Epidemiological and clinical study of acne vulgaris among Libyan patient in Benghazi

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CERTIFICATION

This thesis entitled **" Epidemiological and clinical study of acne vulgaris among Libyan patient in Benghazi "** prepared by Dr. Amina I. Burwais, under the supervision of Associated prof. Abdul hamid A. Elorfi, has been approved for submission to the faculty of medicine, Benghazi university of medical sciences, Benghazi, Libya in partial fulfillment for the certification of the degree of Master in dermatology and venereology (M.Sc).

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DECLERATION

This is declare that I have not submitted the research work embodied in this thesis

" **Epidemiological and clinical study of acne vulgaris among Libyan patient in Benghazi** " to any other university before.

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DEDICATION

I sincerely dedicate this work to

the pure soul of my mother and my father.

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1.Summary:

Background: Acne is a chronic inflammatory disease of the pilosebaceous units. It is characterized by seborrhea, the formation of the comedones, erythematous papules and pustules, less frequently by nodules, deep pustules. Although the course of acne may be self-limiting, the sequelae can be life long, with pitted or hypertrophic scar formation.

Aim of this study: to evaluate the epidemiological and clinical features of acne vulgaris.

Patients and methods: A prospective study was done. The 150 Libyan patients with clinical diagnosis of acne vulgaris attending dermatology department at Aljomhoria hospital in Benghazi-Libya over one year from Jan.2011 to Dec.2011 were enrolled in this study.

All patients were exposed to detailed history and clinical examination according to the prepared appendix I,II. Clinical severity of acne using the Global Acne Grading System (GAGS).

Results: A total of 150 patients with acne vulgaris were included in the present study, were 103 females and 47 male patients (male : female ratio 1: 2.2). The mean age ±SD was 21±4.7 years the most common age group involved was 16-20 years(46.7%), mean age of onset was 17.2±4.3 years. Family history was positive in 63.1% of patients. Involvement of face was seen in 100% of patients followed by chest 73.3%, back 64.7%. Severity of acne using GAGS were found 32.7% had mild acne, 62.7% had moderate acne and 4.6% had severe acne, none of the patients had very severe with statistically significant (p=o.oo6). The most common risk factor were food(52.7%) followed by emotional factor in 47.3% of patients with statistically significant(p=0.00). Only 6(12٪) male patients were smoker 4(8.5%) of them with history of moderate acne and 2(4.2%) of them with history of mild acne. In female patients 68% had premenstrual flare and 16.5% had cutaneous markers of androgenicity. There was a higher incidence of post- acne hyperpigmentation(74%) and post-acne scar(51.3%). 60.7% of patients with normal body mass index(BMI), 13.3% underweight, overweight and obese (12%).

Conclusions: Acne vulgaris is common disease in Libyan adolescents. Female patients more affected by acne and it's complication of acne of post inflammatory hyperpigmentation more in females but scars more in males. Food and emotional stress were the most commonest exacerbated factor in our patients.

2.Introduction:

Acne vulgaris is a chronic inflammatory multifactorial disease of pilosebaceous unit with hormonal influences on local sebum production (1,2), which lead to hyperproliferation of follicular keratinocytes, abnormal differentiation, and desquamation, with resulting obstruction of the follicles and production of comedones. Propionibacterium acne, a resident commensal bacterium that colonizes the lipid-rich microenvironment of the hair follicle , produces inflammatory mediators that engender the papules, pustules , and later nodular lesions typical of inflammatory acne (2). In addition, increasing evidence from recent studies of large families and twins implicates the importance of hereditary factor in the pathogenesis of acne (3). Lesions are distributed on face , neck , chest , and back (1). Severity of the disease varies markedly from one individual to the other depending upon the interplay of various factors involved in the development of acne vulgaris (4). Most doctors would divide the condition into mild, moderate and severe (5). Mild disease consists of open and closed comedones, moderate acne encompasses more frequent papules and pustules with mild scarring and severe disease contains all of the above, plus nodular abscesses that leads to extensive scarring (6).

Acne is a common skin condition particularly in younger people with an estimated prevalence of 70-87% in adolescent (7,8). The prevalence of acne among adults, estimated around 12% to 14% (9). In contrast, acne remain rare in non – Western population such as Eskimo (8). The proportions of acne vulgaris in hospital – based studies of skin disease in Africa have been reported to be 4.6 % in Ghana, 6.7 % in Nigeria, and up to 17.5 % in South Africa (10). The prevalence of acne varies between sex and age groups, appearing earlier in females than in males, possibly the earlier onset of puberty (11), it is more prevalent in girls under and boys over 14 years of age (12), moreover in the age group over 20, females predominate (13). The most severe forms of acne vulgaris occur more frequently in males, but the disease tends to be more persistent in females (1). In most cases acne subsides in the course of a few years. In up to 20 % of patients acne can persist beyond the age of 20 (13).

Family history of acne is a significant risk factor for acne, hot weather, sweating and certain aspect of diet such as nut, chocolate, fatty food, fried food, eggs, cakes and biscuits ,spices , coffee, tea are believed by some to be aggravating factor in acne (14). Other potential factors that may contribute to acne development and severity include genetic (15), stress (15), and

exogenous exposure to comedogenic substances including tars and medications like corticosteroids (15). Hormones influence on acne are undisputed by shown higher prevalence of acne in male adolescents and about 70% of women complain of premenstrual flare, ultraviolet radiation may enhance the comedogenicity of sebum (1).

Other variants of acne include : 1)Infantile and Juvenile acne ; which mainly affects males, presents as facial acne in children between 3 and 24 months ,and may last up to 5 years of age(1). 2)Acne excoriee ; This variant occurs predominantly in females ,two subgroups exist: one with some primary inflammatory acne lesions, another with almost none ,often associate with some personality or psychological problem (1). 3)Drug-induced acne; acne cause or aggravated by many(1,16) such as glucocorticoids, phenytoin, lithium, isonizid, high-dose vitamin B complex, halogenated compounds(iodides, bromides), epidermal growth factor inhibitors(17). 4) Endocrine acne; should be reserved for cases of acne associated with significant clinically manifest endocrine disease such as Cushing's disease, late- onset congenital adrenogenital syndrome and polycystic ovarian syndrome(1). 5) Externally induced acne ;a) Cosmetic acne: This variant perhaps the greater use potentially comedogenic cosmetics(1) . b)Pomade acne : pomades are greasy preparations used to defrizz curly negroid hair c).Detergent acne : uncommon form of acne develops in patients who wash many times each day(1). d)Mechanical acne; the acne occurs after repetitive physical trauma to the skin(17) characterized by the presence of lichenification and pigmentation(1). 6)Occupational acne ; This acneiform eruption occurs in areas of skin that contact with oil and crude tars(1). 7)Chloracne ; that follows exposure to certain toxic, chlorinated hydrocarbon(1). 8)Tropical acne; a severe acneiform folliculitis may develop in extreme heat. This can be seen in tropical climates or in scorching occupational(17). Severe acne variants ;a) Acne conglobata : It is an uncommon(1), a severe form of nodular acne is most common in teenage males(17) characterized by multiple inflammatory papules and tender nodules which frequently fuse to form multiple draining sinuses(1) b).Acne fulminans : It is an uncommon(1) also known as acute febrile ulcerative acne is the most severe form of nodular acne accompanied by systemic symptoms(17). Gram – negative folliculitis : May occurs in patients with pre-exisiting acne vulgaris treated with long-term oral antibiotics, especially tetracyclines(17). Pyoderma faciale : it was initially believed to be a variant of acne but it is suggested that is more related to rosacea, it mainly affects post-adolescent women (aged 20-40 years)(1). SAPHO syndrome : SAPHO syndrome is manifested by synovitis, acne, pustulosis, hyperostosis and osteitis(17) . Vasculitic / pyoderma gangreosum acne : A few patients ,who had very mild acne, have developed the sudden onset of vasculitic, pyoderma gangerosum –like lesions (1).

Acne is not a trivial disease- the physical, social, and psycho logic morbidity associated with the disease can be profound, and the quality of life in sufferers can be impaired (10). The early severe acne and scarring, with the consequent adverse psychosocial disabilities resulting from feelings of embarrassment, frustration and poor self-esteem (18).

Numerous types of agents are used in the treatment of acne, either alone or in combination, each exerting its effect on one or more of the pathogenic factors include : Antibacterial agents ;Both topical and oral antibiotics are used in treating inflammatory acne including benzoyl peroxide, erythromycin, clindamycin, different comedolytic types like topical retinoids, either these alone or in combination forms. Oral retinoids ;Isotretinoin remains the most effective treatment for acne but is reserved for severe cases, Hormonal agents ; such as Spironolactone, oral contraceptive pill for women, antiandrogens flutamide, finasteride, and cyproterone acetate/ ethinylestradiol. Physical modalities also have been used in treatment of acne such as Lasers and light therapy (19).

3. Review of literature:

3.1.Definition: Acne is a chronic inflammatory disease of the pilosebaceous units. It is characterized by seborrhea, the formation of comedones, erythematous papules and pustules, less frequently by nodules, deep pustules (1). Although the course of acne may be self-limiting, the sequelae can be lifelong, with pitted or hypertrophic scar formation (17).

3.2.Epidemiology:

Acne vulgaris is fairly common and affects 85%-100% of the population at some part of their lives (20). Acne usually starts in adolescence and frequently resolved by mid-twenties (1). Prevalence data shows some variation from study to study, which may related to the population studied and time when the study was performed (1). Various studies on acne prevalence in adolescents show a frequency ranging from 30% - 100%, and have reported up to 91 % of male and 79% of female teenagers being affected by acne (18) .

A study from UK, showed that 56% of boys and 45% of girls between 14-16 years were affected by acne (18).

Generally, inovulation of the disease occurs before age 25, however, great variability in age of onset and resolution occurs. Twelve percent of women and 3% of men will continue to have clinical acne until 44 years of age. A few will have inflammatory papules and nodules into late adulthood (21).

In Population-based studies suggest that acne prevalence is lower in rural societies than in industrialized populations (22). Surveys of disease in some rural African villages in Kenya (23), Zambia (23), and the Bantu in South Africa (23) report far less acne than is found in the descendants of people in these areas who now live in the United Kingdom or the United States. More convincing is the study of schoolchildren from Purus Valley, a rural region in Brazil (23), of 9955 children aged 6 to 16 years, only 2.7% had acne vulgaris. In clinics in the urban areas, there is a clear preponderance of girls seeking treatment. There is also a perception that acne is less prevalent in rural population. This is supported by the data from Varanasi where 21.35% of boys (13–18years) from rural areas had acne versus 37.5% from the urban areas (24).

An evaluation of the difference in acne according to skin color has been performed at the Skin Color Center in New York (25). The mean age of acne onset appears lower in Hispanic subjects compared with Black and Asian subjects. The frequency of acne at teenage is the highest in Hispanic subjects (79.2%) and while the frequency in Black was 59.9% and in Asian was 63.2% subjects. Scarring is more frequent in Hispanic subjects (21.8%), remaining low in

Black subjects (5.9%) with an intermediate frequency in Asian subjects (10.5%). The results are similar concerning severe acne with nodular lesions: Hispanic (25.5%), Black (18%) and Asian subjects (10.5%).

3.3.Risk factors:

3.3.1.Genetic:

A possible role for genetic factors in the development of acne is based on the observation that relatives of affected individuals are at increased risk of developing acne compared with unrelated individuals. However, relatives share similar environments as well as genes (26). A genetic background is also supported by Goulden et a (27), who found that the risk of adult acne vulgaris in relatives of patients with acne as compared with control patients is significantly higher. Twin studies show that in homozygous twins, 97.9% of siblings develop the disease concomitantly in contrast to heterozygous twins. In a large twin study, with 458 homozygous and 1099 heterozygous twins 81% of the disease variance could be attributed to genetic causes and only 19% to environmental factors (27). A number of studies (3,28) report a strong familial tendency for acne, where the index cases tend to present at a younger age (3). Racial and ethnic factors may also contribute to differences in prevalence, severity, clinical presentation and sequelae of acne (29).

3. 3.2. Smoking:

The relationship between smoking and acne vulgaris is controversial (4). One study showed a linear relationship between acne prevalence and the number of cigarettes smoked daily (30). However, another study suggested that severe acne was less common in smokers compared to nonsmokers (30). A more recent cross-sectional study has concluded that the anti-inflammatory effects of smoking may inhibit the development of papulopustular acne, more so in girls than boys (31). Many of the adverse and beneficial effects of cigarette smoke, which contains nicotine and many other chemicals, might result from the ability of cigarette smoking to suppress the immune system (31).

3.3.3. Hormones :

The role of hormones, particularly as a trigger of sebum production and sebaceous growth and differentiation, is well known. Excess production of hormones, specifically androgens, growth hormones (GH), insulin growth factor 1(IGF-1), insulin, corticotrophin releasing hormone (CRH), and glucocorticoids, is associated with increased rates of acne development (16). The

surveys from all regions consistently showed a significantly higher prevalence of acne in males than in females, probably because of men's high levels of androgen (3). Androgens are thought to play a crucial role in the pathogenesis of acne. This notion is supported by clinical observation of acne onset around puberty and flare during menstruation or hyperandrogenic states(15). The role of insulin in acne development is also supported by the high prevalence of acne in women with polycystic ovary syndrome (PCOS), a condition associated with insulin resistance, hyperinsulinemia, and hyperandogenism (32).

3.3.4.Diet:

Diet-induced changes in hormonal and cytokine homeostasis represent the most likely environmental factor underlying the development of acne (33). However, the precise role of diet in the pathogenesis of acne remains unclear and controversial, and many dermatologists continue to propagate the conviction that acne is independent of diet (30). Some authors have reported that the hormones in milk, such as IGF-1, 5α-reduced steroids, and α-lactalbumin, may survive milk processing and affect the pilosebaceous unit (22). Milk consumption also increases IGF-1 production, which has been associated with ovarian androgen production in premenarchal girls and acne in adult women (22). Low–glycemic-load diets and increased ingestion of ω-3 polyunsaturated fatty acid can decrease inflammatory acne lesions (34). It was hypothesized that milk and dairy products carry hormones and bioactive molecules that have the potential to aggravate acne. In another epidemiologic study, data were presented to suggest that high glycemic load foods (sugared foods) were the explanation for rising prevalence of acne in developed societies (35). Hyperglycemic food intake results in increase IGF1and a decrease in insulin like growth factor binding protein 3 (IGFBP3) leading to hyperandrogenism, seborrhea, and follicular hyperkeratosis (35). Omega-6 fats are precursors to proinflammatory mediators and have been associated with the development of inflammatory acne (36). In contrast, high levels of omega-3 fatty acids have been shown to decrease inflammatory factors (37), and may reduce acne risk by decreasing IGF-1 levels and preventing hyperkeratinization of sebaceous follicles (22).

3.3.5.Stress:

Stress is frequently implicated in aggravation of acne (vide supra) while acne itself induces stress (30). Acne flares up in stressful conditions, including psychological and emotional stress has been supported by earlier researchers (24,38). Recent experimental studies demonstrated that CRH has a role in promoting lipogenesis in human sebocytes (9), and that the CRH system is highly expressed on acne skin, especially on the sebaceous gland (39).

3.3.6.Sunlight:

Sunlight is generally beneficial to acne although poralens and ultraviolet radiation (PUVA) therapy may sometimes induce or aggravate acne (30).There is also a report of Europeans developing a type of acne after a beach holiday (acne Mallorca)(40). A similar phenomenon has been observed in India and is locally referred to as 'Goa acne' (30). Furthermore, ultraviolet radiation may enhance the comedogenicity of sebum (1).

3.3.7.Menstruation and acne (Premenstrual flare):

About 70% of women complain of a flare 2–7 days premenstrually (1). Possibly it is related to a premenstrual change in the hydration of the pilosebaceous epithelium(1). The menstrual cycle is characterised by changes in hormonal concentration and levels of DHEAS (dehydroepiandrosterone sulfate) may rise in pre-menstrual period and DHEAS has been reported to facilitate initiation of acne (41). This may account for the increase in acne during premenstrual period (41). Progesterone and estrogen have pro- and anti-inflammatory effects, and alteration or modulation of these hormones may be another explanation (30).

3.3.8.Climate:

Some studies, have detected seasonal variability in acne vulgaris, with the colder months associated with exacerbation and the warmer months showing improvement (11). Other studies have shown that climatic/ seasonal variations may affect the severity of acne (42). Previous study (43) had reported that humidity favours bacterial growth and it is noteworthy that Propionibacterium acnes has been implicated in the perpetuation of acne vulgaris (41). The increase in severity of acne during rainy season may be a result of increase in the growth of Propionibacterium acnes (4).

3.3.9.Pregnancy and acne:

Pregnancy has an unpredictable effect on acne. Pre-existing acne may aggravate or remit during pregnancy (30).

3.3.10.Drug-induced acne:

The best known causative drugs are halogenated compounds such as iodide and bromide, progestogens, oral contraceptive pill, corticosteroids, isoniazid, and lithium. Recently, a new class of therapeutic agents epidermal growth factor receptor (EGFR)- antagonists (gefitinib, erlotinib, cetuximab) have been recognized as a trigger of acneiform eruptions (44).

3.4.Aetiopathogenesis:

The pathogenesis of acne is a multifactorial, but four basic steps have been identified

1) Excess sebum production(seborrhoea)

2) Follicular epidermal hyperproliferation (comedogenesis)

3) The presence and activity of Propionibacterium acnes

4)Inflammation

Lastly ,included in pathogenesisis the role of Matrix metalloproteinases(MMPS) (1,17,32).

3.4.1.Excess sebum production (Seborrhoea):

Active sebaceous glands are a prerequisite for the development of acne (1). Sebaceous activity is predominantly dependent on androgenic sex hormones of gonadal or adrenal origin (1). Abnormally high levels of sebum secretion could thus result from high overall androgen production, increased availability of free androgen, due to a relative reduction of sex hormone binding globulin (SHBG) or an amplified target response mediated either through 5α-reduction of testosterone or an increased capacity of the intracellular receptor to bind androgens (1). Sebum consists of a mixture of squalene, wax and sterol esters, cholesterol, polar lipids and triglycerides (1). Linoleic acid is significantly reduced in epidermal and comedonal lipids, and this may relate to ductal hypercornification(1). Patients with acne produce more sebum than those without acne, although the quality of sebum is same between the two groups (17). Triglycerides, may have a role in acne pathogenesis and broken down into free fatty acids by P.acne, normal flora of the pilosebaceous unit (17). 5α-Reductase, the enzyme responsible for converting testosterone to potent DHT (dihydrotestosterone) has greatest activity in areas of skin prone to acne, the face, chest, and back (17). Recent work has implicated substance P in the pathogenesis of acne (19). Through the promotion of proliferation and differentiation of sebaceous glands. CRH and CRH receptors have been detected recently in human sebaceous glands (19). CRH induces the synthesis of sebaceous lipids in vitro (45) Rosenfield et al. (46) found that sebaceous lipid synthesis is stimulated by the presence of both androgens and peroxisome proliferator-activated receptor (PPAR) ligands. In addition to androgen receptors, PPAR receptors are abundantly present in human sebaceous glands (45). Among them, PPARα has been associated with lipid synthesis. One of the strongest natural PPARα a ligands is the 5-

lipoxygenation product leukotriene B4, whose precursor, arachidonic acid, was shown to induce sebaceous lipogenesis in cultured human sebocytes (45).

3.4.2.Follicular epidermal hyperproliferation: (Comedogenesis)

An important feature in the aetiology of acne is the presence of ductal hypercornification, which can be seen histologically as microcomedones, and clinically as blackheads, whiteheads and other forms of comedones such as macrocomedones. There is a significant correlation between the severity of acne and the number and size of follicular casts (microcomedones) (1). Hyperproliferation of the follicular epithelium leads to formation of microcomedones, which are the first acne lesions and can be found in normal-looking skin (45). The very early stage of acne lesion development, namely the beginning of microcomedones, is associated with vascular endothelial-cell activation and involvement of inflammatory events (45) which corroborates the suggestion that acne may represent a genuine inflammatory disorder without involvement of bacteria in its initiation (45). Comedones are due to abnormalities in the proliferation and differentiation of ductal keratinocytes. They represent the retention of hyperproliferating ductal keratinocytes/ corneocytes in the duct. Androgens may play an important role in comedogenesis. There is a correlation between comedone numbers in early acne and DHEAS levels (1). Cells of the pilosebaceous duct have androgen receptors (1), and 5α-reductase type I is also present in these cells both in health and in disease (1). Many studies showed that IL-1 is present in normal sebaceous glands, IL-1α induced hyperproliferation of follicular keratinocytes (45).

