Section: Miscellaneous

Original Research Article

CLINICAL AND MICROBIOLOGICAL PROFILE OF DIABETIC FOOT OSTEOMYELITIS AND THE ROLE OF HYPERBARIC OXYGEN THERAPY (HBOT) AS AN ADJUVANT: A CROSS-SECTIONAL STUDY

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Abstract

Background: The objective of this study is to understand the clinical and microbiological profile of diabetic foot osteomyelitis (DFO). We also tried to understand the efficacy of hyperbaric oxygen therapy (HBOT) as an adjuvant along with conventional methods like intravenous antibiotics and wound debridement in managing DFO. **Materials and Methods:** A cross-sectional study was carried out on 52 patients who were diagnosed with DFO in between 2020 – 2022 and followed them up for 1 year. Their demographic and microbiological profiles along with treatment details were collected. After taking informed consent, they were subjected to HBOT. Wound healing response was assessed with pre and post analysis of digital photographs of ulcers and TCPO2 levels of the patient. Necessary ethical clearance was obtained. The data was analyzed using SPSS 16 and data was correlated. **Result:** Among the 52 patients in our study population, 39 patients were male.73.1% patients were found to have severe neuropathy. Mean ESR was found to be 78.Serum creatinine values were measured pre and post HBOT and was found to be 1.16±.55 and 1.01±.34.(p value =0.003) respectively. Gram negative organism especially Pseudomonas and Proteus were found predominantly. Mean no. of HBOT sessions required was 18.09±9.1. Mean number of days for healing of wound required was about 56 days. Wound was completely healed in 33 patients, partially healed in 8 patients and not healed in 2 patients. None of our patient required amputations post HBOT. **Conclusion:** Osteomyelitis should be ruled out in every case of diabetic foot infection. HBOT can be used as a safe and effective treatment that aids as an adjuvant in managing chronic osteomyelitis. Along with the conventional methods, it can decrease the rate of amputation. We did not observe any adverse events associated with HBOT in our study.

INTRODUCTION

Approximately 194 million people are diagnosed with Diabetes globally and by 2025 the diabetic population might be around 333 million. Worldwide, India is recognized as the diabetic capital with an estimate of 35 million people suffering from diabetes at the moment. By 2025 this figure might reach around 73.5 million.[1,2] Diabetes and diabetic foot infection (DFI) go hand in hand.[3] An Indian data showed about 25% of the population may end up with severe DFI that may lead to amputation.[4] The most terrifying and frequent complication of diabetes is DFI when compared with myocardial infarction, cerebrovascular accidents, nephropathy and retinopathy.[5] About 10-15 % of moderate and 50 % of severe DFI are complicated by Osteomyelitis.[6] DFO should always be ruled out in diabetic patients who present with ulcers or soft tissue inflammation over bony prominences of long duration. Large or deeper wounds with discharging sinus have more probability of an underlying DFO. The likelihood of amputation is higher in DFI when complicated with DFO. MRI can diagnose early DFO when compared with plain radiographs.[7] The chances of amputation

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can be minimized if DFO is diagnosed earlier and can be managed efficiently.[8,9] Hyperbaric oxygen therapy (HBOT) can be used as an adjuvant in treating osteomyelitis effectively along with antibiotic therapy and surgical interventions. HBOT has favorable effect in managing sinuses in chronic DFO and increases oxygen levels in both infected and uninfected bones.[10] The aim of our study is to understand the clinical and microbiological profile of diabetic foot patient and the role of HBOT as an adjuvant mode of treatment in DFO

MATERIALS AND METHODS

We conducted a hospital based retrospective study in a multi-speciality hospital situated in South India. Study group was composed of patients diagnosed with clinical features of diabetic foot infection (DFI) complicated with osteomyelitis (OM). All patients included in the study presented to us during the year 2020 to 2022 and we followed them up for one year. All ulcers with duration of more than 4 weeks referred from other centers or reported to us directly were included. We also obtained informed consent from all patients. All institutional ethical norms were obtained (Study Approval Reference No: SUT/IECHSR/ 2022-010). We excluded all ulcers of less than 4 weeks of duration. Our study population included a total of 52 patients. We collected demographic details from the patient. We concurrently gave standard treatment like glycemic control, culture specific antibiotics, wound debridement, moist wound environment, and nutritional care.

