‘A SYSTEMATIC CLINICAL UPDATE ON KERATOSIS PILARIS’

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ABSTRACT:-

Keratosis pilaris (KP) It's a harmless Skin issues which is sometimes genetically organized characterised by skin lesions, The cause of this illness is still completely unreported but various hypothesis are submitted which shows the partially understanding of their etiology. The types, keratosis pilaris that is keratosis pilaris atrophicans and keratosis pilaris rubra is described here. The cause of keratosis pilaris is considered to be sometimes genetically, so the genomics property are studied which shows a clear demonstration that how the keratosis pilaris is genetically organized. The completely curable treatment for KP is not available but the various treatments are available but there are certain acids which is used in the treatment of KP. However the curative treatment of the KP for till date is laser treatment or therapy, but it has a various side effects so the acid topical treatment is used.

INTRODUCTION:-

Keratosis pilaris It is typical dermatologic the condition is considered towards be a genetic heredity disorder which passes generation to generation in autosomal dominant pattern(1,2).It generally starts to begin in the puberty and also may causes in children which is mostly seen in females as compare to male(2).The racial difference can also been seen in keratosis pilaris as well as the seasonal variation can also being noted some of the conventional medicine are available(3,4). The keratin is referred to called cornification., denotes the cytodifferentiation ,The steps which keratin cells undergo. a transition from there post-germinative stage in the beginning of the bottom zone towards a mature, damaged cellular. These cells become filled in vitamins and constitute An external surface which is both chemically and operationally independent known to be the The upper layer corneum, which contains keratin. This layer exhibits unique properties and functions due to the presence of keratin (5).

It mostly occurs at the upper arms, buttocks, thighs and also depending upon the types it also occurs in back , cheeks and other body parts are also being noted but some peoples does not able to recognize this as it is not painful and looks like common rashes on skin(2,6). It is characterized by small red bumpy papulosquamous follicular hyperkeratosis on erythematous skin which does not has accurate etiology considered to be caused due to the abnormal or hyper keratinization also it is mostly seen in the person with dry skin condition(2,7,8). The pathophysiology is completely not understood but various hypothesis are being submitted regarding keratosis pilaris(6).

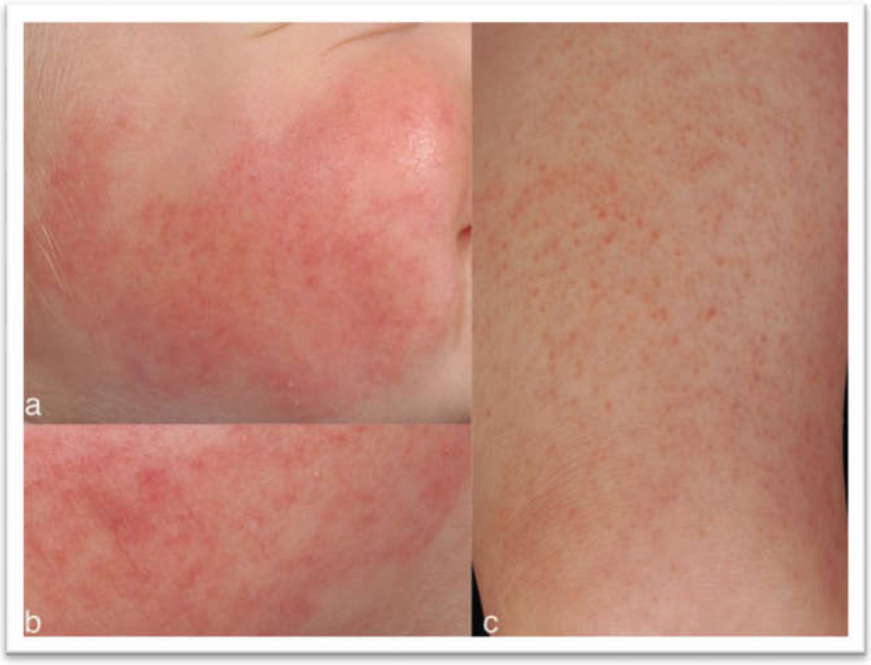


Fig1:- A diagram showing the keratosis pilaris (9)

The keratolytic, retinoids and other skin surface application are used and the most effective therapy is laser therapy but the laser therapy has many disadvantages(7). The level of tolerance exhibited by patients towards the KP's roughness its visual characteristics varies. greatly, often deviating from the clinical signs. The extent of associated morbidity is likely to be overestimated. KP serves as a widespread illness that impacts approximately 40% from people., with a higher prevalence of In excess of 80 percent% among adolescent females. However, adolescent girls among adults, as Stannus identified KP for just 20 percent in adult females. Despite its common occurrence, the organic course based this stage, that's part a significant Patient worries, remains unexplored (10). The disorder is known to occur sporadically in many cases, and it is presumed that these cases are the outcome of an inborn defect. However, They are several notifications of genetic diseases. dominant along with X-linked partial ethnicity. Although KPA is not typically Linked to any both mentally or physically. abnormalities, it It took place observed to conjunction has wool hairs as Noonan's disorders, monosomy is 18p, and additional genetic conditions like delays in growth & disorders of the central nervous system system as well as tooth irregularities, as well as undescended testes(11). Various treatment options have been employed to address these conditions, including the application of topical keratolytics, vitamin D3 analogues, antibiotics, This includes the application of topical and topical antioxidants. However, the outcomes achieved through these approaches have been somewhat restricted. Given the significant impact these pathologies can have on an individual's social life, there is a growing demand for a more efficacious treatment. Consequently, alternative techniques involving cyclic dyeing lights (the PDLs) as the mineral titanyl phospho laser beams (KTP lasers), and powerful glowing light have been explored as potential solutions(12).

