Original Article

Skin Changes on the Face Caused by Over-the-counter Cosmetic Creams: An Observational Study of Clinical and Dermoscopy Features

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ABSTRACT

Introduction: One of the most often prescribed medications in dermatology is TCS (Topical Corticosteroids). Misuse and extended usage of TCS over the face cause "Topical steroid damaged/dependent face" (TSDF). The adverse effect of prolonged topical Hydroquinone (HQ) complicates with Exogenous Ochronosis (EO). Here, we have evaluated clinical and dermoscopic features in the facial skin that is affected by the application of TCS and HQ and attempted to correlate them with histopathological features. **Objectives:** To evaluate clinical, dermoscopic, and histopathological features of EO and TSDF. And to compare features with the duration and potency of TCS. **Materials and Methods:** This was a cross-sectional observational study carried out at a tertiary care hospital. The research included a total of 70 patients who had clinical signs of EO or TSDF. Their demographic information, clinical characteristics, and dermoscopy results were noted. Skin biopsy was done in a few lesions (6 from TSDF and 1 from EO) and statistical analysis was done. **Results:** Dermoscopic features were diffuse red dots (94.28%), brown globules (84.3%), terminal hair (88.6%), vessels (90%), and white structureless areas (61.43%). Features such as curvilinear brown to grey pigment globules, linear vessels, and follicular obliteration suggestive of EO were found in 11 (15.71%). Focal atrophy of the epidermis, focal parakeratosis, dilated capillaries with extravasation of erythrocytes, and perivascular and perifollicular infiltration was noted in histopathology. **Conclusion:** Dermoscopic features due to TCS and HQ were correlated with histopathological changes and it also creates awareness about the long-term adverse effects of inadvertent use of TCS.

Keywords: Topical Corticosteroids, Hydroquinone, Dermoscopy, Cosmetic cream, Awareness.

INTRODUCTION

In the Indian subcontinent, people have a mindset of looking fair which leads to the usage of many cosmetic creams on the face. Hence, many over-the-counter (OTC) topical preparations consisting of corticosteroids and hydroquinone are easily available. Topical corticosteroid (TCS) is among the most widely utilized medications in dermatology because it provides quick relief of symptoms in almost all inflammatory dermatoses. Sulzberger and Witten initially presented it as compound F (hydrocortisone) in 1952.[1] Based on the cutaneous vasoconstrictive property the TCS is divided into seven classes. Class I: super potent corticosteroids, Class II: high-potent corticosteroids, Class III: medium- potent corticosteroids, Class IV and V: medium- potent corticosteroids, Class VI: low-potent corticosteroids, Class VII: least-potent corticosteroids.[2] Corticosteroids have melanopenic, anti-

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pruritic, immunosuppressive, and anti-inflammatory action. Although it is a useful drug, it is known to cause substantial local, systemic as well as psychological negative effects when used excessively or incorrectly.[3]

In the Indian market, TCS is readily available as an over-the-counter drug. Improper use and long-term usage of the drug without medical supervision, especially on the face, has negative consequences that Lahiri and Coondoo have marked as TSDF.[4] TSDF is defined as the indiscriminate, unsupervised, irrational, or extended use of TCS that produces a variety of cutaneous symptoms and signs and psychological dependence on the substance, as well as permanent or semi-permanent damage to the skin on the face.[5,6] It is characterized by telangiectasia, perioral dermatitis, dryness, acneiform eruptions, pustules, erythematous papules, rosacea such as features, and red face syndrome. Treating it has become a battle for both patients and dermatologists. Early identification of TSDF is needed before they become irreversible. The TSDF diagnosis is primarily on the basis of its clinical manifestations. The adverse effect of prolonged topical hydroquinone (HQ) complicates exogenous ochronosis (EO) which is typified by pigmented blotches in caviar-like patterns with depigmented macules.[7]

