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Research Article

A preliminary study of serum Procollagen III N-terminal peptide (PIIINP) in Acne scar patients

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Abstract

Background: Serum PIIINP is a collagen III precursor that has been linked to many inflammatory diseases ending in fibrosis such as burn, scleroderma and liver cirrhosis. The study aimed at assessment of serum PIIINP in acne scar patients in adults >18 years. **Methods**: The study was conducted on 30 patients attending at Dermatology Outpatient Clinic of Minia University Hospital. in the period from January 2022 till November 2022. Patients were divided into 2 groups: 15 patients with acne scars and 15 individual as a control group, Serum PIIINP was assessed in each patient using Human procollagen type 3 ELISA Kit from BT LAB (Bioassay Technology Laboratory**)**, China, and by using of Huma reader 3700, Germany. **Results**: Acne scar patients had significantly higher levels of serum PIIINP, compared to that of control group. **Conclusion:** Serum PIIINP is predictor for ongoing scarring processes in acne scar patients and can be a useful serum biomarker in assessment of acne scar patients.

Keywords: PIIINP; Acne; Acne scar

Introduction

Acne vulgaris is disease of pilosebaceus unit. It presented in form of comedons and inflammatory papules, pustules and nodulo-cystic acne. Healing sequence of acne vulgaris, according to its severity, is post-inflammatory erythema (PIE), post-inflammatory hyperpigmentation (PIH), and scarring [(1.2)].

Acne severity might not only be due to a specific Cutibacterium acnes strain, but also related to multiple host and environmental factors that could potentially yield different level of activation of innate immunity in severe acne. Early and intense inflammatory events in the epidermis have indeed been shown to contribute to the development of scars [(3, 4)].

Acne scars are classified into atrophic and hypertrophic types and most them are in the form of atrophic lesions. Aberrant collagen degradation and production during the healing process leads to acne scars. Atrophic scars are presented in 80-90 % of cases. In atrophic acne scars devastating degradation of elastic fibres and collagen fibres occurred in the dermis, followed by their incomplete recovery [(5, 6, 7)].

Amino-terminal peptide of type III procollagen (PIIINP) is a peptide that released from the precursor peptide, during the synthesis and deposition of type III collagen, a fibrillar collagen that is abundant in a variety of internal organs and skin. Increased amounts of type III

collagen are present in many systemic diseases linked to tissue fibrosis and excessive scarring such as systemic sclerosis, liver and kidney fibrosis, and its serum concentration has shown promise as a biomarker of increased collagen turnover and or accumulation [8, 9].

The present work was aimed to measure of serum PIIINP in acne scar patients

Patients and methods:

The present study was conducted on 30 patients divided into 2 groups: 15 patients with acne scars and 15 individual as a control group, attending at Dermatology Outpatient Clinic of Minia University Hospital. The study was performed in the period from January 2022 till November 2022. Inclusion criteria; untreated acne scar patients. Exclusion criteria; Patients below 18 years, patients with active acne lesions at time of examination and in the past three months, hepatic patients, patients with rheumatoid arthritis or any collagen or fibrosing diseases, patients with significant traumatic or burn scar were also excluded.

Ethical consideration:

Ethical approval was granted by the Ethical Committee of the Faculty of Medicine, Minia University with approval number (217/01/2022). Before data collection, written informed consents were obtained from patients after supplying comprehensive information about the nature of the study.

Clinical assessment:

Each patient was subjected to:

1- History taking: Age, sex, acne onset, duration.
2- Clinical examination: **A-** Local examination of the face; to evaluate type of acne scars. B- General examination**;** for signs of systemic diseases such as liver cirrhosis, rheumatoid arthritis and any collagen disease or any fibrosing disorder.
3- Digital photography for the face of each patient, by Canon DS126621 camera, made in Taiwan.

