"A STUDY OF CLINICAL, DERMOSCOPIC AND HISTOPATHOLOGICAL CORRELATION IN FOLLICULAR KERATOTIC DISEASES"

BY

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DISSERTATION SUBMITTED TO BLDE (Deemed to be university), VIJAYAPUR

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MD

IN

DERMATOLOGY VENEREOLOGY AND LEPROSY

UNDER THE GUIDANCE OF

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I hereby declare that this dissertation entitled "A STUDY OF CLINICAL, DERMOSCOPIC AND HISTOPATHOLOGICAL CORRELATION IN FOLLICULAR KERATOTIC DISEASES" is a bonafide and genuine research work carried out by me under the guidance of Dr. KESHAVMURTHY.A.ADYA, Associate Professor, Department of Dermatology Venereology and Leprosy, at BLDE (Deemed to be university) Shri B.M. Patil Medical College and Research centre, Vijayapur.

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LIST OF ABBREVIATIONS

1. NPL- Non- polarised light

2. PL- Polarised light

3. URTI- Upper respiratory tract infection

4. LS- Lichen spinulosis

5. KP- Keratosis pilaris

6. PRP- Pityriasis rubra pilaris

7. Follicular LP- Follicular lichen planus

8. LPP- Lichen planopilaris

9. FFA- Frontal fibrosing alopecia

10. PPAR- Peroxisome proliferator activated receptors

11. PLGS- Piccardi- Lassuer- Graham- Little syndrome

12. HPE – Histopathological examination

ABSTRACT

Background: "Follicular keratotic disorder is an abnormal keratinization affecting the follicular orifices and clinically characterized by hyperkeratotic follicular papules affecting various sites". Dermoscopy is a non-invasive diagnostic tool and differentiates closely resembling diseases as well as possibly prevents need for an invasive biopsy.

Objective: This study was aimed to find the correlation between clinical, dermoscopic and histopathological findings in follicular keratotic diseases and to establish the dermoscopic criteria in the diagnosis of follicular keratotic diseases.

Methods: This was a hospital based prospective cross-sectional study of patients clinically diagnosed with follicular keratotic diseases, irrespective of age, between 2018 and 2020.

Results: The study consisted of 76 patients with a mean age of 26.7±2.4 years. The most common follicular keratotic disease observed was phrynoderma 22(28.9%) followed by keratosis pilaris 21(27.6%). The predominant dermoscopic finding was perifollicular scaling 73(96%) and keratotic plug 65 (85%). The most common histopathological feature was epidermal hyperkeratosis, dilated follicular infundibulum, follicular plug and dermal lymphocytic infiltration. The clinical and dermoscopic features showed a significant statistical association with the histopathological findings ($P<0.006$).

Conclusion: Dermoscopy is a simple, non-invasive diagnostic tool that helps in differentiating and diagnosing the closely resembling follicular keratotic diseases.

Key Words: Follicular keratotic diseases, Dermoscopy

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LIST OF ALGORITHM

INTRODUCTION

A dermoscope (dermatoscope) is a non-invasive, diagnostic tool which visualizes subtle clinical patterns of skin lesions and subsurface skin structures not normally visible to the unaided eye. It has also been called a skin surface microscope, epiluminescence microscope or episcope. Some dermoscopic patterns are observed consistently with certain diseases and these could aid for their diagnosis.

Basically, a dermoscope is functionally similar to a magnifying lens but with the added features of an inbuilt illuminating system, a higher magnification which can be adjusted, the ability to assess structures as deep as in the reticular dermis, and the ability to record images[1].

Dermoscopy is similar to magnifying lens with several add-on features like:

- It has a specialized illuminating system such as visible light, polarized light and ultraviolet sources
- It has adjustable magnification
- Its ability to visualize deeper structures up to the reticular dermis, and
- Advantage to capture the findings as the digital images for documentation and comparison later[2].

This diagnostic aid must be used in conjunction with a thorough clinical history and examination of skin lesions. Dermoscopy and clinical examination, increases the diagnostic accuracy by 5% to 30% compared to clinical visual inspection alone, depending on the type of skin lesion and experience of the physician[3].

The role of dermoscopy as a diagnostic tool is gaining importance over time as many disorders are being reported where dermoscopy play a role not only in diagnosis but also in monitoring the course of disease[4].

The field of dermoscopy is relatively untapped and provides ample opportunities for original observations. The diagnostic utility of dermoscopy in follicular keratotic disorders has not been explored so far.

Follicular keratotic disorder is an abnormal keratinization affecting the follicular orifices and clinically characterized by hyperkeratotic follicular papules affecting various sites.

Follicular keratotic diseases can be classified as

a) Primary follicular keratotic diseases: Phrynoderma, keratosis pilaris, lichen spinulosis and pityriasis rubra pilaris

b) Follicular variants of Psoriasis, Eczema, Lichen Planus.

The present study has been undertaken to find the correlation between clinical, histopathological and dermoscopic findings in follicular keratotic diseases and propose diagnostic dermoscopic criteria.

Formulating objective and reproducible dermoscopic criteria would assert the clinical diagnosis and differentiate closely resembling diseases as well as possibly prevent the need for an invasive biopsy.

OBJECTIVE OF THE STUDY

1) To find the correlation between clinical, dermoscopic and histopathological findings in follicular keratotic diseases.

2) To establish the dermoscopic criteria in the diagnosis of follicular keratotic diseases.

REVIEW OF LITERATURE

Dermoscopy

German dermatologist Johann Saphier (1920) introduced the term “dermatoscopy”. The term “dermoscopy” was later coined by Goldman. Various synonyms used for dermoscopy include: dermatoscopy, epiluminecsence microscopy, skin surface microscopy and incident light microscopy. The first dermoscope was developed in 1989 by Stolz and Braun- Falco[5].

Dermoscope is a hand-held non-invasive diagnostic tool, which magnifies not only the subtle surface features of skin lesions but also unveils few skin subsurface structures which are imperceptible to the naked eyes and even to the magnifying lens[1]. It is a link between macroscopic clinical dermatology and microscopic dermatopathology[6].

Follicular keratotic diseases can be diagnosed with a higher sensitivity and specificity as compared to clinical examination by dermoscope. Thus dermoscopy obviates the need for invasive skin biopsy in diagnosis of follicular keratotic diseases.

Other added advantages of dermoscopy over histopathology are:

- It is easy to use and is less time consuming.
- It is an office procedure that facilitates quick interpretation of skin lesions.
- Helps the observer to focus on the lesion
- Can be used for post-treatment follow-up
- Provides facility for storage of images for future analysis and comparision[2].

Principle of dermoscope:

The main principle of dermoscopic visualization is to magnify the skin lesions with lenses along with illumination using different light sources[7]. Normally, any light ray that passes through the skin gets either reflected, refracted, diffracted or absorbed and this depends on the type of the skin(Figure 1)[8]. In dry scaly skin, the light gets reflected whereas in smooth oily skin the light reaches the deeper dermis and hence improves the visibility of the skin sub-surface. The latter principle is used in case of contact technique dermoscopy by visualizing the skin lesion following application of linkage fluids like oil (immersion oil, olive oil, and mineral oil), water, an antiseptic solution, glycerin and gels [9].

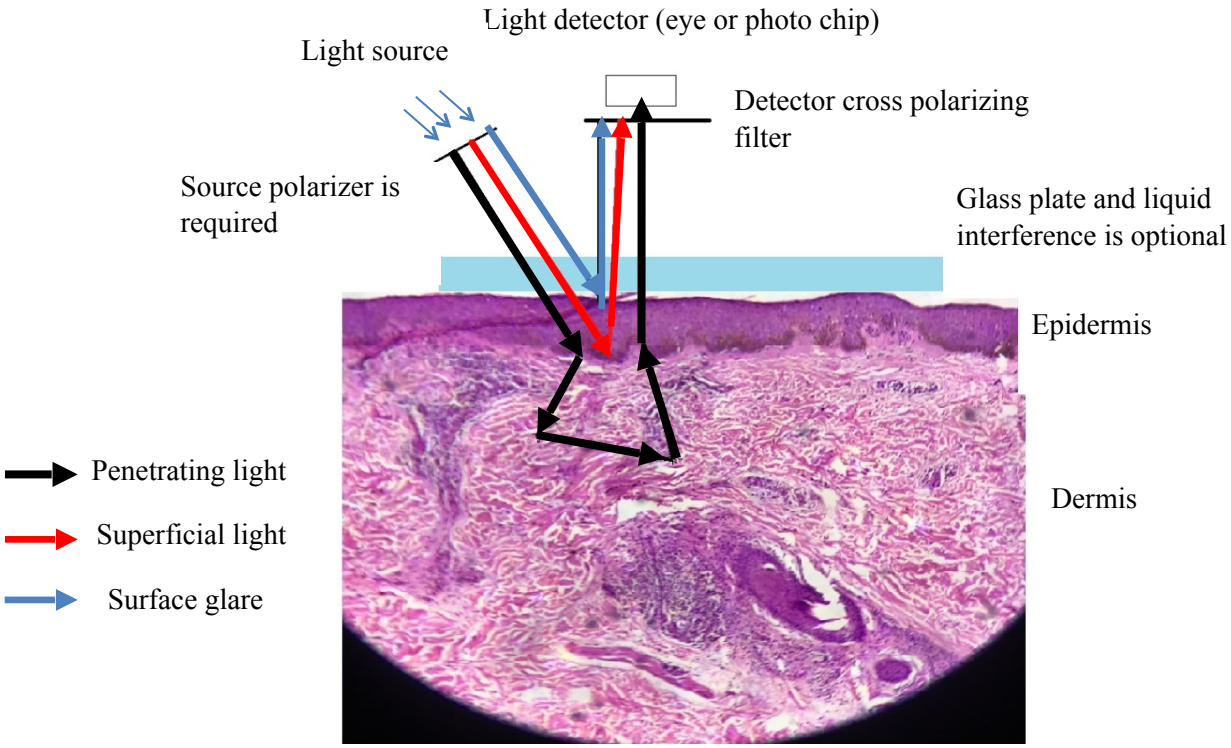


Figure 1: Optics of polarized and non-polarized light in dermoscopy

Parts of dermoscope:

The different parts of dermoscope are as follows[1]

1. *Achromatic lens*: Most instruments provide a magnification of 10X, but higher magnification of upto 1000X can be achieved with video-dermoscope.
2. *In-built illumination system*: Light emitting diodes (LED) are the standard sources that provide high intensity white light and consume 70% less power than classical halogen lamps, which emit yellow light. Illumination can also be altered by turning off a set of LEDs. Videodermoscope uses polarized light which allows them to display the subsurface features of skin lesions without using contact plates and linkage fluid.
3. *Power supply*: Hand-held instruments are powered by batteries or have rechargeable handles.
4. *Display system*: Hand-held dermoscope have a see-through viewing window, while the video-dermoscope can be connected to a computer or other display devices or it may have its own display screen.
5. *Contact plate*: Large contact plate (20mm diameter) and small contact plate (8mm diameter) are the parts of contact technique dermoscopy. The contact plates are made up of multilocated silicone glass which can be sterilized with methylated spirit or 2% glutaraldehyde. Boiling or autoclaving at 134^0 C for 5minutes also serves the purpose. Some of these plates are graduated with scales and others are non-graduated.
6. *Inbuilt photography system*: These have become an essential component of a dermoscope except in the hand-held dermoscope. The camera may be either an attachable conventional or a digital camera, or an in-built video camera. Supporting software, for the capture, storage, retrieval and even interpretation of images is incorporated in the latter cases.

Types of dermoscopy instruments:

Marghoob *et al* [10] reviewed various models of dermoscopes and categorized them into the following types:

a) *Dermoscopes without image capturing facility*: These are hand-held, otoscope-like instruments that lack an inbuilt camera or any other image capture facility. However, cameras can be attached to some of these instruments with an adaptor. It incorporates four different colored polarized light, viz white, blue (surface pigmentation), yellow (superficial vessels) and red (deep pigment and vessels), to facilitate better visualization of skin structures based on the principle that, depth of penetration of light is proportional to the wavelength.

b) *Dermoscopes with image capturing facility*: These instruments either have an inbuilt image capture system or have a camera attached for photography. Also, whole body photography (body mapping) is possible with this instrument. Some have special lenses, which can be mounted onto a conventional or a digital camera. Both clinical and dermoscopic pictures of 10X magnification can be taken. A video dermatoscope has a higher resolution camera fitted to the hand piece and the image is seen on the computer screen. Small videos can be taken with this instrument, as well.

c) *Dermoscopes with image capture facility and analytical capability*: These instruments are mainly used in countries where the incidence of melanoma is high, mainly for pre-operative assessment of pigmentd lesion. Archieved images of the patient can be compared with the new ones. Any significant change in the lesion produces different colour signals. An artificial neural network mechanism helps to judge whether a melanocytic nevus is benign or not.

Technique of dermoscopy:

The dermoscope can be used either by contact or non-contact techniques. In contact technique dermoscopy, using the non-polarized light (NPL), the glass plate or contact plate is applied to the surface of the lesion with an interface fluid. In non-contact technique, using the polarized (PL) there is no contact with the ski surface, which gives an added advantage of avoiding nosocomial infections[11].

Polarised light offers better visualization of structures located deeper in the skin, whereas NPL allows for improved visualization of more superficial structures[3].

The dermoscope facilitates the visualization of skin in a horizontal view; hence the vessels that run parallel to the skin surface are visualized as lines, while the vessels, those run perpendicular are visualized as loops. Vessels are better visualized by the non-contact technique technique, as it doesn't compress the vascular structures[12].

IMMERSION FLUID

In dermoscopic examination, the most preferable linkage is the immersion oil[1].

Linkage or immersion fluid can be divided into four groups:

i) Water-based gels

ii) Oils

iii) Disinfectant solutions and

iv) Water

The characteristics of an ideal immersion liquid are:

i) Cheap and easily procurable

ii) Makes structural parameters of skin lesions well visible, without changing color

iii) Should produce less air-bubbles

iv) Non-volatile

v) Can be used in special locations like circumocular skin

vi) Should not lead to very matte or excessive bright light.

In identification of the pigment network, immersion oil is more appropriate as an immersion fluid. For structural components other than pigment network, ultrasound gel or immersion oil can be used. In dermoscopic examination of non-pigmented skin lesions, ultrasound gel is a better alternative because it is cheap and easily removable from the skin whereas immersion oil is not preferred, as it contains chlorinated paraffin and dibutyl phthalate, which have teratogenic, fetotoxic and carcinogenic effects.

An evidence-based study by Gewirtzmanet *et al*[13] showed that a 70% alcoholic solution gives best results in terms of image clarity, eliminating air bubbles, and better patient tolerance, as it has less strong odour. Alcohol potentially decreases the rate of transmission of infections, it is better used in inflammatory dermatoses.

Glass has a refractive index (1.52) almost similar to that of skin (1.55) and hence when placed over linkage fluid coated skin (as in contact plates), further enhances transillumination of the lesion. Ultrasound gel is useful in performing dermoscopy of solid curved areas, particularly the area surrounding the nail plate[14]. It is also preferred for examination of nail bed, mucosa, genitals and eyelids[1]. By using gel, the entire curved area of the nail can be viewed as the viscose gel fills up and remain in the space between the surface to be viewed and the contact plate unlike liquids which escapes out.

Main categories of dermoscopic criteria

Each disease is dermoscopically typified by one or two predominant criteria. A "predominant" criterion is a structure seen in larger part of the lesion, prevailing other coexisting features. The frequent structures seen in inflammatory skin diseases includes scales, structures associated to hair follicle and vessels. The most important parameters to be evaluated when dermoscopically examining skin eruptions are

1A. Scales colour

a. *White*: This is the most frequent scale colour observed in primary and secondary follicular keratotic diseases and other diseases like papulosquamous and erythematosquamous skin diseases.

b. *Yellow*: Yellow crusts are a result of serum extravasation, and yellow scales, a result of serum mixed with keratin. Yellow crusts and scales represent dermoscopic hallmark of all types of dermatitis, and histologically corresponds to spongiosis.

c. *Brown*: Pigmented parakeratosis may occur in several dermatoses and results in brown coloured scales. Brown scaling may also be a result of exogenous pigmentation.

1B. Scales distribution

a. *Diffuse*: Scales covering all the surfaces of the lesion. Diffuse scale is non -specific of any diagnosis as it can be seen in several hyperkeratotic dermatoses.

b. *Central*: Here, scales are accentuated in the centre of the lesion. This scaling pattern cannot be considered as specific, although it is quite frequently seen in psoriasis.

c. *Peripheral*: Scales are mainly distributed at the periphery sparing the centre. It is a classic sign of pityriasis rosea but also seen in other diseases like tinea corporis.

d. *Patchy*: Random and asymmetric distribution of scales. This is seen in several diseases.

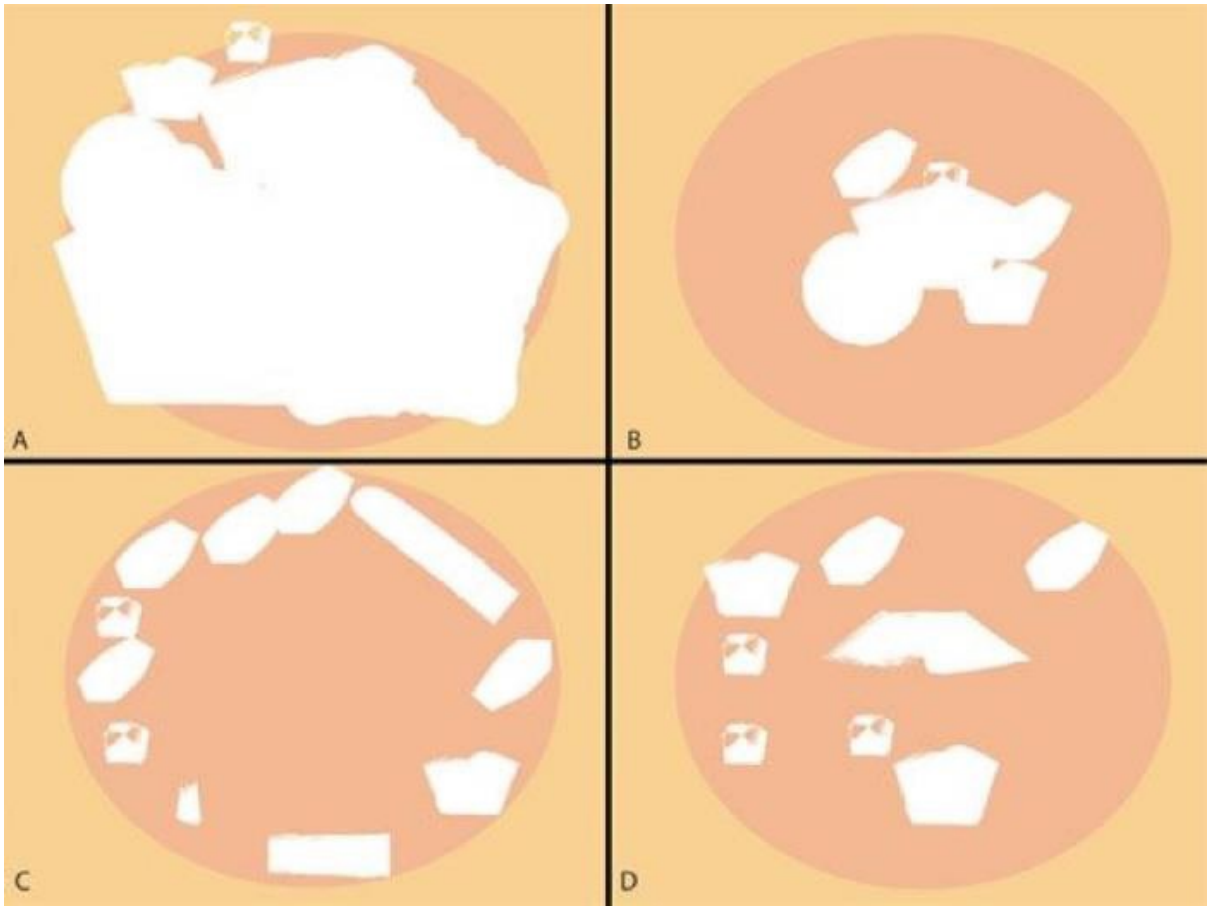


Figure 2 : Distribution of scales: A)Diffuse B)Central C)Peripheral D)Patchy

2. Follicular criteria

a. *Follicular plugs*: Keratin plugs of white or yellow color filling the follicular openings. It is a dermoscopic hallmark of early stage discoid lupus erythematosus but also seen in several diseases including follicular kearatotic diseases.

b. *Follicular red dots*: This represents perifollicular inflammation and vasodilatation. Typically, they are seen in discoid lupus erythematosus but also seen in follicular mucinosis.

c. *Perifollicular white colour*: A white coloured circle surrounding each hair follicle and/or between follicles. It might correspond to perifollicular fibrosis(e.g., DLE), epidermal hyperplasia (e.g.,hypertrophic lichen planus), perifollicular depigmentation (e.g.,Vitiligo)

d. *Perifollicualr pigmentation*: Pigment accentuated around the hair follicles. It represents the first sign of repigmentation in vitiligo and can also be seen in some alopecias[15].

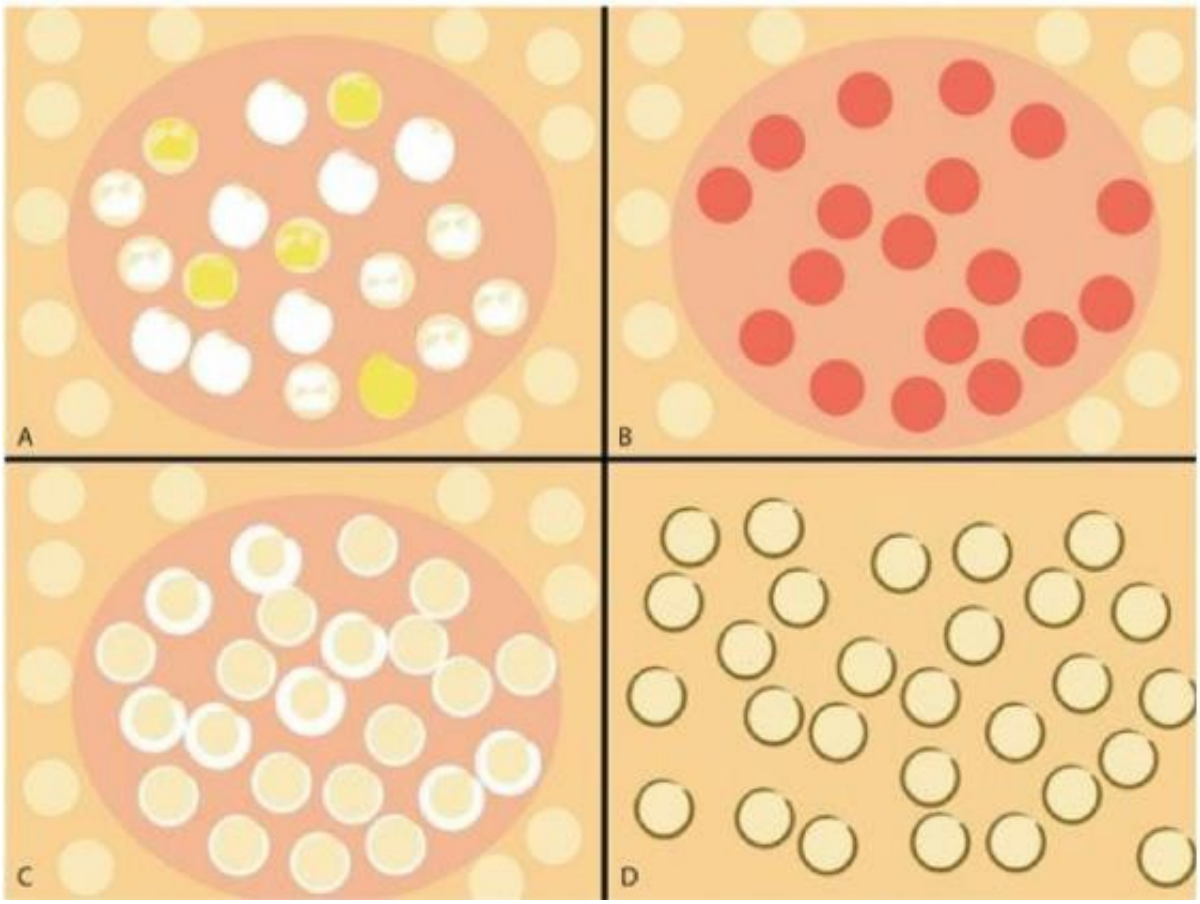


Figure 3: Follicular criteria: A)follicular plugs B)Follicular red dots C)Perifollicular white colour D)Perifollicular pigmentation.

