"A CROSS SECTIONAL STUDY OF ACNE VULGARIS WITH SPECIAL REFERENCE TO SERUM ZINC LEVELS AT KLE'S DR. PRABHAKAR KORE HOSPITAL AND MRC, BELGAUM"

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DISSERTATION

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ENDORSEMENT BY THE HOD, PRINCIPAL / HEAD OF THE INSTITUTION

This is to certify that the Dissertation entitled "**A Cross-sectional study of acne vulgaris with special reference to serum zinc levels at KLE'S Dr. Prabhakar Kore Hospital and MRC, Belgaum**" is a bonafide research work done by the Candidate having Reg. No. BT 0108002

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LIST OF ABBREVATIONS USED

ACTH	=	Adrenocorticotrophic hormone
C3	=	Complement
CD4	=	Cluster differentiation
CH	=	Cutaneous hyperandrogenism
CPA	=	Cypropterone acetate
DHA	=	Dehydroepiandrosterone
DHEAS	=	Dehydroepiandrosterone sulphate
DHT	=	Dihydrotestestorene
EE	=	Ethinyl estradiol
GH	=	Growth hormone
HAIR-AN Syndrome	=	Hyperandrogenism,insulin resistance,acanthosis nigricans
IGF	=	Insulin growth factor
IL	=	Interleukin
ILT	=	Intralesional steroid
MSH	=	Melanocyte stimulating hormone
P.acnes	=	Propioniobacterium acnes.
POD	=	Polycystic ovarian disease
RBP	=	Retinol binding protein
SAHA	=	seborrhoea,acne,hypertrichosis and androgenetic alopecia
SAPHO	=	Synovitis, acne conglobata, palmoplantar pustulosis, hyperostosis, and osteitis
SHBG	=	Sex hormone binding globulin
SER	=	Sebum excretion rate
TNF	=	Tumor necrosis factor

ABSTRACT

Background and objectives: Acne Vulgaris is a common and chronic dermatological disorder, mainly affecting the adolescents and young adults, involving the pilosebaceous follicles of the face and upper trunk. It is clinically characterized by polymorphic lesions such as comedones, papules, pustules, nodules and occasionally cysts. Scarring is the most dreaded complication of acne, for it scars both skin and the mind.

The objectives of the study are to determine the association of serum zinc levels with acne vulgaris, to study the clinical features of acne vulgaris and to observe relationship between acne vulgaris and certain aetiological and predisposing factors like season, diet and heredity, etc.

Materials and Methods: The present study is a one year cross sectional study from November 2008 to October 2009. Patient's demographic data, symptoms, location of lesions, risk factors, associated systemic disease were noted in a pre- tested and pre-designed proforma after taking informed and written consent. Diagnosis was established by history and clinical examination. All the diagnosed cases of acne vulgaris were subjected to grading and serum zinc levels were estimated by immunoturbidometry method.

Results: In the present study, the serum zinc levels were studied in 70 acne patients. Serum zinc levels were not significantly low in acne patients of different grades of the same age group. There was no significant difference in percentage distribution of patients in group A (low zinc levels) and group B(normal zinc levels) in different grades of acne($p=0.9$,not statistically significant).Therefore there was no association between serum zinc levels and severity of acne.

Conclusion: There was no co-relation between the severity of acne and serum zinc levels.

Key words : Acne vulgaris and serum zinc.

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INTRODUCTION

Acne vulgaris is a chronic inflammatory disorder of the pilosebaceous duct characterised by polymorphic lesions of comedones, papules, pustules, nodules and cysts. It occurs most commonly in adolescents and young adults. It has lot of psychological impact on teenage.

Sulzberger and Zaidems in their article stated that "There is no single disease that can cause more psychological trauma, more maladjustment between parent and children and feelings of inferiority than does acne".[1]

There are many myths about acne like its infectivity and relation to chocolate etc. It is unfortunate that etiology of such a common condition still has many controversies and is unclear. Recently it has been shown that consumption of foods with high glycemic index has led to aggravation of acne.

Zinc levels in serum and skin has received the attention of many researchers in the field. It is believed that there is direct correlation between the serum zinc levels and severity of acne. Zinc and vitamin A are essential for normal keratinization of epithelium. Zinc is responsible for release and synthesis of retinol binding protein, which in turn maintains the normal levels of vitamin A in skin. Zinc also stabilizes androgen synthesis in the skin. The role of other trace elements like copper, iron, magnesium etc. have also been studied but there is no consensus among the researchers as to their significance in acne.

The serum zinc levels in acne in various studies contradict each other. Many of the workers have concluded that there is no change in serum zinc levels and acne, whereas others have found a remarkable decrease in the levels.

AIMS & OBJECTIVES

AIM :

To prove low serum zinc levels are associated with severity of acne

PRIMARY OBJECTIVES:

- To associate serum zinc levels with acne vulgaris.

SECONDARY OBJECTIVES:

- To study clinical features of acne vulgaris.
- To observe relationship between acne vulgaris and certain aetiological and predisposing factors like season, diet, heredity, etc.

REVIEW OF LITERATURE

HISTORICAL ASPECTS

Aristotle was the first person to use the word 'Ionthoi', which is a Greek term for acne which means, the first growth of beard. Roman physicians used term for term 'varus' for the disease but this did not last long. **Grant (**1951) found that **Aetius** had used word 'Acnae' in about 542 AD. **Gorreus** in 1578 wrote that, "Acne is a small hard papule in the face."[4]

Acne is derived from transcription error for the word "Akme" which in Greek means height of anything including the height of growth.[5]

Hebra (1868) used the term 'stone-pocks' for acne while **Radcliff-Crocker**(1903) used stone-pock as synonym.

Grant (1951) thought that Egyptian word 'Aku-t' found in the Ebers Papyrus meaning boils, pimples and pustules, may have been accepted by the Greeks.

In 19th century **William Bateman** divided acne into 3 main clinical types, namely-simplex, punctata and Indurata.

In1840, **Fuchs** for the first time used the term 'Acne vulgaris'.[4]

Early thoughts on etiology and pathogenesis of acne:

The fact that acne appeared at puberty was recognised by the Greeks 2500 years ago. **Riolanus**(1638) was the first to note an association between acne and disordered menstruation. **Ionston**(1648) linked acne with virility and repression, stating, "vari infect young people that are inclined to venery".

Plenck (1783) expressed the view that acne could be cured by marriage. He also related the occurance of acne in young people to a rich diet and copious secretion of semen. He noted the disappearance of acne in later teens. ***Bateman*** (1813) considered that black points in acne were due to small worms or grubs. ***Alibert*** (1837) stressed that acne sufferers gambled all night or lived in constant anxiety. ***Simon*** (1842) discovered Demodex folliculorum, which he felt might be at times an aetiological factor in acne.

The pathological events taking place in skin in acne were described by ***Virchow*** (1863) and recorded by ***Hebra*** (1868).Virchow regarded acne as an irritative process set up around the hair follicle by the retention of its secretion. Hebra agreed with **Riolanus** when he said that acne occurred frequently in connection with disordered menstruation and disappeared when this function became normal. He also divided acne into idiopathic and symptomatic form. Hebra is also credited for the observation that acne is closely linked with seborrhoea. Hebra freely confessed that he had been unable to find a remedy to prevent acne developing or to vanish it once established. He found many of the drugs commonly recommended for acne to be ineffective. He listed such ineffective remedies as emetics, purgatives, arsenic, the freshly expressed juices, extracts or decoctions of chicory, couch-grass and dandelion and sulphur waters. The arrival of antibiotics on the therapeutic scene made a considerable difference to the modern management of acne.[4]

Unna (1896) described follicular hyperkeratosis as a characteristic histological feature of acne. ***Sulzberger and Baer*** (1949) tried to find the relation between acne and marriage but could find none. Acne Bacillus was discovered at the end of the 19th century. ***Blair and Lewis and Goodhead*** (1970) concluded by their studies that the black color in blackheads is due to melanin.

Zelickson and Motta showed that the black color is due to densely packed horny cells in the infundibulum.[6]

According to some workers black colour is due to oxidation of melanin, interference in transmission of light through compacted epithelial cells, or the presence of certain lipids in sebum.[33,69]

From the Egyptian times zinc oxide and other derivatives have been used to promote wound healing. The essentiality of zinc was first recognized by ***Raulin*** (1869), for the growth of Aspergillus Niger, and for the growth of higher plants by ***Sommer and Lipman*** (1926). As early as 1934, ***Todd*** *et al* showed that zinc is an essential dietary component for rats, 20 years later, ***Tucker and Salmon*** reported that Zinc cures and prevents parakeratosis in pigs.[7]

Zinc deficiency was once considered impossible to occur in humans, due to widespread occurrence of this metal in food and water supplies, but this does not seem to be true now.[8]

Prasad et al in 1961, for the first time demonstrated zinc deficiency in Iranian men. Subsequently similar cases were observed in Egypt. In these patients, zinc deficiency was attributed to a diet consisting mainly of vegetables and whole grain bread, having a high fibre and phytate content. The habit of pica (clay eating) and hook worm infestation played an additional role.[7]

Though Acrodermatitis enteropathica was a well described entity since 1936, its etiology was a mystery for about thirty years. ***Moynahan*** in 1973 linked the disease to zinc deficiency and successfully treated it with zinc supplements. ***Evans and Johnson*** suggested that the impaired absorption of zinc in Acrodermatitis is due to inadequate intestinal levels of a zinc-binding factor secreted by the pancreas, possibly a prostaglandin.

The co-relation between acne and zinc was thought of after an accidental finding that many patients of Acrodermatitis enteropathica developed a papulopustular eruption on the face and upper chest early in the disease.

Michaelsson, Julin, and Vahlquist (1977) were the first to study the role of oral zinc in acne vulgaris. They, in their study, found a beneficial effect on acne with oral zinc and found no additional benefit in patients who were given zinc with Vitamin A.[2] Since then many other workers have found beneficial effects of zinc in acne vulgaris.

NORMAL ANATOMY OF PILOSEBACEOUS DUCT

Pilosebaceous unit consists of hair follicle and sebaceous gland. Pilosebaceous duct is lined by keratinising epithelium through which hair and sebum pass. Along with sebum, epithelial lining and bacteria are discharged through the pilosebaceous canal exit. Ostium refers to the opening of the pilosebaceous unit on the skin surface. Infundibulum is the part of the pilary canal extending from the level of the ostium down to the entrance of the sebaceous duct.

The upper one fifth of the infundibulum is called acroinfundibulum and the lower four fifth below pilosebaceous duct is called the infrainfundibulum.[9]

These two areas of the infundibulum are structurally and functionally different and it is the Infrainfundibulum which takes part in the comedo formation.[10]

Three types of follicle occur on the face:

- Beard follicle
- Vellus follicle
- Sebaceous follicle

It is the sebaceous follicle, with large pores, which bears the brunt of acne. So it is the dynamics with in the follicle which is responsible for the obstruction. The localisation of acne to the face and trunk is determined by the distribution of sebaceous follicles.

Distribution of Sebaceous glands

Sebaceous glands are situated all over the skin with exception to the palms and soles. They develop in the fourth month of fetal life from an epithelial bud from the hair follicle at a point marking the junction of the future infundibulum and isthmus.[4] These glands vary in their location and are largest and most numerous on the face, forehead and upper back. On the scalp, forehead, cheeks and chin there are about 400-900 glands/ sq cm.[11]

Structure of sebaceous glands

Most sebaceous glands are intimately related to the development of hair follicle and usually vary inversely in size with hair follicles. These two structures are collectively referred to as pilosebaceous units and when very large as sebaceous follicles.[11]Sebaceous glands are well supplied with blood vessels but no nerve supply has yet been demonstrated.

It consists of 3 major cell types. These are the undifferentiated, differentiated and mature cells. Adjacent to the basement membrane are the undifferentiated cells. As these cells are pushed towards the sebaceous duct they become differentiated into lipid containing cells. As the lipid increases the mature cells disintegrate forming sebum. Acid hydrolases and phosphatases contained within the lysosomes are known to play a role in the physiological autolysis that occurs in the formation of a holocrine secretion.[11]

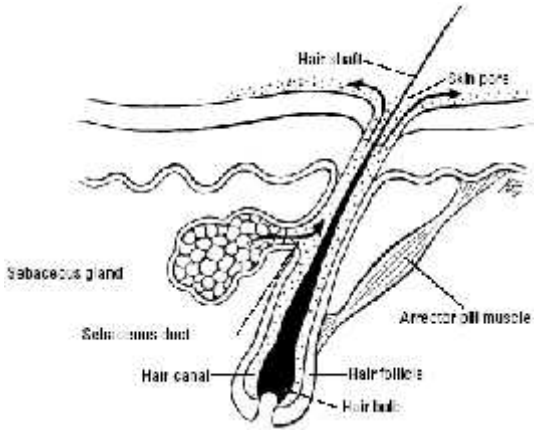


Figure 1 : Structure of pilosebaceous unit

Sebum:

Sebum is formed by the disintegration of lipid containing cells in the sebaceous glands. Sebum is a complex mixture of lipids which varies from species to species It is very difficult to analyse human sebum because the skin surface lipid contains not only sebum but also lipid from the keratinizing epidermis, eccrine and apocrine glands. The exogenous sources of skin surface lipid are cosmetics and ointments used in topical therapy and soaps. When surface lipid is collected from the areas of skin rich in sebaceous gland for example, the forehead-the lipid composition approaches that of pure sebum. The major lipids in sebum are the triglycerides (57.5%), wax esters (26%), squalene (12%), cholesteryl esters (3%) and cholesterol (1.5%). Epidermis contributes triglycerides, cholesterol, cholesterol esters and phospholipids. [11]

Function of sebum

1. Barrier function.
2. Regulation of percutaneous absorption.
3. Antifungal function due to products of hydrolysis.
4. Antibacterial action due to certain surface free fatty acids.
5. Protect skin surface lipids on face by secreting vitamin E.
6. Vitamin D precursor.[33]

Steroid metabolism in the sebaceous gland:

The development and secretory activity of the sebaceous gland are unquestionably under androgen control. The testes synthesize testosterone, the main circulating androgen and delta-5 androstenediol. The adrenal gland is the main source of dehydroepiandrosterone (DHA) and dehydroepiandrosterone sulphate (DHEAS), which is quantitatively the major circulating adrenal androgen. The adrenals also produce androstenedione and delta-5 androstenediol, the latter being an important circulating androgen in women. The ovary is capable of synthesizing testosterone, androstenedione and DHA. Some hormones are transported in bound form, for example testosterone is carried by Sex hormone binding globulin (SHBG). A high level of SHBG signifies a low level of free hormone.[71]

Acne vulgaris is an androgen dependent disorder. Sebaceous glands are specific androgen targets. Sebaceous activity is regulated by androgens of gonadal or adrenal origin.

Seborrhea in patients with acne is due to abnormality of androgen synthesis. 5-α reductase type 1 enzyme activity is higher in skin areas sensitive to testosterone and acne bearing sites, with high sebaceous activity, than in normal skin.

In adults it is higher in areas sensitive to testosterone and acne bearing areas with high level of sebaceous activity. Therefore production of more active metabolite like 5-α dehydrotestosterone from testosterone in the presence of 5-α reductase could be one reason for seborrhoea.

Specific nuclear androgen receptors have been demonstrated in the sebaceous glands. Increased binding of androgens to their respective receptors in skin and a possibly enhanced response of the acne prone sebaceous gland cells to androgen can all be responsible for seborrhoea. [12]

3-beta hydroxysteroid dehydrogenase is distributed evenly throughout the substance of the sebaceous gland and 17-beta hydroxysteroid dehydrogenase is limited to the periphery of the gland. The 3-beta pathway is involved with androgen breakdown whereas 17-beta hydroxysteroid is concerned with androgen production. Their localisation in the sebaceous gland, connects them intimately with the pathogenesis of acne, either due to over production of androgens or to an imbalance of the excretory: synthesis ratio of androgens.[12]

5α-dehydrotestosterone is further reduced to 3-alpha and 3-beta, 17-beta-androstenediols and these substances are excreted in abnormally high quantities by women with acne or hirsutism. They are generally regarded as end point of cellular androgen metabolism. A range of NAD dependent hydroxysteroid dehydrogenase has been histochemically demonstrated in the sebaceous glands from the acne prone areas of human skin. Male or female skin can convert dehydroepiandrosterone to androstenedione, testosterone or epiandrosterone and other derivatives. Dehydroepiandrosterone is known to stimulate sebum production in castrated men or in intact men treated with ethinyl-estradiol.

Hormonal Control of sebum production and secretion:

The fetal zone of adrenal cortex is one of the largest of fetal organs. It develops during the first trimester of pregnancy and is very active in steroid metabolism. This contributes to the development of the fetal sebaceous glands into adult ones. At some determined time after birth, the glands involute due to withdrawal of maternal androgens. With the hormonal changes of puberty, the glands enlarge and produce larger quantities of sebum.

Several factors influence the formation of sebum, but it is predominantly hormonally controlled. Androgens from the testes and the adrenals stimulate the sebaceous gland directly. Progesterone has no major effect. Estrogens exert an inhibitory effect on sebum excretion in both males and females only at doses that exceed the physiologic requirement in females and produce feminization in males. It does not have a peripheral action. It acts by inhibiting hormonal release through the pituitary.[72]

The pituitary gland, in particular, the anterior lobe has an important role in controlling the sebaceous secretion. It releases ACTH and gonadotrophins which act on adrenals and gonads which in turn release androgens which have sebotrophic effect. In males ACTH has negligible effect on sebaceous glands because glands mainly respond mainly to testicular androgens.

In the females ACTH deficiency leads to a decreased sebum secretion rate. Beta MSH has no role to play in the control of sebaceous secretion and thus in the pathogenesis of acne. In acromegaly, GH released by pituitary has sebotrophic effect.[72]

Effect of pregnancy: Burton et al observed only minor fluctuations in the middle and last trimesters of pregnancy but there was a pronounced decrease in the post partum period. Probably a powerful sebotrophic factor is present in pregnancy but its nature is hypothetical.[13]

Oral contraceptives containing a high dose of estrogen reduce the sebum excretion rate (SER) and more progestogenic preparations may exacerbate acne.[72]

Pye, **Meyrick and Burton** (1977) studied the effect of various contraceptive pills on sebum excretion rate in acne patients. They found that predominantly progesterone containing pills produced no effect on the sebum excretion rate, but it was significantly reduced in women taking a more estrogenic pill. It was concluded that progestogens do not exacerbate acne by inducing seborrhea but in doses supplied in the pills, they take away the inhibitory effect of estrogens on the sebaceous glands.[14]

ACNE VULGARIS

Definition:

Acne Vulgaris is a common and chronic dermatological disorder, mainly affecting the adolescents and young adults, involving the pilosebaceous follicles of the face and upper trunk. It is clinically characterised by polymorphic lesions such as comedones, papules, pustules, nodules and occasionally cysts. Scarring is the most dreaded complication of acne, for it scars both skin and the mind.

Genetic factors: Although acne is not an inherited condition, there is inherited predisposition. Several genes are believed to be involved, of which only the gene for cytochrome P-450-1A1 and the gene for steroid 21-hydroxylase are documented.

Positive family history of acne is obtained in 40% of the patients and correlates with more severe disease.

If both parents had acne, 3 of 4 children will have acne. If one parent had acne, then 1 of 4 of the children will have acne.[15] It is found that HLA-DPB1*2402 allele is involved in pathogenesis of acne.

