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A Comparative Study of Therapeutic Response of Melasma To Glycolic Acid (Ga 50%) Versus Trichloroacetic Acid (Tca 10%) For Chemical Peeling

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Abstract
Background: *The treatment of melasma remains a challenge and a mild-moderate improvement is all that is achieved in the majority of patients with the therapeutic options ranging from photo protection, topical hypo pigmenting agents, chemical peels and lasers.* ***Objectives:*** *To compare 50% glycolic acid peel and 10% TCA peel for the treatment of melasma.* ***Material and Methods:*** *We selected 118 participants of melasma aged between 12 and 65 years from the dermatology outpatient department and treated equal numbers with 10% TCA and 50% glycolic acid.* ***Results:*** *Subjective response as graded by the patient showed good or very good response in 88% participants in the glycolic acid group and 84% in the TCA group.* ***Conclusions:*** *Glycolic acid showed highest efficacy in Fitzpatrick type V skin followed by TCA, although there is no significant statistical difference between efficacy of Glycolic acid and TCA in treatment of melasma. For epidermal melasma glycolic acid is preferred peeling agent*

Key Words: *Glycolic acid, TCA, Melasma, Chemical peels.*

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I. Introduction

Melasma is an acquired, chronic, recurrent hyperpigmentary disorder, clinically characterized by symmetric light-brown to bluish-gray macules and patches, with irregular, sharp borders. The pigmentation may be guttate, linear or confluent. Although this disorder has been considered a benign condition, which usually has only aesthetic implication, it may affect self-image and self-esteem, with a negative impact on patient's quality of life.

Melasma is classified into one of three histologic types: epidermal, dermal, and mixed. However, some also include a fourth type known as Wood's light inapparent[1].

As regards management, the therapeutic options range from photo protection, topical hypo pigmenting agents, chemical peels and lasers to a variety of less-tried systemic agents like fish oil, green tea and deoxyarbutin. Although no single agent has proved to be effective for all patients, a combination of two or three agents is often tried to achieve optimum results. In spite of this, the treatment of melasma remains a challenge and a mild-moderate improvement is all that is achieved in the majority of patients[2].

Chemical peeling is the application of a chemical agent to the skin, which causes the controlled destruction of a part or of the entire epidermis, with or without the dermis, leading to exfoliation and removal of superficial lesions, followed by the regeneration of new epidermal and dermal tissues[3]. Chemical peels are a well-known modality of treatment for melasma. The basic mechanism of the action of chemical peels in melasma is the removal of unwanted melanin by causing a controlled chemical burn to the skin. Peels have proved to be useful agents for melasma both as a sole treatment as well as an adjunct to other topical therapies.

Peels are classified as superficial, medium, and deep according to the depth of penetration of the peeling solution. The results of the procedure depend on the chemical used and its concentration, method of application, contact time, skin condition and prior preparation etc. Various agents used for chemical peeling are alpha-hydroxy acids such as glycolic acid, mandelic acid, beta- hydroxyl acid such as salicylic acid and other agents like Jessner's solution, pyruvic acid, trichloroacetic acid, phenol, resorcinol etc[4].

Since there are very few studies done on melasma in this area and considering the high prevalence of melasma among people with Indian skin type there is a need to study treatment modalities of melasma. We took up the study to compare the efficacy of glycolic acid and TCA peel in the treatment of melasma.

II. Material And Methods

118 patients with melasma were included in this single blinded randomized prospective comparative interventional study. All patients were recruited from the Outpatient Clinic of Dermatology and Venereology Department, Prathima Institute Of Medical Sciences, Karimnagar from the period of 2017 to 2019. The study was approved by the Institutional Ethics Committee. All patients were told about the risks of the procedure and a written informed consent was obtained from all patients, before participation in the study.

Patient Selection Inclusion Criteria

1. Those who are willing for study.
2. Newly diagnosed patients without prior treatment.
3. Patients who are regular for follow up.
4. Aged between 12 to 65 years.
5. Skin type IV-VI.
6. Epidermal Melasma
7. Dermal Melasma

Exclusion Criteria

1. Those who aren't willing for study.
2. Those who doesn't turn up for follow up.
3. Pregnancy and Lactation
4. Patients with keloidal tendency.

Wood's lamp examination was done for all patients to determine the type of melasma (dermal, epidermal, mixed). Priming was done for two weeks prior to the peeling procedure to allow a more uniform penetration of the peeling agent. Priming with 0.025% Tretinion cream over the lesions during night time and sunscreen during day time. In this study the patients were divided into two groups, with 59 patients in each group.

Group (A): were treated with 50% Glycolic acid

Group (B): were treated with 10% TCA

Each group was treated for 6 sessions for 2 weeks apart (3 months).

A post auricular test peel was performed in all patients to determine any hypersensitivity to the ingredients of the peeling agent. Patient was enrolled in the study unless patient had any untoward effect either to test peel or priming agent. Peeling procedure initiated after 2 weeks of priming.

Glycolic acid 50%, TCA 10%, spirit, acetone, gauze, cotton- tipped swabs, cold water, Vaseline, Sodium bicarbonate solution materials were used.

Post peel follow up:

During this entire study period the patients were advised to apply a broad- spectrum sunscreen at an interval of 2 hrs during daytime. No other topical treatment was advised. The patients were followed up for an additional 8 weeks to see if there was further improvement, maintenance or worsening of results.

Clinical improvement was assessed by MASI score and Digital photographs.

MASI SCORE (Melasma Area & Severity Index)

MASI score was calculated at baseline and after 1st, 2nd and 3rd month of the peeling procedure. Recorded the percentage of improvement of MASI score for each patient after the end of 3rd month of the treatment, from the baseline score.