3.Vessels

Vessels located in the dermis are generally pink and appear out of focus due to the effect of the dispersion of light through the dermal connective tissue. Those found closer to the surface (immediately under the epidermis), by contrast, are bright red and in focus[16]. Table 1a depicts vessel morphology and 1b vessel distribution pattern.

Vessel morphology

VASCULAR PATTERN	DESCRIPTION	DIAGRAM
Arborising vessels or telengiectasias	In focus, large caliber vessels that branch into finer secondary vessels	
Hairpin vessels	Vessels that double back on themselves and are seen as loops when they are oblique to the surface of the lesion; In keratinizing tumors they are surrounded by a hypopigmented halo	
Crown vessels	Barely branching peripheral vessels that don not cross the centre of the lesion	
Comma vessels	Thick linear curved lines with little branching and occasionally one end that is thicker than the other	
Dotted vessels	Tiny red dots densely aligned next to each other in a very regular fashion	

Glomerular vessels	Large caliber reddish dots formed by tortuous capillaries often distributed in clusters mimicking the glomerular apparatus of the kidney	
Corkscrew vessels	Linear irregular spiral	
Milky red areas/ globules	Out of focus pink-reddish oval or polygonal areas containing atypical linear vessels	
Strawberry pattern	Structureless erythematous areas with heterogenous whitish areas forming a type of pseudo network	
Linear irregular	Straight vessels varying in size and shape	
Polymorphous vessels	Different vascular morphologies in the same lesion	

Table 1a: Vessel morphology

Vessel distribution pattern

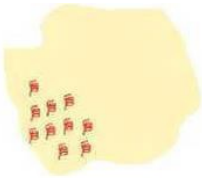
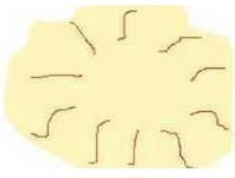
VESSEL PATTERN	DESCRIPTION	DIAGRAM
Regular	Vessels distributed evenly throughout the lesion	
String of pearls	Dotted vessels arranged linearly in a pattern resembling a string of pearl	
Clustered	Tendency of a group together in a lesional area	
Radial	Vessels at periphery of lesion not crossing or occupying the centre	
Branching	Large vessels that branch into smaller vessels	
Irregular	Vascular polymorphism without a specific pattern	
Rope ladder pattern	Short slightly dilated loops that emerge from edges of scar and cross it completely	

Table 1b: Vessel distribution pattern

Follicular keratotic disorders

Introduction

Follicular keratotic disorder is an abnormal keratinization affecting the follicular orifices and clinically characterized by keratotic follicular papules affecting various sites.

Classification

Follicular keratotic diseases can be classified as

1) Primary follicular diseases and

2) Others

Primary follicular keratotic disorders include phrynoderma, keratosis pilaris, pityriasis rubra pilaris and lichen spinulosis.

Diseases other than primary follicular keratosis include follicular eczema, follicular psoriasis and follicular lichen planus.

Phrynoderma

Phrynoderma is a type of follicular keratotic disease. It was coined and described by Nicholls in 1933. The meaning of phrynoderma is “toad skin” and the etiological factors include multiple nutritional deficiencies like Vitamin A, Vitamin B complex, Vitamin E, essential fatty acid deficiency and protein calorie malnutrition.

Phrynoderma mostly affects children and adolescent aged between 5 and 15 years and less commonly seen below 5 years of age and also observed in few lactating mothers. Thus, there is an increased nutritional demand during childhood and lactation, and the lack of good

nutrition due to low socioeconomic status may be responsible for occurrence of phrynoderma[17].

In India, it is commonly seen in low socioeconomic group of population. Although rare in developed countries, it still exists among poor population and is seen among patients with malabsorption from various etiologies and also in hospitalized patients[18].

Phrynoderma has no male or female preponderance and has equal gender distribution. Phrynoderma is more commonly seen in winter season and the flare up of the disease during this season may be due to follicular prominence, which generally occurs in otherwise normal children during cold weather. The site of onset and distribution of lesions indicate importance of pressure and friction in the development of lesions[17].

Clinical features:

Phrynoderma is clinically characterized by follicular keratotic papules of various sizes distributed over the extensor aspects of the extremities, especially over the elbows, knees, neck, posterior axillary folds, and thighs. Manifestations due to deficiency of other vitamins are also evident in most patients. The associated ocular manifestations of vitamin A deficiency are night blindness, xerophthalmia, bitot's spots and keratomalacia[19].

Associated diseases or conditions in phrynoderma:

Xerosis
Pityriasis alba
Night blindness, Bitot's spot, Conjunctival xerosis
Angular stomatitis, glossitis
Lactation
Ichthyosis
Scabies, Impetigo
Helminthiasis
Tinea cruris
Verruca
Herpes simplex infection
URTI, Gastroenteritis
Alopecia areata

Table 2: Associated diseases in phrynoderma

Histopathology

Histopathology reveals epidermal hyperkeratosis, parakeratosis, acanthosis, follicular hyperkeratosis, keratin plugs in the hair follicular orifices, atrophy of the sebaceous glands, perifollicular and perivascular lymphocytic infiltration[17].

Treatment

Topical keratolytics alone- Twice daily x Four weeks
Oral vitamin A supplements 50 000 U/d for 1 month, then 5000 U/d for 2 months[20] or One lakh Units IM Alternate day x Ten injections
Correction of deficiencies of other vitamins a)Vitamin B complex 2 ml IM alternate day x 10 injections b) Vitamin E 400mg Oral Once daily x 4 weeks
Essential fatty acids- Oral Safflower oil 2 tablets with each meal x4 weeks[21]

Table 3: Treatment of phrynoderma

Lichen spinulosis

Lichen spinulosus (LS) is a disorder of keratinization of hair follicles and it was first described by Adamson in 1908[22]. Lichen spinulosis is also known as keratosis spinulosa.

The etiology of the disorder is unknown. However, genetic predisposition may play a role. Other etiologies include atopy, infections, id reaction to fungal infection, drug-related reactions, including reactions to thallium, gold, diphtheria toxin, and arsphenamin[23], HIV infection[24], Crohn disease[25], alcoholics[26], patients taking omeprazole[27].

It is more common in children and slightly more common in boys than girls with no ethnical differences[22] and is characterized by the development of asymptomatic minute, flesh-coloured, follicular horny papules, each with a central spinous process. The papules are grouped and are distributed symmetrically on the trunk, limbs and buttocks with sparing of face, hands and feet. When a patch is rubbed gently with the fingers, it feels similar to a nutmeg grater. The general health of the patient is good[19].

Histopathology

Histopathology is non-specific and shows dilated hair follicle with a keratinous plug and mild perifollicular infiltration[19].

Prognosis

Lichen spinulosus can be ameliorated with topical emollient keratolytics. There is spontaneous remission within 1-2 years; however, few cases lasts for decades.

LS affects only the skin and is not known to be associated with abnormalities of internal organ systems. A patient with lichen spinulosus occasionally presents with pruritus. Otherwise, the disorder mostly is of cosmetic significance. Misdiagnosis can result in inappropriate treatment[28].

Treatment

1. Topical keratolytics like 3% salicylic acid ointment, tretinoin and 12% ammonium lactate solution[28].
2. Topical tacalcitol cream without occlusion twice daily x 4 weeks is found to be effective in few patients[23].
3. Topical salicylic acid gel with and without occlusion for 2 weeks and 8 weeks, respectively.
4. Tretinoin gel at night and hydroactive adhesive application at morning for eight weeks after failure of keratolytic agents for six weeks[22].

Table 4: Treatment of lichen spinulosis

To the best of our knowledge, dermoscopic features of phrynoderma and lichen spinulosis have not yet been reported in the literature.

Keratosis pilaris

Keratosis pilaris (KP) is a follicular keratotic disease characterized by keratin plugs in the follicular orifices with or without perifollicular erythema[29]. It is an autosomal dominant disorder and may occur isolated or associated with other pathologic processes, including follicular inflammation, atrophy, scarring and alopecia (keratosis pilaris atrophicans). Age of onset has bimodal distribution, early childhood and adolescent onset, which improves gradually over years[30]. Females may be affected more frequently than males[31].

Aetiology

KP is an autosomal dominantly inherited disorder but X-linked dominant form in women has been reported. More severe forms have translocations and deletions of chromosome 18p. Family history is often present in keratosis pilaris[19]. Drugs like nilotinib have been implicated in the aetiology of keratosis pilaris or keratosis pilaris atrophicans[32].

Pathogenesis

There is excess formation and/or build-up of keratin around individual hair follicles, due to which hair is unable to reach the surface and becomes trapped beneath the keratin debris giving rise to individual follicular papules (bumps). Mild erythema around the hair follicles is indicative of the inflammation. Often, a small, coiled hair can be seen beneath the papule

Clinical features

KP is characterized by minute, gooseflesh-like, horny plugs at the follicular orifices, distributed on the posterolateral aspect of the thighs, upper arms, gluteal area and legs. There is no grouping and individual follicles show a long strand of keratin glinting when examined

in side light (antenna sign)[33]. Eruptions are usually asymptomatic, except for occasional pruritus. KP becomes more prominent during the winter and improves during summer[29]. The general health of the patient remains unaffected.

Associations of Keratosis Pilaris

Atopy
Scarring alopecia
Ichthyosis vulgaris
Ectodermal dysplasia
Cardio-fascio-cutaneous syndrome
Obesity
KID syndrome
Prolidase deficiency
Down's syndrome[29]
Systemic corticosteroids and lithium
Vemurafenib and sorafenib[33]

Table 5: Associated diseases of KP

Clinical variants

1) *Erythromelanosis follicularis faciei et colli* is a subtype of KP and frequently seen in Asian men. It manifests as follicular hyperkeratosis accompanied by erythema and hyperpigmentation, and affects face, particularly the cheeks and neck[33]. It may be inherited as an autosomal recessive trait[34].

2) *KP atrophicans* is a more inflammatory form of KP resulting in follicular fibrosis and atrophy progressing to scarring alopecia.

Three variants have been recognized as follows:

a) *KP atrophicans faciei*, also known ulerythema ophryogenes or keratosis rubra pilaris faciei atrophicans, affects the cheeks and lateral eyebrows. It is characterized by fixed erythema, follicular plugging, pitted scarring and hair loss. It may be associated with common KP and may be inherited as an autosomal dominant trait.

b) *Keratosis follicularis spinulosa decalvans* is more common in infants and affects the cheeks and nose, characterized by follicular plugging resulting in follicular atrophy. It predominantly involves scalp resulting in cicatricial alopecia and can be associated with palmoplantar hyperkeratosis[33].

c) Atrophoderma vermiculatum manifests in late childhood and has slow progressive course. It affects cheeks and preauricular skin. The follicular plugging evolves towards honeycomb or reticulated atrophy of the skin. Atrophoderma vermiculatum is inherited as an autosomal dominant disorder and both sexes are equally affected[35].

Histopathology

Histopathology shows distended follicular orifice, filled with a keratinous plug that may contain twisted hairs.

Dermoscopic features

In a study conducted by Thomas *et al*, they studied 25 patients with keratosis pilaris, dermoscopy showed coiled hair shafts within the affected follicular infundibula in all the 25 patients, perifollicular erythema was seen in 11 patients and perifollicular scaling in 9[29].

A study conducted by Sonthalia *et al*, showed presence of vellus hairs that are frequently coiled, semi−circular or looped, peri−follicular erythema, peri−pilar casts and hairs emerging in groups of 2 or 3. The study also described presence of vascular ectasias and dyschromic changes (pigmented globules) suggesting post-inflammatory hyperpigmentation[36].

Treatment:

There is no cure or universally effective treatment available for keratosis pilaris (KP) due to genetic predisposition and possible genetic etiology. Inconsistent remissions and variations occur with seasons and hormonal states. The symptoms may remit with increasing age and some cases clear spontaneously without treatment. Keratosis pilaris is generally a controllable but incurable condition.

The results are best achieved with combination therapy.

A) General measures: Use of mild soapless cleansers and emollients
B) **First line** -Keratolytics includes 10% Lactic acid and glycolic acid preparations, 5% salicylic acid cream and urea cream.
C) **Second line** -Topical retinoic acid products such as tretinoin, tazarotene and adapalene. Intermittent dosing of topical retinoids (weekly or biweekly) is well tolerated and combination of topical retinoids with 10% urea containing moisturisers is quite effective. Topical Immunomodulators like Tacrolimus 1% or Pimecrolimus 0.1%- in resistant cases and severe inflammation.
D) **Third line** - In severe KP, Oral isotretinoin is effective but relapse occurs on cessation

E) **Fourth line –** In severe fixed erythema, Pulsed dye laser have been successfully used. Others- Photodynamic therapy using a 2-step combination of a topical photosensitizer (aminolevulinic acid or methyl levulinate) and a light source (sunlight, blue light (417 nm), red light (630 nm), and multiple laser devices)[32, 33].

Table 6: Treatment of keratosis pilaris

Pityriasis rubra pilaris:

Pityriasis rubra pilaris (PRP) is a rare disorder of keratinization characterized by reddish orange scaly plaques, palmoplantar keratoderma and keratotic follicular papules. It is also known as lichen ruber pilaris, Devergie's disease, lichen ruber acuminatus.

Epidemiology:

PRP is an uncommon condition with an incidence between 1 in 5000 and 1 in 50000 with no racial and gender predilection. The acquired forms of PRP have a bimodal age distribution at first and fifth decades whereas the rare familial form starts in early childhood.

Associated diseases:

Autoimmune diseases such as Systemic sclerosis, autoimmune thyroiditis , Myasthenia gravis
Hypogammaglobulinemia, celiac sprue, myositis
Staphylococcal folliculitis or furunculosis
Hypothyroidism, Inflammatory arthritis
Carcinoma of larynx, colon, kidney and lung
HIV Infection

Table 7: Associated diseases of PRP

Pathophysiology:

The pathogenesis of PRP is unknown. The rare genetic form has been linked to gain-of-function mutation in the CARD 14 gene, an activator of nuclear factor kappa light chain enhancer of activated B cells. In sporadic forms, such mutations are rare and streptococcal superantigens have been implicated in children with sporadic forms.

Clinical features:

Patients present with well-defined salmon red or orange red dry scaly plaques that coalesce to form widespread lesion with islands of normal skin (nappes claires). The disease begins initially over the scalp and gradually progress caudally to involve rest of the body. Pruritus may be present in the initial stages of the disease and few patients may become erythrodermic.

Follicular hyperkeratosis may present as 'nutmeg grater' papules over elbows, wrist and back of fingers. Palms and soles may be thickened and fissured with an orange discolouration known as 'PRP sandal'.

The nails are thickened, brittle, dull and rough with splinter hemorrhage. Subungual accumulation of keratinous debris may occur with minimal pitting. The oral mucosa is rarely involved and may resemble lichen planus or a diffuse hyperkeratosis [37].

Clinical variants

Six clinical variants have been described from Type I to Type VI known as Griffith and Gonzales- Lopez classification. The more common generalized sporadic forms Type I and Type III have acute onset and rare familial form of PRP has a slow and gradual onset.

1. Classical adult−onset PRP (type I)

This is the most common type affecting both genders equally with the highest incidence between 40 and 60 years of age. It is characterized by erythematous scaly macules on the head, neck or upper trunk and later profuse erythematous perifollicular papules with a central acuminate keratotic plug develop. Follicular lesions are initially discrete and coalesce to form groups of two or more and gradually submerged in sheets of erythema of a slight orange hue which spreads from head to feet with interfollicular erythema. The scalp shows diffuse *bran−like scaling and* erythroderma may develop within 2–3 months. It usually resolves in 1-3 years. Prolonged erythema may cause peripheral oedema and may precipitate high−output cardiac failure.

2. Atypical adult−onset PRP (type II)

It accounts for 5% of cases and characterized by perifollicular scale and palmoplantar keratoderma and has a chronic course. Patient may show eczematous features and the keratoderma is coarser than in other types.

3. Classical juvenile−onset PRP (type III)

This is the most common childhood form of PRP and affects children 5-10 years age. It is counterpart of type I PRP and has a spontaneous resolution in 1–2 years. Some patients with type III PRP may evolve into type IV PRP and vice versa and there may be recurrence in adult life may be seen.

4. Circumscribed juvenile PRP (type IV)

This is seen in prepubertal children under 12 years of age. It is characterized by well circumscribed plaques of erythema and follicular hyperkeratosis over the elbows and knees.

Patients may have palmoplantar keratoderma. The disease may remit in teenage years as the course is uncertain.

5. Atypical juvenile PRP (type V)

It accounts for 5% cases and most of the familial cases. The disease may be present at birth or early childhood and has a chronic course. It is characterized by erythema, follicular hyperkeratosis and keratoderma is common. Scleroderma−like changes may be present in the hands and feet.

6. HIV−related PRP (type VI)

This form resembles type I PRP and resistant to treatment but may respond to antiretroviral therapy. It is characterized by elongated filiform keratoses on the face and trunk and associated with truncal conglobate acne, hidradenitis suppurativa and lichen spinulosus. The prognosis is poor[37, 38].

Histopathology

Adult onset PRP has a distinctive histopathological findings and may vary according to the stage and evolution of the lesions. It is characterized by acanthosis, hyperkeratosis, alternating orthokeratosis and parakeratosis in both horizontal and vertical direction known as "checkerboard pattern". There is hypergranulosis and irregular acanthosis in the form of a broad and shortened rete ridges, thick suprapapillary plates.

The dermis shows dilated hair follicles filled with dense horny keratin plug and perivascular lymphohistiocytic infiltrates[38].

Dermoscopy

Gaia Moretta *et al* described dermoscopic features of pityriasis ruba pilaris (PRP) lesions showing more irregular linear and dotted vessels, white keratotic plug, yellow peripheral keratotic ring and perifollicular erythema[39].

Sheetanshu Kumar and others in their study described dermoscopic features of erythrodermic PRP as whitish keratotic follicular plugs with peripheral yellowish red areas and multiple linear and dotted vessels arranged in an irregular pattern[40].

A study done by Nair *et al* on dermoscopy of juvenile circumscribed pityriasis rubra pilaris revealed whitish follicular keratotic plugs surrounded by yellowish rings, perifollicular erythema and hair shaft in the center[41].

Prognosis

Classical adult PRP (type I) may progress to erythroderma in few weeks and clears spontaneously in majority of the affected patients. The period of resolution varies from 3years to 20years. Classical juvenile PRP (type III) has a shorter course with remission in one year. Atypical PRP (types II and V) have more limited in extent.

Treatment

Management of PRP depends on extent and severity of the disease and it involves topical and systemic therapies.

A) Topical treatment

This is indicated in localised form of PRP such as type III PRP.

Topical corticosteroids (medium to high potency)
Keratolytics such as 5%-10% urea or 5% Salicylic acid
Emollients
Topical retinoids such as Tretinoin, Tazorotene
Topical Vitamin D derived such as Calcipotriol

Table 8a: Topical treatment of PRP

Topical treatment in association with systemic therapy is recommended to treat hyperkeratosis and palmoplantar keratoderma and reduce scaling, erythema and induration.

B) Systemic treatment

Systemic therapy is indicated in moderate to severe disease and systemic retinoids remains the main stay of treatment in both adults and juvenile forms of PRP. In refractory PRP, biological agents are considered.

First line treatment
Isotretinoin 1mg/kg/day
Acitretin 0.5-0.75mg/kg/day
Second line - Systemic treatment
Methotrexate at a dose of 5mg-25mg/week has a favourable response in Type I PRP
Acitretin + narrowband-UVB
Acitretin + UVA

Acitretin + PUVA
Cyclosporine
Biological agents for refractory forms
Anti- TNF alpha inhibitors (Infliximab, Adalimumab, Etanercept)
IL-23 (Ustekinumab) and IL-17 inhibitors (Sekukinumab)
Other treatments
PDE4 inhibitor (Apremilast) for 4weeks
Extracorporeal photochemotherapy in combination with systemic retinoids + cyclosporine in erythrodermic type I PRP
IV Immunoglobulin in Type II PRP[39]

Table 8b: Systemic treatment of PRP

Secondary follicular keratotic diseases:

Follicular psoriasis:

Follicular psoriasis is an under recognized entity and was first described by McLeod in 1920 and affects adults more commonly than children.

Two clinical subtypes are described: i) Adult form commonly affects females and presents as multiple, discrete, follicle based, hyperkeratotic papules predominantly over the thighs. ii)Second type commonly affects children and presents as asymmetric, grouped, follicular, keratotic papules predominantly affecting the trunk, axilla and extensor aspects of limbs and resembles PRP.

Dark skinned individuals and patients with pre-existing plaque-type psoriasis are predisposed for developing follicular psoriasis, but follicular lesions may be seen without an evidence of psoriatic lesions anywhere else on the body[42].

Dermoscopy

In an article by Behera *et al* dermatoscopic findings of follicular psoriasis revealed a perifollicular white homogenous area, normal looking terminal hair at the centre, perifollicular scaling, multiple red dots/dotted vessels, red globules, twisted red loops and glomerular vessels/bushy capillaries[4].

Histopathology

Histopathological examination shows dilated follicular opening, parakeratotic follicular plugging, follicular hyperkeratosis, hypogranulosis, munro micro abscess, supra papillary thinning, upper dermal dilated and tortuous blood vessels and mild perivascular lympho histiocytic and neutrophilic infiltration[43, 44].

Treatment

Follicular psoriasis is managed conservatively using emollients and adequate intake of fluids and food in patients with erythrodermic follicular psoriasis. Systemic methotrexate at a starting dose of 7.5mg/week for 8 weeks has shown a significant improvement in the follicular lesions[44].

Follicular lichen planus:

Lichen planus is an idiopathic inflammatory disease that affects skin, nails, hair and has a follicular predilection in minority of the patients where it affects the scalp and tends to produce cicatricial alopecia.

There are three variants of follicular LP, namely classic i) lichen planopilaris (LPP), ii) frontal fibrosing alopecia (FFA) and iii) Graham Little syndrome. All three of them cause follicular scarring and hair loss.

i) Lichen planopilaris:

Lichen planopilaris (LPP) is the prototype of lymphocytic cicatricial alopecia and is characterized by inflammation of upper portion of the hair follicle that resulting in follicular scarring and irreversible hair loss. Lichen planopilaris is the most common form of follicular LPand mostly involves the scalp but can also affect other areas of the body with or without concomitant scalp involvement. The term LPP was first introduced by Pringle in 1905.

Pathophysiology:

There is reduced expression of peroxisome proliferator activated receptor γ that regulates these process and loss of function of hair follicle PPAR-γ triggers LPP[45].

Clinical features:

LPP is a chronic condition that affects middle-aged women and men and is characterized by either irregularly-shaped patches of hair loss or diffuse central thinning with peripheral spread. The loss of follicular ostia with perifollicular erythema and scaling of other hair follicles is the clinical hallmark. Patient presents with sever pruritus, pain, tenderness, and burning sensation and often describes it as ‘‘on fire’’. Lichen planus may occur simultaneously on oral or genital mucosa[46].