Ballanger et al. (2006) found more severe acne forms in patients with acne history on the mother's side or on both parental sides than in patients with acne history on the father's side only.[16]

It is not known which etiological factors of acne are inherited. It has been postulated that acne is an exaggerated response of the end organs to, that is, the Pilosebaceous unit to the normal levels of circulating androgens. An alternative explanation is a genetically mediated elevation of circulating androgen.[17]

In a twin study at Leeds, it was observed that identical twins had identical rates of sebum excretion but had a significantly different degree of acne severity.[17]

These findings suggest that sebum excretion is under genetic control and the development of lesions is modified by environmental factors. Studies have shown that some patients with severe acne may have the abnormal XYY chromosome complement. Other features of XYY syndrome were not seen. It has been suggested that the Y -controlled gene regulates Pilosebaceous function directly through the production of an aberrant testosterone. It therefore appears that nodulocystic acne may be an as yet unrecognized but important aspect of XYY syndrome and further investigation is needed.[73,74]

Incidence:

This disease is sufficiently common that it often has been termed physiologic. It is occasionally present at birth and mild cases can be seen in the neonatal period. However it is not until puberty that acne becomes a common problem. In girls acne may precede menarche by more than a year. The greatest numbers of cases are seen during middle to late teen age period and subsequently the incidence decreases. Studies indicate that a slight predominance in males and severe involvement is more common in males, whereas in females acne persists till the third decade.[18]

The largest survey was conducted by **Bloch** (1931) and he found an earlier onset in boys than in girls. The maximum prevalence was later in females (18 years) than the males (17 years).[19]

Forbes in 1946 **Munro Asherman** in 1963 and **Rook** in 1972, recorded the incidence of acne and they concluded that in women a peak incidence and severity occurs between 14-17 years whereas, in men peak age of onset is between 16-19 years.[74]

In a study by **Burton** and **Cunliff** (1971) maximum prevalence occurred at the age of 14 in girls and at 16 in boys. The earlier onset in girls was probably related to earlier onset of puberty in them.[19]

Kligman stated that the true prevalence of acne is 100% in boys and girls and that no one goes through adolescence without a few comedones and papules.

Cunliff and Gould (1979) concluded that clinical acne was not confined to adolescents. Acne was more prevalent in males before 18 years but beyond 23 years it was more prevalent in women and prevalence in men declined. At 40-49 years 3% of men and 5% of women still had acne. At 50-59 years 6% of men and 8% of females had acne.[20]

Little is known about the age at which spontaneous regression of acne occurs. Resolution is not related to reduction of sebum production or surface bacteria. The relationship between ductal hypercornification, inflammatory mediators, changes in the host response and resolution is obscure. It has been postulated that resolution may be associated with specific changes in acne prone hypersecreting glands.[12]

Racial Studies:

Racial studies provide an insight into genetic and environmental factors. Acne is common in North American whites. Spanish persons tend to more commonly develop cystic acne. African Americans have a higher prevalence of pomade acne, likely stemming from the use of hair pomades.[15]

Aetiology:

The basic cause of Acne Vulgaris is still unknown. Currently, it is believed that acne is a multifactorial disease in which, clinical expression depends on the interaction of several factors. The following factors are involved in the pathogenesis of acne:

- Sebaceous gland hyperplasia with seborrhea- a genetic predisposition.
- Abnormal end organ response to the circulating androgens and their increased levels.
- Comedogenesis: Ductal hypercornification and hyperproliferation.
- *Propionibacterium acnes* colonization of the pilosebaceous duct.
- Inflammation and immune response.[21]

Sebaceous gland hyperplasia with seborrhea

The sebaceous glands start to enlarge with androgenic stimulus at approximately 7 to 8 years of age (adrenarche), with a resultant increase in sebum excretion.[21]

Active sebaceous glands are a pre requisite for the development of acne. The sebaceous glands in an acne patient are larger in size due to hyperplasia resulting from increased androgen stimulation, which in turn is under genetic control. Three factors are important in development of acne:

- Sebum excretion rate
- Surface lipid composition
- Sebum outflow resistance.[22]

Acne patients on an average secrete more sebum than normal subjects. The level of sebum co-relates well with severity of disease.[72] Sebaceous activity is dependent on male sex hormones of gonadal or adrenal origin.

High levels of sebaceous secretion could result from increased androgen production or deficiency of Sex hormone binding globulin (SHBG), which results in increased amount of free androgens. Another explanation is a possibility of an amplified end organ (pilosebaceous duct) response to the circulating hormone.

Cove et al found no significant relation between the size of bacterial population and sebaceous secretion.[23]

The role of individual lipid components in causing acne is uncertain. Patients with acne tend to have higher levels of squalene and wax esters, lower levels of fatty acids and a more frequent occurrence of particular free fatty acids.[70]

The reduction in the pilosebaceous duct orifice increases the resistance to the flow of sebum and thus exacerbates acne, especially under tropical and humid conditions, which produces keratin hydration at the orifice.[27]

Abnormal end organ response to the circulating androgens

Acne patients do have excessive androgen production (as may be indicated by hirsutism or significant menstrual dysfunction) and should receive an endocrinologic evaluation.[21]

Darley and co-workers found increased testosterone levels or low SHBG either alone or in combination, in 60% of female patients. They also had an increased amount of free testosterone.

Hyperprolactinaernia was found in 45% of the patients**.**[62]

The plasma testosterone levels are not abnormally high in all males with acne.[12] Local conversion of testosterone to 5 alpha dehydrotestosterone by the enzyme 5 alpha reductase is increased in acne skin compared to normal. This conversion varied among individuals. Differences in the activity of this enzyme at different skin sites might also explain the frequent clinical observation of patients with severe acne at one site and no acne at another. This has proved role of androgen metabolism in sebaceous gland for the development of acne.[12]

Lucky et al found hyperandrogenemia in women with acne and hirsutism. Women with only acne were also found to have elevated levels of testosterone.[24]

Ginsberg et al (1980) found increased levels of dehydroepiandrosterone in women with acne, hirsutism and menstrual irregularity.[25]

But **Sheehan et al** (1988) could not find any relation between acne and other markers of hyperandrogenism. Also significant number of women with raised androgen levels have no acne and women with acne may have normal androgen levels.[26]

Ductal hypercornification (comedogenesis):

Acne patients show ductal hypercornification which produces black heads and white heads. There is a significant co-relation between the severity of acne and the number and size of follicular casts, which are a measure of comedogenesis.

The stimulus for hypercornification could be androgen mediated. It could also be the result of lowered linoleic acid levels in sebum suggesting that ductal bacteria are not needed for the initiation of cornification. In animal experiments, a low linoleate level produced hypercornification and a decreased epidermal barrier function and this made the comedonal wall more permeable to inflammatory substances. Linoleic acid is significantly reduced in epidermal and comedonal lipids and this may relate to ductal hypercornification.[12]

Hypercornification represent the retention of hyperproliferating ductal keratinocytes/corneocytes in the duct.[12] The factors which cause a normal follicle to convert into either a white head or a black head are not known.

Microcomedone formation:

In acne, keratinocytes hyperproliferate and are shed abnormally as cluster or group of cells. Abnormally desquamated corneocytes become densely packed along with monofilaments and lipid droplets in follicle leading to formation of microcomedone, a microscopic lesion not visible to the naked eye.[21]

Abnormal desquamation in pilosebaceous duct:

Several theories have been proposed to explain the abnormal desquamation in duct that occurs in patients with acne.

Guy and Kealey suggested changes in sebum composition or secretion may irritate infundibular keratinocytes, resulting in release of IL-1α.They also showed that addition of IL-1α stimulated abnormal desquamation and led to disruption of the integrity of the follicular wall in organ culture in vitro. Ingham et al showed that high levels of biologically active interleukin-1α (IL-1α) occur in comedones; it is thought that the IL-1α is expressed by follicular keratinocytes.[21]

Abnormal desquamation is due to hyperproliferation and differentiation of ductal keratinocytes. Both of these are due to a relative decrease in sebaceous linoleic acid or due to defect in the 5-α reductase enzyme (type 1) in the infundibulum(leading to increased conversion of testesterone to DHT).[21]

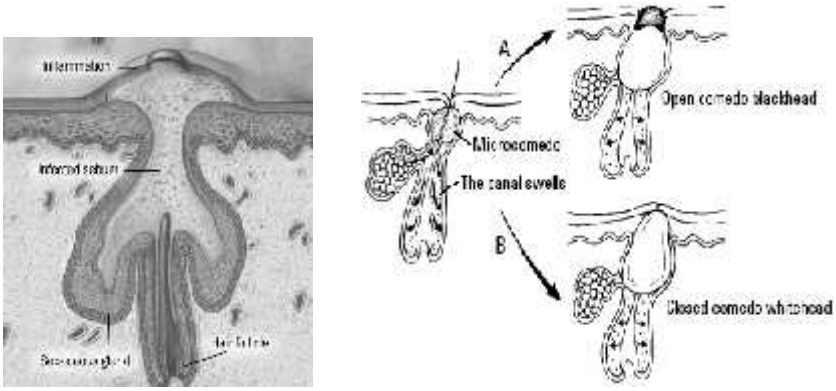


Figure 2 : Acne and Bacteria

Acne is not infectious. The three major organisms isolated from the surface of the skin and the duct of patients with acne are Propionibacterium acnes, Staphylococcus Epidermidis and Malassezia furfur (Pityrosporum).

There are 3 major subgroups of Propionibacteria

- Propionibacterium acnes
- Propionibacterium Granulosum
- Propionibacterium Avidum

Among these P.acnes and to a lesser extent P. Granulosum are the most important. But since they live in association with the S. Epidermidis and M. furfur, it seems that these organisms have some control over the growth of P.acnes.[12]

Initial attempts to quantify the population density of skin surface bacteria failed to find any difference between the number of P. acnes in patients with or without acne. No co-relation has been found between the sebum excretion rate and the size of bacterial population. [23]

Significant co-relation has been found between the Micrococcaceae, propionibacterium and free fatty acid production. The rate of free fatty acid production represents the possible extent of bacterial activity on sebum triglycerides. The level of free fatty acid in sebum does not help in determining the role of bacteria.[23]

The turnover rate of bacteria is greater on skin with a high sebum secretion rate.

Puhvel and **Sakamoto** reevaluated the role of free fatty acids as inflammatory agents in acne. They failed to find any relation between inflammation and free fatty acids. They, thus, concluded that the role of Propionibacterium acnes in the pathogenesis of acne is more complex than merely a source of lipases.[28]

P.acnes has always been thought of as a promotor of inflammation in acne. The inflammatory action was thought to be due to the action of lipase of P.acnes on triglycerides producing free fatty acid. Now, P.acnes is known to produce diffusible leucocyte chemoattractants.[29] Neutrophil ingestion of bacteria and the liberation of hydrolytic enzymes could lead to damage to the follicular wall and thereby generating a foreign body reaction.[75]

Inflammation:

This probably results from biologically active mediators, produced by P acnes which diffuse from the follicle. In the early events of papule formation, a microcomedo is present in 80% of such lesions. Thereafter, CD4 lymphocytes invade the follicular wall, usually leading to disruption. Later, neutrophils migrate to the scene. Ductal rupture is associated with extravasation of lipids, corneocytes, and bacteria into the dermis.[21]

Ductal corneocytes produce Interleukins (IL-l and IL-2) and Tumour Necrosis Factor (TNF) which are involved in inflammation. Cell wall fraction of P. acne is a powerful chemoattractant for polymorphonuclear and mononuclear cells. It also produces a prostaglandin like substance. Direct immunofluorescence studies have shown that in early inflamed and non-inflamed lesions there is an activation of alternate and classical complement pathway. **Dahl and McGibbon** observed the presence of C3 in the walls of dermal vessels of the lesional skin. This suggests the role of complement in the pathogenesis of acne.[30] white heads have greater potential for developing into inflammatory lesion.[31]

Recently it is proposed that *P acnes* activates the toll-like receptor 2 on monocytes and neutrophils leading to the production of multiple proinflammatory cytokines, including interleukins 12 and 8 and tumor necrosis factor. Hypersensitivity to *P acnes* may also explain why some individuals develop inflammatory acne vulgaris while others do not.[15]

The non-inflammatory lesions are known to stimulate alternate pathway for complement activation and this is responsible for the conversion of non-inflamed lesions to inflamed lesions.[31]

C3a and C5a are also produced which together with the release of inflammatory mediators increase the vascular permeability and produce oedema.[31] The total IgG levels are raised in severe acne. These are probably in response to the cell wall component of P acnes mainly and to a lesser extent Staphylococci and Pityrosporum ovale.[32]

The host response to P acnes is important as both classical and alternate pathways are activated. The antibody titre to P.acnes is elevated in acne patients, and this antibody promotes the release of lysosomal hydrolases from polymorphonuclear cells. With the progression of lesions, type III and IV immunological reactions increase, as indicated by an increase in leucocyte migration inhibition in acne patients. The importance of these immunological responses of the host in the production of inflammatory lesions is thus considerable.[33]

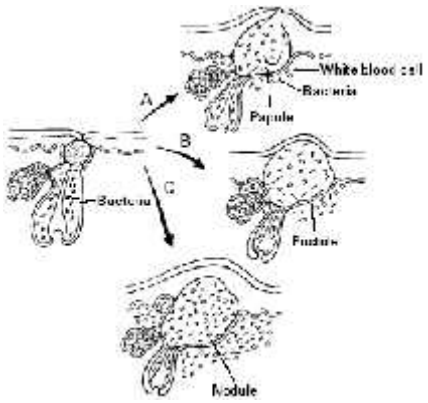


Figure 3 : Conversion of comedons into inflammatory lesions

Pathogenesis of Acne:

Acne rarely develops in certain regions of the body suggesting that, there may be limiting forces possibly related to androgen receptors, critical mass of sebum or bacteria, pore size of the follicle, surface temperature, sebum viscosity, and biochemical composition of sebum or any other related factor. All follicles do not

develop acne and those containing terminal hair are particularly immune. It is because the thick terminal hair prevents blockage of the duct. Acne usually occurs in sebaceous follicles present on the face, chest and back. The initial lesion of acne (micro-comedo) begins. In the lower 4/5th of the follicular infundibulum (infrainfundibulum).

Two important events take place during comedo formation :- A decrease in the dehiscence of horny cells that stick together tightly and form a solid mass that steadily expands. Keratinosomes present in the follicular wall decrease in number during comedo formation. This has been blamed to be responsible for the decrease in lysis of intercellular cementing substance and poor dehiscence of horny cells. Secondly, there is hyperproliferation of the follicular epithelium.

When the horny cells stick together, they form an impacted mass that distends the lumen of the follicle forming a microcomedo. When it grows to a size of 1mm, the microcomedo becomes visible as a closed comedo. With the expansion of horny mass, the lining epithelium becomes thinned out due to pressure. Comedones undergo one of the two fates. They may rupture and incite an inflammatory reaction or they transform into open comedones. Later, the horny mass protrudes through the orifice in the open comedone and the tip darkens. The shrunken sebaceous glands continue to secrete sebum throughout the life of a comedo that streams to the surface through tortuous bacteria filled in comedones.[34]

Factors Affecting Acne

Menstruation and acne:

Menstruation is known to modify acne. Two studies one retrospective and the other prospective, by Cunliff and Foster and Cunliff et al (1974) demonstrated that acne got worse 5-6 days before the onset of menses.[74]

Polycystic Ovarian Disease (POD) is the most commonly associated hormonal disease. This can be detected by ultrasonography but these patients usually do not have other features of POD i.e. Hirsutism, infertility or irregular periods. The presence of ovarian cyst does not relate to the severity of acne.[35]

Williams and Cunliff, used surface microscopy to measure the size of the pilosebaceous duct orifices during the menstrual cycle and came to the conclusion that the duct exit was significantly smaller between the 15th and 20th day. This leads to an obstruction to the flow of sebum resulting in exacerbation of acne premenstrually. Changes in hydration of keratin or in the molecular structure of keratin was thought to be the cause for decrease in the size of the exit but what exactly leads to this change is unknown.[36]

Diet and acne:

Historically, the relationship between diet and acne has been highly controversial. Before the 1960s many dermatologists believed that there was some relationship between acne and diet especially certain food items like fats, chocolates, starchy food, iodides and Vitamins were blamed. However, subsequent studies dispelled these alleged associations as myth for almost half a century.

Recently in last decade studies showed reasonably compelling evidence that high glycemic load diets may exacerbate acne. **Adebamowo et al**, 2005 found that Acne is positively associated with intake of milk (particularly skim milk), instant breakfast drink, sherbet, and cottage cheese. It has been proposed that milk increases comedogenicity through increase of plasma insulin-like growth factor (IGF)-1 level. IGF-1 stimulates synthesis of androgens in both ovarian and testicular tissues and inhibits hepatic synthesis of sex hormone-binding globulin. Milk contains the testosterone precursors (androstenedione and dehydro-epi androsteronesulfate.), 5α-reduced steroids, (5α-androstanedione and 5α-pregnanedione, which are DHT precursors). Both testosterone precursors and 5α-reduced molecules are thought to contribute to the comedogenicity of milk. Both IGF-1 and androgens increase sebum production, which is implicated in acne.[37]

The role of omega-3 fatty acids, antioxidants, zinc, vitamin A, and dietary fiber in acne is unclear and remains to be elucidated.[37]

Rasmussen, in his study observed that 68% of (80 acne patients at a university blamed chocolates and fatty foods for the flare up of their lesions. In a school study conducted at Delhi no significant correlation was found between mean calorie intake in controls and patients.[38]

Experimentally, severe calorie deprivation or dietary manipulation can modify sebaceous gland function. Low calorie diet produces a rapid decrease in sebum secretion.[72]

Iodides have been blamed for aggravating acne but the evidence for this is rather poor. No evidence has been found against flourides which are added to tooth pastes and to drinking water.[76]

The weather:

Sunlight is known to help most people with acne. The reasons for this are varied-

- Camouflaging effect produced initially by erythema and later by pigmentation.
- Bactericidal effects because of increased penetration till the lower dermis, even the bacteria deeply located in the dermis are killed.
- Increased scaling causes unplugging of the blocked Pilosebaceous duct.

Cunliff et al in their studies found :

60% of patients had improvement in sunlight.

20% noticed no change.

20% noticed an increase in their acne lesions.[73]

Deterioration may be secondary to increased sweating especially in hot and humid situations.

Gfesser reported aggravation of acne in 1/3 of their patients in winter and an improvement in 1/3 in summer. Another 1/3 of their patients had a summer aggravation. According to **Mills and co-workers** the aggravation in summer was explained to be due to widespread use of sunscreens. These have been found to be comedogenic and their effect is potentiated by the ultraviolet rays. In some studies Ultraviolet rays is found to increase the comedogenicity of squalene.[39]

Environmental Factors:

Acne is rare in rural areas. It is more common in industrial cities and mining areas because of genetic, dietary and weather differences. Hot and humid environment like in the tropics increases the hydration of stratum corneum which precipitates acne (tropical acne). It is commonly seen on the back, especially in soldiers stationed in the

tropics with backpacks.[40] Workers in kitchen and laundries, due to increased heat and humidity, develop occupational acne.

Psychological factors:

According to Kenyon stress alone is not responsible for induction of acne. However acne can itself induce stress, and picking of the lesions will aggravate the appearance. This symptom is most commonly seen in young women who present with acne excoriee.[12]An increase in the levels of free fatty acids has been noted during periods of stress.[34] Questionnaire studies have shown that many acne patients experience shame (70%), Embarrassment and anxiety (6)%), lack of confidence (67%), impaired social contact (57%) and a significant problem with unemployment.

Severe acne may be related to increased anger and anxiety.[12] According to **KOO**, the psychiatric morbidity associated with acne are the following;[1]

- Impaired self image/ self esteem
- Social impairment
- Depression
- Anger

Patients with Dysmorphophobia may have acne as their primary symptom. Their acne is mild but they are often depressed, obsessional and schizophrenic. They also have a significant risk of suicide.[12]

ZINC AND ACNE VULGARIS

Zinc is a constituent of the earth's crust, combined with carbonate, oxygen, sulfur and silicon. It circulates in nature in its simplest form from rock, to soil, to ocean and may be concentrated from these elements in plants, shellfish, fish and animals.

