

Effect of Low level therapy of Diabetic foot ulcers

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ABSTRACT:

Background: Diabetes mellitus has become a major public health interest because of its incidence, which is rising day to day remarkably. Nearly 15 % of diabetic patients will suffer from DFU in their life span. Conventional treatment is not effective against the non-healing DFUs so in recent days so many adjuvant therapies which have been tried to stimulate healing process are in use. In this study, the role of low level laser therapy on diabetic ulcers was evaluated to reduce the size of ulcer, Faster Wound healing, Control of infection, Cost effectiveness and if secondary procedures like split skin grafting can be avoided.

Materials and Methods: A total of 100 patients with Diabetic foot ulcer fitting the inclusion criteria were included in this study and they were randomly categorized into control and study group. Patients in the study group received treatment with LLLT. Ulcer bed was irradiated locally with red light (660nm). Ulcer size and its depth were used as basis to calculate the duration of exposure to deliver 3–10 J/cm² for 15 to 20 minutes, for 15 days on daily basis. Edge of the ulcer and ulcer floor were irradiated. Conventional dressing was preferred for covering after irradiation and controls were treated with conventional therapy alone which includes dressings with betadine or wet with saline, Course of antibiotic treatment and sloughs off when needed. The size of the ulcer was measured before starting the treatment and on day 15 after starting the treatment. Grade of the ulcer and culture status of the ulcer was also assessed on Day 1 and day 15. Duration of stay in hospital was noted to assess cost effectiveness.

Results: In LLLT group, after completing 15 days treatment complete wound healing was achieved by 66.6% of grade-1 ulcers and 4.4% of grade-2 ulcers and 96.6% of grade-2 ulcers were improved to grade-1. In contrary complete wound healing was not found in grade-1 ulcers of controls and 3.4% of grade-2 ulcers improved to Grade 1 and a majority of ulcers remained as such. In LLLT group only 10 subjects had bacterial growth after completing 15 days treatment and no new growth was found but in controls in a majority of cases (85.5%) growth remained even after-15 and in 18.75% cases, new growth was reported. Reduction in Mean

area of ulcer at day-15 was statistically significant in LLLT group (13.74 ± 11.88 to 3.97 ± 5.41 Cm² and $P < 0.001$) whereas this reaction of mean ulcer area among controls was statistically not significant. (19.09 ± 15.03 cm² to 18.80 ± 17.70 cm² and $P = 0.859$). Mean total cost of the treatment was less compared to conventional treatment group. (2264.3 ± 140 Vs 3588.4 ± 68 Rs)

Conclusion: Laser therapy is painless, cost effective procedure which induces faster granulation, wound contraction and reepithelialisation, thus accelerates complete wound healing hence avoiding secondary procedures like split skin grafting. Control of infection was also better compared to control group.

INTRODUCTION:

Worldwide, Diabetes mellitus has become a major public health interest because of its incidence, which is rising day to day remarkably. [1] Available epidemiological data on the prevalence of DM reported that there was a raise in DM cases. In the year 1985 recorded cases were 30 million cases and were reached to 285 million in 2010 and as per the expectation it may reach to 360 million by 2030 [2]. In majority of DM cases more frequently facing complications were foot ulcers (DFUs). [3, 4] Nearly 15 % of diabetic patients will suffer from DFU in their life span [5, 6] Proper wound caring is very important for DFU otherwise they are the greater source for morbidity, gangrene, amputation. Improper management of DFUs may leads to mortality in some cases. [7, 8] DM patients have 15 times higher risk of lower limb amputation than the normal persons and DFUs cause majorly 50–70% of all lower limb amputations in patients of DM. [5] DFUs may cause notable physical, psychological stress and also affects the productivity which may leads to financial problems and also lowers the patients quality of life. [9].

Most common risk factors leading DFUs were male gender, unusual foot structure, smoking, diabetes for 10 years and greater ,amputations ,worst glycemic control, peripheral neuropathy and arterial diseases. Foot ulcers are usually developed in nearly 15% patients with DM in their life span and among them 6–40% may require an amputation [16]. Still there is a uncertainty about basic pathophysiological factors leading to DFUs, the triad of neuropathy, ischaemia and infections are treated as the routine and most important cause. [10] Low angiogenic response and deficiency of growth factors may be responsible for delayed healing of wounds in DFUs. [11] Conventional treatment is not effective against the non-healing DFUs. [8]

In recent days so many adjuvant therapies which have been tried to stimulate healing process are in use which includes ultrasound, laser therapy and other forms of photo bio modulation, electrical stimulation, hyperbaric oxygen and vacuum-assisted closure [12]. Although laser therapy has been investigated since the 1990s for possible improvements in the healing of wounds, [13, 14] reproducible results not available in literature may stops its wide range of usage in wound healing. In recent days, efficacy of LLLT is completely assessed by conducting properly planned experiments with animal models using different laser wavelengths and fluency. Most of the study findings stated that laser therapy, or low-level laser therapy (LLLT), modulates the expression of inflammatory 3 mediators and leads to a reduction in edema, leukocyte influx, and oxidative stress. [15] Further, LLLT has been shown to stimulate neo vascularisation and collagen remodelling [16] to heal the wounds in faster way. Few of the studies shows that 660 nm wave length shows more viability than

longer wavelength [17]. A study supports that the better results are found with a dose of 3 J/cm² by changing doses of 632.8 nm He-Ne laser irradiation. [18] Low level laser therapy was invented since 1990s to induce wound healing process of different ulcers but its implementation in India was still at budding stage because of less research in this field. Even though many studies have listed in literature on the efficacy of low level laser therapy to treat DFUs [14, 19-23] but in Indian scenario there were minimum number of studies. [24] There is a need in India to accelerate the research on the viability of low level laser therapy to avoid the backlogging in its implementation [7-10].

