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Original Research Article

Assessment of Serum Interleukin-6 (IL -6) Levels and Its Role in Severity of Psoriasis A Hospital Based Case Control Study in M.Y. Hospital, Indore M.P.

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Abstract:

Introduction: Psoriasis is a chronic immuno-inflammatory proliferative skin disease. It is characterized by excessive proliferation of epidermal cells, impaired function of epidermal barrier at the sites of skin lesions and infiltration of skin by activated inflammatory cells. Interleukin 6 (IL-6), a major mediator of the host response to tissue injury and infection, is produced by both epidermal cells and leukocytes in culture. Since immune and inflammatory factors play an important role in the pathogenesis of psoriasis, we aimed to assess the relationship between the serum levels of IL-6 and pathogenesis and severity of psoriasis.

Material and Methods: This cross sectional study included 50 Confirmed & diagnosed cases of psoriasis patients (case group) and 50 age and gender matched healthy subjects (control group). Serum IL-6 levels were measured for both the groups.

Results: In our study the mean serum IL-6 in case group was higher 6.97 ± 5.43 pg/ml than in control group it was 2.22 ± 2.10 pg/ml thus, serum IL-6 level might be useful for evaluating the disease activity of psoriasis as Novel biomarker.

Conclusion: As Interleukin-6 (IL-6) is an important sensitive, diagnostic and prognostic marker in many systemic inflammatory diseases, its detection and serial measurements helps to provide a novel link to evaluate the disease activity, severity and response to treatment in psoriasis.

Keywords: Psoriasis, IL-6, Epidermal cells, Inflammation

Introduction

Psoriasis is a chronic immuno-inflammatory proliferative skin disorder that mainly involves the skin, nails and joints. It is as a squamo-papulous skin disorder characterized by uncontrolled proliferation of keratinocytes and dysfunctional differentiation due to T cell-mediated dysregulation of immune system.

The prevalence of Psoriasis ranges from 2-3% in the general population. [1]Although the disease have higher prevalence in the polar regions of the world, its burden in a tropical/subtropical country like India cannot be underestimated. In India, the prevalence of psoriasis may differfrom region to region due to environmental variability and genetic factors. IL-6 is a pro inflammatory cytokine produced by monocytes, fibroblasts, endothelial cells, adipocytes, and normal human keratinocytes under the influence of IL-17F [2,3,4]. it induces synthesis of acute phase proteins such as CRP, fibrinogen, and hepcidin in hepatocytes, whereas it inhibits production of albumin. IL-6 stimulates the proliferation of Th17 cells and supresses the proliferation of regulatory T lymphocytes and via this pathway it maintains the inflammation. IL-6 stimulates the inflow of T lymphocytes to the epidermis and it participates in the process of growth and differentiation of keratinocytes. [5] Due to the increasing prevalence of psoriasis in India, the present study was conducted in central part of India with an objective to evaluate the serum IL-6 in psoriasis cases and compare them with controls & correlatewith the severity of disease using PASI score (Psoriasis Area and Severity Index).

Materials and Methods:

The present study was conducted in the Department of Biochemistry and Department of Dermatology and Venereology of M.G.M.M.C. & M.Y.H

Hospital Indore, Madhya Pradesh. The study was approved and permitted by the institutional scientific and ethical committee. The period of study was from May 2019 to April 2020. Present study included 50 clinically diagnosed cases of Psoriasis of age group 18-55 yrs of both gender attending Dermatology OPD in M.Y.H. Hospital Indore and 50 apparently healthy age and gender matched controls were taken. The subjects were enrolled for the study after obtaining written consent.

Inclusion criteria:

Cases will include those patients diagnosed with psoriasis attending dermatology OPD, Controls will include healthy individuals without disease, Patients with age group 18 -55 yrs, both gender, ready to sign on informed consent.