Efficacy of the treatment=(MASI score before treatment -MASI score after treatment) ÷ MASI score before treatment × 100.

Clinical efficacy was categorized into:

- **Excellent response**; if more than 75% fall in MASI score.
- **Very good response**; if 50-75% fall in MASI score.
- **Good response**; if 25-50% fall in MASI score.
- **Poor response**; if less than 25% fall in MASI score.
- **No response**: when there was no change in MASI score at the end of the therapy.

Digital photographs were taken for all patients at baseline and after 1st,2nd and 3rd month of the peeling procedure.

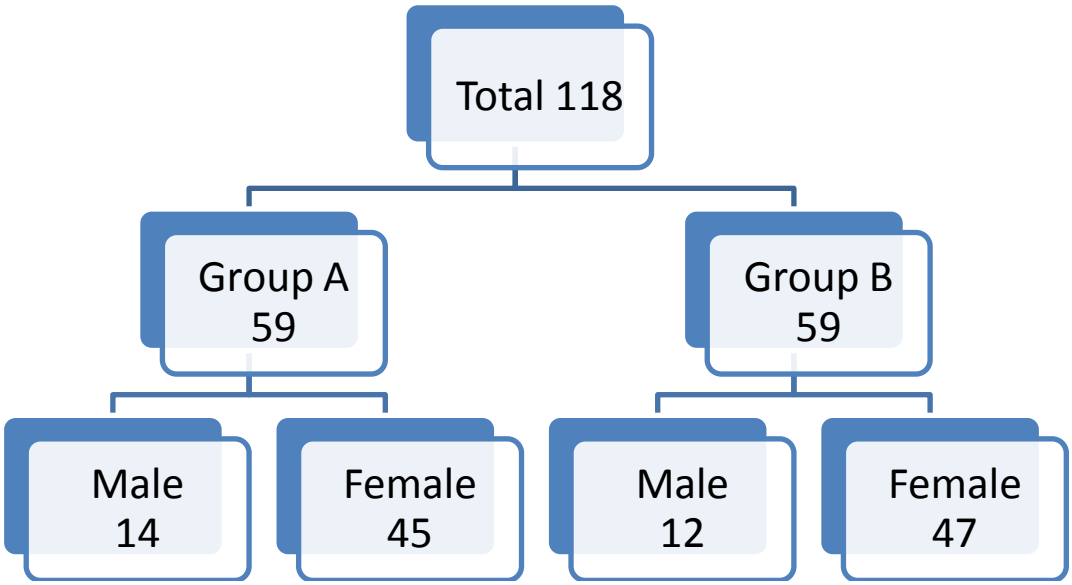
Statistical presentation and analysis:

Statistical presentation and analysis of the present study was conducted, continuous variables are presented as mean ± SD and discrete variables are shown as percentages. Chi square test is used for Categorical variables and t test or Kruskal–Wallis test is used for the Continuous variables. P less than 0.05 was considered significant. Software Statistical Package for Social Science (SPSS), v 20.0 was used.

III. Results

The present study was done to assess the efficacy of glycolic acid, TCA in chemical peeling in 118 patients of melasma who have full filled the selection criteria laid down earlier. The following observations were recorded in the present study.

Figure 1: Study Population



There was no significant difference among the study groups regarding the sex distribution of the patients (P value = 0.686)

Table 1 : Comparison among the study groups according to age of patients

Age	Group A	Group B	Total	Chi-Square	p-Value
≤ 20 Years	3(5.10%)	2(3.40%)	5(4.20%)	1.993	0.76
21-30 Years	8(13.60%)	5(8.50%)	13(11.00%)		
31- 40 Years	27(45.80%)	30(50.80%)	57(48.30%)		
41-50 Years	17(28.80%)	15(25.40%)	32(27.10%)		
> 50 Years	4(6.80%)	7(11.90%)	11(9.30%)		
Total	59(100%)	59(100%)	118		
Mean	36.47	38.68	**t-test : -1.993, p-value : 0.76**		
SD	8.85	8.95			

The youngest patient with melasma was 18 years old while the oldest was 58 years. The mean age of Group A is 36.47 ± 8.85, and Group B is 38.68 ± 8.95.(P value = 0.76) There was no significant difference among the study groups regarding the age of the patients (P value = 0.76)

Table 2 : Comparison among the study groups according to duration of disease of the patients.

Duration of Disease	Group A	Group B	Total	Chi-Square	P-value
≤ 2 Years	21(35.6%)	18(30.5%)	39(33.10%)		
3 - 4 Years	32(54.2%)	33(55.9%)	65(55.10%)		
≥ 5 Years	6(10.20%)	8(13.6%)	14(11.90%)		
Total	59(100%)	59(100%)	118(100%)	0.532	0.67
Mean	3.1	3.22			
SD	1.44	1.54	**p-value: 0.67**		

The mean duration of disease in group A is 3.1 ± 1.44 years, in group B is 3.22 ± 1.54 years. There was no significant difference among the study groups regarding the duration of the disease of the patients (P value = 0.67)

Figure 2: Fitzpatrick skin type of the patients.

