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ORIGINAL ARTICLE

Role of Platelet Rich Plasma (PRP) Therapy on Diabetic Foot Ulcer (DFU): A Prospective Study in Bangladesh

A.B.M. Kamrul Hasan,[1] Md. Abdullah Al Masud,[2] Sahnaz Karim,[3] Daanish Arefin Biswas,[4] Mst. Sabiya Afroz,[5] Noor Mohammad[6]

ABSTRACT

Introduction: Diabetic foot ulcer is a major complication of diabetes mellitus, and is the major component of the diabetic foot. This condition affects up to 15% of all patients with diabetes mellitus. 88% of all lower leg amputations are related to a diabetic foot ulcer. Growth factors from Platelet Rich Plasma (PRP) have shown enhanced wound healing. **Objectives:** To assess the role of PRP therapy on diabetic foot infection. **Methods:** This was a prospective study conducted at Diabetic Foot Care & PRP Center (Diagnostic & Hospital), Sirajganj & Desh PRP Centre, Bogura, Bangladesh from January to June 2022. A total of 65 (sixty-five) patients were included in our study. **Results:** All the cases were diabetes patients. Among the cases male 37 (56.9%) and female were 28 (43.1%). In this study, the age of the patients ranged from 35 years to 75 years. The mean age was 55.0±15.44 years. The 45-65 years age group has the longest diabetic duration. This is statistically significant. The results of the study showed that PRP treatment was successful in 63 out of 65 cases (95.9%), with only 2 cases (3.1%) not achieving complete healing. The most common areas of treatment with significant healing were the back of the right foot (1.5%), the back of the heel of the left foot (9.5%), and the back of the right foot under the little finger (3.2%). **Conclusion:** Foot ulcers have a negative impact on the quality of life of diabetes people. According to the findings of our study, the use of PRP accelerates ulcer healing. These findings demonstrated a viable therapy for foot ulcers. There is a need for more randomized controlled trials to determine the real effectiveness of this therapy.

Keywords: Platelet rich plasma, Diabetes mellitus, Foot ulcer

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INTRODUCTION

Diabetic foot ulcer (DFU) is a major complication of diabetes mellitus and is the major component of diabetic foot. This medical condition affects 15% of all patients with diabetes mellitus. A recent study showed that up to 88% of all lower leg amputations are related to diabetic foot ulcers.[1] A few decades ago, diabetic foot ulcers were treated by vacuum-assisted closure, high voltage pulsed current electrical stimulation and hyperbaric oxygen. Some biological therapies were used in ulcer treatment with an improvement in the time of wound healing.[2] More importantly, the cases of diabetic mellitus patients rapidly increase to 439 million by 2030. The main reason is related to the loss of balance between metalloproteinases (MMPs) and MMP inhibitors.[3,4] This status is enhanced to become serious when combined with ischemia and vascular disease. The vascular injury and ischemia reduced the oxygen and nutrients to the wound.

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So the wound healing mechanism cannot perform as in non diabetic patients. Lack of oxygen and nutrients, epithelial cells in the wound cannot express essential factors for healing such as VEGF and PDGF; almost all of the cells at the wound changed metabolism and activity.[4,5] In recent studies, growth factors from Platelet Rich Plasma (PRP) used for enhancing wound healing were compared to conventional therapies. Wound healing started with the release of local growth factors which attracted stem cells into the wound. PRP decreased cytokine release and increased capillary growth. PRP has also some antimicrobial effects against Candida albicans, MRSA and E. coli.[5-7] These alterations in the structure and function of cells, as well as certain substances at DFUs, slowed and disrupted the normal healing process. Therefore, when diabetes patients develop DFUs, nearly all DFUs cannot be treated, and patients must ultimately undergo lower leg amputation. DFU treatment remains a challenge.

