



OUTCOME OF PRP TREATMENT IN PATIENTS WITH INFRAORBITAL DARK CIRCLES

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Abstract

Infraorbital dark circles are not medically significant, but they are unsightly for many people, especially women, and can arise at any age. PRP speeds wound healing and tissue regeneration.

Objective: To determine outcome of PRP treatment in patients with infraorbital dark circles.

Study Design: This Descriptive study was held in the Dermatology Department of JPMC, Karachi from 31st December 2020 to 30th June 21.

Methods: Patients gave verbal agreement to prospectively collect data. 76 diagnostically qualified patients were included. Quantitative data was given as standard deviation and mean and qualitative factors as percentages and frequency. To determine how effect modifiers affected the result variable, stratification was used. Post stratification chi square test was applied taking p-value ≤ 0.05 as significant.

Results: This study comprised 76 patients who met inclusion and exclusion criteria. The average age and duration of dark circles in our study were 47.14 ± 8.49 years and 5.72 ± 2.24 months. There were 62 (81.6%) successful outcomes and 14 (18.4%) unsuccessful outcomes.

Conclusion: Platelet-rich plasma improves infraorbital dark circles and is best and noninvasive.

Keywords: Platelet-rich plasma, infraorbital dark circle, Facial skin rejuvenation, success outcomes.

INTRODUCTION

Infraorbital dark circles, also known as idiopathic periorbital melanosis, cutaneous hyperchromia of the orbital region, pigmentation or hyperpigmentation and are much prevalent. Bilateral, circular, uniform macules across the infraorbital areas are dark rings¹⁻³. Dark circles can result from infection, inflammation, allergies, and lifestyle. The translucent and thin lower eyelid skin overlying the orbicularis oculi muscle, Excessive pigmentation and shadowing due to skin laxity because of tear trough and aging may cause dark circles. Sun exposure, drugs, hormonal causes, and pigmentary demarcation line extension may also contribute⁴⁻⁵. Aging, subcutaneous fat distribution and skin sagging may worsen it. Treating it is difficult due to its complicated and unknown pathogenesis⁶.

Infraorbital dark circles can cause major cosmetic issues, especially in women, making them look weary and aged and affecting their psychological and social well-being⁷. Eyelid surgery was the third most common surgery in 2013, with 216,000 performed. Soft tissue filler injection was the second most prevalent minimally invasive technique, with 2.2 million performed, up 13% from the previous year. The treatment of infraorbital dark circles depends on the etiology⁸⁻⁹. For extreme pigmentation, utilize topical chemical and bleaching peels. The autologous fat transplantation, fillers and lasers have mixed results. Laser therapy improved clinical assessment by 75.2% (2.8) and 73.1% (2.6) and patient satisfaction scale scores by 74% (2.4) and 71.5% (2.3) at 2 and 4 months, respectively. Despite several treatment strategies in the literature, most results are disappointing. Platelet-rich plasma (PRP) is an autologous suspension of platelets in a small volume of plasma with a platelet concentration above basal blood values, similar to other face rejuvenation and aesthetic dermatology procedures¹⁰⁻¹¹. It may be useful in treating infraorbital dark circles. A recent study found that roughly 80% of PRP patients were satisfied.

PRP comprises numerous angiogenic factors of growth counting transforming growth factor-beta (TGF- β), platelet-derived growth factor (PDGF), vascular endothelial growth factor (VEGF), epidermal growth factor (EGF) and fibroblast growth factor (FGF), to improve regeneration of tissues in medicine and surgery. Few researches have examined the usefulness of PRP for infraorbital dark circles¹²⁻¹³. All these studies had small samples. PRP in infraorbital circles can be more confidently validated by increasing sample size. The results of this study may improve patient management.

METHODS

This descriptive study took place in the JPMC Karachi Dermatology Department from 31st December 2020 to 30th June 21. Using the prevalence of satisfactory outcomes in patients with infraorbital circles undergoing PRP as 80% 5, confidence interval at 95%, and margin of error at 9% in Epi Info 7, the sample size was 76 and non-probability consecutive sampling was used for patient selection.

Criteria for inclusion:

Infraorbital dark circles were diagnosed as operationally defined as lasting over three months.