'Dermoscopy' is an examination of surface and subsurface structures of the skin. It is performed by an instrument called a 'dermoscope' which enables the visualization of skin structures in a magnified way with aid of optical physics and polarization. It is a non-invasive diagnostic complementary tool in dermatology and helps in the precise identification of a variety of inflammatory dermatoses.[8] It shows exactly what is happening in the epidermis and papillary dermis. Hence, it is a reflection of histopathological changes that occur. Thus, each dermoscopic feature correlates well with the histopathological change.[9] Utility of dermoscopy in TSDF and; EO is reported which shows diffuse red areas, focal white areas, brown globules, follicular plugs, Demodex tails, and white hairs, and; obliteration of follicular openings and curvilinear pigment globules respectively. Telangiectasias are noted in both in a variable degree.[10,11] Dermoscopy and histopathological correlation in EO is described.[12] However, the dermoscopic and histopathological correlation of features in TSDF is not described in the literature. Here, the authors evaluated clinical and dermoscopic features in the facial skin that is affected by the application of TCS and HQ, and further compared features with the potency and duration of TCS. An attempt to correlate histopathological features with dermoscopic patterns was made. It may help bring new therapeutic inventions in the future.

MATERIALS AND METHODS

This was cross-sectional observational research conducted on patients presenting to the dermatology outpatient department in a tertiary care hospital connected to "S. Nijalingappa Medical College" in South India between October 2021 and June 2022. Institutional ethical clearance was obtained (SNMC/IECHSR/2021-2022/A-3/1.0). An informed written consent was taken from the participants. **Inclusion criteria:** Patients (over the age of 18) having clinical symptoms suggestive of TSDF or EO. Patients having a history of TCS usage for more than 30 days of continuous use or more than three months of intermittent use and patients who had a history of HQ application (alone or in combination with TCS) for more than 3 months. **Exclusion criteria:** History of rosacea and patients with comorbidities that can cause alterations similar to TSDF (like polycystic ovaries, thyroid disorders, and Cushing's syndrome), and ongoing treatment with oral corticosteroids. Patients were subjected to clinical evaluation. The data regarding demographics, potency, and duration of TCS usage and strength of HQ was recorded. The patients were categorized into 2 groups on the basis of the effectiveness of the TCS used: one used TCS efficiency class I/II and the other used class III/above. Dermoscopy of the target lesion was done with Illuco IDS-1100, 10 X magnification attached to iPhone 12 Pro. Few selected lesions of both TSDF and EO (where patients agreed to skin biopsy) were subjected to histopathological study. Hematoxylin and eosin stains were used. Patients were later educated about the negative impacts of TCS and HQ abuse. Clinical analysis was done by authors HLA, BSA; Dermoscopic assessment was done by authors BSA, CR; Histopathological study was done by author BPN.

Statistical analysis

Data from clinical, histopathological, and dermoscopic studies were tabulated. The statistical data analysis was carried out using "SPSS Statistics" for Windows v20.0 ("SPSS Inc, Chicago, USA"). Continuous variables like duration and age are defined as means±standard deviations. Percentages are used to display discrete variables. Fisher's χ^2 and Chi-square test were applied to statistically express the correlation between qualitative variables like the absence or presence of histopathological and dermoscopic features. $P<0.05$ was deemed statistically significant.

RESULTS

A total of 70 patients were enrolled in the research with females (64, 91.43%) and males (6, 8.57%),

most of them belonging to the age group of 31-40. Females constituted the majority. Twenty-two and 48 patients were using class I/II and class III/above TCS respectively. The most common clinical features included erythema and hypertrichosis in 62 (88.5%) patients each (Figures 1a and 2a). Females outnumbered males with respect to hypopigmentation with p 0.008. Dermoscopic features included diffuse red areas and Demodex tails in 66 (94.2%) and 13(18.5%) patients respectively (Figures 1b and 2b). Features such as curvilinear brown to grey pigment globules, linear vessels, and follicular obliteration suggestive of EO were found in 11 (15.71%) [Figures 3a, 3b, 4a, 4b]. Other types of clinical features are depicted in Table 1, dermoscopic features in Table 2, and in Figures 5a, 5b, 6a, 6b, 7a, and 7b. None of the dermoscopic features were statistically significant when compared in males and females.

There were 32 patients (45.71%) who used TCS for a time more than a year, ranging from one month to six years.