MATERIALS & METHODS

This was a prospective study was conducted at the Department of Transfusion Medicine, Diabetic Foot Care & PRP Center (Diagnostic & Hospital), Sirajganj & Desh PRP Centre, Bogura, Bangladesh from January to June 2022. Sixty-Five (65) patients were included to our study according to the following inclusion and exclusion criteria. The inclusion criteria were patients with DM with planter foot ulcers not healed for more than 3 months, intact distal pulsation and ulcers grade 1 and grade 2 according to Wagner grading system (Figure I). The exclusion criteria were patients with liver cell failure, renal impairment, heart failure, severe cardiomyopathy, bleeding or platelet disorders, malignancies or short life expectations, peripheral vascular disease, major lower limb amputations, low immunity or corticosteroid therapy and ulcers (grade 3, grade 4 and grade 5). Full medical and surgical history taking, general assessment, vascular examination and neurological assessment were done for all patients. Laboratory investigations (pre-operative), x-ray foot, arterial duplex and culture from the ulcers were done routinely. All patients signed the consent. On an outpatient basis, debridement was done for all ulcers, optimization of the patients" general conditions, broad-spectrum antibiotics first then based on culture were described. The size of ulcers was recorded before treatment and every week till complete healing. Offloading for all cases by total contact cast was done. For PRP preparation 25 mL of the patient's blood was collected. The blood was centrifuged at 2000 rpm for 5 min to obtain plasma. Then, this plasma was centrifuged at 3000 rpm for another 5 min to collect platelets at (37 Celsius). Platelets were diluted in 5 mL plasma to form PRP and the rest of the plasma is now considered as Platelet Poor Plasma (PPP). Both were activated by Calcium chloride which leads to gel formation for dressing, and PPP was stored for injection (Figure II). Ulcers were dressed with fibrin gel on the first day. After 3 days daily till the end of the first-week injection with activated PPP Was done. If after 2 weeks, still there is no healing, the procedure can be repeated again (Figure III).

Figure I: Fore foot ulcer

Figure II: Injection of PRP

Figure III: Healed ulcer Preparation of Platelet-rich plasma:

We used a PRP kit (Secquire kit SK50-20) that included sodium citrate tubes, syringes, needles and centrifuge tubes. There were four steps to platelet collection: i. blood sample collection ii. Centrifugation iii. Activation iv. Platelet gel making. The process took 30–45 minutes, from blood collection to the end infusion. Blood (30–40ml) was collected from the patient in 3.8% sodium citrate tubes. The blood was centrifuged (at 1400–1800rpm for 10–12 minutes) after which platelets were carefully removed from above the buffy coat with a sterile pipette and transferred to a new sterile tube. Platelet activation was induced by adding 20mM calcium chloride solution (CaCl2) in a ratio of 1 CaCl2:5 PRP by volume, followed by centrifugation at 3000rpm for 10–15 minutes. Collect in between 2/3rd and 1/3rdarea of the test tube and PRP ready for use. The resulting supernatant was shaken for 30 minutes to form a coagulum. This coagulum, or "platelet gel", was used for wound treatment like ointment on wound area.

Statistical analysis: Data were collected and tabulated and statistical analysis was done with p-value recorded as a significance indicator. The significance of the changes in time for wound healing in the three groups was statistically assessed using a one-way analysis of variance, followed by Bonferroniposthoc multiple comparison by SPSS 20.0 (SPSS Inc., Chicago, IL, US). This CI, being narrow, shows more precise estimates, whereas CIs from small sample sizes tend to be wide, producing less precise results.