- Either gender

The age range is 18-60.

Criteria for exclusion:

- Pregnancy

- Breastfed

If you have a history of pro-coagulative or thrombophilic conditions,

If you have a history of bleeding/clotting disorders,

Platelet count <100,000/mL

This study was done at JPMC Karachi's dermatological clinic. The trial began after hospital ethical committee approval. 76 patients who met inclusion-exclusion criteria following informed consent were studied. All clinically diagnosed patients are checked by a dermatologist with over three years of expertise. In proforma, age, gender, DM, HTN, and smoking were recorded. Photographs were taken before and three months after treatment and scored globally. Patients' satisfaction was assessed at 3 months. The ultimate proforma score was satisfactory based on both scores.

In standard tubes with anticoagulant citrate dextrose solution-formula A (ACD-A) at a 9:1 ratio, 11 ml of whole blood was taken on procedure day. Tubes were centrifuged for 1 spin at 1630 g for 5 min in a multifunctional centrifuge. Plasma and buffy coat were isolated from blood. The buffy coat layer and one-third of the bottom plasma were applied.

All data was entered and analyzed in SPSS 20.0. For quantitative variables including age, dark circle duration, sleep duration, and screen time, descriptive statistics calculated mean and standard deviation. The frequency and percentages of qualitative characteristics like gender, hypertension, smoking, DM, family history, and good outcome were shown. Stratified effect modifiers (age, gender, disease duration, hypertension, smoking, DM, family history, and screen time) were examined for their impact on outcome variables using chi-square test, with p-value <0.05 considered significant

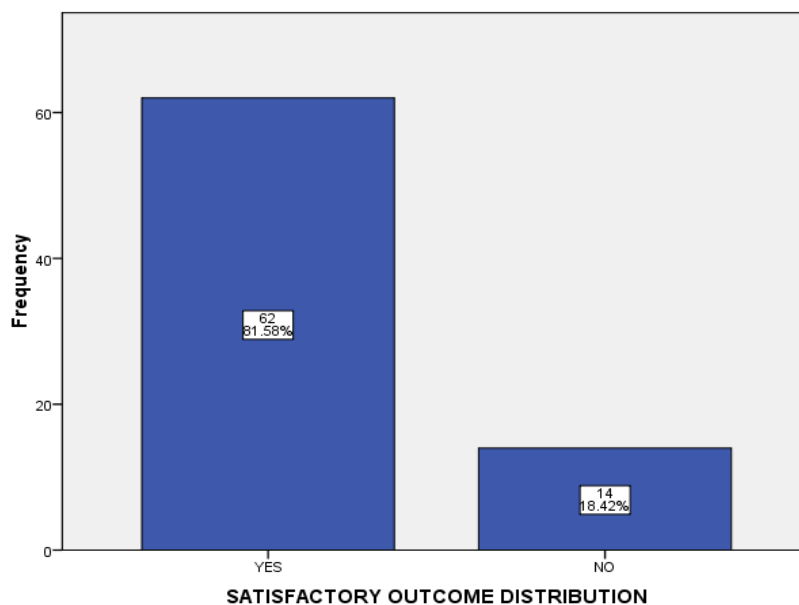
RESULTS

Patients ranged in age from 20 to 60 years of age. The average age and duration of dark circles in our sample were 47.14±8.49 years and 5.72±2.24 months, respectively. As in Table 1.

VARIABLE	MEAN ± SD	STANDARD DEVIATION	MIN-MAX
AGE (YEARS)	47.14	±8.49	20-60
DURATION OF DARK CIRCLE (MONTHS)	5.72	±2.24	3-8

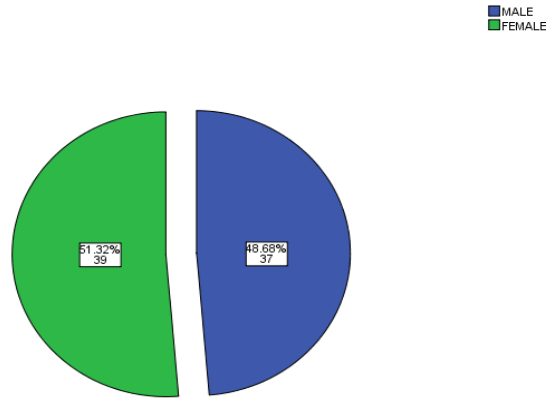
There were 62 (81.6%) patients with successful outcomes and 14 (18.4%) unsuccessful outcomes. As in Figure 1.

