ulcer size. Additionally, IWGDF emphasizes the importance of weighing the potential risks of adverse events and the associated cost savings when considering its application **(Chen et al., 2024)**.

When it comes to pain assessment, no statistically significant differences were observed between the two study groups in mean pain scores either prior to intervention or at the one- and two-month follow-up points. However, a declining pattern in the pain severity throughout the forementioned periods was evident for both study groups. At the three-month follow-up, the HBOT group demonstrated significantly lower mean pain scores compared to the group who received standard care only.

The researchers could attribute this declining pattern of pain severity in both study groups to the improved healing rates in both groups but significantly more in patients who received HBOT compared to those who received standard care alone especially at the three-month follow-up. To the best of our knowledge, there is scarce research investigating the effect of HBOT on the pain level for the patients with DFU. One study provide a comparison of pain level evaluation at the beginning and end of the study (week 12) and found no statistically significant variations in pain level between the standard care group and the adjuvant oxygen therapy in patients with peripheral neuropathy **(Tang et al., 2024)**.

Inevitably, the current study revealed the following additional findings, older patients, with a long history of DM often experience slower healing rates for DFU. Additionally, patients with DFU that have been present for a prolonged period often experience more pain and slower healing. This can be attributed to the fact that aging process together with chronic hyperglycemia may contribute to skin decreased elasticity, diminished blood supply and neuropathy which impair DFU wound healing.

Conclusion:

This study showed that HBOT in combination with standard methods of diabetic foot ulcers management appears to be more effective than standard methods alone that include surgical debridement, antibiotics, and topical daily moist saline dressing with antiseptic solution; as HBOT has better results in wound healing and decreasing pain severity; it provides a significant reduction in the size and depth of the wounds, underpinning the concept that oxygen plays an essential role in wound healing. The current study findings emphasize the importance of a comprehensive treatment approach and provide valuable insights for future clinical practice and research.

Recommendations

- A further study should be conducted on a larger probability sample from different geographical areas in Egypt to generalize the findings.
- Further longitudinal study to evaluate the effect of adjuvant HBOT on different types of wound healing for accurate evidence.
- High-quality RCTs to evaluate the short- and long-term risks and benefits of HBO therapy that are necessary to better inform clinical decisions about the use of HBO to improve recovery.

- Increase nurses' awareness and their ability to identify the "foot at risk," along with new modalities of proper DFU care that may prevent DFU deterioration and thus reduce the risk of amputation.

Author Disclosure statement: The authors declare that they have no competing interests.

Acknowledgement: Special thanks to all participants, hospital team and researchers for their great support of this clinical study. The authors have equally contributed to the article.

References:

Abouzid, M. R, Ali, K., Elkhawas, I., Elshafei, SH.M. (July 20, 2022). An overview of Diabetes Mellitus in Egypt and the significance of integrating preventive cardiology in diabetes management. *Cureus, 14*(7), e27066. Doi: 10.7759/cureus.27066.

Alshmimry, A. H., Jiwani, S. I., Gyasi-Antwi, P., & Adams, G. G. (2021). Effectiveness and safety of hyperbaric oxygen therapy (HBOT) in treating Diabetic Foot Ulcers (DFUs). *Current Research in Clinical Diabetes and Obesity*, 01. https://Doi.org/10.29011/CRCDO-103.100003.

Ambegoda, L. C., Wijesekera, J. R., Panditharathne, K. I., Gamage, R. T., Mudalige, O. S., & Piyasiri, D. M. (2015). Analysis of severity and anatomical distribution of diabetic foot ulcers: A single unit experience. *International Journal of Multidisciplinary Studies, 2*(1), 12. https://Doi.org/10.4038/ijms.v2i1.58.

Armstrong, D. G., Boulton, A. M., & Bus, S. A. (2017). Diabetic foot ulcers and their recurrence. *New England Journal of Medicine, 376*(24), 2367–2375. https://Doi.org/10.1056/NEJMra1615439.

Chen, P., Vilorio, N. C., Dhatariya, K., Jeffcoate, W., Lobmann, R., McIntosh, C., …… & Game, F. (2024). Guidelines on interventions to enhance healing of foot ulcers in people with diabetes (IWGDF 2023 update). *Diabetes/Metabolism Research and Reviews, 40*(3), e3644. https://Doi.org/10.1002/dmrr.3644

Doğruel, H., Aydemir, M., & Balci, M. K. (2022). Management of diabetic foot ulcers and the challenging points: An endocrine view. *World Journal of Diabetes, 13*(1), 27–36. https://Doi.org/10.4239/wjd.v13.i1.27.