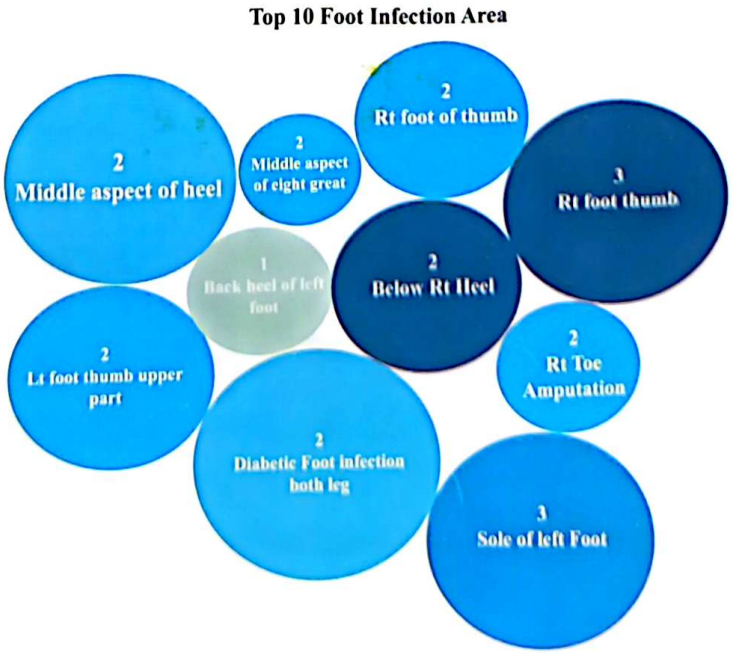


Figure IV: Foot infection area

RESULTS

Total 65 patients were enrolled. All the cases were diabetes patients. In this study, the age of the patients ranged from 35 years to 75 years and the maximum number of cases. Mean age of 55.0±15.44 years. Diabetic history was highest from 45 years to 65 years age group. This was statistically significant. No significant association between the pre-existing medical condition and the distribution among the groups (Figure V). Regarding sex distribution, male 37 (56.9%) and female were 28 (43.1%). Male patients were significant (Figure VI). The infection length side was highest at 6 cm and 4 cm and an average of 2 cm was on both sides (Figure VII). Duration and dose of PRP among the infections area showed that back heel left foot 3 months 1 (1.5%), Back of middle aspect of heel 3 months 1 (1.5%), Back of the foot rt side 1 months 6 (9.5%), Back of the heel left foot 2 months 1 (1.5%), Back of the rt foot in under the little finger 2 months 2 (3.2%), Bellow rt heel 6 months 3 (4.8), Between the front of the middle toe 4 months 2 (3.2%), Diabetic foot infection both leg 6 months 2 (3.2%), Diabetic foot infection lt leg 6 months 1 (1.5%), Diabetic foot infection on 3 months 5 (7.9%), Index toe 2 months 2 (3.2%), Left foot middle finger 4 months 1 (1.5%), Left great toe 12 months 2 (3.2%), Left foot back side 4 month 3 (4.8), Left foot back 4 months 1 (1.5%), Left foot lateral part 6 months 2 (3.2%), Left foot thumb 1 months 2 (3.2%), Left foot thumb and index finger 5 months 5 (7.9%), Left foot thumb upper part 8 months 4 (6.3%), Middle aspect to heel 8 months 2 (3.2%), Middle aspect to right great toe 5 months 8 (12.7%), Right foot of thumb 6 month 6 (9.5), Right foot thumb 15 month 4(6.3%), Rt toe amputation 8 months 6 (9.5) and Sole of left foot 6 months 4 (6.3%) (Figure VIII). PRP dose success rate showed that complete healing were 63 (95.9%) and treatment failwere 2 (3.1%).