The patient was placed in a hyperbaric oxygen chamber (M3 model indigenously made, can accommodate 3 patients at a time.) and the pressure within the chamber was kept at a desired level as per our protocol and patients received 100% oxygen through a modified face mask. The gas concentration level inside the chamber was continuously monitored during the treatment schedule. Our treatment protocol involved administering oxygen to the patient at 2.5 ATA (atmospheric absolute) 90 minutes for 5 days a week. During every HBOT session, the patient was accompanied by a nursing staff to monitor any adverse events. Vitals and blood sugar level were monitored before and after each HBOT session. We also did pre and post analysis of digital photographs of ulcers of the patient. We also assessed TCPO2 level before and after HBOT in selected group of patients (patients who were able to afford the cost of the same). All the patients are subjected to necessary laboratory evaluations and bacteriological study of wounds. We also did Doppler arterial study and biothesiometry in patients who were financially able to afford it. We assessed wound status based on the PUSH and WOCN criteria. [9] Based on these fore-mentioned criteria, we classified wounds into completely healed and partially healed. All cases that did not complete 10 sessions of HBOT were designated as drop out category. Those patients whose wound did not respond to the treatment were included in the non-healed category.

Data Analysis

We used SPSS version 16 20 (SPSS INC, Chicago, IL, USA) for entering and analyzing data. Analyzed frequency and percentage are represented in the form of tables.

RESULTS

Among the 52 diabetic patients included in our study, 39 (75%) were males and 13 (25%) were females.16 of them belonged to the age group less than 50 and the remaining 36 patients were more than 50 of age . 26 (50%) patients were overweight and 8 (15.4%) patients were obese as per calculated body mass index (BMI). Remaining population had a normal BMI. 20 patients (38.5%) had past history of diabetic /non healing ulcers.

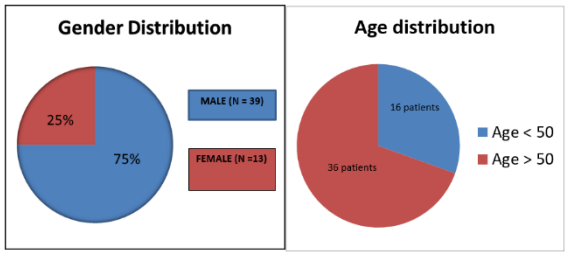

Figure 1: (a, b,) - Gender and Age wise distribution of Study participants.

Around 6 patients (11.5 %) suffered from diabetes for less than 5 years duration, 11 patients (21.2%) for 5-10 years, 25 patients (48.7%) around 10 -15 years , 5 patients since 15 -20 years and 5 patients were diabetic for more than 20 years. 30.8% of patients were smokers. [Table 1].

The various co-morbidities that we noticed among our patients were coronary artery disease (CAD - 21.2%), hypertension (42.3%), peripheral arterial occlusive disease (POAD - 36.5%) and chronic kidney disease (CKD - 34.6%).

Various Ulcer locations include dorsal aspect of toes & fore foot (19.2%), sole surface of toes or fore foot (21.2%), heel pad or calcaneal region(9.6%) , over medial malleolus (1.9%), over lateral malleolus (9.6%), Anterior aspect leg(3.8%), sole surface of mid or hind foot(1.9%) , big toe sole side (28.8%), multiple sites (1.9%) and others (1.9%).Right foot was involved in 23 patients (44.2%), Left foot in 25 patients (48.1%), both feet in 2 patients (3.8%) whereas right and left leg involvement was observed in 1 patient (1.9%) each. 4 patients (7.7%), 3 patients (5.8%) and 1 patient (1.9%) presented to us with pre-gangrenous changes, dry gangrene and wet gangrene respectively. Dry skin was observed in 43 patients (82.7%). Peripheral pulses were palpable in 14 patients (26.9%), weak/feeble among 33 patients (63.5%) and absent in 5 patients (9.6%).43 patients (82.7%) had ulcer with sinus. Out of these 43