MATERIALS AND METHOD:

Study design: The current study was Randomized open labelled control study, with two treatment groups of about 100 patients. Group A: Intervention group (who received laser therapy in addition to standard management), Group B: Control group (standard treatment group). The study population included patients suffering from diabetic foot ulcer. The study was conducted in the department of general surgery, Chettinad hospital and research institute, which is a tertiary care teaching hospital. The recruitment of the participants was conducted over a period of 1 year from June 2016 to July 2017. All the subjects were followed up after 15 days of administering the intervention. Inclusion criteria: (a) Aged between 30 to 80, (b) Good glycemic control ((Patients with fasting blood sugar (FBS) levels measured on two occasions 24 h apart between 90 and 200 mg/dL with glycosylated haemoglobin (HbA1c) levels between 6% and 9% will be included.), (c) Wound size below 10cms and (d) diabetic ulcers from grade 1 to 2. Exclusion criteria: (a) Presence of osteomyelitis, (b) Those with clinical signs of ischaemia and ABI less than 0.9, (c) Patients associated with critical illness who needs intensive care (35).

Randomization:

The recruited participants were randomized into two treatment groups, as per the random number sequence generated using random number tables in Kirkwood B et al, after prior allocation even and odd numbers to each of the intervention groups [14-16]. Allocation concealment: The random number sequence generated was kept in the custody of an independent faculty in the department, who was not part of the study team in serially numbered opaque envelopes as recommended by CONSORT guidelines. Blinding: The study was an open labelled study as both the investigator and participant blinding was not possible, considering the nature of intervention. Study procedure: After obtaining the informed written consent, relevant demographic and clinical parameters were documented in a structure proforma. The exact dimensions of the ulcer were noted and each ulcer was graded using the Wagner grading system as follows.

Wagner Grading System:

Grade 1: Superficial Diabetic Ulcer

Grade 2: Ulcer extension Involves ligament, tendon, joint capsule or fascia

Grade 3: Deep ulcer with abscess or osteomyelitis

Grade 4: Gangrene to portion of forefoot

Grade 5: Extensive gangrene of foot

All patients were joined to the surgical ward and evaluated thoroughly. Both acute as well as chronic ulcers will be included in the study [20]. The size of the ulcer was measured with ruler. Objective assessment of vascularity was done by careful palpation of peripheral pulses and calculation of Ankle brachial index. Colour Doppler imaging of the arterial circulation of lower limbs was performed in patients with feeble or absent [36] and those with signs of ischemia and cases with < 0.9 ABI were excluded from the study. Plain radiographs were used to find the presence of osteomyelitis and those cases were excluded from the study.

Administration of intervention:

All patients in both the groups received the required, conventional treatments of diabetic wound care, including dressing, antibiotics, controlling diabetes, cholesterol, and blood pressure along with aggressive drug treatment and wound debridement when needed, before, after and during the laser therapy procedure. Patients in the study group received treatment with LLLT [21]. Ulcer bed was irradiated locally with red light (660nm). Ulcer size and its depth were used as basis to calculate the duration of exposure to deliver 3–10 J/cm² for 15 to 20 minutes, for 15 days on daily basis. Edge of the ulcer and ulcer floor were irradiated. Conventional dressing was preferred for covering after irradiation and controls were treated with conventional therapy alone which includes dressings with betadine or wet with saline, Course of antibiotic treatment and sloughs off when needed [22-24]. At baseline and day 15, size of the ulcer was measured. Before starting the treatment if there is any evidence of slough in patients, repeated surgical debridement was conducted. Wound swab for culture and sensitivity was taken both in control and study group on day 0 and day 15. Grade of ulcer assessed before starting the treatment and on day 15[25]. Total cost calculated approximately based on duration of hospital stay and dressings keeping per day cost as 50Rs, per dressing cost as 50Rs and per laser sitting cost is 50Rs. Systemic antibiotics were suggested to use with the help of culture sensitivity reports[26]. Good glycaemic control was maintained by having Insulin/oral hypoglycaemic agents (OHA) on the advice of physician. The tools to collect the data required are pretested and informed consent from each patient will be obtained [27-29].

ETHICAL ISSUES:

Ethical clearance was obtained from the Institutional human ethical committee. Informed consent was obtained from each study participant, after explaining the risks and benefits involved in the study and voluntary nature of participation, in a language participant can understand [30-33]. Confidentiality of the study participants was maintained throughout trial conduction and dissemination of the study results. Attempt will be made to use the study for policy modifications and public utility in future.

Statistical methods:

Area of the ulcer was considered as primary outcome variable. The mode of treatment (standard vs Intervention) was considered as primary explanatory variable. Various demographic, diabetes disease related and treatment related parameters were considered as other potential confounding variables [34-36].

Descriptive analysis was carried out by mean and standard deviation for quantitative variables, frequency and proportion for categorical variables. Data was also represented using appropriate diagrams like bar diagram, pie diagram and box plots. [38] Both the study groups were compared at the baseline with respect to all potential confounders. The area of the ulcer was compared between the two groups, using independent sample t-test. The mean differences along with their 95% CI were presented. Association between quantitative explanatory and outcome variables was assessed by calculating person correlation coefficient and the data was represented in a scatter diagram. P value < 0.05 was considered statistically significant. IBM SPSS version 22 was used for statistical analysis [74].