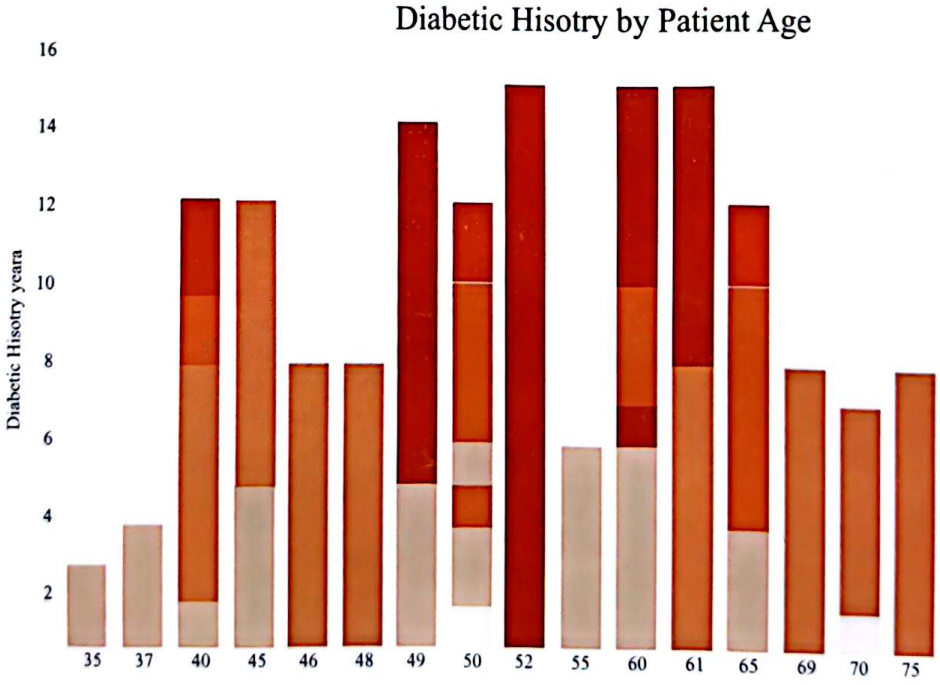


Figure V: Age distribution of diabetic history of patient's age (n=65)

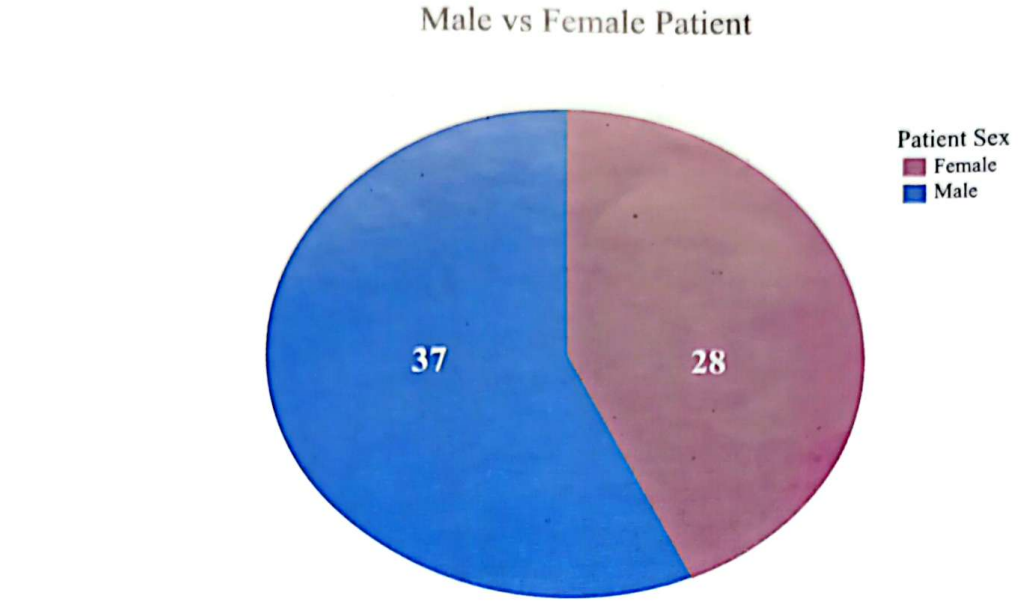


Figure VI: Sex distribution of diabetic history of patients age (n=65)

