Scarring and None Scarring Facial Acne Vulgaris and the Frequency of Associated Skin Diseases

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ABSTRACT:

BACKGROUND:
Acne vulgaris(AV)is chronic inflammatory disease of pilosebaceous unit of young people. Patients with acne with or with out scarring might differ in regard to their immunological background from those free from acne.

OBJECTIVES:
To evaluate the problem of facial AV especially patients with scarring and to determine the frequency of associated skin diseases and to be compared   with acne free control.

METHODS:
A cross sectional randomized controlled epidemiological study was conducted from Oct.2005-Oct. 2006.Three hundred students from Basra University; 132 (44%) males and 168 (56%) females were enrolled, their ages ranged from 18-25 (20.9±1.8) years. They were divided into: *Group A* those free from acne (98 individuals),*Group B* with non scarring facial AV (96 patients), and *Group C* with scarring facial AV (106 patients). History and examination were done for their acne, scarring acne and associated skin diseases. Allen and Smith grading system for AV were used, and a new invented multiparametric scoring system for scarring acne was applied.

RESULTS:
AV was in 98(73.24%) males and   104 (61.9%) females. Scarring was 54 (50.95%) males and 52 (49.05%) females. Greasy skin was the most common type among *Group B* 67 (69.8%) versus 39 (39.8%) among *Group A*(P=0.000029) and was more common among *Group C* 84(79.2%) (P=0.00000001).Family history of AV was nearly similar in A and *B Groups* 55(57.29%) and 56 (52.83%) respectively, while in *Group A* was 39 (39.79%). Family history of scarring acne was in 35(33.02 %) of *Group C*, 16 (16.66 %) of *Group B*, and 3 (3.1%) in *Group A*; (P=0.00000017). The age of onset was similar in *A* and *B Groups* between 15-16 years. Majority of patients in *Group B* had non inflammatory type or mild inflammatory (papular) 65 (67.8%) patients, most of case were mild and moderate 86 (89.58%) patients, while high percent in Group *C* had inflammatory type 95 (89.62%), and more than half of them had severe and very severe types upon grading 56 (52.8%). The aggravating factors were similar in *A* and *B Groups* with stress and hot weather being the leading aggravating factors. Squeezing and digging habit was in 53 (50%) in *Group C* versus 23 (23.95%) in Group *B* (P=0.00024). In most cases of scarring acne, scarring was mild and moderate 85 (80.19%), and the most common type scars was the flat hyperpigmented [50 (47.17%) and 66 (62.26%) respectively].The most common effect of scarring acne on psyche was mild discomfort and mild dysmorphophobia 75 (70.75%).Associated skin diseases were more common among *Group A* 31 (31. 63%) than among *Group B* 22 (22.91%) and least common among *Group C* 14 (13.20%) (P=0.0067) and they were mainly dermatitis and skin infections.

CONCLUSION:
AV might reflect the immunological status especially among patients with scarring. The frequency of skin diseases was much less among patients with scarring acne.

KEY WORDS: acne, skin diseases, immunity, scoring system for   scarring acne.

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INTRODUCTION:
Acne vulgaris is a chronic inflammatory disease of pilosebaceous unit. It is a polymorphic disorder characterized by formation of comedones, papules, pustules, nodules and pseudocysts.
 In some cases, it is accompanied by scarring. Acne is a condition that affect adolescent commonly and usually resolved by the mid twenties and it is of