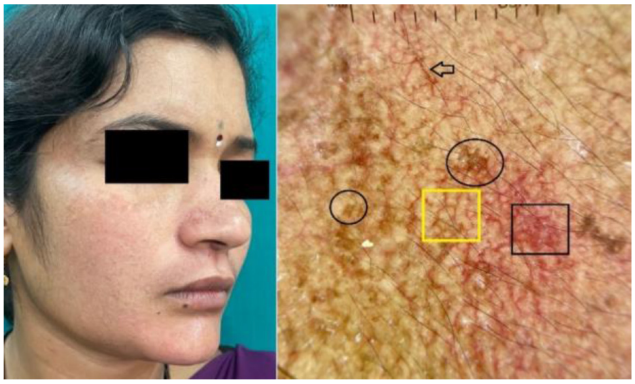

Figure 1a: Clinical image of the topical steroid-damaged face showing diffuse erythema, telangiectasia, and hypertrichosis with rough skin.
Figure 1b: Dermoscopy shows diffuse red areas (black box), brown globules (black circles), and linear and branching vessels (black arrow). Note the vascular polygon (yellow box).

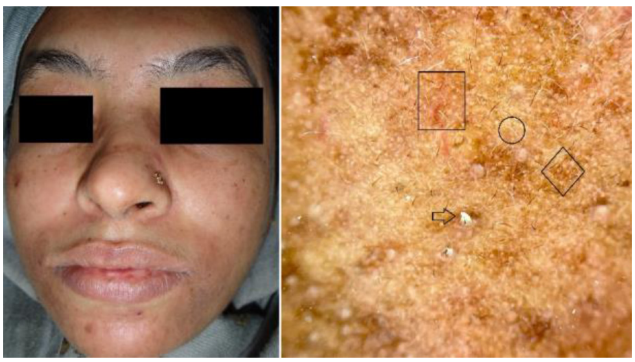

Figure 2a: Clinical image of the topical steroid-damaged face showing diffuse erythema, with dry and rough skin.
Figure 2b: Dermoscopy shows diffuse red areas (box), brown globules (diamond), Demodex tails (arrow), and white hair (circle).

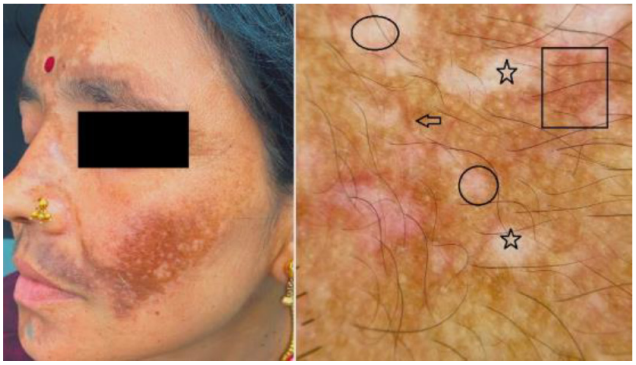

Figure 3a: Clinical image of exogenous ochronosis showing diffuse brown pigmentation with confetti-like white macules.
Figure 3b: Dermoscopy shows diffuse red areas (black box), focal white areas (black stars), and linear vessels (black arrow). Note the obliteration of follicular openings (black circles).

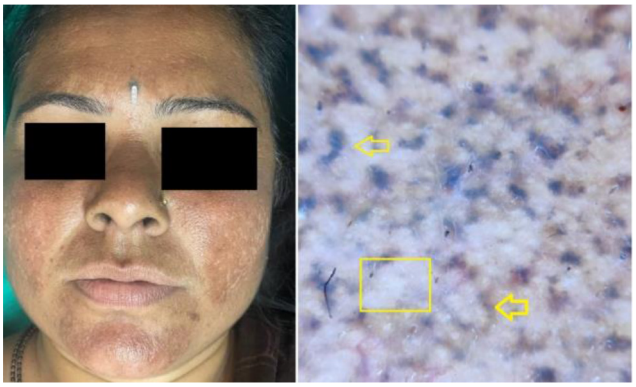

Figure 4a: Clinical image of exogenous ochronosis showing diffuse brown pigmentation with confetti-like white macules and rough skin.
Figure 4b: Dermoscopy shows brown and grey curvilinear pigment structures (black arrows) and obliteration of follicular openings (black box).

Table 1: Clinical findings due to topical corticosteroids and hydroquinone.