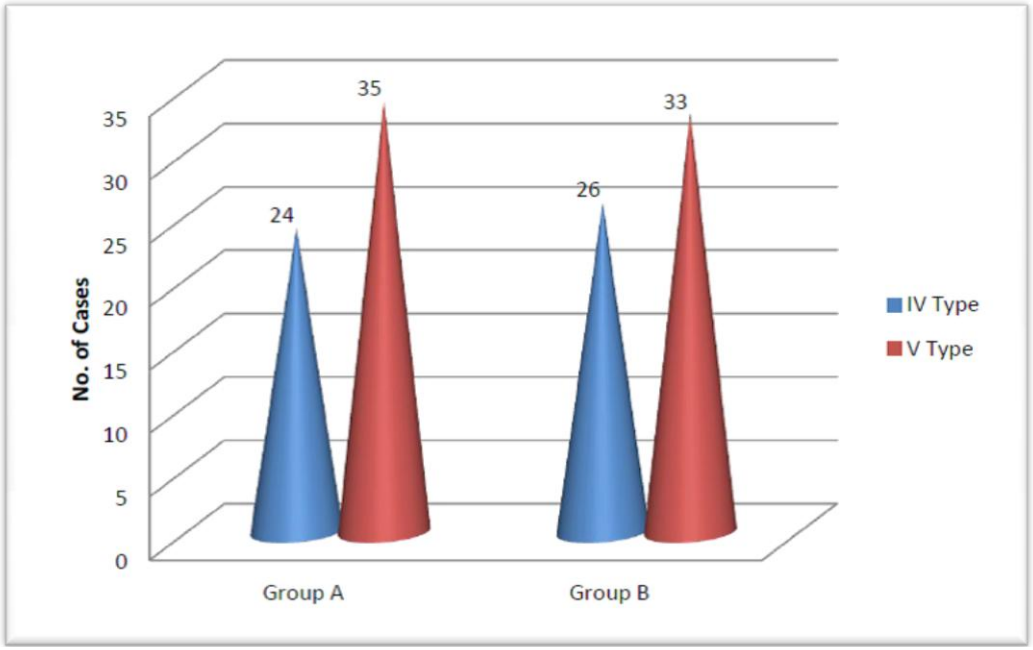


Table 3 : Comparison among the study groups according to MASI score before & after 1st , 2nd and 3rd month of peeling**.**

Group	Pre Peel	After 1 month	After 2 Months	After 3 Months
Group A	13.40 ± 2.10	11.69 ± 2.08	10.02 ± 2.18	7.51 ± 2.73
Group B	12.58 ± 3.46	11.02 ± 3.67	9.85 ± 3.52	7.59 ± 3.21
p-Value	0.12	0.238	0.764	0.89

The results obtained were compared on the basis of MASI score at base line, at the end of 1 month, 2 month and 3 month. In the 2 groups there was constant decrease in MASI scores after peeling procedures

Table 4: Difference between mean score in group A and group B

	Mean	SD	t-value	p-value
Group A				
Pre Peel	13.41	2.1		
After 3rd Month	7.51	2.73	21.01	<0.001**
Group B				
Pre Peel				
After 3rd Month	7.59	3.21	22.81	<0.001**

**p<0.001 is highly significant at 1% level of significance

Table 5: Response level between the groups

Response Level	Group A	Group B	Total	Chi-Square	p-value
Poor	7(11.90%)	6(10.20%)	13(11.0%)		
Good	28(47.50%)	35(59.30%)	63(53.4%)		
Very Good	17(28.80%)	15(25.40%)	32(27.1%)		
Excellent	7(11.90%)	3(5.10%)	10(8.50%)		
Total	59(100%)	59(100%)	118(100%)	2.57	0.461

Regarding the response to treatment in the different study groups,
In group A; excellent response was detected in 7 patients (11.90%), very good response was detected in 17 patients (28.80%) and good response was detected in 28 patients (47.50%). Poor response was seen in 7 patients (11.90%).
In group B; excellent response was detected in 3 patients (5.10%), very good response was detected in 15 patients (25.40%), good response was detected in 35 patients (59.30%) and poor response was detected in 6 patient (10.20%).
There was a statistically significant difference in the study groups as regard to the response to treatment. (p value = 0.461)
Regarding the side effects of the treatment in the different study groups, in group A, there were no side effects in 45 patients(76%); erythema in 6 patients (10.17%); Post inflammatory hyperpigmentation in 3 patients (5.08%).In group B, no side effects were reported in 41 patients (70%); burning sensation in 2 patients (3.39%); Erythema in 6 patients (10.17%); persistant erythema in 3 patients (5.08%); PIH in 3 patients (5.08%) and stinging in 4 patients (6.78%).

IV. Discussion

Melasma, though benign, can be extremely psychologically distressing and has been shown to have a significant impact on quality of life, social, and emotional wellbeing. There is no universally effective specific therapy, and no single therapy has proven to be of benefit to all patients as the sole therapy. The aim of the present study was to evaluate and compare the efficacy of 50% Glycolic acid, 10%TCA peel in treatment of melasma.

Melasma is more common in women of child-bearing age, although men also suffer from the condition and account for 10% of the cases. Melasma affects all races, but is observed more frequently among individuals with skin type IV–VI, especially in women of Hispanic, Caribbean, and Asian origin, who live in areas of intense ultraviolet radiation. There are three clinical patterns – centrofacial, malar, and mandibular – depending upon the area of localization. Histologically, melasma is divided into three types: epidermal, dermal, and mixed. Wood's light causes intensification of pigmentation in epidermal-type melasma, but does not enhance the pigmentation in the dermal type[5]. But this distinction may not be useful in pigmented races. A combination of epidermal and dermal macules is recognized as the mixed type.

AGE:

The youngest patient with melasma was 18 years old while the oldest was 58 years. The mean age of Group A is 36.47 ± 8.85, and Group B is 38.68 ± 8.95.(P value = 0.76) There was no significant difference among the study groups regarding the age of the patients (P value = 0.76)

Thus the present study results were in concurrence with the studies conducted by Javahari et al[6] and Kalla et al[7] with 78% were females and 22% were males. Female to male ratio was 4:1.. Hormonal factors like usage of oral contraceptive pills, thyroid disorders and pregnancy are responsible for high prevalence among the females.