Results:

Table1: Descriptive analysis of GROUP in study group (N=100)

GROUPS	FREQUENCY	PERCENTAGE
Cases	50	50.00%
Controls	50	50.00%

Among the study participants, 50 (50.00%) were Cases and 50 (50.00%) were Controls is Present (Table 1).

Table2: Comparison of mean Age across study groups (N=100)

GROUP	Age Mean ±STD	Mean Difference	95% CI		P value
			Lower	Upper	
Cases	52.1 ± 8.940	-0.38	-4.48530	3.72530	0.855
Controls	52.48 ± 11.57				

The mean Age was 52.1±8.940 in subjects with Cases and mean Age was 52.48 ± 11.57 in subjects With Controls. The mean difference across the group is (-0.38). It is statistically not significant (P Value 0.855) (Table 2).

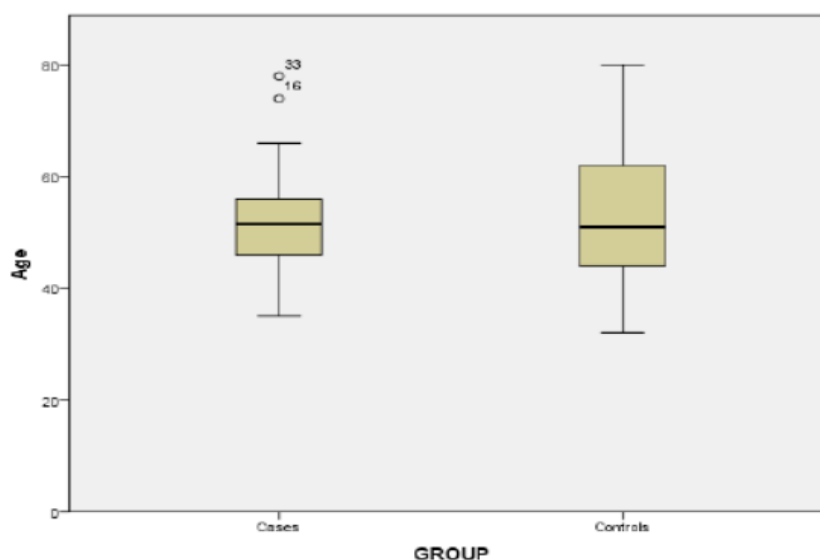


Table3: Association of group with Gender of study population (N=100)

Gender	Groups		Chi Square	P-Value
	Cases (G1=50)	Controls (G2=50)		
Males	26 (52%)	31 (62%)	1.020	0.31
Female	24 (48%)	19 (38%)		

The proportion of subjects with Male in Cases was 26(52%) and with female were 24(48%) whereas the proportion of subjects with male in Controls was 31(62%) and with female was 19(38%). The association of gender with the study groups was statistically not significant (P value0.31) (Table: 3) the proportion of males was slightly higher than females in both cases and controls.

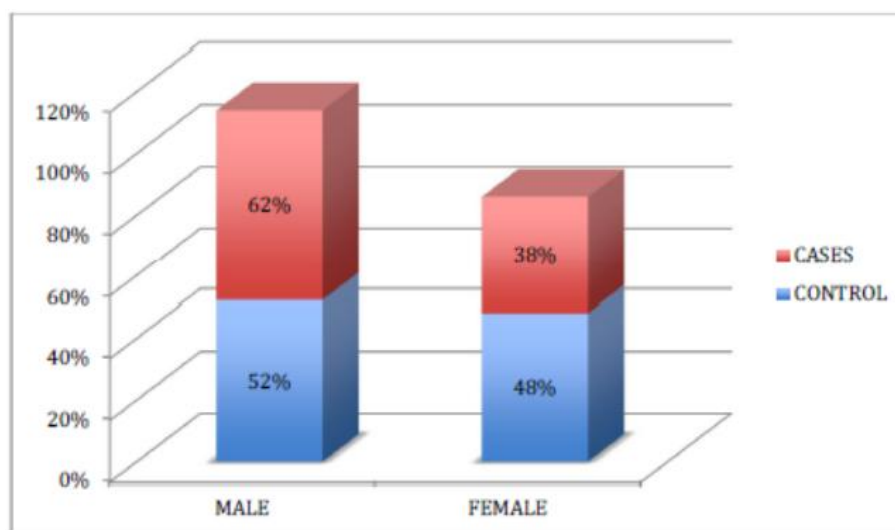


Fig.5 Bar chart of sex distribution in study groups

Table4: Comparison of mean Height cm across study groups (N=100)

Groups	Height (cm) Mean \pm STD	Mean Difference	95% CI		P-value
			Lower	Upper	
Cases	162.6 \pm 6.760	-3.06	-5.49717	-0.62283	0.014
Control	165.7 \pm 5.451				

The mean Height was 162.6 \pm 6.760 in subjects with Cases and mean Height was 165.7 \pm 5.451 in subjects With Controls. The mean difference across the group is (- 3.06). It is statistically significant (P Value 0.014) (Table 4).