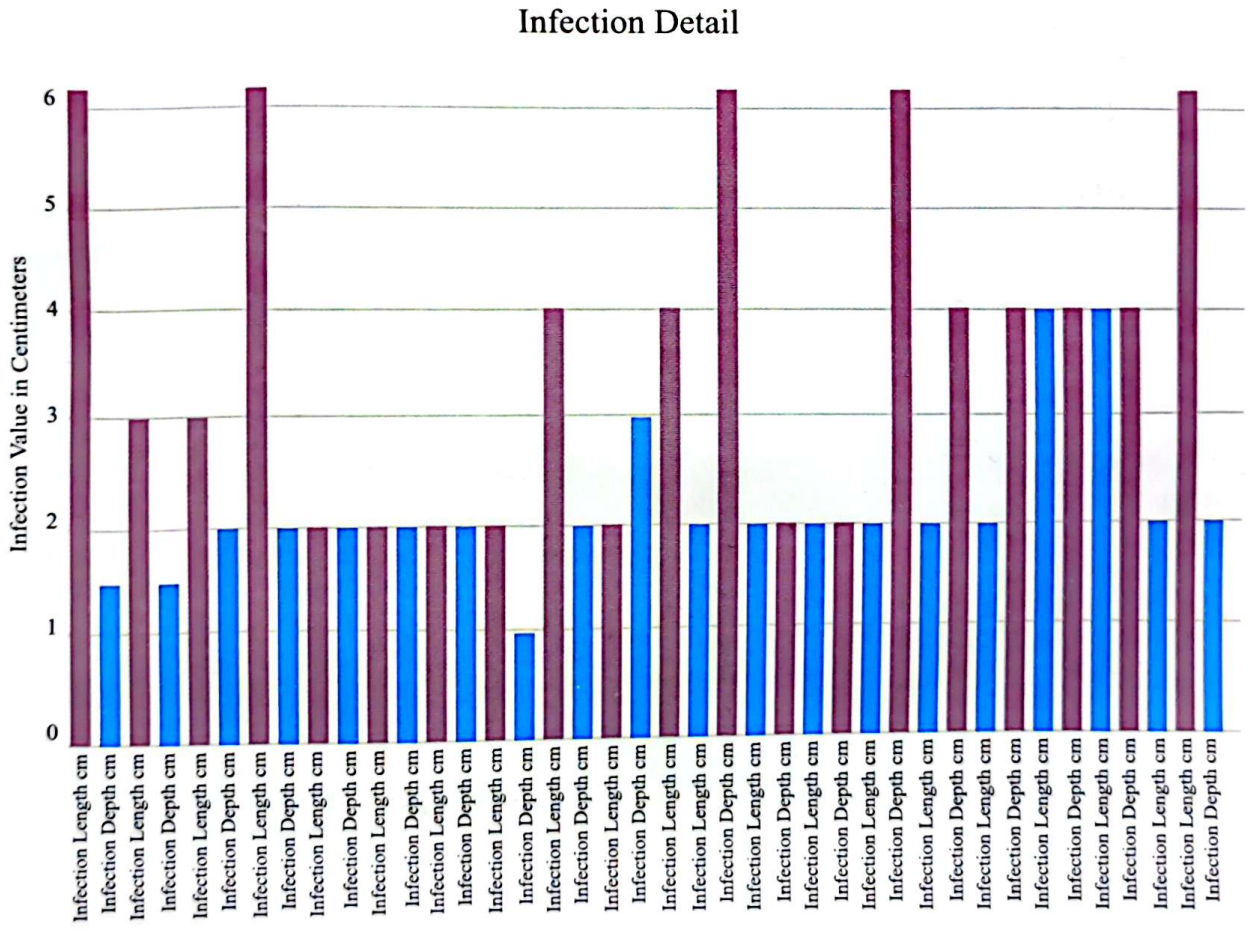


Figure VII: Infection detail of the diabetic history of patients (n=65)