Dermoscopy:

Lichen planopilaris shows preservation of the honeycomb pattern pigmented network with pinpoint white dots that give rise to a starry sky appearance (starry sky pattern). The terminal hairs within and surrounding the alopecic patches shows peripilar casts. Casts often surround a tuft of 2 or more hairs emerging together. Other features include few broken hairs, black dots, and pili torti. Perifollicular blue-gray dots with an annular pattern or "target" pattern are occasionally seen[47].

Nirmal *et al* described dermoscopic features of LPP as perifollicular keratin plugs, white dots in the follicular region, interfollicular area showing crystalline structures (white patches) and speckling with bluegray dots, perifollicular bluegray targets and decrease in number of follicular ostia.

Histopathology

Histopathological examination of the scalp shows basket weave hyperkeratosis, follicular plug, vacuolization of basal cell in the epidermis and bandlike lymphohistiocytic infiltrate in the superficial dermis extending around the infundibulum till the proximal part of the isthmus of the hair follicle with pigment incontinence[48].

ii) Frontal fibrosing alopecia (FFA)

Frontal fibrosing alopecia (FFA) is a form of cicatricial alopecia and a variant of lichen planopilaris. It was first described by Kossard in 1994.

It is characterized by recession of the frontal hairline and may also show recession of the posterior hairline. Loss of eyebrows is an early and a universal finding and body hair loss may be present. There is loss of hair follicles with perifollicular erythema and hyperkeratosis at the marginal line.

iii) Graham–Little syndrome(PLGLS)

Piccardi–Lassueur– Graham–Little syndrome (PLGLS), also a variant of lichen planopilaris, affects women between the ages of 30 and 70 years. It is characterized by widespread follicular keratotic papules on the limbs and trunk and hair loss involving pubic hair, axillary hair, and the eyebrows[49].

Treatment

First line treatment
Topical and intralesional steroids in localized LPP patients
Oral hydroxychloroquine 200mg twice daily in localized and extensive classic LPP patients
A short course of systemic steroids to halt the progression and to improve symptoms in rapidly progressive and severe cases.
Second line
Recalcitrant LPP- Oral Methotrexate 15mg weekly for 6 months
Third line – In severe and recalcitrant LPP
Oral mycophenolate mofetil 0.5 mg twice daily for 4 weeks followed by 1 g twice daily for at least 20 weeks
Oral Cyclosporine 4–5 mg/kg/day for 4–6 months
Oral pioglitazone 15 mg/day for 8 months[50].

Table 9: Treatment of follicular LP

Follicular eczema

Follicular eczema is clinically characterized by follicular papules that are dome shaped and topped with pityriasiform scales. The papules coalesce to form discoid patches and

predominantly involves extensor aspect of forearms and legs. An associated generalized xerosis may be present in few patients.

Histopathology

Skin biopsy shows spongiotic dermatitis localized to upper portion of hair follicle.

Treatment

A midpotent steroid with emollient for 3 weeks has shown a complete resolution of the lesion[51].

METHODOLOGY

Source of data:

Patients presenting to the outpatient Department of Dermatology, Venerology and Leprosy in B.L.D.E (Deemed to be University), Shri B.M. Patil Medical College, Hospital and Research Centre, Vijayapura, were enrolled in the study.

Period of study:

The study was conducted during the period of October 2018 to July 2020.

Study design:

A hospital based prospective cross-sectional study.

Sample size:

Using the expected incidence of follicular keratotic disorders as 1.7%[17], expected sensitivity as 99% and expected specificity 95% and desired precision as 20%, the minimum sample size is 59.

This sample size will give the precision of 20% or less for both sensitivity and specificity.

By using the formula:

$$n = \frac{z^2 p(1-p)}{d^2}$$

where

Z= z statistic at 5% level of significance

d is margin of error

p is anticipated prevalence rate

Hence, the sample size will be 59, using reference article "A Clinical study of 125 patients with Phrynoderma" by Raghunatha *et al*[17].

METHOD OF COLLECTION OF DATA:

Inclusion criteria:

- Patients clinically diagnosed with follicular keratotic diseases irrespective of age, sex or duration of disease.

Exclusion criteria :

- Patients who are on or have received treatment for follicular keratotic diseases.

Methods:

- Informed written consent of the participating patients was taken.
- A prestuctured proforma was used to collect the data.
- Detailed history and thorough clinical examination of all the patients was done.
- Follicular keratotic lesions were evaluated using a hand held dermatoscope Dermalite™ DL3 (3Gen Inc., San Juab Capistrano, CA, USA) under polarized mode.
- Skin biopsy for histopathological examination was performed.
- Dermoscopic and histopathological features of individual follicular keratotic disorders was studied.

LABORATORY INVESTIGATIONS:

- Skin biopsy

Skin biopsy of follicular keratotic papule was taken and sent for histopathology examination. Biopsy was done in strict aseptic condition, using 3mm disposable skin punch. For light microscopy sections were formalin fixed, paraffin embedded and stained with hematoxylin and eosin stain.

- Other investigations like

Complete haemogram

Liver function test and fasting lipid profile was done wherever necessary.

STATISTICAL ANALYSIS:

All characteristics were summarized descriptively. For continuous variables, the summary statistics of mean± standard deviation (SD) were used. For categorical data, the number and percentage were used in the data summaries and diagrammatic presentation. Chi-square (χ^2) test was used for association between two categorical variables.

The formula for the chi-square statistic used in the chi square test is:

$$\chi_c^2 = \sum \frac{(O_i - E_i)^2}{E_i}$$

The subscript "c" are the degrees of freedom. "O" is observed value and E is expected value.
C= (number of rows-1)* (number of columns-1)

The difference of the means of analysis variables between two independent groups was tested by unpaired t test.

The t statistic to test whether the means are different can be calculated as follows:

$$t = \frac{(\overline{x_1} - \overline{x_2}) - (\mu_1 - \mu_2)}{\sqrt{\frac{s_1^2}{n_1} + \frac{s_2^2}{n_2}}}$$

where $\bar{x}_1$ = mean of sample 1

$\bar{x}_2$ = mean of sample 2

n_1 = number of subjects in sample 1

n_2 = number of subjects in sample 2

s_1^2 = variance of sample 1 = $\frac{\Sigma(x_1 - \bar{x}_1)^2}{n_1}$

s_2^2 = variance of sample 2 = $\frac{\Sigma(x_2 - \bar{x}_2)^2}{n_2}$

If the p-value was < 0.05, then the results were considered to be statistically significant otherwise it was considered as not statistically significant. Data were analyzed using SPSS software v.23 (IBM Statistics, Chicago, USA) and Microsoft office 2007.

ETHICAL CLEARANCE:

Institutional ethical committee clearance was undertaken for the study.

RESULTS

A hospital based prospective cross-sectional study was conducted from October 2018 to July 2020. A total of 76 patients with follicular keratotic diseases were included in the present study.

Follicular keratotic disesaes:

Among 76 patients diagnosed with follicular keratotic diseases, primary follicular keratotic diseases 65(85.5%) viz phrynoderma was seen in 22(28.9%)patients, keratosis pilaris 21(27.6%), lichen spinulosis 16(21.1%), pityriasis rubra pilaris in 6(7.9%) patients and secondary follicular keratotic diseases 11(14.5%) i.e.,follicular lichen planus (lichen planopilaris) was seen in 5(6.6%) patients, follicular eczema 4(5.3%) and follicular psoriasis in 2(2.6%) patients. (Figure 4 and 5 and table 10 presents distribution of cases of follicular keratotic diseases included in the study)

Figure 4: Distribution of Cases according to Primary and Secondary follicular keratotic diseases

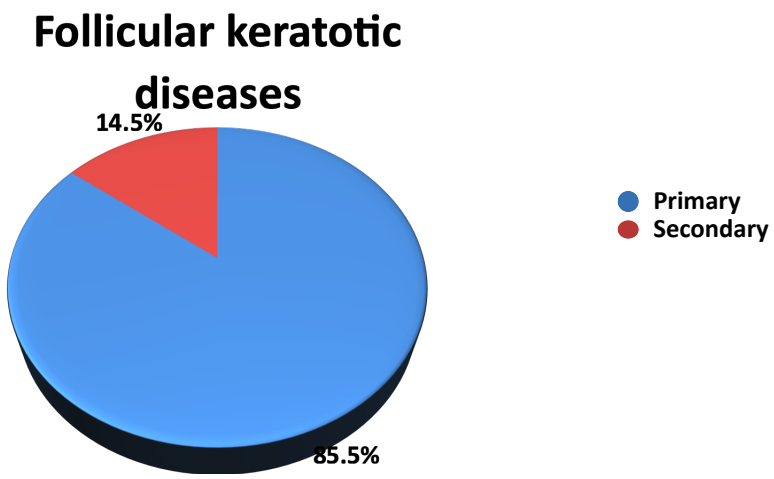
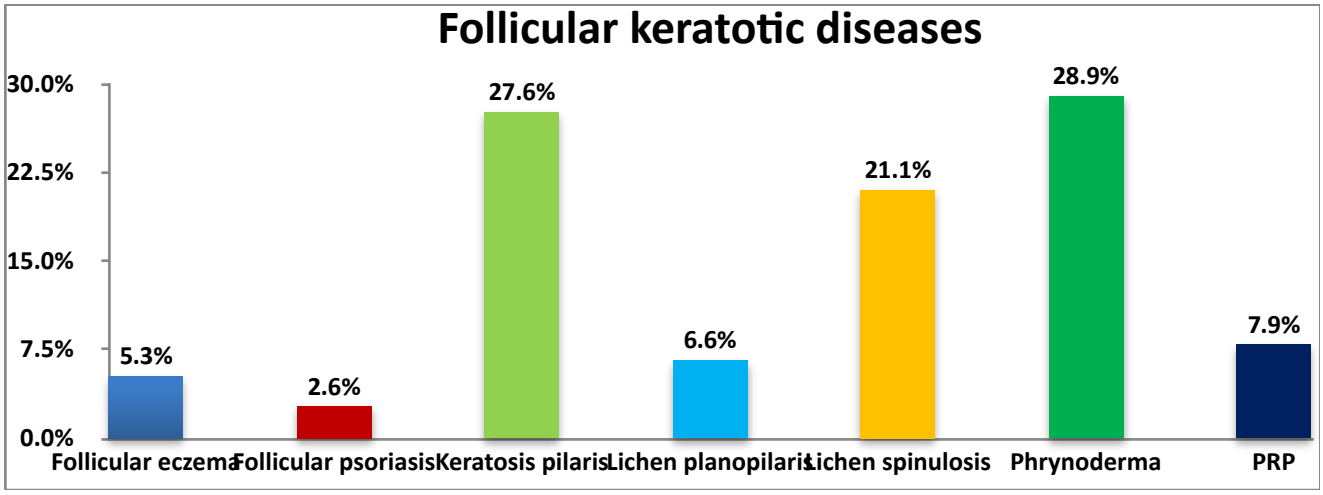


Table 10: Follicular keratotic diseases

Follicular keratotic diseases	N	%
Follicular eczema	4	5.3%
Follicular psoriasis	2	2.6%
Keratosis pilaris	21	27.6%
Follicular Lichen planus(Lichen planopilaris)	5	6.6%
Lichen spinulosis	16	21.1%
Phrynoderma	22	28.9%
Pityriasis Rubra Pilaris	6	7.9%
Total	76	100.0%

Figure 5: Follicular keratotic diseases

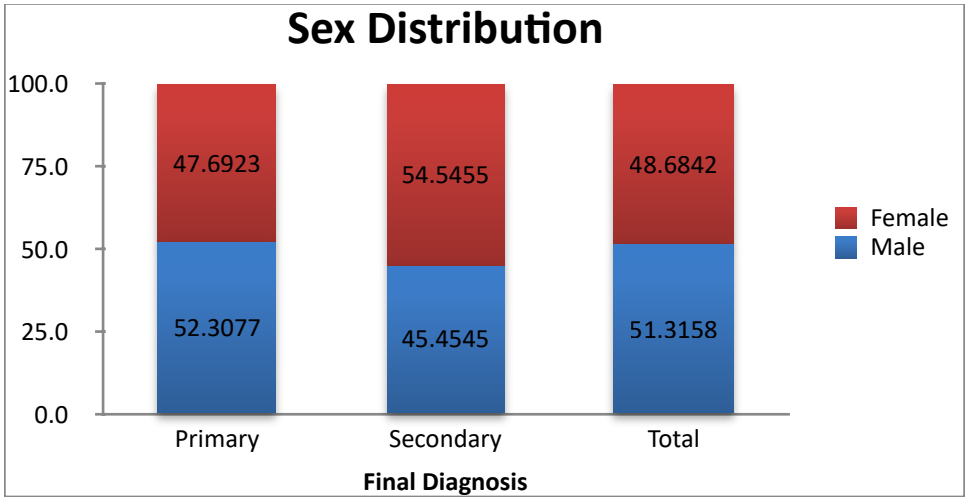


Gender distribution:

Among 76 patients, 39 (51.3%) were males and 37 (48.7%) were females. Males outnumbered females in primary follicular keratotic diseases in the ratio 1.09: 1 and females outnumbered the males in the ratio 1.2: 1 in secondary follicular keratotic diseases.

There was no statistically significant difference in the gender distribution of study population. Figure 6 presents the gender distribution of the patients with follicular keratotic diseases included in the study.

Figure 6: Sex distribution of patients in follicular keratotic diseases



Age distribution:

The age of the patients enrolled in the study ranged from 2 years to 48 years with a mean age of 26.7±2.4years. The age distribution of the study population showed a significant statistical difference (p value < 0.001). Table 11 and Figure 7 presents the age distribution of the patients included in the study.

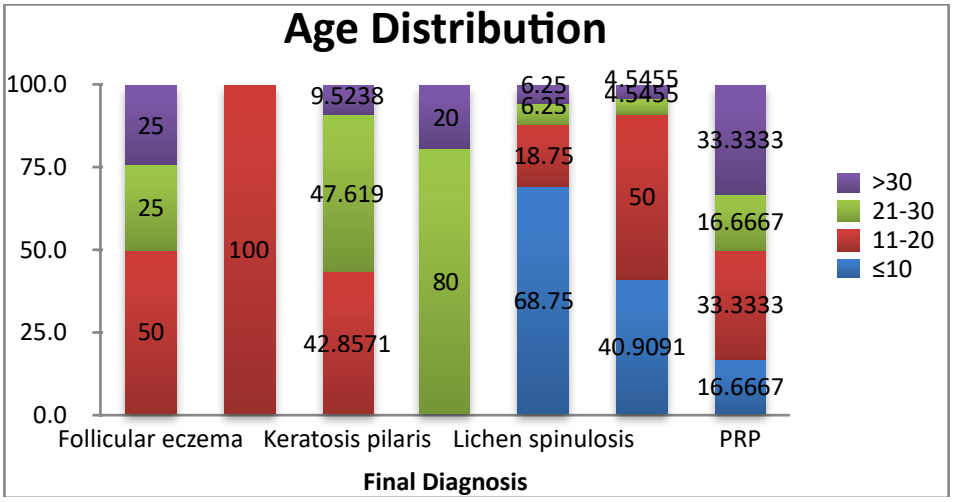
Pre-adolescent and adolescent population in the age group of 11-20 years, constituted the majority of study population with maximum of 29 (38.2%) patients followed by childhood population 21 (27.6%) in the age group ≤10 years followed by adults 18(23.7%) and 8(10.5%) in the age group 21-30 years and > 30years respectively.

Table 11: Age distribution

Follicular keratotic Diseases	Age(years)								p value
	≤10		11-20		21-30		>30		
	N	%	N	%	N	%	N	%	
Follicular eczema	0	0.0	2	50.0	1	25.0	1	25.0	<0.001*
Follicular psoriasis	0	0.0	2	100.0	0	0.0	0	0.0	
Keratosis pilaris	0	0.0	9	42.9	10	47.6	2	9.5	
Lichen planopilaris	0	0.0	0	0.0	4	80.0	1	20.0	
Lichen spinulosis	11	68.8	3	18.8	1	6.3	1	6.3	
Phrynoderma	9	40.9	11	50.0	1	4.5	1	4.5	
PRP	1	16.7	2	33.3	1	16.7	2	33.3	
Total	21	27.6	29	38.2	18	23.7	8	10.5	

Note: * significant at 5% level of significance (p<0.05)

Figure 7: Age distribution of patients in follicular keratotic diseases

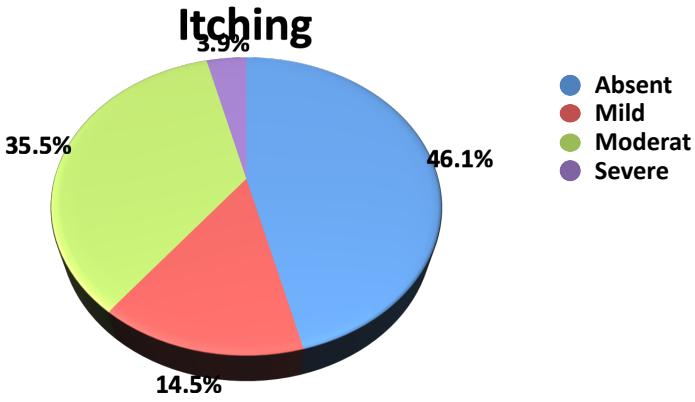


Itching

The lesions were asymptomatic in 35(46.1%) patients, mild itching was present in 11(14.5%), moderate itching in 27(35.5%) patients and severe itching was observed in 3(3.9%) patients. The presence of itching showed a significant statistical difference in the study population.

Itching was maximum in secondary follicular keratotic diseases which included follicular psoriasis 2(100%) patients and follicular eczema 3(75%) followed by primary follicular keratotic diseases i.e., pityriasis rubra pilaris 4 (66.7%) and lichen spinulosis 10(62.5%) patients.

Figure 8: Degree of itching



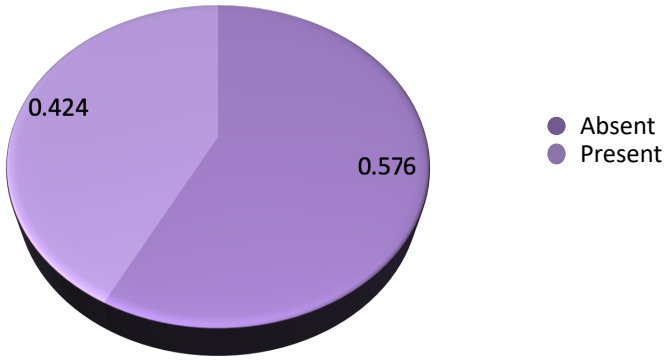
Associated diseases

Only 4(25%) patients of lichen spinulosis had an associated atopic dermatitis. No other follicular keratotic diseases in the study population had associated disorder. Atopic dermatitis in lichen spinulosis showed a significant statistical association (p value 0.015).

Table 12: Associated atopic dermatitis in lichen spinulosis

Atopy	No. of Patients	Percentage
Present	04	25.0
Absent	12	75.0
Total	16	100.0

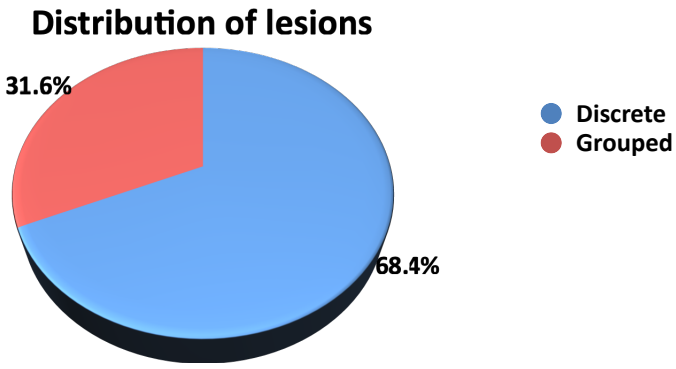
Figure 9: Associated atopic dermatitis in lichen spinulosis



Distribution of lesions

Among 76 patients included in the study, 52 (68.4%) patients showed distribution of lesions in a discrete fashion and 24 (31.6%) patients in a grouped manner. The distribution of lesions of the study population showed a significant statistical difference.

Figure 10: Distribution of lesions



Clinical features:

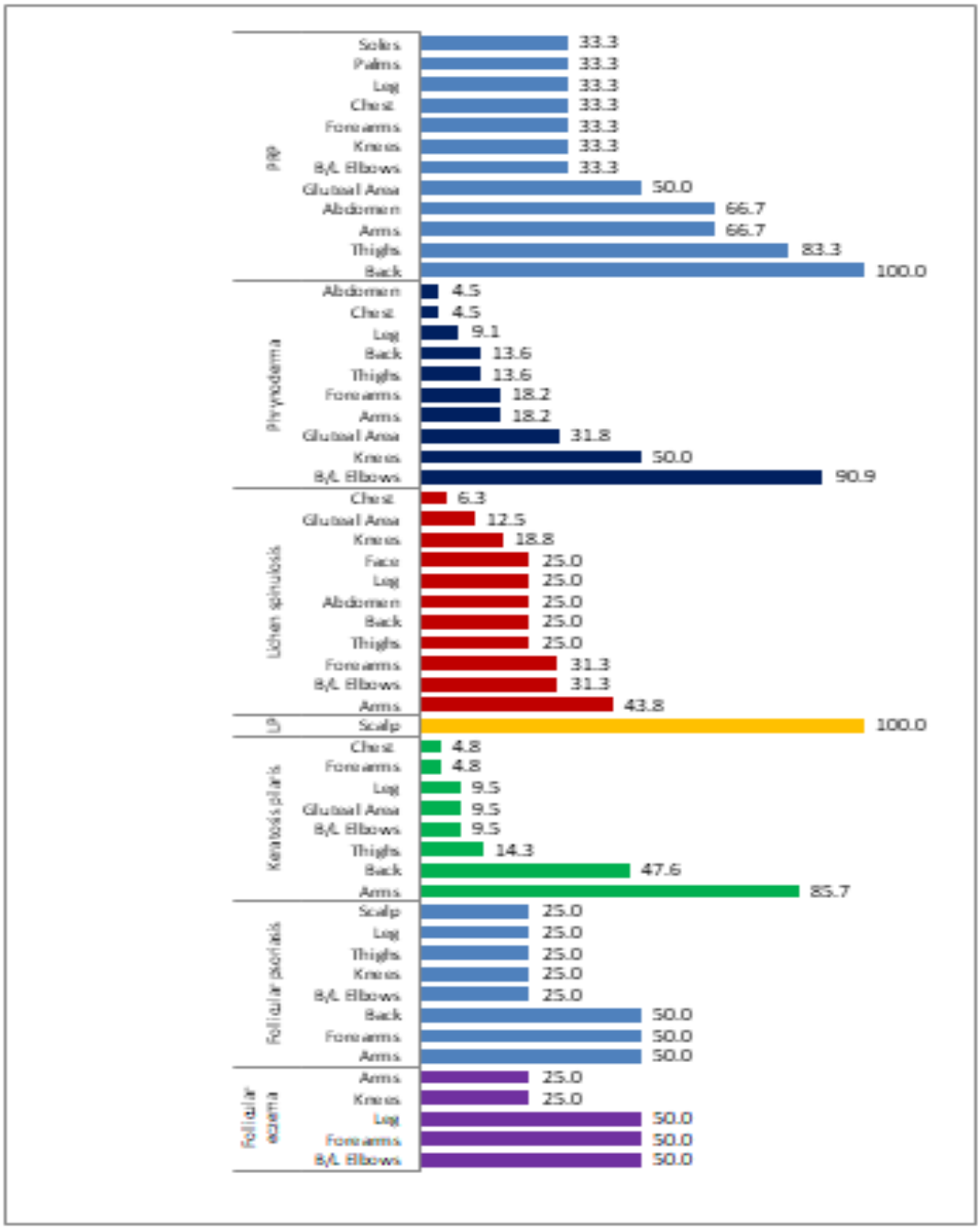
All the patients of primary follicular keratotic diseases had follicular keratotic papules distributed in a grouped and or in a discrete manner, whereas secondary follicular diseases presented with varied type of lesions viz., diffuse hair loss or patchy hair loss over scalp in follicular LP (Lichen planopilaris), follicular papules with scaling over scalp and trunk in follicular psoriasis and skin coloured scaly papules coalescing to form discoid plaque with excoriation marks in follicular eczema. The distribution of lesions according to the site showed a significant statistical association in the study population.

