

## ORIGINAL PAPER

doi: 10.5455/medarh.2018.72.410-413

MED ARCH. 2018 DEC; 72(6): 410-413

RECEIVED: OCT 12, 2018 | ACCEPTED: NOV 25, 2018

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# Serum Concentrations of Interferon Gamma (IFN- $\gamma$ ) in Patients with Psoriasis: Correlation with Clinical Type and Severity of the Disease

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## ABSTRACT

**Introduction:** The etiopathogenesis of psoriasis is still unclear but there is evidence that many of cytokines released by keratinocytes and inflammatory leukocytes may contribute to the induction or persistence of the inflammatory process in psoriasis. **Aim:** The aim of the study was to evaluate serum concentrations of Interferon gamma (IFN- $\gamma$ ) in patients with psoriasis and the healthy subjects and also to assess a possible association between IFN- $\gamma$ , clinical type and severity of disease. **Material and Methods:** The study included a total of 60 patients with psoriasis and 20 healthy subjects in the control group. According to the clinical type of disease, patients with psoriasis were divided into four groups: psoriasis vulgaris (PV), psoriasis erythrodermica (PE), psoriasis pustulosa (PP) and psoriasis arthropatica (PA). Blood samples were collected from all psoriasis patients and from healthy control subjects. Serum IFN- $\gamma$  levels were measured by an enzyme-linked immunosorbent assay (ELISA) technique. The severity of PV was assessed by Psoriasis Area and Severity Index (PASI) score. **Results:** The serum concentration of IFN- $\gamma$  in patients with psoriasis was significantly higher than that in the control group ( $1.91 \pm 1.79$  pg/mL vs  $0.91 \pm 0.38$  pg/mL, respectively). Significantly elevated serum IFN- $\gamma$  concentrations were noticed in patients with PV ( $2.15 \pm 0.30$  pg/mL). There was no statistically significant difference between the mean values of IFN- $\gamma$  compared to the clinical type of psoriasis ( $p > 0.05$ ). In the group of patients with PV 36 (85.71%) patients had mild form of disease with PASI  $< 50$ , and 6 (14.29%) patients had severe disease with PASI  $> 50$ . It was not found statistically significant correlation between serum IFN- $\gamma$  level and PASI score in the group of PV. **Conclusions:** The results of our study indicate that psoriasis is associated with significant changes in the serum concentration of IFN- $\gamma$ . There was no significant correlation between serum IFN- $\gamma$  concentrations, clinical type of psoriasis and severity of PV evaluated with the use of PASI score.

**Keywords:** serum concentration, psoriasis, cytokines, IFN- $\gamma$ .

## 1. INTRODUCTION

Psoriasis is a common chronic inflammatory skin disease that affects 1%-3% of the general population (1). The disease is classified into several clinical types of which the most common is psoriasis vulgaris (PV), and it occurs in 90% of patients (2). The less common type is psoriasis pustulosa (PP) which is characterized by a localized or a generalized formation of a sterile pustules. Psoriasis erythrodermica (PE) and psoriasis arthropatica (PA) are the more severe types of disease and they most frequently occur as a complication of the two previous types of disease. Psoriasis has a multi factorial aetiology, including genetic predisposition, environmental factors, and vascular and immune system disturbances. The histological and immunohistochemical fea-

tures of psoriatic lesional skin consisting of activated memory-effector CD4<sup>+</sup> or CD8<sup>+</sup>, denoted by CD45RO<sup>+</sup>, T cells in the dermis which are primarily CD4<sup>+</sup> cells and epidermis which are predominantly CD8<sup>+</sup> cells (3). Although the etiopathogenesis of the disease is not clear, many studies have shown that levels of cytokines released by keratinocytes and inflammatory leukocytes may contribute to the induction or persistence of the inflammatory process in psoriasis. It is postulated that changes in cytokine production both locally and systemically could be useful in monitoring disease activity. Interferon gamma (IFN- $\gamma$ ) is one of the key proinflammatory cytokine central to many biological processes. The changes in serum IFN- $\gamma$  concentrations were found in many diseases

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such as psoriasis (4), systemic lupus erythematosus (5) and lichen planus (6). In some of these diseases, serum IFN- $\gamma$  concentration correlated with activity and intensity of the disease, and may be used as a prognostic factor.

## 2. AIM

The aim of our study was to evaluate serum concentrations of IFN- $\gamma$  in patients with psoriasis and healthy subjects, and also to determine a possible correlation between IFN- $\gamma$  and clinical type and severity of psoriasis.