Clinical features	Male (%) n = 6	Female (%) n = 64	*P* value
Erythema	5 (83.3)	57 (89.1)	0.67
Hyperpigmentation	5 (83.3)	56 (87.5)	0.77
Telangiectasia	4 (66.7)	37 (57.8)	0.67
Hypertrichosis	5 (83.3)	57 (89.1)	0.67
Scaling	0 (0)	14 (21.9)	0.20
Acne	0 (0)	11 (17.2)	0.27
Wrinkles	1 (16.7)	7 (10.9)	0.67
Hypopigmentation	6 (100)	28 (43.8)	0.008

Statistical difference was found in clinical and dermoscopic features as well in the class of TCS used. Erythema and telangiectasia were appreciated more with class III/above TCS as compared to class I/II. The diffuse red area, white hairs, focal white areas, and EO were prominently seen

Table 2: Dermoscopic findings due to topical corticosteroids and hydroquinone.

Dermoscopic features	Male (%) *n*= 6	Female (%) *n* = 64	*P* value
Diffuse red areas	6 (100)	60 (93.8)	0.53
Brown globules	5 (83.3)	54 (84.4)	0.95
Exogenous ochronosis	1 (6.7)	10 (15.6)	0.95
Terminal hair	5 (83.3)	57 (89.1)	0.67
Focal white area	3 (50)	40 (62.5)	0.55
White hair	2 (33.3)	26 (40.6)	0.73
Follicular plugging	2 (33.3)	14 (21.9)	0.52
Comedones	2 (33.3)	16 (25)	0.66
Demodex tails	0(0)	13 (20.3)	0.22
Vascular structures (dermoscopy)			
Serpentine	2 (33.3%)	44 (68.7%)	0.08
Linear	4 (66.6%)	42 (65.6%)	0.96
Y-shaped	1 (16.6%)	29 (45.3%)	0.17
Polygonal	0(0%)	20 (31.2%)	0.10
Arcuate	1 (16.6%)	10 (15.6%)	0.94
Globular	0 (0%)	6 (9.3%)	0.43

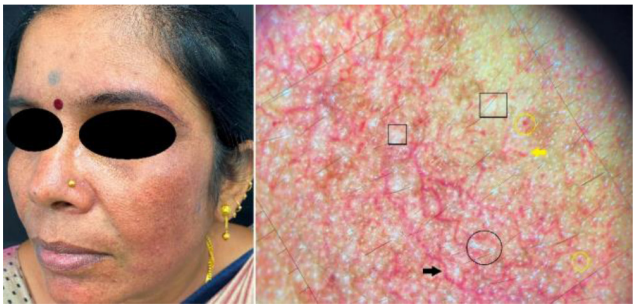

Figure 5a: Clinical image of the topical steroid-damaged face showing diffuse erythema, telangiectasia, hypertrichosis, and acne.
Figure 5b: Dermoscopy shows linear and branching (black arrow), globular (yellow circles), and arcuate (yellow arrow) vessels. Note the focal white areas (black box) and white scales (black circle).

($p < 0.05$) with class III/above TCS. Details are shown in Tables 3 and 4. Morphological types of telangiectasia under dermoscopy included serpentine in 56 (80%), linear in 46 (65.71%), Y-shaped in 30 (42.85%), polygonal in 20 (28.57%), and arcuate vessels in 11 (15.71%). Statistical significance was not found in vascular structures either with duration or potency of TCS. As mentioned above, a skin biopsy was done on a few lesions (6 from TSDF and 1 from EO). Histopathological features included focal parakeratosis, epidermal atrophy, and dilated capillaries with extravasation of erythrocytes. Perivascular and perifollicular infiltration of neutrophils were other findings. In addition, ochre bodies were observed in EO