multifactorial etiology [1,2]. Scarring is a consequence of abnormal resolution or wound healing following the damage that occurs in the sebaceous follicle during acne inflammation. A cell-mediated immune response found to be involved in these inflammatory events but such a response not only contributes to the clearance of antigen but also to tissue damage [1]. In acne patient who where not prone to scarring, it was typical course of type IV delayed hypersensitivity reaction (DHR).Cell recruitment peaked at 48 h, after which there was a decrease in leukocytes, cellular activation and a return to normal level of blood vessels and vascular adhesion molecules in resolving lesions. Of CD4+ T cells, 50% were skin homing memory effectors cells and naive cells, while the remainder where unclassified, which suggest that effective resolution occurred by both nonspecific (innate) and adaptive immune mechanism. On the other hand, in lesions from acne patients who were prone to scar a predominantly adaptive immure response was present which was persistent and up regulated in resolving lesions. The numbers of CD4+ T cells were smaller than those found in lesions of non-scares, but a high percentage of these cells were skin homing memory/effectors cells, suggesting that these patients were sensitized to the causative antigen(s). In addition, the numbers of macrophages, blood vessels and vascular adhesion molecules were high. However, in resolving lesions, there was an up regulation of the response with greater cellular activation, a further influx of macrophages and skin homing memory effectors cells and angiogenesis remain high. Thus, it may be interpreted that, in patients prone to scarring there is a chronic (DHR.) provoked by a persistent antigen. Therefore, we can conclude that the cellular infiltrate was large and active with a greater non specific response (few memory T cells) in early lesions of non scarring acne patients, which subsided in resolution. In contrast predominantly specific immune response was present in scarring acne patients, which was initially smaller and ineffective, but was increased and activated in resolving lesions. Such excessive inflammation in healing tissue is conductive to scarring [3]. The different inflammatory cell profiles elicited by the two patient groups – those with non-scarring and those with scarring acne could explain the different qualities of repair observed. Lymphocytes and macrophages secrete an extensive array of cytokines and growth factors that are known to modulate dermal fibroblast recruitment, proliferation and phenotype, and will affect fibroblast function such as wound remodeling and contraction, both contributory factors in scarring. It is possible that the type and magnitude of the inflammatory response in "resolving" lesions from patients with such a dominant macrophage presence, would lead to abnormal healing and pathological scarring [1]. There are now evidences that the sebaceous gland is an immunocompetent organ [4]. In the other hand the colonization of skin by P. acnes may have an immunomnodulatory role *P.acnes* is unique to humans and this fact may equate with the rather unique composition of human sebum [1]. There is an interesting suggestion that the capacity to develop delayed immune hypersensitivity may be augmented and maintained by *P.acnes*, which colonize sebaceous glands in adults. A sequel of this may be an enhanced immunoregulatory effect, producing some protection against cancer such as leukemia and melanoma which occur with less frequency in acne patients [5, 6]. Also it has been suggested that *P.acnes* which enhances immune responses may provide protection against malignant hematological diseases [7,8]. There is already firm evidence that *P.acnes* promote anticancer activity in animals Administration of *P. acnes* to animal's results in stimulation of the immune system. It addition anti-tumor activity has been demonstrated against variety of neoplasms in animals, in particular leukemia, melanoma, and ovarian and breast carcinomas [9]. The mechanism of *P.acnes* induced immune enhancement is unknown but we can say that acne patients are not usually immunologically misfit [1]. When present in the follicle, *P.acnes* can induce immune response of varying intensity. It has been argued that variations in severity of acne from patient to patient may best be explained by variation in immune response to this pathogen.

The more intense the immune response the more severe the acne [10], and since the scarring usually tend to follow the severe acne;so scarring may be taken as a marker of good immune response. The aim of the present study is to evaluate the different aspects of acne vulgaris and to record the frequency of other skin diseases among scarring and non scarring groups.

PATIENTS AND METHODS:

A cross sectional systematic multistage randomized controlled epidemiological study was conducted on a sample of college students from Basra University in the south of Iraq at the period from the end of October 2005 to the end of October 2006.

A total of 300 students were enrolled in this study. Their ages ranged from 18-25 years with a mean ± SD of 20.9±1.8 years. The number of males was 132(44%) and females 168(56%). The sample collection took place during the 2nd half of February, March, April and beginning of May. Each person included in the study after consent was informed that these data are for the purpose of scientific research. Exclusion criteria included any person whose age above 25 years, his (her) acne was altered by treatment or those were free from facial acne. By the mean of direct interview, a satisfactory history was taken and full examination of the face only in the daylight was done. They were classified into 3 groups: Group A: those who are free from facial acne vulgaris (control group), Group B: those with non-scarring facial acne vulgaris and Group C: those with scarring facial acne vulgaris. The history includes age, sex, skin type (whether dry, normal or greasy), onset of acne (if present), its duration, aggravating factors noticed by the affected individual, squeezing or digging habit, presence of other dermatological diseases, family history of acne with it's scarring tendency among parents and siblings. Examination of the face was done for the type of acne whether non inflammatory (like comedones) or inflammatory like papular, papulopustular or nodulocystic and for assessment of its severity. Grading acne into mild, moderate, severe or very severe by utilizing Allen and Smith method (the over all severity acne grading system) (Table-1) [11]. For those with scarring acne, we used a new multiparametric scoring system (Table-2) since there was no universal scoring system for scarring acne vulgaris in dermatological literatures. In this study we grade scarring acne vulgaris depending on 5 different parameters (each scores 1, 2, 3 or 4 points). This system scores from 5 up to 20 points. Then we count the total score of 5 parameters. Accordingly we divided the severity of scarring into: mild if it scores 5-9, moderate if it scores 10-14 and severe if it scores 15-20.