## 3. PATIENTS AND METHODS

The study was conducted on 60 patients with psoriasis and 20 healthy controls. The planned research is conducted on the basis of the usual approaches the subject method history and objective medical examination. The patients who had received any topical or systemic treatment within previous 3 months were excluded from the study, as well as patients with any diseases based on the immune pathomechanism, which could influence serum concentrations of IFN- $\gamma$ . All patients were divided into 4 groups according to the clinical type of psoriasis: a) psoriasis vulgaris; b) psoriasis pustulosa; c) psoriasis erythrodermica and d) psoriasis arthropatica. The severity of PV, including erythema, induration, scales, and surface, was assessed by the psoriasis area and severity index (PASI) for each patient (7). The control group consist of venous blood samples (5-10 ml) were taken in vacutainer tubes under sterile conditions from all psoriasis patients and controls subjects. Serum IFN- $\gamma$  levels were measured by enzyme-linked immunosorbent assay (ELISA) technique, using Quantikine Human IFN- $\gamma$  Immunoassay (R&D System, Minneapolis, MN, USA). Briefly, this assay employs the quantitative sandwich enzyme immunoassay technique. A polyclonal antibody specific for IFN- $\gamma$  has been precoated onto a microplate. Standards and samples are pipetted into the wells and any IFN- $\gamma$  present is bound by the immobilized antibody. After washing away any unbound substances, an enzyme-linked polyclonal antibody specific for IFN- $\gamma$  is added to the wells. Following a wash to remove any unbound antibody-enzyme reagent, a substrate solution is added to the wells and color develops in proportion to the amount of IFN- $\gamma$  bound in the initial step. The color development is stopped and the intensity of the color is measured. The PASI scores of patients with psoriasis vulgaris and their correlation with serum IFN- $\gamma$  were evaluated.

### Statistical analysis

Statistical analysis of the data was performed using SPSS Version 17. The data are expressed as mean  $\pm$  standard deviation. The test distribution was done by Kolmogorov-Smirnov test, and comparison of mean values between groups were performed by t-test. The data were considered statistically significant if p values were less than 0.05.

## 4. RESULTS

The study group composed of 60 patients with psoriasis (27 female and 33 males; the mean age of the pa-

tients was 52.2 years, ranging from 14 to 85 years), and 20 healthy controls (13 female and 7 male, the mean age 47.40 years, ranging from 21 to 75 years). There was no significant difference in age and female/male ratio between the patients and controls ( $p > 0.05$ ). The mean duration of psoriasis was  $12.9 \pm 11.9$  (range 0.1-43 years). In the total of 60 patients with psoriasis, 42 (70%) had PV, 9 (15%) patients had PE, 6 (10%) patients had PP and 3 (5%) patients had PA. The serum concentration of IFN- $\gamma$  in patients with psoriasis was significantly higher than in the control group ( $1.91 \pm 1.79$  pg/mL vs  $0.91 \pm 0.38$  pg/mL, respectively). Significantly elevated serum IFN- $\gamma$  concentrations were noticed in patients with PV type ( $2.15 \pm 0.30$  pg/mL), compared with patients suffering from PE ( $1.57 \pm 0.68$  pg/mL), PA ( $1.33 \pm 0.53$  pg/mL), and in particular patients suffering from PP ( $1.08 \pm 0.21$  pg/mL) who had the lowest mean serum concentration of IFN- $\gamma$  (Table 1). There was no statistically significant difference between the mean values of IFN- $\gamma$  compared to the clinical type of psoriasis ( $p > 0.05$ ). In a group of patients with PV 36 (85.71%) patients had mild form of disease with PASI  $< 50$ , and 6 (14.29%) patients had severe disease with PASI  $> 50$ . It was not found statistically significant correlation between IFN- $\gamma$  value and PASI score in the group of patients with PV.

Psoriasis		N	IFN- $\gamma$ (pg/ml)	SD	SEM	Minimum (pg/ml)	Maximum (pg/ml)
Clinical type of psoriasis	P. vulgaris	42	2.15	0.30	0.20	0.75	18.61
	P. erythrodermica	9	1.57	0.68	0.22	0.87	2.79
	P. pustulosa	6	1.08	0.21	0.08	0.85	1.43
	P. arthropatica	3	1.33	0.53	0.30	0.83	1.90
F= 0.351; p= 0.789							

Table 1. Serum concentration of IFN- $\gamma$  compared to the clinical type of psoriasis

## 5. DISCUSSION

Psoriasis is common inflammatory, and hyper proliferative skin disease with a widespread prevalence of 2-3% (1). As a chronic inflammatory condition, psoriasis results from an interaction between genetic and immunologic factors in a predisposing environment (8). Although the precise pathomechanism of psoriasis is still unknown, various cytokines derived from T lymphocytes, dendritic cells or keratinocytes, are critically involved in this disease. Psoriasis can be described as a T-cell-mediated disease, with a complex role for variety of cytokines and other factors. It has been hypothesized to be an immune-mediated disorder in which the excessive reproduction of keratinocytes is due to cytokine such as interferon (IFN)- $\gamma$  and tumor necrosis factor (TNF)-alpha secreted by infiltrating CD4<sup>+</sup> and CD8<sup>+</sup> T cells and natural killer cells (9). Cytokines are small, biologically highly active proteins that regulate the growth, function, and differentiation of cells and help steer the immune response and inflammation (10). They play an important role in both physiology and pathophysiology of human skin. The serum cytokine concentration are altered by several process like the production, tissue/cellular deposition, degradation, and elimination of these

molecules; furthermore other tissue sources of cytokines production might exist beside the circulating T cells.