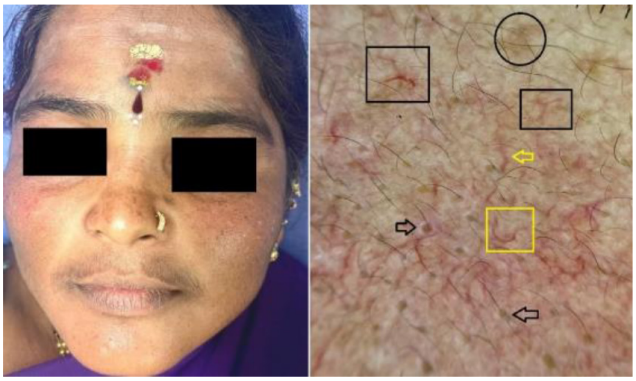

Figure 6a: Clinical image of the topical steroid-damaged face showing diffuse erythema, telangiectasia, hypertrichosis, and acne.
Figure 6b: Dermoscopy shows follicular plugs (black arrows), Y-shaped (black box), arcuate (yellow box), and linear (yellow arrow) vessels. Note the brown globules (black circle).

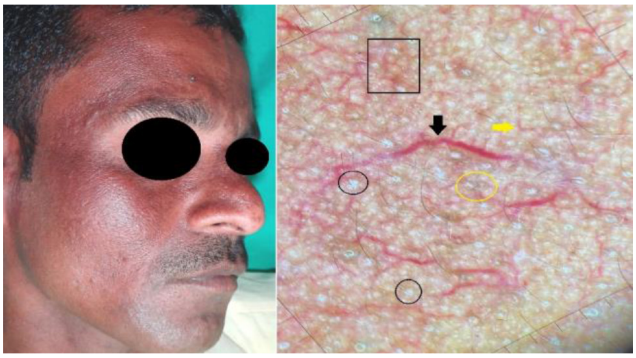

Figure 7a: Clinical image of the topical steroid-damaged face showing diffuse erythema and acne.
Figure 7b: Dermoscopy shows thick linear and branching (black arrow), arcuate (yellow arrow), and polygonal (black box) vessels. Note white hair (yellow circle) and perifollicular scales (black circle).

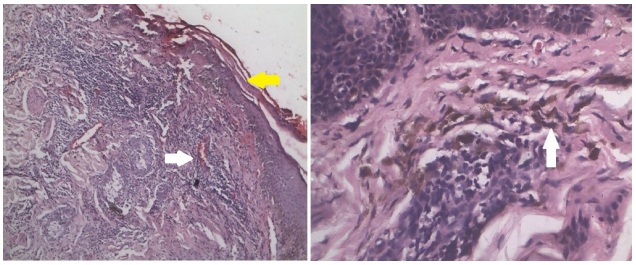

Figure 8a: Histopathology of the topical steroid-damaged face showing focal parakeratosis, epidermal atrophy (yellow arrow), and dilated capillaries with extravasation of erythrocytes. Note the perivascular and perifollicular infiltration of neutrophils (white arrow) [H and E, 10X].
Figure 8b: Histopathology of exogenous ochronosis showing epidermal atrophy neutrophilic infiltrate with ochre bodies (white arrow) [H and E, 40X].

lesions (Figure 8a, 8b). Dermoscopy and histopathological correlation are described in Table 5.

Table 3: Comparison of clinical findings due to topical corticosteroids and hydroquinone based on the potency of the steroid.

Clinical features	The potency of topical steroids		
	Class I /II (%) *n* = 22	Class III (%) *n* = 48	*P* value
Erythema	14 (63.6)	48 (100)	<0.0001
Hyperpigmentation	17 (77.3)	44 (91.7)	0.95
Telangiectasia	3 (13.6)	38 (79.2)	<0.0001
Hypertrichosis	19 (86.4)	43 (89.6)	0.69
Scaling	1 (4.5)	13 (27.1)	0.29
Acne	4 (18.2)	7 (14.6)	0.70
Wrinkles	0(0)	8 (16.7)	0.42
Hypopigmentation	6 (27.3)	28 (58.3)	0.16

Table 4: Comparison of dermoscopic findings due to topical corticosteroids and hydroquinone based on the potency of the steroid.