Among primary follicular keratotic diseases, majority had lesions confined to bilateral elbows 20(90.9%) followed by knees 11(50%), gluteal area 7(31.8%) and back 3(13.6%) in phrynoderma patients, as is depicted in figure 16. In keratosis pilaris, the lesions were predominantly present over bilateral arms in 18(85.7%) patients followed by back 10(47.6%) as can be seen in figure 19. The lesions were confined to bilateral arms 7(48.3%) followed by bilateral elbows and forearms in 5(31.3%) patients each and involved trunk and lower extremities in 4(25%) each of lichen spinulosis patients as is depicted in figure 22. In pityriasis rubra pilaris, majority patients had lesions confined to back 6(100%) and thighs 5(83.3%), abdomen and arms in 4(66.7%) each and gluteal area in 3(50%) patients followed by upper and lower extremities including palms and soles in 2(33.3%) patients as can be observed in figure 25.

Among secondary follicular keratotic diseases, all the 5(100%) patients had lesions over the scalp in follicular lichen planus (lichen planopilaris) and majority of the patients had lesions confined to legs, forearms and elbows 2(50%) each followed by arms and knees in 1 (25%)

patient each in follicular eczema, as can be observed in figure 28. In follicular psoriasis, the lesions were predominantly present over back and upper extremities in 2 patients each (100%) and over scalp and lower extremities in 1patient each (50%) , as is depicted in figure 31 .Figure 11 represents the distribution of lesions according to the site

Figure 11 : Distribution according to lesions



Dermoscopy findings in follicular keratotic diseases

A) Perifollicular and interfollicular area

Among 65(85.5%) primary follicular keratotic diseases, all the patients (100%) of phyrnoderma, lichen spinulosis, pityriasis rubra pilaris and 18(85.7%) patients of keratosis pilaris had perifollicular scaling. Among 22(28.9%) phrynoderma patients, keratotic plug 22(100%) was seen predominantly followed by perifollicular fibrosis 12(54.5%) and perifollicular erythema was observed in 1(4.5%) patient as is seen in figure 17. Among 21(27.6%) keratosis pilaris patients, perifollicular erythema and keratotic pug was seen significantly in 19(90.5%) patients each as can be observed in figure 20. Keratotic plug 10(62.5%) was predominantly found in lichen spinulosis followed by perifollicular erythema 5(31.3%) and perifollicular fibrosis 3(18.8%) as is depicted in figure 23. In Pityriasis rubra pilaris 6(7.9%), keratotic plug 5(83.3%) was significantly seen followed by perifollicular erythema 3(50%) as is seen in figure 26. Normal interfollicular area was seen in all lichen spinulosis patients 16(100%) and hyperpigmented interfollicular area and lichenification was seen in 13(59.1%) and 8(36.4%) phrynoderma patients respectively. In keratosis pilaris, interfollicular area was normal in 13(61.9%) patients, hyperpigmentation in 6(28.6%) and interfollicular erythema was seen in 2(4.8%) patients. In pityriasis rubra pilaris, interfollicular area was normal in 3(50%) patients and erythema, hyperpigmentation, lichenification was observed in 1 (16.7%) patient each.

Among 11(14.5%) secondary follicular keratotic diseases, all the patients 11(100%) had perifollicular scaling. Among 5(6.6%) patients of follicular LP (LPP), keratotic plug was seen in all the 5(100%) patients followed by perifollicular erythema and perifollicular fibrosis in 3(60%) patients each as is depicted in figure

34. Keratotic plug was seen in 3(75%) and 1(50%) patient of follicular eczema and follicular psoriasis respectively. Interfollicular area showed hyperpigmentation in 4(80%) patients in follicular LP and lichenification and hyperpigmentation in 2(50%) and 1(25%) patients of follicular eczema respectively as can be observed in figure 29 and all patients 2(100%) had normal interfollicular area in follicular psoriasis as is depicted in figure 32.

The follicular, perifollicular and interfollicualr lesions dermoscopically showed a significant statistical association.

Figure12 presents the follicular and perifollicular lesions findings dermoscopically

Figure13 presents the interfollicular lesions findings dermoscopically

Table 13: Follicular/ Perifollicular area dermoscopic findings

Follicular/ Perifollicular area findings	Follicular keratotic diseases														p value
	Follicular eczema		Follicular psoriasis		KP		LPP		LS		Phrynoderma		PRP		Total
	N	%	N	%	N	%	N	%	N	%	N	%	N	%	
Perifollicular Fibrosis	0	0.0	0	0.0	0	0.0	3	60.0	3	18.8	12	54.5	0	0.0	18	<0.001*
Perifollicular Erythema	0	0.0	0	0.0	19	90.5	3	60.0	5	31.3	1	4.5	3	50.0	31	<0.001*
Perifollicular Scaling	4	100.0	2	100.0	18	85.7	5	100.0	16	100.0	22	100.0	6	100.0	73	0.225
Keratotic plug	3	75.0	1	50.0	19	90.5	5	100.0	10	62.5	22	100.0	5	83.3	65	0.027*

Note: * significant at 5% level of significance (p<0.05)

Figure 12: Follicular/ Perifollicular area dermoscopic findings

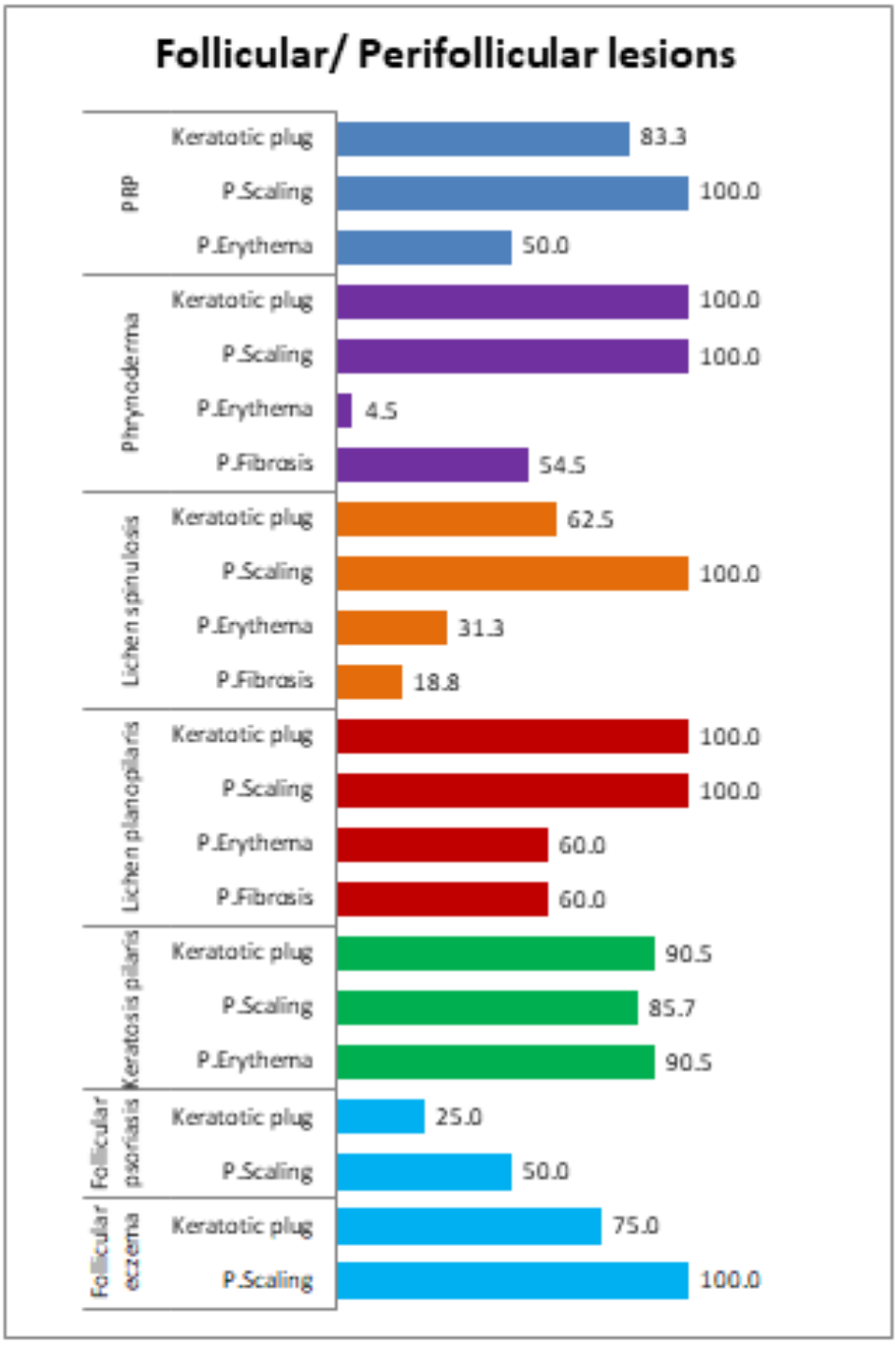
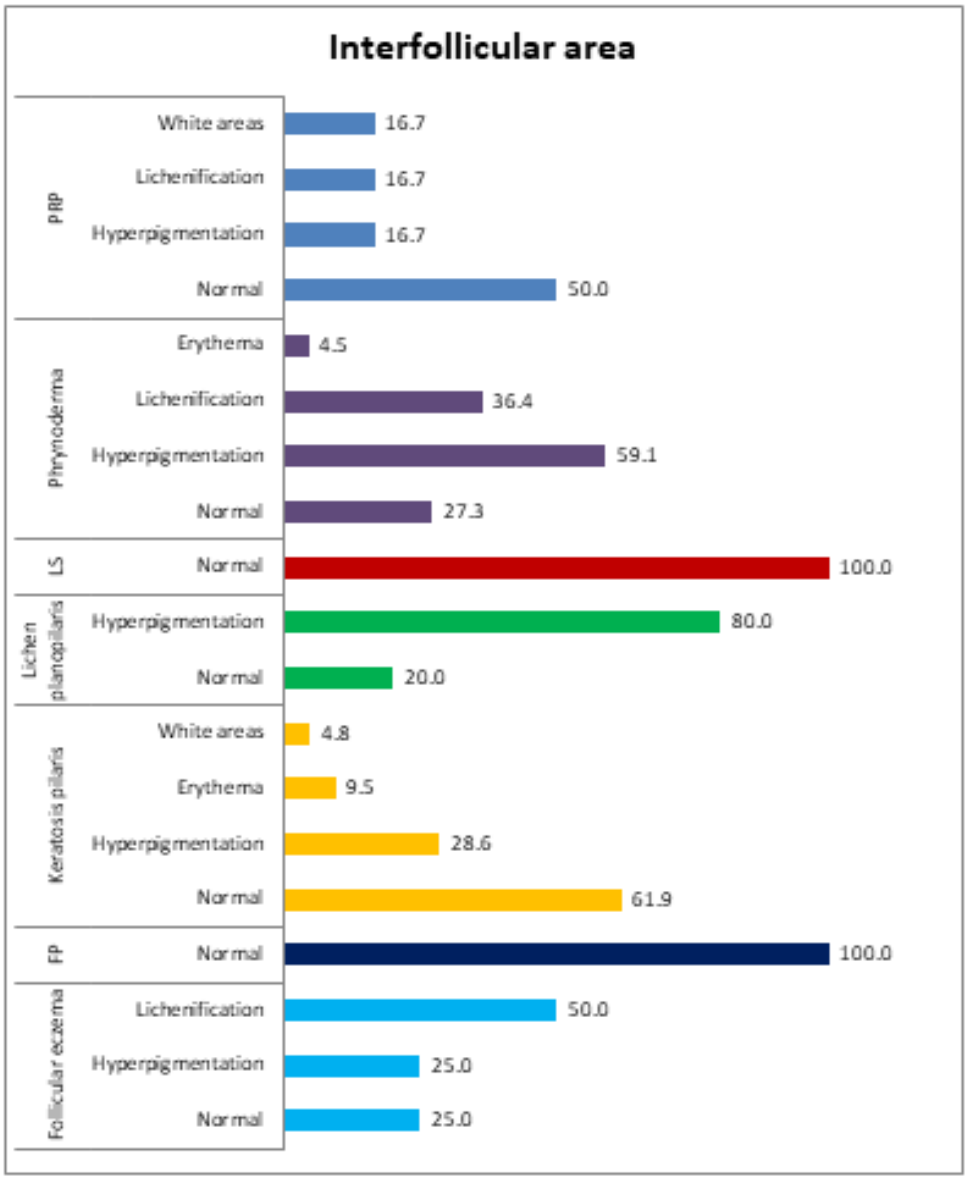


Figure 13: Interfollicular area findings



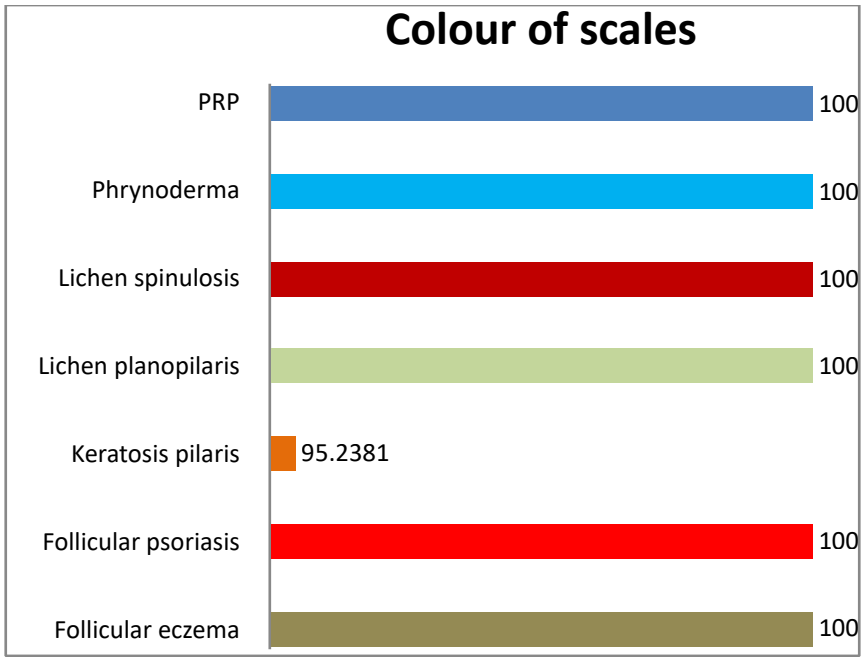
Type of scales

Among 76(100%) patients included in the study group, white scales was observed in all the patients of phrynoderma 22(100%), lichen spinulosis 16(100%), PRP 6(100%), follicular LP 5(100%), follicular eczema 4(100%), follicular psoriasis 2(100%), and 20(95.2%) patients of keratosis pilaris.

Table 14: Colour of scales

Colour of scales	Follicular keratotic diseases														Total	p value
	Follicular eczema		Follicular Psoriasis		KP		LPP		LS		Phrynoderma		PRP			
	N	%	N	%	N	%	N	%	N	%	N	%	N	%		
White	4	100.0	2	100.0	20	95.2	5	100.0	16	100.0	22	100.0	6	100.0	75	0.851

Figure 14: Colour of scales



Hair shaft

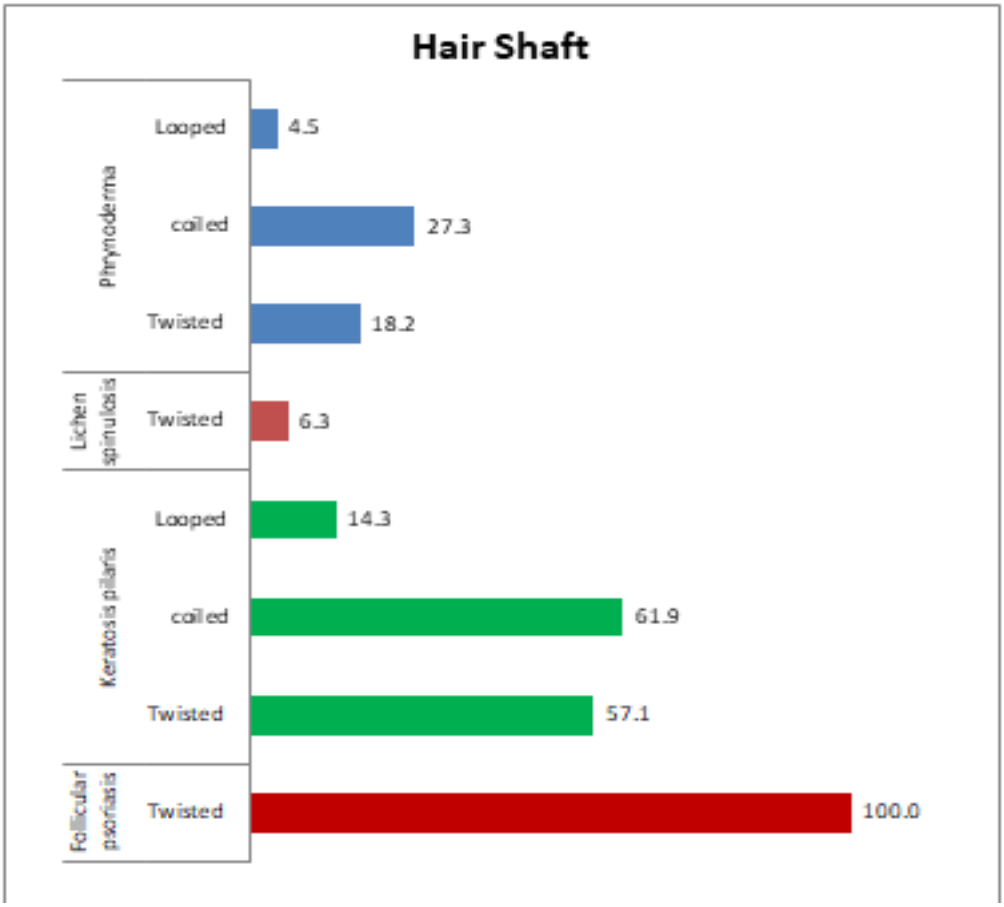
Among 76 patients included in the study population, coiled hair was predominantly found in 13 (61.9%) patients of keratosis pilaris followed by phrynoderma 6(27.3%). Twisted hairs was the predominant dermoscopic finding in follicular psoriasis 2(100%) followed by keratosis pilaris 12(57.1%), phrynoderma 4(18.2%) and lichen spinulosis 1(6.3%). Looped hair was present in 3(14.3%) patients of keratosis pilaris and 1(4.5%) patient of phrynoderma. The hair shaft findings in the study population showed a significant statistical association (p value 0.001). Figure 15 presents the hair shaft findings

Table 15: Hair shaft findings

Type of hair	Follicular keratotic diseases														Total	p value
	Follicular eczema		Follicular psoriasis		Keratosis pilaris		LPP		LS		Phrynoderma		PRP			
	N	%	N	%	N	%	N	%	N	%	N	%	N	%		
Twisted	0	0.0	2	100.0	12	57.1	0	0.0	1	6.3	4	18.2	0	0.0	19	<0.001*
Coiled	0	0.0	0	0.0	13	61.9	0	0.0	0	0.0	6	27.3	0	0.0	19	<0.001*
Looped	0	0.0	0	0.0	3	14.3	0	0.0	0	0.0	1	4.5	0	0.0	4	0.508

Note: * significant at 5% level of significance (p<0.05)

Figure 15: Hair shaft findings



Type of vessel

Red dots were present predominantly in follicular psoriasis 2(100%) followed by follicular eczema 3(75%) and pityriasis rubra pilaris 4(66.6%).

Histopathology

The predominant histopathological findings of follicular keratotic diseases included in the study population was epidermal hyperkeratosis, parakeratosis, orthokeratosis, acanthosis, spongiosis, dilated hair follicle, follicular plugging, perifollicular, perivascular, periadnexal lymphocytic infiltration and dilated capillaries. Thus we report that histopathology alone cannot differentiate and diagnose individual follicular keratotic diseases.

The histopathological findings in the study population showed a significant statistical difference.

Phrynoderma

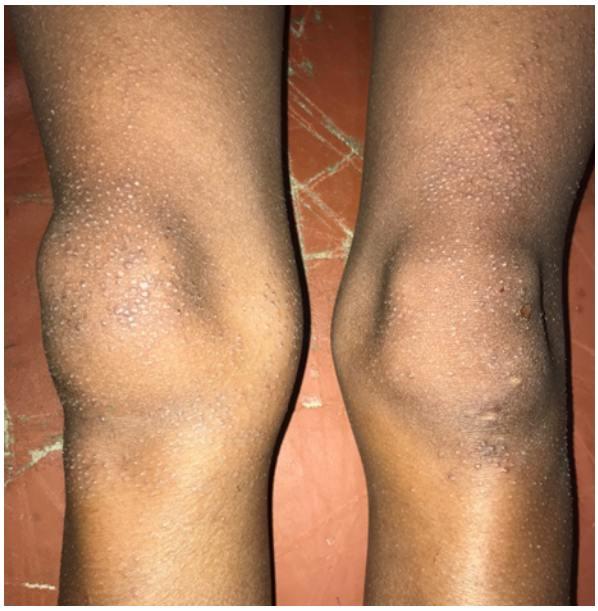


Fig. 16a

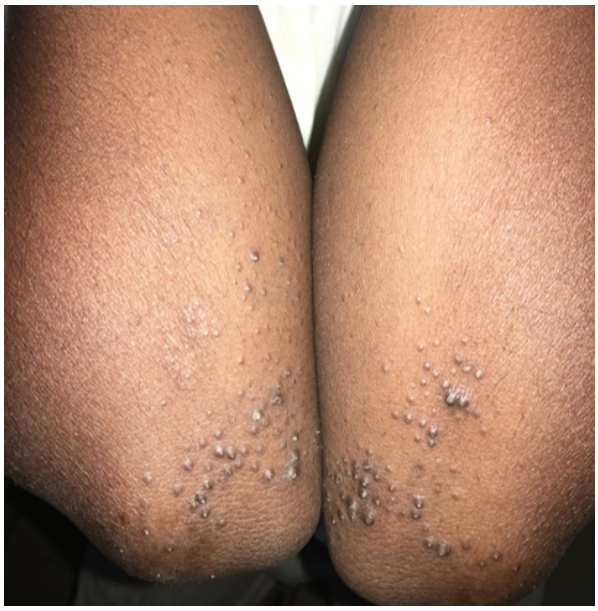


Fig. 16b

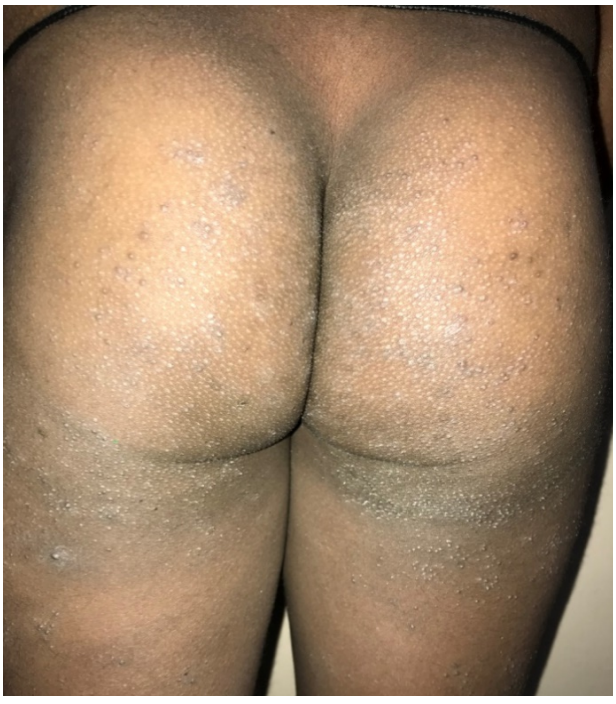


Fig. 16c

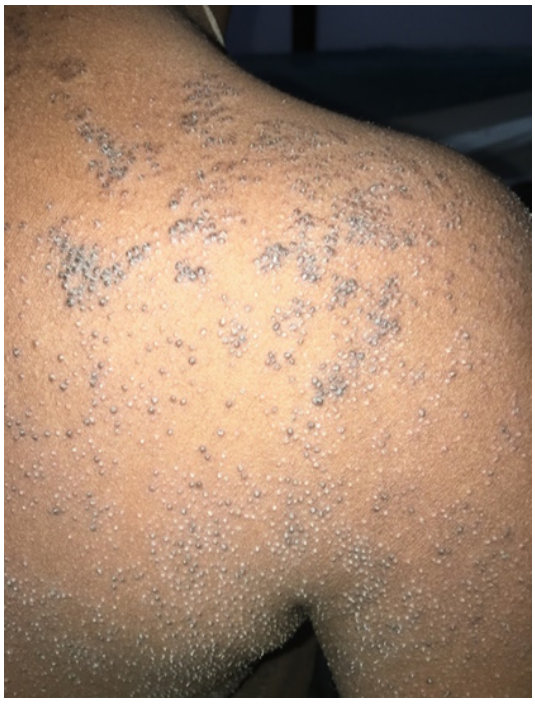


Fig. 16d

Figure 16: Discrete, skin coloured and hyperpigmented follicular papules with central keratinous plug over knees(a), elbows(b), gluteal area(c), back and shoulders(d).