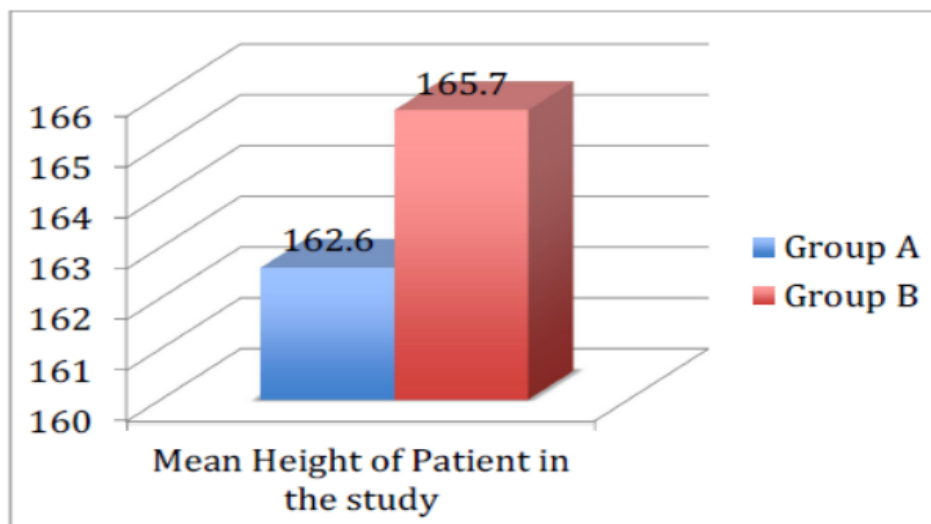


Fig.6 Bar chart of mean height across study group

Table5: Comparison of mean Weight kg across study groups (N=100)

Groups	Height (cm) Mean \pm STD	Mean Difference	95% CI		P-value
			Lower	Upper	
Cases	72.12 \pm 9.518	-0.36	-4.17904	3.45904	0.852
Control	72.48 \pm 9.725				

The mean Weight was 72.12 \pm 9.518 in subjects with Cases and mean Weight was 72.48 \pm 9.725 in subjects With Controls. The mean difference across the group is (- 0.36). It is statistically not significant (P Value 0.852) (Table 5).

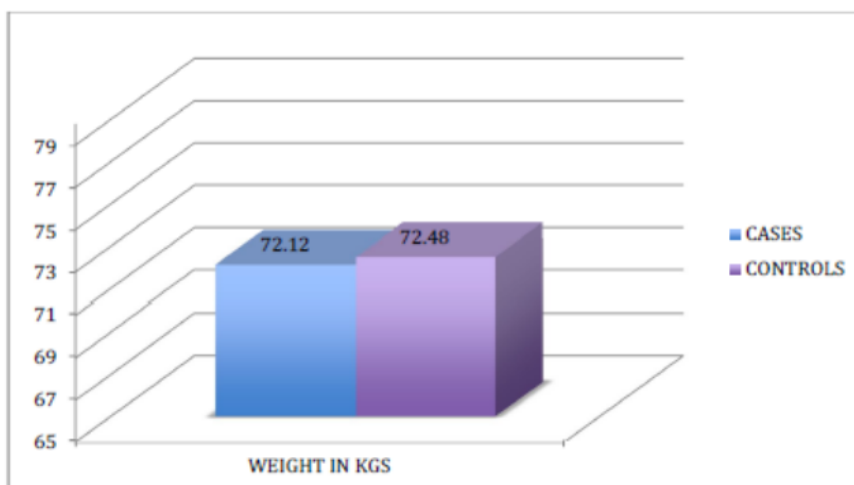


Fig.7 Bar chart of mean weight across study groups.

Table 6: Comparison of mean BMI across study groups (N=100)

Groups	Height (cm) Mean ± STD	Mean Difference	95% CI		P-value
			Lower	Upper	
Cases	27.19 ± 2.554	0.89	0.10382	1.88564	0.079
Control	26.29 ± 2.457				

The mean BMI was 27.19±2.554 in subjects with Cases and mean BMI was 26.29 ± 2.457 in subjects With Controls. The mean difference across the group is (0.89). It is statistically not significant (P Value 0.079) (Table 6).

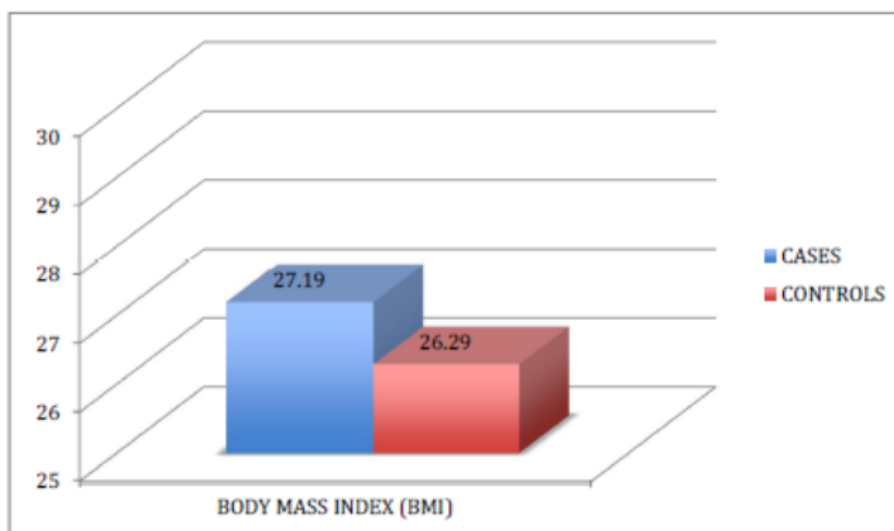


Fig.8 Bar chart of mean BMI across study groups

Table7: Comparison of mean Duration of ulcer in weeks across study groups (N=100)

Groups	Height (cm) Mean ± STD	Mean Difference	95% CI		P-value
			Lower	Upper	
Cases	4.72 ± 3.625	0.10	-1.43918	1.63918	0.898
Control	4.62 ± 4.115				

The mean Duration of ulcer in weeks was 4.72±3.625 in subjects with Cases and mean Duration of ulcer in weeks was 4.62 ± 4.115 in subjects With Controls. The mean difference across the group is (0.10). It is statistically not significant (P Value 0.898) (Table 7).