3.4.3. The presence and activity of Propionibacterium acnes:

Acne is not infectious three major organisms have been isolated from the pilosebaceous ducts of acne patients including P. acnes, Staphylococcus epidermidis and Malassezia furfur (1). Among them, P. acnes is the most important one (1). P.acne is a Gram positive, anaerobic, and microaerobic bacterium in sebaceous follicle(18). Adolescence and its attendant seborrhoea are associated with a significant increase in P. acnes numbers (1), The presence and quantity of P. acnes cultured from skin in individuals with and without acne do not always correlate with the existence of acne or its severity (47). P. acnes can prompt the secretion of a variety of cutaneous anti-microbial peptides (AMPs). AMPs include defensins and cathelicidins and mediate their bactericidal or bacteriostatic action through cell membrane disruption (48). Evidence shows that human β-defensin-1 and human β -defensin-2 have been shown to be increased in acne lesions, and the expression of these defensins seems to be proportional to the degree of inflammation(49).

3.4.4.Inflammation:

Propionibacterium acnes may initiate the inflammatory process by producing neutrophil chemotactic factors. Once neutrophils attracted by bacterial chemoattractants reach the inflamed site, they release inflammatory mediators such as lysosomal enzymes and reactive oxygen species (50). The combination of keratin, sebum and microorganism particularly P. acnes leads to release of proinflammatory mediators and accumulation of T-helper lymphocytes, neutrophils and foreign body giant cells. This in turn causes the formation of inflammatory papules, pustules and nodular lesions. Early cellular infiltrate is lymphocytic seen around blood vessels and duct. Within 12-24 hours polymorphonuclear leucocytes appear but lymphocytes remain in the papule as predominant cell infiltrate. Ductal rupture is not a prerequisite for development of inflammation (51). The inflammation represents a classical type IV immunological reaction (1). Direct immunofluorescence studies have shown that there is activation of the classical and alternative complement pathways in early non-inflamed and in inflamed lesions (1). P. acnes produces many enzymes, including three proteases, lipase, phosphatases and hyaluronate lyase which are implicated in the development of inflammation (1). Additionally, P.acnes to stimulate an upregulation of cytokines by binding Toll-like receptors 2 on monocytes and polymorphonuclear cells surrounding the sebaceous follicle. After binding Toll-like receptor 2,pro-inflammatory cytokines such as IL-1,IL-8,IL-12, and tumor necrosis factors-α are released (17). Leukotriene B4 (LTB4) is a pro-inflammatory mediator synthesized from arachidonic acid in the sebaceous gland. LTB4 induces recruitment and activation of neutrophils and monocytes (1), and contributes to the inflammation (2).

3.4.5.Matrix metalloproteinase role:

Papakonstantinou et al (52) investigated the role of MMPs(Matrix Metalloproteinases) in acne. These enzymes, which include collagenases, gelatinases, stromelysins, and matrilysins, have a prominent role in both inflammatory matrix remodeling and proliferative skin disorders. Sebum Includes several MMPs, which are thought to originate in keratinocytes and sebocytes. In addition, oral isotretinoin can reduce concentrations of MMPs in sebum in parallel with clinical improvement (53**).**

3.5.Acne and hormones :

Sebaceous gland activity and sebum production play a central role in the development of acne. The sebaceous gland is hormonally regulated. Several hormones have been linked to acne and may regulate sebaceous secretion. They include androgens, estrogens, growth hormone,

insulin, ,IGF-1, CRH, adrenocorticotropic hormone(ACTH), melanocortins, and glucocorticoids(16).

3.6.Acne and associated disease :

Acne is a feature of several non endocrine and endocrine diseases . The clinical appearance of acne may help guide or suggest the diagnosis in several of these disorders. Non-endocrine disorder including; **Apert syndrome:** which is a rare autosomal dominant congenital disorder caused by a mutation in the gene encoding the fibroblast growth factor receptor 2 (54).The dermatologic hallmark of Apert syndrome is severe inflammatory and comedonal acne involving the face, chest, back, and unusual sites such as the forearms, buttocks, and thighs (55) . It is typically very resistant to treatment but excellent responses to isotretinoin (18). **SAPHO syndrome**: (Synovitis Acne Pustulosis Hyperostosis Osteitis Syndrome) SAPHO syndrome is characterized clinically by any combination of synovitis, acne, pustulosis, hyperostosis, and osteitis (16). The cause is unknown and it is observed primarily in children, young adults, or middle-aged individuals(16). Skin lesions in SAPHO syndrome are characterized by severe acne fulminans or acne conglobata, palmoplantar pustulosis, or pustular psoriasis(58). Treatment including isotretinoin and Infliximab(16). **Behcet Syndrome:** Recurrent oral and genital ulcerations and uveitis are the originally clinical hallmarks of Behcet syndrome. The acne lesions characteristic which are usually combination with arthritis. The preferred sites are the arms and legs being more commonly involved. Treatment is challenging, and multiple therapies may be induce remissions(16). **PAPA syndrome:** (Pyogenic Arthritis Pyoderma Gangrenosum Acne Syndrome) PAPA syndrome is an another acne variant with systemic symptoms(17), is an autoinflammatory disorder characterized by pyogenic arthritis, pyoderma gangrenosum, and acne. It is inherited in an autosomal dominant fashion. However, acne does affect most individuals with PAPA syndrome and is usually severe nodular acne. It begins in adolescence and proceeds into adulthood (56). Management is challenging. Treatment of acne usually requires isotretinoin (56), infliximab and anakinra (17).

Moreover the endocrine disorder associated with acne including: **Polycystic ovarian syndrome:** PCOS occurs in 3% to 6% of the general population also called Stein – Leventhal syndrome (17). It is the most common hormonal disorder in young women. Its diagnosis relies upon the presence of two out of the three following criteria: (1) oligomennorrhea or amenorrhea; (2) hyperandrogenism or (3) polycystic ovaries as demonstrated by ultrasound(57).) The main abnormality in PCOS is increased ovarian production of androgens,

which is mostly likely caused by abnormal regulation of 17α-hydroxylase, the rate-limiting enzyme in androgen biosynthesis (58). The excess ovarian androgens act locally to cause ovarian dysfunction and peripherally to cause acne and other signs of hyperandrogenism such as hirsutism and androgenic alopecia(58). There is an increased risk of diabetes mellitus and endometrial carcinoma(17). HAIR-AN syndrome, a subset of PCOS,the markers of this syndrome are hyperandrogenism, acne, insulin resistance and acanthosis nigricans (17). Screening laboratory tests to evaluate for hyperandrogenism are include serum DHEAS, total testosterone, free testosterone, and luteinizing hormone/follicle stimulating hormone (LH/FSH ratio) (57). Free testosterone is the most sensitive test for hyperandrogenemia and is a marker for ovarian androgens (57). Cushing syndrome, congenital adrenal hyperplasia, androgen-secreting tumors, and acromegaly (16).

3.7.Clinical features:

Acne is a polymorphic disease, which occurs predominantly on the face and, to a lesser extent, occurs on the back and chest (1). The lesions may be either noninflammatory or inflammatory. The noninflammatory lesions are comedos, which may be either open (blackheads) or closed (whiteheads).The open comedo appears as a flat or slightly raised lesion with central dark-colored follicular impaction of keratin and lipid. The closed comedones, in contrast to the open comedones, may be difficult to visualize. They appear as pale, slightly elevated, small papules and do not have a clinically visible orifice (17). Macrocomedones are large whiteheads or blackheads (usually whiteheads) greater than 1 mm in diameter. Secondary comedones may be produced after exposure to dioxins (chloracne), pomades (pomade acne), topical steroids and other drugs (drug-induced acne) (1). Inflammatory lesions may be superficial or deep, and many arise from non-inflamed lesions (1). The superficial lesions are usually papules and pustules (5 mm or less in diameter), and the deep lesions are deep pustules and nodules. The term nodulo-cystic acne is incorrect, as acne ‘cysts’ are not true cysts because they are not lined by an epithelium and is a more appropriate to describe such lesions as nodules (1). Nodules more frequently occur in males and, if exudative or haemorrhagic, are particularly disfiguring and messy. Moreover nodules may extend over areas of a few to many centimetres, and may be remarkably deep with very little surface involvement. Sinus track acne is due to sinus formation between nodules and/or deep pustules and leads to devastating cosmetic effects and scarring (59). The inflammatory lesions vary from small papules with a red border to pustules to large, tender, fluctuant nodules (17). Whether the lesion appears as a papule, pustule, or nodules depends on the extent and location of the inflammatory infiltrate in the dermis (17). Scarring usually follows deep inflammatory lesions, but may often happen after

superficial lesions in scar-prone patients (1). There are four general types of acne scars : ice-pick, rolling, boxcar, and hypertrophic (17). Moreover, there are 3 basic types of atrophic scars have been described include ice-pick scars, rolling scars, and boxcar scars. Ice-pick scars are narrow ≈ 2 mm in diameter, v-shaped, deep, sharply marginated epithelial tracts that extend vertically to the deep dermis or subcutaneous tissue. The depth reaches below conventional skin resurfacing options (60). Rolling scars occur from dermal tethering, with abnormal fibrous anchoring of the dermis to the subcutis leading to superficial shadowing. Rolling scars are usually wider than 4 to 5 mm and although they are shallow, the subdermal tether precludes treatment from the surface above. Boxcar scars have a flat, u-shaped base with sharply demarcated vertical edges, similar to varicella scars, however they are broader than ice-pick scars, round, polygonal, or linear at the skin's surface. Boxcar scars can be shallow (0.1–0.5 mm) or deep (0.5 mm). Although shallow boxcar scars are within the dermal reach of skin resurfacing treatments, deeper boxcar scars are resistant to improvement in the absence of fullthickness treatment of the scar (61).

Hypertrophic acne scars result from excess proliferation of fibrous tissue, and may be hypertrophic or keloidal in nature (60). Hypertropic acne scars remain reasonably within the confines of the preexisting acne lesion. Keloidal acne scars extend significantly beyond the original site of the preexisting acne lesion (62).

3.8.Acne variants:

3.8.1.Neonatal acne :

Neonatal acne is a common condition occur in up to 20 % of healthy newborn., with a male sex preponderance (17,21). Lesions usually appear around 2 weeks of age and resolve spontaneously within 3 months . It is characterized by small, inflamed papules across the nasal bridge and on the cheeks, however comedones formation is absent (17). Although this cutaneous eruption is a consequence of transplacental transfer maternal androgenic hormones . However recent evidence, , points to an etiologic role for Malassezia species and suggests that the disorder be renamed neonatal cephalic pustulosis (63), and some reports have demonstrated positive cultures of the pustules with Malassezia and improvement with ketoconazole cream (17). Treatment is often not required for this self-limiting disorder , but a topical anti-fungal cream may help (1).

3.8.2.Infantile / juvenile acne :

Infantile and juvenile acne , which mainly affects males , presents as facial acne in children between 3 and 24 months , may last up to 5 years of age (1), although, marked by the presence of comedones , papules , pustules, and nodules can also present on the face and scarring may occur even with relatively mild disease (17). Infantile acne very rarely associated with other clinical features of androgen excess such as hirsutism or premature closure of epiphyses (1). It is caused in part by transient elevation of DHEAS produced by the immature adrenal gland. Usually resolves around 1 to 2 years of age. Treatment usually consist of topical retinoids and benzoyl peroxide. Oral therapy with erythromycin, trimethoprim , or isotretinoin can used in severe or refractory cases (17).

3.8.3.Childhood acne :

Childhood acne may evolve from persistent infantile acne or begin after age 2. It is uncommon and has a male predominance. Grouped comedones, papules, pustules and nodules can occur alone or in any combination, usually limited to the face. The duration is variable, from a few weeks to several years and occasionally extends into more severe pubertal acne. Often there is a strong family history of moderately severe acne (21).

3.8.4.Acne conglobata:

Acne conglobata ,a rare but severe form of acne found most commonly in adult males with few or no systemic symptoms. Lesions occurs on the trunk and upper limbs and frequently extend to the buttocks, however, facial lesions are less common. The condition often presents in the second to third decade of life and may persist into the sixth decade. Conglobata acne is characterized by multiple grouped comedones amidst inflammatory papules, tender, suppurative nodules which commonly coalesce to form sinus tracts. Extensive and disfiguring scarring is frequently a feature (29). In addition, malignant change may occur in chronic scars (1). Hidradenitis suppurativa and dissecting cellulitis of the scalp may be seen with acne conglobata, an association known as the follicular occlusion triad(21). Therapy is difficult, options include long-term high-dose antibiotics, colchicine, dapsone and topical therapy. The management of these patients is very difficult and the effect of treatment often temporary. Several medications have been used, including isotretinoin, intensive high- dose therapy with antibiotics, intralesional glucocorticoids, systemic glucocorticoids, surgical debriderment, surgical incision, and surgical excision. In severe cases, high dosage of isotretinoin as 2 mg/ kg

/ day for a 20 – week course may be necessary (17). However, relapse is common and repeated courses of isotretinoin are frequently required (64).

3.8.5.Acne fulminans :

Acne fulminans (also known as acute febrile ulcerative acne) is the most severe form of nodular acne accompanied by systemic symptoms (17). It is an uncommon condition (1). The etiology uncertain but increased response to p.acnes antigens on skin tests , and depressed response to intradermal purified protein derivatives are in favor of an abnormal immuniologic response (64). The patients are predominantly young males (1). The sudden appearance of massive, inflammatory, tender , oozing , friable , plaques with hemorrhagic crusts characterize acute fulminans. The lesions predominate on the back and chest, however, the face is often not involved this lesion rapidly become ulcerative, and heal with scarring (17). Associated features are fever , polyarthropathy , marked leukocytosis , weight loss , anorexia and general malaise, moreover painful splenomegaly (1) , erythema nodosum (1) and bone pain due to aseptic osteolysis have also been reported (1).

3.8.6.Excoriated acne :

Also known as pickers acne and acne excorie des jeunes fills (21), as the names suggests, occurs primary in young women who picking at their skin, although males may also be affected. Mild acne may be present and is accompanied by extensive excoriations. Comedones and papules are systemically and neurotically excoriated leaving crusted erosions that healed with scar (17). This condition may be a sign of depression or anxiety with an obsessive – compulsive symptom (21). Antidepressants and psychotherapy can be helpful in treating these patients (17).

3.8.7.Mechanical acne : (Acne mechanica)

Acneiform eruptions have been observed after repetitive physical trauma to the skin such as rubbing . This can occur from clothing or sport equipment (17). It is present as a well- defined, lichenified, hyperpigmented papules or plaque interspersed with comedones (17). The mechanism of mechanical acne is unclear. Most patient have a tendency to develop acne and its localization may be caused by an irritant dermatitis of the upper part of the pilosebaceous duct or excessive hydration at that site (1). Treatment is the same as for other forms of acne but, in addition, advice on removal of the causative stimulus is essential (1).

3.8.8.Occupational acne :

3.8.8.1. Oil and tar acne :

This acneiform eruption occurs in areas of skin that are in contact with oils and crude tar (65). Men are more often affected than women, the skin lesion may show comedones and only occasionally frank superficial inflammatory lesions. Lesions can occur within 6 week of exposure on almost any site, but the thighs and lower arms are especially prone (1).

3.8.8.2. Chloracne :

This variant is follows exposure to certain toxic, chlorinated hydrocarbons (1). Chlorinated hydrocarbons are found in fungicides, insecticides, and wood preservatives (17). Chloracne lesions consist of multiple comedones, however inflammatory lesion are infrequent (66). Comedones are often localized on both sides of face, especially the temporal regions, but severe cases may occur on other parts of the body (1). Chloracne classically affects the malar, retroauricular, and mandibular regions of the head and neck as well as the axillae and scrotum (17). Other skin lesions may also occur, including porphyria-like changes, pigmentation, hypertrichosis and palmar and plantar hyperhidrosis (1). Systemic abnormalities are less frequent, and include fatigue, anorexia, neuropathy, impotence, disturbed liver function and hyperlipidaemia (1). Often chloracne and the systemic disturbance may last for many years following exposure (1). Topical therapy with retinoids, long-term oral antibiotic therapy may be needed for inflammatory lesions (1), however a oral isotretinoin does not help (1).

3.8.9.Tropical acne (hydration acne) :

Tropical acne is unusually severe acne occurring in the tropics during the seasons when the weather is hot and humid (21), or in scorching occupational environments (17). Tropical acne occurs mainly on the trunk and buttocks with sparing of the face (17,21). It has many deep, large, inflammatory nodules with multiple drainage areas, resembling acne conglobata (17). It is thought that hydration of pilosebaceous duct pores precipitating inflamed lesions(1). Secondary infection with coagulase – positive staphylococci almost always ensues (17). Systemic antibiotics must be given, moreover more important is removing the patient to a cooler environment (17).

3.8.10.Acne with solar comedones : (Senile comedones, Favre – Rocouchot syndrome)

This form of acneiform eruption seen in elderly people, especially in the periorbital areas (1). It is has been estimated to occur in 6 % of persons more than age 50 years (17). Most patients have had high exposure to ultraviolet radiation, and solar damage to the supporting dermis allows the pilosebaceous duct to become more easily distended with impacted corneocytes (1). Clinically, there are multiple, open, and sometimes closed, comedones superimposed on a sun-damaged skin, usually symmetrically affecting the periorbital areas and cheeks, rarely the lesions are unilateral (67). It can be treated with oral or topical retinoids as well as comodonal extraction and Genitle electrocautery (1,17).

3.8.11.Externally induced acne :

3.8.11.1.Cosmetic acne:

This variant of acne occurs because of the greater use of potentially comedogenic cosmetics (1). The lesions characteristically occur in the perioral area of mature females, especially those who had acne as adolescents and used cosmetics for a long time (1). Compounds such as lanolin, peterolatum, vegetable oils, laureal alcohol, butyl stearate, and oleic acid, are known to be comedogenic substances. Over recent years, cosmetic products have been specifically formulated as noncomdogenic, and more critical evaluation of the problem suggests that it is an infrequent cause of acne (64). Treatment with topical retinoids or benzyl peroxide is usually successful (1).

3.8.11.2. Pomade acne :

Pomades are greasy preparation used to deffriz curly negroid hair .The rash similar to cosmetic acne and consists predominantly of many non-inflamed lesions around the forehead and other areas and may extend into hairless skin (1). It may also coexist with true acne. Restriction of the use of pomades is essential , and the treatment of choice is with topical retinoids (1).

3.8.11.3.Detergent acne :

This uncommon form of acne develops in patients who wash many times each day, in the mistaken hope of improving their existing acne. Trauma and the alkalinity of soap are likely to be involved in the mechanism. Several bacteriostatic soaps contain weak acnegenic compounds, such as hexachlorophene (1). Pustular and papular lesions are most noticeable (1).

3.8.12.Gram – negative folliculitis :

Gram – negative folliculitis occurs in patients who have had moderately inflammatory acne for long periods and have been treated with long- term antibiotics, mainly tetracyclines (21). The lesions appear as either papulopustules concentrated around the nose or as deep-seated nodules. Culture of these lesions may reveal Enterobacter, Klebsiella, or Escherichia in papopustules or Proteus in the nodules (17). Therapy usually involves stopping the current antibiotics and replacing them with either ampicillin or trimethoprim, the response usually slow and relapse is common. Isotretinoin is the treatment of choice (1).

3.8.13. SAPHO Syndrome:

SAPHO syndrome is characterized clinically by any combination of synovitis, acne, pustulosis, hyperostosis, and osteitis (16). The cause is unknown and it is observed primarily in children, young adults, or middle-aged individuals (16). Chronic multifocal recurrent osteomyelitis is a common feature and mostly affects the sternum, pelvis, lower jaw, and clavicles. The osteomyelitis is usually sterile or may show presence of Propionibacterium acnes (16). The disease may represent an immune reaction to particularily skin or bacterial antigen (1). Skin lesions in SAPHO syndrome are characterized by severe acne fulminans or acne conglobata, palmoplantar pustulosis, or pustular psoriasis (16). To manage musculoskeletal symptoms, steroidal and nonsteroidal antiinflammatory drugs are the mainstay of therapy. For acne and palmoplantar pustulosis, retinoids, isotretinoin and Infliximab has been used with success (68).

3.8.14. PAPA Syndrome :

PAPA syndrome , another acne variant with systemic symptoms (17), is an autoinflammatory disorder characterized by pyogenic arthritis, pyoderma gangrenosum, and acne. It is inherited in an autosomal dominant fashion and is caused by a mutation in the CD2 binding protein 1 (56,69). Manifests clinically during childhood with recurrent and destructive arthritis (69). Pyoderma gangeronsum does not always present in affected individuals (16). However, acne does affect most individuals with PAPA syndrome and is usually severe nodular acne. It begins in adolescence and proceeds into adulthood (56). Management is challenging. Treatment of acne usually requires isotretinoin (56,69). There are reports of successful treatment with infliximab and anakinra (16).

3.8.15.Acne aestivalis :

Also known as Mallorca acne , this a rare form of acne starts in spring , progresses during the summer , and resolves completely in the fall (21). It is a monomorphous eruption, consist of multiple, uniform, red, popular lesions seen after sun exposure (17). Comedones and pustules are absent or sparse (21). Almost all cases have occurred in women, mainly 20 to 30 years old. The lesions are common on the shoulders, arms, neck , and chest (17). Acne aestivalis does not response to antibiotics but benefits from application of retinoic acid (21).