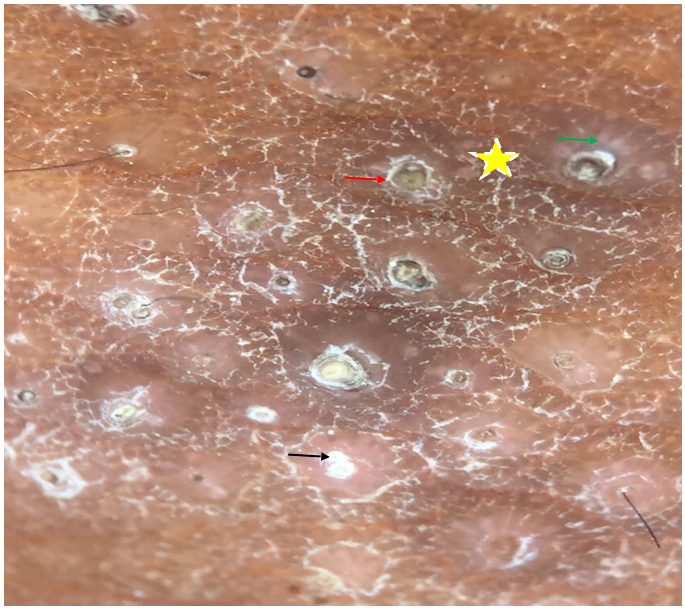


Figure 17: Dermoscopy of phrynoderma shows perifollicular scaling (red arrow), keratin plug (black arrow), perifollicular fibrosis(green arrow), interfollicular area hyperpigmentation and lichenification (yellow star).

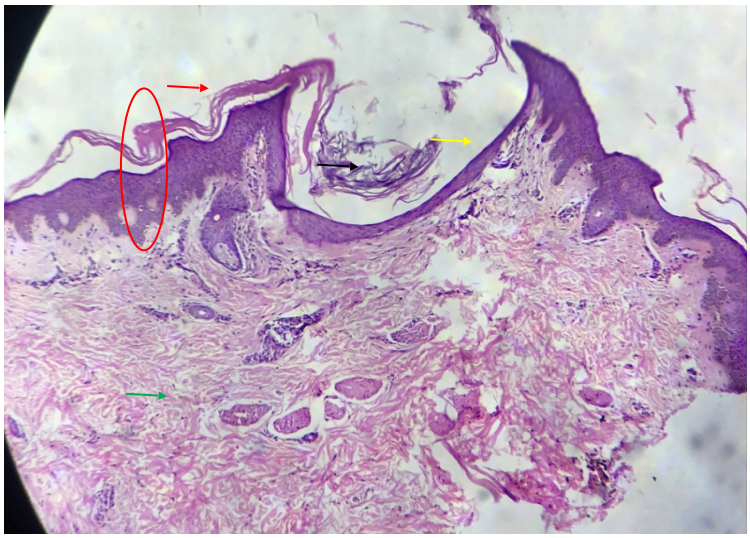


Figure 18 : Histopathology (H and E 10x) of phrynoderma shows epidermal hyperkeratosis (red arrow), increased epidermal thickening (red ring), dilated follicular infundibulum (brown arrow), keratin plug (black arrow), dermal fibrosis (green arrow)

Keratosis pilaris

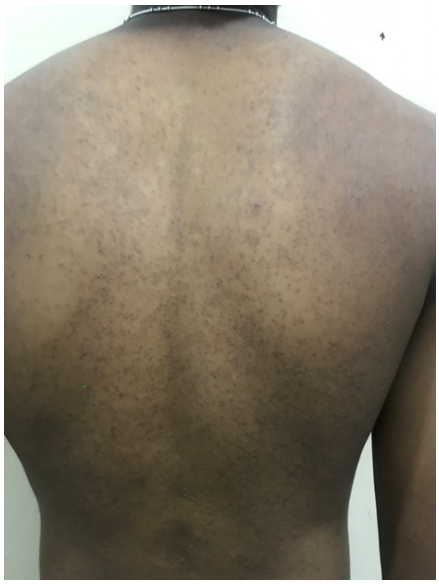


Fig. 19a

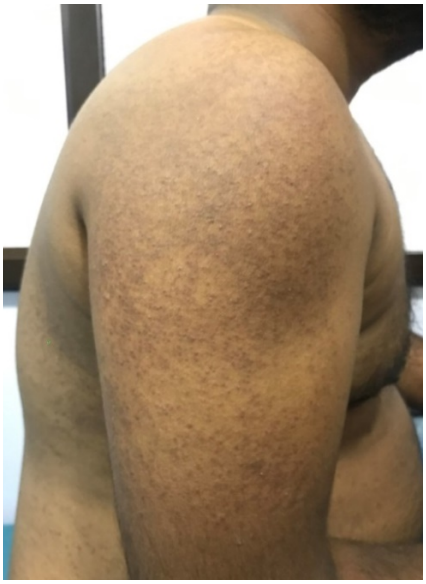


Fig. 19b

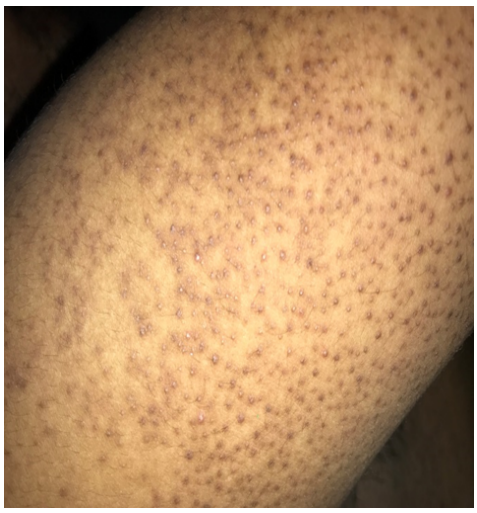


Fig. 19c

Figure 19: Multiple discrete erythematous and hyperpigmented follicular keratotic papules over back (a) and posterior aspect of upper arms(b). Close up view (c) of keratotic papules.

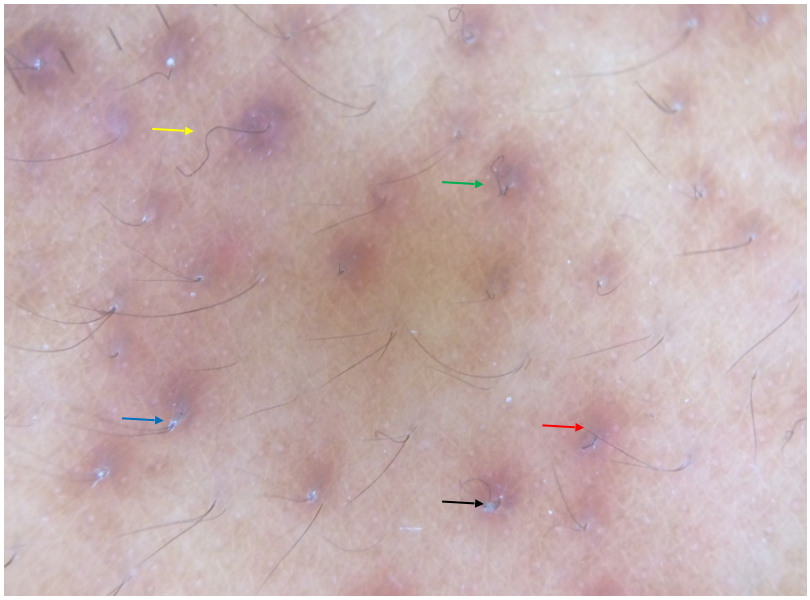


Figure 20: Dermoscopy of keratosis pilaris shows perifollicular scaling (blue arrow), perifollicular erythema (red arrow), keratotic plug (black arrow), coiled hair (green arrow) and twisted hair (yellow arrow).

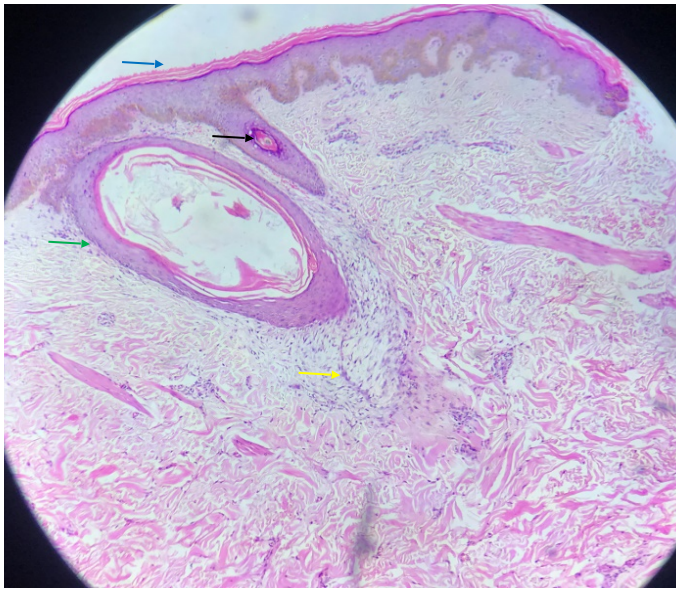


Figure 21: Histopathology (H and E 10x) of keratosis pilaris shows epidermal hyperkeratosis (blue arrow), orthokeratosis, dilated follicular infundibulum (green arrow), keratin plug (black arrow), perifollicular lymphocytic infiltration (yellow arrow).

Lichen spinulosis

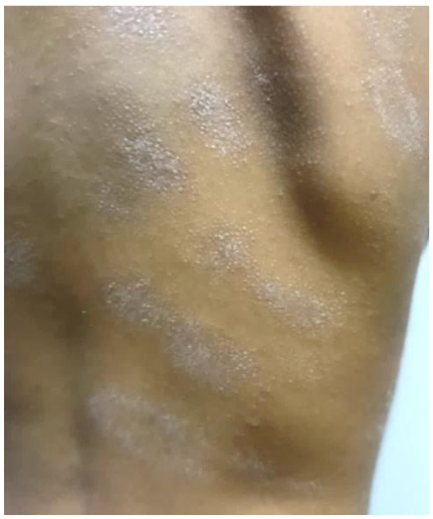


Fig. 22a

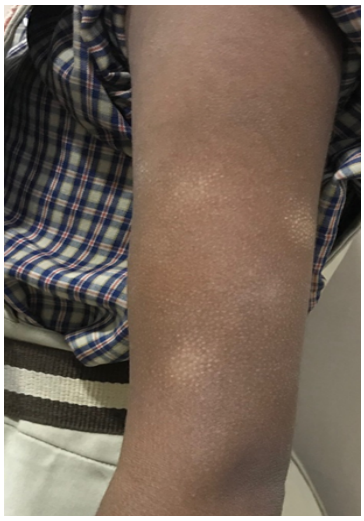


Fig. 22b

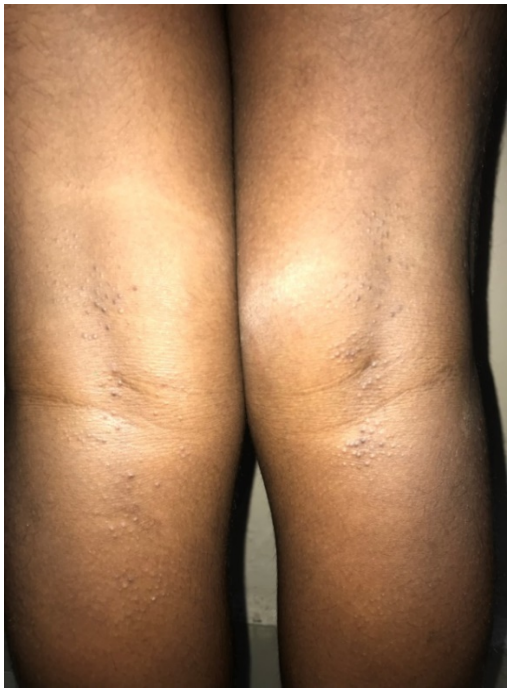


Fig. 22c

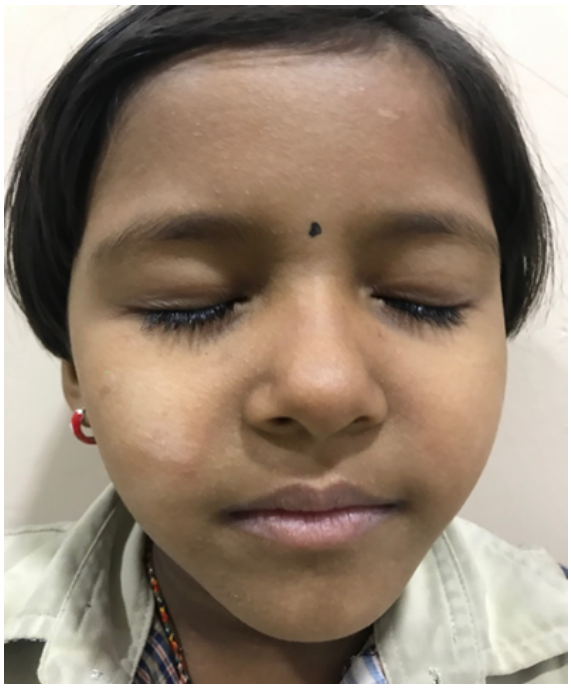


Fig. 22d

Figure 22: Multiple flesh coloured follicular keratotic papules with central spinous process present over back (a), arms (b), posterior aspect of thighs and legs (c). Figure 22d: associated atopic dermatitis: hypopigmented scaly plaques over face.

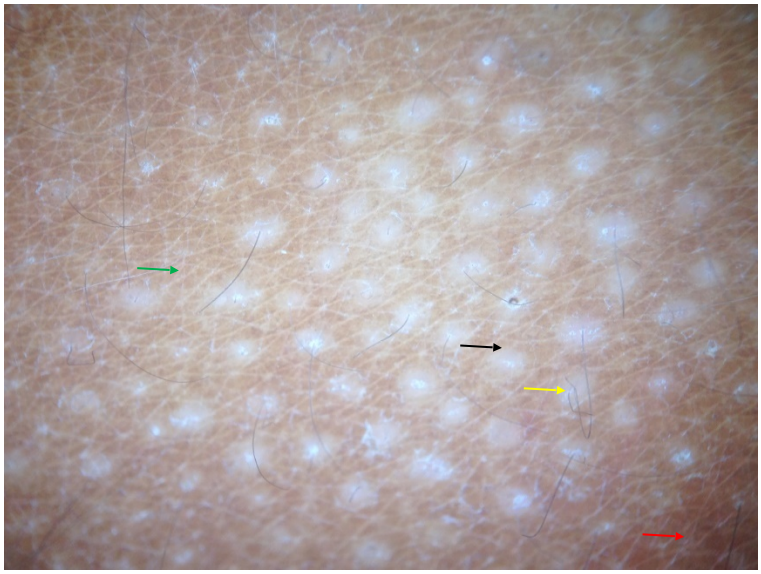


Figure 23: Dermoscopy of lichen spinulosis shows perifollicular scaling (red arrow), keratin plug (black arrow), perifollicular white area (yellow arrow) and normal interfollicular area (green arrow).

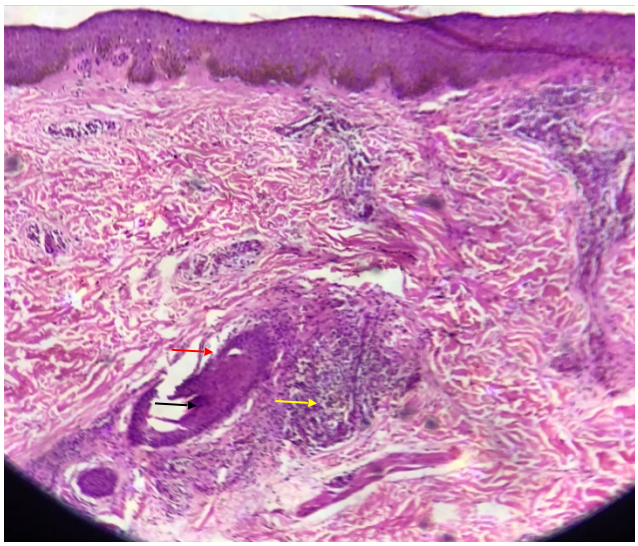


Figure 24: Histopathology (H and E 10x) of lichen spinulosis shows normal epidermis, dilated follicular infundibulum (red arrow), keratin plug (black arrow), perifollicular lymphocytic infiltration (yellow arrow).

Pityriasis rubra pilaris

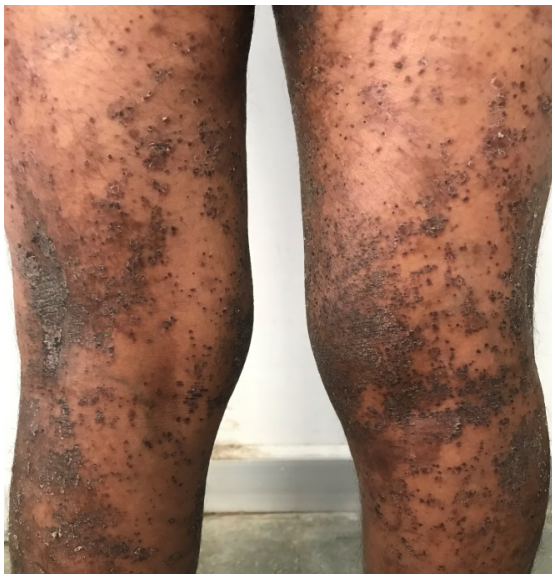


Fig. 25a

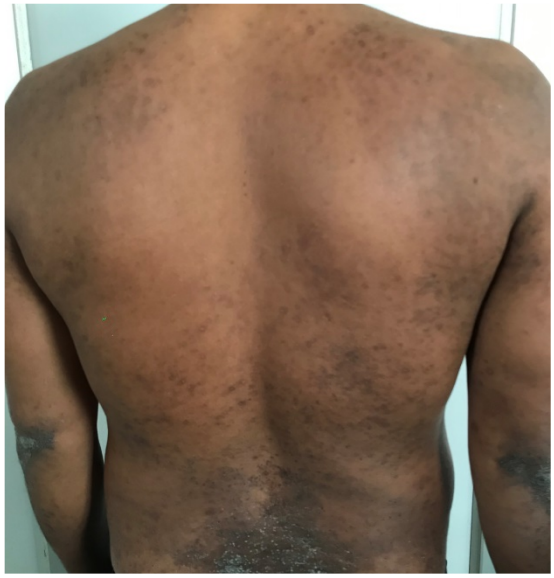


Fig. 25b

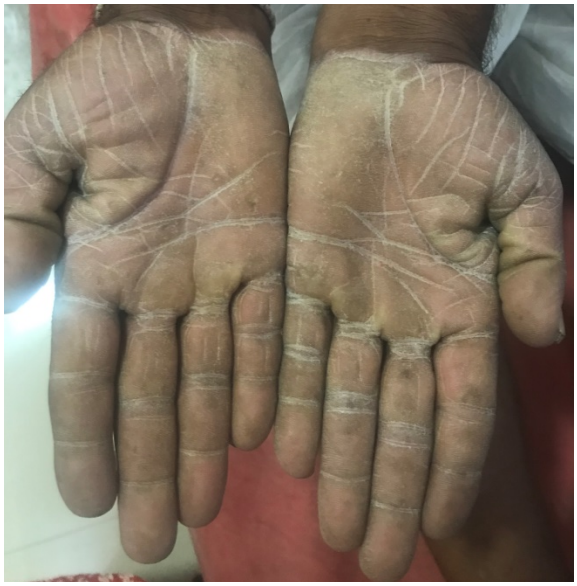


Fig. 25c

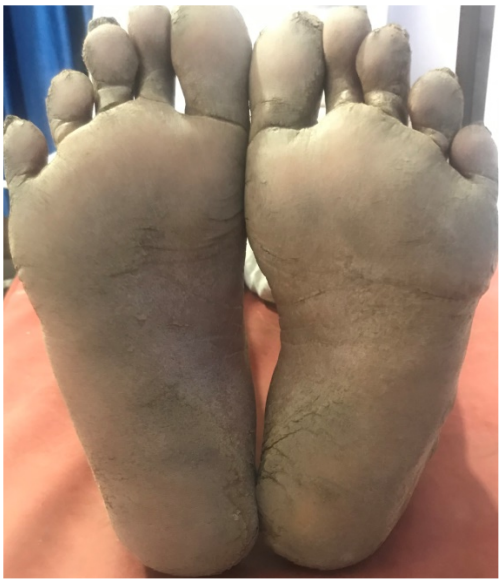


Fig. 25d

Figure 25: Multiple hyperpigmented small follicular keratotic papules with islands of sparing present over lower extremities (a), trunk (b), palms (c) and soles (d).

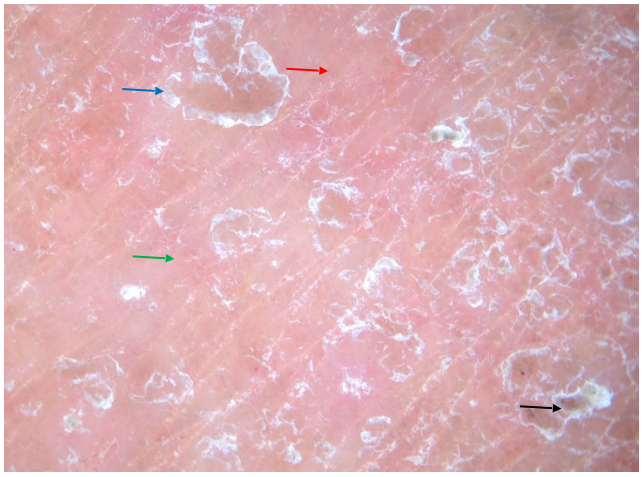


Figure 26: Dermoscopy of pityriasis rubra pilaris shows perifollicular scaling (blue arrow), keratotic plug (black arrow), perfollicular/interfollicular erythema (red arrow), red dots (green arrow).