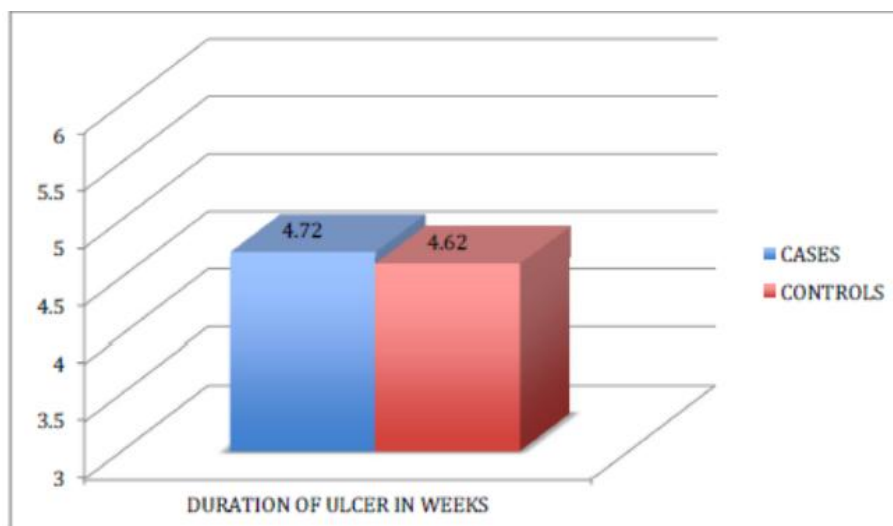


Fig.9 Bar chart of mean Duration of ulcer in weeks across study groups

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Parameters	Cases(G1) Mean±STD	Control(G2) Mean± STD	Mean Difference	95% CI		P- value
				Lower	Upper	
Day-1 area	13.74±11.88	19.09±15.03	-5.3490	-10.72	0.028	0.051
Day-15 area	3.97±5.41	18.80±17.70	-14.8330	-20.02	-9.638	<0.001
Changes in area	9.77±7.83	0.28±11.37	9.4836	5.607	13.359	<0.001

The mean Day-1 area was 13.74±11.88 in subjects with Cases and mean Day-1 area was 19.09 ± 15.03 in subjects With Controls. The mean difference across the group is (-5.349). It is statistically significant (P Value 0.051). The mean Day-15 area was 3.97±5.41 in subjects with Cases and mean Day-15 area was 18.80 ± 17.70 in subjects With Controls. The mean difference across the group is (-14.83). It is statistically significant (P Value <0.001) the mean Changes in area was 9.77±7.83 in subjects with Cases and mean Changes in area was 0.28± 11.37 in subjects With Controls. The mean difference across the group is (9.48). It is statistically significant (P Value <0.001) (Table 9).

Table 9: Comparison of mean Height, Weight, BMI, Duration of ulcer in weeks, Area of ulcer in Day1&15 and change in area of ulcer .(N=100)

Parameter	Tracheotomy		P value
	Cases(G1) Mean± STD	Control(G2) Mean ±STD	
Age	52.1 ± 8.940	52.48 ± 11.57	0.855
Height (cm)	162.6 ± 6.760	165.7 ± 5.451	0.014
Weight (kg)	72.12 ± 9.518	72.48 ± 9.725	0.852
BMI	27.19 ± 2.554	26.29 ± 2.457	0.079
Duration of ulcer week	4.72 ± 3.625	4.62 ± 4.115	0.898
Day 1 ulcer width in cm	4.384 ± 2.599	5.15 ± 2.536	0.139
Day 1ulcerlength	3.03 ± 2.898	3.278 ± 1.136	0.575
Day1 area	13.74 ± 11.88	19.09 ± 15.03	0.051
Day 15 ulcer width in	2.05 ± 2.105	5.062 ± 2.908	<0.001

cm			
Day 15 ulcer length	1.18 ± 1.114	3.094 ± 1.322	<0.001
Day 15 area	3.975 ± 5.414	18.80 ± 17.70	<0.001
Change in area	9.771 ± 7.836	0.287 ± 11.37	<0.001

Table 10: The change in the grade of ulcer in GROUP A (N= 50)

Day-1	DAY – 15		
	GRADE -2	GRADE -1	COMPLETE HEALED
Grade2 (N=29)	0(0.00%)	28(96.6%)	1(3.4%)
Grade1 (N=21)	0(0.00%)	7(33.33%)	14(66.67%)

In study group A, among the 50 subjects 29 were grade ulcers and 21 were grade ulcers on day 1. At the end of 15+ days, number of grade2 ulcers that remained in grade2 was nil. Out of 29 grade2 ulcers 28 (96.6%) improved to grade1 and ulcer was completely healed at day 15. Among 21 grade ulcers, (33.33%) remained in grade 1, 14 (66.67%) ulcers completely healed at the end of 15 days (Table11).

Table11: The change in the grade of ulcer in group B (N= 50)

Day-1	DAY – 15		
	GRADE -2	GRADE -1	COMPLETE HEALED
Grade2 (N=26)	23(88.46%)	3(11.53)	0
Grade1 (N=24)	0(0.00%)	24(100%)	0

In study group B, among the 50 subjects 26 were grade ulcers and 24 were grade ulcers on day 1. At the end of 15 days, number of grade2 ulcers that remained in grade2 was23 (88.46%) and ulcers (11.53%) improved to grade1. Among 24 grade1 ulcers all remained in grade1 and nil, (0.00%) ulcers completely healed at the end of 15 days. (Table12).