3.8.16.Hidradenitis suppurativa : (Acne inversa)

Hidradenitis suppurativa is a chronic disease characterized by recurrent abscess formation, primarily within the folded areas of skin that contain both terminal hairs and apocrine glands (21). It' s histological studies reveal the follicular hyperkeratosis is followed by rupture of the follicular epithelium, and release of keratin, sebum, bacteria, and hairs into the dermis. The resulting Inflammatory process engulfs the apocrine gland, leads to rupture of the overlying skin, fibrosis, and sinus tract formation Secondary bacterial infection with Staphlococcus aureus(S.aureus), Streptococcus pyogenes, and various Gram-negatlve organisms may occur (21). It is occasionally associated with severe nodular acne, often of the conglobate type (1). There is often a family history and the onset is usually in late adolescence; the disease may persist up to the age of 40 or 50 years (70,71). It is a post-pubertal process that affects women approximately four times as often as men. Affected patients are often overweight (21). It is a persistent disease that affects the axillae, breasts, and the genital and perianal areas, and may sometimes spread extensively on to the buttocks and lower back (1). There is clinical evidence of comedones (often polyporous), papules, pustules, deep nodules, large abscesses, sinus track formation and scarring. There is much discharge from the inflammatory lesions, which makes the simple activities of sitting, walking, working and sexual relationships at times almost impossible. Pain is a common feature; the foul smell is often (1). Aetiological factors such as hyperandrogenism, obesity, smoking and local irritation which may be relevant aggravating factors (1). Therapeutic options include long-term antibiotics as used in acne but in high doses, topical retinoids, topical antiseptic washes, oral isotretinoin, oral zinc, and potent topical, intralesional and intermittent pulsed oral steroids. More recently, finasteride 5 mg/day has been reported to be successful (1) as has infliximab (71).

3.8.17.Acne keloidalis : (nuchae)

Acne keloidalis is most frequently encountered in young adult black (21). It is not associated with acne vulgaris and is a primary cicatricial alopecia variant (21). Clinically distinctive lesions begin as follicular pustules and papules and progress to persistent firm papules or coalesce into hairless keloid-like plaque (17). Mild form may be treated with topical or intralesional corticosteroids or systemic antibiotics , and / or cryotherapy (17). Severe form Surgical excision of affected skin and CO2 laser therapy are the most effective treatment (17,21).

3.8.18.Acne miliaris necrotica: (Acne Varioliformis)

The primary lesion in acne miliaris necrotica is a pruritic or painful erythematous follicular based- papule that develops central necrosis and crusting and heal with a varioliform scar (17). The lesions are concentrated on the nose, forehead, and anterior scalp, but may spread primary to the trunk. It has a chronic course (17). Possible treatments include systemic antibiotics and oral isotretinoin (17).

3.8.19.Virally induced acne :

Acne can occur at unusual sites and at unusual ages with little involvement of commonly affected sites. An acneiform rash has been reported at the site of previous herpes zoster infection. A very small number of patients with severe acne and significant glandular fever responded poorly to oral antibiotics and oral isotretinoin. It was proposed that the viral illness in some way played an important role in the poor response (72).

3.8.20.Pyoderma faciale : (Rosacea fulminans)

This was initially believed to be a variant of acne but it is suggested that it is more related to rosacea (73). It is uncommon, and occurs in patients who usually have mild skin disease that suddenly erupts producing many pustules and nodules, especially on the face. However it mainly affects post-adolescent women (aged 20– 40 years), often following a period of stress (1). It is distinguished from acne by the absence of comedones, rapid onset, fulminating course, and absence of acne on the back and chest (20). In contrast to acne fulminans, there are usually no systemic symptoms (1). Rosacea fulminans has been reported in association with Crohn's disease (1) and daily ingestion of high-dose vitamin B supplements (73). Oral antibiotic treatment is ineffective, however treatment with low does isotretinoin alone or in combination with oral glucocorticoids . clofazimine for 4 to 5 month have been reported beneficial (17).

3.8.21.Vasculitic / pyoderma gangrenosum acne :

This variant of acne occurs in a few patients, who previously had very mild acne, which developed the sudden onset of severe vasculitic, pyoderma gangrenosum-like lesions (1). Very significant scarring is the inevitable consequence (1). It is probably an immunological reaction to p.acne. Such patients appear to be unresponsive to oral isotretinoin alone, but in combination with oral steroids and azathioprine (1).

3.8.22.Drug – induced acne / acneiform eruption (acne medicamentosa):

By definition, acne medicamentosa is acne caused or aggravated by medications, drug-induced acne is characterized by a monomorphic eruption of papules and pustules, and classically involves the trunk rather than the face, moreover open and closed comedones are typically absent. Corticosteroids, orally, topically, intranasally, intrathecally and ACTH by injection, may provoke an acneiform reaction (74). A follicular eruption may appear as early as 2 weeks after initiation of systemic or topical steroids (17). Although discontinuation of the steroid is the primary treatment, conventional acne treatments including retinoid and antibiotics are also beneficial (16).

3.8.22.1.Lithium :

Several studies of adverse side effects of lithium demonstrate that acne may affect 33% to 45% of patients treated with lithium (75). Acne lesions may involve typical sites of acne vulgaris but may also present on the legs and arms (16). Management with topical or oral antibiotics are usually effective (75).

3.8.22.2.Isoniazid :

Isoniazid is known to cause an acneiform eruption consisting of inflammatory pustules with open and closed comedones. The onset is abrupt and there is greater predominance of comedones than inflammatory lesions. Patients who are slow acetylators are more common affected (16).

3.8.22.3.Phenytoin :

The antiepileptic drug phenytoin caused increased levels of testosterone , resulting in hyperandrogenism (76), which ultimately stimulates the pilosebaceous unit (76-77). In one study, 80.3% of patients on phenytoin developed acne compared with 30.2% in non-epileptic females (77).

3.8.22.4.Iodides and bromides :

Iododerma refers to skin lesions caused by exposure to substances with iodine. Tender pustules that coalesce into crusting plaques and nodules are hallmark of iododerma . The face , along with regions high in sebaceous activity, is primarily affected (16). In contrast to acne vulgaris, all people and all ages were affected(1). Antibiotics and removal of the offending agent are beneficial (16).

3.8.23.Epidermal Growth Factor Receptor Inhibitor – association eruption :

EGFR inhibitors are a class of antineoplastic drugs which includes gefitnib, cetuximab, erlotinib, and trastuzumab. They are commonly used in treatment of carcinomas of lung, breast, and colon (16). A perifollicular, papulopustular eruption on the face and upper torso is frequently associated with use of these drugs and used to assess response to drug clinically (17), however comedones are not present (78) .It occurs as quickly as 7 days after initiation of treatment (78),and it occurs in up to 86% of patients(17). Although the etiology is not completely understood, it is thought to result directly from EGFR blockade of the hair follicle (79). Rapid response to conventional acne treatment such as benzyoyl perioxide, retinoids, and topical or oral antibiotics has been reported (78,79).

24.Folliculitis on the scalp and acne:

3.8.24.1.Scalp folliculitis :

About 1% of acne patients complain of, or are found on examination to have, small papules or pustules in the scalp. Patients receiving treatment with oral isotretinoin may develop a pustular scalp folliculitis, which is either due to S. aureus infection or may arise for unknown reasons (1).

3.8.24.2.Folliculitis decalvans :

Folliculitis decalvans is a chronically progressive disorder of the hairy scalp that leads to scarring alopecia and atrophy (80–81). The aetiology is unknown (1). In some patients, it is associated with very severe acne often acne conglobata and hidradenitis suppurativa, forming part of the so-called poral occlusion triad (1). Staphylococcus aureus is usually cultured from these pustules, but whether this is a primary or secondary process is unclear (17). Systemic antibiotics, particularly in combination with rifampin, systemic and /or topical steroids, and systemic retinoids may also helpful (17).

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3.8.24.3.Dissecting folliculitis of the scalp (perifolliculitis capitis abscedons et suffodiens):

This condition is more frequently seen in Afro-Caribbean males (82–83). It is a chronically progressive inflammatory disease of the scalp similar to nodular acne of the face and trunk (1). The primary lesions are follicular and perifolllcular erythematous papules which progress to abscesses. This disease is likely a variant of acne vulgaris; it closely resembles acne conglobata and hidradenitis suppurativa. Coagulase-positive S.aureus may be found in the lesions (21). The pathogenesis is occlusion of the follicular pores and a subsequent granulomatous response to the ruptured duct contents (1). The lesions characteristically last many years and are cosmetically very unpleasant, painful and foul smelling (82). Response to therapy is poor(1), however some cases reported success with oral isotretinoin, systemic antibiotics, systemic steroids, and dapsone (17). Surgical incision and drainage, excision with grafting, /or x-ray epilation are occasionally used for refractory cases (17).

3.9.Laboratory tests (investigations) :

The majority of patients will have a negative medical illness history and examination will revealed no abnormality except acne lesions, thus requiring no further workup. Endocrinologic testing is indicated in the presence of acne and evidence of androgen excess, or when patients show no abnormal signs and symptoms but have recalcitrant acne when hormonal manipulation is unsuccessful (15).

Normal total testosterone and DHEAS obtained 2 weeks prior to the onset of menses, along with imaging may exclude an androgen secreting tumor of the adrenals or ovaries. DHEAS levels may be normal in late-onset congenital adrenal hyperplasia (LOAH) and highly elevated in adrenal tumors (21). Testosterone levels may be high in patients with ovarian tumors (21). Measurement of LH and FSH and free testosterone may add to clinical suspicion of PCOS (21). Testosterone levels may be high in patients with PCOS with an associated increased LH/FSH ratio(>3)(21). LOAHis typically associated with elevation in 17-hydroxyprogesterone (21). SHBG can be measured and is increased with oral contraceptive pills, moreover hyperprolactinemia is not uncommon in hyperandrogenic patients and must be excluded prior to diagnosis of PCOS (84).

However, the possibility that other hormones may affect the sebaceous glands, either directly or by enhancing their response to androgens, should not be neglected as in acromegaly, the rate of sebum excretion is high and correlates with skin thickness and GH levels (1).

3.10.Complications:

All types of acne lesions have the potential to resolve with sequale . Almost all acne lesions leave a transient macular erythema after resolution (17), moreover in darker skin types, post-inflammatory hyperpigmentation may persist months after resolution of acne lesions (17). However, in some individuals, acne lesions may result in permanent scarring (17).

3.10.1. Osteoma cutis : Calcification, is an uncommon complication of acne and usually needs treatment (86). The calcification occurs in areas of inflammation and presents as small 2-4 mm persistent papules, which are slightly firm to touch and usually skin or ivory coloured. The lesions are often suspected to be persistent closed comedones. The only successful treatment is carbon dioxid laser therapy (1).

3.10.2. Pyogenic granuloma: Pyogenic granuloma is a rare complication of healing severe nodular and acne fulminans (1), and occur more frequently following high-dose of isotretinoin therapy (1). The lesions can be either be left alone or, if single treated with cautery .Moreover multiple lesions, usually responsed to clobetasol priopionate cream topically twice daily over a 2-3 week period (1).

3.10.3. Solid facial edema: It is a persistent ,firm facial swelling that is an uncommon, though distressing ,result of acne vulgaris or acne rosacea. Both corticosteroids and isotretinoin have been reported to be effective treatment (21).

3.10.4. Recent evidence has shown that acne results in significant psychological problems, such as stigmatization from peers, lower self-esteem, interpersonal difficulties, anxiety, depression and higher unemployment rates (86). Severe psychological consequences such as depression, eating disorder and body dysmorphic disorder are common among people with acne (87).

3.11.Histopathology:

Biopsy of lesions in acne vulgaris is not needed as it is a clinical diagnosis. Comedones reveal a thinned epithelium and a dilated follicular canal filled with lamellar lipid-impregnated keratinous material. In pustular cases there are folliculocentric abscesses surrounded by a dense inflammatory exudate of lymphocytes and polymorphonuclear leukocytes. In addition to these finding, indolent nodular lesions frequently show plasma cells, foreign body giant cells, and proliferation of fibroblasts. Epithelial-lined sinus tracts may form (21).

3.12.Differential diagnosis :

The diagnosis of acne is usually straight forward, although some conditions may occasionally confused with acne (88).

3.12.1.Rosacea:

A disease characterized by lacks of comedones, nodules, or scarring and occurs in older patients. The presence of facial flushing that is induced by heat, hot food or alcohol is a useful pointer towards a diagnosis of rosacea. Patients may also have occular involvement, but rarely have truncal lesions (1).

3.12.2.Milia:

They are characteristic white papules on a background of non-inflammed skin may resemble closed comedones (88). They are predominantly infraorbital in distribution and are whiter (1). They are very common and can occur in association with, although unrelated to, acne (1).

3.12.3.Perioral dermatitis:

Is a common acneiform disorders in children and young adults, and This condition characterized by papules and pustules, typically without comedones, that are usually distributed near the eyes, nose, and mouth (88).

3.12.4.Bacterial folliculitis:

Clinically appears as erythematous papules and pustules that rarely mistaken for acne. These lesions typically involve the buttocks and posterior thighs of diaper wearing children,however, they may also appear in other locations (88).

3.12.5.Pityrosporum folliculitis:

It is likely, but unproven, to be host reaction to Malassezia furfur, which is normal skin commensal (89). Presents on the upper trunk as moderately ill-defined superficial plaques among which are scattered many papules or pustules (1). It does not usually response well to isotretinoin (1), moreover response to topical imidazoles is often poor (1). This disorder may be distinguished from acne by the absence of facial lesions and by positive potassium hydroxide test result (88).

3.12.6.Demodex folliculitis:

They present as a persistent acne-like eruption on the face that does not respond to acne therapy (88). Best diagnostic help is the therapeutic response to metronidazole or topical permethrin (1).

3.12.7.Plane wart:

Particularly on the face can also cause confusion with acne (1).

3.12.8. Pseudofolliculitis barbae:

This is a disorder more common in black men, which appear as a small, fragile, dome-shaped pustule occurs at the infundibulum (ostium or opening) of a hair follicle often on the bread area (17).

3.12.9.Acneiform drug eruptions:

Unlike acne vulgaris, drug induced acne is characterized by monomorphic eruption of papules and pustules, and classically involves the trunk rather than the face. Open and closed comedones are typically absent (16).

3.12.10.Keratosis pilaris:

A common disorder in pediatric dermatology practice, is characterized by hyperkeratotic papules, associated with hair follicles typically involving the cheeks, outer arms, and dorsal thights (88). This condition usually confused with acne when it is inflammatory (88).

3.12.11.Angiofibromas:

Formerly referred to as adenoma sebaceum, are encounter in the setting tuberous sclerosis, an autosomal dominant multiple hamartoma syndrome (90). These papules may resemble to acne, but are typically translucent are located in mid facial region, generally appear earlier than acne typically at approximately 4-6 years of age and are not accompanied by comedones (88).

3.12.12.Acne necrotica (varioliformis):

Is associated with itching and small-pox like scars, usually on the trunk. Biopsy shows a necrotizing lymphocytic folliculitis (1). It can be mistaken for severe acne excoriée, but the response to isotretinoin can be excellent (91).

3.12.13.Zinc deficiency:

The severe papulopustular eruption associated with zinc deficiency can be mistaken for marked acne and several cases have been reported after prolonged intravenous feeding without zinc supplementation (1).

3.13.Treatment :

The choice of acne treatment is based principally on the type of acne lesions and the severity of acne. In addition, the presence of scarring and/ or significant psychiological and social disability may be indication for more aggressive therapy relative to the acne grade (64).

3.13.1. Topical treatments:

3.13.1.1.Topical retinoid:

Topical retinoids are the mainstay of acne treatment because they treat comedones , which are the primary lesions in acne (19). Topical retinoids prevent the formation of new comedones and inflammatory lesions, they also have anti-inflammatory properities (92), many studies have shown similar effects of adapalene, tretinoin, and tazarotene (93-94). Maximal clinical improvement is usually seen within 3-4 months. The major adverse effects associated with topical retinoid use include burning, irritation, scaling, and redness (89).

3.13.1.2.Topical antimicrobials/antibiotics:

Available antimicrobials/antibiotics include benzyl peroxide, clindamycin, erythromycin, sodium sulfacetamide, and azelaic acid. Topical antimicrobials and antibiotics are useful in the treatment of mild to moderate inflammatory acne (95).

Benzyl peroxide ; is a topical bactericidal agent that reduces P. acnes by generating reactive oxygen species in the sebaceous follicle. It is available in various preparations ranging from 1 to 10% (96). It recommended that erythromycin and clindamycin be used concomitantly with topical benzyl peroxide. Patients may be instructed to use one product in the morning and one in the evening (53). Combination therapy usually eliminates or reduces bacterial resistance moreover,it is more effective than either the individual components alone (97).

Sodium sulfacetamide ; is an antibacterial agent. It is available in topical lotions and medicated pads at concentrations of 10%. Sodium sulfacetamide can also be formulated with 5% sulfur, which has both keratolytic and antibacterial proprieties, as a lotion or wash (89).

Azelaic acid ; is a naturally dicarboxylic acid that has been used in the treatment of acne, as well as benign pigmentary disorders. It possesses bacteriostatic activity against P. acnes, as well as anti-inflammatory properties. Azelaic acid is also a natural inhibitor of tyrosinase, which explains its efficacy in treating hyperpigmentation (96).

3.13.3.Others topical agents :

Dapsone ; is a synthetic sulfone with both antiinflammatory and antimicrobial properties (95,98). Recently, a new topical formulation, dapsone 5% gel was approved by the FDA as a new therapy for inflammatory acne (99). It has been proposed that its action may be the result of a direct inhibition of leukocyte trafficking and the generation of chemical mediators of inflammation by leukocytes. Alternatively, it might act indirectly in acne by altering the levels and /or activity of propionibacteria (100).

Picolinic acid gel 10% ; picolinic acid is an intermediate metabolite of the amino acid tryptophan . It has antiviral, antibacterial, and immunomodulatory properties. It is safe and effective treatment for inflammatory and non inflammatory lesions in patients with mild to moderate acne vulgaris (101).

Salicylic acid ; Its comedolytic properties but less potent than topical retinoids. It often is used when patients cannot tolerate a topical retinoid because of skin irritation (97).

3.13.2.Systemic treatments :

3.13.2.1.Antibiotics:

Antibiotics such as tetracyclines (oxytetracycline, tetracycline chloride, doxycycline, and minocycline), trimethoprim, and macrolide antibiotics(erythromycin) have been a mainstay of treatment for moderate and severe acne and treatment resistant forms of inflammatory acne (98).

Lymecycline:

Lymecycline is a second-generation, semisynthetic tetracycline, with improved oral absorption, enhanced tissue penetration, and slower elimination than tetracycline (98).

Azithromycin:

Azithromycin is a methyl derivative of erythromycin that effectively inhibits significant intracellular pathogenesis, as well as Gram-positive and Gram-negative aerobic and anaerobic

bacteria, including p.acne (98).It has been found to be effective in treating noninflammatory and inflammatory acne lesions (102).

Doxycycline:

Doxycycline at a subantimicrobial dosage have been shown to reduced both inflammatory and noninflammatory lesions, however no resistant strains of p.acne has been repoted (103).

Minocycline:

Minocycline was approved by the US food and drug Administration (FDA) for moderate to severe inflammatory acne vulgaris in patients over 12years old (98).

3.13.2.2.Isotretinoin:

Systemic isotretinoin(13-cis retinoic acid) has revolutionized the treatment of severe acne. It is the only drug that targets all four pathogenic factors of the disease, and is the most inhibitor of sebum production (98). Isotretinoin is approved for the treatment of severe nodular acne, it is also useful for acne that either treatment resistant or producing physical or psychological scarring (97). Isotretinoin is recommended at a dosage at 0.5-2.0 mg/kg/day. Although it may cause initial flaring, this can be minimized with a beginning dosage of less than 0.5mg/kg/day, for longer time periods, for cumulative dosage of 120-150mg/kg (104). Its most serious adverse effect is teratogenicity and the risk of severe damage to the fetus (21), and other side effects include those of the mucocutaneous, musculoskeletal, and ophthalmic systems, as well as headache and central nervous system effects. Most of the adverse effect are temporary and resolve after drug is discontinued (105).

3.13.3.Hormonal therapy:

Oral contraceptives:

Oral contraceptive become accepted therapeutic alternative for the treatment of acne in woman. All combination oral contraceptive pills have a net effect of increasing SHBG and decreasing circulating free testosterone and therefore, have the potential to improve acne (106). The third-generation progestins, desogestrel, norgestimate, and gestodene have the lowest intrinsic androgen activity (17). Two oral contraceptives are currently FDA approved for the treatment of acne (Ortho tri-Cyclen and Estrostep) (17).