Table 1: Grading System for Scarring Acne.

	Score parameter	1	2	3	4
1	No. of scars	≤ 10	11-20	21-30	>30
2	area Involved of the face	≤ ¼	>¼-½	>½-¾	>¾
3	Type of scars	Flat	Depressed	Hypertrophic	Keloid
4	Color of scars	Skin colored	Erythematous or hypopimented	Hyperpigmented	Bluish or grayish
5	Effect on psyche	No effect or mild discomfort	Mild dysmorphophobia	Moderate dysmorphophobia	Severe dismophophbia or social withdrawal.

RESULTS:

The number of subjects included in this study was 300 persons. The different aspects of the study were shown according to type of group. The age sex distribution is as follow: *Group A*: 98 subjects (32.7% of total), 34 (34.7%) males and 64 (65.3%) females, with male to female ratio = 1:1.9.The mean age was 20.95 ± 1.8 years. *Group B*: 96 subjects (32% of total), 44 (45.8%) males and 52 (54.2%) females with male to female ratio = 1:1.2.The mean age was 20.93 ± 1.57 years. *Group C*: 106 (35.3% of total), 54 (50.95%) males and 52 (49.05%) females with male to female ratio = 1.03:1.The mean age was 21.05 ± 1.6 years. The frequency of facial acne vulgaris (scarring and non scarring) among males was 74.24% (98 out of 132), while in females was 61.9 %(104 out of 168 subjects), so there is male predominance among acne sufferers in general (P =0.032). The number of males was slightly higher among *Group C*, but not to the degree that is statistically significant,54(50.95%) versus 52(49.05%), (P =0.890). The greasy skin was 67(69.8%) versus 39(39.8%) among *Group A* (P =0.000029) and it is more obviously predominant among *Group C* (79.2%), P value = 0.00000001. Family history of acne was positive in 54.96 %(111 out of 202) total acne sufferers ;(Group B and C). Positive family history of acne was about similar in both *Groups B* and C, 55 (57.29%) and 56 (52.83%) respectively. There was statistically significant association between acne and family history of acne (P=0.039). Family history of scarring type of acne was positive in 3 (3.1%) of *Group A*, 16 (16.66%) of *Group B* and 35 (33.02%) of *Group C* indicating that there was significant relationship between scarring acne and family history of such type of acne, (P=0.00000017). Age of onset of acne vulgaris in *A* and *B*: Its seems that there was no difference between non scarring

and scarring type of acne regarding the age of onset of acne, was 52.97% (107 out of 202 subjects) have the age of onset at 15-16 years. Types of acne among *Group B*: The non inflammatory and papular type of inflammatory acne was the predominant lesions in 65 subjects (67.7%) of non scarring acne group. Severity of acne in *Group B*: Most of the cases of non scaring facial acne vulgaris were mild and moderate acne, 48 (50%) and 38 (39.58%) respectively, while severe and very severe cases were present in 8 (8.34%) and 2 (2.08%) respectively. Types of acne among *Group C*: The study showed that the inflammatory type was seen in 95 (89.62%) of patients, with the papulopustular and nodulocystic type represented together 64.15% of total, and when we compared the presence of inflammatory type of acne with that among *Group B*: 60 out of 96 (60%), we find that there was a statistically significant difference (P=0.000005) meaning that the inflammatory type of acne was significantly more common among *Group C*. Severity of acne among *Group C*: Most of the cases of scaring acne occur in those with moderate, severe and very severe acne with the severe and very severe type representing together (52.84%). Aggravating factors among both *Groups B* and *C*: The leading aggravating factors of acne vulgaris that were noticed by patients are:

1-Stress.26.73%
2-Hot weather and sweating.22.77%
3-Premenstrual in females.19.23%
4-Spicy foods.12.87%
5-Sweety foods.10.39%
6-Fatty foods.4.95%
7-Hair epilation.4.95%
8-Sun exposure.3.46%
9-Cosmetics application.2.97%
10-Hand contact.1.98%

The stress and hot weather were the main aggravating factors among both *Groups B* and *C*, while the others were comparable in both groups. Squeezing and digging habit among *Groups B* and *C*: Squeezing and digging habits were more common among *Group C* in comparison with *Group B* (50% versus 23.95%) (P.value =0.00024). The onset of scarring in Group *B, C*:

In more than half of cases 62 (58.49%), scarring started from the beginning of having acne in both males and females and there is another smaller peak of onset for scarring 3 years after the onset of acne in 18 (16.98%) subjects. According to our scoring system, 50 (47.17%) subjects, of those with scarring facial acne vulgaris have moderate scarring, while the mild scarring was found in