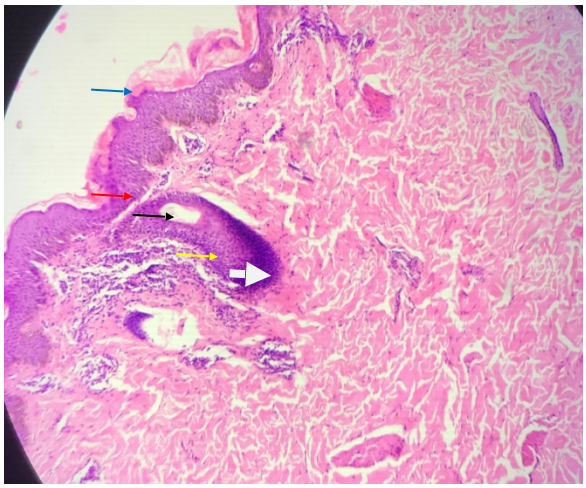


Fig. a (H and E 10x)

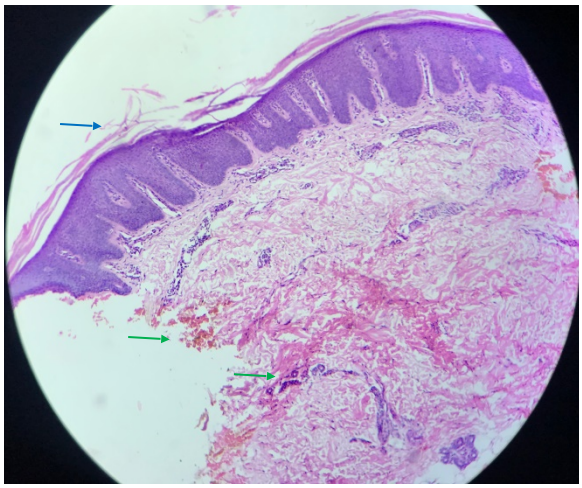


Fig. b (H and E 4x)

Figure 27: Histopathology of pityriasis rubra pilaris epidermal hyperkeratosis (blue arrow), orthokeratosis, broad and short rete ridges (red arrow), dilated follicular infundibulum (yellow arrow), keratin plug (black arrow), perifollicular lymphocytic infiltration (white arrow) and dilated capillaries & RBCs (green arrow).

Follicular eczema

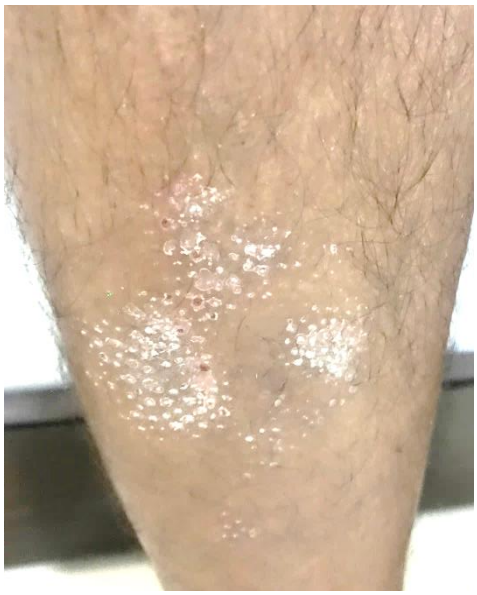


Figure 28: Multiple skin coloured scaly keratotic follicular papules coalescing to form plaques with excoriation present over lower leg

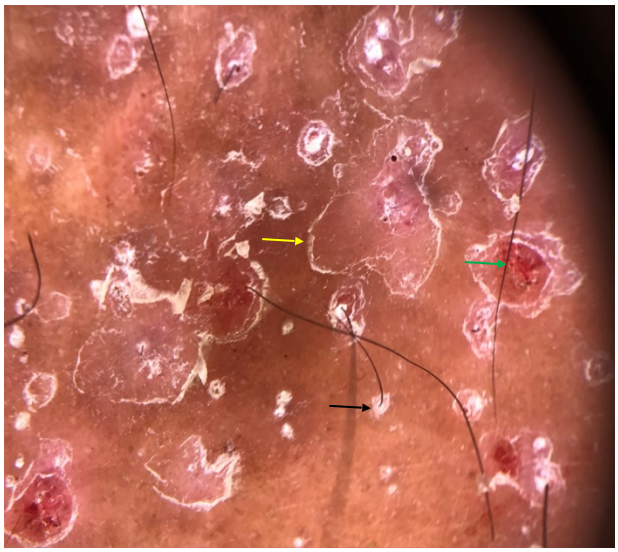


Figure 29: Dermoscopy of follicular eczema shows perifollicular scaling (yellow arrow), keratotic plug (black arrow), irregular red dots (green arrow).

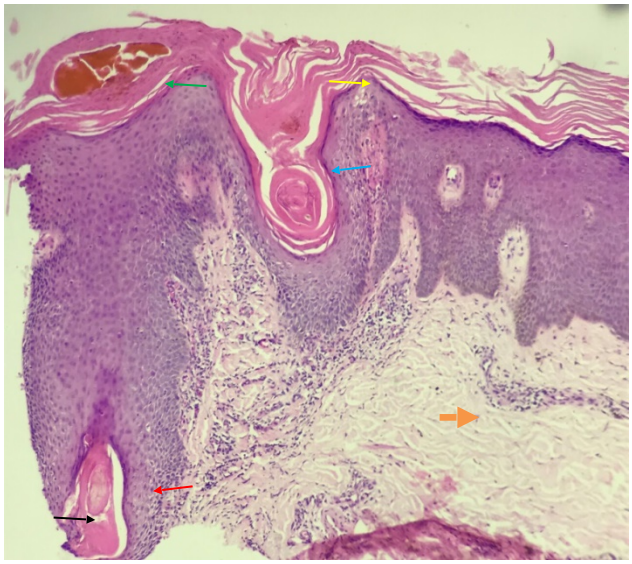


Figure 30: Histopathology (H and E 10x) of follicular eczema shows epidermal hyperkeratosis (yellow arrow), parakeratosis, spongiosis, dilated follicle (blue arrow), keratin plug (black arrow), perifollicular hyperkeratosis, spongiosis (red arrow), dilated blood vessels and RBCs (green arrow), dermal lymphocytic infiltration (orange thick arrow).

Follicular psoriasis

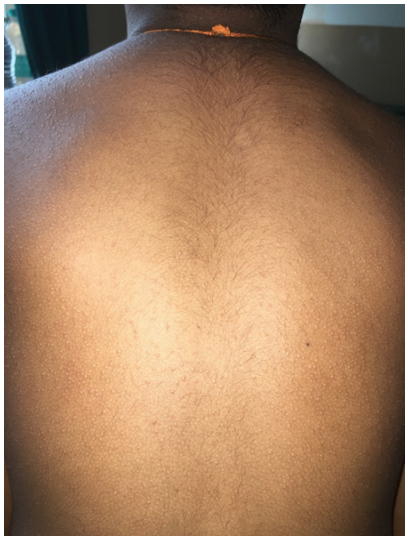


Figure 31a

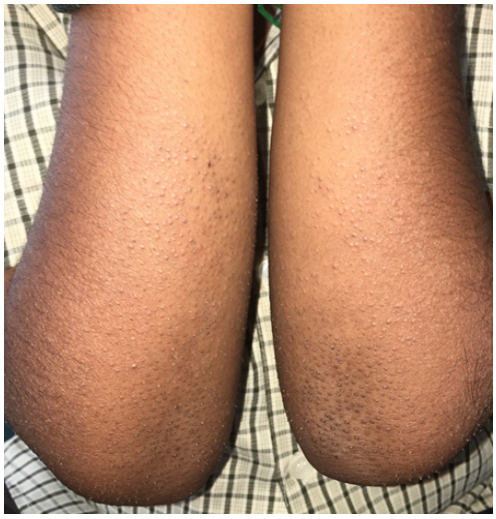


Figure 31b

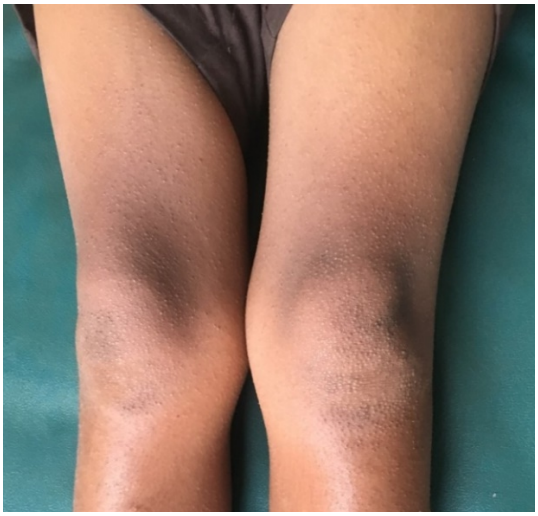


Figure 31c

Figure 31: Multiple small scaly keratotic follicular papules over back (fig 31a), forearms (fig 31b) and thighs & legs (fig 31c).

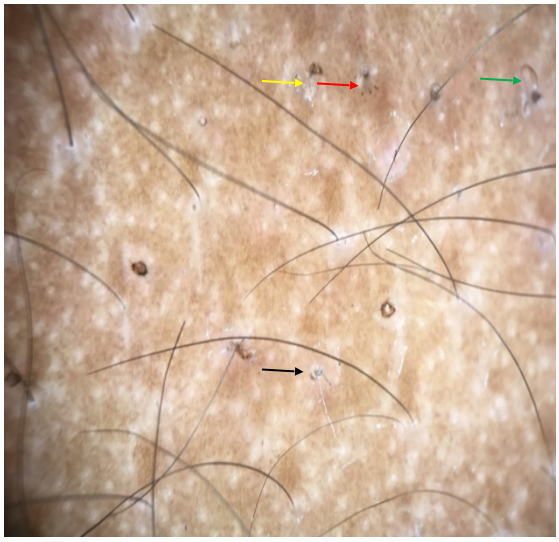


Figure 32: Dermoscopy of follicular psoriasis shows perifollicular scaling (yellow arrow), keratin plug (black arrow), perifollicular regular red dots (red arrow), twisted hair (green arrow).

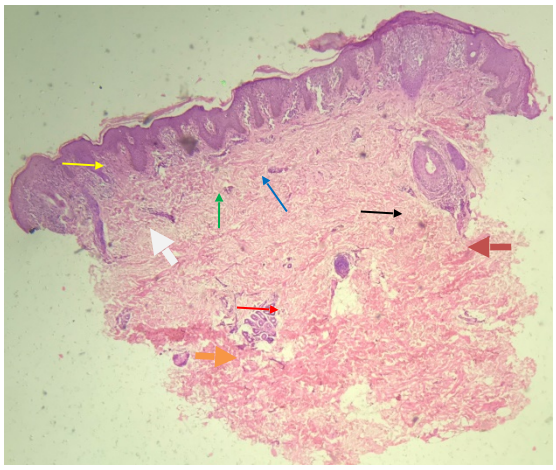
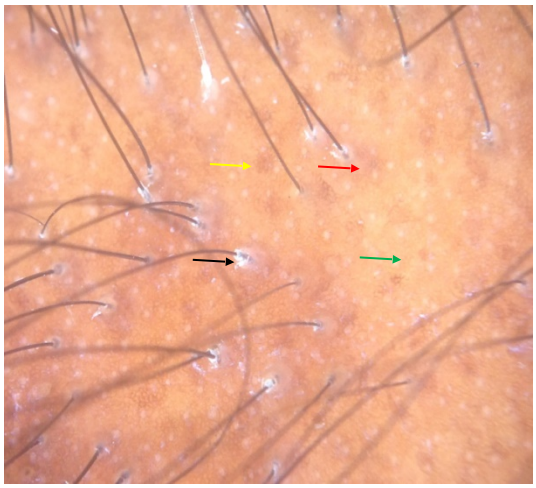


Figure 33: HPE(H and E 4x) of follicular psoriasis shows epidermal hyperkeratosis (yellow arrow), elongated rete ridges (thick white arrow), camel foot (green arrow) and club shaped (blue arrow) rete ridges, dilated hair follicle (black arrow), dilated capillaries (red arrow), perifollicular (thick maroon arrow) and perivascular lymphocytic infiltration (thick orange arrow).

Follicular LP (Lichen planopilaris)



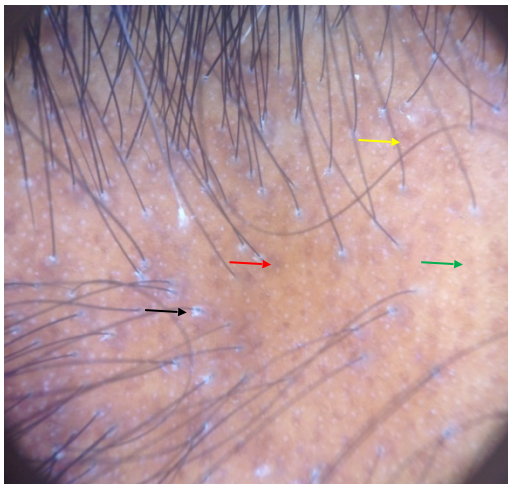
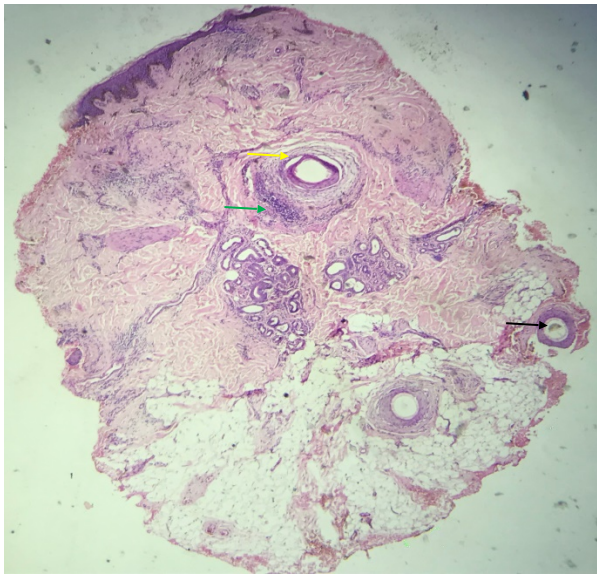


Figure 34a **Figure 34b**

Figure 34: Dermoscopy of follicular LP (Lichenplano pilaris) shows perifollicular erythema (red arrow), peripilar cast (black arrow), interfollicular area blue gray dots (yellow arrow), reduced follicular ostia (green arrow).



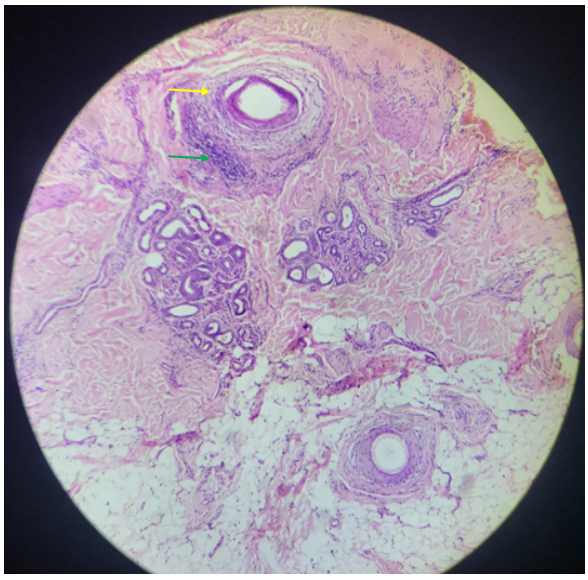


Figure 35a (H and E 4x) **Figure 35b (H and E 10x)**

Figure 35: Histopathology of follicular LP (lichen planopilaris) shows dilated hair follicle (yellow arrow), keratin plug (black arrow), perifollicular lymphocytic infiltration (green arrow).

DISCUSSION

Follicular keratotic disorder is an abnormal keratinization affecting the follicular orifices, clinically characterized by keratotic follicular papules affecting various sites and histologically characterized by hyperkeratosis, parakeratosis, dilated hair follicle, keratin plug, perifollicular and periadnexal lymphocytic infiltration.

Dermoscopy is a noninvasive inexpensive technique that can easily and quickly detect the inflammatory and infectious diseases[53]. The use of dermoscopy to assert the clinical diagnosis and differentiate closely resembling follicular keratotic diseases is the highlight of the current study.

In this cross-sectional study, we report findings in 76 patients with follicular keratotic diseases. Among 76 patients, primary follicular keratotic diseases were seen in 65(85.5%) patients and secondary follicular keratotic diseases in 11(14.5%) patients. Among 76 patients, 39 (51.3%) were males and 37 (48.7%) were females. Male to female ratio was 1.05:1 with no much gender predilection. The age of the patients enrolled in the study ranged from 2 years to 48 years with a mean age of 26.7±2.4years. Pre-adolescent and adolescent population in the age group of 11-20 years, constituted the majority of study population with maximum of 29 (38.2%)patients followed by childhood population 21 (27.6%) in the age group ≤10 years.

Primary follicular keratotic diseases

Phrynoderma

Phrynoderma is a type of follicular keratosis that occurs due to multiple nutritional deficiencies such as Vitamin A, Vitamin B-complex, Vitamin E and Essential fatty acid deficiency and protein-calorie malnutrition[17]. Among 65 patients of primary follicular keratotic diseases, we report phynoderma in 22 (28.9%) patients.

Among 22 patients, 12(54.5%) were males and 10(45.45%) were females. Majority of phrynoderma patients were in the age group 11-20years {11(50.0%)} patients followed by < 10years {9(40.9%)} patients. Phrynoderma was predominantly seen in school students 20(90.9%), which was comparable to the study done by Raghunatha *et al* [17] , comprising of 125 patients, with 79 (63.2%) male and 46 (36.8%)female and the age of the patients ranged from 3-26 years, with a mean of 10 ± 4.3 years and mostly affecting the school students 94.4%. Also the study done by Raghunatha *et al*[17], reported familial occurrence of phrynoderma in 3 patients. In our study, no family history of phrynoderma was observed.

Cutaneous manifestation in the form of discrete 12(54.5%) or grouped 10(45.5%), follicular, skincoloured papules with central keratotic plugs was present in all (100%) patients of phrynoderma. The lesions were predominantly distributed over the extensor aspects involving elbows 20(90.9%), knees 11(50.0%), gluteal area 7(31.8%), extensor arms and forearms in 4(18.2%) patients each, thighs and back 3(13.6%) patients each, legs 2(9.1%), chest and abdomen 1(4.5%) each . The lesions were asymptomatic in 11(50.0%) patients, associated with mild itching in 4 (18.2%) and moderate itching in 7(31.8%) patients. Raghunatha *et al*[17] in his study also noted that elbows 123(98.4%) was the predominant site involved followed by knees 100(80%). However, in their study lesions were asymptomatic in 114 (91.2%) patients and mild itching was present in 11 (8.8%) patients.

The dermoscopic findings of the phrynoderma patients included in the study population showed keratotic plug and perifollicular scaling in all 22(100%) patients followed by perifollicular fibrosis in 12(54.5%). Interfollicular area showed hyperpigmentation in majority of the patients 13(59.1%) followed by lichenification in 8(36.4%) patients. Coiled hair was observed in 6(27.3%) patients followed by twisted hairs in 4(18.2%). To the best of our knowledge, dermoscopic features of phrynoderma have not yet been reported in the literature.

The predominant histopathological findings observed in phrynoderma were epidermal hyperkeratosis, parakeratosis, dilated hair follicle and keratin plug, periadnexal, perivascular and perifollicular lymphocytic infiltration and periadnexal lymphohistiocytic infiltration which were compatible with the study by Raghunatha *et al*[17] in which epidermal hyperkeratosis, acanthosis, follicular plugging, follicular hyperkeratosis, perivascular and perifollicular lymphocytic infiltration were observed.

In our study, we observed that dermoscopic findings in phrynoderma such as perifollicular scaling correlate to epidermal hyperkeratosis histopathologically. Similarly, interfollicular area lichenification corresponding to epidermal thickening; keratotic plugging and perifollicular fibrosis dermoscopically ,correlates histopathologically with dilated follicle, follicular plugging and dermal fibrosis respectively. Hence, we report that in phrynoderma the dermoscopic findings correlate with the histopathological features in the study population.

Lichen spinulosis

Lichen spinulosus (LS) is a disorder of keratinization of hair follicles due to atopy, infections, id reaction to fungal infection, drug-related reactions[23]. Among 65 patients of primary follicular keratotic diseases, we report lichen spinulosis in 16 (21.1%) patients.

Our study showed equal preponderance in males 8(50%) and females 8(50%) and was more commonly seen in children < 10 years (68.8%) and adolescents of 11-20years {3(18.8%)} followed by adults 20-40 years {2(12.6%) patients} . A study done by Hawsawi *et al* [22] and Kim *et al* [23] reported male preponderance which was a slight variation from our study and also noted that lichen spinulosis was more commonly seen in children <10 years which was similar to our study. The majority of the patients had moderate itching 10 (62.5%), 1 (6.3%) patient had mild itching and lesions were asymptomatic in 5 (31.3%) patients. Kim *et al* [23] in their study reported lesions were asymptomatic and mildly pruritic.

The cutaneous manifestation in the form of multiple skin coloured scaly keratotic papules with central spinous processes arranged in groups 12 (75%) and in discrete manner 4 (25%) was observed in all 16 (100%) patients. The lesions were distributed symmetrically over arms 7 (43.8%), followed by forearms and elbows in 5 (31.3%) patients each, very closely followed by thighs, legs, abdomen in 4 (25%) patients and knees , gluteal area in 3 (18.8%) patients, which was in accordance with the studies done by Hawsawi *et al* [22] and Kim *et al* [23]. Among 16 patients of lichen spinulosis, 4(25%) patients had history of personal atopy and presented with hypopigmented scaly plaques over face. However, there was no family history in any of our patients. Hawsawi *et al* [22] in his study noted that there was no family or personal history in lichen spinulosis patients.

The dermoscopic findings of lichen spinulosis observed in the study population predominantly included perifollicular scaling in all 16(100%) patients followed by keratotic

plugging in 10(62.5%) and perifollicular erythema in 5(31.3%) patients and it was also found that interfollicular area was normal in all 16(100%) patients and twisted hair was noticed in only 1(6.3%) patient. To the best of our knowledge, dermoscopic features of lichen spinulosis have not yet been reported in the literature.

The histopathology in lichen spinulosis showed normal epidermis, and there were no significant changes in the epidermis. The dermis showed dilated follicular infundibulum with follicular plugging and perifollicular, perivascular, periadnexal lymphocytic infiltration which was in accordance with the study by Kim *et al* [23] which showed dilated hair follicles with a keratotic plug surrounded by mild perivascular lymphocytic infiltrations.

In our study we noticed that dermoscopic findings like normal interfollicular area and keratin plug corresponds histologically with normal epidermis, dilated infundibulum and follicular plugging respectively. Thus, we report that in lichen spinulosis the dermoscopic findings correlates with the histopathological features in the study population.

Keratosis pilaris

Keratosis pilaris (KP) is an autosomal dominant disorder characterized by keratinous plugs in the follicular orifices with or without perifollicular erythema[29]. Among 65 patients of primary follicular keratotic diseases, we report keratosis pilaris in 21 (27.6%) patients.

Among 21 patients of keratosis pilaris, 10(47.6%) were males and 11(52.4%) were females. Females slightly outnumbered the males in the ratio 1.1:1. Keratosis pilaris was predominantly seen in adults 12 (57.1%) followed by adolescents 9(42.9%) in the age group 21-40 years and 11-20 years respectively which was in correlation with the study done by Poskitt *et al*[31] comprising of 49 patients, where 30 were females and 19 were males and the

age of the patients ranged from 2 to 40 years, with a mean of 20 years. Family history of keratosis pilaris in first degree relatives was present in 2 (9.5%) of our patients which was similar to a study by Poskitt *et al*[31] where 19 (39%) patients had a positive family history in first degree relatives. However, there were no associated diseases observed in our study whereas Poskitt *et al* [31] in his study noted associated atopic diseases like eczema, asthma in 37% patients.