DURATION OF DISEASE:

In the present study, mean duration of disease in group A is 3.1 ± 1.44 years, in group B is 3.22 ± 1.54 years. There was no significant difference among the study groups regarding the duration of the disease of the patients (P value = 0.67).
In a study by Bari et al[8] reported the duration of disease from 4 months to 12 years, with mean duration of 3.6 years. Hence the present study findings were in consistent with the above study.

CORRELATION BETWEEN EFFICACY OF TREATMENT WITH AGE GROUP

Correlation between efficacies of treatment with age of patients revealed an inverse relation where the patients with younger age had higher efficacy of the treatment than the elders in different study groups(r= 0.659) (p value < 0.0001).

Correlation between efficacies of treatment with duration of melasma revealed an inverse relation where the shorter duration of melasma had higher efficacy of treatment (r= - 0.098) (p value < 0.457)

Kalla et al[7] in their study also showed an inverse relationship between duration of disease and response to the treatment.

In the present study regarding the efficacy of treatment, there was a highly statistically significant difference in MASI score after treatment among the two study groups. There is no significant statistical difference between the efficacy of Glycolic acid and TCA in the treatment of melasma.

PRE DISPOSING FACTOR

In group A, 71.19% of the patients reported sunlight as the precipitating factor, followed by Hormonal (13.55%), family history (10.17%) and Cosmetics (5.10%).

In group B, 72.90% of the patients reported sunlight as the precipitating factor followed by Hormonal (13.60%), family history (8.50%) and Cosmetics(5.10%). There was no significant difference among the study groups regarding the duration of the disease of the patients (P value 1.0)

In a study by Dogra et al reported sunlight (74%), followed by pregnancy (44%), hormonal factors (24%)[9]. In an another study by Bari et al reported sunlight (79%) as the main precipitating factor, followed by pregnancy (44%), Hormonal factors (14%)[8]. Thus the findings in the present study were in accordance with the previous studies.

PATTERN OF MELASMA OF THE PATIENTS:

Most of the patients have Centrofacial followed by malar and mandibular pattern of Melasma. There was no significant difference among the study groups according to pattern of melasma of the patients (P value = 0.853).

In the present study regarding the efficacy of treatment, there was a highly statistically significant difference in MASI score after treatment among the two study groups.

Response level between the groups:

Regarding the response to treatment in the different study groups,

in group A; excellent response was detected in 7 patients (11.90%), very good response was detected in 17 patients (28.80%) and good response was detected in 28 patients (47.50%). Poor response was seen in 7 patients (11.90%).

In group B; excellent response was detected in 3 patients (5.10%), very good response was detected in 15 patients (25.40%), good response was detected in 35 patients (59.30%) and poor response was detected in 6 patient (10.20%).

There was a statistically significant difference between the study groups as regard the response to treatment. (P<0.001)

Hence the present study was in consistence with the Puri N study[10].

Glycolic acid :

In Group A there was highly significant decrease in mean MASI score from the baseline to the end of the treatment.

In a study by Puri N 35 % Glycolic acid peel was used for the treatment of Melasma[10]. In this study 70% of the Participants showed good or very good response. It was concluded that 35% GA was an effective peeling agent in the treatment of melasma.

In the present study also 93% of the participants showed excellent or very good or good response to the 50% GA peel. Hence the present study was in consistence with the Puri N study[10].

In an another study by Rashmi Kumari et al used 35% GA in the treatment of melasma. In her study the average MASI Score in the GA group decreased from 12.59 ± 7.58 at base line to 4.56 ± 2.98 at 12 weeks. A Significant decrease in MASI Score from baseline to 12 weeks was observed in GA group with statistically significant results (P < 0.001) [11].

In our study the average MASI Score in the GA group decreased from 13.40 $\pm$2.10 at base line to 7.51 ± 2.73 at 12 weeks. A Significant decrease in MASI Score from baseline to 12 weeks was observed in GA group with statistically significant results (P<0.001)

The beneficial effect of glycolic acid is due to its smallest molecular weight of all the alpha hydroxyl acids which become more active and penetrates the skin more deeply, diminishes corneocyte adhesion in the upper layers of the epidermis, causing an epidermolytic effect, facilitating the removal of melanized keratinocytes,

leading to melanin pigment loss and acceleration of skin turnover. GA directly inhibits melanin formation in melanocytes as well.

In Ball AKL et al study, the efficacy of superficial glycolic acid peels alone in the management of melasma was done. Though improvement was seen in 88% of patients, most of them had mild (32% patients) and moderate (40% patients) improvement. Marked improvement was seen in only 14% patients[12].

In our study also 88.10% of the participants of Group A showed excellent or very good or good response to the 50% GA peel.

TCA PEEL:

Trichloroacetic acid (TCA) peel is a cost effective, simple office procedure used for a plethora of indications like acne, postinflammatory hyperpigmentation, melasma, xanthelasma, solar lentigines and actinic keratosis.

Sonia Valkova et al in their study, a statistically significant decrease in average MASI scores after treatment was observed in both Group I and Group II (Group I – MASI before treatment 13,8±9,4; after treatment 5,0±1,2; t=18,9; p<0,001; Group II - MASI before treatment 14,6±7,7; MASI after treatment 6,2±1,9; t=16,3; p<0,001)[13]. No statistically significant difference was found between MASI values after the two therapeutic regimens (t=0,12; p>0,05), as well as among MASI scores of patients with phototypes II, III and IV (MASI after treatment for phototype II - 6,0±2,7, for phototype III - 6,8±1,5 and for phototype IV - 7,7±2,2; t=0,25; p>0,05).