Dermoscopic features	Class I /II (%)	Class III (%)	*P* value
Diffuse red areas	18 (81.8)	48 (100)	0.002
Brown globules	16 (72.7)	43 (89.6)	0.72
Exogenous ochronosis	11 (50)	0 (0)	<0.0001
Terminal hair	19 (86.4)	43 (89.6)	0.69
Focal white areas	7 (31.8)	36 (75)	0.001
White hair	2 (9.1)	26 (54.2)	<0.0001
Follicular plugging	6 (27.3)	10 (20.8)	0.55
Comedones	7 (31.8)	11 (22.9)	0.43
Demodex tails	2 (9.1)	11 (22.9)	0.17
Vascular strucutres (dermoscopy)			
Serpentine	16 (72.7%)	40 (83.3%)	0.30
Linear	14 (63.6%)	32 (66.6%)	0.80
Y-shaped	10 (45.4%)	20 (41.6%)	0.76
Polygonal	8 (36.3%)	12 (25%)	0.32
Arcuate	5 (22.7%)	6 (12.5%)	0.27
Globular	2 (9.1%)	4 (8.3%)	0.91

DISCUSSION

TCS is among the most often recommended topical drugs. However, widespread exploitation and misuse of the face results in TSDF.[13] The key factor contributing to abuse is the wide availability of medications as cosmetic creams or fairness creams. Furthermore, EO results are due to the prolonged use of HQ. It is well known that many preparations which are perceived as cosmetic creams by people have combined ingredients of TCS and HQ.[7] TSDF represents a difficult issue for both the patient and the attending dermatologist. Initially, the patient could begin taking TCS for certain mild cases of dermatosis like melasma or acne. At first, the anti-inflammatory, as well as vasoconstrictive influences of TCS, lead to what seems to be a resolution of the main dermatosis, but their continued use leads to epidermal atrophy, dermal degeneration structures, and collagen degradation within a few months.[14] A variety of mechanisms, such as rebound vasodilation and the production of pro-inflammatory cytokines by prolonged intermittent steroid exposure, cause a rosacea-like eruption.[15] In this research, a typical female preponderance was observed. It was in concordance with the previous studies.[13,16] The higher cosmetic concern and self-conscious nature of women may have been the cause for the outnumbering of women over men in TCS abuse. Most of the patients in our research were between the ages of 20 and 40, which was also widely documented in various studies that demonstrated this age group's susceptibility. This is owing to reaching the age of marriage, beginning a new job, and active involvement in society.[13,16,17]

Table 5: Histopathological correlation of dermoscopic features due to topical corticosteroids and hydroquinone.

Parameters	Dermoscopic features	Histopathological correlation
Background colour	Reddish brown	Extravasation RBCs
Globules/ pigment pattern	Brown globules	Increased Melanin in the epidermis
	Focal white areas	Epidermal and dermal atrophy
Vessels	Telangiectasia	Dilated vessels
Scales	present	Focal parakeratosis

One month to six years was spent on the TCS application. But the majority of the patients (45.71%) utilized TCS for more than a year. About 68.5% of patients utilized TCS with the potency of class III/above, similar to another Indian research. Several of our patients have utilized triple-combination creams comprising TCS, an antibiotic, and an antifungal (so-termed cocktail creams), which are readily available due to their low cost. OTC accessibility is among the main factors contributing to the increase in steroid abuse, necessitating the development of legislative measures to halt the OTC sales of TCS. Most often reported signs of TCS abuse include acne melasma, and as a fairness product.[13,16,18]

Presenting complaints in this work were pigmentation, itching, redness, and acne. Repeated application of TCS causes nitric oxide inhibition, which causes chronic vasoconstriction, when TCS is withdrawn, the

endothelial nitric oxide is released causing vasodilatation and consequent erythema.[19,20] Therefore, mechanisms like rebound dilation of blood vessels and release of cytokines and "nitric oxide" are thought to be responsible for the expansion of facial erythema, burning sensation, and itching. The typical clinical symptoms reported in TSDF patients include dyspigmentation, erythema, and papulopustular lesions. In our study, in addition to this, we also found hypertrichosis in a high percentage (58.57%), in concordance with research conducted by Sethi *et al*.[16] Dermoscopy is a non-invasive instrument that was originally used to diagnose skin malignancies, but has now expanded its scope of use to many inflammatory skin conditions.[21]