Zinc is a trace element that is necessary for epithelial differentiation and normal pubertal growth. It exists in high amounts within the skin and especially the epidermis. Its importance for human metabolism has been noted by the dramatic improvement of acrodermatitis enteropathica following zinc supplementation. A case of acrodermatitis enteropathica was reported, where severe acne also completely resolved with zinc treatment.[64]

Zinc is an element found in the structure of many metalloenzymes that play a role in important functions such as protein synthesis, DNA and RNA replication and cell division. Zinc is therefore required for growth and development. It plays a role in delayed type hypersensitivity reactions, regulation of inflammation, normal keratogenesis, cell membrane stabilization and many enzymatic reactions. Zinc is also a structural component of many hormones such as growth hormone, insulin, sex hormones and thymulin and influences the activity of these hormones.[64]

Foodstuffs of animal origin, including the dairy products and sea food are good sources of zinc. Legumes, nuts, grains and green leafy vegetables are also good sources of zinc.

Meat and fish products are the best sources of nutrition for zinc content and bioavailability.

The zinc in food of animal origin is absorbed better than zinc in food of grain origin. The phytates present in grains bind zinc and decrease its absorption. Zinc deficiency is a common mineral deficiency in our country where 70-80% of the daily calorie requirement is derived from grains and grain products. [64]

Zinc deficiency can be due to genetic or acquired causes. Genetic zinc deficiency leads to “acrodermatitis enteropathica”, characterized by red, patchy and scaly dermatitis involving the face, periorificial and anogenital regions, papulopustular, psoriasiform or vesiculobullous eruptions of the acral regions, and alopecia. Acquired zinc deficiency can be associated with alcoholism, chronic diseases, malabsorption due to jejunoileal bypass and consumption of food with a high phytate content such as some high-fiber vegetable and grains.[64]

The zinc deficiency in acne patients has been associated with nutritional deficiency, dieting patients, decreased absorption, and increased excretion with sweat or feces. The inflammatory reaction in acne patients is another factor decreasing serum zinc levels.

It forms an essential trace element in the human body. Most laboratories have found a reference value of 70-120µg zinc per 100ml serum which is equivalent to 11-18 µmol per litre.[55] Zinc levels in blood fall within hours of stress such as surgical trauma, myocardial infarction or inflammation. A protein called leucocyte endogenous mediator is released by the active phagocytes, which lowers the zinc levels. Zinc is essential for the activity of at least 90 enzymes, which participate in all the major metabolic pathways. It is essential for all phases of cell cycle. It also stabilizes the lysosomal plasma membrane. Deficiency of zinc occurs from inadequate dietary intake, increased body losses, malabsorption or intravenous feeding.

Assessment of body zinc status is rather difficult. Serum zinc levels are subject to acute variations. Determination of urinary zinc is also unreliable. At present, the best criterion for detecting zinc deficiency is an unequivocal clinical response to zinc administration. [56]

Role of Zinc in Acne vulgaris:

The essential trace metal Zinc has been linked to numerous biological processes in man. The initial link between zinc deficiency and acne was made as early as the 1970s by Michaelsson and Fitzherbert who reported the improvement of acne upon supplementation of zinc in zinc-deficient patients.[65]

It plays an important role in the activity of various enzyme systems, helps to stabilize macromolecules and biological membranes and influences the activity of macrophages.

There are conflicting reports in literature regarding the value of oral zinc therapy in acne vulgaris. The acne-like papulopustular lesions in zinc deficiency and their rapid improvement with zinc supplementation have led some investigators to assess the relationship between serum zinc levels and acne. These studies are few in number but have shown that patients with acne have low serum zinc levels although these levels do not correlate with the severity of disease. Some authors have therefore combined zinc to inflammatory acne treatment, and it is still used with varying rates of success.

In a study by **Demetree et al,** the effect of zinc on sebum excretion rate was recorded. They found an inverse relation between the group mean serum zinc level and group mean sebum excretion rate, after starting the patients on zinc sulfate

therapy for several weeks. The subjects noticed an improvement in their oily skin, with development of dryness, and also in their acne lesions. This improvement was accounted for by an enhanced metabolism of androgens by a zinc dependent hydroxysteroid dehydrogenase. [63]

Another mechanism binding zinc deficiency and acne development involves the "retinol binding protein" (RBP). Retinol binding protein (RBP) is a specific transport protein and its plasma level reflects the amount of vitamin A available to the tissues. **Smith et al** conducted a study to know the effect of zinc deficiency on the metabolism of retinol binding protein in rat and found that zinc was essential for the release and synthesis of the retinol binding protein in the liver.[2]

So zinc is thought to influence vitamin A transport and utilization directly or indirectly through some enzymes and prevent keratinization and follicular obstruction. The serum levels of zinc and retinol binding protein were compared in patients with acne and in controls. Patients with severe acne were found to have lower levels of retinol binding protein and zinc than patients with mild acne and healthy individuals.

Oral administration of zinc has been found to be effective in the treatment of acne. The possible mechanism of action of zinc is through the release of vitamin A, which is supposed to be deficient in patients with acne vulgaris. [2]

From a mechanistic point of view, the role of zinc in the treatment of acne vulgaris is not well understood. Several studies noted a reduction in local skin microbial parameters such as the Propionibacterium acnes count and free fatty acids levels. Zinc appears to target P. acnes specifically and does not affect Staphylococcus spp. Whether zinc is effective against Micrococcaceae has yet to be determined as

existing data appear controversial. A possible mechanism for this antimicrobial effect is inhibition of P. acnes lipase by zinc.

The effect of zinc on inflammatory cells and especially on granulocytes is the most important mechanism relevant to acne.[65]

Treatment with zinc gluconate improved polymorphonuclear chemotaxis in patients suffering from acne. Zinc also plays a regulatory role in control of phagocytosis, stabilizes macromolecules and lysosomes. It also activates complement during inflammatory reaction. Studies with laboratory animals have shown that zinc inhibits histamine secretion from mast cells and prevents inflammatory phenomena. This suggests a role for zinc as an inflammation modulating agent in skin.

An additional proposed mechanism for the benefit of zinc in the treatment of acne is suppression of sebum delivery, perhaps by anti-androgenic activity. Damage to the zinc-dependent enzyme systems in androgen synthesis is thought to be another mechanism explaining zinc deficiency and development of acne vulgaris. It has been shown that testosterone converts mostly into DHT with the reductase enzyme and that zinc inhibits the reductase enzyme.

Interestingly, zinc appears to enhance the topical absorption of erythromycin. This observation alludes to a possible benefit in combining erythromycin with zinc salts. In summary, zinc is thought to be linked to acne through direct effects on the microbial-inflammatory equilibrium, as well as possible facilitation of topical antibiotic absorption.

HISTOPATHOLOGY OF ACNE

Comedone: A comedo contains keratinized cells, sebum and some organisms, but in routinely prepared sections, only keratinized cells are seen because xylene used in processing removes the lipid material. There is infundibular dilation and thinning of follicular wall. In closed comedone there is normal or less follicular ostia. In open comedone there is widening of follicular orifice. In both comedones there is mild mononuclear inflammation situated in vessels around papillary dermis.[41]

Papules: The follicular papules of acne are characterised by a predominantly lymphocytic infiltrate, arranged around a follicle containing either a closed comedo or a microcomedo. Small areas of follicular wall degeneration may also be seen on careful searching.[41]As the comedo enlarges, the sebaceous gland undergoes atrophy. **Kligman** carried out a detailed histological study of comedo and showed that a comedo begins in the infrainfundibulum where the entire epithelial lining undergoes a change in the pattern of cornification. The granular layer becomes more prominent and the horny cells become more distinct and sturdy. Instead of sloughing into a loose disorganizing mass, the horny cells begin to pack together into lamellae of dense eosinophilic horn. Ultrastructurally, the granular layer cells have few tonofilaments and large keratohyaline granules. The lamellar granules are decreased in the intercellular spaces of the cornified layer in a comedo. Multiple intracellular lipid inclusions have been found within the cells of stratum corneum and granulosum.[77]

Pustule: Extreme attenuation of follicular wall may lead to rupture. Release of follicular contents into superficial dermis it generates an inflammatory response initially mediated by neutrophils and later by histiocytes and foreign body giant cells.[41]

Inflammatory nodule: Release of follicular contents into deeper dermis. Cyst like follicular dilation with deep rupture leading to neutrophilic and granulomatous inflammation throughout the dermis.[41]

Cystic acne and Acne fulminans: Extensive inflammation leading to dermal necrosis with abscess formation.[41]

CLINICAL FEATURES

Acne patients usually present with a greasy skin which is usually due to seborrhea. There is a direct relation between the severity of acne and seborrhea but not all patients with seborrhea have acne. This point is proved by the fact that patients with Parkinsonism and Acromegaly also have seborrhea but not acne.[74]

Lesions of Acne:

The lesions of acne are polymorphic and consist of comedones, papules, pustules, nodules, cysts, macules and scars. Post inflammatory pigmentation and pyogenic granuloma may also occur.

Comedones: These are the non inflammatory lesions of acne. They can be either open or closed.

Open comedones: These are commonly referred to as Blackheads. These are between 0.1 to 3 mm. in diameter. They are flat or slightly raised lesions with central dark coloured follicular impaction of keratin, lipid, melanin and bacteria. These take a few weeks to develop and can be easily expressed out with a comedone extractor. On expression, a greyish white structure is extruded. The black tip of the structure consists of melanin which was previously thought to be due to oxidation of surface lipids. In an ultrastructural study of comedones by **Zelickson and Mottaz**[6] the

amount of melanin found was minimal and thus could not be attributed to the black colour. They concluded that the dark colour may be due to a large number of densely packed horny cells located in the superficial infundibular region of the sebaceous follicle and to the numerous bacteria and their break down products.

Closed Comedones: These are also called white heads. This represents a pilosebaceous duct distended with inspissated ductal material, the orifice of which is hardly visible to the naked eye. They appear as pale, slightly elevated, small papules. Stretching of the skin aids in detecting the lesions which are not extractable. Of the typical white heads 25% resolve within 3 to 4 days and 75% develop into inflamed lesions. Larger ones last for weeks to months. Since the closed comedones are the potential precursors for the large inflammatory lesions, they are of considerable clinical importance. All comedones cannot be clearly classified as open or closed. Some show black melanized centre with a white halo. Such lesions constitute 40% of comedones but not classified officially with a name. The term Intermediate non inflammed lesions or even "blight head" has been used for such lesions.[76]

Open and closed comedones are primary comedones.

Secondary comedones: Rupture and re-encapsulation or epithelisation of comedones creates secondary comedones. Polyporous comedones are secondary comedones.

Polyporous comedones are also called fistulous comedones or double or triple comedones. Groups of adjacent comedones and follicles are linked up by rupture and re-encapsulation. They are typical of Acne conglobata.

Comedo naevus (Naevus comedonicus): This uncommon naevus is a developmental defect of the hair follicles, and the associated sebaceous gland may be normal, hypoplastic or hyperplastic. Scalp, face and trunk are common sites to be involved. It may be present at birth or develop later.

Familial comedone: This uncommon genetic disorder shows autosomal inheritance. Polyporous comedones and cysts are seen and scarring may follow.

Solar comedones: These are commonly seen in the elderly, especially in the periorbital areas. Solar damage to the supporting dermis allows the pilosebaceous duct to become more easily distended.

Macrocomedones: Larger than 1mm.

Sand paper comedones: Small but large number of closed comedones on forehead.

Submarine comedones: Large and deep comedones.

Papules: These usually arise from comedones. 50% arise from microcomedones of normal skin, 25% arise from white head, 25% remainder from black heads.

There are 2 types of papules:

- Less Active papules: less red, smaller than active lesions reach up to 4mm diameter, last longer. Resolve via macule or develop into active papule or pustule.
- Active papules: Resolve via macule or indirectly via a less active papule.[11]

Pustules: These are of two types-

- The first type is a superficial pustule formed as a result of obstruction and inflammation in the upper part of the Pilosebaceous canal. This is not tender and lasts for a few days. It usually resolves following puncture most often by the patient himself.

- The second type is a much deeper lesion where the lesion is present both in the epidermis and dermis. This arises from a preexisting inflammatory papule or nodule and may persist for 4-7 days. It resolves in two to six weeks through a papular phase.[76]

Nodules: These are deep-seated structures, larger in size and take 8 weeks before completely resolving through a papular phase.

Cysts: These are rare but when they occur they are quite disfiguring. They may be unilocular or multilocular and when aspirated with a thick bore needle drain thick viscid creamy yellow material. Sometimes the cysts are widespread and affect the face, back, chest and neck. Even the scalp may be affected. The lesions may coalesce, producing boggy areas associated with Sinuses, necrosis, and granulomatous inflammation called Acne Conglobata.

Morphogenesis of acne lesions:

The morphogenesis of acne is a dynamic process. Most lesions exhibit a polymorphic appearance rather than resolve directly. The inflamed lesions can be divided into superficial and deep types. The superficial lesion includes active papules, less active papules, less active pustules and macules- an important end phase of most inflamed lesions. Deep lesions are either nodules, deep pustules or, the cysts. There is no set pattern of behavior characteristic for each morphogenic type, but there is a tendency to follow one or two routes. Less active papules resolve predominantly via a macule; for them the popular routes are either to become more or less inflamed or pustular. Less active pustules mostly resolve via a macule or become papular. Active papules, active pustules and nodules mainly resolve via a less active lesion and subsequently through a macular phase. The mean life span of less active papules is 5

days and active papules, 9 days. Less active pustules and active pustules survive for 5 and 6 days respectively. Nodules can exist for 4 weeks or longer. However, it is not possible to predict how long a lesion will last, when it is first seen and it varies with individuals.

Scarring of acne: Scarring follows only those lesions which effect the deeper dermis like the nodules and the deep seated pustules. Scarring can also result from more superficial inflamed lesion. It has been observed that some patients are more prone for scarring. In some patients the scars may improve with time because of remodelling of skin with time while in others it may persist for a very long period. There are fundamentally two types of tissue response in acne scarring:

- Increased tissue formation: This gives rise to hypertrophic and keloidal scars
- Loss of tissue: This can give rise to either ice-pick scars, depressed fibrotic scars, superficial and deep soft scars.

Post inflammatory pigmentation is a non-specific feature of inflammation, usually seen in the colored skin. This can be prevented by starting the treatment early. They take up to 18 months to fade.[76]