IFN- $\gamma$  is a helper T-cell 1 (Th1)-derived cytokine and plays a critical role for both innate and adaptive immunity against viral and intracellular bacterial infections and tumor control. In the normal skin, IFN- $\gamma$  promotes growth arrest of normal keratinocytes (11). It is considered as a key cytokine in the pathogenesis of psoriasis. The suggested mechanisms are that IFN- $\gamma$  mediates interactions between inflammatory T cells and keratinocytes, facilitating T-cell migration to lesional epidermis (12). It induces antiapoptotic protein BCLx and alters the expression of the apoptotic catalytic enzymes, cathepsin D and zinc- $\alpha$ 2 glycoprotein, in psoriatic skin, thus promoting keratinocyte proliferation playing a major role in psoriasis pathogenesis (13). The level of IFN-gamma measured by immunohistochemical methods and PCR in the psoriatic epidermis was measured at ten-fold higher concentrations than in the healthy epidermis (14). Moreover, the intradermal administration of IFN- $\gamma$  into nonlesional skin of psoriatic patients causes the appearance of lesions at the inoculation site (15). The study by Sharon et al. confirmed previously reported data that cytokine IFN- $\gamma$  was elevated in the serum of psoriatic patients. In addition, the results of these authors' research have shown that the serum IFN- $\gamma$  concentration in psoriatic patients is correlated with the clinical disease severity index (PASI) (16).

The study by Moustafa et al. found that the level of IFN- $\gamma$  in psoriatic patients was significantly higher than the control group of healthy subjects. A significant correlation between the PASI value and the level of IFN- $\gamma$  in the serum of patients was also established (17). The results presented in our study demonstrate that the mean serum levels of IFN- $\gamma$  were significantly elevated in patients with psoriasis in comparison to healthy subjects, and this results are in agreement with a clinical studies performed by previous authors. This may provide evidence about role of IFN- $\gamma$  in psoriasis pathogenesis. The suggested mechanisms are that IFN- $\gamma$  is capable of inducing the expression of intercellular adhesion molecule 1 (ICAM-1) and HLA-DR, thus mediating interactions between inflammatory T cells and keratinocytes, facilitating T-cell migration to the lesional epidermis. IFN- $\gamma$  also stimulates the release of a number of cytokines, such as interleukin IL-1, IL-6, IL-8, TNF- $\alpha$ , and inflammatory mediators, in addition to inducing the expression of ICAM-1, HLA-DR, and vascular ICAM-1 on keratinocytes and endothelial cells, thereby attracting lymphocytes from circulation.

The findings of our study showed that it was no statistically significant difference between the mean values of IFN- $\gamma$  compared to the clinical type of psoriasis ( $p > 0.05$ ). The significantly elevated serum IFN- $\gamma$  levels were detected in patients with psoriasis vulgaris while the lowest serum levels of IFN- $\gamma$  was found in patients with psoriasis pustulosa. Yamamoto et al. indicate in their study that the concentration of IFN- $\gamma$  correlates with the clinical characteristics of pustular psoriasis, as well as the concentration of IL-6, IL-10 and TNF- $\alpha$  (18).

In our study, it was no found statistically significant correlation between IFN- $\gamma$  and PASI score in the group of patients with psoriasis vulgaris, and this results is in agreement with the results of Almahzangy and Gaballa (19). In contrast with results of our study, Shoeib et al. found a significant positive correlation between PASI score and level of IFN- $\gamma$  in all clinical types of psoriasis (plaque, erythrodermic and guttate) (20). This explained that IFN- $\gamma$  has a role in psoriasis pathogenesis but it is not the proximal regulator or sole player in this process.

## 6. CONCLUSION


In conclusion, the current study underscores the important role of IFN- $\gamma$  in the development of psoriasis. The measurement of serum IFN- $\gamma$  may allow for better prediction and monitoring of psoriasis activity, and it would be more useful to differentiate psoriasis from other skin diseases, such as seborrheic dermatitis or parapsoriasis, especially in cases where there is a doubt in skin histology. Further investigations are required to clarify the pathogenic role and clinical significance of IFN- $\gamma$ , and these findings may provide important clues to assist in the development of new therapeutic strategies for patients with psoriasis.

- Author's Contribution: N.O.K. and E.K.H. gave substantial contribution to the conception or design of the work and in the acquisition, analysis and interpretation of data for the work. Each author had role in drafting the work and revising it critically for important intellectual content. Each author gave final approval of the version to be published and they are agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.
- Conflicts of interest: There are no conflicts of interest.
- Financial support and sponsorship: None.

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