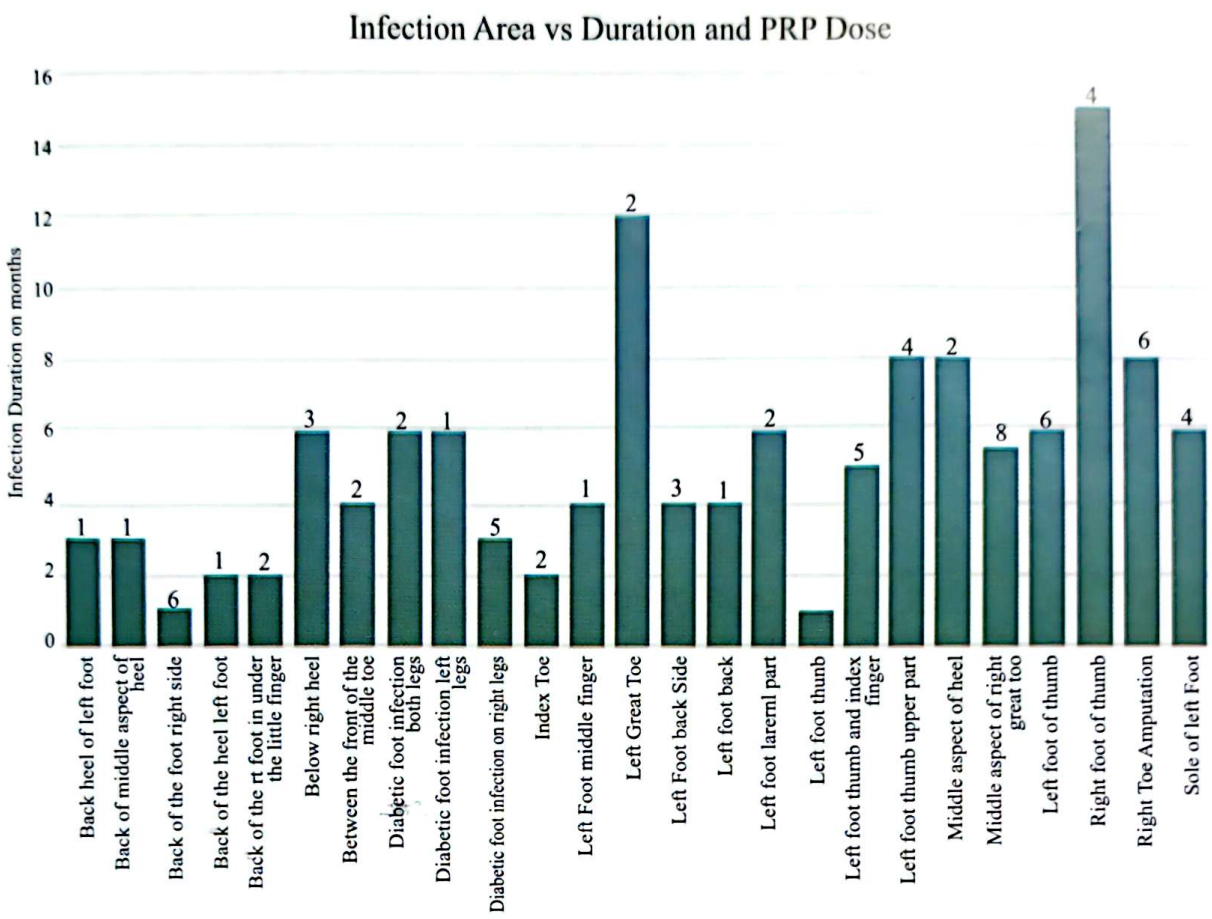
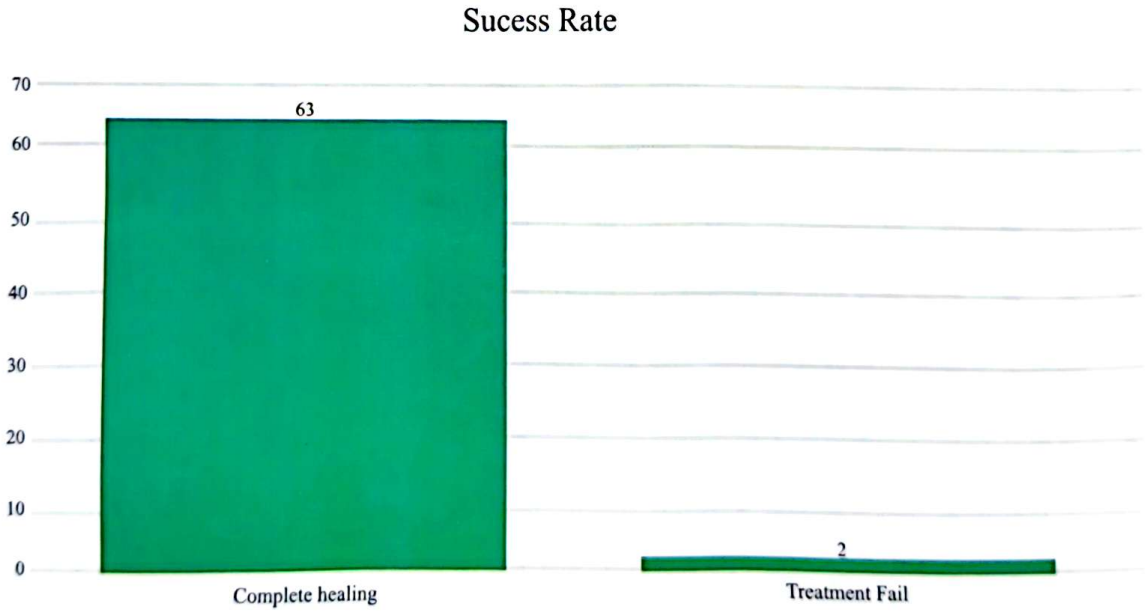


Figure VIII: Infection area vs duration and PRP dose of diabetic patients (n=65)



All the time treatment fail due to Paitent neglagency.