Cutaneous lesions were discrete, erythematous or hyperpigmented, minute, gooseflesh-like, scaly horny plugs at the follicular orifices distributed symmetrically over posterolateral aspect of upper arms 18(85.7%) and back 10 (47.6%) followed by posterolateral aspect of thighs in 3 (14.3%) and gluteal area 2 (9.5%) patients which was in accordance with the study by Poskitt *et al* [31], wherein the most predominant sites were arms (92%) followed by legs (59%), face (41%), buttocks (30%). The lesions were asymptomatic 16 (76.2%), in majority of our patients and 4 (19%) had mild itching.

The predominant dermoscopic findings in the lesions of keratosis pilaris included in the study population are perifollicular erythema and keratotic plug in 19 (90.5%) patients followed by perifollicular scaling 18(85.7%). The interfollicular area showed hyperpigmentation 6(28.6%) and erythema in 2 (9.5%) patients. Coiled hair was predominantly seen in 13(61.9%) patients followed by twisted hairs 12 (57.1%) and looped hairs in 3 (4.3%) patients. This was in concurrence with the study by Thomas *et al* [29], where they observed perifollicular erythema 11(44%), perifollicular scaling 9(36%), coiled 10(40%) and looped hair 5(20%). Sonthalia *et al*[36] also noted a similar findings such as perifollicular papular erythema, irregular coiled and twisted hairs.

The histopathological examination revealed epidermal hyperkeratosis, dilated follicular infundibulum, keratin, follicular plugging, sebaceous gland hypertrophy, perifollicular

parakeratosis and orthokeratosis, perifollicular, periadnexal and perivascular lymphocytic and lymphohistiocytic infiltration. This was consistent with the study done by Sonthalia *et al*[36] where they observed dilatation of follicular infundibulum and plugging with focal peri-infundibular parakeratosis, and perifollicular lymphocytic infiltrate.

In our study we observed that dermoscopic findings like perifollicular scaling and keratin plug corresponds histologically with epidermal hyperkeratosis, dilatation of follicular infundibulum and follicular plugging respectively. Hence, we report that the dermoscopic findings of keratosis pilaris correspond to the histopathological features in the study population.

Pityriasis rubra pilaris

Pityriasis rubra pilaris (PRP) is a rare chronic papulosquamous disorder of keratinization characterized by reddish orange scaly plaques, palmoplantar keratoderma and keratotic follicular papules[37]. Among 65 patients of primary follicular keratotic diseases, we report pityriasis rubra pilaris in 6 (7.9%) patients.

Among 6 patients, 4(66.7%) were males and 2 (33.3%) were females. Males outnumbered the females in the ratio 2:1. In our study, we noticed bimodal age distribution affecting equally the children and adults in the age group 11-20 years and > 30 years in 2 (33.3%) patients each respectively followed by < 10 years and 21-30 years in 1(16.7) patient each. Thus, we report classical adult onset PRP (type 1 PRP) and classical juvenile onset PRP (type 3 PRP) in 3 (50%) patients each. Ross *et al*[52] in his study noted no gender predilection which did not correspond with our study and age of the patients ranged from 5 to 87 years with median age 61 years showing bimodal age distribution which was in accordance to our study. We did not observe family history of PRP nor associated diseases in the study population enrolled.

Majority of the patients enrolled in the study presented with moderate itching 4 (66.7%) and few had severe 2(33.3%) itching over the lesions. The lesions were discrete, brown to hyperpigmented keratotic follicles coalescing to form plaques with white scales 6 (100%) and islands of sparing. The lesions were distributed predominantly over back 6 (100%) and thighs 5 (83.3%) followed by arms 4 (66.7%) and abdomen 4 (66.7%), gluteal area 3 (50%), elbows, knees, forearms, chest, legs, palms and soles in 2 (33.3%) patients each. We observed palmoplantar hyperkeratosis in 2 (33.3%) of our adult patients. The distribution of lesions was in concurrence to the study done by Ross *et al*[52], in which majority of the patients had lesions over trunk, extensor aspects of elbows and knees, thighs.

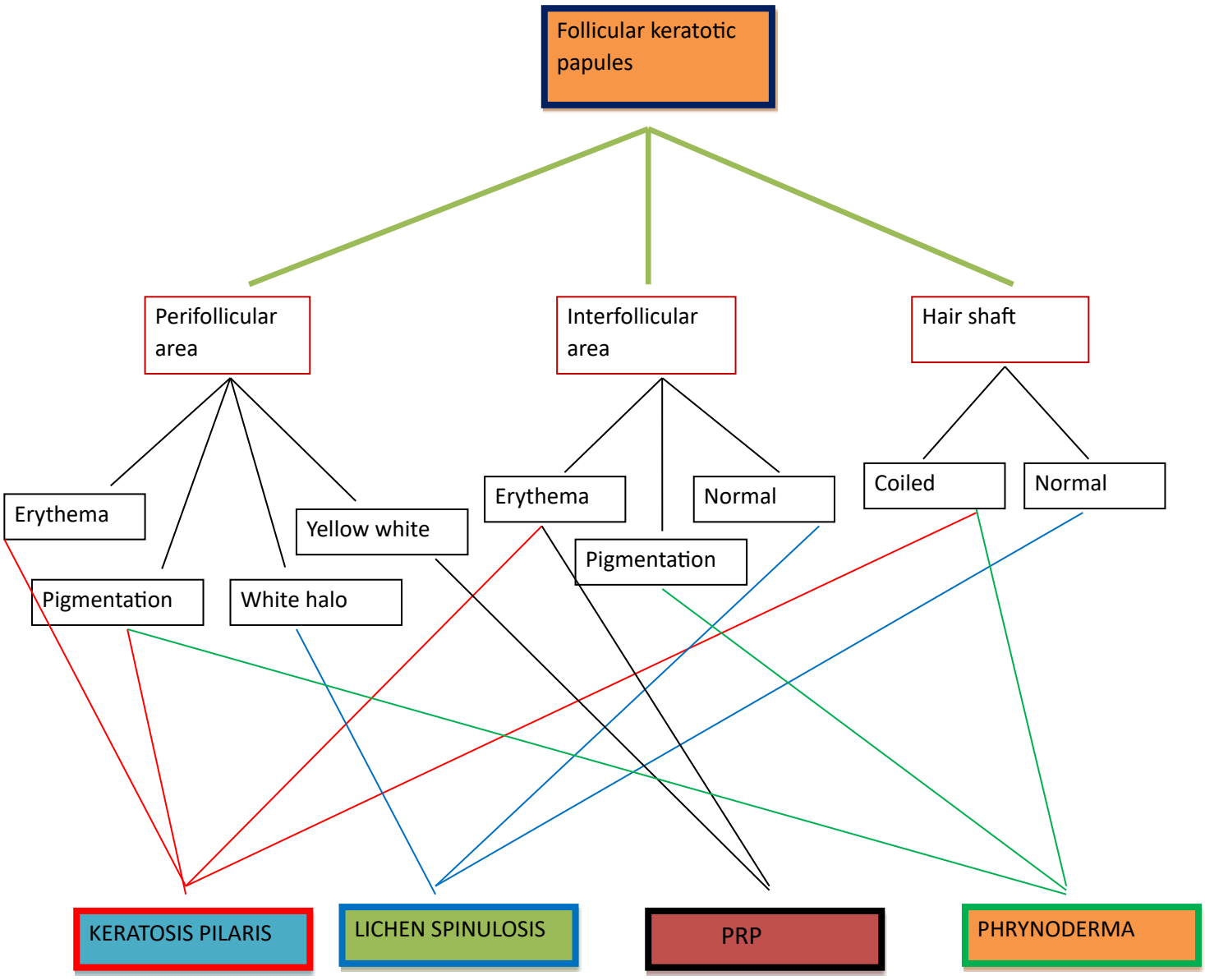
The predominant dermoscopic findings in the study population were perifollicular scaling 6 (100%) and keratotic plugging 5 (83.3%) followed by perifollicular erythema 3 (50%). Interfollicular area was normal in 3 (50%) patients followed by interfollicular erythema, hyperpigmentation, lichenification in 1 (16.7%) patient each. The red dots arranged in an irregular pattern was noted in 4 (66.7%) patients. We did not observe significant hair shaft changes in PRP dermoscopically. A similar dermoscopic finding was observed in a study conducted by Moretta *et al* [39], Sheetanshu Kumar[40], Nair *et al*[41] with whitish follicular keratotic plugs with peripheral yellowish rings, perifollicular erythema, hair shaft in the center, irregular dotted red vessels. However, all our patients 6(100%) had perifollicular white scales and we did not observe orange yellow scales or peripheral yellowish rings dermoscopically, which is suggestive of yellowish orange scales being less commonly observed in dark skinned individuals.

The predominant histopathological features of PRP were epidermal parakeratosis, hyperkeratosis, orthokeratosis, spongiosis, acanthosis, broad and shortened rete ridges, dilated hair follicle with keratin plugging, dilated capillaries, perifollicular, perivascular,

periadnexal lymphocytic infiltration and periadnexal lymphohistiocytic infiltration. This was in comparision with the study done by Sehgal *et al* [38] and Nair *et al*[41] where they observed acanthosis, hyperkeratosis, alternating orthokeratosis and parakeratosis in both horizontal and vertical direction "checkerboard pattern", hypergranulosis and irregular acanthosis, broad and shortened rete ridges and dermis showed dilated hair follicles filled with dense horny keratin plug and perivascular lymphohistiocytic infiltrates.

In our study we observed that dermoscopic findings like perifollicular scaling and keratin plug corresponds histologically with epidermal hyperkeratosis, dilatation of follicular infundibulum and follicular plugging respectively. Irregular arrangement of red dots dermoscopically correlates to dilated capillaries histologically. Hence, we report that the dermoscopic findings of PRP corresponds to the histopathological features in the study population.

In our study, we observed that histopathological examination of primary follicular keratotic diseases showed epidermal changes such as hyperkeratosis, parakeratosis, orthokeratosis, acanthosis and dermal changes like dilated follicular infundibulum, follicular plug, dilated capillaries and perifollicular, periadnexal and perivasculay lymphocytic infiltration. Thus we report that histopathology alone cannot differentiate and diagnose individual primary follicular keratotic diseases, hence dermoscopy plays an important role in aiding diagnosis of the same. Figure presents an algorithm for diagnosing primary follicular keratotic diseases dermoscopically.



Secondary follicular keratotic disorders

Follicular psoriasis

Follicular psoriasis is an under recognized entity and affects adults more commonly than children. Among 11(14.5%) secondary follicular keratotic diseases, follicular psoriasis was observed in 2 (2.6%) patients.

Among 2 patients, 1(50%) was male and 1 (50%) female. Both (100%) the patients were children with age < 15 years. This was in accordance with the study by Patil *et al*[44], where one third of the follicular psoriasis in children was noted without gender predilection. One patient (50%) had a family history of palmoplantar psoriasis in first degree relative. Although personal history of plaque type psoriasis has been reported in literature, no family history has yet been reported.

The lesions were multiple, small discrete follicular keratotic papules with white scales present predominantly over back, arms, forearms in both patients 2(100%) followed by scalp, elbows, knees, thighs and legs in one (50%) patient each ,sparing mucosa, nails, palms and soles. Both 2(100%) the patients had moderate degree itching. This was in concurrence with the study done by Behera *et al* [4], where lesions were predominantly present over thighs and lower legs.

The predominant dermoscopic finding observed were perifollicular scaling 2(100%), keratotic plug 1(50%) with normal interfollicular area 2(100%) and twisted hairs 2(100%). Regular arrangement of follicular red dots was observed in both the patients 2(100%). Behera *et al* [4] also came up with similar findings of perifollicular scaling, multiple red dots and red globules.

The histopathological examination showed epidermal hyperkeratosis, parakeratosis, elongated, camel foot, club shaped rete ridges, dilated hair follicle, perivascular and perifollicular lymphocytic infiltration and dilated capillaries. This was in consistent with the study by Behera *et al*[4], Patil *et al*[44], where they noted parakeratosis, hypogranulosis, elongated rete ridges, suprapapillary thinning of epidermis, and perivascular lymphohistiocytic and neutrophilic infiltrate in the dermis with follicular plugging, ostial parakeratosis, dilated and tortous blood vessels.

The dermoscopic findings such as perifollicular scaling and regularly arranged blood vessels corresponds to hyperkeratosis and dilated capillaries histologically in the study population. Thus, we report that the dermoscopic findings of follicular psoriasis corresponds to the histopathological features in the study population.

Follicular lichen planus (Lichen planopilaris)

Lichen planopilaris is the most common form of follicular LP and is characterized by inflammation of upper portion of the hair follicle that resulting in follicular scarring and irreversible hair loss[45]. Among 11(14.5%) secondary follicular keratotic diseases, follicular lichen planus was observed in 5 (6.6%) patients.

Among 5(6.6%) patients, 4 (80%) were females and 1(20%) patient was male. Females outnumbered males in the ratio 4:1. Follicular LP (LPP) was predominantly seen in adults 5(100%) age > 20years. Ochoa *et al*[46] in his study noted that lichen planopilaris is commonly seen in middle aged adults, equally affecting males and females. However, our study showed a female preponderance.

The lesions were follicular scaly papules with diffuse thinning of hairs and or scarring alopecia over the scalp 5(100%). Perifollicular erythema with scaling was observed in majority of the patients 3(60%). The lesions were asymptomatic 3(60%) in majority of the patients whereas mild and severe itching was noted in 1 (20%) patient each. We did not notice lichen planus lesions over mucosa or other body sites in the study population. This was consistent with the study by Ochoa *et al*[46], where LPP presented with irregularly shaped patchy hair loss or as diffuse central thinning with peripheral spread and perifollicular erythema and scaling.

The dermoscopic findings of LPP in the study population includes perifollicular keratin plug 5(100%), perifollicular scaling 5(100%), perifollicular erythema and perifollicular fibrosis in 3(60%) patients each, interfollicular area blue gray dots, white dots and reduced follicular ostia in all the patients5(100%). Nirmal *et al*[48] turned up with a similar finding of perifollicular erythema, peripilar tubular cast, granular grey dots and white dots.

Histopathological examination revealed epidermal hyperkeratosis, basal cell vacuolisation, pigment incontinence in the basal layer, dilated follicular infundibulum, keratin plug, band like lymphocytic infiltration in the upper dermis. This was in accordance with the study by Nirmal *et al*[48], where he observed basket weave hyperkeratosis, follicular plugging, basal cell vacuolization in the epidermis and bandlike lymphohistiocytic infiltrate in the superficial dermis along with pigment incontinence.

The dermoscopic findings such as tubular cast corresponds to follicular plugging histologically, bluegray dots to melanophages due to pigment incontinence and white dots to dermal fibrosis. Hence, we report that the dermoscopic findings of lichen planopilaris corresponds to the histopathological features in the study population.

Follicular eczema

Follicular eczema is a secondary follicular keratotic disease usually affecting the extensor aspect of the extremities[51]. Among 11(14.5%) secondary follicular keratotic diseases, we report follicular eczema in 4 (5.3%) patients.

Among 4 patients, 3 (75%) were males and 1 (25%) patient was female. Follicular eczema was observed equally in paediatric age group (11-20 years) and adults (>21 years) in 2 (50%) patients each. Majority of the patients had moderate itching 3 (75%) and 1 (25%) patient had mild itching. There was no history of personal or familial atopy in any of our patients. Sardana *et al*[51] in his study reported follicular eczema in paediatric age group and there was no family or personal history of atopic dermatitis which was in accordance to the current study.

The lesions were multiple scaly skin coloured follicular papules that coalesced to form plaques with excoriation marks distributed predominantly over legs 2 (50%), forearms 2 (50%) and elbows 2 (50%) followed by knees and arms in 1 (25%) patient each. This was compatible with a study done by Sardana *et al*[51], where he noted that lesions were predominantly present over extensor aspects of forearms and legs.

The dermoscopic features of follicular eczema includes perifollicular scaling 4 (100%) and keratotic plug 3 (75%), interfollicular area lichenification 2 (50%) and hyperpigmentation 1 (25%) and irregularly arranged red dots in 3 (75%) patients. To the best of our knowledge, dermoscopic features of follicular eczema have not yet been reported in the literature.

The predominant histopathological findings in the study population were epidermal hyperkeratosis and spongiosis, dilated follicular infundibulum with keratin plug, perifollicular spongiosis, perifollicular orthokeratosis, perifollicular, perivascular, periadnexal

lymphocytic infiltration and periadnexal lymphohistiocytic infiltration and dilated capillaries. Sardana *et al*[51] in their study noted a similar finding of spongiotic dermatitis localised to the upper portion of hair follicle.

Thus, we report, dermoscopic findings of follicular keratotic diseases corresponds and showed a significant statistical association with the histopathological features.

The current study is the only cross-sectional study undertaken till date to assess the correlation between clinical, dermoscopic and histopathological features of follicular keratotic diseases.

CONCLUSION

"Follicular keratotic disorder is an abnormal keratinization affecting the follicular orifices and clinically characterized by hyperkeratotic follicular papules affecting various sites". "Dermoscopy is a non-invasive, quick, OPD based diagnostic tool[53] and differentiates closely resembling diseases as well as possibly prevents need for an invasive biopsy. In the current study, dermoscopy had an important role in diagnosing the individual follicular keratotic diseases; so also did the clinical and dermoscopic features show a significant statistical correlation with the histopathological findings.

The following conclusions were drawn from the study:

1. Preadolescents and adolescents were the commonest age group affected in follicular keratotic diseases followed by children.

2. Males and females were equally affected.
3. The associated disease with follicular keratotic disease was atopic dermatitis.
4. The patients of secondary follicular keratotic diseases had moderate itching while the lesions were asymptomatic in primary follicular keratotic diseases.
5. Follicular scaly keratotic papules were the universal cutaneous findings in the entire study population.
6. Perifollicular scaling and keratotic plug were the predominant dermoscopic finding observed in the study population.
7. Epidermal hyperkeratosis, parakeratosis, dilated follicular infundibulum, follicular plugging, perifollicular and periadnexal lymphocytic infiltration were the predominant histopathological finding.

8. Dermoscopy has an important role in diagnosing and differentiating individual follicular keratotic diseases.
9. The clinical and dermoscopic features were found to have significant association with histopathological findings.

Thus, dermoscopy can be considered as an important tool in diagnosing individual follicular keratotic diseases and possibly prevents the need for an invasive biopsy.

SUMMARY

A hospital based, prospective cross-sectional study was conducted between October 2018 to July 2020 to determine the correlation between clinical, dermoscopic and histopathological features of follicular keratotic diseases.

With the aid of dermoscopy and histopathology, the features of follicular keratotic diseases were determined, and further analysed statistically for the presence of correlation between clinical, dermoscopic and histopathological features.

Following are the salient findings of this study:

1. Preadolescents and adolescents were the common sufferers of follicular keratotic diseases with no gender predilection.
2. Follicular keratotic scaly papules were the hallmark cutaneous manifestation observed in all the study population.
3. Perifollicular scaling and keratotic plug were the predominant dermoscopic finding observed in all the study population.
4. Epidermal hyperkeratosis, parakeratosis, dilated follicular infundibulum, follicular plugging, perifollicular and periadnexal lymphocytic infiltration were the predominant histopathological findings observed in the study population.

Dermoscopy is a quick and important tool that helps in differentiating and diagnosing a closely resembling follicular keratotic disease.

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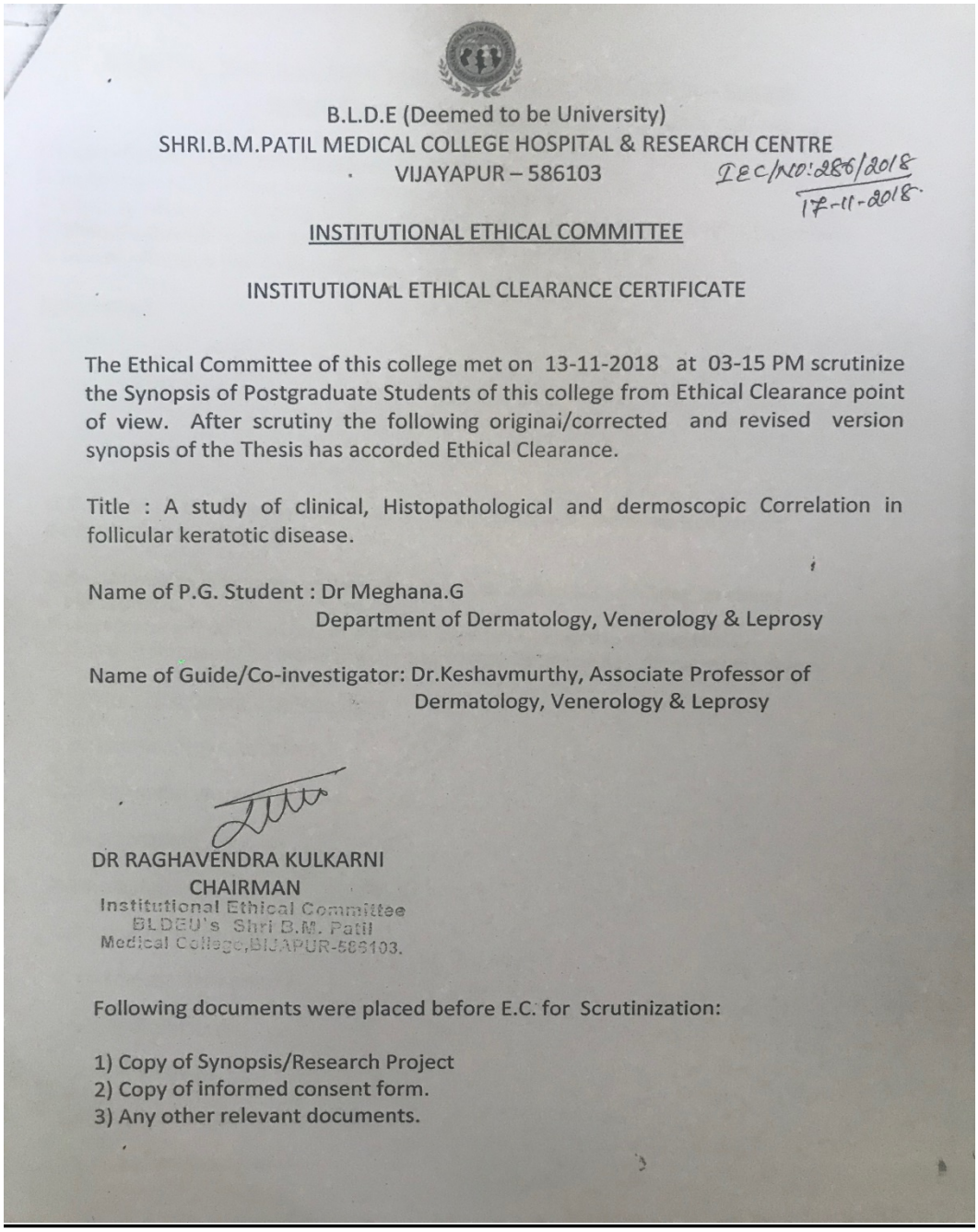
ANNEXURES

ETHICAL CLEARANCE CERTIFICATE



B.L.D.E (Deemed to be University)
SHRI.B.M.PATIL MEDICAL COLLEGE HOSPITAL & RESEARCH CENTRE
VIJAYAPUR – 586103

IEC/NO:286/2018
17-11-2018.

INSTITUTIONAL ETHICAL COMMITTEE

INSTITUTIONAL ETHICAL CLEARANCE CERTIFICATE

The Ethical Committee of this college met on 13-11-2018 at 03-15 PM scrutinize the Synopsis of Postgraduate Students of this college from Ethical Clearance point of view. After scrutiny the following original/corrected and revised version synopsis of the Thesis has accorded Ethical Clearance.

Title : A study of clinical, Histopathological and dermoscopic Correlation in follicular keratotic disease.