EPIDEMIOLOGY:-

It affect nearly 50-80% at the age of puberty and nearly 40% of adults, the sites of occurring the disease is mostly upper firearms, the legs, with posterior nearly percentage is in The armpits (92%), the lower legs (59%), or the thigh area (30%) (13). Some records also seen the summertime improve season when it get worsen through wintertime. season ,it also more frequently seen in the person with dry skin condition, it can be connected with the condition with person occurring atopy ,obesity, ischthyosis vulgaris , ectodermal dysplasia , down's syndrome. This condition is far more prevalent within women. more versus boys nearly occurs 80% in puberty in females. In some cases there was no family history but in some of the cases there is family history (6,13).

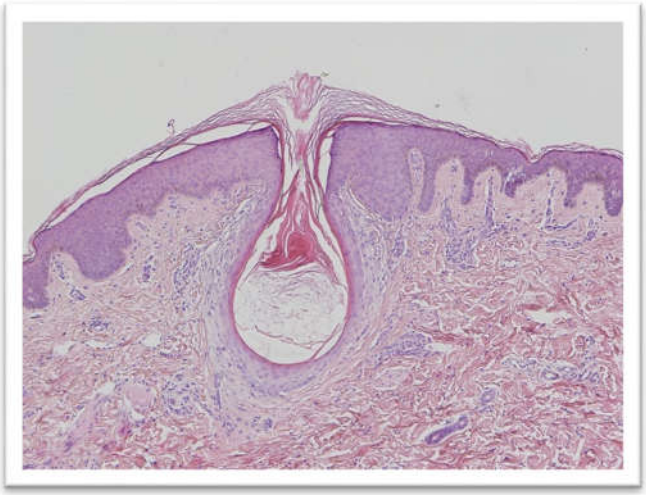
The juvenile onset pityris rubra may link with hypoparathyroidism and brachyonychia which is a abnormal keratinization disorder (14). The effective rate with genetics for R501X The genetic sequencing rate was satisfactory , while in 2282del4 it was 98.7 prcent . The genetic determined for Other genotypes having no impact. show any significant deviations from the expected frequencies (15). The atopic dermatitis considered as hyperlinear palms and soles (16). Skin disease on schoolchildren account for 6-24%was analysed in Saudi Arabia (17). The skin disease of Mexico children were found to be are mostly the patient of 0-17 year (18).

DIAGNOSIS OF KERATOSIS PILARIC:-

After careful examination of the symptoms and clinical findings, The person involved has been identified at KP. it patient displayed clustered small papular lesions accompanied by burning as a feeling of burning. These infections revealed localized a specific areas, including an expandable element in The top back, arm, chest area, and upper arms and legs. Moreover, their presence in a familial history with a similar condition proved valuable in excluding other potential disorders (4). Keratosis pilaris (KP) It is prevalent skin a state defined by its presence in small, challenging bumps on the skin's surface. These bumps, known as papules, are typically around 1 mm in size and can have a spiny texture. One distinguishing feature of KP is the presence of fine-coiled, fragile hair within the papules. The papules may appear in clusters or be scattered across the affected area, and there may be subtle redness around the hair follicles. Diagnosis typically encompasses a comprehensive evaluation of the patient's medical background and a thorough physical examination. However, dermoscopy can serve as a valuable tool in assisting with the diagnosis process and monitoring the effectiveness of treatments. Dermoscopic observations may reveal various indicators such as excessive pigmentation, redness around hair follicles, flaking, dilation of blood vessels in the dermis, enlarged openings of hair follicles, curled or twisted fine hairs, and the presence of keratin plugs. While keratosis pilaris (KP) generally does not cause any discomfort, it can occasionally lead to itching and aesthetic concerns (6).

HISTOLOGY:-

A hyperkeratotic papule from the patient's right upper arm underwent histologic investigation, which revealed an enlarged and infundibulum fungal that has a keratotic plugging made Cells which are orthokeratotic, enclosed as a slight permeation of lymphohistiocytic germs or distinct fibrosis . Disease stage is the main factor influencing histology. All forms of follicular keratoses include the formation of keratotic plugs at the infundibulum's follicular hole. Furthermore, it can be challenging to distinguish between various structures in light of histology during the underlying phase of the illness. The follicle in the upper corium is surrounded by a lymphocytic infiltration that contains a small number of neutrophilic granulocytes. A rise on perifollicular



fibro over The condition's growth in atrophic variants. Atrophic hair follicles, cutaneous sclerosis, and the development of horn sores are all present in the atrophic stage. Many dilated lymphatic and blood vessels are also apparent (1).