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patients, 34 patients (65.4%) had wound discharge associated with sinus. 20 patients (38.5%) had associated cellulitis. 26 patients (50%) had callus formation. Claw toes were noticed in 24 patients (46.2%).11 (21.2%) patients were found to have Charcot joint deformity. Only 15 patients (28.8%) used modified diabetic foot wear. 86.5 % (45 patients) of study population used footwear both indoors and outdoors whereas the remaining 13.5% (7 patients) used footwear both inside and outside of home.

Diagnosis of osteomyelitis was proved clinically in 11 patients (21.2 %), only radiographs in 1 patient (1.9%), clinically and radiographs in 31 patients (59.6%), clinically and MRI in 4 patients (7.7%), clinical plus radiographs and MRI in 5 patients (9.6%).

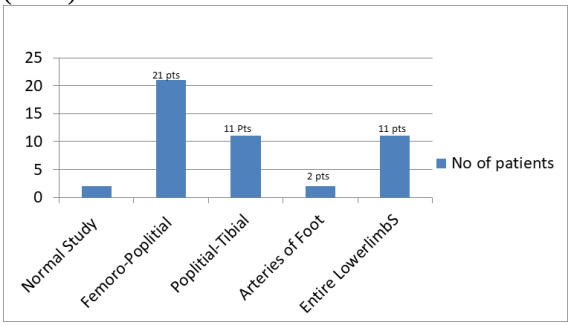

Figure 2: Arterial Doppler findings

Arterial Doppler was done in 47 patients. 2 patients (3.8%) had normal study. We observed femoro-poplitial involvement in 21 patients (40.4%), popliteal-tibial involvement in 11 patients (21.2%) and arteries of foot in 2 patients (3.8%). In 11 patients (21.2%) the entire arteries of lower limbs were involved. Diffuse atherosclerotic involvement with calcification was noticed in 21 patients (38.5%), without calcification in 13 patients (25%), moderate involvement of arteries in 9 patients (17.3%) and mild involvement in 3 patients (5.7%). Monophasic flow pattern was observed in 12 patients (23.1%), diphasic flow pattern in 27 patients (51.9%) and triphasic flow pattern in 6 patients (11.5%).2 patients (3.8%) demonstrated absent blood flow. ABI was performed in 49 patients. Out of these 49 patients, 16 patients (30.8%) had abnormal values.

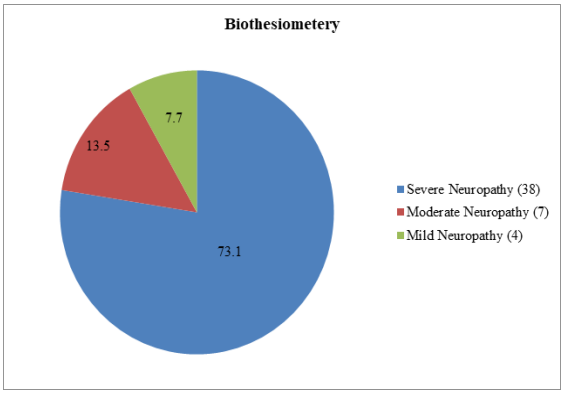

Figure 3: Biothesiometry

Use of Biothesiometry was done in 51 patients .38 patients (73.1%) had severe neuropathy, 7 patients (13.5%) had moderate neuropathy and 4 patients (7.7%) had mild neuropathy.

