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Assessment of Serum Interleukin-17 As a Prognostic Factor in Patients with Postburn Scars

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ABSTRACT

Background: Postburn scars are defined as abnormal wound healing after burn, which results in disfigurement and psychological stress. The factors determining the figure and the severity of the upcoming scar after burn are still unclear. But there are many studies suggesting that inflammation is the initiating step of developing postburn scars. Interleukin-17 is an inflammatory factor that has the ability to promote the T cells activation leading to chronic inflammation. Also, interleukin-17 was proved to increase the skin fibrosis resulting in delayed wound healing. If we find a strong relation between the severity of postburn scars and the level of serum interleukin-17, we can target it and suppress the inflammation in the treatment protocol of burn to avoid extensive postburn scars.

Objective: This study aimed to find a link between serum intrleukin-17 and the severity of the resulted scar following burn injury so when targeting this cytokine during the early inflammation, we can avoid sever pathological scar later.

Patients and methods: Sixty patients having scars from burns were collected for the study. The scars were assessed utilizing Vancouver score scale (VSS). A serum sample was taken from each patient to estimate the serum level of interleukin-17 using ELISA kit.

Results: The study showed a statistically significant strong positive correlation between the levels of interleukin-17 and the severity of the postburn scars and confirmed the results of previous studies that serum interleukin-17 is higher in more recent scars.

Conclusion: Interleukin-17 may have a role as a factor increasing the chance of formation of sever scars after burn and targeting this inflammatory mediator early after burn may be of great value to avoid the development of sever postburn scar.

Keywords: Postburn scars, VSS, Interleukin-17.

INTRODUCTION

Postburn scars are defined as the scars that develop as a complication of burn injury, taking different forms with variable disfigurements depending on many factors either extrinsic or intrinsic [1]. Scars that develop after superficial burn injuries are usually non-hypertrophic, sometimes with only slight change in skin colour. However, deeper burns commonly progress to pathologic obtrusive scars as hypertrophic scars [2].

Patients with severe postburn scars often experienced limited mobility, skin contracture, aesthetical problems making the patient estranged from society, and a dramatic change in the quality of life [3].

There is great improvement in the critical care of patients exposed to massive burn injury using the best optimum fluid and electrolyte replacement together with the use of updated surgical techniques that has significant impact on the survival rate of those patients. However, the resulting scars remain a long lasting memory of the accident to such patient and to all the surroundings. Minimising the scarring and decreasing the pathologic alterations during the healing process after burn remains one of the main requirements for the patients [4]. So, the care given for any burn patient should include the best treatment options to reach the best possible cosmetic outcome. After injury, both damaged tissues and activated platelets, start inflammatory reactions by attracting immune cells to the site of injury to arouse a stage of proliferation and during this stage, wound area also decreases in size by the action of wound contraction. After that, tissue reaches the remodelling stage. Finally, this stage ends by the organisation of collagen fibrils resulting in the normal appearance of the scar. The abnormal scar formation is characterized by abnormal organisation and proliferation of fibroblasts [5].

The pathophysiology of how the different types of scars with variable severity are formed has not fully comprehended. It has proved in many studies that inflammation has the principal role in modulation and arrangement of collagen during the formation of the scar and the severity of inflammation correlated positively to the final appearance of the resulted scars [6, 7].

Interleukin-17 (IL-17) is one of the inflammatory cytokines produced by CD4+T cells [8]. Its role is to activate T helper cells and stimulate the production of IL-6, IL-8 and the subsequent inflammation. Numerous earlier researches demonstrated the upregulation of IL-17 in keloids and hypertrophic scars [9]. Moreover, IL-17-stimulated mice showed accelerated fibrosis, which increased the infiltration by macrophages, causing a delay in the healing process of wounds and occurrence of excessive inflammation [10].

Additionally, IL-17 induces the production of stromal cell-derived factor 1, which increases the collection of Th17 cells from the circulatory system. This may result in excessive infiltration of T cells by

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this positive feedback mechanism resulting in chronic inflammation at the wound site [11].

This study was designed to find a link between serum interleukin-17 and the severity of the post burn scars as the existence of this correlation could be the key to develop a treatment protocol that can selectively block specific pathways within the early stage during wound healing and may have a role in preventing unwanted pathological scar formation.