Spironolactone:

Spironolactone is an anti-androgen its effects by blocking androgen receptors at higher doses (97).

Cyproterone acetate:

Cyproterone combined with ethinyl estradiol(in form of an oral contraceptive) have been found to be effective in treatment of acne in females (97). Higher doses have been found to be more effective than lower doses (97).

Flutamide:

Flutamide, a non-steroidal antiandrogen, but its use is limited because of the potential of hepatic failure (97).

Oral corticosteroids:

Because of their anti-inflammatory activity, high-dose systemic glucocorticoids may be benefit in the treatment of acne (17). One study demonstrated that low dose corticosteroids suppress adrenal activity in patients who have proven adrenal hyperactivity (97).

Metformin (Insulin sensitizing agents)

Metformin, a biguanide, is the most commonly used insulin sensitizer for treatment of PCOS. At dosage 1500mg daily for 14 months has been shown to reduce hirsutism in women PCOS, and improved mild acne, with no changes in sebum excretion rates (107). Metformin treatment resulted in a decline of insulin, as well as total and free testosterone, thus leading to improvement of clinical signs of hyperandrogenism, such as acne (108).

3.13.4.Miscellaneous therapy:

Intralesional steroids: Intralesional corticosteroid injections are effective in treatment of individual acne nodules (97).

Chemical peels:

Both glycolic acid-based and salicylic acid-based peeling preparations have been used in the treatment of acne (97).

Cemedo removal:

Cemedo removal may be helpful in the management of comedones resistant to other therapies (97).

3.13.5.Phototherapy and laser:

Light, laser, and photodynamic treatments are all currently being utilizing in the treatment of acne. Blue and red light target different pathogenetic factors in acne. Blue light(405-420nm) reacts with porphyrins produced by p.acne, creating reactive oxygen species that damage the bacteria cell wall and cause bacterial death. Red light (660nm) is anti-inflammatory. Both wave lengths of light may improve acne in some individuals (106).

3.13.6.Photodynamic therapy (PDT):

Photodynamic therapy involves the use of a photosensitizer along with a light source. Photosensitizer that can be used for PDT include aminolevulinic acid(ALA)and methyl aminolevulinate(MAL). Light sources that can be used include a blue light, red light or intense pulse light (53). ALA- and MAL-PDT seem to be an efficient treatment for inflammatory acne (98).

3.13.7.Diet:

Dietary intervention using low glycemic load carbohydrate may have therapeutic potential in the treatment of acne because of the beneficial endocrine effects these diets possess. A large interventional study has demonstrated that diet rich in low glycemic foods reduced serum testosterone and fasting glucose while improving insulin metabolism and increasing SHBG (33). These endocrine changes are consistent with those known to promote normal follicular cell proliferation and to reduce sebum production (33).

3.14.Treatment for acne scars:

3.14.1.Topical and injectable:

Topical or injectable treatments that have been suggested for prevention or treatment of scarring include vitamins A, E, C; zinc; colchicines; corticosteroids; hyaluronidase; cyclosporine; honey; onion extract; 5-fluorouracil; bleomycin; retinoids; verapamil; pepsin; hydrochloric acid; and formalin (109-110). Vitamin E is a major lipophilic antioxidant in plasma, membranes, and tissues, and has been used for its anti-inflammatory effects. Vitamin C is also known to have anti-inflammatory activity. Topical vitamin C has been shown to

enhance collagen production in human skin and has also been reported to stimulate collagen synthesis. Zinc is an element that is required in wound healing, and has been shown to reduce the cellular and genetic damage caused by oxidative stress and enhance resistance to skin fibroblasts. Topical retinoids have been used to improve the appearance of keloids, hypertrophic scars, and superficial scars (109). Intralesional corticosteroid injection can be used for hypertophic scars and keloids (110). Corticosteroids exhibit multiple immunomodulatory and anti-inflammatory properties that reduce the expression of cytokines, cellular adhesion molecules, and other enzymes related to the inflammatory cascade (110). Intralesional triamcinolone injections can help to decrease the production of collagen, decrease inflammation, and stimulate collagen resorption (110).

3.14.2.Surgical management:

Surgical management is the best route for ice-pick, rolling, and boxcar scars. Many surgical procedures have been used including: punch excision, punch grafting, radiofrequency ablation, nonablative laser resurfacing, dermal filler, and dermal grafting and chemical peels (62).

3.14.3.Laser Resurfacing:

Both ablative and nonablative lasers are used for treatment of acne scarring. Ablative lasers include CO2, erbium:YA G, and Fraxel lasers. These lasers emit high-energy pulses of light to remove thin layers of skin, with little thermal damage to the adjacent tissue. Ablative lasers produce epidermal ablation, thermal contraction of the dermis, upregulate type I collagen fibers, and promote dermal remodeling (111). Distensible, undulated acne scars respond better to ablative effects of the CO2 laser because the more extensive thermal injury produces greater collagen shrinkage and skin tightening (111). Nonablative are Q-switched neodymium: yttrium-aluminum-garnet (Nd:YAG) laser treatment was found to smooth the surface, decrease stiffness, and increase compliance (17).

3.15.Course and prognosis:

The disease usually appears in adolescences, the period in which sexual hormones increases, simultaneously and usually disappears in the second half of the third decade of life (112). Acne develops earlier in females than males (1), which may reflect the earlier onset of puberty (1). However, to some degree, acne may persist beyond adolescence in a significant proportion of individuals, particularly women (29). Younger men tend to have an oiler complexion and more severe widespread disease than young women. Women may experience a flare of their papulopustular lesions a week or so before menstruation (21). Even after the disease has ended,

acne scars and dyspigmentation are not uncommon permanent negative outcomes (53). The course is one several years´ duration followed by spontaneous remission (17). The extent of involvement varies and spotaneoues fluctuations in the degree of involvement are the rule than exception (17) Over all, the prognosis for acne favorable (17). Successful and early treatment of acne is very important and delayed or failure in treatment causes probably irretrievable sequele (112).

4.Aim of the study :

The aim of this study is :

To evaluate the epidemiological and clinical features of acne vulgaris in Libyan patients attending dermatology department in Benghazi.

5.Patients and methods:

5.1.Patients:

In this prospective open-non controlled study a total of 150 Libyan patients with the clinical diagnosis of acne vulgaris attending dermatology department at Aljomhoria hospital in Benghazi – Libya over one year y from Jan. 2011 to Dec. 2011 were enrolled in this study.

5.2.Methods:

Each patient was subjected to thorough a detail history and clinical examination according to the prepared appendix I, II.

Exclusion criteria included non Libyan patients, drug induced acne and other acneiform eruptions. The parameters evaluated included age, gender, marital status, occupation, age of onset, duration of acne, family history of acne, aggravating factors, dietary relation, history of smoking, relation to menstrual cycle, marks of androgenicity, seasonal variation, previous or current acne treatment and past medical and drug history, skin photo type, type of acne scar, post-acne hyperpigmentation.All patients were examined under good illumination using magnified lens.

Grading of acne vulgaris was done by using the Global Acne Grading System (GAGS) (113). This grading divided the face, chest and back into six locations (forehead, each cheek, nose, chin, chest and upper back) The six locations are graded separately on a 0–4 scale depending on the most severe lesion within that location (0= no lesions, 1= comedones, 2= papules,3= pustules and 4= nodules). The score for each area is the product of the most severe lesion, multiplied by the area factor i.e local score = factor x grade (0–4). These individual scores are then added to obtain the total score. For the total score between 1 and 18, the patient is classified as mild while for the total score between 19 and 30, the patient is classified as moderate. If the total score is between 31 and 38, then the grade is severe and if more than 39 then it is very severe . We calculated Body Mass Index (BMI) from weight (in kilogram) divided by height in square meter(m^2). (underweight <18.5, normal 18.5-24.99, overweight 25-29.99, obese 30-34.99, morbid obesity ≥35)

5.3.Statistical analysis:

Data was analyzed using SPSS (Statistical package for social science) version 18. Descriptive statistic: Mean , median, mode and standard deviation , minimum and maximum value were calculated. Analytic statistic: x^2 test & was used to compare the distribution of the variables , t-test was used to compare the means of two group , difference will be considered significant when p value ≤ 0.05 .Data was presented in tables and figures.

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6.Result:

A total of 150 patients with acne vulgaris were included in the present study; 103(68.7%) of the patient were female, their mean age ± SD was 21.7±4.9 years and 47(31.3%) of the patient were male as shown in figure 1 , their mean age ± SD was 19.4±3.8 years. Male to female ratio was 1: 2.2.

The age of the patients varied from 12 to 36 years with the mean age ± SD was 21±4.7 years. Figure 2 shows that the most common age groups involved with acne vulgaris was between16-20 years constitute 70(46.7%) of the patients and age group 21-25 years constitute 45 patients(30%). Ninety one(60.7%) of the patient under study had a normal body mass index (BMI) , where as underweight seen in 20(13.3%) of the patients and overweight and obese seen in 18(12%) of the patients for each is reported in table 1 and figure 3. The commonest Fitzpatrick's skin photo type was type IV that constitute 126(84%) of the patients, type III seen in 15(10%), and type V seen in 7(4.7%) of the patients. Figure 4 shows distribution of patients according to skin phototypes.

The disease duration ranged from 3 weeks to 25 years with median duration of 3.8 years. In 100 patients (66.7%) the duration of the disease was 1-5 years.

The Mean age of onset of acne vulgaris in the patients under study was 17.2±4.3 years (range 11-32 years). The mean age of onset in male patients was 16.1±3.3 years which is earlier compared to female patients whose mean age of onset was 17.6±4.7 years. However, this was not statistically significant(p=0.300). In this study we found that the majority of the patients were student 103(68.6%), and 21(14%) were housewife, while 6(4%) were employers as shown as figure 5.

Face was involved in all the patients, however, face alone was involved in 150 (100%) of the patients. The chest was involved in110(73.3%), and the back in 97(64.7%) of the patients(Fig. 6).

According to the global acne grading system (GAGS) 34(33%) of the female and 15(31.9%) of the male patients had mild acne, and 68(66%) of the female and 26(55.3%) of the male patients had moderate acne, where as 1(1%) female and 6(12.8%) male patients had severe acne, none of the patients understudy had very severe grade. This difference was statistically significant as shown as table 2 and figure 7,8. No statically association between duration of acne, age of onset and sexes with severity of acne vulgaris in both sexes.

Regarding the marital status majority of the patients 145(96.7%) were single while 5(3.3%) of the patients were married.

Family history of acne vulgaris was seen in 65(63.1%) of female patients and 32(68.1%) of the male patients, there was no a statistically significant difference in family history of acne vulgaris between both sexes as shown as figure 9. The family history of acne vulgaris in the first degree relative were seen in 59(90.8%) of female patient while in male patients seen in 28(87.5%), and history of acne vulgaris in the second degree relative was seen in 6(9.2%) of female patient and 4(12.5%) of the male patients as reported in figure 10, this was statistically insignificant.

Among the precipitating factor seen in our patient as shown table(3), food was the commonest factor seen in 79(52.7%) of the patients. Figure 11shows the types of food that were most often believed by acne patients to aggravate their acne condition: chocolate (53.2%), tuna (43.1%), fatty food (26.6%), spicy food (24.1%), eggs (22.8%), diary product(8.9%) and coca cola (5.1%). Emotional factors as aggravating factor was seen in 71(47.3%) of the patients, 62(60.2%) of them were female patients and 9(19.1%) were male patient as shows in table 4 and this difference was statistically significant. Seasonal variation was observed in 51(34%) of the patients, 35(23.3%) of patient has their disease exacerbated in summer, and 16(10.7%) of the patients their disease showing flaring in winter. Smoking aggravating the disease in 6(12.8%) of male patients figure 12.

Only 6 (12.8%) male patients were smokers 4(8.5%) of them with history of moderate acne and 2(4.2%) of them with history of mild acne.

Eighteen of the female patients (17.5%) gave history of irregular menstrual periods. Seventy (68%) of the female patients gave history of premenstrual flare and exaggeration of their lesions during the cycle seen in 6(5.8%), and in post cycle period in 13(12.6%) of them as shows in figure 13.

Clinical features suggestive of hyperandrogenicity were observed in 17(16.5%) of the female patients including hirsutism in 10(9.7%), female pattern alopecia in 4(3.9%) and acanthosis nigricans in3(2.9%) as shown in table 5 and figure 14, however none of those patients fulfill the criteria for HAIRAN syndrome.

Table(6) or figure(15) show distribution of patient according to acne vulgaris complication. Post-acne hyperpigmenation was observed in 111(74%) of the patients as shows table 7 and figure 16, and post-acne scar seen in 77(51.3%) of the patients. The most common type of post-acne scar was boxcar seen in 49(32.7%) of the patient, 27(26.2%) of them where females while 22(46.8%) where males, then followed by ice pick scar seen in 32(31.1%) of female patients and 14(29.8%) of the male patients, and rolling scar seen in13(12.6%) of female and in male patients seen in 11(23.4%) of them, and hypertrophic scar seen in one (2.1%) male patient.

Regarding the histories of the patients, of the 150 patients, of 87(58%) patients used topical, 41(27.3%) patients used systemic treatment and 22(14.7%) not used treatment as shows as figure 17.

Table 1: Distribution patients according to body mass index .

Body mass index	No.	%
Normal	91	60.7
Under weight	20	13.3
Over weight	18	12
Obese	18	12
Morbid obesity	3	2
Total	150	100

Table 2: Distribution of patients according to severity of acne by global acne grading system & sex.

Severity	Male		Female		Total	
	No.	%	No.	%	No.	%
Mild	15	31.9	34	33	49	32.7
Moderate	26	55.3	68	66	94	62.7
Sever	6	12.8	1	1	7	4.6
Total	47	100	103	100	150	100

Table 3 : Distribution of patients according to history of exacerbated factors.

Exacerbated factors	No.	%
Food	79	52.7
Emotional factor	71	47.3
Summer time	35	23.3
Winter time	16	10.7

Table 4 : Distribution of patients according to exacerbated by emotional factor & sex.

Emotional factor	Male		Female		Total	
	No.	%	No.	%	No.	%
Yes	9	19.1	62	60.2	71	47.3
No	38	80.9	41	39.8	79	52.7
Total	47	100	103	100	150	100

X^2 = 21.8 df=1 p = 0.00(Significant).

Table 5: Marker of androgenicity in female with acne.

Marker of androgenicity	No.	%*
Hirsutism	10	9.7
Acanthosis nigricans	3	2.9
Female androgenic alopecia	4	3.9

***Percentage from 103 females.**

Table 6 : Distribution of patients according to acne complication.

Complications	Male		Female		Total	
	No.	%	No.	%	No.	%
Hyperpigmantation	32	68.1	79	76.7	111	74
Ice pick scars	14	29.8	32	31.1	46	30.7
Rolling scars	11	23.4	13	12.6	24	16
Boxcar scars	22	46.8	27	26.2	49	32.7
Hypertrophic scars	1	2.1	0	0	1	0.7

Table 7: Distribution of patients according to post acne hyperpigmentation.

Hyperpigmentation	No.	%
Yes	111	74
NO	39	26
Total	150	100

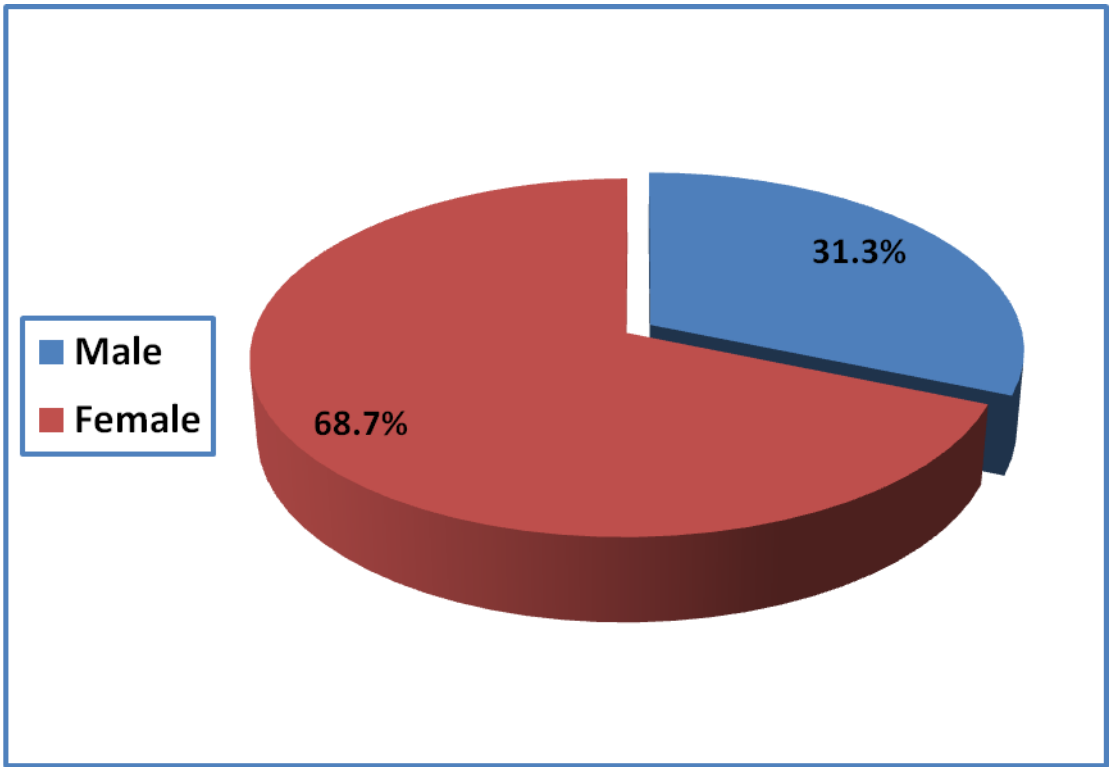


Fig. 1: Distribution of patients according to sex.

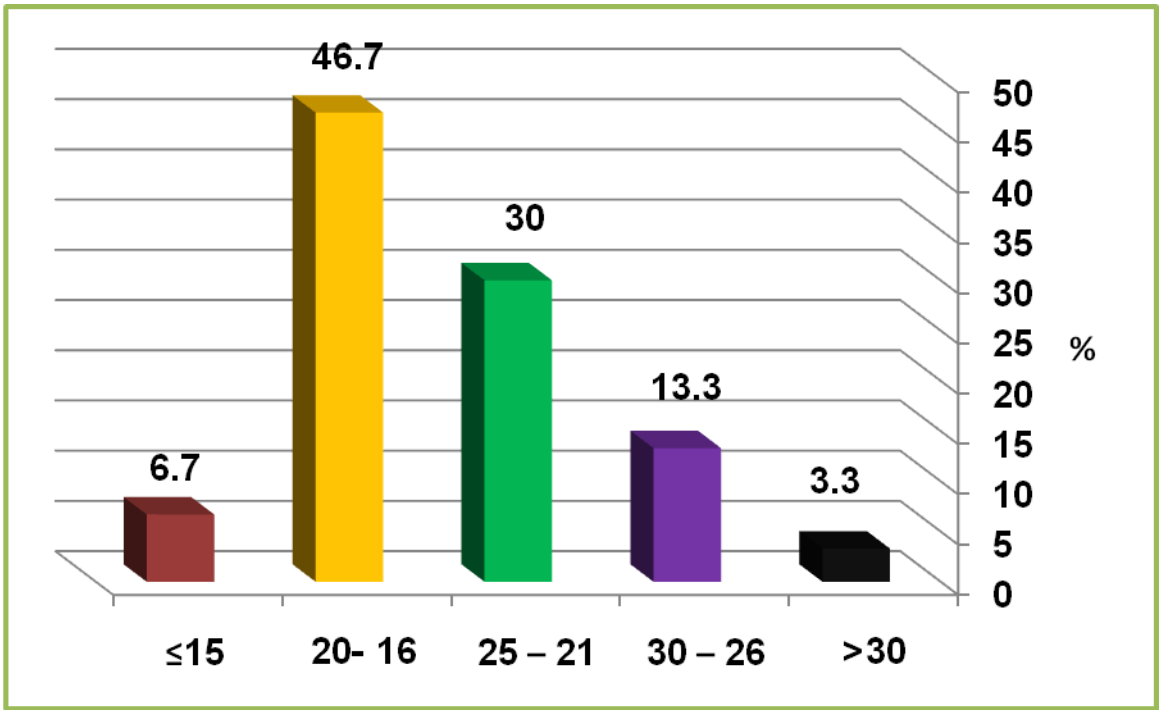


Fig. 2: Distribution of patients according to age.