FIGURE-1: SATISFACTORY OUTCOME DISTRIBUTION n=76



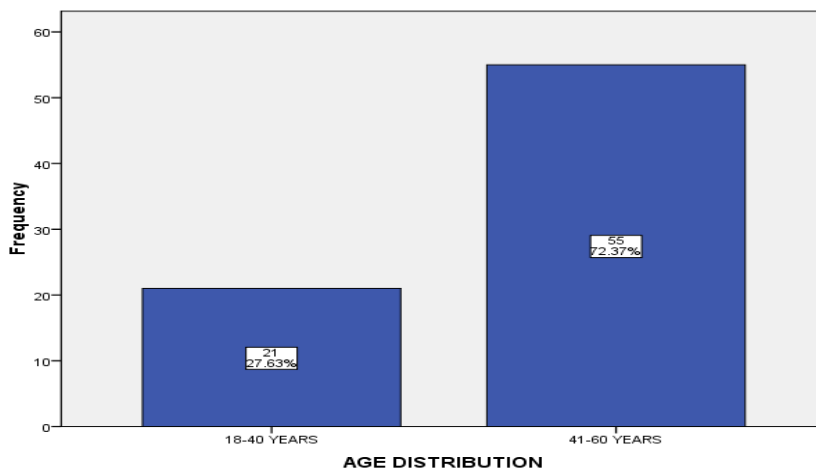
Of 76 patients, 37 (48.7%) were male and 39 (51.3%) female. As in Figure 2.

FIGURE-2: GENDER DISTRIBUTION, n=76



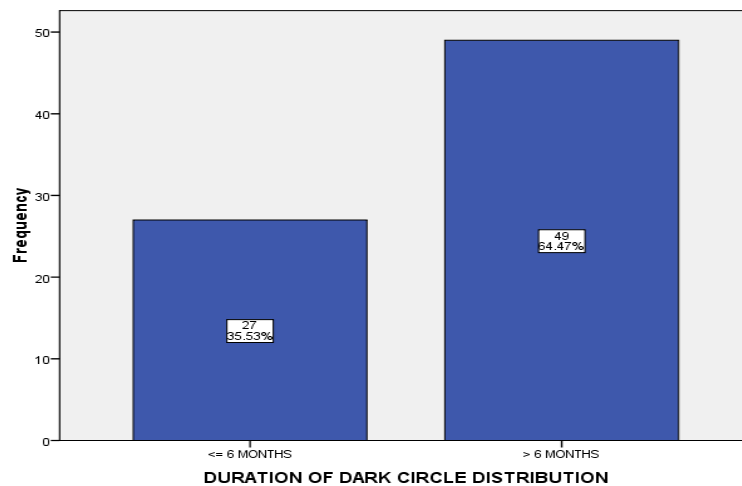
Age distribution showed that 21 (27.6%) and 55 (72.4%) of 76 patients were 18-40 and 41-60 years old. Figure 3.

FIGURE-3: AGE DISTRIBUTION, n=76



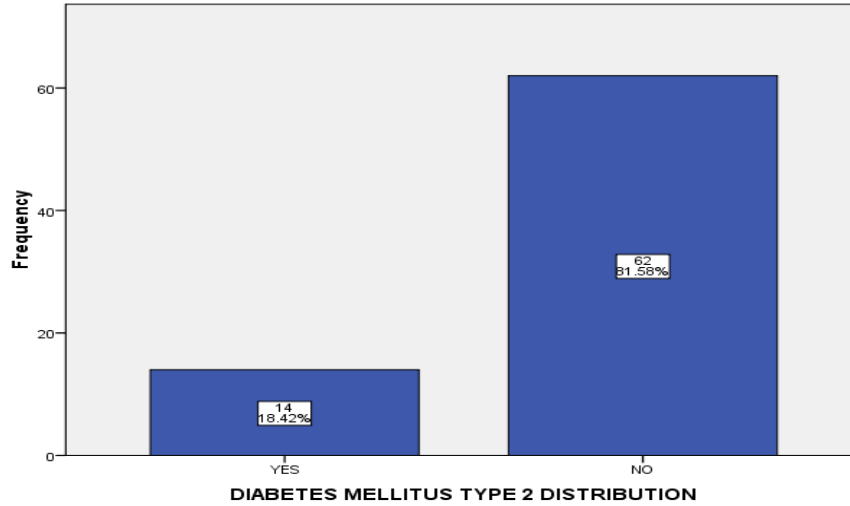
The frequency distribution of dark circle duration revealed that 18.4% of 76 patients had duration \leq 6 months and 81.6% had duration $>$ 6 months. Figure 4.