Table 12: Culture positive status on day 1 and day 15 in group A (N= 50)

Day-1	DAY – 15	
	GROWTH	NO GROWTH
Growth(N=31)	10(32.25%)	21(67.74%)
No growth(N=19)	0(0.00%)	19(100%)

In group A, 31 subjects had bacterial growth in their ulcers on day and the remaining 19 had no bacterial growth. Out of the 31 subjects with bacterial growth, 10 people still had growth at the end of 15 days and 21 had no growth at 15 days. Among 19 people with no growth at baseline, none of them have developed new growth at day 15. (Table13)

Table 13: Culture positive status on day 1 and day 15 in group B (N= 50)

Day-1	DAY – 15	
	GROWTH	NO GROWTH
Growth(N=34)	29(85.25%)	5(14.71%)
No growth(N=16)	3(18.75%)	13(81.25%)

In group B, 34 subjects had bacterial growth in their ulcers on day-1 and the remaining 16 had no bacterial growth. Out of the 34 with bacterial growth, 29(85.25%) people still had growth at the end of 15 days and 5(14.71%) had no growth. Among 16 people who had no growth at baseline, in 3(18.75%) cases bacterial growth was found and in the remaining 13(81.25%) cases bacterial growth was not found (Table14).

Table14: Comparison of mean area of the ulcer within each study group before and after intervention (N=100)

Parameter	Mean± SID	PAIRED T-TEST P-VALUE
Cases		
Day-1 area	13.74±11.88	<0.001
Day-15 area	3.97±5.41	
Controls		
Day-1 area	19.09±15.03	0.859
Day-15 area	18.80±17.70	

The mean area of the ulcer was 13.74±11.88 in among cases, which has reduced to 3.97± 5.41 Cm² on day 15, which was statistically significant (P Value <0.001). Among the controls, the mean area of the ulcer was reduced only minimal from 19.09±15.03 Cm² on day 1 to 18.80± 17.70 on day 15, which was statistically not significant (P Value 0.859) (Table 14).

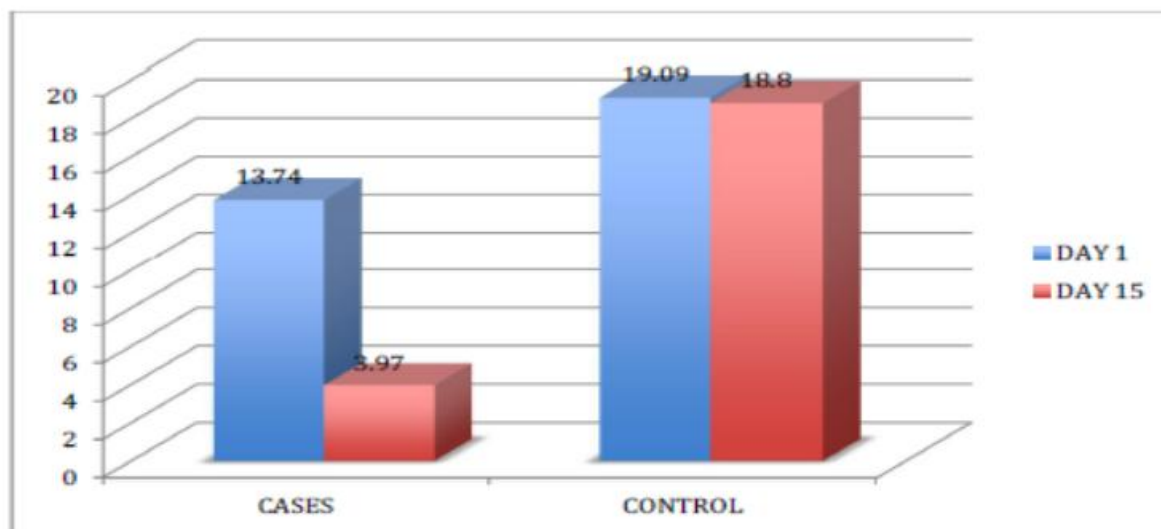
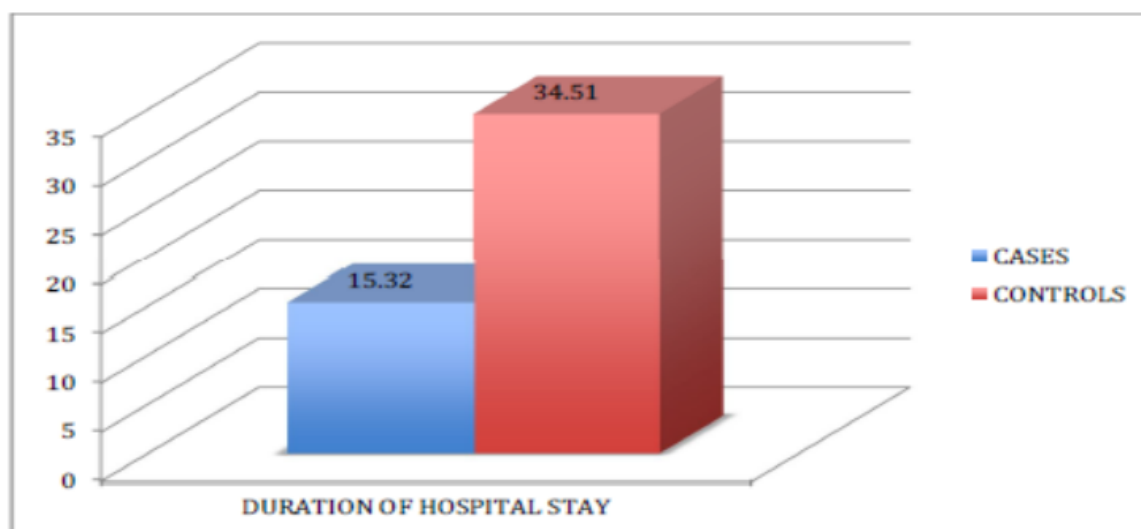


Fig .10 Bar chart of Change in mean area of ulcer before and after intervention between two study groups.