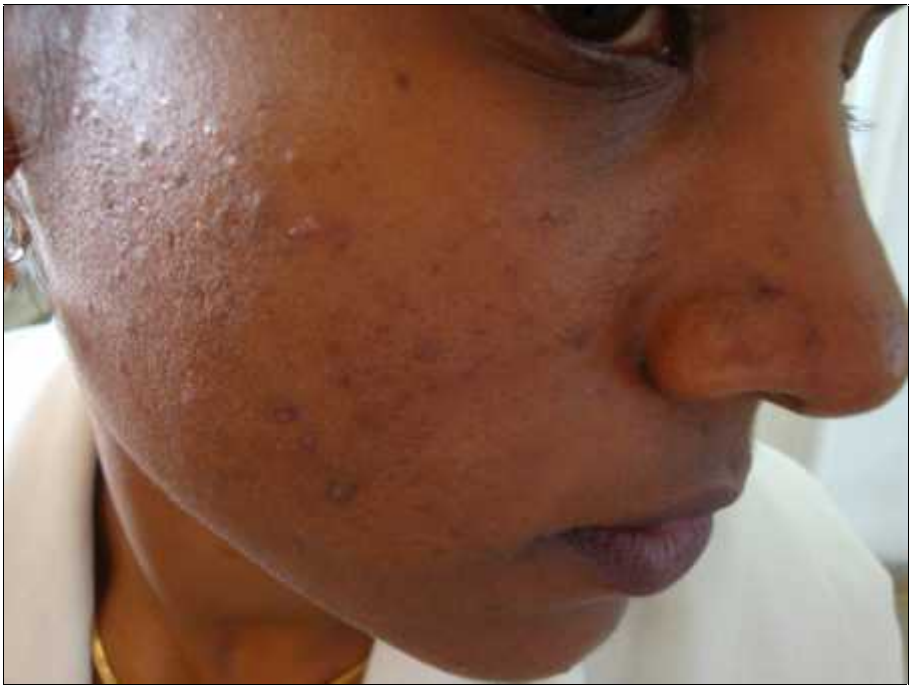


Figure 4 : Comedones & post acne pigmentation

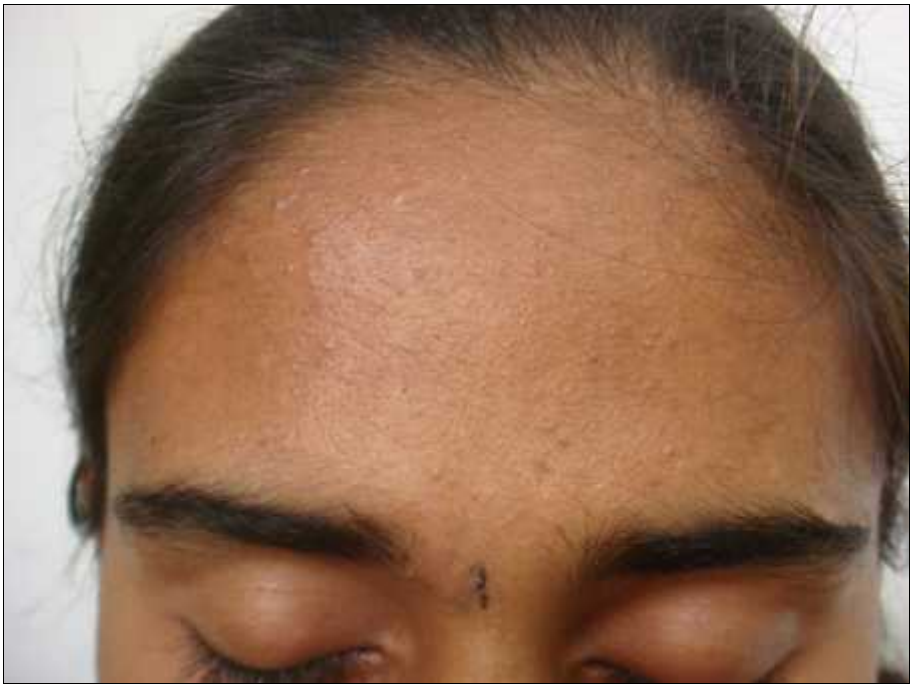


Figure 5 : Comedonal acne

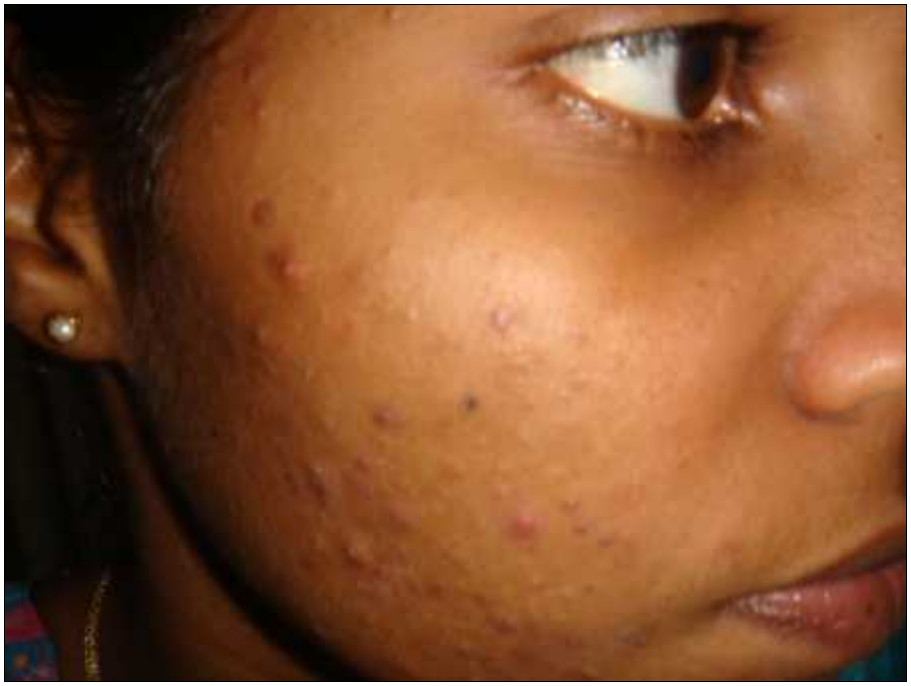


Figure 6 : Papulopustular acne

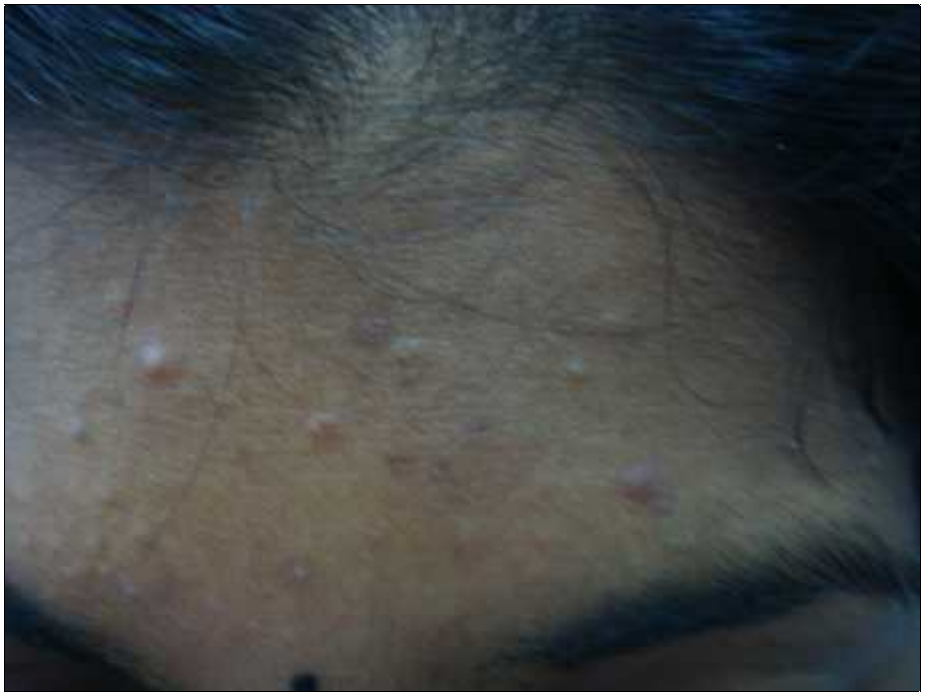


Figure 7 : Papulopustular acne

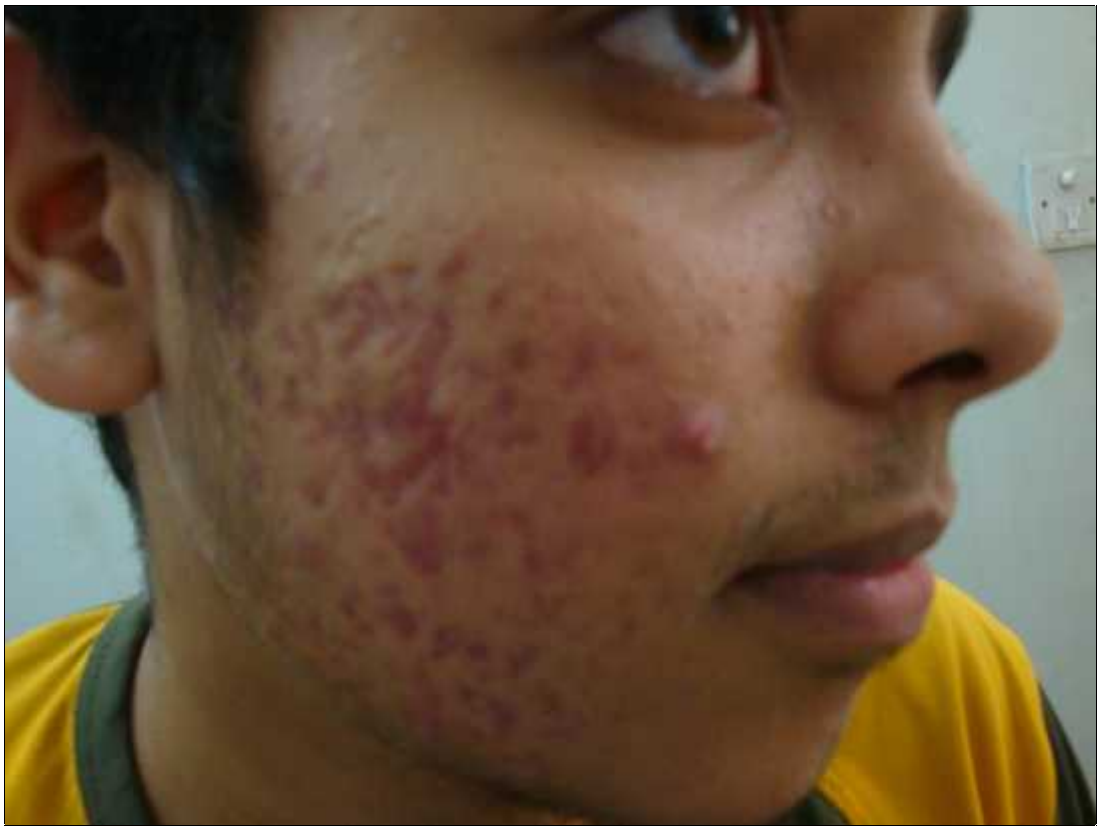


Figure 8 : Erythematous scars and nodule

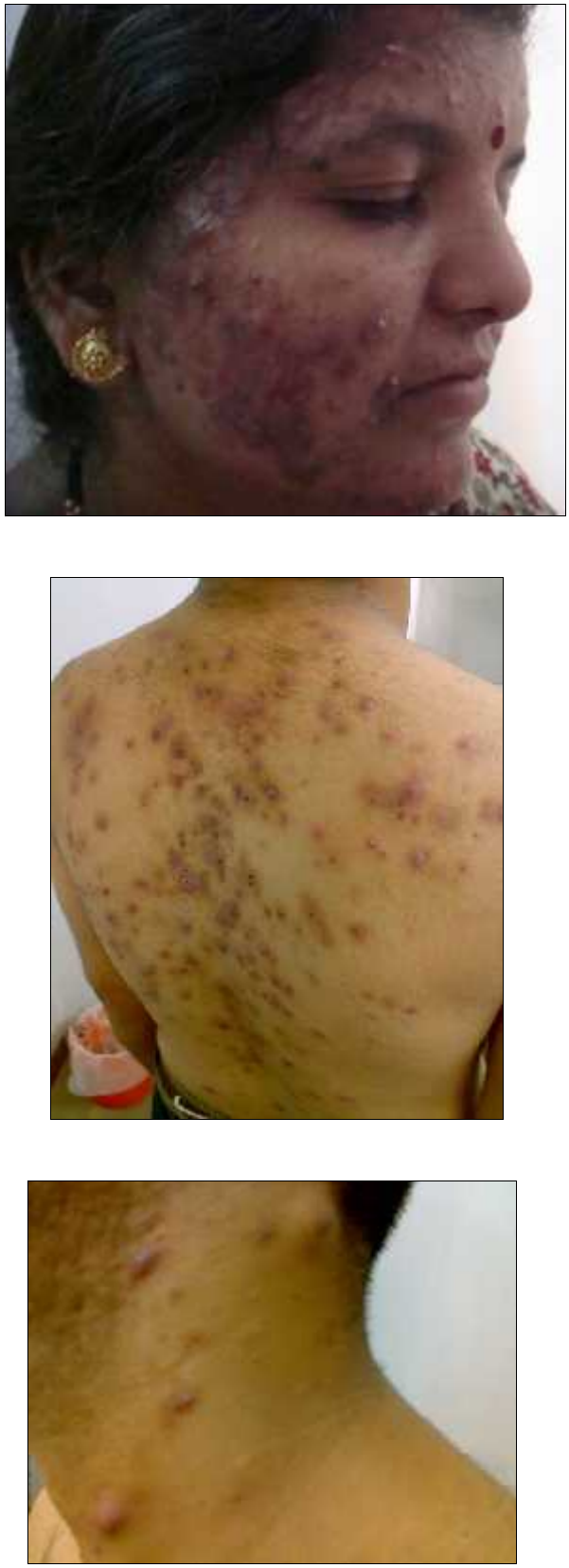


Figure 9 : Nodulo cystic acne

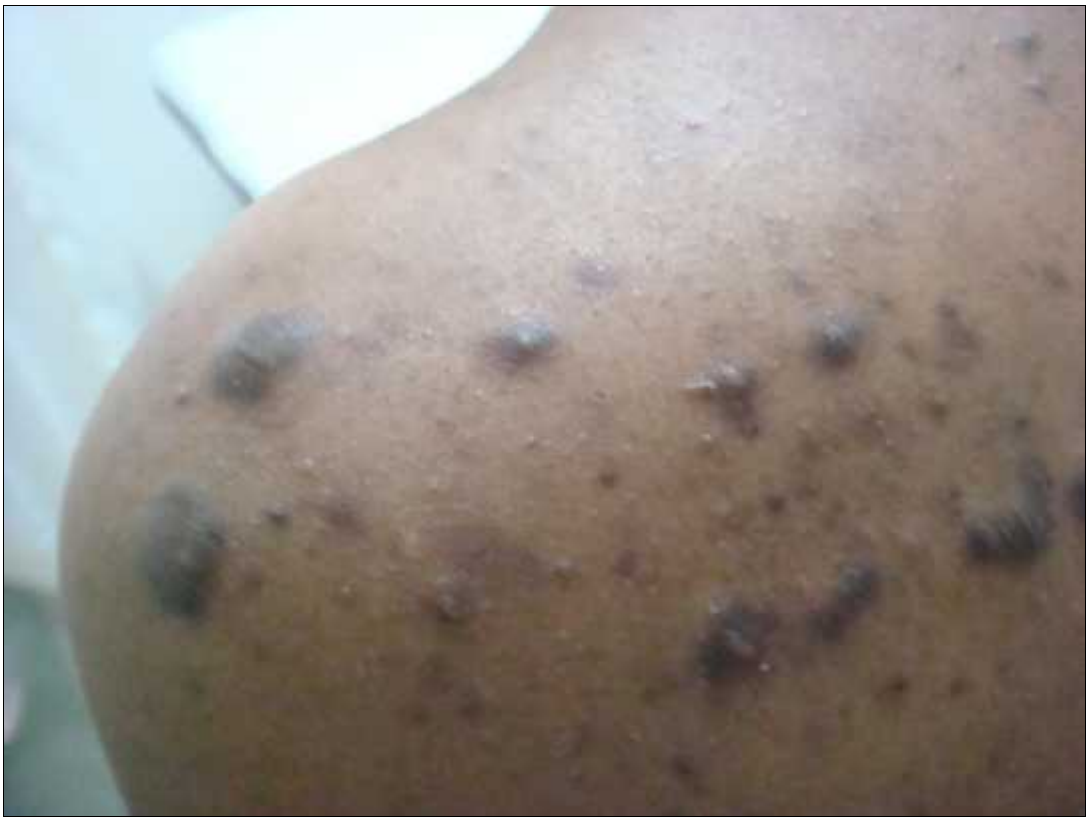


Figure 10 : Keloidal acne

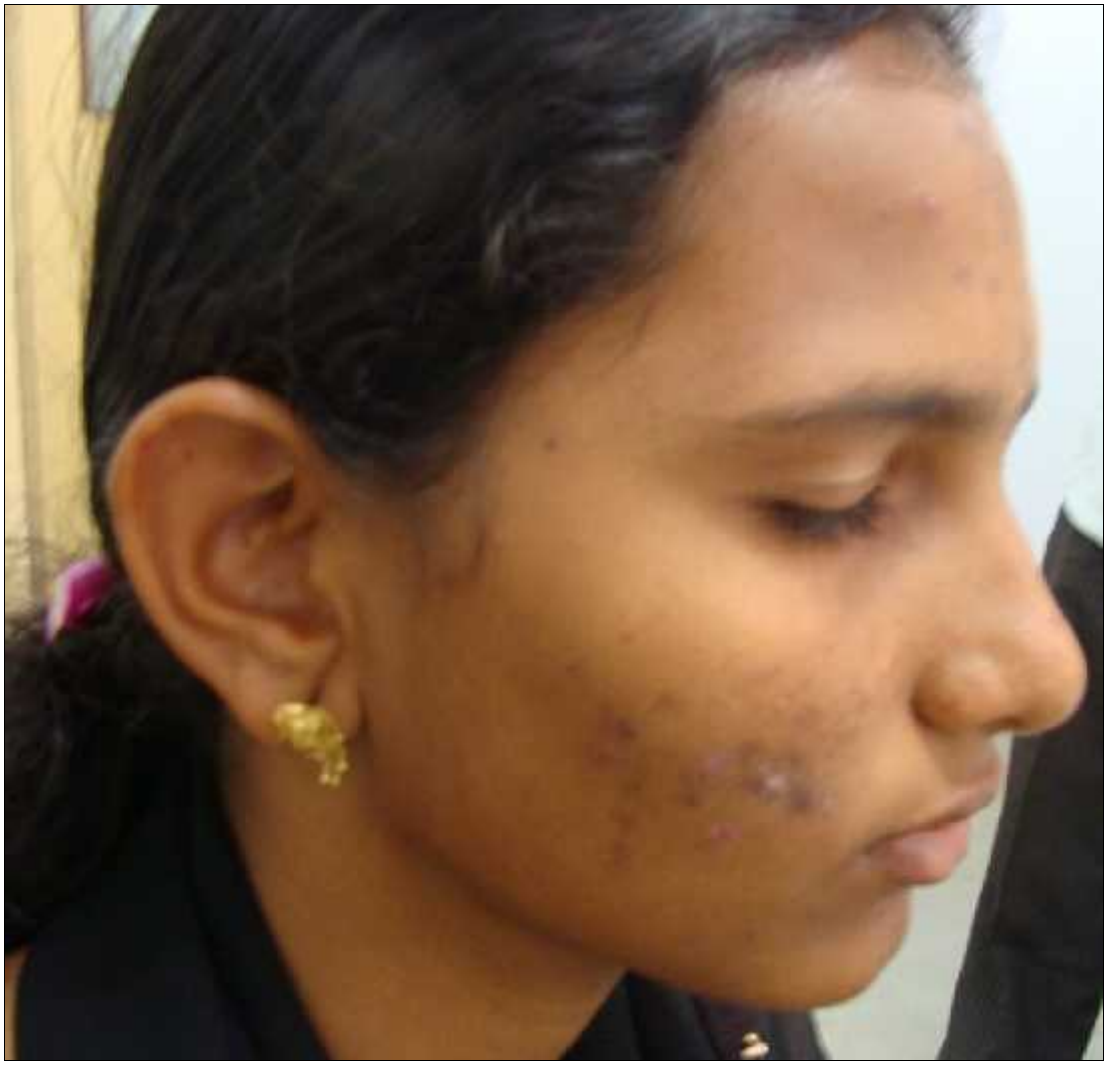


Figure 11 : Acne excoriae

RARE COMPLICATIONS OF ACNE VULGARIS:

Follicular macular atrophy: This is also known as perifollicular elastolysis. It is characterised by soft palpable perfollicular lesions most commonly seen on the trunk. **Pyogenic Granuloma**: This occurs most frequently following Isotretinoin therapy. **Osteoma Cutis**: This occurs due to calcification of the acne scars and can be seen on X-ray.

Solid Facial Oedema: This complication is non responsive to antibiotics, but fortunately it is very rare. Isotretinoin is used for treating this condition.

Hidradenitis Suppurativa and Dissecting Cellulitis of the scalp are commonly associated with Acne Conglobata.

CLASSIFICATION OF ACNE

Many attempts have been made to classify acne on the basis of severity of the disease, but to date, a widely accepted standardized classification does not exist. **Witkowski and Simons** (1966) introduced an evaluation technique where the lesions were counted and the sum used as a score.[43]

Pillsbury (1970) used the presence or absence of deep seated and inflammatory lesions as the basis of devising a four level grading system. **Frank**(1971) recommended a system based on the type of predominant lesion present and a severity numbering system.[43]

Michaelsson (1977) evaluated their respective acne treatment results by counting each type of lesion and multiplying the count with the respective severity index.

A sum of these indices was taken as the severity index.[43]

Cook et al used photography to grade acne on a 0-8 scale. The patients were photographed and their acne scored on grades of 0,2,4 and 8, by comparing it with the reference card. Their definition of grades, to quote, very few pustules or perhaps 3 dozen papules' was very vague.

Allen and **Smith** (1982) extended the photographic technique. They added a palpation criteria to the photographs and improved the acne assessment by giving a grading scale for comedones (0-8). They found their method superior to lesion counting. [43]

Burke and **Cunliff** (1984) reported their assessment technique which is entirely subjective, based on inspection and palpation of the skin. Training is essential for using this technique. It's also called the Leeds technique. The scale resulting from these trials is subdivided into 0.25 units from 0-2, i.e. 0.25, 0.5, 0.75, 1.0, 1.25, 1.5 and l.75. Grades 0.25 - 0.75 represent physiological acne or acne minor. Grades 1.0 and above represents clinical acne or acne major. Above grade 2, the acne is subdivided into 0.5 divisions.[44,45]

The major conclusions drawn at the consensus conference on acne classification in 1990 at Washington were as follows:

- A strictly quantitative definition of acne severity cannot be established because of the variable expression of the disease.

- The clinical diagnosis of severe acne should be based on the presence of any of the following characteristics: Persistent or recurrent inflammatory nodules, extensive papulopustular disease, ongoing scarring, presence of sinuses and purulent discharge from the lesions.

- Additional factors that designate severity are the psychological circumstances, occupational difficulties and inadequate therapeutic responsiveness.

VARIANTS OF ACNE

Disorders manifesting as comedones and manifesting as papulopustular lesions are included in this group.

Neonatal and Infantile acne: Mild acne is present in up to 20% of the newborns. The cause of neonatal acne is not known but appears to be related to stimulation of the neonatal sebaceous glands with maternal and infant androgen, particularly those derived from the hyperactive neonatal adrenal gland.[40] Lesions are usually mild and disappear by 1 to 3 months as the sebaceous glands involute and scarring is absent. Infantile acne is differentiated from neonatal acne by its appearance later in infancy, usually from third to sixth month and by the presence of more numerous lesions. The cause is not known, but it is postulated to be related to precocious secretion of androgens by the gonads. No relation has been seen between acne in pregnancy and development of neonatal acne but family history is commonly present in these patients. It occurs more commonly in male children. In a recent study, it has been found that there is a higher incidence and greater severity of acne in teenage years in patients with a history of infantile acne.[46] But if acne does not subside even after 5 years, adrenal hyperplasia has to be ruled out.

Acne Majorca or Mallorca or Aestivalis. This condition occurs in spring or summer. This condition was attributed to heavy exposure to ultraviolet rays. Histopathologically, cysts were found in the dermis which occasionally ruptured. Sebaceous glands were atrophied.

Drug induced acne: Numerous drugs can give rise to acneiform eruptions. The most common drugs that cause acneiform lesions are;

Corticosteroids, anabolic steroids, ACTH and androgens.

Antitubercular drugs like INH and Rifampicin.

Phenytoin, lithium, disulfiram and thiouracil.

Halogens like Iodides and bromides when ingested can cause acneiform eruptions due to halogen deposition in the skin.

Drug induced acne are clinically characterized by sudden onset, occurrence at any age and at any site, mainly the trunk, monomorphic in presentation and lack true comedones.[33]

Acne mechanica or Frictional acne: This occurs secondary to chronic friction either due to headbands worn by hippies or in violinists on neck (fiddler's neck).

Acne detergicans: This type of acne is seen in people who wash their faces frequently, due to the comedogenic effect of certain types of soaps.

Occupational Acne: This consists, of acneiform eruptions caused by various industrial compounds. They may be described as chloracne and as chemical acne.