Assessment of serum PIIINP:

Two ml of peripheral venous blood sample was withdrawn from each subject on plain tube, then left to clot for 20 minutes at room temperature then centrifuged at 3000 RPM for 20 minutes. Expressed serum were frozen consecutively and stored at -20°C until to be used for determination of Human procollagen type 3 using Human procollagen type 3 ELISA Kit from BT LAB (Bioassay Technology Laboratory**)**, China, and by using Huma reader 3700, Germany.

Statistical analysis:

The collected data were coded, tabulated, and statistically analyzed using SPSS program (Statistical Package for Social Sciences) software version 24. Descriptive statistics were done for parametric quantitative data by mean, standard deviation, minimum & maximum of the range. Independent samples T-test was used to compare serum PIIINP of the studied population and the control individuals. The significance of the result was assessed in the form of p value that was differentiated into (Non-significant when p value > 0.05 and Significant when p value ≤ 0.05).

Results

Socio-demographic data

The present study was conducted on 30 patients divided into 2 groups: 15 patients with acne scars and 15 individual as a control group. Acne scar group: the patients were 8 males (53%) and 7 females (47%). Their ages at time of examination ranged from 19 to 42 years, with a mean ±SD of 27.4±7.09 years. Control group: age of the participants were 7 males (47%) and 8 females (53%). Their ages at time of examination ranged from 19 to 33 years, with a mean ±SD of 23.4±4.5 years (Table 1)

Clinical assessment:

Clinical assessment of the studied group revealed acne onset ranged between 12 to 21 years, with a mean ±SD of 16.7 ±2.9

years, acne scar duration range of 6 to 27 years, with a mean ±SD of 10.5 ±5.7 years. An atrophic scar is manifested in 14 patients (93.3%), while hypertrophic scar in one patient (6.7%). (Table 2, figure 1).

Serum PIIINP assessment:

In acne scar patients, the serum PIIINP level ranged from 3 to 6 micrograms/L with a mean ±SD of 3.97 ±0.82 micrograms/L. In control patients, the serum level of PIIINP ranged from 2.1 to 4.2 micrograms/L with a mean ±SD of 3.43 ±0.57 micrograms/L. Serum PIIINP in acne scar patients were statistically significant higher than that of control group (p = 0.04) (table 3).

Table 1: Demographic data of the studied groups

	Acne scar group (n=15)	Control group (n=15)	P value
Age (years)			
Mean±SD	27.4±7.09	23.4±4.5	0.07
Range	19-42	19-33	
Sex			
Man	8(53%)	7 (47%)	0.9
woman	7(47%)	8(53%)	

Table 2: Clinical assessment of acne scare patients

	Acne scar group (n=15)
Age of onset (years)	
Mean±SD	16.7 ±2.9
Range	12-21
Duration of acne (years)	
Mean±SD	10.5 ±5.7
Rang	6-27
Type of acne scar	
Atrophic scar	14 (93.3 %)
Hypertrophic scar	1 (6.7 %)