Hassan, S. (2020). Application of protection motivation theory to diabetic foot care behaviors in Egypt. *Journal of Diabetes & Metabolic Disorders,* 1-5.

International Diabetes Federation. *IDF Diabetes Atlas*, 10th ed. Brussels, Belgium: 2021. Available at: https://www.diabetesatlas.org. accessed at 27-9-2024.

Lam, G., Fontaine, R., Ross, F. L., & Chiu, E. S. (2017). Hyperbaric oxygen therapy: Exploring the clinical evidence. *Advances in*

Skin & Wound Care, *30*(4), 181-190.

Laopoulou, F., Kelesi, M., Fasoi, G., Vasilopoulos, G., & Polikandrioti, M. (2020). Perceived social support in individuals with diabetic foot ulcers: A cross-sectional survey. *Journal of Wound Ostomy & Continence Nursing*, *47*(1), 65-71.

Mariam, T. G., Alemayehu, A., Tesfaye, E., Mequannt, W., Temesgen, K., Yetwale, F., & Limenih, M. A. (2017). Prevalence of diabetic foot ulcer and associated factors among adult diabetic patients who attend the diabetic follow-up clinic at the university of Gondar Referral Hospital, Northwest Ethiopia, 2016: Institutional-based cross-sectional study. *Journal of Diabetes Research,* 2879249. https://Doi.org/10.1155/2017/2879249.

Mousa, A. S., Shehata, M. S., & Salem, M. M. (2020). Comparative study between treatment by vacuum-assisted closure (VAC), treatment by Hyperbaric Oxygen Therapy and traditional treatment of Diabetic Foot Infection. *The Egyptian Journal of Hospital Medicine, 81*(4), 1810–1814. https://Doi.org/10.21608/ejhm.2020.120449.

Oley, M. H., Oley, M. C., Tjandra, D. E., Sedu, S. W., Sumarauw, E. R., Aling, D. R., ... & Faruk, M. (2020). Hyperbaric oxygen therapy in the healing process of foot ulcers in diabetic type 2 patients marked by interleukin 6, vascular endothelial growth factor, and PEDIS score: A randomized controlled trial study. *International Journal of Surgery Open, 27*, 154-161.

Paul C. P, Rajiv S. J, I-Chant A. C, Dana C. L, & Carrie C. (2017). *Research Methods in Psychology*. 3rd ed. American Edition Licensed under a Creative Commons Attribution-Non Commercial-Share Alike 4.0 International License, available at: Research Methods in Psychology – Simple Book Publishing (wsu.edu).

Putri, I. L., Alyssa, A., Aisyah, I. F., Permatasari, A. Y., Pramanasari, R., & Wungu, C. K. (2024). The efficacy of topical oxygen therapy for wound healing: A meta-analysis of randomized controlled trials and observational studies. *International Wound Journal, 21*(7), e14960. https://Doi.org/10.1111/iwj.14960.

Santema, T. B., Lenselink, E. A., Balm, R., & Ubbink, D. T. (2016). Comparing the Meggitt-Wagner and the University of Texas wound classification systems for diabetic foot ulcers: Inter-observer analyses. *International Wound Journal, 13*(6), 1137–1141.

Sari, N. F., & Fawzy, A. (2024). A deep dive into the role of hyperbaric oxygen therapy in enhancing Burn Wound Healing. *International Journal of Medical Science and Clinical Research*

Studies, 4(05), Article 05.https://Doi.org/10.47191/ijmscrs/v4-i05-30

Shah, P., Inturi, R., Anne, D., Jadhav, D., Viswambharan, V., Khadilkar, R., Dnyanmote, A., & Shahi, S. (2022). Wagner's Classification as a Tool for Treating Diabetic Foot Ulcers: Our observations at a Suburban *Teaching Hospital. Cureus, 14*(1), e21501. https://Doi.org/10.7759/cureus.21501