PATIENTS AND METHOD

This study is categorized as an observational, cross-sectional study that was conducted on sixty patients presented to the Dermatology Outpatient Clinic of the National Research Centre suffering from postburn scars.

Exclusion criteria: Patients under 18 and over 50 years old. Patients receiving systemic immunosuppressant treatment. Pregnancy and lactation. Patients with any immunological disease.

Patients were subjected to the following: Thorough history taking and clinical evaluation. Clinical examination of the scars to be evaluated by VSS that was calculated depending on the data on table (1).

Vancouver score scale:

It is a scar assessment numeric score, used widely to evaluate any scar either in the clinical practice or research studies. It depends on evaluation of four characteristics of the scar which are: vascularity, height, pliability, and pigmentation. As shown in table 1, each characteristic is given a score and then added together to get the final score that ranges from 0 to 13 [12].

Table (1): The Vancouver Scare Scale (VSS)

Pigmentation (0-2)	Normal	0
	Hypopigmentation	1
	Hyperpigmentation	2
Vascularity (0-3)	Normal	0
	Pink	1
	Red	2
	Purple	3
Pliability (0-5)	Normal	0
	Supple	1
	Yielding	2
	Firm	3
	Banding	4
	Contracture	5
Height (0-3)	Normal (flat)	0
	0-2 mm	1
	2-5 mm	2
	>5 mm	3

1. Three ml blood sample was taken from each patient under complete aseptic condition.
2. Serum interleukin-17 was measured for each patient by ELISA (Enzyme Linked Immune Sorbent Assay).

Ethical approval: This study was done after the agreement of The Ethical Committee, Dermatology Department, National Research Centre (NRC). The study was conducted in accordance with the principles specified in the Declaration of Helsinki for Human Subject Experimentation. All patients in the current trial provided informed written permissions, and their privacy rights were constantly monitored.

Statistical analysis

SPSS version 23.0 was used on an IBM PC for data analysis. Explanation of quantitative variables given by the Shapiro-Wade test of normality as Mean ± SD, median, and IQR. A breakdown of qualitative factors shown as percentages and numbers. When comparing quantitative variables between the two groups in non-parametric data (SD > 30% mean), the Mann-Whitney test was used. When comparing quantitative variables between more than two groups in non-parametric data (SD > 30%mean), the Kruskall Wallis test was used. For linear relationships between variables, Spearman correlation test was used. When the p-value was equal to or less than 0.05, it was deemed significant.

RESULTS

Clinical and demographic characteristics of the 60 study participants: All patients were exposed to burn for not more than 5 years and with scar surface area of a lower order than 50% of their bodies surface area.

Table (2): Demographic data of the patients

	Median (IQR)	**Range**
Age (years)	34.5 (31-37)	28-39
BMI	28 (26-32)	21-39
Vancouver score	7 (7-9)	4-9
Serum interleukin 17 (pg/ml)	54.9(50.7-68.4)	24.8-76.4

Correlation between serum interleukin-17 and Vancouver scores of patients:

It was discovered that there was a statistically highly significant positive correlation between the serum level of interleukin-17 and the Vancouver score scale of the postburn scars of patients ($r = 0.863$, $p = 0.001$) as shown in figure (1).