In the present study also MASI score decreased from 13.40 ± 2.10 to 7.51 ± 2.73 in group A and 12.58 ± 3.46 to 7.59 ± 3.21 in group B at 12 weeks. No statistically significant difference was found between MASI values of the two therapeutic groups. This is in accordance with Sonia Valkova et al.

MASI score before and after treatment in Epidermal melasma patients:

GA & TCA are time tested and has shown good response in epidermal melasma patients in Asia. In an another study by Achar A et al, There was good to fair response in patients with epidermal melasma, in comparison to patients with mixed melasma, while no significant improvement was seen in dermal melasma patients. The present study was in consistent with the Achar A et al study[14].

In epidemal melasma patients, treated with Glycolic acid the percentage change in MASI score (70%) is more than the TCA peel (65%).

MASI score before and after treatment in Dermal melasma patients.

In dermal melasma patients, treated with TCA the percentage change in MASI score(19.75%) is more than the GA peel (14.95%). Dermal melasma has often been resistant to topical treatments, but marked improvement was seen in patients who had failed other topical treatments with tretinoin, hydroquinone and steroids.

SIDE EFFECTS OF PEELING:

In glycolic acid group, erythema and PIH was reported in 15.23% of the patients in each complication.

In TCA peel, erythema, burning sensation was noticed in 13.56%, PIH seen in 5.08%. stinging sensation was seen in 6.78% patients. In comparison to GA peel TCA has more incidence of side effects.

Rivas SH et al reported erythema and stinging as complications[15]. Similarly sarkar et al reported only focal erythema and stinging as side effects[16]. Rendon M et al reported complications in the form of PIH.[17]

V. Conclusion

The present study was undertaken to assess the therapeutic efficacy of chemical peeling with Glycolic acid and Trichloroacetic acid in melasma patients.

In the present single blinded, randomized, prospective, comparative interventional study 118 patients of melasma were divided into 2 groups, A & B with 59 patients in each group. Group A and B were treated with 50% glycolic acid & 10% TCA respectively for 2–4 minutes once every 2 weeks for three consecutive months. MASI score was calculated at baseline and after 1st, 2nd and 3rd month of the peeling procedure.

In all the groups the maximum number of patients were in the age group of 31 to 40 years with mean age of 36.47 ± 8.85 and 38.68 ± 8.95 for group A and B respectively. Females were affected more than the males in the ratio of 4:1 The mean duration of the disease for group A & B is 3.1 ± 1.44 and 3.22 ± 1.54 respectively.

In Group A, 71.19% of the patients reported sunlight as the precipitating factor, followed by hormonal (13.55%), family history (10.17%) and cosmetics (5.1%). In Group B, 72.90% of the patients reported sunlight as the precipitating factor, followed by hormonal (13.60%), family history (8.50%) and cosmetics (5.10%). This clearly proves the role of multiple factors in the etiopathogenesis of melasma.

Epidermal, mixed and dermal melasma was observed in 47.45%, 30.5% and 22.05% of the patients respectively. The most frequent Fitzpatrick skin type was V (57.62%) followed by IV(42.38%). In majority of

the patient the pattern of melasma was centrofacial (51.70%) followed by malar (44.90%) and mandibular (3.40%).

In the present study; there was no significant difference among the study groups regarding the clinical data as regards age, duration of the disease, predisposing factors, Fitzpatrick skin phototype, pattern of melasma and Wood's light examination of the patients, hence the results can be comparable.

Glycolic acid showed the highest efficacy in Fitzpatrick type V skin followed by TCA, although there is no significant statistical difference between the efficacy of Glycolic acid and TCA in the treatment of melasma. For epidermal melasma glycolic acid is preferred peeling agent.

Correlation between efficacies of treatment with age of patients revealed an inverse relation where the patients with younger age had higher efficacy of the treatment than the older ($r = -0.623$) (p value< 0.05).

Correlation between efficacies of treatment with duration of melasma revealed an inverse relation where the shorter duration of melasma had higher efficacy of treatment than the longer duration. ($r = -0.634$) (p value <0.05).

Regarding the side effects of the treatment in the different study groups, in group A, there were no side effects in 45 patients(76%); erythema in 6 patients (10.17%); Post inflammatory hyperpigmentation in 3 patients (5.08%).

In group B, no side effects were reported in 41 patients (70%); burning sensation in 2 patients (3.39%); Erythema in 6 patients (10.17%); persistant erythema in 3 patients (5.08%); PIH in 3 patients (5.08%) and stinging in 4 patients (6.78%).

There was no statistically significant difference in regard to the efficacy between group A & group B (p value = 0.472). Compared to TCA, Glycolic acid is safe peeling agent.

Based on the observations noted in the present study, it may be concluded that the melasma occurs predominantly in young female adults with most common clinical presentation of centrofacial pattern and malar pattern seen frequently with type IV and V fitzpatrick skin types. The main predisposing factors for melasma are sunlight, followed by hormonal, pregnancy, family history and cosmetics.

Glycolic acid showed the highest efficacy in Fitzpatrick type V skin followed by TCA, although there is no significant statistical difference between the efficacy of Glycolic acid and TCA in the treatment of melasma. For epidermal melasma glycolic acid is preferred peeling agent. Compared to TCA, Glycolic acid is safe peeling agent. In young patients with short duration of melasma better response to the treatment was noticed.