Wound culture and sensitivity was done in 51 patients .43 samples (82.7%) were positive for bacterial growth. Gram negative organisms (25 patients; 48.1%) were more common compared to gram positive organisms (8 patients; 15.4%). Mixed growth was found in 10 samples (19.2%). 13 samples showed multiple drug resistance. Among gram negative organisms, Pseudomonas aeruginosa grew in 8 samples, Proteus in 7 samples, E.coli and Klebsiella in 4 samples each.1 sample had a combination of Pseudomonas and Klebsiella. Staph. Aureus is the only gram positive organism that grew and 2 of the samples grew MRSA.

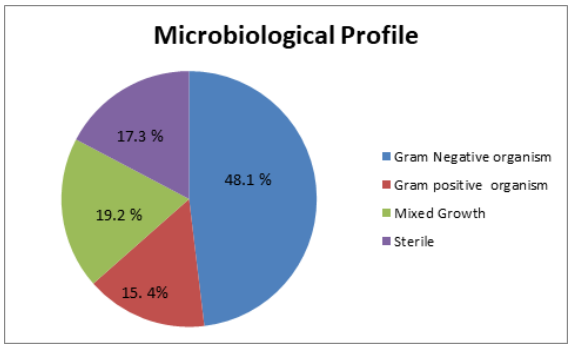

Figure 4: Wound Culture and Sensitivity

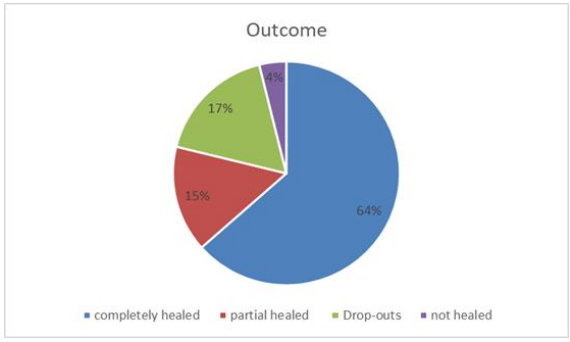

Figure 5: Outcomes for Study participants

We treated all the patients with hyperbaric oxygen therapy (HBOT), wound debridement, intravenous (IV) antibiotics and other supportive measures. Cleaning and dressing of wound were done on alternate days. Mean number of sessions of HBOT required was 18.09±9.1. Mean number of days required for wound healing was 56 days. Minimum number of days required for healing was 38 days.44 patients took less than 100 days to heal while remaining 8 patients took more than 100 days to heal. Mean age of patients who took less 100 days for wound healing was 58.86±11.88 while it was around 52.12 ± 9.65 for those who required less than 100 days to heal (p value =0.147). TcPo2 levels were also assessed before and after HBOT. Prior to HBOT, Tcpo2 belonged to range in between 37.25 – 56 mmHg of which the mean value was 51 mmHg. Post HBOT it belonged to a range of 48 - 67 mmHg,

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where the mean value was 63 mmHg. 17 patients (32.7%) in our study required only oral antibiotics, 7 patients (13.5%) required only iv antibiotics, 27 patients (51.9%) had both oral and iv antibiotics and 1 patient (1.9%) received none.8 patients (15.4%) required only 1 course of antibiotics , 15 patients (28.8%) required 2 courses , 23patients (44.2%) needed 3 courses and 5 patients (9.6%) had more than 3 courses of antibiotics. 31 patients required a combination of iv antibiotics.

The wound was completely healed in 33 patients (63.5%), partially healed in 8 patients (15.4%) and not healed in 2 patients (3.8%). 9 patients dropped out from receiving HBOT. We noticed recurrence of ulcer among 16 patients (30.8%) during the follow up period and majority of wounds in that group healed during follow up period itself. None of the patients required post HBOT amputations.

Table 1: Duration of Diabetes.

Duration of diabetes	No of patients
Less than 5 years	6 patients (11.5 %)
5-10 years	11 patients (21.2%)
10-15 years	25 patients (48.7%)
15-20 years	5 patients (9.6%)
More than 20 years	5 patients (9.6%)

Table 2: Co-Morbidities as per study subjects

Various Co-morbidities	%
Coronary artery disease	21.2%
hypertension	42.3%
Peripheral arterial occlusive disease	36.5%
Chronic Kidney Disease	34.6%

Table 3: Ulcer Location with Clinical Presentations.