Table15: Comparison of mean total duration of hospital stay between two study groups (N=100)

	Mean± SID	PAIRED T-TEST P-VALUE
Duration of Hospital stay(Days)		
Cases	15.32±3.17	0.003
Controls	34.51±4.22	
Total cost of the treatment(Rs)		
Cases	2264.3±140	<0.001
Controls	3588.4±68	

The mean total duration of hospital stay was 15.32±3.17 days in subjects of cases and among controls mean total duration of hospital stay was 34.51±4.22, which was statistically significant (P Value 0.003). Among the cases, the mean total cost of treatment of the ulcer based on hospital stay and number of dressings was 2264.3±140 Rs and among controls it was 3588.4±68, which was statistically significant (P Value <0.001) (Table 16).

**Fig 11. Bar chart of mean total duration of hospital stays in days between two study groups****Discussion:**

Diabetic foot ulcers are the most common complications of Diabetes Mellitus (DM) and conventional wound healing therapies is not that much effective for DFUs and if proper treatment was not given to the DFUs they may herald severe complications.[44] Wound healing can be initiated by treating with a beam of Electromagnetic radiations or laser. In the existing literature, few studies are available in this area. [14, 19-24] The current study was aimed to assess the adequacy of a treatment modality with Low- Level Laser Therapy (LLLT) for diabetic foot ulcers [12]. Our study population constitutes of total 100 participants and were randomly divided into two groups' cases and controls with 50 participants in each. The mean Age of cases was 52.1±8.940 whereas in controls mean Age was 52.48 ± 11.57. The mean difference across the group is (-0.38). The proportion of males was slightly higher in both cases and controls 26(52%) &31(62%) than

females 24(48%) & 19(38%). Like our study Kajagar, B. M. et al [14] study recorded that mean age of both cases and controls was 54.35 ± 6.84 and 50.94 ± 8.11 respectively. The proportion of males and females was equal (2:1) in both cases and controls. [7-10]

In our study, the mean Height was 162.6 ± 6.760 cm in Cases and 165.7 ± 5.451 cm in Controls. The mean difference across the group was statistically significant (P Value 0.014). similar findings were reported in the study of Hopkins, J. T. et al [21] Mean height was 174.8 ± 11.7 cm in laser group and 176.4 ± 7.8 cm sham group. In the current study, the mean weight was 72.12 ± 9.518 in cases and 72.48 ± 9.725 in Controls. The mean difference across the group was statistically not significant (P Value 0.852). The mean BMI was 27.19 ± 2.554 in cases whereas 26.29 ± 2.457 in controls. Mean difference was statistically not significant. (P-Value 0.079). In the study of Hopkins, J. T. et al [21] Mean mass was 76.9 ± 16.3 kg in laser group and 75.5 ± 12.6 kg in the sham group.

In the current study mean Duration of ulcer was 4.72 ± 3.625 weeks in Cases and 4.62 ± 4.115 weeks in Controls. The mean difference across the group is (0.10). It is statistically not significant (P Value 0.898) Like the current study, the study by Kajagar, B. M. et al [14] have shown that median duration of ulcer in the treatment group was 4 weeks at baseline and it was 5 weeks for controls. As per the study of Kaviani, An et al [22] mean duration of ulcer was $11.48.8 \pm 8.5$ months in laser group and 8.8 ± 3.6 months in the placebo group. The mean Day-1 area was 13.74 ± 11.88 in cases and mean Day-1 area was 19.09 ± 15.03 in controls. The mean difference between the groups was statistically significant (P Value 0.051). At Day-15 mean area was 3.97 ± 5.41 in cases and 18.80 ± 17.70 in Controls. Mean difference across the groups was showing statistical significance (P Value < 0.001) [37]. The mean changes in the area were 9.77 ± 7.83 in subjects with Cases and mean Changes in the area was 0.28 ± 11.37 in subjects With Controls. Statistically significant mean difference across the two groups was found (P < 0.001) [37]. Results of the study by [14] study also a similar, in LLLT group mean size of the ulcer at base line was 2608.03 mm² and it was 2747.17 mm² in controls [38]. At the end of 15 days treatment, in treatment group final area of ulcer was 1564.79 mm² where as in controls 2424.75 mm² was the final area of ulcer. Mean reduction in ulcer area was $1043.20266.62$ mm² in LLLT group and in controls it was reported as $1043.20 - 266.62$ mm². Mean difference between two groups was significant (P < 0.010). Findings of the study of [22] were similar to the present study. Mean area of ulcer at baseline was 10.7 ± 25.7 cm² in laser group and 7.8 ± 11 cm² in placebo group. Mean difference was statistically not significant. After 2 weeks of treatment, there was a great reduction in ulcer size of LLLT group than the placebo treatment group (58 10.4% vs. 23.5 14.1%; p $\frac{1}{4}$ 0.046) [40-43]. After 4 weeks of treatment, reduction of ulcer size was greater In LLLT group subjects than the placebo treatment group (73.7 10.2% vs. 47.3 15.4%; p $\frac{1}{4}$ 0.03).