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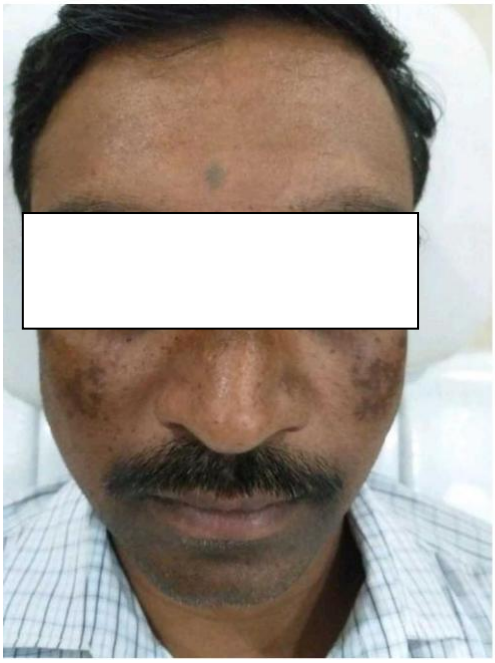
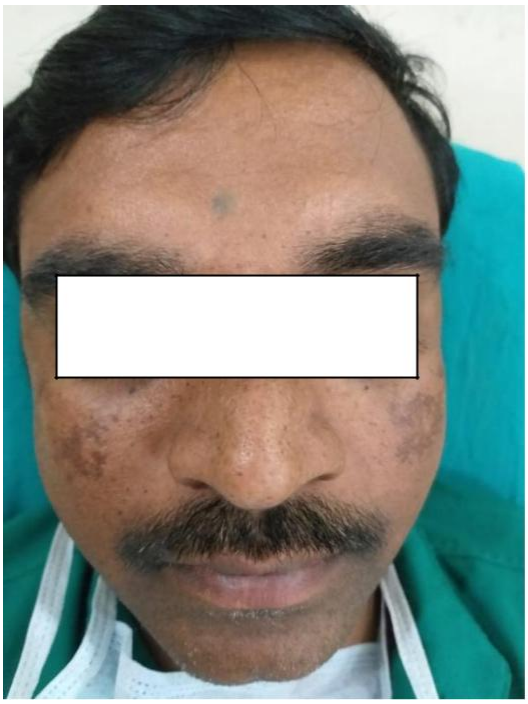
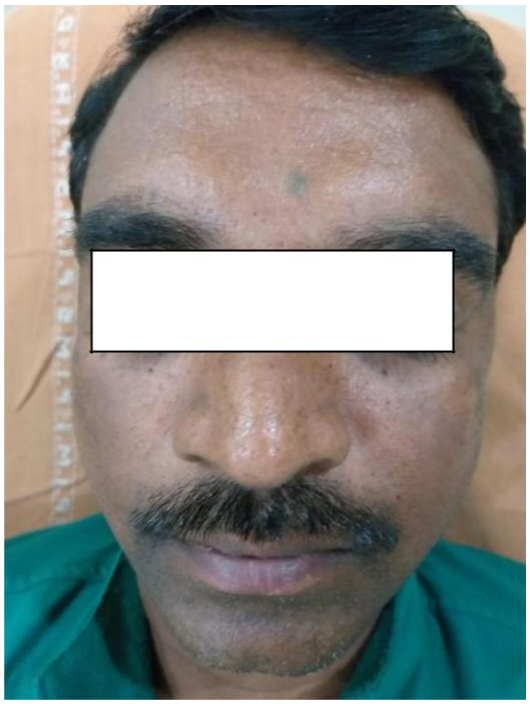
Digital photographs