McDonalds Acne : It is the acne found in teenage workers in McDonald's Restaurant. It is due to repeated exposure to oil vapour during cooking.[79]

Chloracne is caused by aromatic chlorinated hydrocarbons, used in insulators and insecticides. Contact with heavy oils, cutting oils, waxes and coal tar derivatives give rise to *chemical acne.* These are also called *oil acne.* They are distributed on the extremities and are non-inflammatory in nature. Vegetable oils used in cosmetics *(cosmetic acne)* and in cheap pomades (*Pomade acne)* can also give rise to acneiform eruptions.[33] Cosmetics containing lanolin, petrolatum, lauryl alcohol and oleic acid are comedogenic.[12]

Acne Excoriee: This is seen mainly in females with acne, who might be having mild acne but aggravate it by scratching or playing with it. There is always an underlying psychic stress or a personality disorder. These patients require psychotherapy together with the acne treatment.[33]

Severe Acne variant:

Acne Conglobata: This is a highly inflammatory and chronic disease seen commonly in males. It is clinically characterised by comedones, papules and pustules but mainly cysts and burrowing intercommunicating abscesses with irregular scarring. It is commonly associated with Hidradenitis Suppurativa. It has a very chronic course and is very difficult to treat.

Pyoderma Faciale: This refers to exacerbated purulent acne of the face. There is a sudden development of highly inflammatory acne lesions in patients with mild acne. It is usually seen in women aged 20-40 years.

Acne Fulminans: Patients are predominantly males. They develop extensive inflammatory lesions, especially over the trunk with fever, malaise, polyarthritis and weight loss. It is caused due to an immunological reaction to Propionibacterium acnes. The treatment of choice is Prednisolone 40mg /day tapered over a month.[12,33]

DIFFERENTIAL DIAGNOSIS

Rosacea: This usually occurs in an older age group (30-50 years) and lacks comedones, nodules, cysts and scarring. Occasionally, patients may have both Acne and Rosacea. Usually the muzzle area of the face is involved characterised by erythema and telangiectasia. Ocular involvement and photosensitivity is also known in Rosacea.

Milia: These are commonly confused with whiteheads. But milia usually occur in the infraorbital area and are whiter.

Gram negative folliculitis: This occurs as a complication of acne therapy with long term antibiotics. It is usually caused by Proteus group of anaerobic bacteria and the condition is very difficult to treat.

Perioral dermatitis: It is a distinct clinical entity and occurs more frequently in females. It is characterised by itchy papules and plaques around the mouth, follows the use of flourinated topical steroids for a long time.

Pityrosporum folliculitis: These are mildly itchy lesions seen on the upper trunk commonly. They consist of papules and pustules on an erythematous base. Pityrosporum ovale is always found in the follicles. It shows good response to topical imidazoles.

Molluscum contagiosum: It is viral infection caused by pox group of virus. When extensive, it can be easily mistaken for closed comedones.

Folliculitis: Both Candidal and Staphylococcal folliculitis can be mistaken for acne lesions. Material cultured from the swab will give a clue to the diagnosis.

Acne Agminata: This condition is characterised by brownish papules especially in the periorbital area. They heal spontaneously in one to two years with scarring

Others: Plane warts, pseudo folliculitis barbae, hyperalimentation acne due to zinc deficiency, tuberous sclerosis, acne varioliformis, acneiform eruptions of Behcet's disease and dental sinus.[76]

THERAPY FOR ACNE VULGARIS

Topical therapy:

- **Cleansing:** The simple hygienic measure of regular washing of face with soap and water has been recommended in order to remove keratinous plug and also in reducing the associated seborrhoea. Many persons also believe that acne is related to poor hygiene. Yet there is no evidence that lack of washing is associated with acne or that frequent washing improves the condition. Too vigorous cleansing and scrubbing can aggravate the inflammatory phase of acne. Normal washing does not affect the follicular reservoir of lipids—the site of acne pathology.[21]

- **Exfoliants:** Elemental sulfur is the oldest therapy for acne and is still used. It is keratolytic, anti-bacterial and anti-oxidant. But it is argued that sulfur has a dual paradoxical role in acne. It hastens the resolution of visible papulopustules while insidiously promoting the formation of new comedones from which inflammatory lesions spring, thus establishing a vicious cycle.[48] Thus, it is not so commonly used nowadays.

Resorcinol is another exfoliant which like sulfur, acts by producing irritation and consequent peeling and exfoliation. But these are not effective for deeply rooted comedones.

Salicylic acid in propylene glycol (5%) is useful as a keratolytic agent, but now replaced by better agents like Benzoyl peroxide.

Benzoyl Peroxide is a bactericidal agent. It acts by releasing free oxygen radicals which oxidize the bacterial proteins of the sebaceous gland. It is effective in reducing the comedones. It is available in concentrations of 2.5, 5 and 10% in a gel formulation. Contact sensitivity is observed in 1-3 % of patients.[48] It bleaches clothes and hair.

Topical antibiotics: These antibiotics act by bacteriostatic effect and by reducing inflammation.

Clindamycin phosphate is available in 1% concentration in a gel form. It reduces both ductal and surface counts of P. acnes. Since there have been a few reports of Pseudomembranous colitis in patients using it, they should be warned to stop the therapy as soon as intestinal symptoms occur.

Erythromycin is very effective and non sensitizing. It acts mainly by reducing free fatty acid content of the follicular duct. It is available as 1.5% and 2% solution, 2% ointment and in combination with Benzoyl peroxide gel.[48]

Tetracycline hydrochloride is as effective as Erythromycin but causes temporary yellow staining of the skin. Its efficacy is increased when it is given with an initial course of oral tetracycline.

Topical retinoids:

a) Inhibit the formation of and reduce the number of microcomedones (precursor lesions).

b) Reduce mature comedones. Reduce inflammatory lesions

c) Promote normal desquamation of follicular epithelium.

d) Some may be anti-inflammatory

e) Likely to enhance penetration of other drugs

f) Likely to maintain remission of acne by inhibiting microcomedo formation, thus preventing new lesions

- **Retinoic acid (Tretinoin):** It is a synthetic vitamin A preparation for topical use. It is available in gel and cream form in the concentration of 0.025%, 0.05% and 0.1 %. It is the most effective comedolytic agent. It inhibits the formation of comedones and helps in expelling the existing ones by increasing the epidermal cell turn over and decreasing the cohesiveness of the horny cells. It also decreases the normal cell layers of the stratum corneum and thus helps in the penetration of other topical agents. It should be started with a lower concentration in fair complexioned patients because of its irritant properties. It causes erythema and drying. It also has a photosensitizing property and thus night application is advised.

Adapalene is a third generation retinoid available as cream, gel, and solution in 0.1% concentration. More recently, adapalene has demonstrated equivalent efficacy to tretinoin microsphere gel 0.1% and tretinoin cream 0.05%, as well as greater tolerability than tretinoin cream 0.025%.

Tazarotene, available as a gel or cream in 0.05% or 0.1% concentrations

- **Azelaic acid**: It is a dicarboxylic acid derivative derived from Pityrosporum ovale. It suppresses P.acnes and reduces keratohyalin granules and is similar in efficacy to benzoyl peroxide and retinoic acid. It was initially used for hyperpigmentation that followed the acne lesions.[12]

- **Zinc sulfate** : 2% zinc sulfate solution has been tried in acne with little success.[49] In another study, combination of 4% erythromycin lotion and 1.2% zinc sulfate reduced sebum output significantly.
- **Metronidazole gel:** 2% Metronidazole gel has been found to be better than 5%benzylperoxide gel alone in a clinical trial.[50]
- **Aluminium chloride hexahydrate:** It is antiperspirant and antibacterial agent. It may be useful in cases of acne in which sweating is prominent or appears to be aggravating the disease.[48]

Dapsone gel 5%: It appears to be an effective, safe, and well-tolerated treatment for acne vulgaris, with a rapid onset of action. A potential mechanism of action of dapsone in acne could be the direct inhibition of leukocyte trafficking and the generation by leukocytes of chemical mediators of inflammation. However, it is also possible that, as a sulfone with structural similarities to trimethoprimsulfamethoxazole and other sulfonamides, topical dapsone may act indirectly in acne by altering the levels and/or activity of propionibacteria located in the upper third of the follicles. Local signs and symptoms of acne and cutaneousirritation such as skin dryness and erythema may develop.[66]

Systemic Therapy:

This is indicated in patients with grade 2, 3 and 4acne. There are three main groups of oral therapy-antibiotics, retinoids and Hormones. Others are Dapsone, Zinc sulfate and Clofazamine.

Antibiotics: These suppress the growth of normal cutaneous flora primarily P.acnes. As the bacteria are decreased, even the free fatty acid level is slowly diminished. They also interfere with the cellular inflammatory functions and directly inhibit the

extracellular lipases responsible for generation of inflammatory compounds. Antibiotics can be evaluated only after 6-8 weeks.

Tetracycline: It is less expensive, has few side effects and is best tolerated for long periods of time. Tetracycline is effective in low doses because high concentrations are achieved within sebaceous glands. Initially the therapy is started with 250mgs four times daily and decreased to maintainence dose of 250-500mg/day, once improvement is seen. It should be taken on empty stomach half an hour before food, because food interferes with its absorption.

Side effects: Gastrointestinal irritation, Candidal vaginitis, Gram negative folliculitis and yellowish discoloration of teeth in children below 12 years of age.

Erythromycin: It is used in the dose of 250 mg qid. It is the usual second choice of drug. It is the drug of choice in children below 12 years and pregnant women.

Azithromycin: Azithromycin is one of the antibiotics that has been recently prescribed for treatment of acne which is at least as effective as doxycycline and minocycline.

There are several regimens of oral azithromycin in acne treatment:

According to Kapida *et al* - 500 mg orally thrice weekly whereas the recommended dose of Parsad *et al* is 500 mg once a day for four days per month

Recommended dose by Fernandez-Obregon is as 250 mg orally three times a week.

All of them are given over a 12-week period.[51]

Minocycline: This is used in patients who are unresponsive to other antibiotics. It is a lipid soluble drug and penetrates the sebaceous follicle more effectively. Therapy is

started with 50mg/day and slowly increased to 100 mg/day. It has better patient compliance because of the single dose regimen. It can cause hyperpigmentation. It has lowest risk for bacterial resistance over time.[52]

Doxycycline is equally effective in doses of 100 mg/day, but photosensitivity is greater with this drug.

Trimethoprim-sulfamethoxazole: It has also shown a fatty acid decreasing capacity. Usually given in the dose of 400-80mg/day or two double strength tablets per day.

Oral Zinc therapy: A beneficial effect has been noted with oral zinc sulfate 600 mg daily in case of severe acne. It is taken after meals to minimize the gastrointestinal sideeffects. Non-steroidal anti-inflammatory drugs, such as ibuprofen and benoxaprofen have shown to reduce inflammatory lesions.

Dapsone: This has been tried with varying success. It is less effective than Isotretinoin**.** It is given in the dose of 50mg per day for 6 months. It is used for nodulocystic acne,can be used as alternative to antibiotics in pustular acne in poor patients.[52]

Clofazamine: Has been seen to be effective in Acne fulminans but should not be used as the first line of treatment. It is used in the dose of 200mg three times a day.

Oral Vitamin A: This has been advocated, but failed in other controlled studies. It is less effective than tetracycline and erythromycin.[48]

Hormonal therapy: This is useful only in females because in males it leads to feminization. Various hormonal regimens exist for reducing the sebaceous production. Hormonal therapy is an excellent choice for female patients with acne who have SAHA syndrome, polycystic ovarian syndrome (PCOS), HAIR-AN

syndrome (hyperandrogenism, insulin resistance, acanthosis nigricans) or cutaneous hyperandrogenism (CH), late onset adult acne, in refractory acne, nodulocystic acne where isotretinoin is contraindicated.[52]

The most popular combination is ethinylestradiol 35 µg plus cyproterone acetate 2 mg (EE-CPA). Besides decreasing ovarian production of androgens, EE-CPA also increases SHBG which, in turn, binds free circulating testosterone.

A newer combination oral contraceptive containing EE 20 µg and drospirenone 3 mg is available and is indicated in patients intolerant to EE-CPA.

Hormonal therapy is contraindicated in patients with personal or family history of thromboembolism, and should be used with caution and with greater justification in cases with family history of breast or uterine malignancies, in mature adults, in the presence of depression, hypertension, or other internal medical problems.[52]

Side effects of hormonal therapy : Menstrual abnormality, occasional fluid retention and melasma.

Antiandrogens like *Cyproterone acetate:* It is given as 50-100 mg for first ten days of the EE-CPA cycle for 5-10 cycles.

Spironolactone (100-200 mgs) for 6 months is of considerable benefit. It acts by reducing the sebum excretion rate.

Low dose Glucocorticoids leads to suppression of adrenal androgens and thus lead to reduction in sebaceous secretion. In severe forms of acne - nodulocystic acne, acne conglobata, and acne fulminans, and in acne flares evoked by other systemic therapies.

Intralesional steroids: triamcinolone (ILT) 2.5-5 mg/ml.

Ketoconazole: It has been tried in a single daily dose of 200 mg. A statistically significant decrease in the sebum excretion rate has been seen. It acts through its anti-androgen effect.

Isotretinoin: This drug has revolutionized the life of patients with severe acne. It is given in an initial dose of 0.5 to 1 mg/kg/day, It is usually given for a period of 4-5 months. Its effect continues for upto 2months of stopping drug. The most important feature of Isotretinoin is relative lack of relapse after the drug has been stopped. **Norris** and **Cunliff** have reported that younger patients, having a short duration disease and those having truncal acne relapse earlier.

Isotretinoin has a sebostatic effect. It acts by reducing the size of the sebaceous glands and sebum by 90%. It has potent comedolytic action, by normalization of ductal hypercornication and loss of cell to cell adhesion. It does not directly affect P. acne but suppresses it by reducing its nutrient supply and by reducing the size of the follicular space where P. acne grows.

It acts as anti-inflammatory by decreasing chemotaxis of polymorphnuclear leucocytes and monocytes.

It is indicated in following-severe acne-nodulocystic acne, difficult acne(acne conglobata, acne corporis, adult acne, androgenic acne, severe infantile acne, acne fulminans, and SAPHO syndrome)and refractory acne(less than 50% improvement with conventional therapy consisting of oral antibiotics and topical combinations) mild to moderate acne where scarring is imminent. Cutaneous side effects: Cheilitis, Facial erythema, irritant dermatitis, photosensitivity, xerosis, other-hairloss, dry nose and eyes. Most of these are reversible on discontinuation of the drug.

Systemic side effects: teratogenicity, arthralgia, myalgia, vertebral hyperostoses and Benign Intracranial hypertension. Depression and suicidal ideation are controversial.[52]

Adjunctive therapy:

Chemical peeling.

Acne surgery: Comedo expression.

Draining of cysts and abscesses.

Intralesional steroids.

Cryoslush.

Laser therapy for acne scars.

Cosmetic camouflage.

Iontophoresis.

Chemical peeling:

Salicylic acid peeling: Salicylic acid is a beta-hydroxy acid. It is a hydroxyl derivative of benzoic acid and represents a carboxylic acid attached to an aromatic alcohol, phenol.

Salicylic acid is an excellent keratolytic agent. It is thought to function through solubilization of intercellular cement, thereby reducing corneocyte adhesion. Because of its lipophilic nature, salicylic acid has a strong comedolytic effect. Salicylic acid affects the arachidonic cascade and thus exhibits anti-inflammatory capabilities. It also helps in controlling seborrhea. A history of allergy to aspirin, and pregnancy and lactation are contraindications.

Side effects : Transient hyperpigmentation and superficial crusting may be seen in areas of inflammatory acne. Patients with Fitzpatrick skin type III may experience darkening during desquamation due to increased melanin sloughing. Minor side effects include superficial crusting, edema and transient purpura in the lower eyelid areas, hypopigmentation, transient dryness and hyperpigmentation, which resolves quickly.[67]

Glycolic acid peeling: It is a alpha-hydroxy acid. It is mainly used to treat post-acne pigmentation. It is a superficial peeling agent. Erythema and exfoliation are side effects. In dark skinned individual there is risk of post inflammatory hyperpigmentation.

Acne scar classification: Broadly, acne scars are classified as atrophic and hypertrophic. The European acne group (ECCA) has renamed the atrophic acne scars as V-shaped (ice-pick), U-shaped (boxcar), and W-shaped (rolling).

Treatment of acne scars:

As atrophic scars are the most common and face is the priority area, they are directed toward atrophic scars.

Surgical techniques: Punch excision of ice-pick scars is easy and gives good early result; occasionally there is secondary widening. Punch autograft is used when treating deep ice-pick scars. The donor site is usually postauricular skin. Subcision involves subcutaneous sectioning of dermal adhesions with a sharp needle (1.5 inch, 18 Gauge, Nokor). It is often associated with neocollagenosis, and the technique is good for V, U, and W scars.[52]

Resurfacing techniques: These include TCA peeling, phenol peeling, microdermabrasion, laser abrasion, selective thermolysis with Fraxel laser, and

resurfacing by radiofrequency and electrosurgery. The objective is to restore skin contour by inducing neocollagenosis. Resurfacing is indicated in U and W scars. The main complication is erythema which persists for weeks. There is also risk of pigmentation. Spot TCA peeling is a good technique for V and deep U scars. A sharp stick (toothpick) soaked in 62% or 100% TCA is brought in contact with the target and the contact is maintained till whitening appears. It is a painful procedure and multiple sessions are required. In a study by Lee et al .62% TCA gave good results in 82% versus 94% with 100% TCA. [52]

Microdermabrasion: This involves planning of the skin by mechanized means utilizing the projection of micromarbles consisting of aluminum oxide on scars. Six to seven sessions, at two week intervals are needed. In one session, twenty passes are made on each area until superficial bleeding appears. Six to seven session microdermabrasion has low efficacy and may be useful in superficial U scars.[54] Chemabrasion is when microdermabrasion is combined with a peeling agent.

Lasers: Intense Pulse Light (IPL) acts by heating the dermis and stimulating neocollagenosis. It has weak activity and may be helpful in red, hypertrophic scars. Light-Emitting Diode (LED) does not warm but acts by photomodulation. It is a safe and painless procedure but the efficacy is low. It is being used for superficial U scars, erythema (acne macules), and pigmentation. Ablative laser resurfacing, although effective, is associated with excessive tissue reaction as erythema and edema, and complications such as pigmentation and scarring. It is less suited for skin types V-VI. Fractional photothermolysis, a new concept, using 1,550-nm erbium-doped fiber laser (Fraxel®) appears to be very promising. It creates microscopic thermal wounds to achieve skin rejuvenation without significant side effects. In a study from USA, 53 patients (skin types I-V) with mild to moderate atrophic facial scars were treated with

three treatment sessions at monthly intervals. Clinical improvement averaged 51-75% in nearly 90% of patients. Clinical response rates were independent of age, gender, or skin type. Side effects included transient erythema and edema in most patients, but no dyspigmentation, ulceration, or scarring. It was concluded that atrophic scars can be effectively and safely reduced with 1,550-nm erbium-doped fiber laser.[52]

585 om Flashlamp-Pumped Pulsed Dye Laser was used for treatment of hypertrophic facial scar.

Fillers: The aim is to lift the depression caused by scars, by injecting a filler underneath. There are several options. Resorbable filler such as hyaluronic acid is a good option. It lasts for 6-12 months. It is expensive but safe. It is indicated for scars with gentle slopes and no sclerosis. Nonresorbable fillers carry the risk of granuloma formation.

Iontophoresis has been tried for atrophic acne scars. Its main advantage is its non-invasiveness.[53] Recently lasers have been successfully used in the treatment of acne scars.

MATERIALS AND METHODS

Totally 23242 patients attended the outpatient department of Skin, STD and Leprosy and KLE Hospital and Research Centre between 1st December 2008 and 30th November 2009.

Among these 70 cases were selected for the present study according to formula sample size = pq/d^2 [p-prevalence=85%, q = (100-p), d(error) = 9% of p]. Only patients who had not taken any zinc therapy were selected for study. A detailed history was taken from each patient regarding his/her age, sex and occupation. An elaborate note was made about the age of onset, treatment, seasonal variation, cosmetics usage, relation to food, manual picking, and diet.