Fig2:- a diagram showing dilated infundibulum

after dermascopy (19)

The keratosis pilaris (KP) papules are formed due to an excess accumulation of keratin in the openings on the follicles hair, resulting in the emergence for horny plugs that widen the infundibulum of the follicle. In the layer underlying the epidermis and perifollicular regions, It has a mild infiltration on lymphohistiocytic the cells surrounding blood vessels. The epidermis shows slight thickening of the outer layer of skin (hyperkeratosis), reduced granular layer (hypogranulosis), and blockage of the follicles. Although there may be localized abnormal keratinization in The strata corneum, your skin's uppermost surface, known as cells affected by this condition do not remain throughout the hair follicle. The previously keratin spike lengthens deeply enters a follicle of hairs or can lead to thinning It includes glands that produce sebum, follicle walls, etc arrector pili muscles. in particular, a plug is composed of layers of hardened keratin and often traps one or more twisted and fragile hairs (20).

Indeed! Histological observations using hematoxylin and eosin staining to examine epidermolytic hyperkeratosis (EHK) do not offer a definitive diagnosis, but they do reveal distinct characteristics. These include significant hyperkeratosis, vacuolar disintegration in the uppermost granule layer, coarser keratohyaline particles, with an extensive granular layer, of the skin. In some cases, deeper granular cells may resemble keratohyaline granules, and the concentration of abnormal keratinization(21).

ETIOLOGY AND PATHOGENESIS

Pathogenesis of the keratosis pilaris a still completely unidentified, but There is one various hypothesis are involved regarding these. The most acceptable theory was considered to be abnormal keratinization (13). It is most often believed to cause by the abnormal or hyperkeratinisation, in some cases the patient visualisation is done in which the more amount of skin cell debris are builds up beside the hair follicles of an individual in which the hair gets trapped under the skin cell debris (2).

The secondly hypothesis is believed to be the hair shaft with patient despite of removal of hair it include the coiling of the hairs under the skin debris, the hair shaft get rupture the hair follicles skin . This does not has any known aetiology and considered to be held the Papulosquamous disease (22).This is characterised by the scaly papules and plaques it is believed to be sometimes the genetic disorder and believed to be cause in autosomal dominant pattern(6).

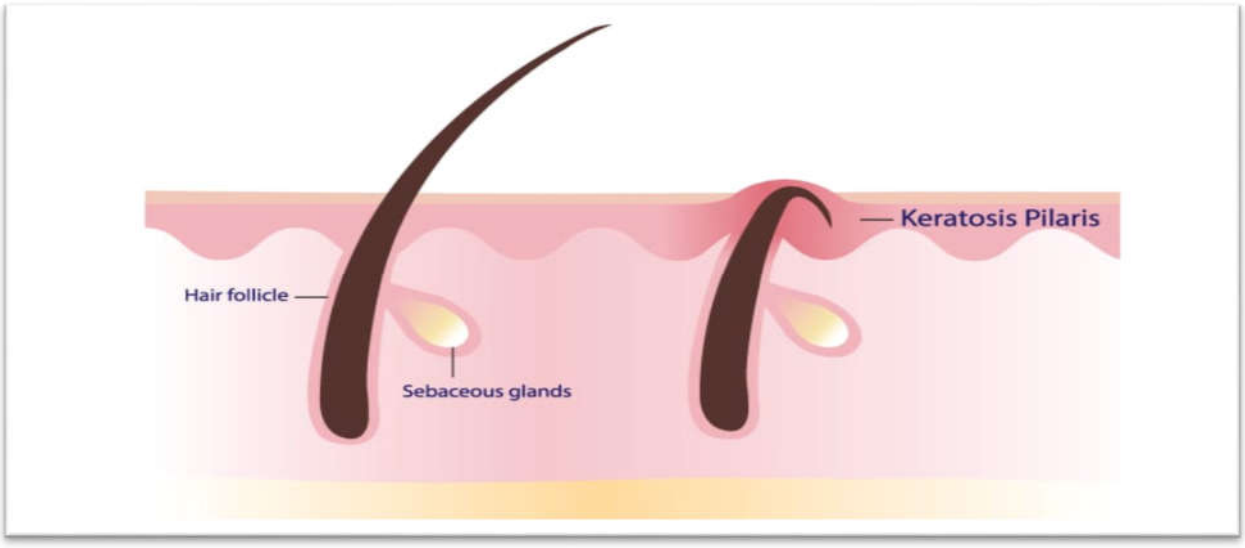


Fig3:- A diagram showing pathophysiology of normal and disease KP (23)

In some studies it is found to believe that it may cause from the decrease in the fillagrin. The research primarily focused on FLG (Filaggrin), an essential protein found in the epidermis that performs a crucial part in the creation of corneocytes on that skin's natural moisturizing factor.