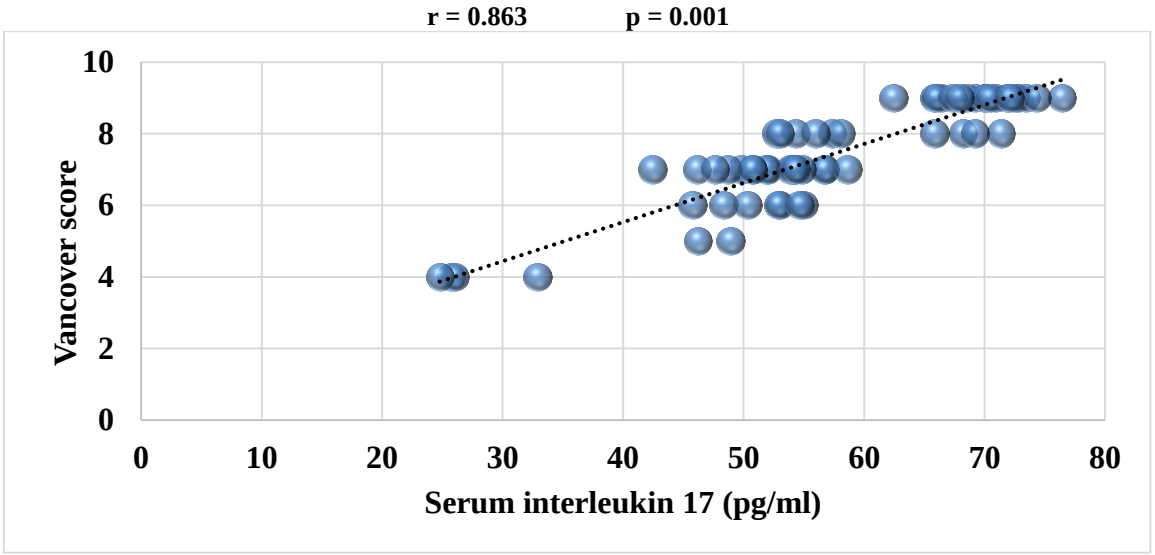

Figure (1): Correlation between serum interleukin-17 and Vancouver score

Relation between serum interleukin-17 and age of patients:

It was found that there was a highly significant positive correlation between the serum level of interleukin-17 and age of patients as it increase with patient of older age (r = 0.443, p = 0.001) as shown in figure (2).

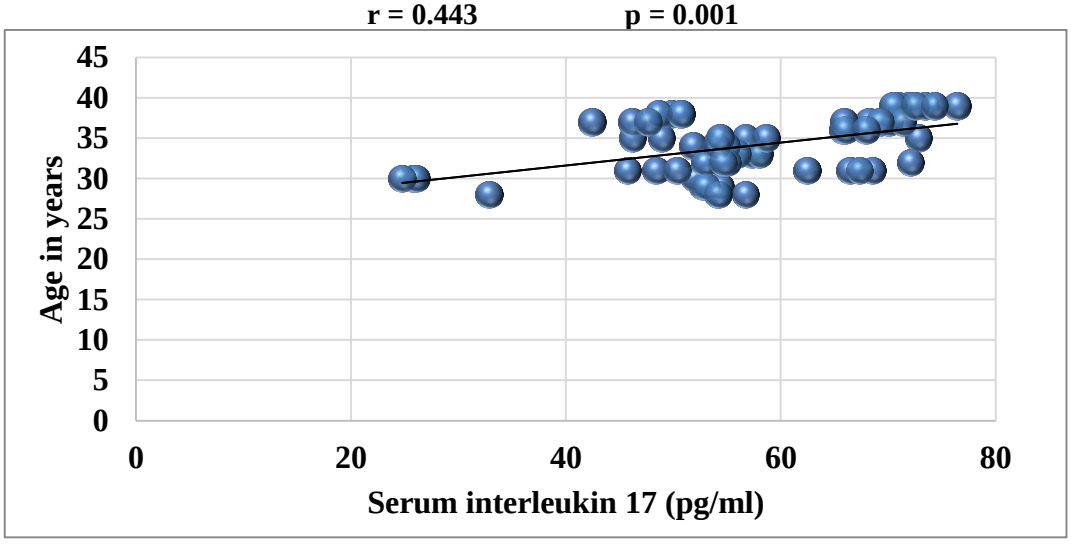

Figure (2): Correlation between serum interleukin-17 and age of patients

Relation between level of serum interleukin-17 and duration of the scars:

A statistically significant negative correlation was discovered between the serum level of interleukin-17 and the duration of the scar as it was higher in patients with recent scars (r = -0.316, p = 0.014) as shown in figure (3).