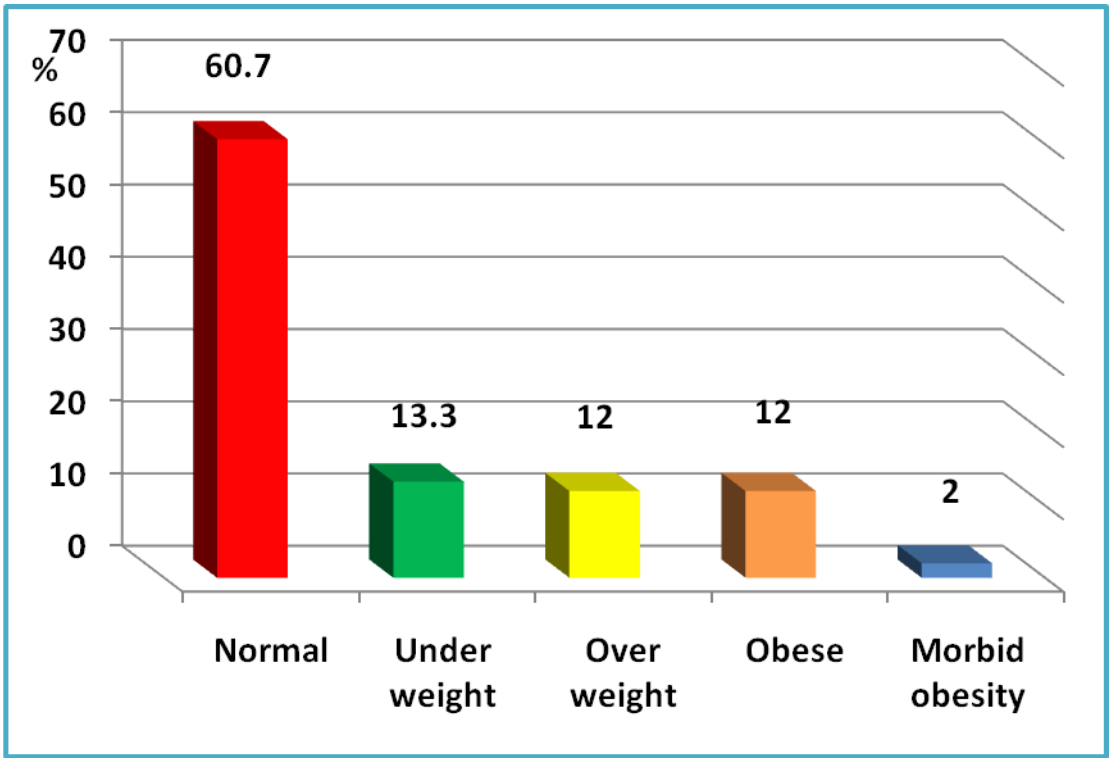


Fig. 3: Distribution patients according to body mass index .

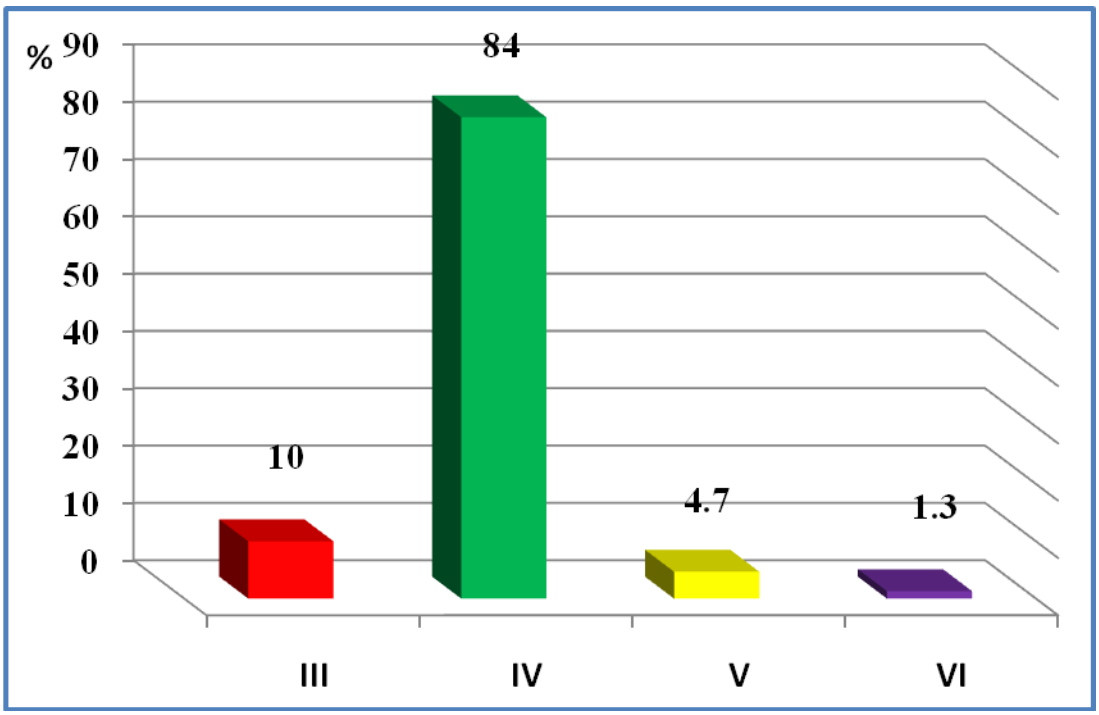


Fig. 4: Distribution of patients according to skin phototypes.

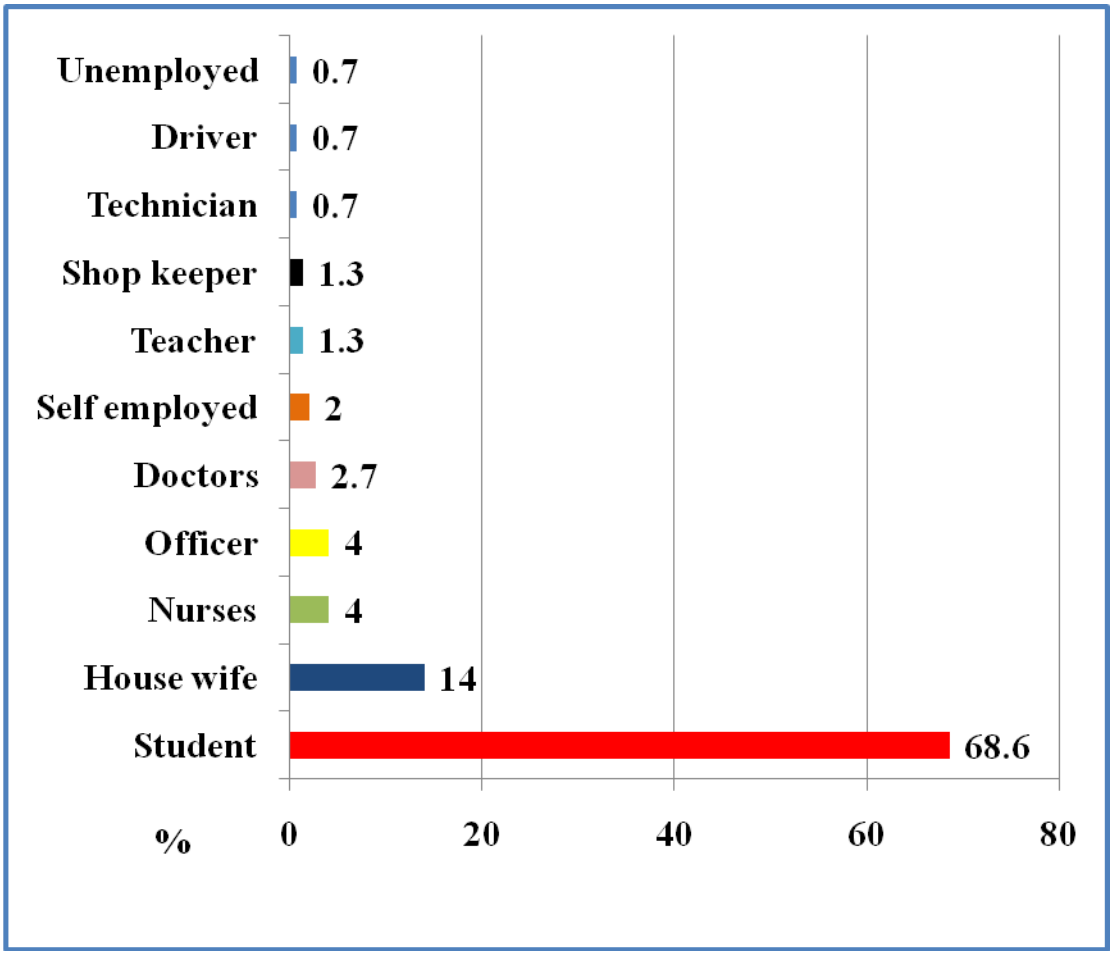


Fig. 5: Distribution of patients according to occupational status.

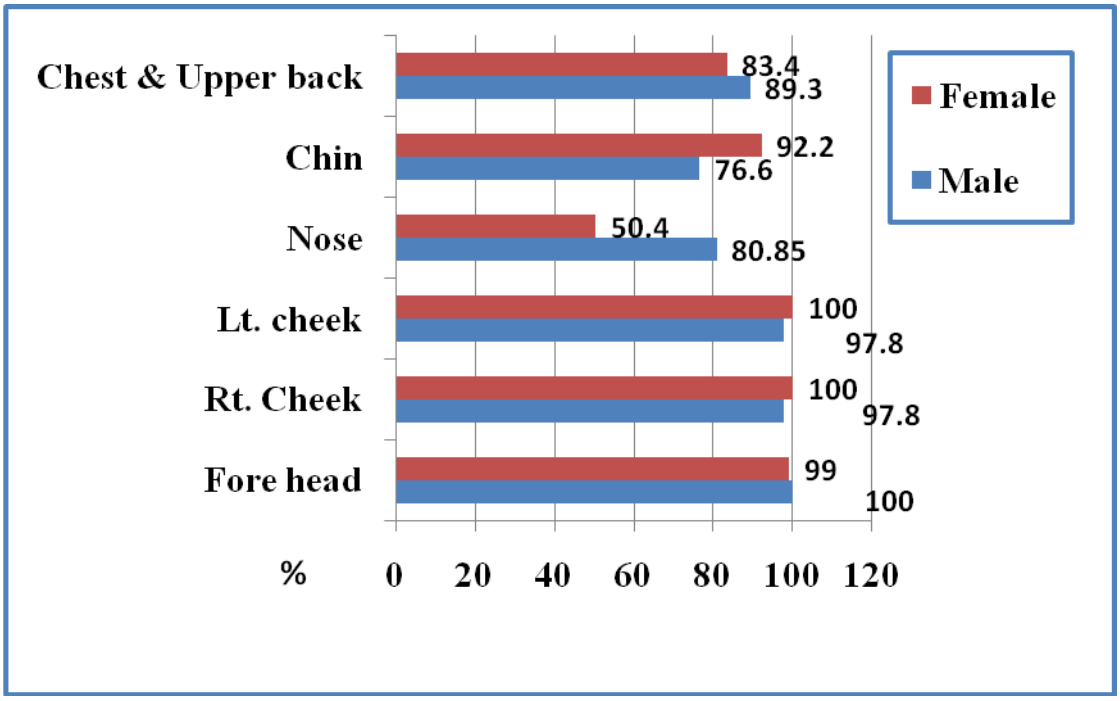
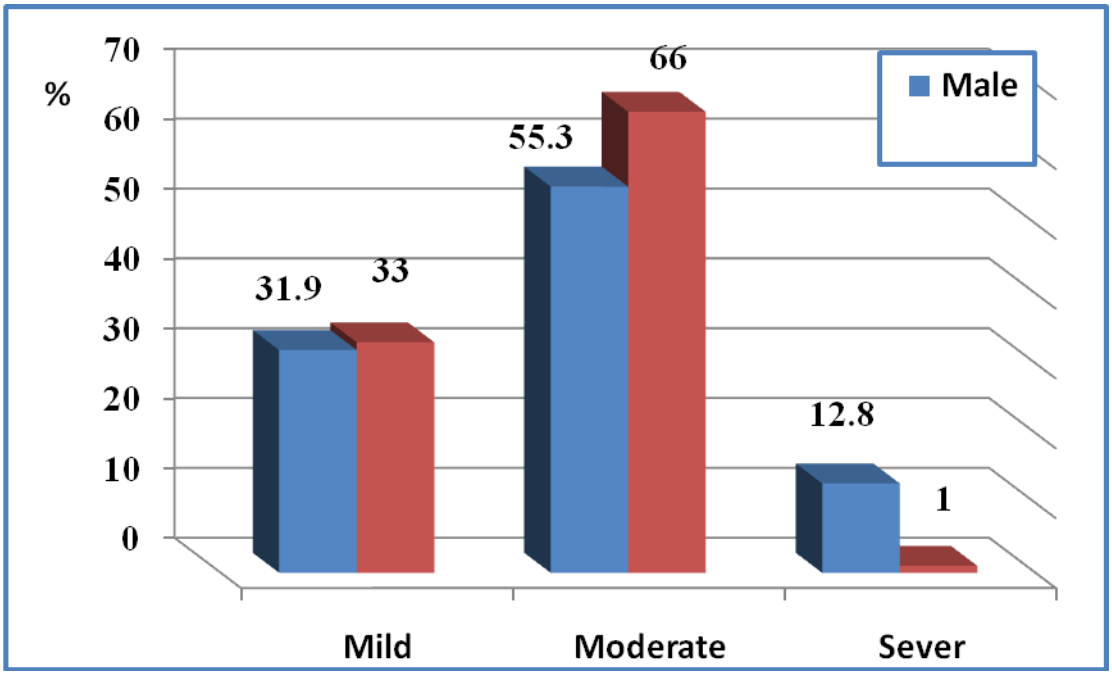


Fig.6: Distribution of patients according to site of acne.



X^2 =7.791 df=2 p = 0.020(Significant).

Fig. 7: Distribution of patients according to severity of acne by global score & sex.

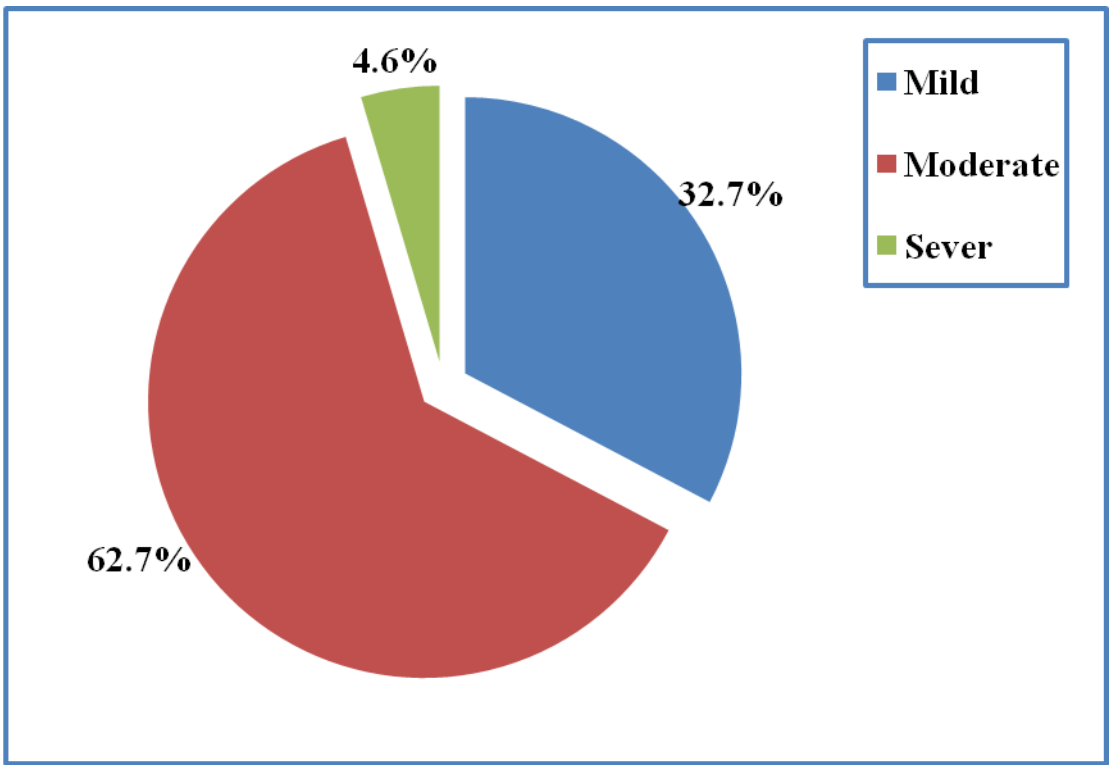
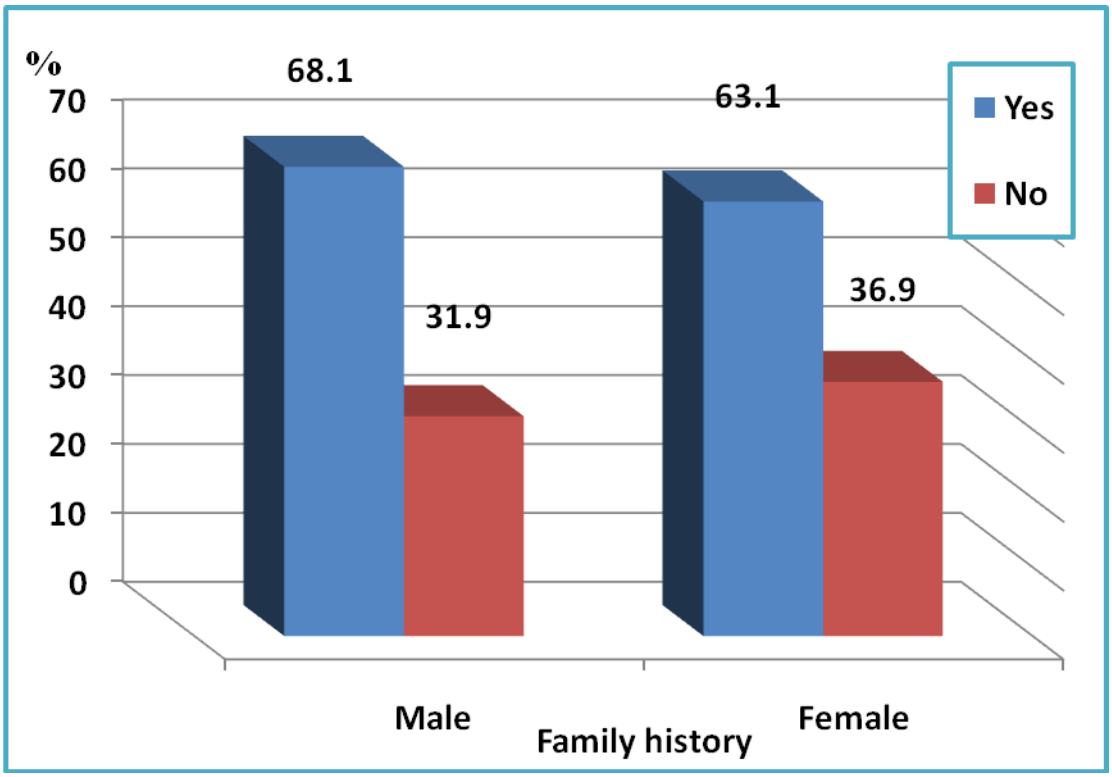


Fig. 8: Distribution of patients according to severity.



P=0.684

Fig. 9: Distribution of patients according to family history of acne &sex.

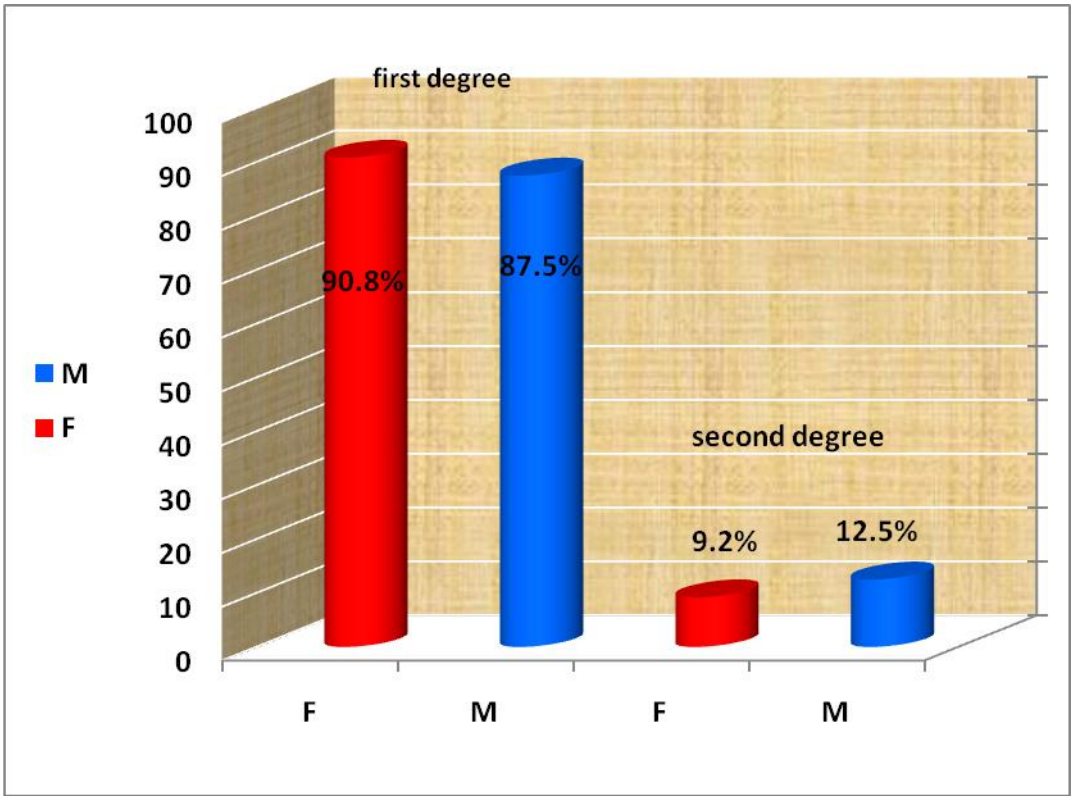


Fig.10: Distribution of patients according to degree family with history of acne & sex.