Mutations in FLG have been linked to xerosis cutis, a condition characterized by dry and rough skin, which also affects the protective epithelial barrier. Normally, FLG aids in maintaining the acidity of the skin, protecting it against damage from sunlight, and contributing to the natural moisture of the stratum corneum. To investigate further, the researchers examined FLG genotypes in 20 patients with keratosis pilaris (KP) and analyzed the skin's morphology using both light and electron microscopy. Their objective was to evaluate any potential structural changes in the epidermis associated with KP and determine whether there is a specific impairment in the skin barrier among KP patients with FLG null mutations (24).

IMPACT OF KERATOSIS PILARIS:-

Its psychosocial impact, especially on their body-image, socialization, as well as sexual, is in particular notable among young adolescents. However, there's limited documentation on this aspect, potentially underestimating its impact. Studies like Kootiratrakarn et al.'s a Thai case determined who over 40 per cent of KP cases greatly impacted one's quality of life and sense of self, with effective treatments showing improvements in bodily satisfaction, anxiety, and depression . Yet, such studies often lack broader applicability due to being single-center trials. A less commonly reported variant, keratosis pilaris rubra (KPR), characterized by pronounced redness alongside KP, can also have social implications. KPR on his cheeks, experiencing embarrassment and discomfort, avoiding physical education classes due to self-consciousness. Such examples highlight the substantial impact of KP and its subtypes on individuals, emphasizing the need for further research into these psychosocial aspects(6,25).

TYPES OF KERATOSIS PILARIS

The keratosis pilaris a categorised into many forms , it includes :

1.Keratosis pilaris rubra

2.Keratosis pilaris atropicans

1.KERATOSIS PILARIS RUBRA:-

A clinical variant of keratosis pilaris (KP) known as keratosis pilaris rubra (KPR) is distinguished by the presence of numerous tiny papules within a background and redness. This condition is commonly observed on the outside of the upper limbs, face, and trunk .this can be distinguished about follicularis faciei et colli erythromelanosis the presence of from keratosis pilaris atrophicans and erythema by the absence of tissue wasting. Despite the absence of a universally accepted treatment, Topical therapies like keratolytics and emollient (such as urea, lactate, and salicylic acid), as well as vitamin-D analogs, steroid medication, and retinoids, frequently yield unsatisfactory results in managing this condition (26).

Keratosis pilaris rubra is a common but underreported keratosis pilaris variation characterized by significant involvement and more apparent pruritus without atropy or hyperpigmentation. Keratosis pilaris (KP) is a prevalent non-threatening disarray with an unidentified cause. Usually, it appears as a rash characterized by symmetrical, painless, clustered keratinized bumps on cheeks and lateral and medial portions of the proximate limb. In some cases, KP may also affect the neck, torso, buttocks, and rarely, it may become generalized. If erythema is present, Usually minor, it only affects the skin. surrounding a hair follicles. This condition often has a familial pattern, and it is thought to have a dominant autosomal pattern. manner without any specific racial or gender predisposition. Keratosis pilaris commonly develops during early childhood and frequently resolves by adulthood in many patients (27).

2. KERATOSIS PILARIS ATROPICANS:-

Keratosis pilaris KPAF, or atrophicans faciei, alternatively referred to to be ulerythema ophryogenes is a very uncommon condition. that is established through the presence of little , red, Keratotic papules begin on the face. These papules eventually lead to both focal baldness and atrophy. This circumstance primarily affects the eyebrows and is considered uncommon. There are genetic and clinical similarities between KPAF and other scarring alopecias that exhibit follicular hyperkeratosis, such as tosis follicularis about atrophoderma vermiculatum spinulosa Decals. A Few experts have grouped pilaris keratosis atrophicans, a collective term used for multiple medical conditions (28). The term "acne pilaris atrophicans" defines a class with genetic skin conditions that manifest as three separate physical objects: atrophoderma vermiculatum (AV), keratosis follicularis spinulosa decalvans (KFSD), and a condition known as keratosis pilaris atrophicans faciei (KPAF). (29).

The more comprehensive term "keratosis pilaris atrophicans" (KPA) is used to collective together these diseases. These disorders are categorized based on variations in their location, as well as the level of inflammation and atrophy. Throughout the literature, there are numerous terms for these disorders, which can often be perplexing and cause confusion(30).

- It is associated with erythematous follicularis papules which used to cause or the eyebrows. The first account of Ulerythema ophryogenes dates back to 1889 when Taenzer, a member of Unna's clinic, provided its initial description(31). There were numerous papules on the parietal scalp that exhibited slight itchiness and excessive keratinization. These papules were surrounded by a red halo and were limited to the inflamed skin. Additionally, hair loss was observed as a consequence (32).
- Also associated with Follicle keratosis spinulosa decalvans. Keratosis spinulosa decalvans follicularis, in addition referred to to be keratosis follicularis Decalvans, the initially as stated by Lameris the Netherlands as ichthyosis/ollicularis. Siemens, who examined Dutch patients and members of the original Bavarian family, put forward the term KFSD (33,34).
- Keratosis pilaris atrophicans faciei also occurs in cheeks, trunk and limb (34) .

- The noonan syndrome was also associated with these disorder ,it was found to be associated in a patient with congenital heart disease (35).
- Erythromelanosis follicularis Faciei is also a one of the variant of keratosis pilaris , it is also asymptomatic skin lesion (9).It is considered to be an inflammatory process disease (36).