FIGURE-4: DURATION OF DARK CIRCLES DISTRIBUTION, n=76



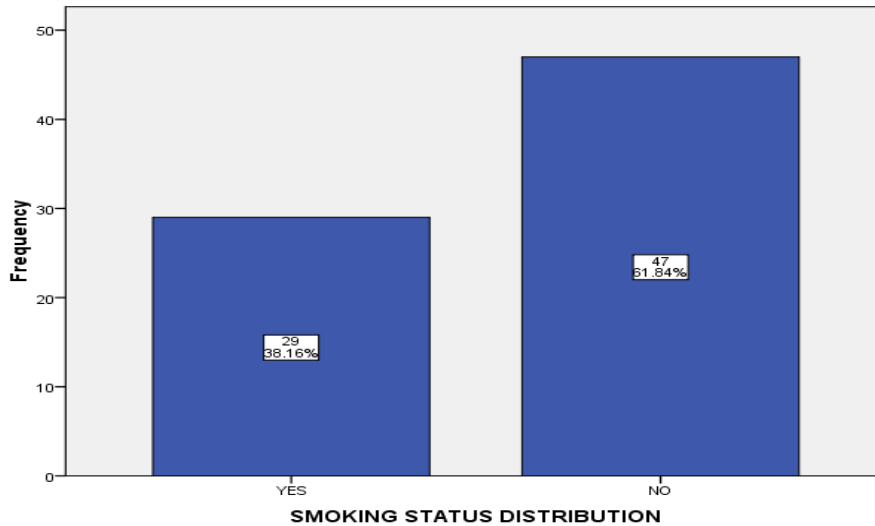
According to the frequency distribution, 14 (18.4%) of 76 individuals had diabetes type II and 62 (81.6%) did not. As seen in Figure 5.

FIGURE-5: TYPE 2 DIABETES MELLITUS DISTRIBUTION n=76



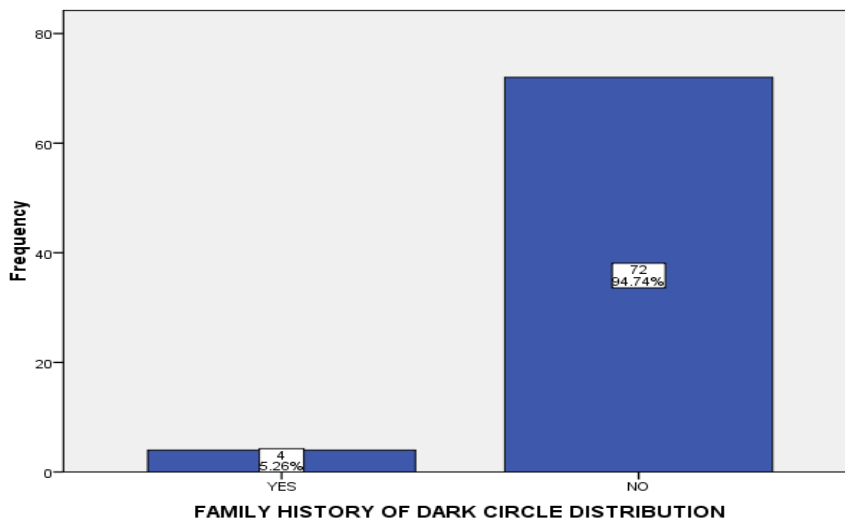
Hypertension was present in 18 (23.7%) of 76 individuals and absent in 58 (76.3%). See Figure 7. Out of 76 patients, 29 (38.2%) smoked and 47 (61.8%) did not. See Figure 6.