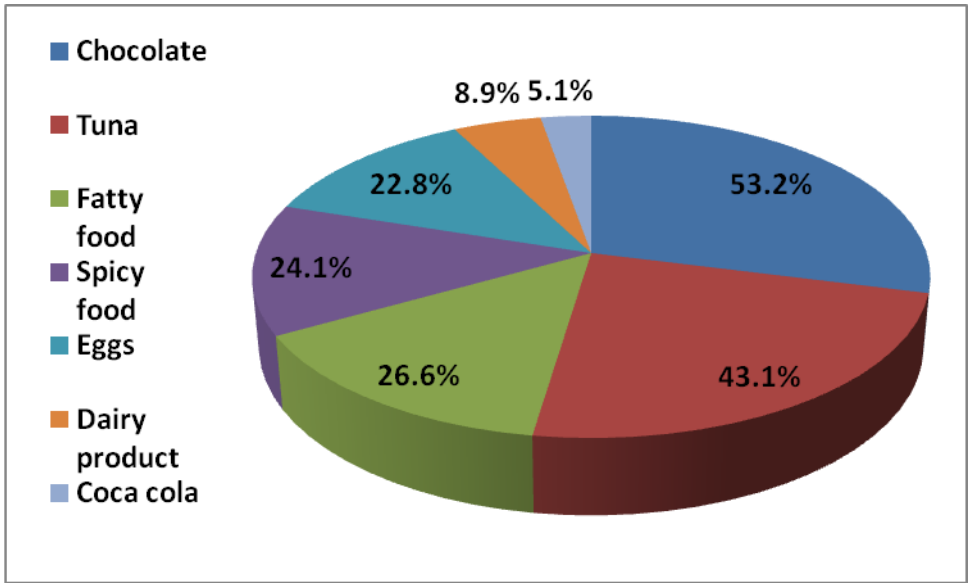


Fig 11. Distribution of patients according to types of foods.

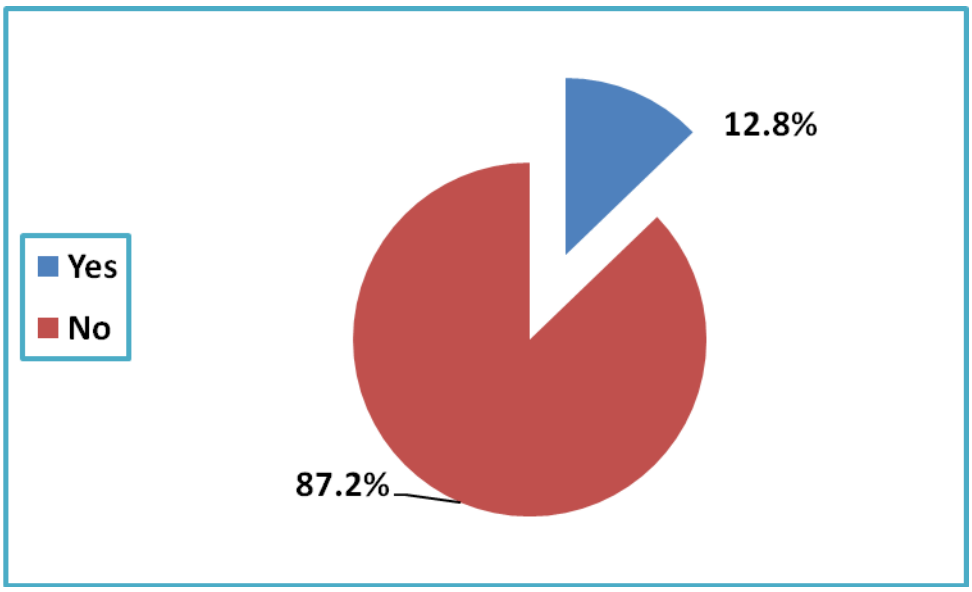


Fig. 12: Distribution of male patients according to smoking status.

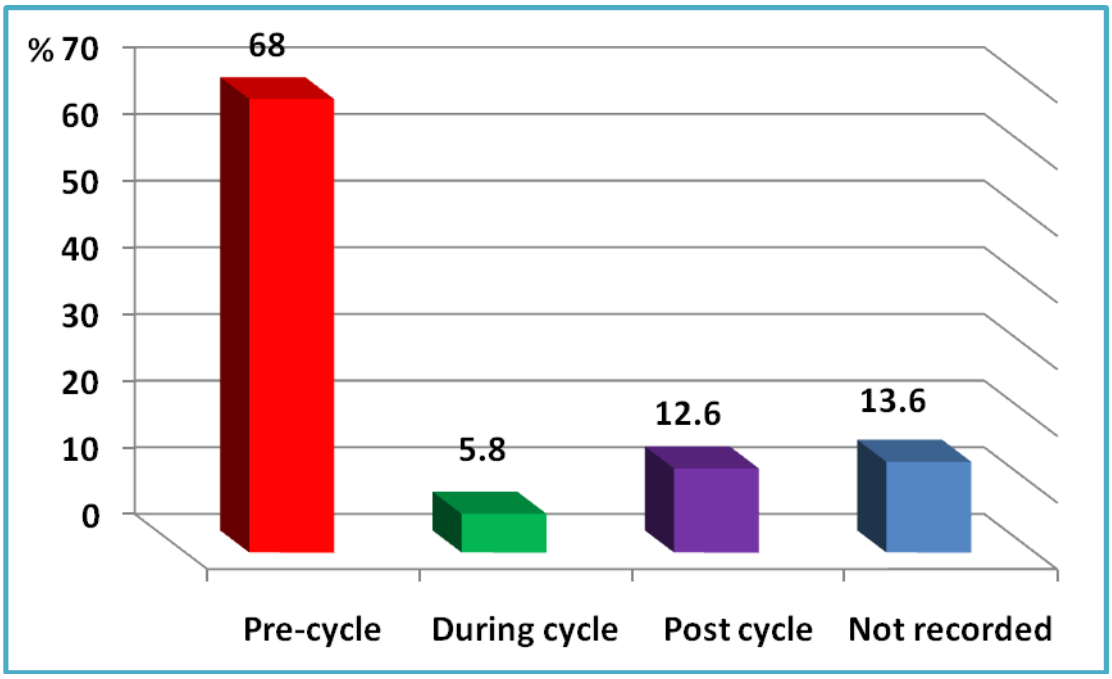


Fig. 13: Distribution of patients according to relation of severity of disease and menstrual cycle.

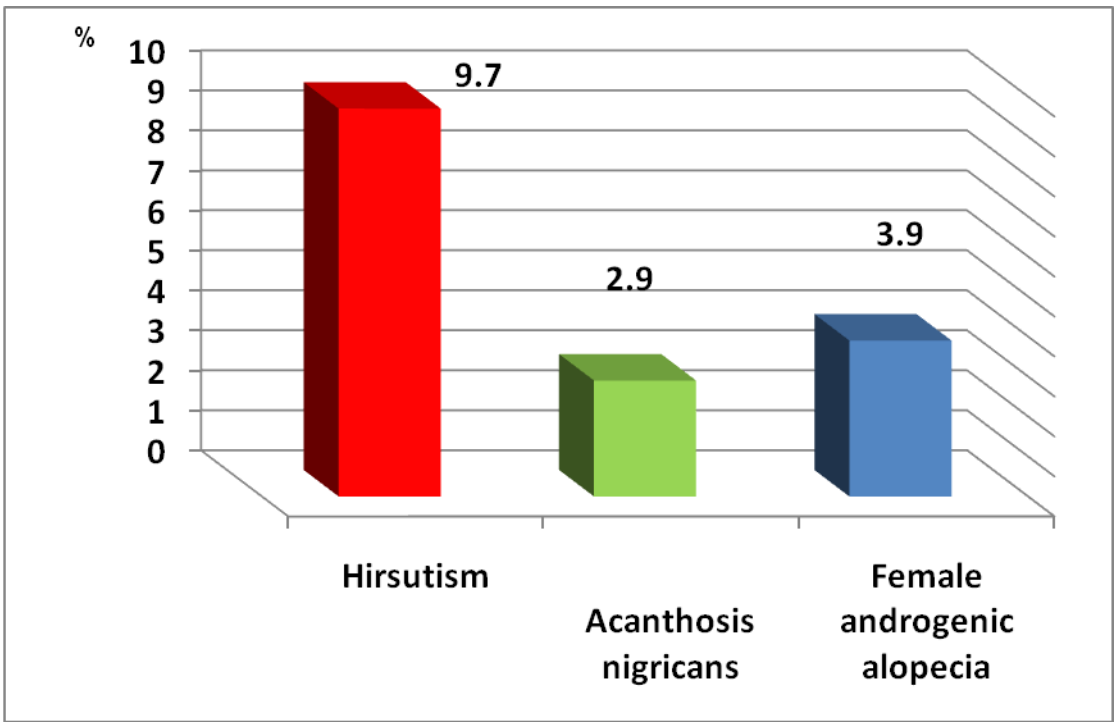


Fig. 14:Marker of androgenicity in females with acne.

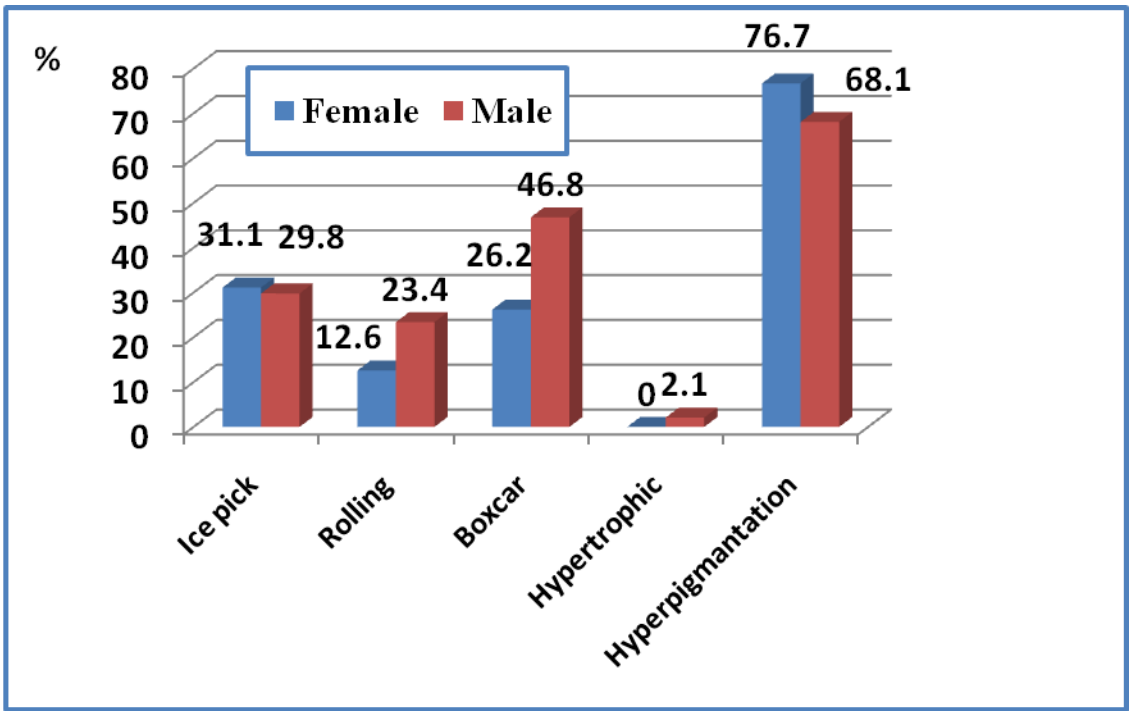


Fig.15: Distribution of patients according to acne complication.

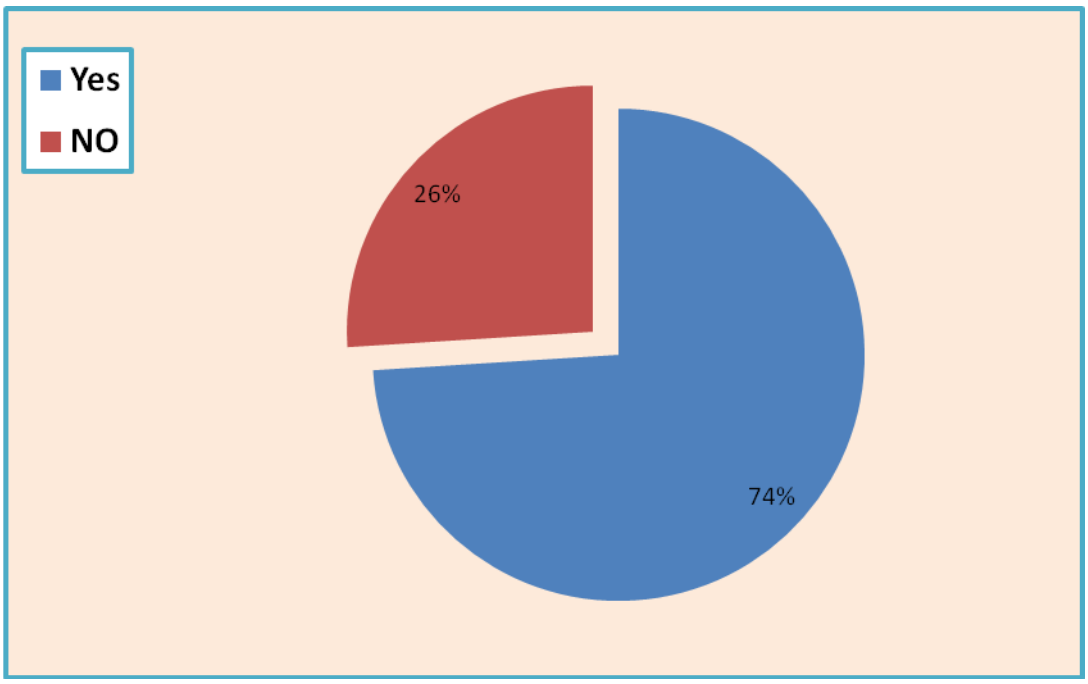


Fig. 16: Distribution of patients according to post acne hyperpigmentation.

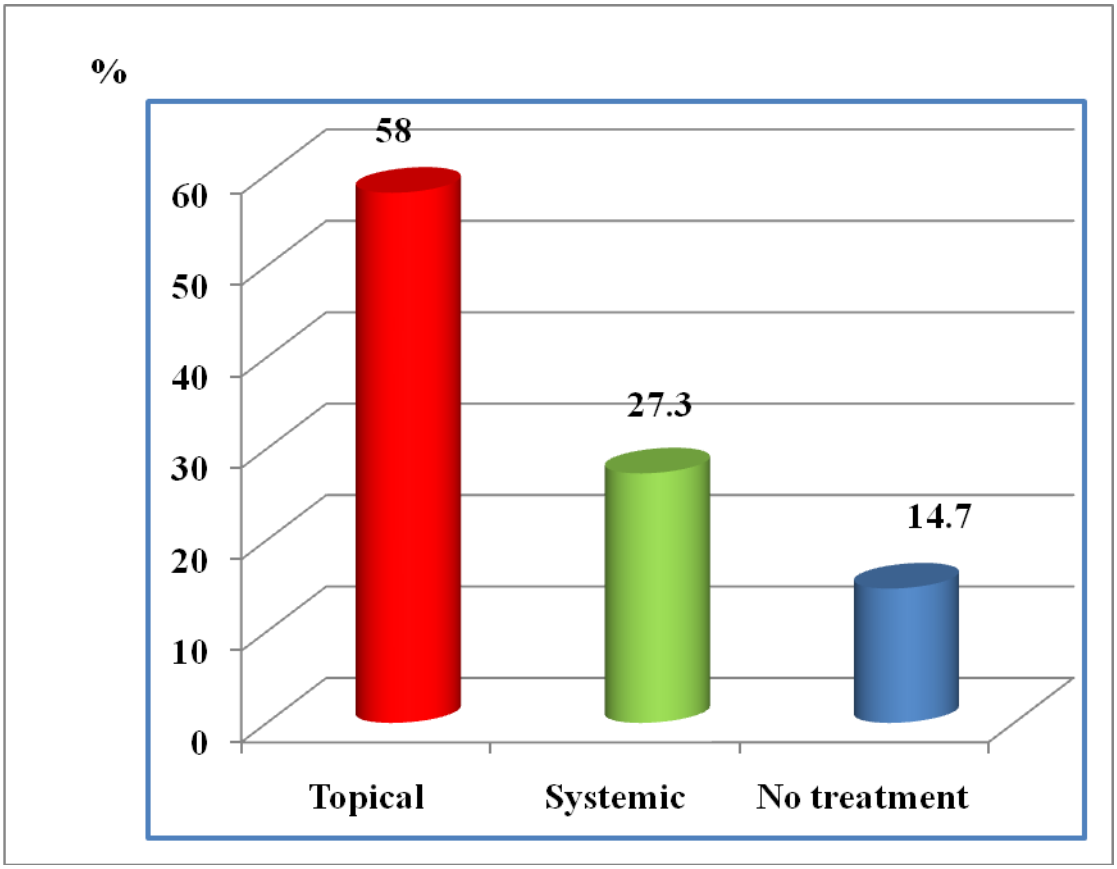


Table 17: Distribution of patients according to previous treatment.

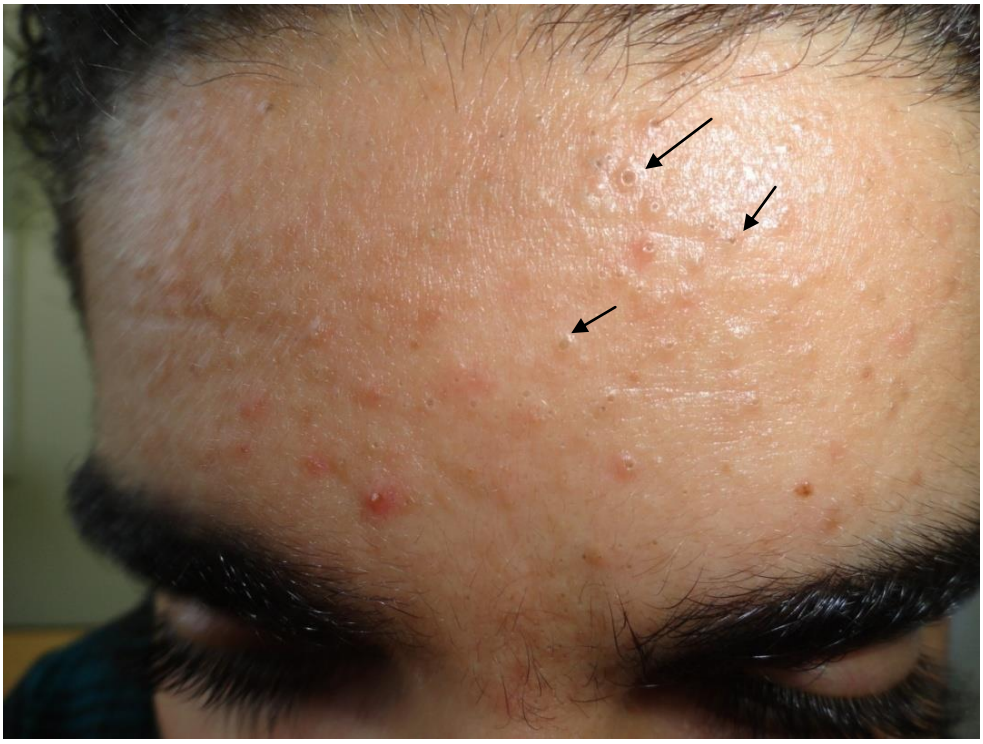


Figure 18. Multiple open comedones on the forehead.