Name of P.G. Student : Dr Meghana.G
Department of Dermatology, Venerology & Leprosy

Name of Guide/Co-investigator: Dr.Keshavmurthy, Associate Professor of Dermatology, Venerology & Leprosy

DR RAGHAVENDRA KULKARNI
CHAIRMAN
Institutional Ethical Committee
BLDEU's Shri B.M. Patil
Medical College,BIJAPUR-586103.

Following documents were placed before E.C. for Scrutinization:

1) Copy of Synopsis/Research Project
2) Copy of informed consent form.
3) Any other relevant documents.

CONSENT FORM

B.L.D.E (Deemed to be university) SHRI B.M PATIL MEDICAL COLLEGE

HOSPITAL AND RESEARCH CENTRE, VIJAYAPURA-586 103

INFORMED CONSENT FOR PARTICIPATION IN DISSERTATION/RESEARCH

TITLE OF THE PROJECT : A STUDY OF CLINICAL, DERMOSCOPIC AND HISTOPATHOLOGICAL CORRELATION IN FOLLICULAR KERATOTIC DISEASES.

PG GUIDE : DR. KESHAVMURTHY A ADYA

PG STUDENT : DR. MEGHANA G

PURPOSE OF RESEARCH:-

I have been informed that this project will determine the correlation between clinical, histopathological and dermoscopic features in follicular keratotic diseases.

BENEFITS:-

I understand that my participation in this study will help the investigator in establishing the diagnosis of follicular keratotic diseases.

PROCEDURE:-

I understand that relevant history will be taken and I will undergo detailed clinical examination.

RISK AND DISCOMFORTS:-

I understand there is no risk involved and I will experience no discomfort during the clinical examination.

CONFIDENTIALITY:-

I understand that medical information produced by this study will become a part of my hospital records and will be subjected to the confidentiality and privacy regulation of the said hospital. Information of a sensitive personal nature will not be a part of the medical records, but will be stored in the investigator's research file.

If the data are used for publication in the medical literature or for teaching purposes no names will be used and other identifiers such as photographs and audio or videotapes will be used only with my special written permission. I understand I may see the photographs, videotapes and hear the audiotapes before giving this permission.

REQUEST FOR MORE INFORMATION:-

I understand that I may ask more questions about the study at any time concerned. Dr Meghana G is available to answer my questions or concerns. I understand that I will be informed of any significant new findings discovered during my participation.

REFUSAL OR WITHDRAWAL OF PARTICIPATION:-

I understand that my participation is voluntary and I may refuse to participate or may withdraw consent and discontinue participation in this study at any time without prejudice.

INJURY STATEMENT:-

I understand that in the unlikely event of injury to me resulting directly from my participation in this study and if such injury were reported promptly, then medical treatment will be available to me, but no further compensation will be provided. I understand that by my agreement for my participation in this study, I am not waiving any of my legal rights.

I have explained to (patient's / relevant guardian's name) the purpose of the study, the procedures required, and the possible outcome to the best of my ability in patient's own language.

_____ _____

Investigator / P. G. Guide Date

I confirm that …….(Name of the PG guide / chief researcher) has explained to me the research, the study procedures that I undergo and the possible risks and discomforts as well as benefits that I may experience. I have read and I understand this consent form. Therefore, I agree to give my consent for my participation as a subject in this research project.

_____ _____

Participant / guardian Date

_____ _____

Witness to signature Date:

PROFORMA

Department of Dermatology, Venerology and Leprosy

S.NO: Date:

Name: OP NO:

Age/sex Occupation:

Contact no:

Address:

HISTORY:

1. Presenting feature :

2. Past history:

   Any previous treatment received:

3. Family history:

CUTANEOUS EXAMINATION

Site:

Lesions: Grouped/Discrete

Itching:

PROVISIONAL CLINICAL DIAGNOSIS:

HISTOPATHOLOGY REPORT:

OTHER INVESTIGATIONS:

DERMATOSCOPIC FINDINGS

Table 1: Follicular and perifollicular lesions

PERIFOLLICULAR FIBROSIS	
PERIFOLLICULAR ERYTHEMA	
PERIFOLLICULAR SCALING	
KERATOTIC PLUG	
INTERFOLLICULAR AREA	

Table 2: Color of scales

SCALE COLOR	
WHITE	
YELLOW	

Table 3: Type of hair

TYPE OF HAIR	
TWISTED HAIR	
COILED HAIR	
SEMICIRCULAR HAIR	
LOOPED HAIR	

Table 4: Type of vessel

TYPE OF VESSEL	
RED DOTS	
RED GLOBULES	
RED LOOPS	
GLOMERULAR VESSELS	

FINAL DIAGNOSIS:

KEY TO MASTER CHART

M - Male

F - Female

P - Present

A - Absent

d - Days

w - Weeks

m - Months

y - Years

N - No

Dn - Done

Em - Emollient

Elb - Elbows

Kn - Knees

GA - Gluteal area

Th - Thighs

Arm - Arms

FA - Forearms

Bk - Back

Ch - Chest

Abd - Abdomen

Leg - Legs

Slp - Scalp

Pm - Palms

Sl - Soles

Fc - Face

HP - Hypopigmented patch

\+ - Present

\- - Absent

HPE - Histopathological examination

HK - Hyperkeratosis

PK - Parakeratosis

OK - Orthokeratosis

ET - Epidermal thinning

MH - Malphigian hyperplasia

B&S - Broad & short

PF - Perifollicular

PV - Perivascular

PA - Periadnexal

SG - Sebaceous glands

BV - Blood vessels

D. Hair follicle - Dilated hair follicle

LH - Lymphohistiocytic

HT - Hypertrophy

RD - Red dots

\+ - Present

\- - Absent

PHR - Phrynoderma

KP - Keratosis Pilaris

LS - Lichen spinulosis

PRP - Pityriasis rubra pilaris

LPP - Lichen planopilaris

FE - Follicular eczema

FP - Follicular psoriasis

SL N	OP N	Age	Sex	Atopy	Itch	Duration	Topical	Family h/o	Distribution of lesions																HPE	Epidermal Changes								Dermal	Inflammation(lymphocytic infiltration)			LH infiltration		Hair changes								Follicular & PF findings dermoscopically				Interfollicular area					Colour of scales		Type of hair			Type of Vessel	Diagnosis
									Elb	kn	GA	Th	Arm	FA	Bk	Ch	Abd	leg	Slp	Pm	Sl	Fc	Grouped	Discrete		HK	PK	OK	Acanthosis	Spongiosis	Basal layer	Rete ridges	Fibrosis	fibrosis	PF	PV	PA	PF	PV	D. Hair follicle	keratin	Follicular plug	PFPK	PFOK	PF Spongiosis	BV	SG	PF. Fibrosis	PF .Erythema	PF .Scaling	Keratotic plug	Nrmal	Hyperpigmentation	Lichenification	Erythema	white areas	White	yellow	Twisted	coiled	Looped		
1	47547	14	M	A	P	3m	N	A	P	A	A	A	A	A	A	A	A	A	A	A	A	A	-	+	Dn	+	+										+			+								A	A	P	P	-	+	+	-	-	P	A	A	P	A	A	PHF
2	307073	9	F	A	A	1m	Em	A	P	P	P	A	A	A	A	A	A	A	A	A	A	A	-	+	N																							P	A	P	P	+	-	-	-	-	P	A	A	P	A	A	PHF
3	164050	40	F	A	A	15d	N	A	P	A	A	A	A	A	A	A	A	A	A	A	A	A	-	-	N																							A	A	P	P	-	+	-	-	-	P	A	A	A	A	A	PHF
4	266375	9	M	A	A	1m	N	A	P	P	P	P	A	A	A	A	A	A	A	A	A	A	-	+	N																							A	A	P	P	-	+	+	-	-	P	A	A	A	A	A	PHF
5	303306	10	M	A	A	3m	N	A	P	A	A	A	A	A	A	A	A	A	A	A	A	A	-	-	N																							A	A	P	P	-	+	+	-	-	P	A	A	A	A	A	PHF
6	164451	8	F	A	A	2.5y	Em	A	P	P	A	A	A	A	A	A	A	A	A	A	A	A	+	-	Dn	ET				+						+												P	A	P	P	+	-	-	-	-	P	A	P	P	A	A	PHF
7	61148	9	F	A	P	15d	N	A	P	P	A	A	A	A	A	A	A	A	A	A	A	A	-	+	N																							A	A	P	P	-	+	-	-	-	P	A	A	P	P	A	PHF
8	436190	13	M	A	A	1m	N	A	P	P	P	P	P	A	P	P	A	A	A	A	A	A	-	-	N																							P	A	P	P	-	+	-	-	-	P	A	P	A	A	A	PHF
9	366325	9	F	A	A	4m	N	A	P	P	P	A	P	P	P	A	A	P	A	A	A	A	-	+	N																							P	A	P	P	+	-	-	-	-	P	A	P	A	A	A	PHF
10	236750	13	M	A	P	5m	N	A	P	A	A	A	P	A	A	A	A	A	A	A	A	A	-	-	N																							P	A	P	P	+	-	-	-	-	P	A	A	A	A	A	PHF
11	425988	12	F	A	A	3y	N	A	P	P	A	A	A	A	A	A	A	A	A	A	A	A	+	-	N																							P	A	P	P	-	+	-	-	-	P	A	A	A	A	A	PHF
12	282600	13	F	A	A	1 m	N	A	P	A	A	A	A	P	A	A	A	A	A	A	A	A	-	+	Dn	MH									+		+			+	+	+						P	A	P	P	-	+	+	-	-	P	A	A	A	A	A	PHF
13	290239	14	M	A	P	1m	N	A	P	A	A	A	A	A	A	A	A	A	A	A	A	A	-	-	N																							P	A	P	P	-	+	+	-	-	P	A	A	A	A	A	PHF
14	254020	13	F	A	P	1w	N	A	A	P	P	A	A	A	A	A	A	A	A	A	A	A	-	-	N																							A	A	P	P	-	+	-	-	-	P	A	P	P	A	A	PHF
15	23922	15	F	A	P	2w	N	A	P	P	A	A	A	A	A	A	A	A	A	A	A	A	+	-	Dn	+									+	+	+			+		+						P	A	P	P	-	+	-	-	-	P	A	A	A	A	A	PHF

16	303445	11	M	A	P	4m	N	A	A	A	A	P	P	A	P	A	A	A	A	A	A	A	-	+	N																							A	A	P	P	+	-	-	-	-	P	A	P	P	P	A	KP
17	366297	12	M	A	A	6m	N	A	P	A	A	A	A	A	A	A	A	A	A	A	A	A	-	+	Dn											+	+			+	+							A	A	P	P	+	-	-	-	-	P	A	A	A	A	A	PHF
18	1890	10	M	A	A	1m	N	A	P	A	A	P	A	A	A	A	A	A	A	A	A	A	+	-	N																							A	A	P	P	+	-	-	-	-	P	A	A	A	A	A	PHF
19	162743	13	M	A	A	1y	Em	A	P	A	A	A	A	A	A	A	A	A	A	A	A	A	-	+	N																							A	A	P	P	-	+	+	-	-	P	A	A	A	A	A	PHF
20	119401	14	F	A	A	1 y	N	A	A	A	A	A	P	A	A	P	A	A	A	A	A	A	-	+	N																							A	P	A	P	+	-	-	-	-	P	A	A	A	A	A	KP
21	170468	32	M	A	A	4m	N	A	P	A	A	A	A	A	A	A	A	A	A	A	A	A	-	+	N																							A	P	P	P	+	-	-	-	-	P	A	P	A	A	A	KP
22	298731	25	M	A	A	4 y	Em	A	A	A	A	A	P	A	P	A	A	A	A	A	A	A	-	+	N																							A	P	A	P	+	-	-	-	-	P	A	P	P	A	A	KP
23	423323	20	F	A	A	5 y	Em	A	A	A	P	A	P	A	P	A	A	A	A	A	A	A	-	+	N																							A	P	P	P	-	+	-	-	-	P	A	A	A	A	A	KP
24	403916	23	M	A	A	5 y	Em	A	A	A	A	A	P	A	P	A	A	A	A	A	A	A	-	+	N																							A	P	P	P	-	+	-	-	-	P	A	P	A	A	A	KP
25	249209	26	M	A	A	2 y	N	A	A	A	P	P	P	A	P	A	A	A	A	A	A	A	-	-	Dn								+	+		+	+			+	+		+					A	P	P	P	-	+	-	+	-	P	A	P	P	A	A	KP
26	253573	26	M	A	A	3 y	N	P	A	A	A	A	P	A	A	A	A	A	A	A	A	A	-	+	Dn										+	+		+	+	+	+	+						A	A	P	P	-	+	-	-	-	P	A	A	P	A	A	KP
27	213161	18	F	A	A	1 y	N	A	A	A	A	A	P	A	A	A	A	A	A	A	A	A	-	+	N																							A	P	P	A	+	-	-	-	-	P	A	A	A	A	A	KP
28	215839	30	F	A	P	1 y	N	A	A	A	A	A	P	A	A	A	A	A	A	A	A	A	-	+	Dn										+	+	+			+		+					H	A	P	P	P	+	-	-	-	-	P	A	P	P	A	A	KP
29	328126	22	M	A	A	1 m	N	A	A	A	A	A	P	A	P	A	A	A	A	A	A	A	-	+	Dn			+							+	+				+		+		+				A	P	A	P	-	+	-	-	-	A	A	P	P	A	A	KP
30	364340	11	F	A	A	3 m	N	A	A	A	A	A	A	A	A	A	A	P	A	A	A	A	-	+	Dn	ET										+				+								A	P	P	P	+	-	-	-	-	P	A	P	P	A	A	KP
31	307225	16	F	A	A	2 m	N	A	P	A	A	A	A	A	A	A	A	A	A	A	A	A	-	-	N																							A	P	P	P	+	-	-	-	-	P	A	A	P	A	A	KP
32	248426	28	F	A	P	3 y	N	A	A	A	A	A	A	P	A	A	A	A	A	A	A	A	+	-	N																							A	A	P	A	+	-	-	-	-	P	A	A	A	A	A	FE
33	240981	2	F	A	P	8d	N	A	A	A	A	A	P	A	P	A	P	A	A	A	A	A	+	-	N																							A	A	P	A	+	-	-	-	-	P	A	A	A	A	A	LS
34	251178	11	F	A	P	15	N	A	A	A	A	A	P	A	A	A	P	A	A	A	A	A	-	-	N																							A	P	P	A	+	-	-	-	-	P	A	A	A	A	A	LS
35	35705	7	M	A	P	6m	N	A	A	A	A	P	A	A	A	A	A	P	A	A	A	A	+	-	N																							A	P	P	A	+	-	-	-	-	P	A	A	A	A	A	LS
36	17490	28	F	A	P	2 m	Em	A	A	A	P	P	A	A	P	P	P	P	A	A	A	A	-	-	Dn		+(focal)					B&S			+	+												A	A	P	P	-	-	-	-	+	P	A	A	A	A	R	PRP

37	240947	14	M	A	P	1m	N	A	A	A	A	P	P	A	P	A	P	A	A	A	A	A	-	-	Dn		+ (focal)	+		+		B&S			+	+	+			+		+						A	P	P	A	+	-	-	-	-	P	A	A	A	A	A	PRP
38	281492	7	M	A	P	10 (	N	A	P	P	P	P	P	A	P	A	P	A	A	A	A	A	-	-	Dn					+						+	+									dila		A	P	P	P	-	-	+	-	-	P	A	A	A	A	R	PRP
39	167656	48	M	A	A	5 y	Em	A	A	A	A	P	A	A	P	A	A	A	A	P	P	A	-	-	N																							A	A	P	P	+	-	-	-	-	P	A	A	A	A	R	PRP
40	26461	40	M	A	P	1y	Em	A	P	P	P	P	P	P	P	P	P	P	A	P	P	A	-	+	Dn	+	+					B&S																A	A	P	P	-	+	-	-	-	P	A	A	A	A	A	PRP
41	292763	12	M	A	P	10c	N	A	P	P	A	A	P	P	A	A	A	A	A	A	A	A	-	+	N																							A	A	P	P	-	-	+	-	-	P	A	A	A	A	R	FE
42	304354	31	M	A	P	3 m	N	A	A	A	A	A	A	A	A	A	A	P	A	A	A	A	-	+	Dn	+									+	+	+			+	+	+		+	+			A	A	P	P	-	+	-	-	-	P	A	A	A	A	R	FE
43	364750	16	M	A	P	1 y	N	A	P	A	A	A	A	A	A	A	A	P	A	A	A	A	+	-	N																							A	A	P	P	-	-	+	-	-	P	A	A	A	A	R	FE
44	294867	8	M	P	P	2m	N	A	A	A	A	A	P	P	A	A	A	A	A	A	A	H	+	-	N																							A	A	P	A	+	-	-	-	-	P	A	A	A	A	A	LS
45	295482	4	F	P	P	1m	N	A	A	A	A	A	A	A	A	A	P	A	A	A	A	H	+	-	N																							A	A	P	P	+	-	-	-	-	P	A	A	A	A	A	LS
46	216112	23	F	A	P	1m	N	A	A	A	A	A	A	A	A	P	A	A	A	A	A	A	-	+	Dn										+	+	+			+								A	A	P	P	+	-	-	-	-	P	A	A	A	A	A	LS
47	256994	10	F	A	P	1m	N	A	A	A	A	P	P	A	A	A	P	A	A	A	A	A	-	+	N																							A	P	P	P	+	-	-	-	-	P	A	A	A	A	A	LS
48	262511	4	F	A	P	1m	N	A	P	P	P	P	P	P	P	A	A	P	A	A	A	H	-	+	Dn										+	+	-			+								P	A	P	A	+	-	-	-	-	P	A	A	A	A	A	LS
49	332925	3	M	A	A	1m	N	A	A	A	A	A	A	A	P	A	A	A	A	A	A	A	+	-	N																							A	A	P	P	+	-	-	-	-	P	A	A	A	A	A	LS
50	401734	4	M	P	P	1m	N	A	P	P	A	A	A	A	A	A	A	P	A	A	A	A	-	-	N																							A	A	P	A	+	-	-	-	-	P	A	A	A	A	A	LS
51	449027	15	M	A	P	2y	N	A	P	A	P	P	A	A	A	A	A	P	A	A	A	A	+	-	Dn										+	+	-			+								P	A	P	P	+	-	-	-	-	P	A	A	A	A	A	LS
52	433949	25	F	A	A	1y	N	A	A	A	A	A	P	A	A	A	A	P	A	A	A	A	-	+	N																							A	P	P	P	+	-	-	-	-	P	A	A	A	A	A	KP
53	440272	19	F	A	P	2y	N	A	A	A	A	P	P	A	P	A	A	A	A	A	A	A	-	+	N																							A	P	P	P	-	+	-	-	-	P	A	A	A	A	A	KP
54	434889	3	M	A	A	2m	N	A	P	P	A	A	A	A	A	A	A	A	A	A	A	A	+	-	N																							A	P	P	P	+	-	-	-	-	P	A	A	A	A	A	LS
55	434650	9	F	A	A	3m	N	A	P	A	A	A	A	P	A	A	A	A	A	A	A	A	+	-	N																							A	P	P	P	+	-	-	-	-	P	A	A	A	A	A	LS
56	286285	30	F	A	P	1 y	N	A	A	A	A	A	A	A	A	A	A	A	P	A	A	A	-	+	Dn										-	+	+	+		+		-						P	P	P	P	-	+	-	-	-	P	A	A	A	A	A	LPP
																	A																																														
57	191019	25	M	A	A	3 m	N	A	A	A	A	A	A	A	A	A	A	A	P	A	A	A	-	+	Dn	ET					PI				+,s		+			+		-						P	P	P	P	-	+	-	-	-	P	A	A	A	A	A	LPP
58	290532	38	F	A	A	5 y	N	A	A	A	A	A	A	A	A	A	A	A	P	A	A	A	-	+	Dn										+					+								A	P	P	P	-	+	-	-	-	P	A	A	A	A	A	LPP

59	143659	30	M	A	A	10y	N	A	A	A	A	A	P	A	P	A	A	A	A	A	A	A	-	+	N																							A	P	P	P	+	-	-	-	-	P	A	P	P	P	A	KP
60	29855	9	M	A	P	3m	N	A	P	A	A	A	A	A	A	A	A	A	A	A	A	A	+	-	N																							P	A	P	P	-	+	-	-	-	P	A	A	A	A	A	PHF
61	40300	25	F	A	A	3m	N	A	P	P	A	A	P	P	A	A	P	P	A	A	A	A	-	+	N																							P	P	P	P	-	-	-	+	-	P	A	A	A	A	A	PHF
62	71348	6	F	P	P	1w	Em	A	A	A	A	A	P	P	A	A	A	A	A	A	A	H	+	-	N																							P	A	P	P	+	-	-	-	-	P	A	P	A	A	A	LS
63	50472	11	M	A	A	2 w	N	A	A	A	A	A	P	A	A	A	A	A	A	A	A	A	-	+	N																							A	P	P	P	+	-	-	-	-	P	A	A	A	A	A	KP
64	339197	30	F	A	P	1 y	N	A	A	A	A	A	A	A	A	A	A	A	P	A	A	A	-	+	Dn										+	-	-			+	+	+						P	A	P	P	+	-	-	-	-	P	A	A	A	A	A	LPP
65	345974	27	F	A	A	1 y	N	A	A	A	A	A	A	A	A	A	A	A	P	A	A	A	-	+	Dn						PI				+	+	+			+	+	+						A	A	P	P	-	+	-	-	-	P	A	A	A	A	A	LPP
66	301385	8	M	A	A	6m	Em	A	A	A	P	A	A	P	P	A	A	A	A	A	A	A	-	+	Dn																							P	A	P	P	-	-	+	-	-	P	A	A	A	A	A	PHF
67	404344	11	M	A	A	1m	Em	A	P	P	A	A	A	A	A	A	A	A	A	A	A	A	+	-	N																							A	A	P	P	-	-	+	-	-	P	A	A	P	A	A	PHF
68	404344	11	M	A	A	1m	Em	A	A	A	A	A	P	A	P	A	A	A	A	A	A	A	+	-	N																							A	A	P	P	+	-	-	-	-	P	A	A	A	A	A	LS
69	322637	31	M	A	A	5y	N	A	A	A	A	A	P	A	P	A	A	A	A	A	A	A	-	+	N																							A	P	P	P	-	-	-	-	+	P	A	P	P	A	A	KP
70	345904	25	F	A	A	6 y	N	P	A	A	A	A	P	A	A	A	A	A	A	A	A	A	-	+	N																							A	P	P	P	+	-	-	-	-	P	A	P	P	A	A	KP
71	98154	16	F	A	P	1 y	N	A	A	A	A	A	P	P	P	A	A	A	A	A	A	A	-	+	Dn		+		+	+					-	+	-									+		A	P	P	P	+	-	-	-	-	P	A	A	A	A	R	PRF

72	476820	11	F	A	P	1m	N	A	A	A	A	A	P	P	P	A	A	A	P	A	A	A	-	+	Dn	+	+					elongated,camelfoot,clubshaped			+	+	-											A	A	P	P	+	-	-	-	-	P	A	P	A	A	R	FP
73	304354	31	M	A	A	6m	N	A	A	A	A	A	A	P	A	A	A	A	A	A	A	A	+	-	N																							A	A	P	P	+	-	-	-	-	P	A	A	A	A	A	LS
74	252204	28	F	A	A	2 y	Em	A	A	A	A	A	P	P	A	A	A	A	A	A	A	A	-	+	N																							A	P	P	A	+	-	-	-	-	P	A	A	P	A	A	KP
75	314194	20	F	A	A	2 y	Em	A	A	A	A	A	P	A	P	A	A	A	A	A	A	A	-	+	N																							A	P	P	P					+	-	P	A	P	P	P	A	KP
76	392726	11	M	A	P	2 y	Em	P	P	P	A	P	P	P	P	A	A	P	A	A	A	A	-	+	Dn	ET										+												A	A	P	P	+	-	-	-	-	P	A	P	A	A	R	FP