FIGURE-6: SMOKING STATUS DISTRIBUTION n=76



Out of 76 patients, 04 (5.3%) had family history of dark circle and 72 (94.7%) did not. Figure 9.

FIGURE-9: FAMILY HISTORY OF HAVING DARK CIRCLES DISTRIBUTION, n=76



Only 29 (78.4%) of males achieved satisfactory outcomes, while 08 (21.6%) did not. While 33 (84.6%) and 06 (15.4%) females obtained unsatisfactory results. P-value 0.48. According to Table 2.

GENDER	SATISFACTORY OUTCOME		TOTAL
	YES	NO	
MALE	29 (78.4%)	08 (21.6%)	37 (100%)
FEMALE	33 (84.6%)	06 (15.4%)	39 (100%)
TOTAL	62 (81.6%)	14 (18.4%)	76 (100%)
P-VALUE	0.48		

51 (82.3%) urban residents had satisfactory outcomes, while 11 (17.7%) did not. Whereas 11 (78.6%) and 03 (21.4%) rural residents obtained satisfactory results. P-value 0.74. As shown in Table 3.

TABLE-3: SATISFACTORY OUTCOME ACCORDING TO RESIDENCE STATUS, n=76

RESIDENCE STATUS	SATISFACTORY OUTCOME		TOTAL
	YES	NO	
URBAN	51 (82.3%)	11 (17.7%)	62 (100%)
RURAL	11 (78.6%)	03 (21.4%)	14 (100%)
TOTAL	62 (81.6%)	14 (18.4%)	76 (100%)
P-VALUE	0.74		

Family history of dark circle was stratified by good outcome into 04 (100%) and 00 (00%) patients. Those without a dark circle family history experienced 58 (80.6%) and 14 (19.4%) bad outcomes. P-value 0.32. Table 4.

TABLE-4: SATISFACTORY OUTCOME ACCORDING TO FAMILY HISTORY OF DARK CIRCLES, n=76

FAMILY HISTORY OF DARK CIRCLES	SATISFACTORY OUTCOME		TOTAL
	YES	NO	
YES	04 (100%)	00 (00%)	04 (100%)
NO	58 (80.6%)	14 (19.4%)	72 (100%)
TOTAL	62 (81.6%)	14 (18.4%)	76 (100%)
P-VALUE	0.32		

Patients in the illiterate, primary, secondary, and higher educational groups had satisfactory outcomes at 03 (75%), 04 (50%), 22 (81.5%), and 33 (89.2%). Among illiterate, primary, secondary, and higher education patients, 01 (25%), 04 (50%), 05 (18.5%), and 04 (10.8%) achieved satisfactory outcomes. P-value 0.07. According to Table 5.

TABLE-5: SATISFACTORY OUTCOME ACCORDING TO EDUCATIONAL STATUS

EDUCATIONAL STATUS	SATISFACTORY OUTCOME		TOTAL
	YES	NO	
ILLITERATE	03 (75%)	01 (25%)	04 (100%)
PRIMARY	04 (50%)	04 (50%)	08 (100%)
SECONDARY	22 (81.5%)	05 (18.5%)	27 (100%)
HIGHER	33 (89.2%)	04 (10.8%)	37 (100%)
TOTAL	62 (81.6%)	14 (18.4%)	76 (100%)
P-VALUE	0.07		

DISCUSSION

Infraorbital dark circles are hard to assess and have a complex aetiology. Dark circles are not a medical concern, but they should be thoroughly assessed to determine the best therapy for this

unsightly problem. The complicated architecture and physiology of the orbital area make it important to analyze various infraorbital zones, as earlier research have shown¹⁴⁻¹⁵.

Our study included 76 participants who met inclusion and exclusion criteria. The average age and duration of dark circles in our study were 47.14 ± 8.49 years and 5.72 ± 2.24 months. There were 62 (81.6%) successful outcomes and 14 (18.4%) unsuccessful outcomes.