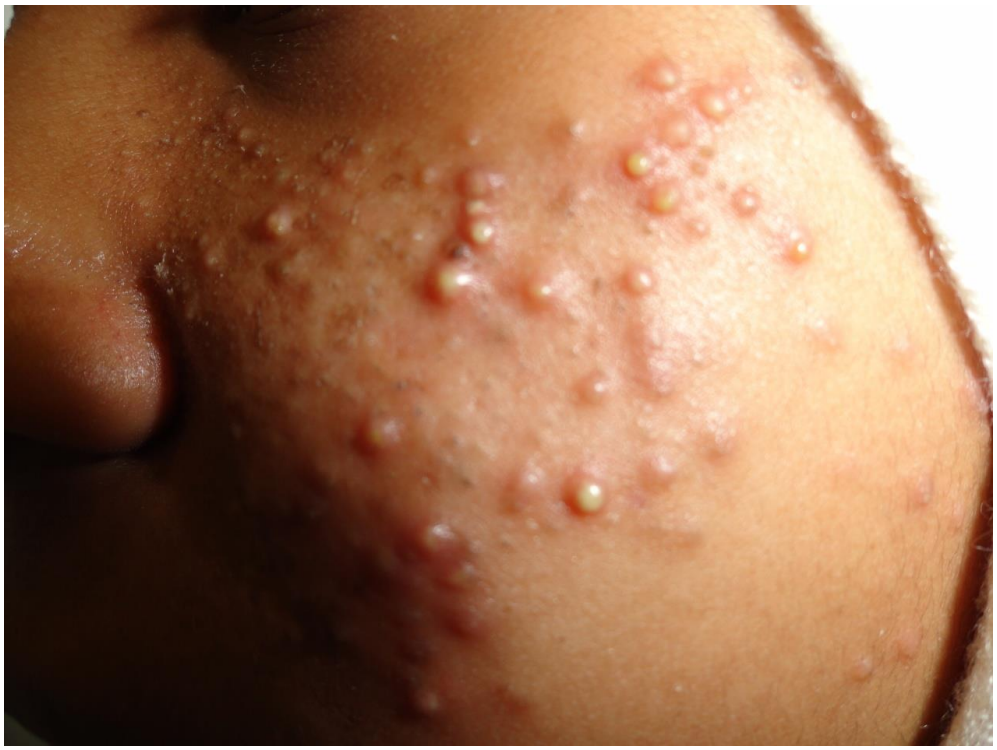


Figure 19. Papules , pustules and black comedones on cheek.

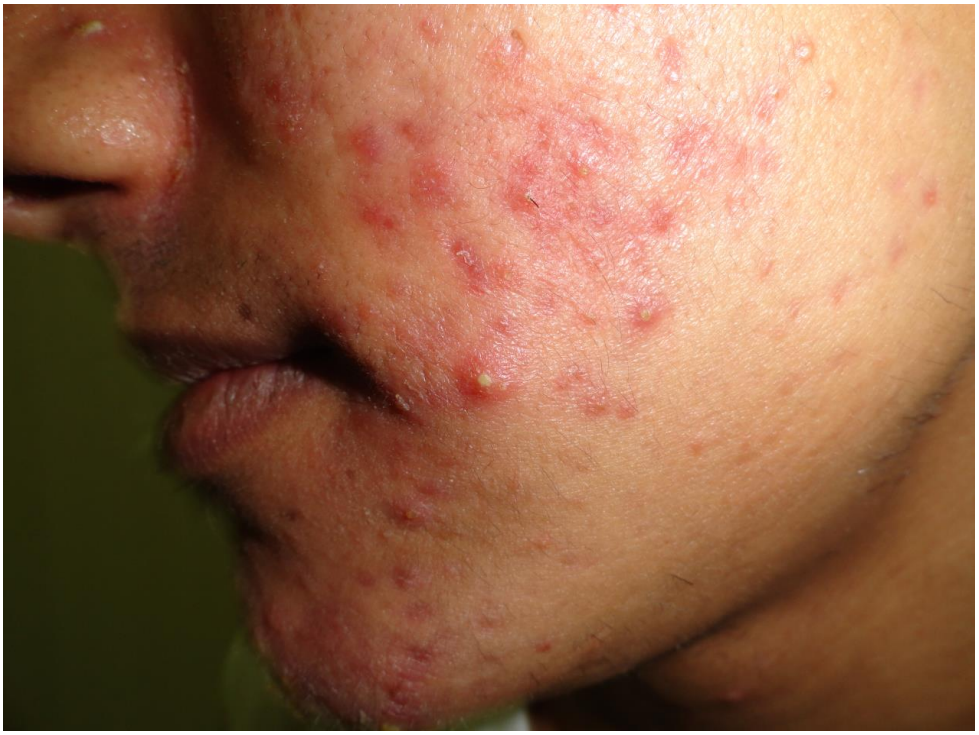


Figure 20. Close-up of the cheek showing comedone, erythematous papules, pustules and scars.

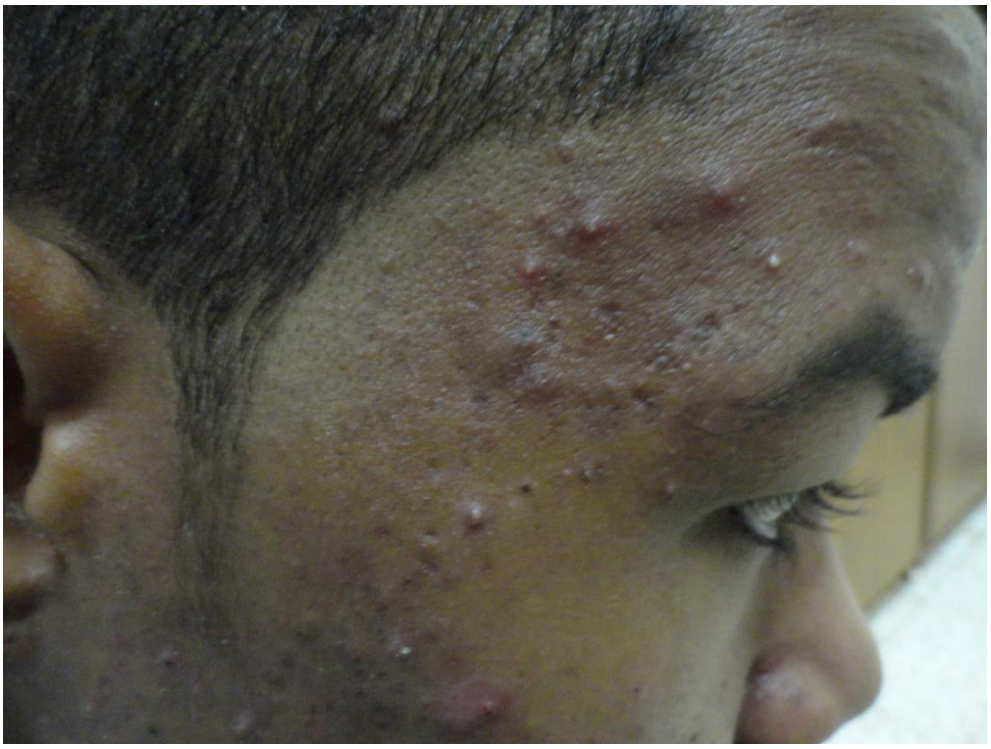
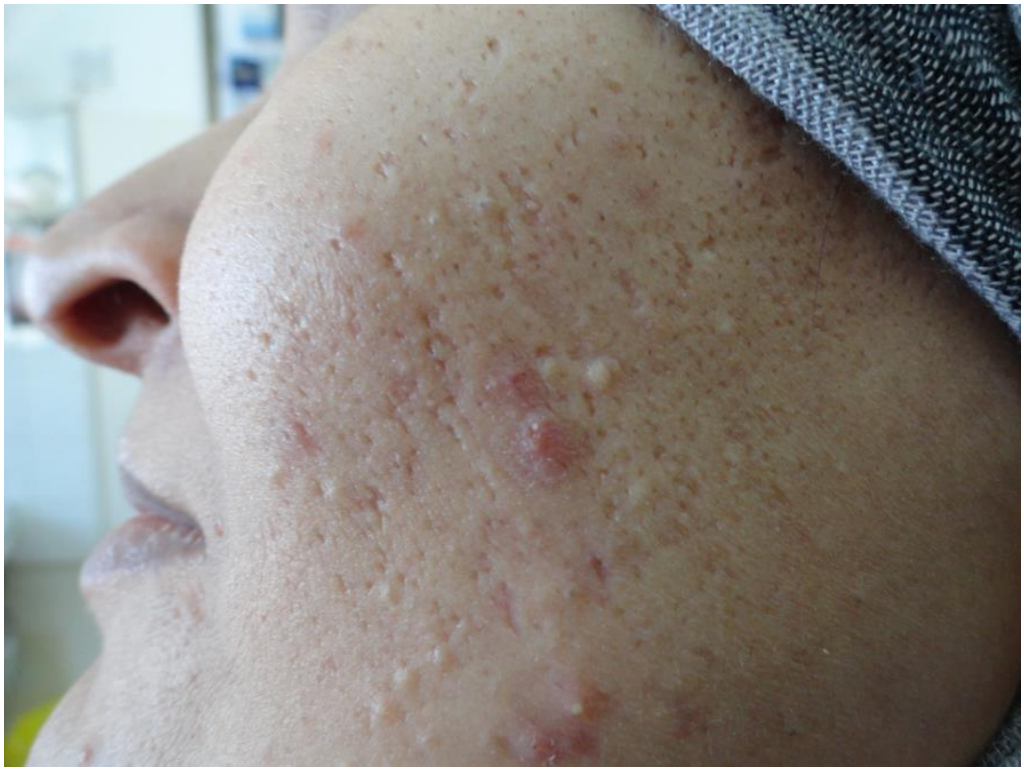


Figure 21 . Pustules with erythema, scars, postinflmmatory hyperpigmentation in skin phototype V.



Figuer 22 . Open, closed comedone, pustule with significant scars.

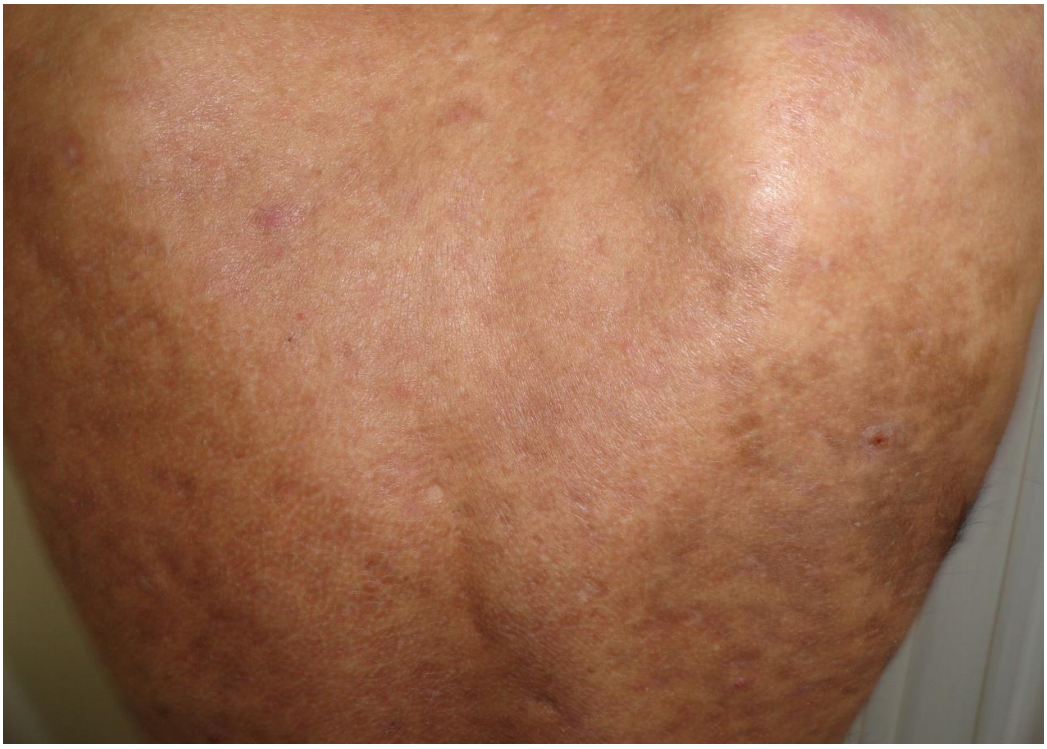


Figure 23. Many depressed scars and postinflammatory hyperpigmentation on the back.

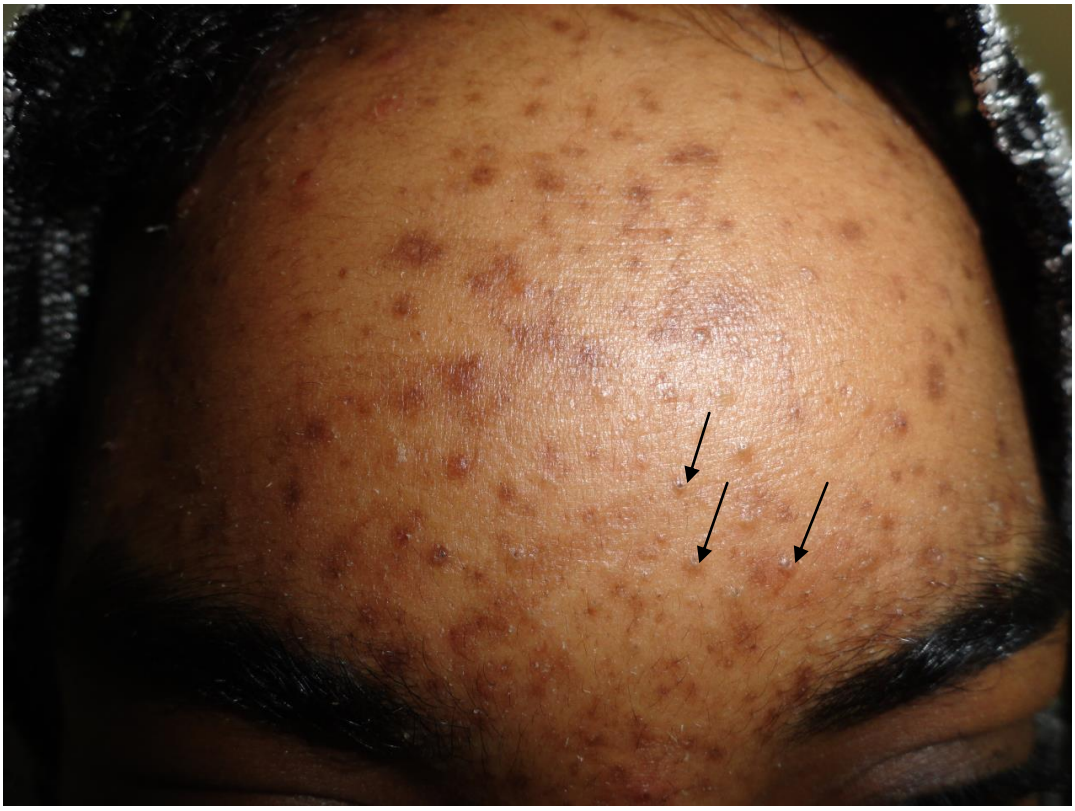


Figure 24. Postinflmmatory hyperpigmentation with black comedone on forehead.

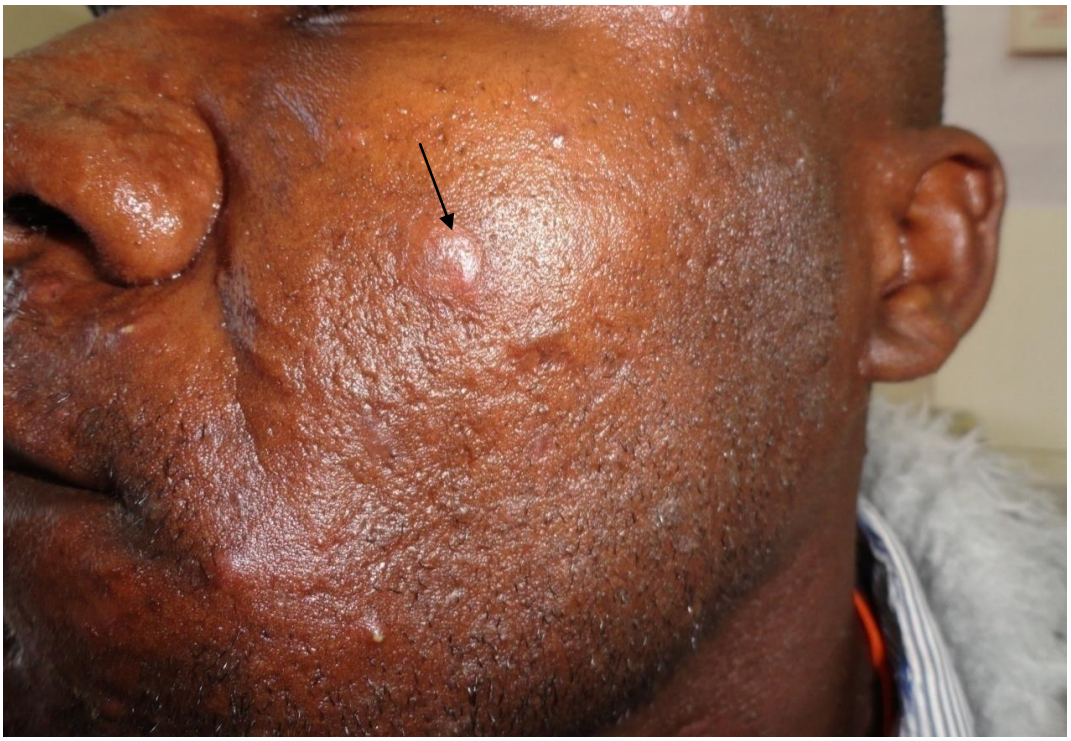


Figure 25. Pustules and nodules seen on the left cheek and forehead with little scar.

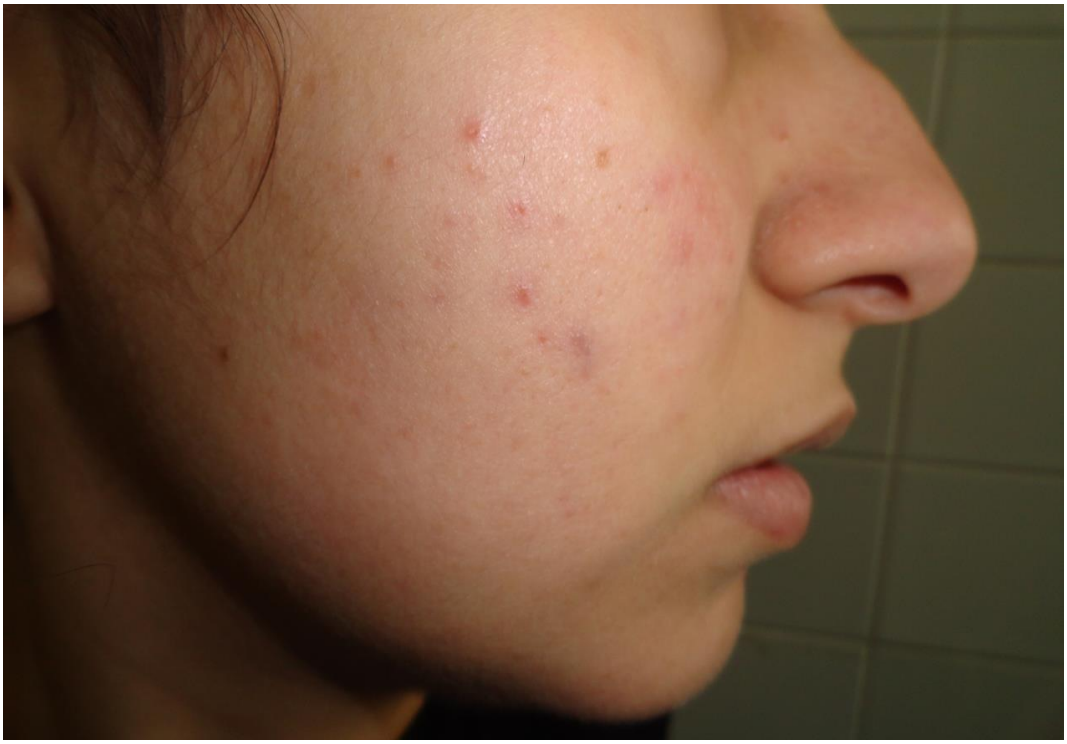


Figure 26. Libyan female patient with mild acne vulgaris.