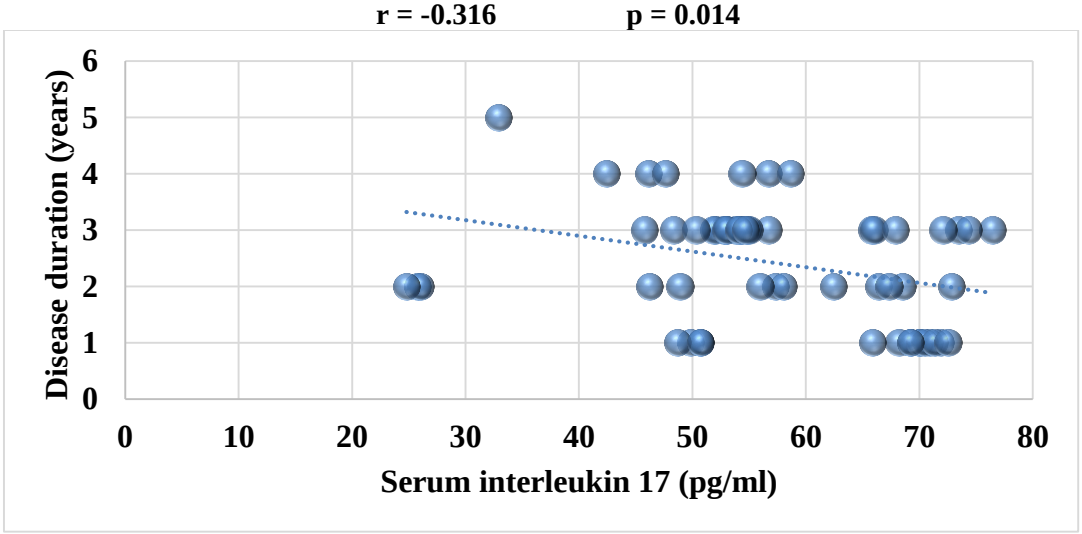

Figure (3): Correlation between serum interleukin-17 and scar duration.

DISCUSSION

The idea of this study was to find a link between serum intrleukin-17 and the severity of the resulted scar following burn injury so when targeting this cytokine during the early inflammation, we can avoid sever pathological scar later.

Interleukin-17, according to previous studies, was proved to be elevated in hypertrophic scar tissue. Also, there was a study that tried to inject recombinant IL-17 into the wound area during early inflammatory stage and the result was aggravation of fibrogenesis and increases the inflammation. However, on depleting macrophages that mediates the effect of IL-17 by clodronate liposomes, the fibrogenesis and inflammation was blocked [13]. **Lucas *et al.*** [14] suggested that early depletion of macrophages would be beneficial in decreasing the risk of scar formation and that opinion was based on the fact that inflammation and remodeling of tissues are necessary for normal healing of wounds but in appropriate degrees otherwise keloids and hypertrophic scars may develop. Also, it was observed that excessive inflammatory cells during remodeling stage correlates with the severity of development of pathological scars by affecting fibroblast proliferation and differentiation, and also collagen deposition [14].

Many studies have proposed different forms of anti-inflammatory treatments to decrease the chance of development of abnormal scar but, most of them have been evaluated only during the remodelling phase of wound healing. Researches that evaluate, and try the anti-inflammatory therapies at these early stages were very limited, because moderate inflammation in early stage is required for wound healing, and for preventing any possible infection [14-16].

Botulinum toxin was tested as a treatment to improve the scar appearance but with limited effect as regards the size of the scars [15]. So, more specific, and recent early interventions such as trying to suppress the accumulation of macrophages, instead of using general anti-inflammatory treatments, may be more promising. To this point, more research may be needed to study the exact role of the immune cells and the inflammatory mediators during wound healing and subsequent scar formation, therefore providing new therapeutic modalities for normal healing of wounds. Moreover, developing treatments that selectively block certain pathways within the early stages of the process of healing may have prophylactic effects that antagonize the formation of a pathological scar [16].

To prevent the formation of a pathological scar during wound healing has become a goal. To develop a novel combination therapeutic modality, a comprehensive cause effect relation among key cells and molecules within scar pathogenesis should be found.

We could prove through our study that there was a strong significant correlation between serum interleukin-17 and the severity level of the scar, so we recommend further investigations targeting these cytokines in early stage of wound healing to avoid the occurrence of a sever pathological scar.

CONCLUSION

In a word, interleukin-17 may have a role as a factor increasing the chance of formation of sever scars after burn and targeting this inflammatory mediator early after burn may be of great value to avoid the development of sever postburn scar.

Conflict of interest: None.
Fund: None.

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