Ulcer location	Frequency (n)	Percentage (%)
Dorsal aspect of toes & fore foot	10	19.2
Big toe sole side	15	28.8
Sole surface of toes fore foot	11	21.2
Heel / Calcaneal region	5	9.6
Over medial malleolus	1	1.9
Over lateral malleolus	5	9.6
Anterior aspect leg	2	3.8
Multiple sites	1	1.9
Sole surface of mid or hind foot	1	1.9
others	1	1.9

Table 4: Diagnosis of DFO using Imaging.

Diagnosis of DFO	N (Frequency)
Only Clinical	11
Only Radiographs	1
Clinically + Radiographs	31
Clinically +MRI	4
Clinically +Radiographs +MRI	5

Table 5: Laboratory Variables distribution as per study participants

Variables	Mean ± SD/ Median (IQR)
Hb	11.33 ± 2.06
CRP (Initial)	22.26 (5.03 - 39.5)
CRP (Final)	5.45 (3.2 - 7.70)
ESR Initial	78 (37.75 - 112.25)
Creatinine (Initial)	1.16 ± 0.55
Creatinine (Final)	1.01 ± .34
Albumin	3.67 ± 0.59
Total Protein	7.27 ± 0.54
FBS	156.4 ± 55.02
PPBS	236.05 ± 75.81
Hba1c	8.68 ± 1.96

Table 6: Wound Culture and Sensitivity

Micro Organism	N (Frequency)
Pseudomonas Aeruginosa	8
Proteus mirabilis	7
Escherichia coli	4
Klebsiella	4
Pseudomonas and Klebsiella	1

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Staphylococcus Aureus	8

Table 7: Management based on HBOT, antibiotics and Supportive measures

Variables	Mean ± SD
Days Of Heal	56 (38 - 76)
Number Of HBOT	18.09 ± 9.1
Pre-Tcpo2	51 (37.2 – 55. 6)
Post-Tcpo2	63 (48 - 67)

DISCUSSION

One of the major causes of amputations due to non-traumatic etiology is diabetic foot disease. Patients diagnosed with diabetes are more prone to have peripheral neuropathy, poor circulation to the lower limbs and multiple foot bio mechanic issues. Hence in diabetic patients, it is important to distinguish between soft tissue infections like cellulitis from osteomyelitis (OM) as the latter requires a more intense therapy. [11, 12] The risk of amputation escalates when complicated with infection and in an inadequately managed DFO. [13-15]

Around 45-65 % patients with diabetic foot infection (DFI) have an underlying POAD. [16] 19 patients (36.5 %) had a previous diagnosis of POAD in our study. However 45 out of 47 patients who underwent arterial Doppler study showed abnormal involvement of vessels. It is found that a chance of OM is higher in patients with ulcers with exposed joint or bone and of size more than $2cm^2$. [17] Forefoot (90%) is the most common site of foot OM. Other sites include midfoot and hind foot (5% each). The first metatarsal head, fifth metatarsal head and the calcaneum forms the "tripod of the foot". They function as the weight bearing bones and are more prone to develop osteomyelitis. [18] Sole surface of toes / forefoot (21.2%), dorsal aspect of toes / forefoot (19.2%) followed by heel / calcaneal region (9.6%) and lateral malleolus (9.6%) were the affected sites observed in our study. As a result of loss of protective sensations among diabetic patients, they are unaware of trauma (eg: foreign body penetration, blistering or abrasions).

Foot deformities are end products of motor neuropathy and can lead to development of new ulcers from local pressure exerted from footwear. Once the skin is disrupted, organisms of pathogenic nature can enter and affect subcutaneous and deeper structures.[19] In our study 38 patients (73.1%) were found to have severe neuropathy while 7 patients(13.5%) and 4 patients (7.7%) had moderate and mild neuropathy respectively. It could be said from our study that patients with diabetic foot osteomyelitis can have a strong association with underlying neuropathy and POAD.