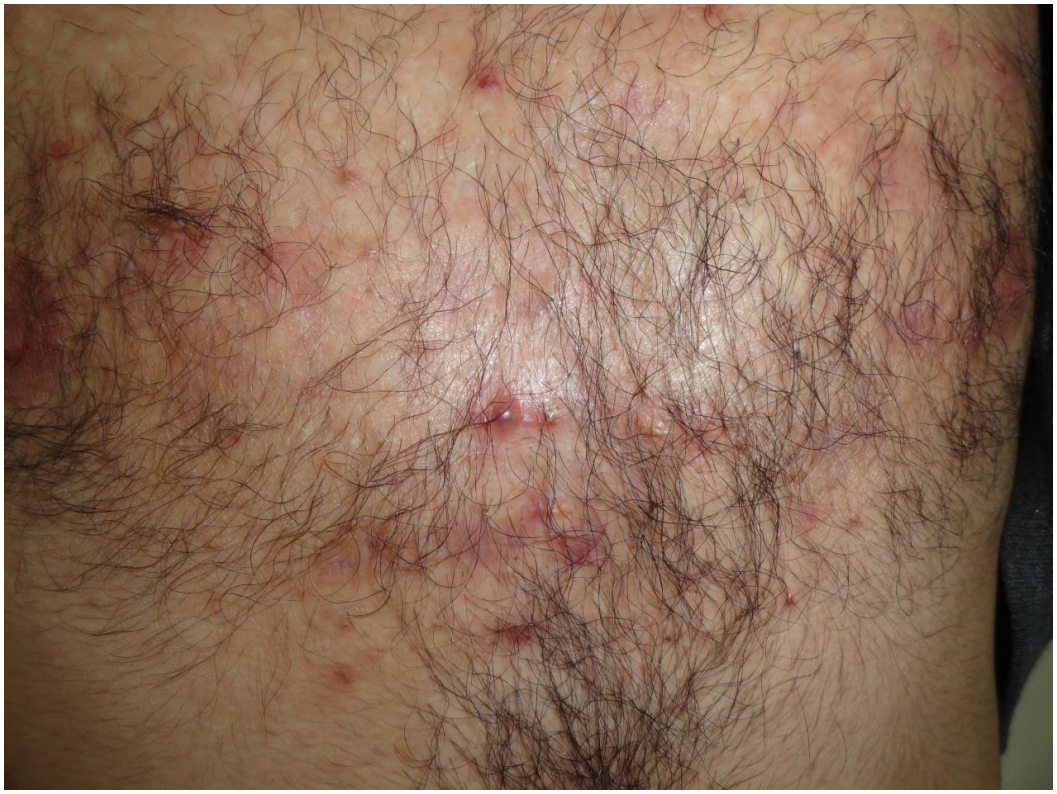


Figure 27. Moderate pustular acne with erythma on the chest.

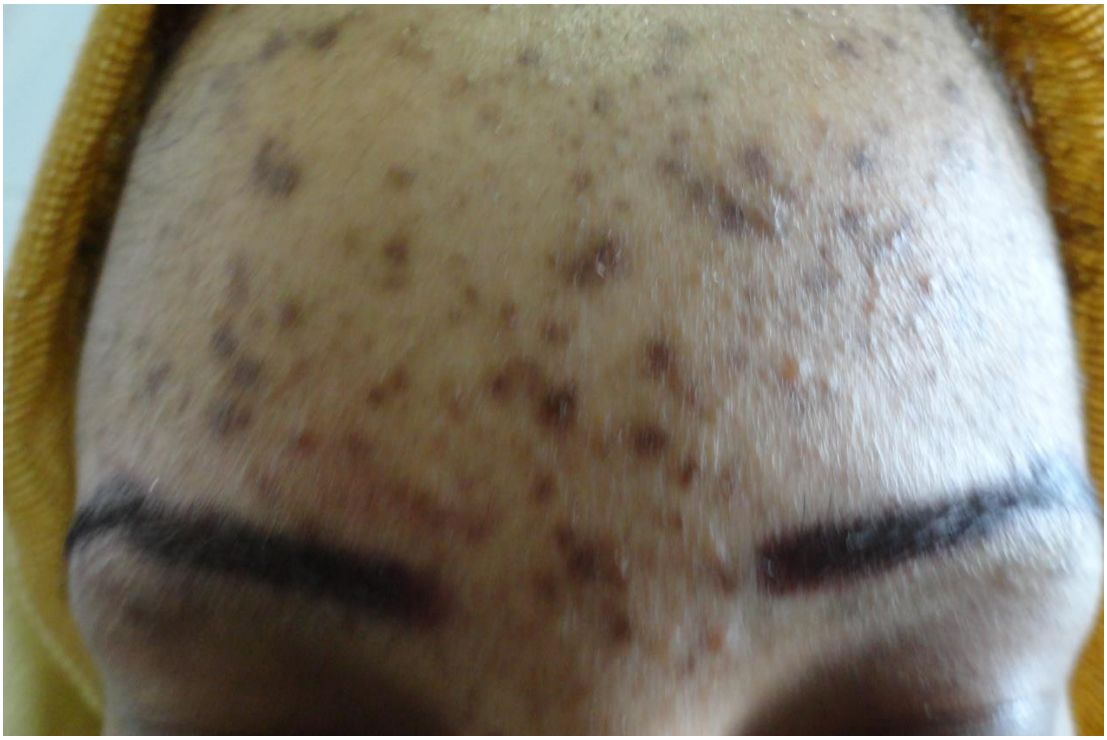


Figure 28. Postinflmmatory hyperpigmentation on forehead.

7.Discussion:

Acne vulgaris is a chronic disease that is virtually universal in adolescence(1). There are many myths about factors that might helper or aggravate acne including diet, premenstrual flare, sweating, ultraviolet radiation, occupation, smoking and stress (1).

The present study revealed a female preponderance in agreement with observation of AI-Ameer et al(42) and Ikaraoha et al(41) who found a female preponderance in their studies. However Aditytan et al (4) reported a male preponderance. Females were significantly more likely to use acne treatment and more likely seek medical care for acne(115).

The mean age of the onset among our patient was 17.2 years, which is higher as compared to the finding of Adityan et al 15.97years (4).

Approximality half (46.7%) of the patients understudy were in the age group of 16-20 years followed by 21-25 years(30%), as also observed by Adityan et al (59.8%) in 16-20 years (4).

The mean age of the subjects in the present study was 19.4±3.8 years similar to the study by Adityan et al in south India 19.78±4.94 (4). However our study was in contrast with previous study(4) who noted that the mean age of presentation of their patients was 25.58 years.

Many people have the impression that acne and obesity are related in the present study more than half (60.7%) of the patient had normal BMI. Previous study(8) showed that adult men with acne were significantly heavier than men without acne. However, the authors showed that this association was dependent on age, because weight was not associated with acne in adolescents aged 15-19 years. In contrast, previous study (8) showed mild peripheral insulin resistance in female acne sufferers that was not associated with obesity or menstrual irregularities.

The improvement of acne in summer and exacerbation in winter is a conventional dermatological opinion. Studies done in past regarding seasonal variation in acne vulgaris(4). In our study, seasonal variation was observed only in 34% of the patients with exacerbated in summer time in majority of them in agreement with an Indian study which showed that

majority of patients with acne vulgaris worsened during summer (116). However, this observation in contrast with study done in A Saudi Arabian whose shown that acne exacerbates in winter and often improves in summer(42).

The relationship between smoking and acne vulgaris is controversial(4), only 12.8% male patients were smokers, 4(8.5%) of them with history of moderate acne and2(4.2%) of them with history of mild acne this observation in agreement with study done by SZ Ghodsi et al(28) whose found no association between acne severity and smoking, in contrast previous studies(4) there were noted that smoking is likely to bear a positive correlation with acne. According to Rombouts et al. (31), daily cigarette consumption and duration of smoking appeared to be significantly protective in the development of inflammatory acne in girls. No significant association was detected among boys. An explanation for the association between smoking and acne is unknown, impaired vasoreactivity, collagen synthesis and wound healing may be partially responsible for the effect of smoking on the development of acne (31). Smoking also has immunosuppressive effects and affects cells from the innate immune system such as macrophages, natural killer cells and neutrophils, and from the adaptive immune system, such as T and B lymphocytes(31).

Premenstrual flare was noticed in more than two-third(68%) of female patients in our study in agreement with study done by Cunliffe WJ, Gollnick HPM(40) whose reported premenstrual flare of acne in 70% of females patient. In contrast with study done by Kairavee D, Vivek C (117) whose noted in their study only 19% of female had experience of premenstrual exacerbation. The explanation offered is hydration-induced cyclical narrowing of the pilosebaceous orifice between 16-20 days of the menstrual cycle(40). However, the mechanism for this blockage is not known(4) Khanna and Pandh(118). noticed a mean reduction in the noninflammatory and inflammatory lesions count during the postmenstrual period.

Hyperandrogenism is a common cause of irregular menses in adolescent females, and affects 5–7% of adult women (119). Girls and women with PCOS or hyperandrogenism may present a

variety of concerns and symptoms, including irregular periods, excess hair growth, acne, and obesity (119). The incidence of hirsutism and irregular menses observed in earlier studies(4) varied between 0% to 21% and 15.5% to 48%, respectively. The corresponding figures in our study were 9.7% and 17.5% respectively. Study done by Vexiau P et al(120) whose shows that acne in adult women is frequently associated with clinical hyperandrogenism. However, study done by Adityan B and Thappa DM(4) whose observed no association between severity of acne vulgaris and clinical markers of androgenicity.

Acne vulgaris occurs in sites, which are rich in pilosebaceous units. It was noted in our study that face was involved in all the patients with acne vulgaris, chest was involved in 73.3%, back was involved in 64.7%.

In our study, the grading of acne vulgaris among our patients was made by The Global Acne Grading System (GAGS) (113). GAGS is a clinical grading system for the severity of acne. More than half of male patients having moderate acne and over one-third of female patient, male patients under study had more severe acne vulgaris than female patients and this difference was statistically significant($p= 0.020$). similar observation has been reported in previous study (4).

Many studies confirm the importance of heredity as a prognostic factor for acne. Family history of acne is associated with earlier occurrence of acne, increased number of retentional lesions and therapeutic difficulties(12).In our study approximality two third(63.1%) of patients with positive family history of acne vulgaris in agreement with study done by Xu et al(121), showed that the risk of acne vulgaris occurring in a relative of a patient was significantly greater than for the relative of an unaffected individual. In contrast study done by Adityan et al(4). Whose found family history was positive in 42% of the cases. In one study, researchers found that 50% of the adults with acne had a first degree relative parent, sibling and child who had acne. This suggests, that some people may have a genetic Predisposition(11).

The role of diet in the development of acne has been controversial(122). Diet as a cause of acne has been long debated. Smith et al(8), suggest that nutrition-related lifestyle factor may influence the pathogenesis of acne. Over half(52.7%) of patients in our study show flaring of their acne lesion by food, half of them due to consumption of chocolate in agreement with study done by Green and Sinclair(123) which reported the dietary factors(chocolate, oily and fatty food and high sugar content foods) as exacerbating factors in acne. Regular consumption of food with a high glycemic index elevates serum insulin concentrations, which may stimulate sebocyte proliferation and sebum production(22), suppress SHBG concentrations and raise androgen concentrations, and contribute to acne(22). However Fulton et al(124) and Anderson(125) found that there was no association between the consumption of chocolate bars and acne, sebum production and composition, and comedogenicity. Less than half of patients (47.3%) understudy, show flaring of their lesions by emotional factor in agreement with earlier researches (126,127) whose finding of acne flares up in stressful conditions, including psychological and emotional stress. However Mosam et al(128) found that severity of acne was not significantly correlated with psychological distress. It is well- known that stress can influence sebaceous gland function by inducing changes in the neuroendocrine system moreover stress can elicit substance p release from peripheral nerves (129).

Post inflammatory hyperpigmentation is a common complication of acne vulgaris particularly in pigmented skin (1). 74% of patients understudy showed post-acne hyperpigmentation in agreement with study done Kane et al(130), noted that 67.7% of their patients had post-acne pigmentation However Adityan et al(4) observed only in 24.6% of their patients.

Scarring is a well-known consequence of acne, but it is commonly attributed to inflammatory lesion regardless of their severity(9), in present study about 51.3% of patients having post acne scars. Boxcar scars were the most common type noticed in 32.7% of the patients, in agreement with study done by Rajar et al(11) who noted that 59% of their patients had post-acne scar. In contrast to study done by Taylor et al(25) who noted only 5.9% of their patients had post-acne

scarring. This suggests that the retention lesions, and in particular the macrocomedones, can leave scars. This may be a result of the involvement of the extracellular matrix proteins detected in acne lesions (9). The occurrence and incidence of scarring is still not well understood, however there is considerable variation in scarring between one person and another, indicating that some people are more prone to scarring than others. Scarring frequently results from severe inflammatory acne that occurs deep in the skin. But, scarring also may arise from more superficial inflamed lesions(11).

8.Conclusion :

- 150 patients with clinical diagnosis of acne vulgaris.
- The ratio was higher in females than males 2.2 : 1 and the mean age ±SD was 21.7±4.9 years, most patients were in the age group of 16-20 years (46.7%) and majority of patients were students (68.6%).
- 91(60.7%) of patients with normal BMI(Body Mass Index) no association between acne and obesity.
- The commonest site of involved in acne vulgaris was face.
- There were 49 patients(32.7%) with mild acne, 94(62.7%) with moderate acne, 7(4.6%) with severe acne and none of them with very severe acne.
- Diet 79(52.7%) was the most common predisposing factor followed by emotional factor detected in 71(47.3%) of patients (p=0.00). Seasonal variation was observed only in 51 patients(34%), 35 patients(23.3%) exacerbated in summer and 16 patients (10.7٪) in winter.
- 68% of female patients gave history of premenstrual flare up.
- Seventeen of our female patients(16.5%) had cutaneous markers of androgenicity and the most common marker was hirsutism(9.7%).
- Scarring and hyperpigmentation the sequelae of acne were observed in77 ⟨51.3%⟩ and 111⟨74%⟩ of patients.
- Men who were smokers had mild and moderate acne vulgaris.

9.Rercomendation :

- A large study including more number of patients over a long period of time.
- A laboratory screening for the patients with acne vulgaris including hormonal assay.
- Screening female patients using ultrasound scanning to rule out associated polycystic ovarian syndrome (PCOS).

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Appendix (I)

(History)

Serial no. ……..

Age……..Sex ……
Marital status ……
Occupation ……
Duration of acne ……..
Age at onset of acne ……
Effect of Diet ……..
Seasonal variation a)Summer ……
b)Winter …….
Emotional factors ……
H\O smoking …….
Family H\O acne …….
Menstrual history : Regular …… Irregular ……

Relation of acne to cycle
(Pre – menstrual Flare) ……
(Post – menstrual Flare) ……..

Hirsutism ……

Medical illness ……
Drug history .....
Treatment for acne
Topical ……..
System ……..
Other ……

Appendix (II)

(clinical examination)

a)General dermatological examination :

Skin type I….. II……III……. IV……. V….. VI……

Hair ……

Nail ……

M.m ……...

b)Local examination for acne vulgaris :

Site affected : Face …… Chest …… Back ……...

Site	No lesion (0)	Comedone (1)	Papules (2)	Pustules (3)	Nodules (4)	Local score Factorxgrade
Forehead						2x
Right cheek						2x
Left cheek						2x
Nose						1x
Chin						1x
Chest&Upper back						3x
Total						

GAGS=

(mild 1-18, moderate 19-30, severe 31-38, very severe > 39)

Scars

Ice pice …… Rolling……...

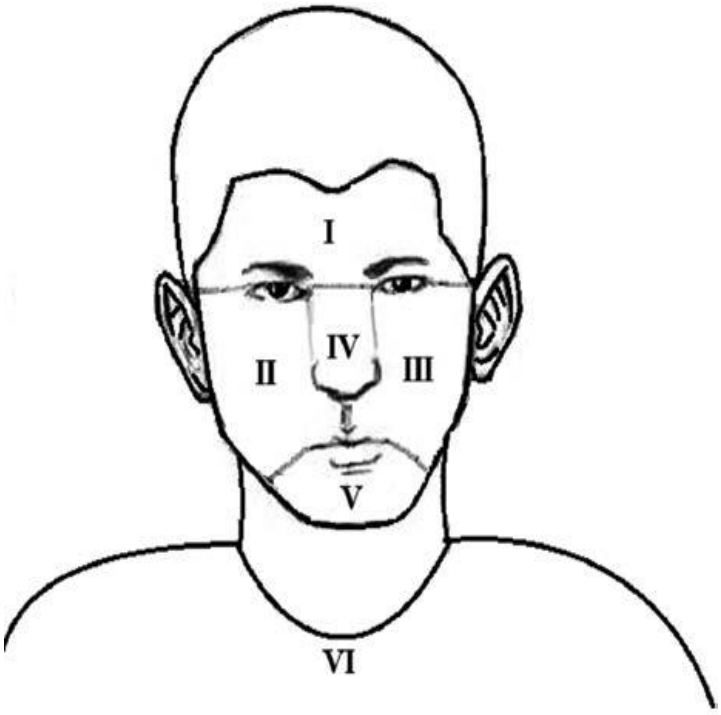
Boxcar ……. Hypertrophic…….

Postinflmmatory :

Hyperpigmentation …… Hypopigmention .....

Body weight ……kg Body height …….

Body mass index = weight(kg)／(height(m))^2



The six locations (I-VI) of the global acne grading system (114).

الدراسة الوبائية والسريرية من حب الشباب الشائع بين المرضى الليبيين في بنغازي

خلفية :حب الشباب هو مرض التهابي مزمن من الوحداتالشعرية الدهنية ويتميز بزيادة أفراز الدهون و تشكيل بثور, حطاطات (زوائد) ملتهبة ودماميل, وأقل كثيرا من قبل العقيدات, دماميل عميقة. على الرغم من أن حب الشباب بطبيعة الحال قد تكون محدودة ذاتيا ، يمكن أن تكون له عواقب طول الحياة، مع تشكيل ندوب محفرة أومتضخمة.

الهدف من هذه الدراسة : لتقييم ميزات الوبائية والسريرية من حب الشباب .

المرضى و الطرق : تم إجراء دراسة مستقبلية إلي 150 مريض ليبي مع التشخيص السريري من حب الشباب وكانوا يحضرون إلى قسم الأمراض الجلدية في مستشفىAljomhoria في بنغازي -ليبيا خلال سنة واحدة من Jan.2011 إلى Dec.2011وتم تسجيلهم في هذه الدراسة.

تعرض جميع المرضى للتاريخ المفصل و الفحص السريري وفقا ل استعداد التذييل الأول والثاني.وشدة حب الشباب السريرية باستخدام نظام الدرجات حب الشباب العالمية (GAGA)

النتائج : شملت ما مجموعه 150 مريضا بحب الشباب في هذه الدراسة و كان 103 من الإناث و 47 من الذكور(نسبة الذكور: الإناث 1 : 2.2) . وكان متوسط العمر 21 ± SD سنوات وكان في الفئة العمرية الأكثر إصابة 16-20 سنة (46.7٪) ومتوسط سن البدء 17.2 ± 4.3 سنوات . التاريخ عائلي إيجابي في 63.1 ٪ من المرضى. والوجه متأثر في جميع المرضي 100 ٪ثم يليه الصدر 73.3٪, الظهر 64.7 ٪ . تم العثور على شدة حب الشباب باستخدام (GAGA)كان 32.7 ٪ حب الشباب الخفيف ، وكان 62.7 ٪ حب الشباب معتدل، وكان 4.6٪ حب الشباب الشديد ،ولم يكن هناك أيا من المرضى لديهم حب شباب شديد جدا وكانت هناك أيضا علاقة بين معدل حب الشباب وشدته (p=0.006) .وهناك عوامل خارجية تؤثر علي تنشيط أو زيادة حدته و كان عامل الخطر الأكثر شيوعا الغذاء (52.7 ٪)، يليه عامل الإجهاد العاطفي (47.3٪) (p=0.00) وكان6

(12.8٪) فقط من المرضى الذكور المدخين و 4 (8.5 ٪) منهم من حب الشباب المعتدل و 2 (4.2 ٪) منهم من حب الشباب المعتدل. في المرضى من النساء كان 68 ٪ يحدث لهن تهيج ما قبل الحيض ، وكان 16.5 ٪ من علامات الجلدي التذكيرية . كان هناك نسبة أعلى من فرط تصبغ ما بعد حب الشباب (74 ٪) و ندب حب الشباب في مرحلة ما بعد (51.3 ٪) . 60.7 ٪ من المرضى الذين يعانون من مؤشر كتلة الدهون الطبيعي(BMI) ، 13.3 ٪ يعانون من نقص الوزن ، زيادة الوزن والسمنة (12 ٪) .

الاستنتاجات : حب الشباب هو من الأمراض الشائعة في المراهقين الليبية. .و المرضى من النساء أكثر تأثرا بحب الشباب و من حيث مضاعفات المرض فالتصبغ مابعد حب الشباب أكثر في الإناث ولكن ندوب أكثر في الذكور . وكان الطعام و الضغط النفسي من العوامل الأكثر تفاقم في مرضانا.