Patients were also asked about history of acne in the family. Each patient was examined thoroughly and a note was made of the distribution of lesions, type of lesions and associated skin and systemic diseases.

The acne lesions in each patient were graded according to the grading method described by Tutakne and Chari.

Fasting venous blood was collected from each patient. The blood was centrifuged at 2000 rpm for 15 minutes and the serum was collected in a plastic container with an air tight cap, labelled. Glass containers were deliberately avoided to prevent zinc contamination from glass.

The serum samples were analysed 'for zinc levels at the KLES HOSPITAL .*Serum immunoturbidometry method* was the method used for estimation of serum zinc levels. This is one of standard method of estimation of serum zinc levels.

Figure 12 : Zinc Kit

Figure 13 : Photometer

OBSERVATIONS AND RESULTS

Out of the total 23242 patients who attended the Out Patient Department during the study period, 1158cases of acne vulgaris were diagnosed. The incidence of acne vulgaris amounted to 5%. Among these, 70 cases were selected for the present study using formula pq/d^2

Table 1 : Age Incidence

Age in Years	No. of Cases	Percentage
11 - 15	4	5.714%
16 - 20	33	47.142%
21 - 25	28	40%
26 - 30	4	5.714%
31 - 35	1	1.428%

Maximum prevalence was seen in the 16-20 years age group (47.14%). The 31-35 years age groups had an incidence of 1.428% respectively. The oldest patient was of 32 years and the youngest was 12 years old.

Graph 1 : Age Incidence

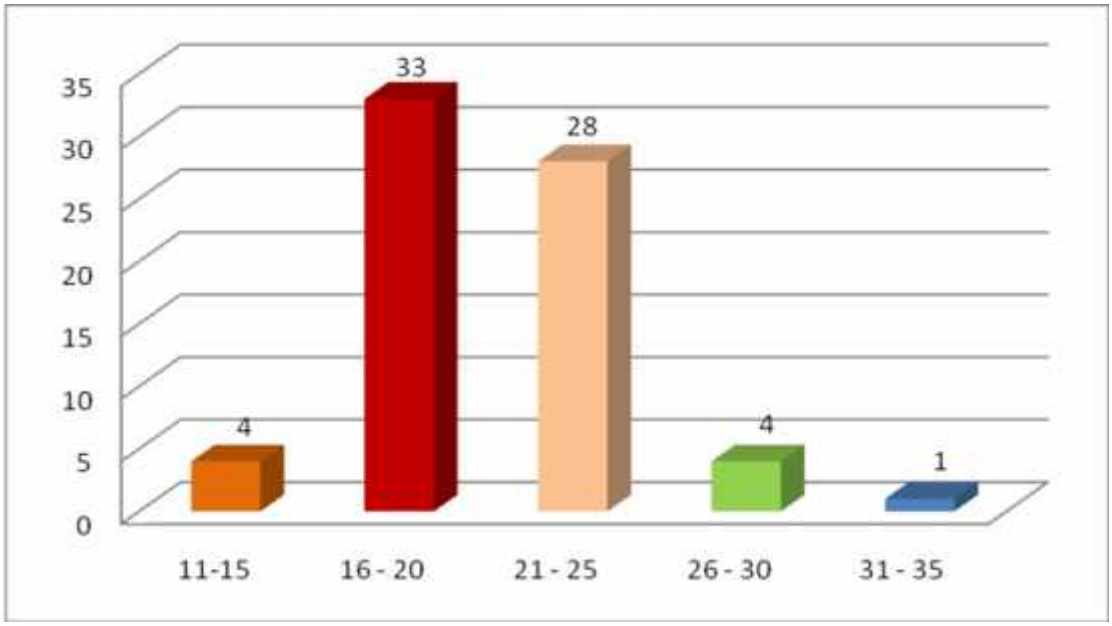


Table 2 : Sex Incidence

Sex	Males	Females
No. of cases	36	34
Percentage	51.43%	48.57%

36 patients out of 70, were males (51.43%) and 24 were females (48.57%). The incidence in males was slightly higher than in females, with a male to female ratio of 1.0588:1.

Graph 2 : Sex Incidence

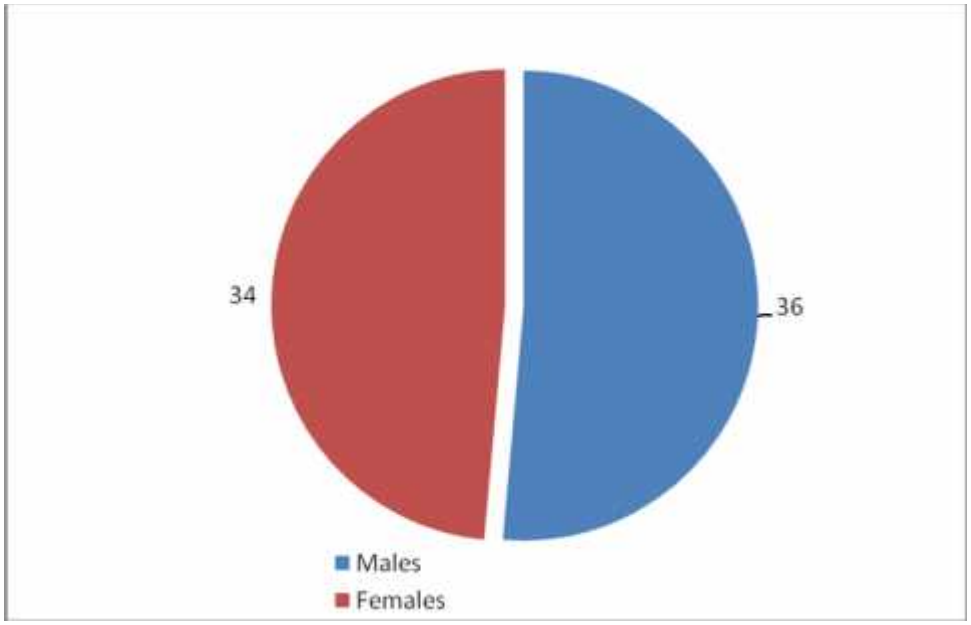


Table 3 : Age and Sex distribution

Age in Years	Males	Females
11-15	2	2
16 - 20	16	17
21 - 25	17	11
26 - 30	1	3
31 - 35	0	1

Maximum cases were seen in the 16-20 years age group in both the sexes. Among these, the male prevalence was 48.48% and the female prevalence was 51.52%. Maximum prevalence in males was seen at 18years and in females at 18 and 19 years. All other age groups had almost equal sex incidence.

Graph 3 : Age and Sex distribution

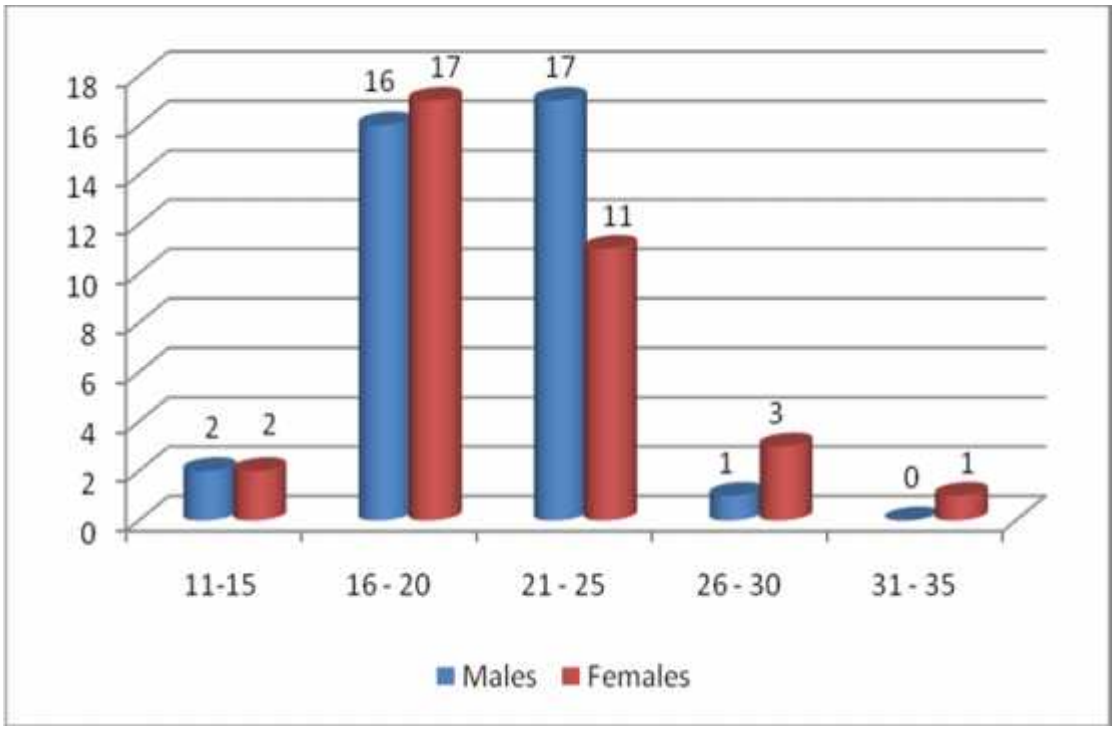


Table 4 : Distribution of lesions

Site	No. of patients	Percentage
Face	39	55.71%
Face, back	7	10%
Face and chest	2	2.85%
Face and arms	1	1.43%
Face, chest and back	10	14.28%
Face, chest and arms	1	1.43%
Face, back and arms	3	4.28%
Face, chest, back and arms	7	10%

39 patients (55.71%) patients had acne lesions exclusively on face. Face was involved in all the 70 patients. 7 patients (10%) had lesions on face and back. 2(2.85%) of them had lesions on face and chest. 1patients (1.43%) had lesions on face and arms.10 patients(14.28%) had lesions on face, chest and back sites.1(1.43%) of them had on face, chest and arms, 3(4.28%) of them had lesions on face, back and arms. Remainder 7(10%) had lesions on all four sites.

Graph 4 : Distribution of lesions

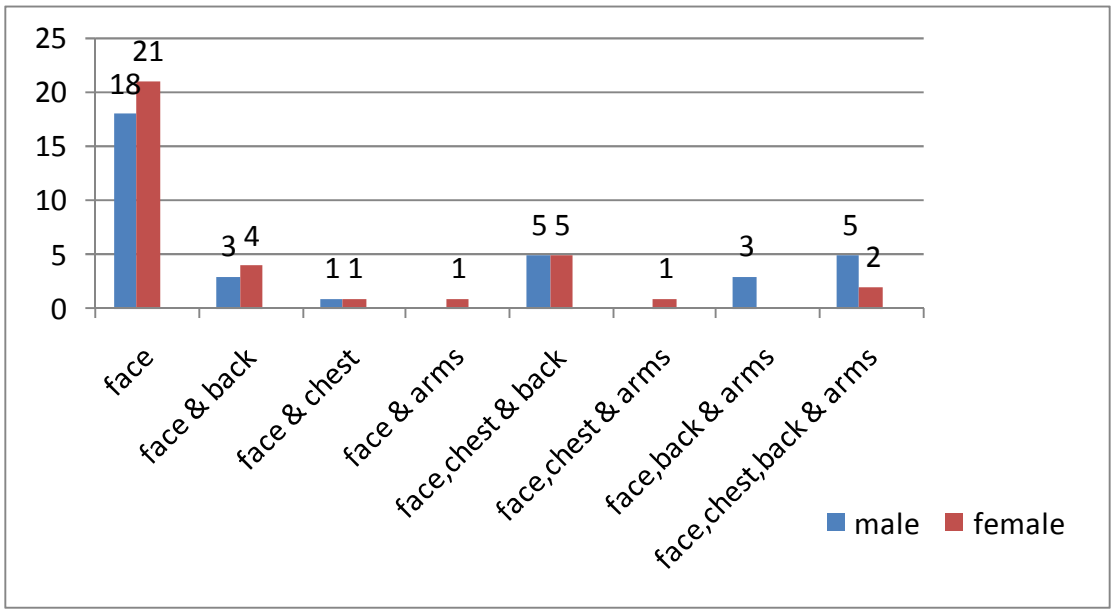


Table 5 : Severity of acne

Grades	Male	Female	%
Grade I	10	8	25.714
Grade II	12	28	57.142
Grade III	9	1	14.28
Grade IV	2	0	2.85

Majority of patients-40 (57.142%) had grade II acne. 10(14.28%) and 2 (2.85%) belonged to grade III and IV respectively.

Graph 5 : Severity of acne

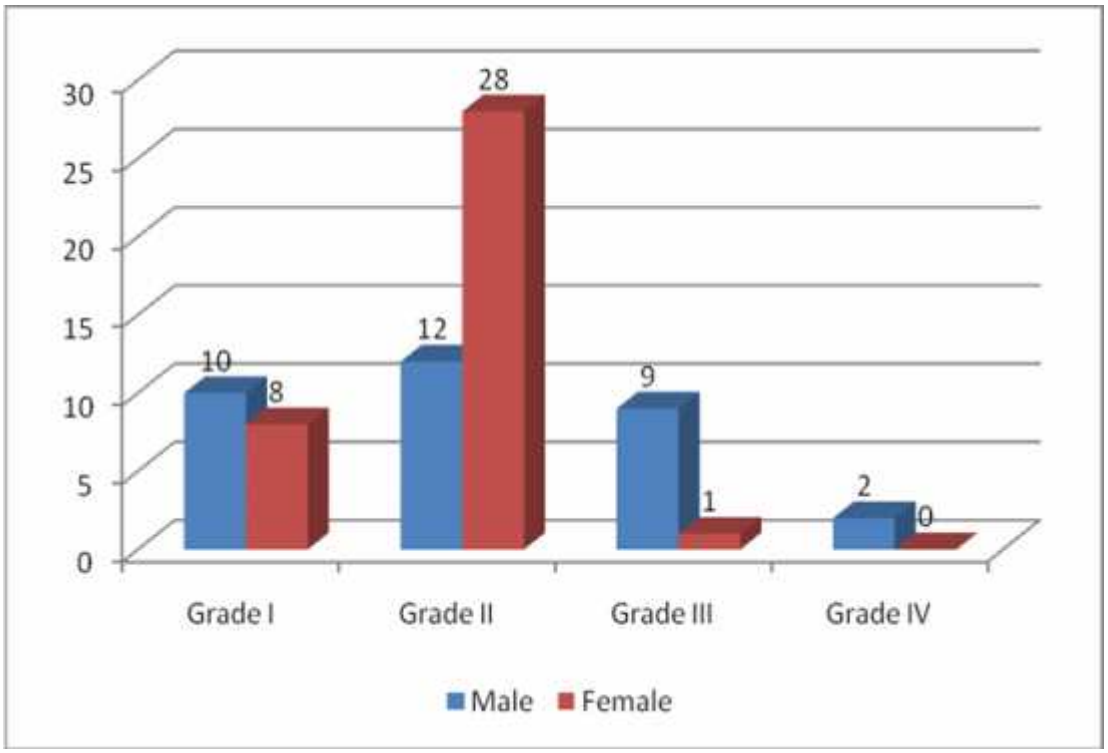


Table 6 : Occupation

Occupation	No. of patients	Percentage
Students	65	92.85
Labourer	1	1.428
House wife	3	4.285
Officer	1	1.428

Most of the patients were students 92.85%(65). Remainder were house wives and 1 officer and 1 labourer.

Graph 6 : Occupation

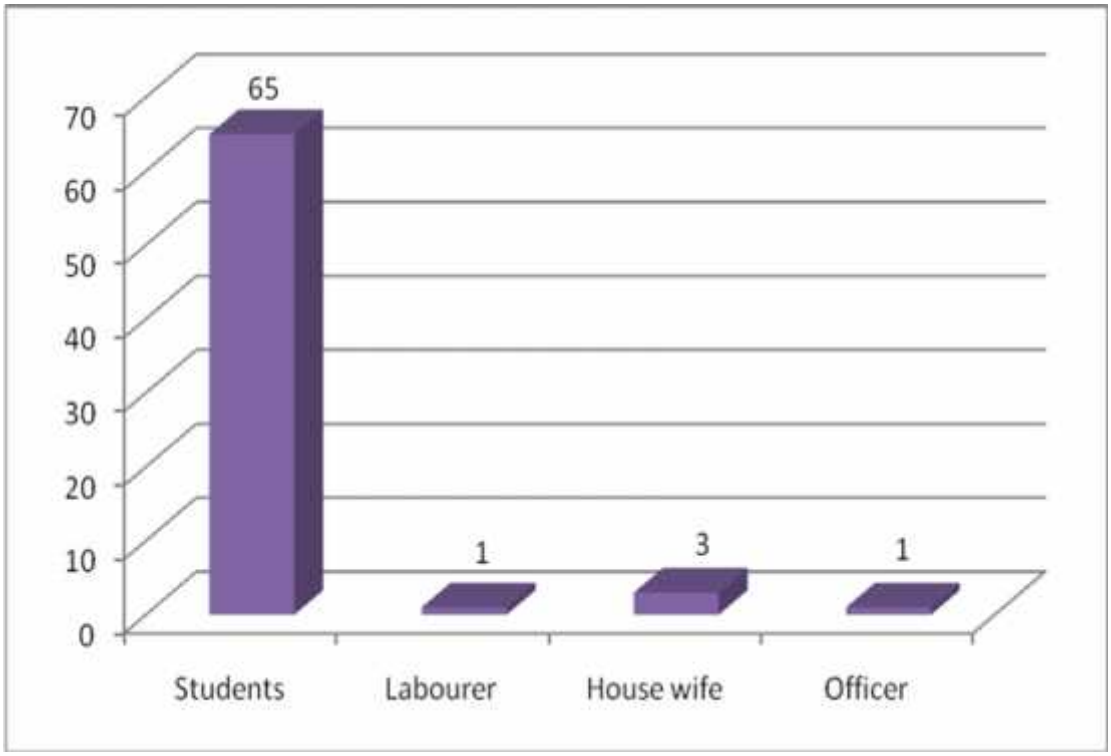
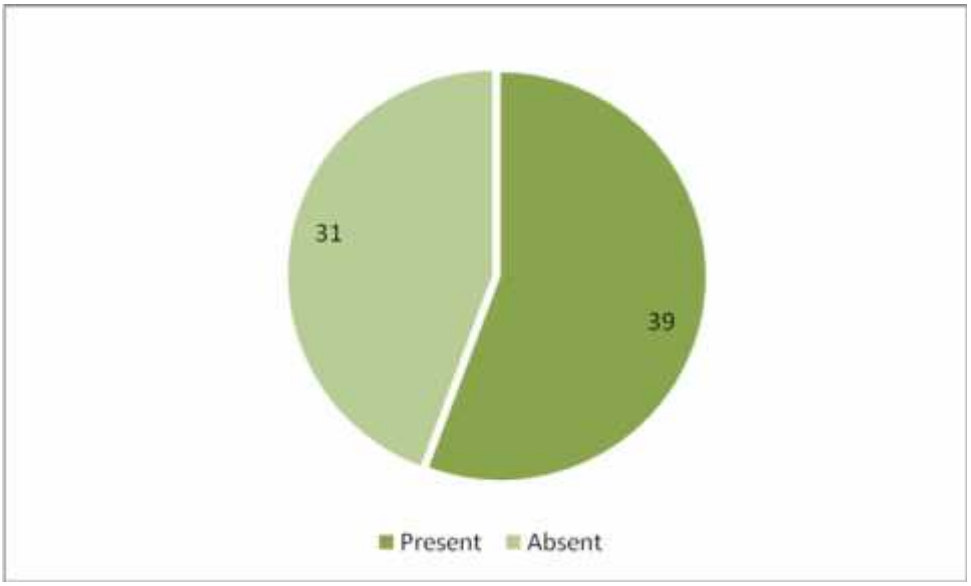


Table 7 : History of manual picking

History	No. of Patients	Percentage
Present	39	55.71
Absent	31	54.29

39 patients gave a history of manual picking and among these, 20 were males and 19 were females.

Graph 7 : History of manual picking



Personal History:

Diet: 30 patients (42.857%) in the present study were purely vegetarians and the rest were non-vegetarians.