Figure IX: Success rate of PRP dose of diabetic patients (n=65)

DISCUSSION

One of the most common causes of ulcers is growth factor abnormality. Platelets are considered a rich source of growth factors. PRP enhance wound healing by either the barrier effect to prevent bacterial invasion into the wound or the growth factors stimulating wound healing.[4]A total of 65 patients were enrolled. Mean age of the patients was 55.0±15.44 years. Diabetic history from 45 years to 65 years was the highest age group. Male and female were 37 (56.9%) and 28 (43.1%) respectfully. Various types of PRP systems exist with variable platelet, leukocyte, and growth factor concentrations. Chronic inflammatory responses against foreign invaders are made possible by leukocytes including lymphocytes, monocytes, neutrophils, eosinophils, and basophils. Recent evidence has shown that leukocyte levels within PRP may have controversial effects on wound healing.[8] Of the studies included in the review, Perez Zabala et al.,[9] reported using leukocyte-poor PRP with high average healing rates of 1.46 cm2/wk. Complication rates after the topical application of PRP were low. Besides the 2.2% incidence of transient wound infections and 0.3% incidence of contact dermatitis, no other adverse effects were reported. The complication rates were significantly lower compared to the 11.1% incidence of wound infection and 0.8% incidence of skin maceration among patients receiving conventional wound treatment. However, further higher-quality studies with randomized controlled trials are necessary to justify the use of PRP over more cost-effective treatment methods. Most publications apply PRP only on the wound but we apply both activated PRP and PPP. Plasma Rich Protein enrich the wound with multiple growth factors for cell migrations and neo-angiogenesis while PPP contains nutrients for healing.[10] Figure VIII showed detailed results of different areas affected and treated. Saad et al.,[11] compared the results of both PRP and PPP on ulcer healing and showed that healing in PRP group was faster ($P < 0.005$) than PPP. Our findings mirrored those of Lone et al.,[12] who used PRP to treat DFUs. They showed that 62.85% of patients developed granulation tissue by the end of the second week and 77.78% of patients reached 100% granulation at the end of the 3rd week.[13]Also, McAleer et al.,[14] reported good results of PRP in chronic foot ulcers in a 57-year-old man. Another study reported the synergistic effect of both autologous adipose tissue and PRP in a case study of a diabetic 65-year-old male patient who had a foot ulcer for 3 years.[15] Scimeca et al.,[16] published the successful result for the treatment of chronic plantar diabetic ulcers in a 49-year-old man using PRP.[17] Figure IX showed that the PRP dose success rate of complete healing is 63 (95.9%) and treatment fall 2 (3.07%). A retrospective cohort of 599 patients with diabetic foot ulcers was published and reported complete healing in 50% of patients undergoing PRP treatment and 41% of patients not treated with PRP.[18] Future studies can improve by designing more prospective comparative trials, increasing study sizes, and standardizing clinical outcome measures such as healing rates, percentage of ulcers completely healed, and ulcer area at baseline and final follow-up. Another possible limitation of this review is that other relevant studies on this topic could have been excluded, despite conducting a systematic search.

CONCLUSION

Foot ulcers affect the quality of life of diabetic patients. In our study, the results confirm that the use of PRP and PPP increases the ulcer healing rate. These results provided a promising method for ulcer treatment. The future of PRP therapy is promising and still evolving. PRP is being used increasingly in fields such as dermatology, cosmetic surgery, and dentistry, as well as sports medicine and orthopedics. Further randomized controlled studies that show clinical outcome improvement in multiple parameters are necessary to evaluate the true efficacy of this treatment.

Conflict of Interest: None

Source of Fund: Nil.

Authors' Contribution: All authors contributed to this present study.

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