Radiological imaging plays an important role in the diagnosis and management of DFO. Plain radiography can be adequate to detect DFO. [20] MRI was found to be more accurate, sensitive ($p<0.1$) as well as specific in comparison to other diagnostic scans. MRI should be carried out in patients where plain radiographs turn negative for DFO. MRI also provides better details and extent of infective process so that further treatment could be planned appropriately [21]. We were only able to do MRI in patients who were able to afford it. The Erythrocyte sedimentation rate of 70mm/h is considered as the adequate cut-off in the prediction of DFO. [22] The mean ESR Level observed in our study is 78.

A very important step in selecting the required antibiotic is to find the causative organism. It can be done via soft tissue as well as bone tissue culture and sensitivity. [23] Gram positive organism especially staphylococcus aureus was predominantly isolated in a study by Embil JM et al. [24] whereas gram negative organism, mainly pseudomonas followed by proteus species predominantly shown in our study. Organisms resistant to antibiotics complicate antimicrobial therapy. A prolonged duration of antibiotic therapy for about 4 to 6 weeks is required without surgical intervention in managing DFO. [25] However in our study population, 23 patients (44.2%) required 3 courses and 5 patients (9.6%) required more than 3 courses of antibiotics. Around 31 patients required combination of intravenous antibiotic.

Hyperbaric oxygen therapy (HBOT) involves the patient breathing 100% oxygen at an atmosphere above sea level in a monoplace or multiplace chamber using a specially designed tight face mask. HBOT can be used effectively in soft tissue infections of skin such as cellulitis and OM by improving hypoxia especially caused by antibiotic resistant organisms [26] Adequate antibiotics cannot reach the bone due to the relative inadequacy of blood vessels. [27] It has been proven in both in vitro and in vivo studies that HBOT improves tissue oxygenation in ischemic tissue and thereby promoting it's healing. It increases the leukocyte phagocytic activities in the wound and infected bone. HBOT also promotes new vessel and bone formation to pack the dead space with both bony as well as vascular tissue. Other ways HBOT improves healing is by increasing osteoclastic activity to remove dead bone tissue and inhibiting growth of anaerobic organism within affected tissue.[28] Multiple case control and cohort studies have proved the efficacy of HBOT as an adjuvant , mainly in refractory cases of DFO.[29] HBOT has kept infection under check in 60-85% of cases with chronic refractory OM HBOT also reduces chances of amputation in DFI.[30,31] Mean number of HBOT sessions required in our study was about 18.09 ± 9.1.] Mean number of days for healing of wound required was about 56 days. In our study , it was found that

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33 patients, 8 patients and 2 patients had completely healed , partially healed and failed treatment outcomes on follow up. None of our patient required amputations post HBOT. Additionally, HBOT helps in better glycemic control and improves markers of atherosclerosis and inflammation. [32] HBOT also improved renal function status in our patient group. We observed a decrease in creatinine levels post treatment and this effect may be due to the improvement in wound healing and infection control. [33]

CONCLUSION

Diabetic foot Osteomyelitis (DFO) should be ruled out in all cases of diabetic foot infections. Probability of OM increases with the severity of DFI. OM can have associations with underlying neuropathy and peripheral vascular disease. In our study, 33 of 52 patients were successfully treated with a combination of hyperbaric oxygen therapy (HBOT), antibiotics and wound debridement while 16 patients had recurrence of ulcer. It can be used as a safe and effective treatment that aids as an adjuvant in managing DFO. OM increases the chances of amputation. Early detection of OM and HBOT along with the conventional methods can decrease the rate of amputation and help in saving limbs. We did not observe any life threatening adverse event associated with HBOT in our study.

Limitation

The limitation in our study is that it is a cross-sectional study and not a randomized control trial. Another limitation is that our sample size is small.

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