Exclusion criteria:

Subjects on Vitamin D & calcium supplementation, subjects receiving OCPs, patients on corticosteroids treatment, history of liver disease and renal diseases, history of autoimmune diseases like-Alopecia, pernicious anemia, diabetes mellitus, other inflammatory disorders - IBD, COPD, DVT, connective tissue disorder, history of chronic diseases, pregnancy.A PASI score is a tool used to measure the severity and extent of psoriasis. A PASI score of < 5 indicates mild chronic plaque psoriasis, score of 5–10 represents moderate chronic plaque psoriasis, score of >10 describes severe chronic plaque psoriasis. The maximum PASI score is 72.

Investigation Procedure:

Venous blood (5 ml) sample was withdrawn with aseptic precautions from the antecubital vein following overnight fasting. The blood sample was collected in clot activator tube and serum was separated. The serum was analysed for biochemical investigations on same day and remaining samples were preserved for further biochemical investigations at -20°C.Measurement of Serum IL-6 is done by Enzyme Immunoassay (EIA) on Thermo-fisher ELISA reader in clinical Biochemistry laboratory of M.Y.Hospital Indore.

Data Collection and Statistics:

The data were tabulated on excel sheet & analyzed by appropriate statistical methods. Minitab Version 17.0 was used for calculating the p values. Results on continuous measurements were presented as Mean ± SD. P value < 0.05was considered significant and p value < 0.001 considered as highly significant. Comparison of mean between the two groups was done using Unpaired 't' test, comparison of means of more than two groups was done using One-way ANOVA followed by Post hoc Tukey test. Correlation between two parametric variables was done using Pearson Coefficient of Correlation.

Results:

The mean serum IL-6 in control group was 2.22 ± 2.10 pg/ml, while in the case group it was 6.97 ± 5.43 pg/ml with statistically significant p value (p value< 0.001**), showing a higher serum IL-6 level in case group. (Table 1 & Figure 1) In our study we have found that according to PASI score mean IL-6 in mild psoriasis was 2.69 ± 1.75 pg/ml and in severe type it was 8.98 ± 5.42 pg/ml (Table 2 & Figure 2) which was statistically very significant with p value < 0.001**.

Table 1: Biochemical parameter IL-6 in control & case group

Biochemical Parameter	Control Group (n=50) (Mean ± S.D)	Case Group (n=50) (Mean ± S.D)	t value	p value
Serum IL-6 (pg/ml)	2.22 ± 2.10	6.97 ± 5.43	5.75	< 0.001** (Highly Significant)

Figure1: Biochemical parameter IL-6 in control & case group

Table 2: Comparison of mean IL-6 according to PASI score

PASI Score		No.	IL-6 (pg/ml) [Mean ± SD]	F value	P value
< 5	Mild	16	2.69 ± 1.75	20.27	< 0.001** (Highly Significant)
> 10	Severe	34	8.98 ± 5.42		
	Total	50	6.97 ± 5.43		