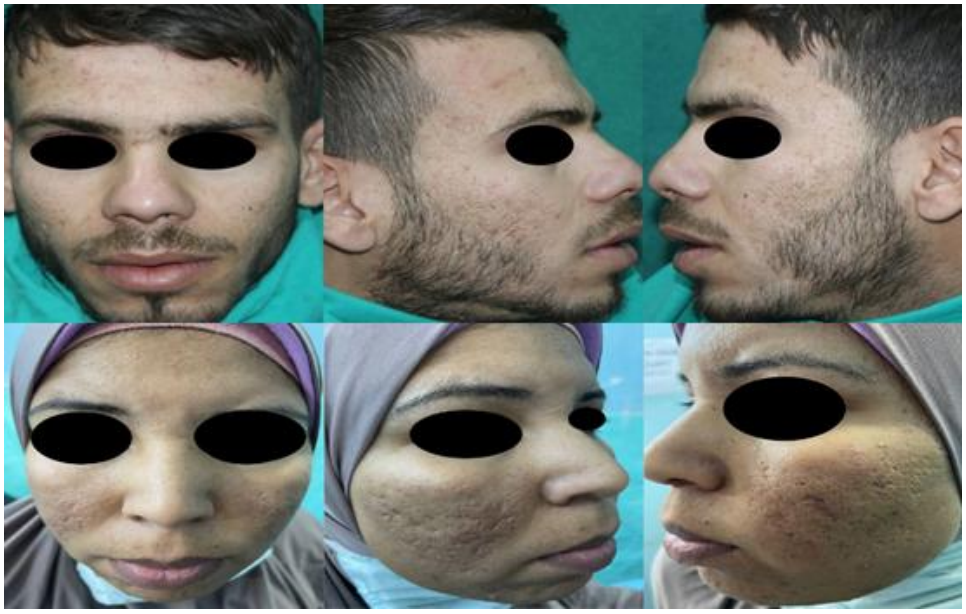

Figure 1: patients with atrophic acne scars

Table 3: Serum PIIINP in the studied groups

	Acne scar group (n=15)	Control group (n=15)	P value
Serum PIIINP (micrograms/L) Mean±SD Range	 3.97 ±0.82 3-6	 3.43 ±0.57 2.1-4.2	 0.04

Discussion

The present work was conducted on 30 participants; 15 acne scar pateitns and 15 contropl individual. We excluded patients with active acne lesions during last 3 months to exclude ongoing follicular inflammation which affect scar process. Pathogenesis of active acne lesions is multi factorial including propionibacterium acnes, androgen activity and increased sebum production. It stimulates the follicular inflammation and ruptures which stimulate the wound healing process resulting in scar production [10, 11, 12].

We noted a higher incidence of atrophic scars, in comparison the hypertrophic scars, in the studied patients. Our results come the finding of **Jacob et al, 2001** and **Moon et al, 2019** [6, 13].

To the best of our knowledge the current study is the first study that assesses serum PIIINP in sera of acne scar patients. In acne scar group the serum levels of PIIINP was significantly higher than control, meaning that serum PIIINP reflect acne scarring process, and this is similar to Abdel-Magiud et al., 2020, who measured serum collagen III in acne scar patients and mentioned that there is a decreased serum collagen III with procedural treatment, and highlighted that serum collagen III can be a useful marker of collagen turnover in post-acne scarring, enabling the assessment of improvements in response to different therapeutic modalities[14]. Similarly serum PIIINP can be used as a marker for ongoing synthesis or degradation of type III collagen fibrils [15].

Moreover, **Soylemezoglu et al., 1997** agree with us, as they reported correlations between serum and urine levels of collagen III and the severity of renal fibrosis in their study [16].

Our results are consistent with findings from **Vassiliadis et al., 2011** study in which they found a significant correlation between levels of collagen III in urine and skin fibrosis induced in a mouse model [17].

Also our results are supported by **Ulrich et al., 2022** in which they found that serum PIIINP has increased in the sera of burnt patients, during post-burn scar formation. As well as, serum PIIINP correlates with the pre- and post-operative Burn Scar Index and with the PIIINP immune-staining in scar tissue [18].

Also our results is supported by **Pettersson-Pablo et al., 2021** who have mentioned that the amino-terminal peptide of type III procollagen (PIIINP) is a peptide that released from the precursor peptide during the synthesis and deposition of type III collagen in the skin [8].

Another study which was conducted by **Jensen et al., 1997** it was mentioned that, during collagen degradation, these molecules may be released, and hence soluble N-propeptides for type III collagen reflect both degradation and synthesis. So circulating levels of PIIINP may originate from ongoing synthesis or degradation of type III collagen fibrils with PIIINP on their surface [15]. These data supporting our data as serum PIIINP was significantly higher in acne scar patients when compared with control.

Conclusion

Serum PIIINP is correlated to acne scar. It can be a useful biomarker in assessment and predicting of the progression and severity of scars in acne patients

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