None of them had any bowel or bladder disturbances or insomnia.

History of drug intake: One of the female patient was taking growth hormone daily.

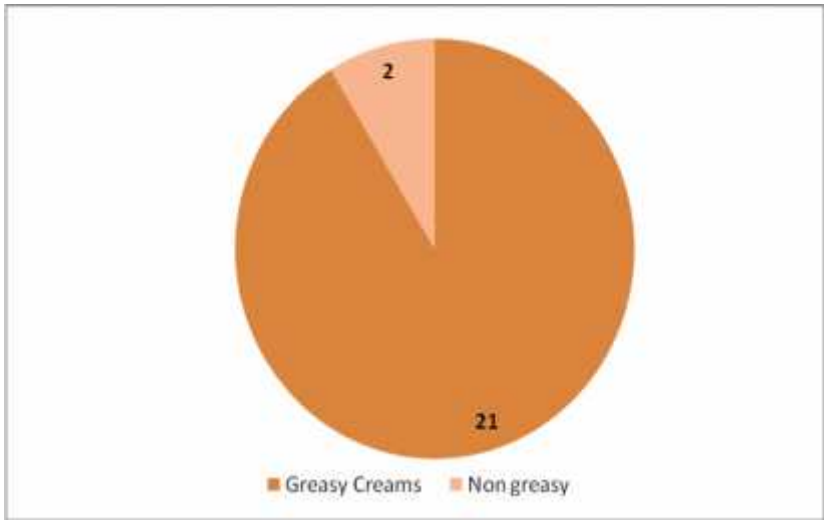
History of premenstrual flare: Among the female patients, 28 gave a positive history of premenstrual flare up of their lesions. The others did not notice any change.

Table 8 : Type of Cosmetics and topical applications used

Type of Application	No. of Patients	Percentage
Greasy Creams	21	30
Non greasy	2	2.857

Majority of the patients (30%) gave a history of using greasy moisturising creams and fair and lovely cream.

Graph 8 : Type of Cosmetics and topical applications used



Skin type:

42 (79.24%) of the patients described their skin type as oily. 7 (13.20%) of the patients called it dry. The rest of them could describe their skin type neither as oily nor as dry.

Table 9 : Family history of acne

History	No. of Patients	Percentage
Present	27	38.57
Absent	43	61.43

27 (38%) of the patients gave a positive family history of acne. At least one parent was affected in 19 (70.37%) of these cases and a positive history in the siblings was present in 8 (29.73%) of the cases.

Graph 9 : Family history of acne

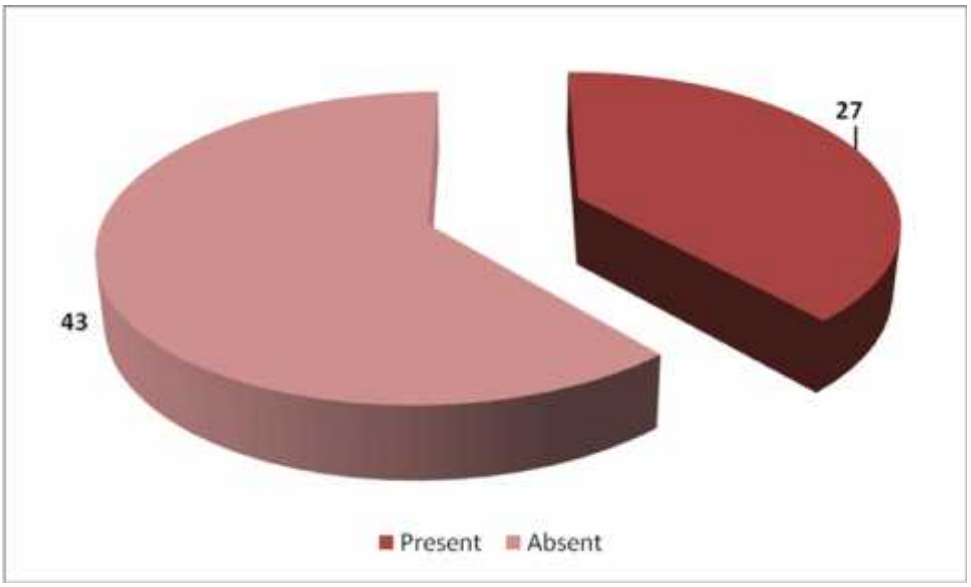


Table 10 : Associated skin diseases

Skin Disease		No. of Patients
Telangiectasia		--
Milia		--
Hirsutism		--
Hair changes		1 with canities and telogen effluvium
Nail changes		
seborrhea		54
Perioral lesions		3
Other skin disorders-	Tinea versicolor	2
	Vitiligo and PIH	1
	Pyoderma	2

Systemic diseases:

None of the patients had any systemic diseases, except for one patient who had Upper respiratory tract infection.

Laboratory Investigation:

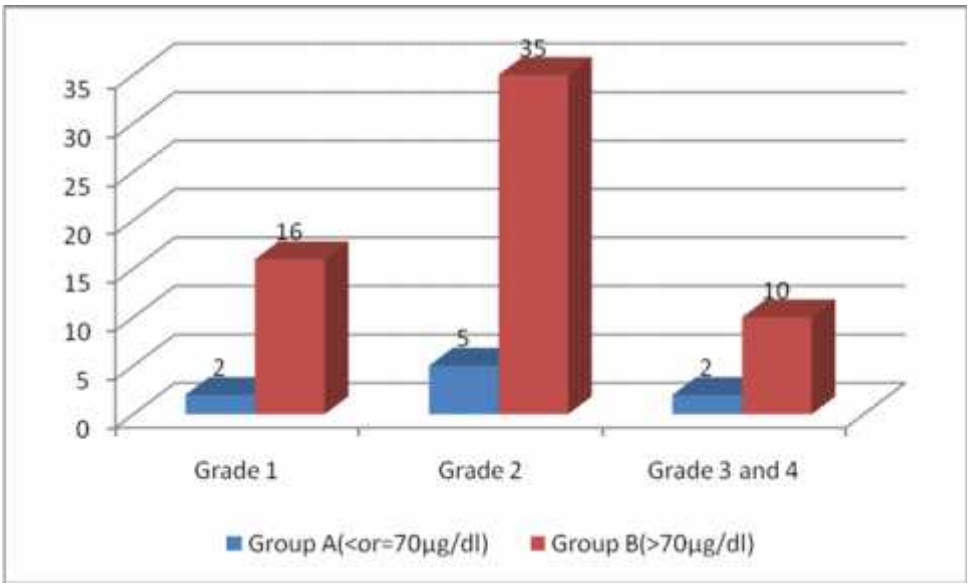
Table 11 : Serum zinc levels in different grades of acne

Grades of acne	Group A(<or=70µg/dl)	Group B(>70µg/dl)	Total
Grade 1	2(11.1%)	16(88.9%)	18
Grade 2	5(12.5%)	35(87.5%)	40
Grade 3 and 4	2(16.6%)	10(83.4%)	12

Percentage of distribution of patients of both Group A and B in all grades of acne is same. (χ^2=0.209, degree of freedom=2, Probability = 0.90). Since probability P>than 0.05, it is not significant. Therefore there is no correlation or association between serum zinc levels and grades of acne

There is no difference in percentage of distribution of patients of both groups A and B in all grades of acne. Null hypothesis is proved so there is no association or correlation between serum zinc levels and grades of acne.

Graph 10 : Serum zinc levels in different grades of acne



DISCUSSION

Age incidence:

Out of 23242 patients who attended the outpatient department during the study, 1158cases of acne vulgaris were seen. The incidence of acne thus amounted to 5%. Out of these, 70 cases were selected for the present study as per formula samples size=pq/d^2.

In a Swiss study, done by Bloch, it was found that 18-year-olds had the highest prevalence of clinical acne on the face-35%in men and 23% in women. It started earlier in boys (10years) than in girls (11 years), whilst the maximum prevalence was later in girls (l8years) than the boys (17 years).[19]

According to study of Schafer acne was present in 26.8% overall, and was more prevalent in men (29.9%) than women (23.7%).[60]

Hinrichsen et al and Hamilton et al found that acne started earlier and reached its maximum prevalence earlier in girls than in boys. The above studies had contradictory findings.[19]

In a study done by Adityan B and Thappa D.M at JIPMER, most patients were in the age group of 16-20 years (59.8%) and 21-25 years (19.4 %).The majority being either college (33.3%) or school (33%) students. [68]

In our study the "maximum prevalence of acne was in the age group of 16-20years (47.14%). In boys, the maximum prevalence was at 18years (22.23%) and for girls it was at 18 and19years (both ages showed same prevalence of 17.65%). This finding was in accordance with the studies done by Bloch as well as Thappa.

Gotz et al observed that only 7% of cases developed acne before the age of 12 years and 40% experienced acne after they were 16 years.[4] In the present study, 5.7% developed acne between 11-15 years of age and 94.3%of the patients developed acne after 16 years. Maximum cases had their age of onset between 16-20 years age group. This finding coincides with the above finding. The reason for this finding is attributed to the increased androgen secretion with puberty.

The correct incidence and prevalence of acne could not be assessed in our study due to the small size of the study group.

Most of the studies have been done in schools comprising of adolescents, where as our study was not restricted to the adolescents only, patients who attended the clinic with acne as their presenting complaint were included in the study.

Family History:

Cunliff et al (1975) in one study, found that 82% of the patients had a history of acne in at least one sibling and in 60% a history of acne was obtained from one or both the parents.[17]

A survey in Germany showed that acne had been present in one or both parents of 45%of school boys with acne but in only 8% of parents of boys without acne.[12]

In our study, 38.57% of patients had a family history of acne. 70.37% of among these patients had a history of acne in at least one of the parents and remainder 29.63% of patients gave a history of acne in siblings. Heredity seems to have a role in the etiology of acne but it is not the only factor.

Relation to menstruation:

Cunliff et al (1974) demonstrated that acne worsens 5-6 days before the onset of menses.[4] **Cunliff and Cotterill** (1976) observed that 60-70% of the females notice a deterioration in their acne lesions, in the premenstrual week.[73] Vaswani and **Pandhi** (1991) found a significant decrease in the inflammatory and non-inflammatory lesions in the post menstrual phase. Some studies report premenstrual exacerbation between 27 and 70%.[60]

In our study, 28 (82.35%) of the females gave a history of premenstrual worsening of their acne lesions. This finding is in co-relation with all the above studies. The reason for this exacerbation has been attributed to hydration of the ductal pores premenstrually, causing increased resistance to sebum out flow. This leads to ductal obstruction and thus to the aggravation of lesions.[36]

Seasonal variation:

There is a wide spread consensus that acne generally improves in summer but there is no proof regarding it. Cunliff et al observed that 60% of the patients improved in summers, 20% did not notice any change and another 20% had an aggravation of their lesions in summer.[73] Gfesser et al (1996) in their studies, found regression of acne in summers in one third of the patients and summer exacerbation in another third of the patients. In the rest one third, no seasonal variation was found.[39] In the present study, 28.57% of the patients reported a summer exacerbation and 5.71% had winter exacerabation. None of the patients reported any improvement in summer, which is in contrast with the above two studies. 65.716% of the patients did not notice any seasonal variation.

The explanation for summer exacerbation is the comedogenic effect of ultraviolet radiation. Excessive sweating, especially in a tropical climate, can lead to blockage of duct and thus increase in acne.[27]

Relation to diet:

A controversy has long raged on the role of diet in the pathogenesis and management of acne. In a study by Rasmussen et al, 60% of the patients felt that chocolates and fatty foods were responsible for the flare up of their acne lesions. Fulton et al did not find any effect of large amount of chocolates, milk, cold drinks and nuts on the acne lesions.[58] Vaswani and Pandhi did not find any relation between diet and the severity of lesions in their study.[38]

El-Akawi *et al* reported that, of 166 Jordanian male and female untreated clinic patients with acne, participants believed that their acne was aggravated by nuts (89%), chocolate (85%), cakes/biscuits (57%), oily food (53%), fried food (52%), eggs (42%), or milk, yogurt, and cheese (23%).[62]

In 2001 Green and Sinclair in their study showed following results: 41% (*n*= 88) of medical students believed diet aggravated acne; 12% of these 88 blamed chocolate.[62]

In the present study 40% of the patients felt that fatty food including fried and oily food stuffs (21.428%), non- vegetarian food (14.285%) and chocolates (4.285%) were responsible for the flare up of their acne lesions. This finding is in agreement with the Rasmussen study and Green and Sinclair study but the reason for lower percentage could be a smaller size of the study group. Also, many of the patients were not in the habit of eating chocolates. Our findings were in contrast to those of Fulton et al and the reason for this is that their findings were based on the clinical trials and not on history as in our study.

Type of cosmetics used:

Many of the cosmetics have comedogenic effect.[12]There is a misconception among the acne patients that acne is caused by dirty skin. Thus most of them end up washing their faces frequently with soaps and cleansers. In the process they cause more harm to the already inflamed skin. Many of the patients have greasy skin and inspite of it may try to hide their lesions with harmful cosmetics. Moisturizers on a greasy skin will only serve to enhance the existing oiliness.[40] In the present study, 30% of the patients gave a history of using greasy cosmetics, 2.857% gave history of usage of non-greasy cosmetics. Besides 54(77.14%) of the patients described their skin type as oily. Thus all these factors could have aggravated their acne.

Distribution of lesions:

In a study it was found that most of the lesions were present on the face. 60% of the patients had lesions on the back, 15% had also on the chest and only 1 % had lesions on chest and back but no lesions on the face.[74] In the present study, all the patients had lesions on the face. 41.42% of the patients had acne on the back also and 30% had lesions on the chest. Lesion distribution varies with individuals and there is no definite pattern of lesional distribution described.

Seborrhoea: One of the striking features of acne is a greasy skin, but all patients with seborrhoea do not have acne. **Munro Asherman** interviewed 490 subjects and found the incidence of dandruff to be 26% in patients with acne.[74] In the present study, 54(77.14%) subjects with acne gave a history of seborrhoea. Our findings are not the same as the above studies, the reason being a small study group.

Clinical assessment of acne:

Different grading methods have been used for measuring the severity of acne, but to date, a widely accepted standardized classification system does not exist. A clinically meaningful objective assessment of Acne Vulgaris is very important when relating the relative merits of therapeutic substances in this condition. The assessment techniques usually employed are lesion counting, grading systems and photographic methods and each method has its positive and negative features.

Gibson et al (1984) compared different methods of evaluation including, lesion counting, visual tactile grading and photography. They concluded that a well thought out clinical grading system is the best overall method as it provides a meaningful assessment with speed and reasonable accuracy.[45] Photography has a disadvantage that it cannot include the palpatory findings. **Michaelsson** evaluated their respective acne treatment results by counting all the evident lesions and multiplying with the respective severity index for each lesion. In the present study, 1-4 scale was used as described by **Tutakne** and **Chari.** It's an arbitrary method of grading acne severity but a very quick and convenient one.[33]Since the present study did not include any therapeutic trial, this method fulfilled the requirement of clinical assessment. This method helps in evaluating the patients and to choose the modality of treatment.

Grade 1-Mainly comedones and occasional papules.

Grade 2-Comedones,papules and occasional pustules.

Grade 3-Mainly pustules and nodules.

Grade 4-Nodules and Cysts.

Burton et al found that in 14-16 years age group virtually 100% of the girls and 100% of the boys had grade I acne, which was considered to be subclinical acne according to their grading system. 56% of the girls and 78% of the boys had grade II acne.[19]

In the present study, 18 patients (25.714%) had grade I acne. 40 patients (57.142%) had grade II acne. Most of the patients in this study belonged to grade II. 40% were females and 17.142% were males. 10(14.28%) had Grade III and 2(2.8%) had grade IV acne and totally 12patients (17.142%) had severe acne. Among these grade III and IV 11(15.714%) were males and 1(1.428%) was female. Our findings were different from the above studies because their grading system was different and included only adolescents and also comprised of a large study group. Though the grading method used in the present study, is similar to those used by many others, it has not been used in any study. It's just an arbitrary method of clinical assessment.

Serum zinc levels:

The normal values of serum zinc levels appear to be rather uniform all over the world. Most laboratories have obtained a reference value of 70-125µg/100ml.[55]

Serum levels in acne patients have been studied by many workers with varying results. Michaelsson et al were the first to study zinc in relation to Acne Vulgaris. In their study (1977) they demonstrated as slight decrease in the serum zinc level in male patients with severe acne. Female patients did not show any definite change.[2] They also found a definitive decrease in serum levels of retinol binding difference in serum zinc levels between acne patients and healthy controls. Similarly, El-Saaiee et al could not demonstrate any change in zinc levels between acne patients and control. In all the above studies, they demonstrated a beneficial affect of oral zinc in acne.

Michaelsson (1990), studied both epidermal and serum zinc levels in acne and other skin disorders. He found low zinc levels in, the epidermis, inspite of normal levels in the serum. Amer et al (1982) demonstrated a significantly lower levels of serum zinc levels as compared to controls, in both male and female acne patients with higher grades of acne.[58]

Their results were lower than those of Michaelsson et al. Women, whether diseased or healthy, showed a significantly lower mean serum zinc levels as compared to men. Michaelsson et al, in contrast, did not show any decrease in the levels in females.

Ghorpade et al (1982) studied serum zinc levels in 46 cases of Acne Vulgaris and 20 controls and found a significant decrease in the zinc levels in both males and females as compared to normal controls of same age. The levels were slightly lower in male patients but this difference was not statistically significant. Madadi et al (1993) studied serum zinc levels and other trace elements in acne patients and found significant decrease in the serum zinc levels as compared to controls.

They however did not study the differences in male and female patients.[3]In the present study, the serum zinc levels were studied in 70 acne patients. Serum zinc levels were not significantly low in acne patients of different grades of the same age group There is no significant difference in percentage distribution of patients in group A (low zinc levels) and group B(normal zinc levels) in different grades of acne(p=0.9,not statistically significant).Therefore there is no association between serum zinc levels and different grades of acne.

Our findings were similar to Michaelsson et al (1978) and El-Saaiee studies. Few workers have found zinc levels to be significantly low only in males with severe

acne and others have found it decreased in both male and female acne patients irrespective of their acne score and yet others have found no change in the serum zinc levels between acne patients and normal controls. The beneficial effect of oral zinc is yet another fact observed by many workers.[2]All these findings link zinc and acne in some way, which is not completely understood.

How reduced serum zinc level induces acne can be explained in many ways, which are directly or indirectly related to zinc metabolism. Vitamin A is essential for the normal epithelial development. Zinc is involved in the maintenance of normal plasma transport of Vitamin A by regulating the levels of retinol binding protein in the blood. It is possible that these patients have real zinc deficiency leading to defective synthesis of retinol binding protein and a resultant deficiency of Vitamin A.[2] If zinc Levels in serum are low, it leads to abnormal epithelial keratinization, thus precipitating or aggravating acne. Zinc stabilizes androgen synthesis.[3]A decreased serum zinc level leads to increased androgenic hormone production which controls the activity of enzyme hydroxysteroid dehydrogenase at the skin and sebaceous gland level. Many workers have found a beneficial effect of zinc therapy in acne. This is another proof that relative zinc deficiency occurs in acne.

Michaelsson et al (1977) have kept the possibility of stress and inflammatory process in acne, as responsible factors in low zinc levels. All these facts conclude that zinc has some role to play in Acne Vulgaris. But whether acne itself leads to low serum zinc levels or the low zinc levels precipitate acne is yet to be studied.

SUMMARY

Among the 70 cases that were studied, maximum cases of Acne Vulgaris were seen in the age group of 16-20 years (47.14%). Males had maximum prevalence at 18 years and females at 18 and as well as 19years. The youngest patient was 12 years old and the oldest was 32 years old.

Over all incidence among males was 54.71% and among females it was 45.28%.