GENOMICS:-

Autosomal dominant inheritance may be responsible for the genetic aetiology of KP, as evidenced by its occurrence in approximately 39% individuals who have a medical family history of the illness (10). By performing a genomic analysis on thirteen consanguineous Pakistani patients affected by KPA, researchers successfully identified a pathogenic variant in the LRP1 gene. This variant, designated as KP1245R, is a novel homozygous missense variant and has been determined to be responsible for autosomal recessive KPA and KP (37). Within the LDL family, LRP1 serves as an important player in endocytic processes. However, in patients with this particular mutation, the levels of LRP1 are diminished in fibroblasts, resulting in a decline in the Cellular absorption of α2-macroglobulin, and its ligand (38).

Additionally, There is a supporting proof indicating which alterations desmoglein 4 might contribute to its development of autosomal recessive Keratosis Pilaris Atrophicans (KPA) (39). In most cases, KPAF is passed down via autosomal dominant lines fashion alongside insufficient penetration. Nevertheless, sporadic occurrences of the condition have also been well-documented (40). Inheritance of AV can also occur with a pattern of dominant autosomal genes, although The regularity of sporadic cases is higher (40,41). Erythromelanosis condition is linked to keratosis pilaris, which manifests on the shoulders as well as the arms' extensor sides. This family history is described in some studies (42,43). The probable genetic cause for the condition in all three affected family members is most likely due to father-given dominant autosomal inherited. It may be possible, though, that each of the children's mutations came from their mom and have nothing to do with the father's illness., thus providing evidence for X-linked inheritance (44).

A rare condition is keratosis follicularis spinulosa decalvans. genetic situations that affects the process of keratinization. It passes down through a the X-linked manner it is distinguished by the participation with both Skin around the eyes and skin. Initially, it was identified as an X-associated genetic disease. Nevertheless, there have been instances where Additionally, irregular and autosomal dominant genetic processes have been noted observed (45). A presence of the gene variant has been linked to decreased levels of the protein and a decrease in the cellular absorption of α2-macroglobulin (α2M). Considering the involvement Furthermore, genetic processes which are both autosomal dominant or irregular are being seen. propose a potential process of disease within our household, which is attributed to the dysregulation of the inflammatory response mediated by LRP1 (46).

Atrichia, photophobia, which is and The condition follicularis are a primary subcutaneous dermis manifestations observed in individuals affected by this uncommon genetic condition. The

underlying cause of this disorder can be attributed to mutations occurring within a gene. responsible for containing the location 2 of the membrane-bound transcription factor peptidase (MBTPS2). The severity of these symptoms may vary among affected individuals (47).

TREATMENT:-

- ACID

Acid is a prevalent ingredient found in numerous acne-fighting products, primarily due to its efficacy in unclogging the pores. One notable acid, glycolic acid, functions by disrupting the interconnections among the human skin's outermost protective layer and, consisting of the epidermis and decreasing cells of the skin. Consequently, this process initiates an stripping impact that reduces the accumulation of Skin cells that have died as well as excess crude oil within the openings, ultimately Which results in a more refined and blemish-free complexion (2). Acid is a widely utilized ingredient in numerous acne-fighting products due to its ability to effectively unclog the pores. One such acid, glycolic acid, functions by disrupting the connections amongst the skin's outermost protective layer, composed of dead skin cells and dermal tissue. Consequently, in process induces a tearing impact that reduces the accumulation of Skin cells that have died as well as excess oil within the openings, ultimately leading to a more clarified complexion (48).

Glycolic acid, derived from sugar cane, belongs to a group of compounds called alpha-hydroxy acids (AHAs). AHAs consist of Five different groups, namely Glycolic acid is an acid. (found in Sugar from cane), Lactose (obtained with breastmilk), acid phosphoric (present in citrus or lemons), Acid with malic acid (derived with apple and pear trees), and tartaric acid (extracted to cherries). When applied to in skin, glycolic acid interacts with the outermost layer, effectively disintegrating it via breaking down keratin along with other binders deceased tissues in unison (49). The total amount of cellular retinoic acid-binding protein (CRABP) substantially increased. observed on patches psoriatica. However, no increase was observed in the levels of CRBP, or cellular retinol-binding protein when in contrast to non-lesional psoriasis and humans skin that is normal (50).

- KINASE INHITORS

It inhibition of tyrosine kinases by kinase inhibitors has been observed to exert an influence on keratosis pilaris and its closely related variants. These enzymes, responsible for transmitting growth signals within cells, are effectively blocked by kinase inhibitors, thereby impeding cell growth and division (2). Vemurafenib, another noteworthy kinase inhibitor, has garnered attention in the scientific community. It functions as a BRAF inhibitor and is utilized in the management of metastatic melanoma, a form of skin cancer where the melanocytes, responsible for pigment production, undergo malignant changes (51).