Case-1
Treatment with GA peel

Pre peel **After 1 month**



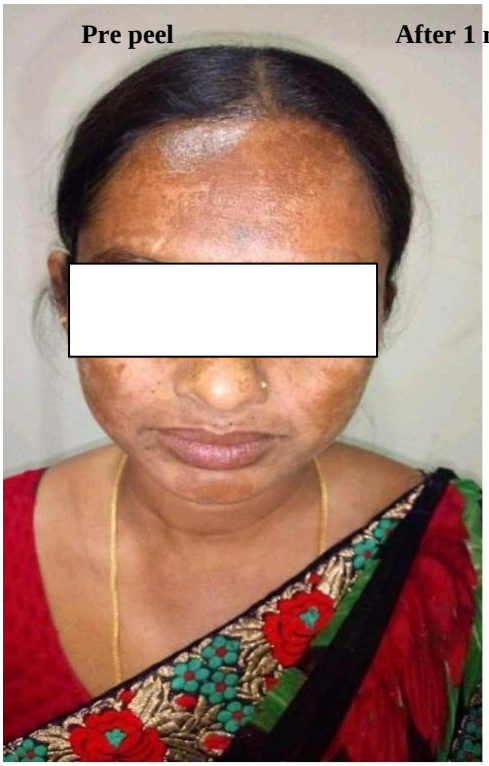

After 2 months **After 3 months**

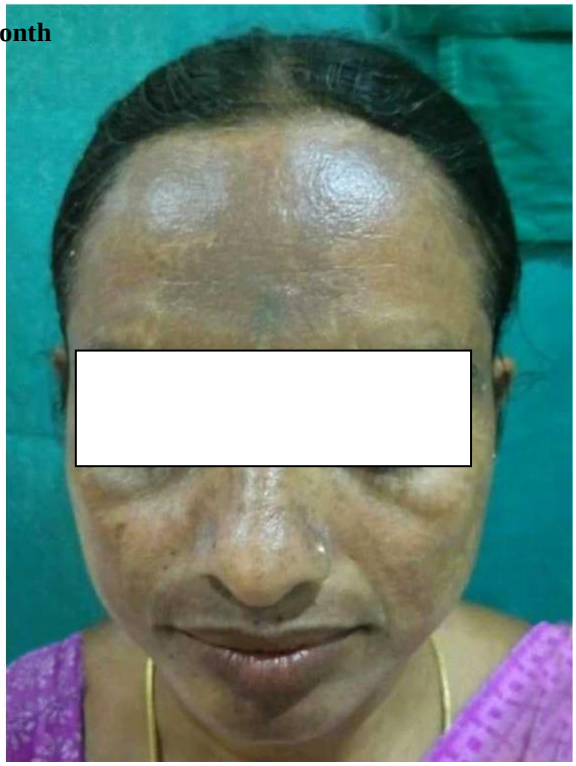



Case -2

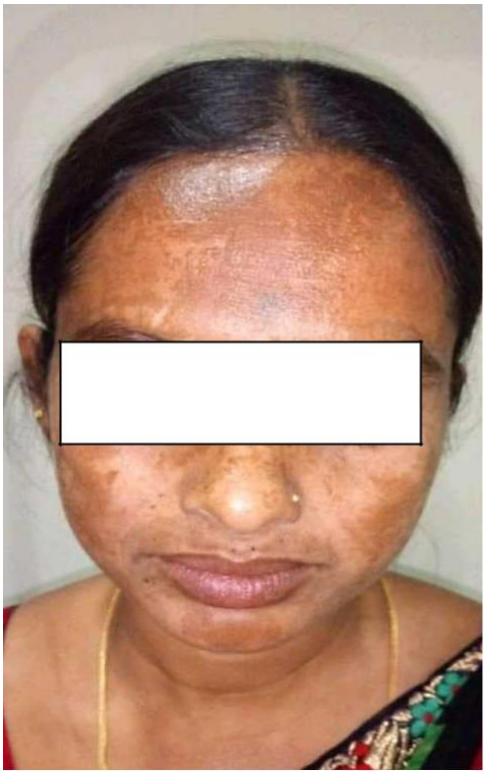
Treatment with GA peel

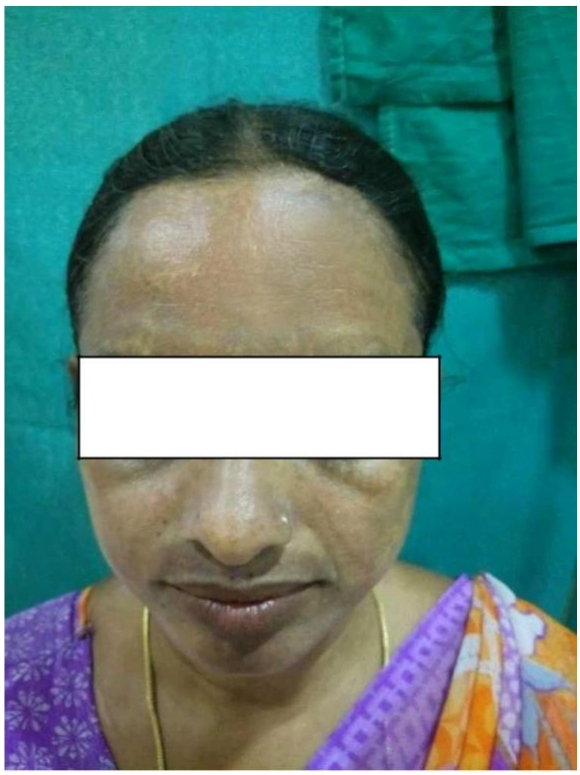
Pre peel **After 1 month**





After 2 months **After 3 months**

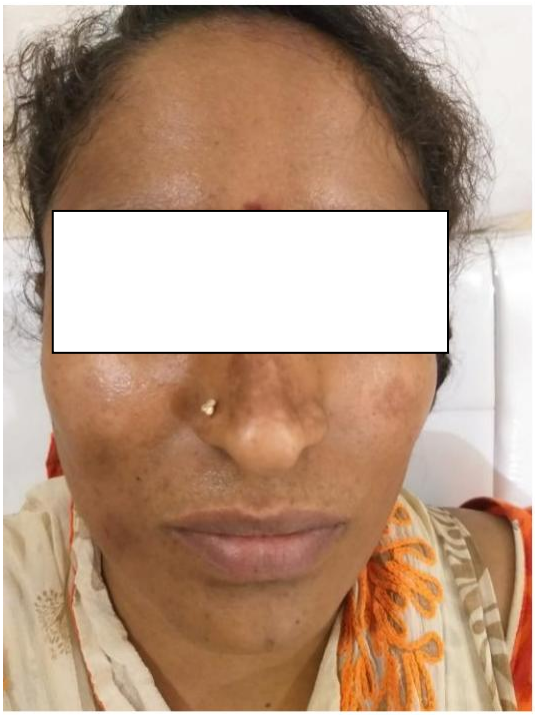