Male : Female ratio in this study was 1.0588:1. A slight male preponderance was noted. Most of the patients were students 38.57% of the patients gave a family history of acne, either in the siblings or the parents. Thus, this agrees with the fact that hereditary predisposition is present in Acne Vulgaris, but other factors are also involved. 82.35% of female patients gave a history of premenstrual flare up of their lesions. Most of the cases in the present study belonged to grade II acne (57.14%). Severe acne (grade III and grade IV) cases amounted to 15.174%, and among these 91.67% were males and 8.33% were females. Thus, males had more severe acne than females. 55.174% of the patients gave a history of manipulating their lesions. 28.57% of the patients reported a summer exacerbation and 5.71% had winter exacerbation. None of the patients had any improvement in their lesions in summer. 40% of the patients related worsening of their lesions to fatty food, non-vegetarian food and chocolates. Though this was a subjective finding, it was quite significant in our study. 77.14% of the patients had seborrhea as an associated feature. There was no co-relation between the low serum zinc levels and severity of acne.

CONCLUSION

Among the 70 cases studied, maximum cases were seen in the 16-20 years age group (47.14%). Male to female ratio was 1.0588:1. A significant family history was noted.

Summer and premenstrual exacerbations were observed. Seborrhea was an important associated feature. A significant number of patients blamed diet for aggravation of their lesions. Most cases belonged to grade II acne. Males had more severe acne than females. Serum zinc levels were not significantly low in acne patients of different grades of the same age group. There was no co-relation between the severity of acne and serum zinc levels.

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PROFORMA

"ONE YEAR CROSS SECTIONAL STUDY OF CORRELATION OF SERUM ZINC LEVELS WITH SEVERITY OF ACNE VULGARIS AT KLE PRABHAKAR KORE HOSPITAL AND MRC BELGAUM."

Case No. ☐ OP /IPNO: ☐☐☐☐☐☐☐☐

Name: First name ☐

Last name ☐

Age: ☐ **Years**

1. Male
2. Female ☐

Occupation:

1. Labourer
2. Housewife
3. Officer ☐
4. Any other

Is the patient eligible for study? ☐ 1-yes 2-no

Has informed consent been taken? ☐ 1-yes 2-no

I.D.NO: ☐ ☐ ☐

Chief complaints:
Rised lesions **Site** ☐ Duration ☐

History of present illness:

1.Lesions:

White heads present ☐ absent ☐

Black heads present ☐ absent ☐

Rised solid lesions present ☐ absent ☐

Pus filled lesions present ☐ absent ☐

Nodular present ☐ absent ☐

Painful yes ☐ no ☐

2 Age of onset- ☐ years

3 Distribution of lesions

Cheek present ☐ absent ☐

Nose present ☐ absent ☐

Forehead present ☐ absent ☐

Chin present ☐ absent ☐

Chest present ☐ absent ☐

Arms present ☐ absent ☐

4 H/O drug intake

Hormones ☐

Steroids ☐

Anti-Tb drugs ☐

PUVA therapy ☐

5 H/O seasonal variation

Summer increases ☐ decreases ☐

Winter increases ☐ decreases ☐

6 Type of cosmetics used

Greasy ☐ non greasy ☐ others ☐

7 Relation to food-

H/o flare up of lesions on taking

Non veg ☐ oily food ☐ Chocolates & cakes ☐

8 H/O manual picking of lesions : yes☐ no☐

9 Skin type: oily☐ dry ☐ combination☐

10.H/O Chronic Diarrohea: present ☐ absent ☐

11H/O Pre-menstrual flare up: yes ☐ no ☐

12 **PAST HISTORY**

H/O Similar complaints yes☐ no☐

H/O Medication yes☐ no☐

13 **FAMILY HISTORY**

H/O Similar complaints in

Mother☐ father☐ brother☐ sister☐

14**PERSONAL HISTORY**

Diet ☐ Appetite☐ sleep☐ stress☐

bowel & bladder ☐ habits☐

15 **MENSTRUAL HISTORY**

Age of menarche- ☐

Attained menopause- yes ☐ no ☐

16 **GENERAL PHYSICAL EXAMINATION:**

Built poor ☐ moderate☐ well☐

Nutrition- poor☐ moderate☐ well ☐

Pallor-☐ icterus☐ cyanosis☐ Edema☐

Lymphadenopathy ☐

Odour ☐

/Vitals- pulse rate(per min) ☐☐

Blood pressure ☐ mm of hg

Temp ☐ deg centigrade

weight ☐ in kg

respiratory rate ☐

CUTANEOUS EXAMINATION

Distribution of lesions:
Face:

Cheek	present ☐	absent ☐
Nose	present ☐	absent ☐
Forehead	present ☐	absent ☐
Chin	present ☐	absent ☐

OTHER SITES

Chest	present ☐	absent ☐
Back	present ☐	absent ☐
Arms	present ☐	absent ☐

Types of lesions

	Comedones Open closed	Papules	Pustule	Nodule	Cyst	Scar	Keloid
Type							
Size							
Erythema							

ASSOCIATED SKIN CHANGES

Telangiectasia present ☐ absent ☐

Milia present ☐ absent ☐

Hirsutism present ☐ absent ☐

Hair changes present ☐ absent ☐

Nail changes present ☐ absent ☐

Mucous membrane present ☐ absent ☐

Seborrhoea present ☐ absent ☐

Perioral lesions present ☐ absent ☐

Palmar lesions present ☐ absent ☐

SYSTEMIC EXAMINATION

Cardiovascular system ☐ 1-Normal : 2-Abnormal

Respiratory system ☐ 1-Normal: 2-Abnormal

Nervous system ☐ 1-Normal: 2-Abnormal

Per abdomen ☐ 1-Normal: 2-Abnormal

INVESTIGATIONS

Serum zinc levels

INFORMED CONSENT FORM

I.D.NO ☐☐☐

You are invited to participate in our research study titled

"A ONE YEAR CROSS SECTIONAL STUDY OF CORRELATION OF SERUM ZINC LEVELS WITH ACNE VULGARIS AT KLE'S PRABHAKAR KORE HOSPITAL."

The study is conducted by a Post-graduate student in M.D Dermatology, from J N Medical College, Belgaum.

Respected sir/madam, we request you to enroll yourself to participate in our study as, you are eligible for participating in this study. During the study you will be asked some questions in detail regarding your presenting complaints.

PURPOSE OF STUDY

The purpose of this study is to estimate serum zinc levels in acne vulgaris patients and associate serum zinc levels with acne vulgaris. You are being asked to participate in this research because you have been clinically diagnosed as suffering from the disease, acne vulgaris. All patients attending the outpatient department, who are diagnosed to have this disease, will be requested to participate in this study during the period of one year. This study will be conducted in J. N. Medical College, Belgaum.

PROCEDURE & STUDY

Should you choose to participate, you will be asked to give a detailed history of your disease, undergo a physical examination, and consent to a blood investigation. You will undergo a serum zinc estimation.

RISKS & BENEFITS

You may undergo a slight degree of discomfort during the process of investigation, which may include a slight amount of pain and bleeding. However, all necessary steps and precautions will be taken to ensure your safety. The result of you taking part in this research would help health care providers towards a better understanding of this disease, and thus we will be able to provide improved patient care.

ALTERNATIVES

If you decide not to participate in this study, you will still be receiving the usual standard care for your disease.

PRIVACY & CONFIDENTIALITY

Your privacy will be respected and all information collected about you during the course of this study will be kept confidential. Your identity will remain undisclosed.

INSTITUTIONAL POLICY

The J.N.Medical College will provide, within limitations of laws of state of Karnataka, facilities and medical attention to patients who suffer as result of participating in its projects. In the event you believe that you have suffered any physical injury as a result of your participation in this study, you may contact KLES Hospital and MRC on Telephone No.95 831 2473777.

FINANCIAL INCENTIVES

You shall not be receiving any payment or any financial incentives for participating in this study.

AUTHORISATION TO PUBLISH RESULTS

The results of this study may be published for scientific purpose or presented to a scientific group. Your identity, however, will be maintained confidential at all times.

VOLUNTARY PARTICIPATION

Your participation in this study is voluntary. Your decision whether or not to participate will neither affect the care of your current disease, nor your future relations with the doctor or the hospital. You are free to discontinue participation in this study at any time and for any reason. In case you need further information regarding your rights as a study participant, you may please contact Dr. V D Patil, Principal and Chairman of the Ethical Committee, J N Medical College, Belgaum on telephone no. 95 831 473777.

STATEMENT OF CONSENT

I.D.NO: ☐ ☐ ☐

I Mr/Ms/Mrs _____ volunteer & consent to participate in this study. I have read the consent or it has been read to me. The study has been fully explained to me and I may ask questions at any time. By signing this consent form I am signing the consent form after having read or been read for me in vernacular language, including the risks and benefits and having all my questions answered.

Participant's name:

Signature of left thumb imprint of participant:

Witness' name:

Signature of witness:

Investigators Name:

Signature of Investigator:

Date:

Place:

If the participants are Minor (under 18), the parents sign the form, rather than the parents.

KEY TO MASTER CHART

Bro		=	Brother
Comb		=	Combination skin type
Com		=	Comedone
Fa		=	Father
Inc		=	Increase
Pap		=	Papule
Pus		=	Pustule
Sex	M	=	Male
	F	=	Female
Sis		=	Sister
Nv		=	Non-vegetarian
V		=	Vegetarian

MASTER CHART

SNO	Name	Age	Sex	Age of onset	Occupation	History of drug intake	Seasonal variation	Cosmetics	Relation to food	Manual picking	Skin type	Premenstrual flare up	Food habits	Family history	Disturbution of lesions	Type of lesions	Grade	Seborrhea	Associated skin disease	Serum Zinc level
1	Yaseen s.m	25	m	23	student		Inc in summer		NV		oily		nv		Face, back	Com,pap	2	+		122
2	Darshini s.t	12	f	12	student			greasy			dry		nv		Face	Com,pap	2			106
3	Reshma s s	18	f	16	student					+	dry	+	nv	fa	Face, back	Com,pap,pus	2			50
4	Kush k.r	20	m	18 1/2	student					+	oily			bro	Face	Com,pap,pus	2	+		120
5	Sheshendra v r	17	m	16	student					+	oily		nv		Face, back, chest, arms	Com,pap,pus	2	+		98
6	Sunil s.d	18	m	16	student			greasy			comb		v		Face	Com,pap,pus	2	+		167
7	Ravi.m,n	18	m	16	student			greasy			oily		v		Face, back, chest, arms	Com,pap,pus,nod	3	+		102
8	Mahesh.I.H	22	m	21	student			greasy		+	oily		v	fa	Face, back, arms	Com,pap	2	+		128
9	Sangeeta R.R	30	f	30	worker			greasy			oily	+	nv		Face	Com,pap	2	+		80
10	Tejashree D.P	19	f	19	House wife						comb	+	v		Face	Com,pap	2			112
11	Shailaja S.A	28	f	16	student					+	oily		nv	mot	Face, arms	com	1	+		88
12	Girija S.D	23	f	23	nurse		Inc in winter	greasy			oily	+	v		Face	Com,pap,pus	2	+		142
13	Prashant M.R	22	m	22	army		Inc in summer		Oily food	+	oily		v		Face	Com,pap,nod,scar	3	+	furuncle	120
14	Sheela S.M	15	F	15	Student	Growth hormone		greasy			oily		v		Face	Com,pap	2	+		132
15	Adarsh B.K	15	M	14	Student			greasy			oily		nv		Face, back, chest	Com,pap,pus	2	+	Canities,telogen effluvium	116

SNO	Name	Age	Sex	Age of onset	Occupation	History of drug intake	Seasonal variation	Cosmetics	Relation to food	Manual picking	Skin type	Premenstrual flare up	Food habits	Family history	Disturbution of lesions	Type of lesions	Grade	Seborrhea	Associated skin disease	Serum Zinc level
16	Jyothi N.Y	18	F	13	Student		Inc summer	greasy			oily		v		Face	Com,pap	2	+		160
17	Hanumant N.B	18	m	16	student	steroids					dry		nv		Face, back, arms	Com,pap,pus	2		folliculitis	150
18	Ajay K.S.K	16	m	15	student				nv	+	comb		nv		Face	Pap,pus,scar	2			123
19	Vinata B.B	17	f	16	student				choc		oily	+	v		Face, back	com	1	+		106
20	Rajani S.M	19	f	19	student			greasy		+	oily		v		Face	Com,pap	1	+		106
21	Ravi K.R.M	18	M	17	student				nv		oily		nv	sis	Face, back, arms	Com,pap,pus	2	+		108
22	Archana S.J	19	f	19	student					+	oily	+	v	fa	Face	Pap,pus	2	+		58
23	Heena K.S.S	18	F	18	Student				nv	+	comb		nv		Face	Com,pap,pus	2			54
24	Vimal D.G	25	f	24	student		Inc summer		Oily food		oily	+	v	sis	Face, back	Com,pap,pus	2	+		83
25	Ratan.S.P	17	m	13	student		Inc summer			+	oily		v	sis	Face	Com.pap	2	+	PIH,vitiligo	119
26	Basappa V.P	21	m	18	student						comb		v		Face, back, arms	Com,pap	2			102
27	Lingaraj B.M	22	m	22	student			greasy	nv		comb		nv		Face	nodule	3			115
28	Sandeep V.N	20	m	18	student					+	comb		v		Face	Com,pap,pus,nodule	3		Tinea versicolor	67
29	Nilofer M.B	18	m	18	student			greasy		+	oily	+	nv	mot	Face	Pap,pus	2	+		88
30	Satish K.M	23	m	22	student						comb		v		Face	Com,pap,pus	2			115
31	Basavaraj S.Y	15	M	14	Student					+	comb		nv	mot	Face	Com,pap,pus	1	+	Tinea versicolor	96
32	Ashwini A.M	24	f	17	student		Inc summer				oily	+	v	mot	Face, back	Pap,pus,scar	2	+		92

SNO	Name	Age	Sex	Age of onset	Occupation	History of drug intake	Seasonal variation	Cosmetics	Relation to food	Manual picking	Skin type	Premenstrual flare up	Food habits	Family history	Disturbution of lesions	Type of lesions	Grade	Seborrhea	Associated skin disease	Serum Zinc level
																				104
33	Shashidhar V.H	18	m	17	student				Oily food	+	oily		nv	mot	Face	Com,pap,pus	1	+		75
34	Harsh K.S	19	M	16	student		Inc summer				oily		nv		Face	Com,pap,pus	1	+		112
35	Thabusum J.J.P	22	f	22	student			greasy		+	dry		nv	mot	Face	Com,pap	2			100
36	spoorthi	19	f	18	student			greasy		+	oily	+	nv		Face, chest, arms	Com,	1	+		100
37	Pramila.S.K	22	f	22	student		Inc summer	Non greasy			oily	+	nv		Face	Com,pap,pus	2			102
38	Reshma.N.A	27	F	24	student		Inc summer				oily	+	nv		Face	Com,pap,pus	2	+		102
39	Praveen B.P	23	m	19	student		Inc winter			+	oily		nv	bro	Face	Com,pap,nod	3	+		98
40	Sheela U.M	25	f	25	House wife					+	oily				Face	Com,pap	2	+		82
41	Harpreet K	20	f	18	student		Inc summer		Choc cake	+	oily	+	nv		Face, back, chest, arms	Com,pap	2	+	Perioral lesions	477
42	Jismol J	18	F	18	student			greasy	oily	+	oily	+	nv		Face, back, chest	Com,pap,scar	2	+		110
43	Ravi K.S.S.R	25	m	16	student		Inc summer		Oily food	+	oily		v	Fa,sis	Face, back, chest	Pap,pus,nod,cyst, scar	4	+		538
44	Roopali.D.P	25	f	23	student		Inc summer				oily	+	v		Face	Com,pap,pus	2	+		97
45	Elna J.K.U	19	f	19	student			greasy	Nv,oily	+	oily	+	nv	fa	Face	Com,pap	1	+		123
46	Sangita P.R	18	f	18	student						dry		v	mot	Face, back, chest, arms	Com,pap	2	+		108
47	Deepa A.K	20	f	19	student		Inc summer		oily	+	oily	+	v		Face, back, chest	Com,pap,pus	2	+		136
48	Mahesh M.K	22	m	21	student		Inc summer	other	Nv,oily	+	oily		nv		Face, back, chest	Com,pap,pus,nod	3	+		98

SNO	Name	Age	Sex	Age of onset	Occupation	History of drug intake	Seasonal variation	Cosmetics	Relation to food	Manual picking	Skin type	Premenstrual flare up	Food habits	Family history	Disturbution of lesions	Type of lesions	Grade	Seborrhea	Associated skin disease	Serum Zinc level
49	Anil G.M	22	m	22	student		Inc summer				oily		nv		Face, back	Com,pap,pus	1	+		109
																				105
50	Akshay A.B	21	M	19	student		Inc winter		Nv,oily	+	oily		nv		Face, back	Com,pap	2	+		121
51	Ajeesh S.D	23	M	23	student						oily		v		Face, back, arms	com	1	+		102
52	Sudha.D.U	32	f	22	House wife		Inc winter	greasy		+	oily	+	nv	mot	Face, chest	Com,pap,pus,nod	3	+	Perioral lesions	120
53	Vishwanath.L.G	21	m	14	student		Inc summer			+	oily		nv	Mot,sis	Face	Com,nodule	3	+		399
54	Ribika S.K	20	f	16	student		Inc summer		Nv,oily	+	oily	+	nv		Face, back	Com,scar,keloid	1	+	keloids	110
55	Hanumant Y.M	21	m	21	student				oily		oily		v		Face, back, chest	Com,pap,pus	1	+		102
56	Reshma M.P	20	f	18	student		Inc winter	greasy		+	comb	+	v	mot	Face	Com,pap,pus	2			108
57	Iranna B.S	18	m	15	student		Inc summer			+	oily		nv		Face, chest	Com,pap	1			48
58	Vibhav M.S.K	18	m	15	student		Inc summer				comb		nv	Fa,mot	Face, back, chest, arms	Com,pap,nod	3			108
59	Gouri A.B.V	18	f	14	student			greasy		+	oily	+	v		Face, back, chest	Com,pap,pus	2	+		88
60	Anjana P.P	24	f	22	student		Inc summer		oily		oily	+	nv		Face, back, chest	pap	2	+		59
61	Fawas A.K	22	m	22	student						oily		nv		Face	nod	3	+		38
62	Rakesh S.M	23	m	22	student						oily		v	bro	Face	Com,pap	1	+		63
63	Nutan V.M	25	f	24	student			greasy			oily	+	nv	sis	Face	Com,pap,pus	1	+		110
64	Arathianna M	22	f	22	student			greasy	choco	+	oily	+	nv		Face	Com,pap	2	+		60

SNO	Name	Age	Sex	Age of onset	Occupation	History of drug intake	Seasonal variation	Cosmetics	Relation to food	Manual picking	Skin type	Premenstrual flare up	Food habits	Family history	Disturbution of lesions	Type of lesions	Grade	Seborrhea	Associated skin disease	Serum Zinc level
65	Manjunath J.K	17	m	17	student		Inc summer		nv	+	dry		nv		Face	Com,pap	1	+		100
66	Dilkush B.G	25	m	18	student		Inc summer			+	oily		nv	fa	Face	pap	2	+		102
																				106
67	Ashwath S.G	19	m	14	student		Inc summer		Oily ,spicy	+	oily		v	Fa,mot	Face	Com,pap,nod,scar	3			107
68	Laxmi S.G	19	f	16	student		Inc summer		oily	+	oily	+	v	fa	Face, back, chest	Com,pap	2	+	Perioral lesions	130
69	Ashwini C.K	21	f	21	student				oily	+	oily	+	nv		Face, back	Com,pap,pus	2	+		106
70	Hanumant D.G	29	m	18	student					+	oily		nv		Face, back, chest, arms	Com,pap,pus	2	+		115

SNO	Name	Age	Sex	Age of onset	Occupation	History of drug intake	Seasonal variation	Cosmetics	Relation to food	Manual picking	Skin type	Premenstrual flare up	Food habits	Family history	Disturbution of lesions	Type of lesions	Grade	Seborrhea	Associated skin disease	Serum Zinc level