A follow-up after three and six months revealed moderate to good improvement in wrinkles (74.1,77.9%), nasolabial fold (51.9%,57.2%), periorbital dark circles (47.8,60.9%), and skin stiffness (52.3%,60.9%). The only circles of statistical significance (P value 0.031) were dark ones. In terms of periorbital dark circles (47.9%,74%), wrinkles (39.1%, 43.5%), and nasolabial folds (4.3%, 13.1%), therapeutic physicians observed moderate to good improvement¹⁶⁻¹⁷. Folds (P value 0.025) and dark circles (P value 0.008) showed statistical significance. In terms of periorbital dark circles (34.8%, 52.2%), wrinkles (26.1%, 34.8%), and nasolabial folds (4.4%, 13%), the second dermatologist demonstrated moderate to good improvement (P value 0.025). After three months, 80% of patients showed improvement, according to Mehryan et al. 90% of patients regarded their treatment as excellent or adequate, with a mean score of 1.7 on a 0-3. Three was the mean satisfaction score¹⁸⁻¹⁹. The injection caused burning in every patient. Only a small, temporary dermatorrhagia was an adverse impact. There were no significant or enduring adverse effects noted. Three months apart, Banihashemi et al. administered PRP twice to thirty patients. At three and six months, the majority of patients reported fair to extraordinary results for nasolabial folds, periorbital wrinkles, dark circles under the eyes, and skin firmness. Only 17% of patients experienced minimal or no improvement with their therapy. The treatment success was dependent on the patients, the treating physician, and another independent physician. The best outcomes were less wrinkles and dark circles²⁰⁻²¹.

To treat periorbital hyperpigmentation, Al-Shami administered three PRP injections each month to fifty patients. Results were reported by 4% of patients as excellent, 12% as substantial, 46% as fair, and 38% as poor. According to the medical evaluation, 60% of cases improved somewhat or significantly. More than half of the patients expressed satisfaction or high satisfaction with the outcomes²²⁻²³.

16 instances were studied by Kang et al. With infraorbital wrinkle treatment, 12.5% were ecstatic, 25% were quite satisfied, and 56.3% were satisfied. 62.5% of patients were satisfied with the infraorbital tone improvement, whereas 37.5% were extremely happy with it. Three reviewers blindly evaluated the cases and determined that 12.5% had improved, 18.8% had been fair, 56.3% had been terrible, and 12.5% had not. After PRP, the erythema index decreased from 8.52 to 7.37.

Elasticity improvement as evaluated by a cutometer was observed in 12 people by Cameli et al. Like in our experiment, there are three appointments every month for treatment²⁴. The canthal, forehead, cheeks, and nasolabial region were all treated. Medical outcomes for fine wrinkles and skin texture were good in 37.5% of cases, sufficient in 37.5%, and insufficient in 25% of cases²⁵.

CONCLUSIONS

Platelet-rich plasma rejuvenates skin and treats infraorbital dark circles safely and effectively. The treatment was successful, patient satisfaction was high, and no major side effects occurred. Further studies should quantify the minimum PRP volume to make therapy more pleasant. Dark circles are caused by many circumstances; thus, identification is required before therapy. Dark circles may have multiple causes, so doctors should be familiar with various treatments and address them individually.

REFERENCES

1. Sarkar R, Ranjan R, Garg S, Garg VK, Sonthalia S, Bansal S. Periorbital Hyperpigmentation: A Comprehensive Review. *J Clin Aesthet Dermatol*. 2016 Jan;9(1):49–55.
2. Freitag FM, Cestari TF. What causes dark circles under the eyes? *Journal of Cosmetic Dermatology*. 2007 Sep;6(3):211–5.