Dermoscopy assists in the recognition of TSDF and EO before they become irreversible. In this study, dermoscopic findings in TSDF were diffuse red areas, brown globules, terminal hair, vessels, and focal white areas. Other features included Demodex tails and follicular plugging. Demodex tails appear as whitish gelatinous specs in the follicular opening. These findings were similar to other reported studies.[16] TCS causes inhibition of keratinocyte proliferation in the epidermis, and inhibition of synthesis of collagen and fibroblasts in the dermis resulting in epidermal and dermal atrophy.[22] This could explain diffuse red areas were due to dilated capillaries and extravasation of erythrocytes in the dermis, which makes easy visibility of vasculature due to the thin epidermis. Follicular plugging was due to follicular hyperkeratosis. Brown globules were due to increased epidermal melanin content which was probably secondary to the underlying melasma. Dermoscopy of EO showed dark grey-brown structures or "globules" that are grouped in an annular and arcuate pattern, providing a curvilinear and "wormy" appearance. On histopathology, characteristic short, stout, curvilinear, 'banana shaped' ochre-colored fibers of varying thickness were noted in the papillary dermis. These were in accordance with the previous reports in terms of dermoscopy and histopathology of EO.[23,24] Furthermore, vascular changes were due to capillary dilatation and pigment curvilinear structures were due to melanin in the epidermis and dermis with epidermal changes.

Various vascular structures are described in TSDF and EO in dermoscopy including linear, serpentine, Y-shaped, polygonal vessels.[11,16,25] Polygonal vessels are linear vessels with branches forming a network; Y-shaped vessels are linear vessels with one lateral branch. Similar vascular changes were observed in this study. We also noted C-shaped, arciform or arcuate vessels. However, statistical significance was not observed in vascular structures. Clinical changes such as erythema (p 0.0001), telangectasia (p 0.0001), and diffuse red areas (p 0.002) were prominently seen with TCS belonging to the class III potency, and they were statistically significant. This suggests that more damage was seen with TCS of higher potency. With a rising duration of TCS, dermoscopic features were more pronounced. However, statistical significance was obtained for telangiectasia, focal white areas, and white hairs with a usage duration of more than 3 months. In those continuing it for a longer duration, polygonal vessels have been predominant. Most of the dermoscopic features were significantly more in females compared to males. Men have an overall 10-20% thicker skin than women which could be the reason for greater damage seen with females.[26]

TSDF must be differentiated from other conditions causing red face, like erythemato-telangiectatic rosacea (ER), lupus erythematosus, contact dermatitis, and tinea faciei. It is possible with the use of dermoscopy. Though polygonal vessels are present in both TSDF and ER, the presence of focal white areas, terminal hairs, and white hairs favors TSDF. The presence of salmon-colored follicular spots surrounded with white halos known as the inverse strawberry pattern is seen in lupus erythematosus, yellow scales, dotted vessels, and sero-crusts in contact dermatitis.[27] Tinea faciei is characterized by perifollicular scale, peripheral red dots, and brown globules.[28] Thus, dermoscopy helps to differentiate TSDF and EO from various other facial dermatoses.

In this study, dermoscopic features due to TCS and HQ were correlated with histopathological changes. This study creates awareness about the long-term adverse effects of the inadvertent use of TCS. This would assist the treating physician to recognize features of TSDF, EO and act accordingly in treating and counseling. Limitations of this study include a smaller number of patients being included and only a few lesions being subjected to histopathological analysis.

CONCLUSION

Dermoscopy is a new diagnostic technique for TSDF and EO. This study revealed various dermoscopic findings of TSDF and EO with histopathological correlation. It showed a correlation between the dermoscopy features and duration/potency of TCS use. Thus, dermoscopy helps in the early detection of TSDF and EO before it is clinically apparent. Further studies on dermoscopy in therapeutic monitoring of TSDF and EO are recommended.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

ABBREVIATIONS

TCS: Topical corticosteroids; **TSDF:** Topical steroid damaged/dependent face; **HQ:** Hydroquinone; **EO:** Exogenous ochronosis; **OTC:** Over-the-counter ; **ER:** Erythemato-telangiectatic rosacea

SUMMARY

Misuse of TCS over the face is quite common. It is very crucial to make people aware of the possible side effects of these drugs and the severity of the problems associated with their irrational and unregulated use. Dermoscopic features of TSDF and EO along with histopathological correlation have been explained in this study. This would help the attending physician to recognize the features of TSDF and EO and act accordingly in treatment and counselling.

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