Ulcer Grade: In the current study, among 50 subjects of a Group A study participants 29 were grade-2 ulcers and remaining 21 were grade 1 ulcers at baseline [45-46]. After 15 days grade -2 ulcers were improved. Among 29 grade 2 ulcers, 28(96.6%) were upgraded to grade-1 and 1 ulcer was healed completely at 15th day [48-51]. At day 15, in 21 Grade 1 ulcers majority (66.67%) of ulcers were healed completely but 33.33% were retained as such in grade-1 of 50 group B participants, 26 were grade-2 ulcers and remaining 24 were grade 1

ulcers at 1st day [52-56]. After 15 days of treatment, 88.46% of grade-2 ulcers remained as such and 11.53% of wounds improved to grade-1, out of 24 grades -1 ulcer all remained as grade-1 and no wound got healed completely. In the past literature, very minimal number of studies has shown interest on grades of ulcer [64], study have shown findings similar to our study. 21 open wounds were treated with low level laser therapy and at the end of 9 weeks of treatment, the major proportion of wounds (61.9%) improved significantly. 42.8% were closed completely, minimum improvement was found in 14.3% cases and no change was reported in 23.8% wounds.

Bacterial growth status:

In our study among Group A participants, at base line 31 subjects had bacterial growth in their ulcers and the remaining 19 had no bacterial growth [57-59]. At the end of 15 days in 31 cases with bacterial growth, growth was absent in 67.74% cases and in 32.25% cases growth still remained. In 19 cases with no growth at day-1, growth was not developed even after 15 days [60-65]. Among group-B study participants, at base line 34 subjects were having bacterial growth and the remaining 16 had no growth. At day 15 in 34 subjects with bacterial growth 85.25% of cases were still showing growth and 14.7% had no growth. In 16 cases with no growth at day-1, 81.25% of cases had no growth but in 3 subject's growth was observed after 15 days of treatment. A study conducted by [70] findings were also in agreement with current study findings. He studied 60 patients of diabetic foot ulcer and positive for culture. After 10 days of treatment, among treatment group subjects 66.66% were showing culture positive results and 33.3% were with negative culture reports. In controls (N=30) 80% of subjects had positive cultures and in 20% of subjects were culture negative [73-76].

Ulcer Size:

In our study reported that the mean area of the ulcer was 13.74 ± 11.88 among cases, which has reduced to 3.97 ± 5.41 Cm² on day 15, statistically significance (P Value <0.001). Among the controls, the mean area of the ulcer was reduced only minimal from 19.09 ± 15.03 Cm² on day 1 to 18.80 ± 17.70 on day 15, which was statistically not significant (P Value 0.859) [77-83]. Like our study findings [14] have reported in his findings as the mean initial area of the ulcer was 2608.03 mm² in cases and was reduced to 1564.79 mm² after 15 days of treatment whereas in controls initial area was 2747.17 mm² and reduced to 2424.75 mm² [21]. Mean reduction was minimal in controls when compared to cases, agreed with the current study findings and shows that after conducting follow up tests for days 6, 8 and 10 days observed that wound size was reduced in laser group than the sham group for both treated as well as untreated wounds and the difference in size reduction between the two groups was statistically significant, they have reported that there was a great reduction in ulcer area of LEPT group than the placebo group (193.0 mm² Vs 14.7 mm²) with statistically significant difference in ulcer area between two study groups (P=0.0002) [70].

Cost of the treatment:

In current study among cases mean total duration of hospital stay was reported as 15.32 ± 3.17 days and it was reported as 34.51 ± 4.22 days among controls. The mean difference was statistically significant (P Value 0.003)., The mean total cost of treatment was 2264.3 ± 140 Rs in cases where as in controls it was 3588.4 ± 68

Rs , which was statistically significant (P Value <0.001). Few of the existing studies by Pertille et al [75], Yosuf MK et al [76] and Feitosa, M. C et al [20] also supports the fact that the low level laser treatment was the pain less, most effective and a low cost treatment with less side effects.[20, 75, 76].

Conclusion:

In LLLT group, after completing 15 days treatment complete wound healing was achieved by 66.6% of grade-1 ulcers and 4.4% of grade-2 ulcers and 96.6% of grade-2 ulcers improved to grade-1. In contrary complete wound healing was not found in grade-1 ulcers of controls and 3.4% of grade-2 ulcers improved to Grade 1 and a majority of ulcers remained as such. In LLLT group only 10 subjects had bacterial growth after completing 15 days treatment and no new growth was found but in controls in a majority of cases (85.5%) growth remained even after-15 and in 18.75% cases, new growth was reported [88]. Reduction in Mean area of ulcer at day-15 was statistically significant in LLLT group (13.74 ± 11.88 to 3.97 ± 5.41 Cm² and $P < 0.001$) whereas this reduction of mean ulcer area among controls was statistically not significant. (19.09 ± 15.03 cm² to 18.80 ± 17.70 cm² and $P = 0.859$). Mean total cost of the treatment was less compared to conventional treatment group (2264.3 ± 140 Vs 3588.4 ± 68 Rs)[90]. In conclusion, Laser therapy is painless, cost effective procedure which induces faster granulation, wound contraction and reepithelialisation, thus accelerates complete wound healing hence avoiding secondary procedures like split skin grafting. Control of infection was also better compared to control group.

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