- STEROIDS

Steroids are known to exert an influence on keratosis pilaris, being classified as one of the compounds that affect this condition. By diminishing inflammation, both topical and systemic steroids actively combat acne disorders (52). Steroids have been identified as one of the substances that have an impact on keratosis pilaris. Both topical and systemic steroids play a crucial role in reducing inflammation and directly combating acne-related conditions (2).

- LASER THERAPY

Among the laser treatments currently accessible for the treatment of cutaneous vascular lesions, the PDL stands out for the exceptional safety margin, especially when considering its application in children. However, That is crucial to recognize that it's possible impact a PDL on the inflammatory component of KPA remains uncertain, which might explain the absence of its usage in treating this particular disorder (11).

Other laser therapy involves the various laser treatment they are :-

- laser treatment with 810-nm (53)
- Fractional carbon dioxide laser
- Potassium Titanyl phosphate laser

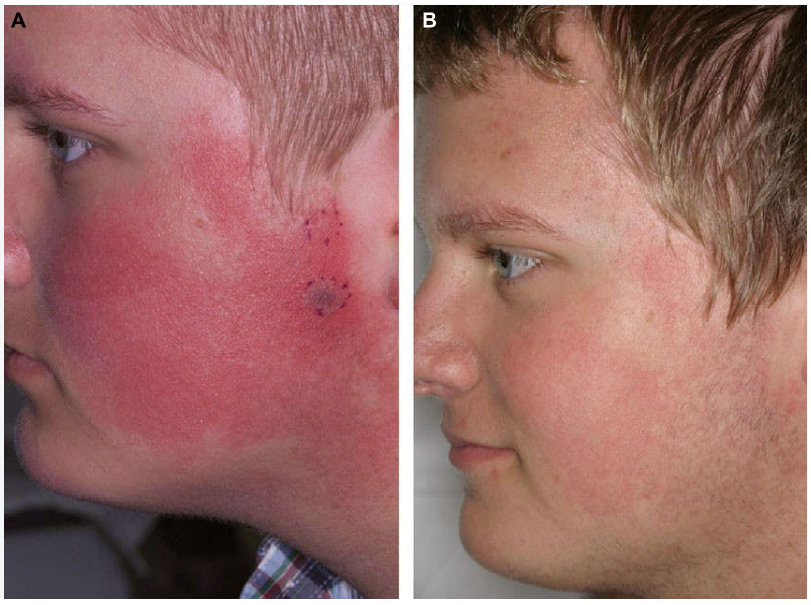


Fig4:- A diagram showing the KP after treatment with laser therapy and before treatment with laser therapy (25)

CONCLUSION:-

According to various studies which has been reported on this paper concluded that various treatments are available for this but the effective treatment is laser therapy, but it has various side effect ,so various topical application like some acid ,steroid and kinase inhibitor are used .so now till the date the most convenient treatment is to use acid containing products.

FUTURE PROSPECT:-

By the use of this review article the connection between the pathophysiology and treatment can be connected easily, for this the experimental work is necessary and the convenient treatment confirmation is possible according to types of KP.

REFERENCE:-

1. Arnold AW, Buechner SA. Keratosis pilaris und Keratosis pilaris atrophicans faciei. JDDG - Journal of the German Society of Dermatology. 2006 Apr;4(4):319–23.
2. Reddy S, Brahmbhatt H. A Narrative Review on the Role of Acids, Steroids, and Kinase Inhibitors in the Treatment of Keratosis Pilaris. Cureus. 2021 Oct 20;
3. Ravipati A, Pradeep T. Seasonal variability in public searches of keratosis pilaris: How the internet can illuminate a pattern in public interest. Dermatol Ther. 2020 Nov 1;33(6).
4. Vipinsha RS, Prathibha CKB, Anandaraman PVS. Aveda management of keratosis pilaris - A case report. J Complement Integr Med. 2021 Mar 1;18(1):223–30.
5. Reddy N, Parveen S, Allahuddin S. Evaluation of Oral Vitamin-A Clinical Response in Keratinized Skin Diseases. IOSR Journal of Dental and Medical Sciences (IOSR-JDMS) e-ISSN [Internet]. 2019;18:33–6. Available from: www.iosrjournals.org
6. Wang MA, Wilson A, Murrell DF. A Review of the Scoring and Assessment of Keratosis Pilaris. Vol. 9, Skin Appendage Disorders. S. Karger AG; 2023. p. 241–51.
7. Kaune KM, Haas E, Emmert S, SchÖn MP, Zutt M. Successful treatment of severe keratosis pilaris rubra with a 595-nm pulsed dye laser. Dermatologic Surgery. 2009 Oct;35(10):1592–5.
8. Maghfour J, Ly S, Haidari W, Taylor SL, Feldman SR. Treatment of keratosis pilaris and its variants: a systematic review. Vol. 33, Journal of Dermatological Treatment. Taylor and Francis Ltd.; 2022. p. 1231–42.
9. Ziller F, Leclerque C, Bartholdt E, Habeck JO, Feldmann-Böddeker I. Melanom-rezidiv nach 45 jahren. Vol. 13, JDDG - Journal of the German Society of Dermatology. Wiley-VCH Verlag; 2015. p. 49–51.
10. Poskitt L, Wilkinson JD. Natural history of keratosis pilaris. Vol. 130, British Journal of Dermatology. 1994.