33.02 %(35 subjects) and the severe scarring in 19.81 %(21 subjects). The study showed that the most common type of scars was the flat type 47.17% (50 subjects), followed by the atrophic type 35.85 %(38 subjects), then the hypertrophic type 10.38 %(11 subjects) and the least common was the keloid type 6.6 %(7 subjects). Keloidal and hypertrophic types of scars were more common in males than females (11.11% and 14.81% versus 1.92% and 5.77% respectively) (P=0.012), while the flat type of scars was more common in females (57.69% versus 37.04% in males) (P=0.033). The most common type of scars according to the color was the hyperpigmented (62.26%, 66 subjects) type and it was the commonest among both males and females followed by the skin colored type (21.7%, 23 subjects) then the hypopigmented (11.32%, 12 subjects) and the least was the discolored (bluish or grayish) type (4.72%, 5 subjects,). The effect of acne scarring on the psyche: Acne scarring sufferers have mild dysmorphophobia in 37.73 %(40 subjects) of cases, while 33.02% (35 subjects) of cases reported that they had only mild discomfort. Moderate dysmorphophobia was present in 18.87% (20 subjects), while severe dysmorphophobia and social withdrawal was present in 11(10.38%) subjects. The frequency of associated skin diseases in the 3 groups: The presence of different other dermatological diseases was more common among *Group A*, 31 subjects (31.63%) than those with *Group B*, 22 subjects (22.91%) and the least among *Group C*, 14 subjects (13.2%). This difference was statistically significant P value = 0.0067. (Table2) Different types of dermatitis were significantly more common among *Group A* than *Group B*; 15 subjects (15.31%) versus 7 subjects (7.29%) and Group *C* 4 subjects (3.77%) and this association was statistically significant (P value =0.011), while the infectious diseases, were more common among *Group A*, 12 subjects (12.24%), than among *Group B*, 4 subjects (4.17 %) and the least common were among *Group C*, 4 subjects only (3.77%). (P value =0.0261). Other skin diseases such as autoimmune, connective tissue diseases, navi, urticaria and others had no proven significant association. Skin diseases if present; they were associated to those with mild types of scarring; flat and atrophic types: 6 subjects (42.68%) and 7 subjects (18.42%) respectively, and less associated with severe types of scarring; hypertrophic and keloid type: 1 subject (9%) and 0 subjects (0%) respectively. This association was statistically significant, (P value =0.01).

Table 2 :Comparing the frequency of different skin diseases in the 3 groups of patients with acne vulgaris.

disease	Acne free group (n=98)	Non scarring acne group (n=96)	Scarring acne group(n=106)	P value
Different type of dermatitis (atopic,seborrhoeic ,.discoid,contact, pompholyx, photosensitivity, pityriasis alba)	15 (15.31%)	7 (7.29%)	4 (3.77%)	0.011
Infectious disease like recurrent boil,recurrent herpes simplex ,viral warts,tinea ,Baghdad boils	12 (12.24%)	4 (4.17%)	4 (3.77%)	0.0261
Autoimmune diseases like Vitiligo,psoriasis	3 (3.06%)	1 (1.04%)	2 (1.89%)	Not significant
Congenital naevi	0	3(3.12%)	0	Not significant
urticaria	0	1(1.04%)	2(1.89%)	Not significant
Connective tissue diseases	0	1(1.04%)	0	Not significant
Others:drug rash,pityriasis rubra pilaris,pityriasis lichenoides chronica, ,hairfall,hirsutisim, ,melasma.	1 (1.02%)	5 (5.21%)	2 (1.89%)	Not significant
Total	31(31.63%)	22(22.91%)	14(13.20%)	0.0067

DISCUSSION:

Acne vulgaris is a very common condition among young people that might be associated with scarring and disfiguring. The present study showed that acne vulgaris in general was more common in males than in females (74.24%) versus (61.9%) (P value = 0.032) and this fact was proved by many other published studies [12, 13]. Results indicate that facial scarring nearly equally affects both male and females and this finding had been reported before [14]. Regarding the skin type, greasy skin was more common among acne sufferers than acne free subjects; In addition, it was more common among those with scarring acne to the degree that it can be considered as a risk factor for scarring acne.