Shukla, U., Kumar, A., Anushapreethi, S., & Singh, S. P. (2020). Evaluation of the efficacy of Hyperbaric Oxygen Therapy in the management of Diabetic Ulcer using Bates-Jensen Wound Assessment Tool. *Anesthesia, Essays and Researches, 14*(2), 335–342. https://Doi.org/10.4103/aer.AER_68_20

Suriadi, H, Aris, D., & Imran, i. (2021). Reliability study of a new wound classification system for patients with diabetes. *Clinical Practice, 18*(4), 1672–1677. https://Doi.org/10.37532/fmcp.2021.18(4).1672-1677

Swaminathan, N., Awuah, W. A., Bharadwaj, H. R., Roy, S., Ferreira, T., Adebusoye, F. T., ….. & Papadakis, M. (2024). Early intervention and care for Diabetic Foot Ulcers in Low- and Middle-Income Countries: Addressing challenges and exploring future strategies: A narrative review. *Health Science Reports, 7*(5), e2075.https://Doi.org/10.1002/hsr2.2075

Tai, C. H., Hsieh, T. C., Lee, R. P., & Lo, S. F. (2021). Prevalence and medical resource of patients with Diabetic Foot Ulcer: A nationwide population-based retrospective Cohort Study for 2001–2015 in Taiwan. *International Journal of Environmental Research and Public Health, 18*(4), 1891. https://Doi.org/10.3390/ijerph18041891

Tang, T. Y., Mak, M. Q., Yap, C. Q., Boey, J. C., Chan, S. L., Soon, S. Y., ….. & Goh, W. X. (2024). An observational clinical trial examining the effect of Topical Oxygen Therapy (Natrox^{TM}) on the rates of healing of chronic Diabetic Foot Ulcers (OTONAL Trial). *The International Journal of Lower Extremity Wounds, 23*(2), 326-337.https://Doi.org/10.1177/15347346211053694

Tao, L., & Yuan, X. (2024). Efficacy and safety of hyperbaric oxygen therapy in the management of diabetic foot ulcers: A systematic review and meta-analysis. *International Wound Journal, 21*(3), e14507. https://Doi.org/10.1111/iwj.1450

Tasman, J., Clegg, D. J., Carver, C., Adabala, S., Buckley, M. R., Goldman, M. H., & Roberson, P. N. E. (2024). Assessing the influence of rural residence and economic distress on lower extremity risk stratification among diabetic foot ulcer patients utilizing the Wound, Ischemia, and Foot Infection (WIfI) classification system. *Journal of Diabetes and Its Complications, 38*(8), 108814. https://Doi.org/10.1016/j.jdiacomp.2024.108814

Tong, T., Yang, C., Tian, W., Liu, Z., Liu, B., Cheng, J., …. & Zhou, B. (2020). Phenotypes and outcomes in middle-aged patients with diabetic foot ulcers: A retrospective cohort study. *Journal of Foot and Ankle Research, 13*, 24.https://Doi.org/10.1186/s13047-020-00386-z

Vahwere, B. M., Ssebuufu, R., Namatovu, A., Kyamanywa, P., Ntulume, I., Mugwano, I., ….. & Nasinyama, G. W. (2023). Factors associated with severity and anatomical distribution of diabetic foot ulcer in Uganda: A multicenter cross-sectional study. *BMC Public Health, 23,* 463. https://Doi.org/10.1186/s12889-023-15383-7

Vinkel, J., Holm, N. R., Jakobsen, J. C., & Hyldegaard, O. (2020). Effects of adding adjunctive hyperbaric oxygen therapy to standard wound care for diabetic foot ulcers: A protocol for a systematic review with meta-analysis and trial sequential analysis. *BMJ Open, 10*(6), e031708.https://Doi.org/10.1136/bmjopen-2019-031708

Xia, N., Morteza, A., Yang, F., Cao, H., & Wang, A. (2019). Review of the role of cigarette smoking in diabetic foot. *Journal of Diabetes Investigation, 10*(2), 202–215. https://Doi.org/10.1111/jdi.12952

Wagner F. W., (1981). The dysvascular foot: A system for diagnosis and treatment. *Foot & Ankle, 2*(2), 64–122.https://Doi.org/10.1177/107110078100200202

Yisak Alemayehu, R. N., & Kiwanuka, F. (2019). Hyperbaric oxygen therapy: Indications, benefits and nursing management. *International* 23 (2), 156-68.