3. Park SR, Kim HJ, Park HK, Kim JY, Kim NS, Byun KS, et al. Classification by causes of dark circles and appropriate evaluation method of dark circles. *Skin Res Technol*. 2016 Aug;22(3):276–83.
4. Park KY, Oh IY, Moon NJ, Seo SJ. Treatment of infraorbital dark circles in atopic dermatitis with a 2790-nm erbium: yttrium scandium gallium garnet laser: a pilot study. *J Cosmet Laser Ther Off Publ Eur Soc Laser Dermatol*. 2013 Apr;15(2):102–6.
5. Mehryan P, Zartab H, Rajabi A, Pazhoohi N, Firooz A. Assessment of efficacy of platelet-rich plasma (PRP) on infraorbital dark circles and crow's feet wrinkles. *J Cosmet Dermatol*. 2014 Mar;13(1):72–8.
6. Ahmed NA, Mohammed SS, Fatani MI. Treatment of periorbital dark circles: Comparative study of carboxy therapy vs chemical peeling vs mesotherapy. *J Cosmet Dermatol*. 2019 Feb;18(1):169–75.
7. Ellabban NF, Eyada M, Nada H, Kamel N. Efficacy and tolerability of using platelet-rich plasma versus chemical peeling in periorbital hyperpigmentation. *J Cosmet Dermatol*. 2019 Dec;18(6):1680–5.
8. Nguyen HT, Isaacowitz DM, Rubin PA. Age- and fatigue-related markers of human faces: An eye-tracking study. *Ophthalmology*. 2009;116:355–60.
9. Gendler EC. Treatment of periorbital hyperpigmentation. *Aesthet Surg J*. 2005;25:618–24.
10. Rohrich RJ, Pessa JE. The fat compartments of the face: Anatomy and clinical implications for cosmetic surgery. *Plast Reconstr Surg*. 2007;119:2219–27.
11. Pessa JE, Zadoo VP, Mutimer KL, Haffner C, Yuan C, DeWitt AI, et al. Relative maxillary retrusion as a natural consequence of aging: Combining skeletal and soft-tissue changes into an integrated model of midfacial aging. *Plast Reconstr Surg*. 1998;102:205–12.
12. Nakra T. Biplanar contour-oriented approach to lower eyelid and midface rejuvenation. *JAMA Facial Plast Surg*. 2015;17:374–81.
13. Friedmann DP, Goldman MP. Dark circles: Etiology and management options. *Clin Plast Surg*. 2015;42:33–50.
14. Roh MR, Chung KY. Infraorbital dark circles: Definition, causes, and treatment options. *Dermatol Surg*. 2009;35:1163–71.
15. Epstein JS. Management of infraorbital dark circles. A significant cosmetic concern. *Arch Facial Plast Surg*. 1999;1:303–7.
16. Goldberg RA, McCann JD, Fiaschetti D, Ben Simon GJ. What causes eyelid bags? Analysis of 114 consecutive patients. *Plast Reconstr Surg*. 2005;115:1395–402.
17. Watanabe S, Nakai K, Ohnishi T. Condition known as “dark rings under the eyes” in the Japanese population is a kind of dermal melanocytosis which can be successfully treated by Q-switched ruby laser. *Dermatol Surg*. 2006;32:785–9.
18. Guerrero D. Dermocosmetic management of the red face and rosacea. *Ann Dermatol Venereol*. 2011;138(Suppl 3):S215–8.
19. Sidle DM, Decker JR. Use of makeup, hairstyles, glasses, and prosthetics as adjuncts to scar camouflage. *Facial Plast Surg Clin North Am*. 2011;19:481–9.
20. Bierman A, Figueiro MG, Rea MS. Measuring and predicting eyelid spectral transmittance. *J Biomed Opt*. 2011;16:067011.
21. Darlenski R, Surber C, Fluhr JW. Topical retinoids in the management of photodamaged skin: From theory to evidence-based practical approach. *Br J Dermatol*. 2010;163:1157–65.
22. Draelos ZD. Skin lightening preparations and the hydroquinone controversy. *Dermatol Ther*. 2007;20:308–13.
23. Nordlund JJ, Grimes PE, Ortonne JP. The safety of hydroquinone. *J Eur Acad Dermatol Venereol*. 2006;20:781–7.
24. Garcia A, Fulton JE., Jr The combination of glycolic acid and hydroquinone or kojic acid for the treatment of melasma and related conditions. *Dermatol Surg*. 1996;22:443–7.
25. Amnuait T, Maneenuan D, Boonme P. Evaluation of caffeine gels on physicochemical characteristics and in vivo efficacy in reducing puffy eyes. *J Appl Pharm Sci*. 2011;1:56.