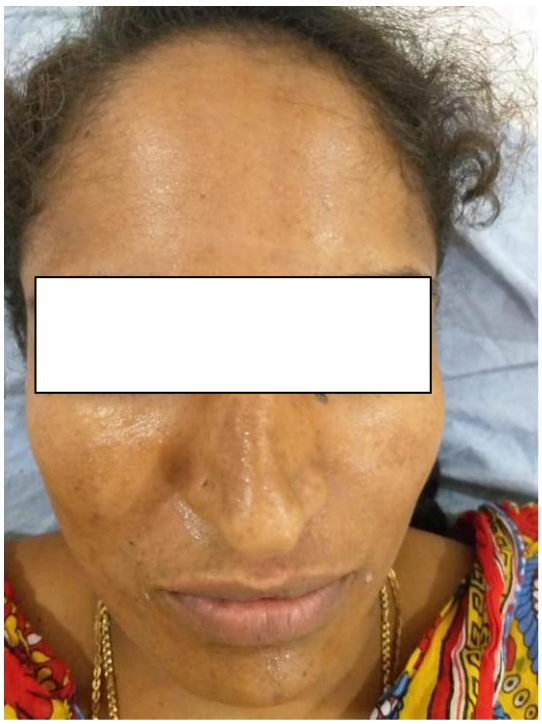


Case – 3

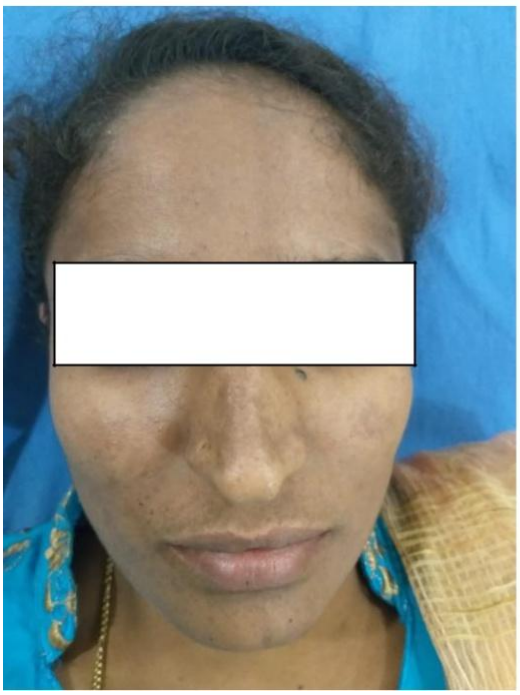
Treatment with TCA peel

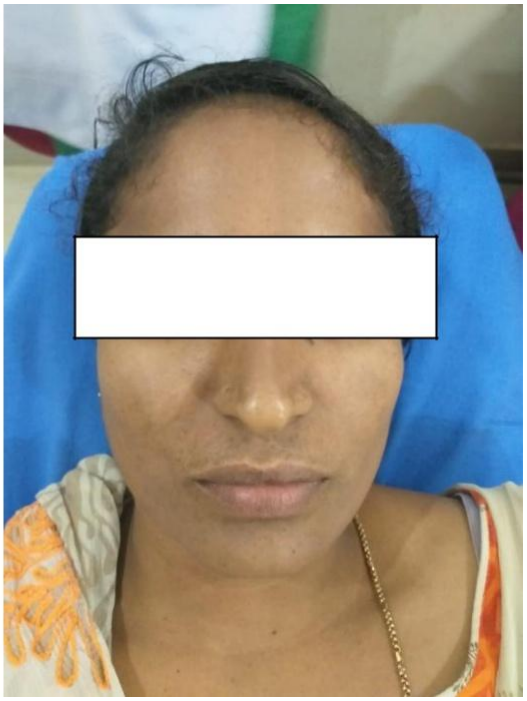
Pre peel **After 1 month**





After 2 months **After 3 months**

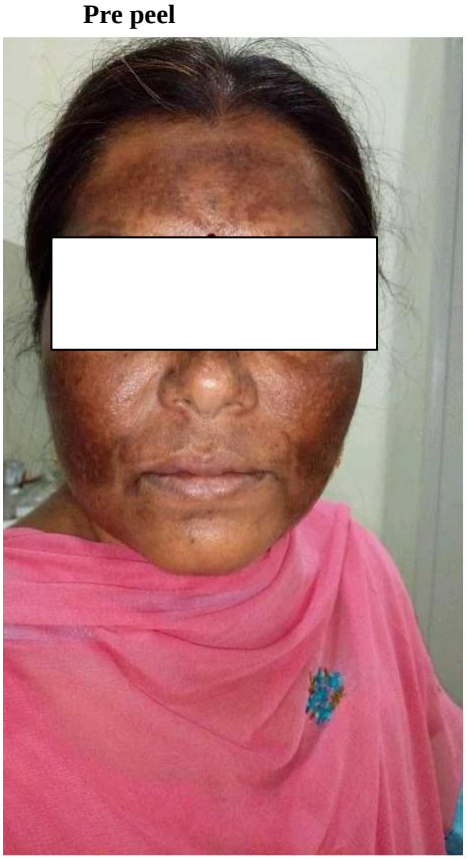


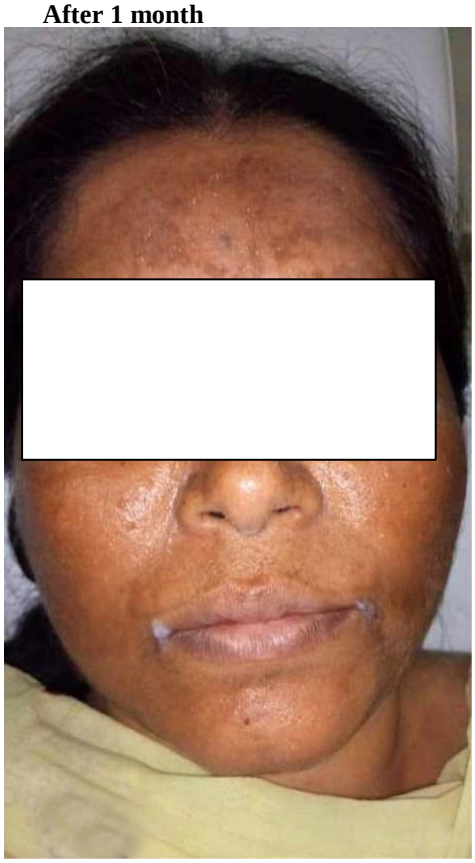


Case – 4

Treatment with TCA peel

Pre peel **After 1 month**





After 2 months **After 3 months**