This observation has been studied before but no attention was paid to greasy skin in scarring acne [15]. Family history of acne vulgaris was nearly similar in both non-scarring and scarring groups and was significantly higher than that in acne free group. So, family history of acne is an important risk factor [16]. Family history of scarring type of acne was significantly more common among those with scarring acne as compared with those with non scarring type and acne free group indicating that the family history of scarring type of acne was a significant risk factor for developing scarring acne. This observation has not been adequately studied before. The age of onset of acne was nearly similar in both scarring and non-scarring acne groups, the majority of both being at 15-16 year indicating that the age of onset of acne was not a predicative factor for development of scarring.

This result was comparable to previous Iraqi study in which the mean age of onset of acne in males and females was 16.5 years [16]. Regarding the type of acne among non scarring group, we found that the mild types; the non inflammatory and papular type of inflammatory represented the majority of the cases, followed by moderate acne.While among those with scarring acne the reverse was true, where the majority of them had inflammatory type of acne, and this finding was statistically significant when compared with non scarring acne group, and upon grading for severity of acne, the severe and very severe types made together more than half of cases. These findings indicate that the more inflammatory type and the severe acne were important   risk factors for scarring. This finding was observed in a previous study [14]. The aggravating factors for acne were comparable in both scarring and non-scarring groups with stress and hot weather being the leading aggravating factors. Squeezing and digging habit was significantly more common among scarring group; indicating that this attitude may help to induce or aggravate scarring, an observation which has not been appreciated before. The onset of scarring in more than half of cases started with the onset of acne it self with another smaller peak after three year. This delay time reported between the onset of acne and the onset of scarring might be real, but could be related to the delayed subjects' awareness of the scars. Previous studies suggested that a time delay of three years between the onset of acne and ultimate degree of scarring [14].

When we graded the severity of scarring, we found that the majority had mild and moderate scarring and only minority had severe type of scarring. This grading was obtained according to our invented new scoring system since there was no global system for grading of scarring acne. Regarding the type of scars, the flat type was the most common one followed by the atrophic then the hypertrophic types and the least common was the keloid type. The keloid and hypertrophic types of scars were obviously more common among males than females; similar finding had been previously observed [14]. The most common type of scars according to the color was the hyperpigmented type followed by the skin colored then the hypopigmented and lastly the discolored type (bluish or grayish). These finding were consistent with the dark complexion of Iraqi population; this observations had not been recorded before. As a regard to the effect of scarring on the psyche, mild dysmorphophobia was the most common effect, while severe dysmorphophobia and social withdrawal was present in minority of cases with male predominance. This might be due to the more severe types of scarring among males, although the sum of moderate and severe dysmorphophobia was higher in females than in males and this could attributed to females' greater awareness of minor blemish; an observation which had been noticed for acne in general [17]. The frequency of different skin diseases were recorded more frequent among the acne free group than in those with non scarring acne group and they were less common among the scarring acne group and this was a statistically significant difference .These findings might indicate that people who had acne might have better immunological defense system than those who were acne free, that was especially true in cases of dermatitis and skin infections which were less common among acne sufferers and least common among those with scarring. We also found that the frequency of the dermatological diseases decreased with the increase of the severity of scarring. These observations were to the best of our knowledge reported for the first time. These finding could be explained on bases that acne may provide good immunological defense, as acne mostly associated with greasy skin (seborrhea), and the sebum by it self is protective against fungal and bacterial infections and forms a barrier against different irritants and pathogens [5,6]. In addition, acne is mostly associated with colonization of the skin with *P.acnes*, which may have an immunological role, producing some immunological

enhancement through increasing the capacity to develop and maintain type four immune response (delayed hypersensitivity reaction-DHR) [1,10-11]. There is augmented DHR. Which is maintained by *P.acnes*, and as a sequel of this there may be enhanced immunoregulatory effect, producing some protection against cancer such as leukemia and melanomas which occur with less frequency in acne patients [5,6]. In addition scarring acne is mostly associated with severe form of acne where there is more seborrhea and colonization with *P.acnes* (inflammatory type).Also the type of inflammation differs from that of non scarring in being predominant adaptive immune response which is persistent and up regulated in resolving lesions resulting in chronic delayed type hypersensitivity reaction which is more specific and prolonged than in non scarring type of acne [1,3]. Accordingly, we can conclude that scarring is associated with more sebum, more *P.acnes*, more severe inflammation and more intense immune response. These observations might explain why other skin disease like infections and dermatitis were the least common among those patients with scarring type of acne and decrease with the increasing severity of scarring, where there is more intense underlying immunological defensive reaction.

CONCLUSION:

Acne vulgaris in general and scarring acne in particular were associated with decreasing frequency of other skin diseases and that might be due to good underlying immunity. Thus the acne particularly the scarring type although destroying and disfiguring but it could be a marker of good immunological status.

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