11. Treatment of keratosis pilaris atrophicans with the pulsed tunable dye laser SM Clark, CM Mills & SW Lanigan.

12. Alcántara González J, Boixeda P, Truchuelo Díez MT, Fleta Asín B. Keratosis pilaris rubra and keratosis pilaris atrophicans faciei treated with pulsed dye laser: Report of 10 cases. Journal of the European Academy of Dermatology and Venereology. 2011 Jun;25(6):710–4.

13. Thomas M, Khopkar US. Keratosis Pilaris Revisited: Is It More Than Just a Follicular Keratosis? Int J Trichology. 2012 Oct;4(4):255–8.

14. Rasi A, Soltani-Arabshahi R, Zahra ;, Naraghi S, Rasi D, Arabshahi S. 218 CUTIS ® PEDIATRIC DERMATOLOGY Circumscribed Juvenile-Onset Pityriasis Rubra Pilaris With Hypoparathyroidism and Brachyonychia.

15. Novak N, Baurecht H, Schäfer T, Rodriguez E, Wagenpfeil S, Klopp N, et al. Loss-of-function mutations in the Filaggrin gene and allergic contact sensitization to nickel. Journal of Investigative Dermatology. 2008;128(6):1430–5.

16. Mevorah B, Marazzi A, Frenk E. The prevalence of accentuated palmoplantar markings and keratosis pilaris in atopic dermatitis, autosomal dominant ichthyosis and control dermatological patients. Vol. 112, British Journal of Dermatology. 1985.

17. Al-Saeed WY, Al-Dawood KM, Bukhari IA, Bahnassy AA. Prevalence and pattern of skin disorders among female schoolchildren in Eastern Saudi Arabia [Internet]. Available from: www.smj.org.sa

18. Del Pozzo-Magaña BR, Lazo-Langner A, Gutiérrez-Castrellón P, Ruiz-Maldonado R. Common Dermatoses in Children Referred to a Specialized Pediatric Dermatology Service in Mexico: A Comparative Study between Two Decades. ISRN Dermatol. 2012 Oct 14;2012:1–5.

19. Oro-Ayude M, Feito M, Quintana-Castanedo L, Beato-Merino MJ, De Lucas R. Keratosis pilaris-like eruption secondary to nilotinib in a child. Pediatr Dermatol. 2020 Sep 1;37(5):968–9.

20. Pediatric dermatology.

21. Rout DP, Nair A, Gupta A, Kumar P. Epidermolytic hyperkeratosis: Clinical update. Clin Cosmet Investig Dermatol. 2019;12:333–44.

22. Fox BJ, Odom RB. Continuing medical education Papulosquamous diseases: A review*. Vol. 12, AmeRicaN ACaDemY OF DerMaTOLOGY. 1985.

23. httpswww.healthkart.comconnectkeratosis-pilaris-its-causes-symptoms-and-treatment.

24. Gruber R, Sugarman JL, Crumrine D, Hupe M, Mauro TM, Mauldin EA, et al. Sebaceous gland, hair shaft, and epidermal barrier abnormalities in keratosis pilaris with and without filaggrin deficiency. American Journal of Pathology. 2015 Apr 1;185(4):1012–21.

25. Schoch JJ, Tollefson MM, Witman P, Davis DMR. Successful treatment of keratosis pilaris rubra with pulsed dye laser. Pediatr Dermatol. 2016 Jul 1;33(4):443–6.

26. Eckburg A, Kazemi T, Maguiness S. Keratosis pilaris rubra successfully treated with topical sirolimus: Report of a case and review of the literature. Pediatr Dermatol. 2022 May 1;39(3):429–31.

27. Marqueling AL, Gilliam AE, Prendiville J, Zvulunov A, Antaya RJ, Sugarman J, et al. Keratosis Pilaris Rubra A Common but Underrecognized Condition [Internet]. Available from: http://archderm.jamanetwork.com/

28. Baden HP, Byers HR. Clinical Findings, Cutaneous Pathology, and Response to Therapy in 21 Patients With Keratosis Pilaris Atrophicans [Internet]. Available from: http://archderm.jamanetwork.com/

29. Lesher JL, Callaway SR. Keratosis Pilaris Atrophicans: Case Series and Review. Vol. 21, Pediatric Dermatology. 2004.

30. Rand R, Baden HP. Keratosis Follicularis Spinulosa Decalvans Report of Two Cases and Literature Review [Internet]. Available from: http://archderm.jamanetwork.com/

31. Davenport DD. Ulerythema Ophryogenes Review and Report of a Case. Discussion of Relationship to Certain Other Skin Disorders and Association With Internal Abnormalities [Internet]. Available from: http://archderm.jamanetwork.com/

32. Stojanović S, Vučković N, Jovanović M. Overlap Between Ulerythema Ophryogenes and Keratosis Follicularis Spinulosa Decalvans: a Case Report. Serbian Journal of Dermatology and Venereology. 2015 Sep 1;7(3):129–38.