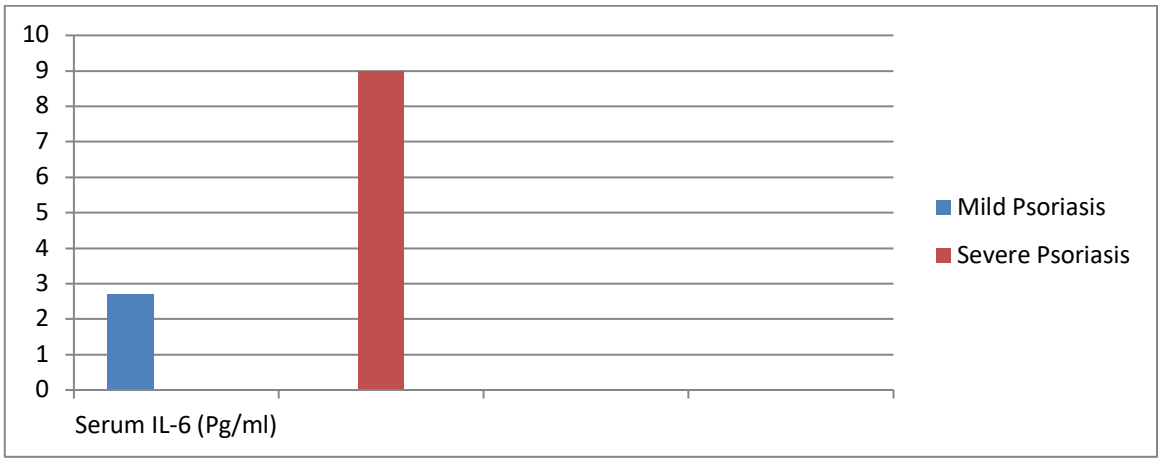

Figure 2: Table 2.Comparision of mean IL-6 according to PASI score

Discussion:

Psoriasis is characterized by increased proliferation of epidermal cells, an inflammatory infiltrate consisting of T cells and neutrophils and vascular proliferation. The primary defect in psoriasis patient is abnormal keratinocytes proliferation. [6] The very initial lesion of psoriasis is characterized by infiltrate of inflammatory mononuclear cells in the upper layer of dermis with slight changes in the epidermis. [7]Sustained inflammation is one of the hallmark of psoriasis due to which there is uncontrolled, excessive proliferation and dysfunctional differentiation of epidermal cells.

Psoriasis shows traits of an autoimmune disease on an auto inflammatory background. [8] Cytokines are small, biologically active proteins that regulate the growth, function and differentiation of cells and influence the immune response and inflammation. Keratinocytes secrete a number of cytokines that either activate or suppress immune responses. [9]The precise mechanism of involvement of cytokines in psoriasis remains unclear but, in some researches, it has been found that cytokines including IL-6 may directly contribute to the epidermal hyperplasia,seen in psoriatic epithelium and affect the functions of dermal inflammatory cells. Some studies have proven elevated levels of IL-6 in the skin and serum of patients with psoriasis. [10, 11] It is a marker of disease activity and its concentration is proportional to the severity of skin changes in psoriasis. [12]In our study serum IL-6 levels were found significantly increased (p value < 0.001) in all the psoriatic patients as compared to controls. The mean serum IL-6 levels in case group (6.97 ± 5.43 pg/ml) were higher than in control group (2.22 ± 2.10 pg/ml).Findings of our study was in concordance with the study by Abanmi A et.al., [13] Mizutani H et al., [14] and Ozer Arican et al., [15] who found raised levels of baseline IL-6 in psoriatic patients than in normal healthy subjects.

In our study serum IL-6 level has shown positive and statistically significant correlation with severity of disease. Out of the 50 patients, 16 patients had mild degree of psoriasis with mean IL-6 levels 2.69 ± 1.75 pg/ml and 34 patients had severe degree of psoriasis with mean IL-6 levels 8.98 ± 5.42 pg/ml, signifying that as severity of psoriasis increases IL-6 level increases. The higher mean IL-6 levels were seen in severe psoriasis while levels were lower in mild psoriasis.

This result is also supported by study of Szepietowski JC et. al.,[16]who revealed that patients of psoriasis had significantly higher levels of IL-6 than healthy controls and patients with severe disease had significantly higher levels of IL-6 and concluded that IL-6 may be considered as a valuable marker of severity of psoriasis that could be used to monitor disease activity and its treatment. So according to the findings of our study we can say that, serum IL-6 level might be a useful index for evaluating the disease activity of psoriasis as Novel biomarker.

Conclusion:

In our study psoriasis patients have markedly raised serum levels of IL-6 as compared to controls and show a positive correlation with the disease severity. Further studies by dermatologist and medical practitioner are essential to detect the association. We suggest screening of all the patients of psoriasis for serum IL-6 estimation at

initial visits. Further large scale prospective studies are needed to establish the cause effect relationship.

Limitation of the Study: The limitation of this study lies in its relatively small sample size.

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