33. Keratosis Pilaris Atrophicans One Heterogeneous Disease or a Symptom in Different Clinical Entities? [Internet]. Available from: http://archderm.jamanetwork.com/

34. Maroon M, Tyler WB, Marks VJ. Keratosis Pilaris and Scarring Alopecia [Internet]. Available from: http://archderm.jamanetwork.com/

35. Pierini DO, Pierini AM. Keratosis pilaris atrophicans faciei (Ulerythema ophryogenes): a cutaneous marker in the Noonan syndrome. British Journal of Dermatology. 1979.

36. Rand R, Baden HP. Keratosis Follicularis Spinulosa Decalvans Report of Two Cases and Literature Review [Internet]. Available from: http://archderm.jamanetwork.com/

37. Klar J, Schuster J, Khan TN, Jameel M, Mäbert K, Forsberg L, et al. Whole exome sequencing identifies LRP1 as a pathogenic gene in autosomal recessive keratosis pilaris atrophicans. J Med Genet. 2015 Jul 3;52(9):599–606.

38. Akay BN, Parlak N, Saral S, Akyol A. Retina dekolmaninin eşlik ettiği iktiyozis folikülaris, alopesi ve fotofobi sendromlu bir olgu. Turkderm Deri Hastaliklari ve Frengi Arsivi. 2014;48(2):108–10.

39. Cohen-Barak E, Danial-Farran N, Hammad H, Aleme O, Krauz J, Gavish E, et al. Desmoglein 4 mutation underlies autosomal recessive keratosis pilaris atrophicans. Vol. 98, Acta Dermato-Venereologica. Medical Journals/Acta D-V; 2018. p. 809–10.

40. Sardana K. Follicular disorders of the face. Vol. 32, Clinics in Dermatology. Elsevier Inc.; 2014. p. 839–72.

41. Barron DR, Hirsch AL, Buchbinder L, Pomeranz JR. Folliculitis Ulerythematosus Reticulata: A Report of Four Cases and Brief Review of the Literature. Vol. 4, Pediatric Dermatology. 1987.

42. Yanez S, Velasco JA. Familial erythromelanosis follicularis faciei et colli an autosomal recessive mode of inheritance. Vol. 18, Clinical and Experimental Dermatology. 1993.

43. Türel A, Öztürkcan S, Turhan M, Türkdo P, Saçar T. Erythromelanosis Follicularis Faciei et Colli Associated with Keratosis Pilaris in Two Brothers. Vol. 23, Pediatric Dermatology. 2006.

44. Bellet JS, Kaplan AL, Selim MA, Olsen EA. Keratosis follicularis spinulosa decalvans in a family. J Am Acad Dermatol. 2008 Mar;58(3):499–502.

45. Chauhan RK, Sankhwar S, Tripathi R, Pandey SS. A rare presentation of keratosis follicularis spinulosa decalvans in female twins. Vol. 84, Indian Journal of Dermatology, Venereology and Leprology. Wolters Kluwer Medknow Publications; 2018. p. 645.

46. Klar J, Schuster J, Khan TN, Jameel M, Mäbert K, Forsberg L, et al. Whole exome sequencing identifies LRP1 as a pathogenic gene in autosomal recessive keratosis pilaris atrophicans. J Med Genet. 2015 Jul 3;52(9):599–606.

47. Nemer G, Safi R, Kreidieh F, Usta J, Bergqvist C, Ballout F, et al. Understanding the phenotypic similarities between IFAP and Olmsted syndrome from a molecular perspective: the interaction of MBTPS2 and TRPV3. Arch Dermatol Res. 2017 Oct 1;309(8):637–43.

48. Searle T, Ali FR, Al-Niaimi F. The versatility of azelaic acid in dermatology. Vol. 33, Journal of Dermatological Treatment. Taylor and Francis Ltd.; 2022. p. 722–32.

49. Wiegmann D, Haddad L. Two is better than one: The combined effects of glycolic acid and salicylic acid on acne-related disorders. J Cosmet Dermatol. 2020 Sep 1;19(9):2349–51.

50. Siegenthaler G, Saurai JH, Salomon D, Mérot Y. Skin Cellular Retinoid-Binding Proteins and Retinoid-Responsive Dermatoses' Key Words. Retinol • Retinoic acid • Etretin • Retinoid-binding proteins • Cellular retinoic acid-binding protein • Cellular retinol-binding protein • Serum retinol-binding protein. Vol. 173, Dermatologica. 1986.

51. Boyd KP, Vincent B, Andea A, Conry RM, Hughey LC. Nonmalignant cutaneous findings associated with vemurafenib use in patients with metastatic melanoma. Vol. 67, Journal of the American Academy of Dermatology. Mosby Inc.; 2012. p. 1375–9.

52. The prevalence and descriptive epidemiology of atopic dermatitis in Singapore school children. Epidemiology/Health Services Research.

53. Ibrahim O, Khan M, Bolotin D, Dubina M, Nodzenski M, Disphanurat W, et al. Treatment of keratosis pilaris with 810-nm diode laser a randomized clinical trial. JAMA Dermatol. 2015 Feb 1;151(2):187–91.