University of Thi-Qar Journal of Science (UTsci)
ISSN Onlin:2709-0256, ISSN Print: 1991-8690 Volume (9), No.1 AUG 2022

Evaluation of Interleukin6 (IL-6) levels in Atopic Dermatitis Patients in Thi-Qar province

Amel A. Naji
Ministry of health –Diabetes/ and Endocrinology Specialist Center
Ministry of Health
Nasiriyah / Iraq
Amal95@sci.utq.edu.iq

Hind M Mousa
Pathological Analysis Department
Faculty of Science, University of Thi-Qar, IRAQ
Nasiriyah / Iraq
Hindmousa_pa@sci.utq.edu.iq

***Abstract*—IL-6 is a pro-inflammatory marker seen in the circulation of atopic disease. The study comprised 90 people of both genders, 45 of whom were patients, and the same number served as controls. Blood samples were obtained from both groups, and the serum levels of IL-6 were estimated using an IL-6 ECLIA kit by Electro-chemilumenescence Immunoassay. The findings of the present study referred that there were elevated sera levels of IL-6 (12.26pg/ml) in AD patients in contrast to the control groups (4.05pg/ml) with a significant difference . Also, The results revealed an increase in the levels of IL-6 in severe AD patients compared with control group with highly statistically significant(P≤ 0.01). According to the results of the current study, it can be concluded that IL6 plays a critical role in the pathogenesis of dermatitis, and its elevated levels correlate with the clinical severity of the disease pathogenesis of AD.**

Keywords— Atopic Dermatitis , Inflammation , IL-6 .

I. INTROUDUCTION

IL-6 is a pleiotropic cytokine with pro-inflammatory, anti-inflammatory, and immune modulating functions on numerous cell and tissue types (Tanaka *et al.*,2014; Schaper and Rose-John, 2015). It is produced by numerous immune cells including T cells, neutrophils, macrophages, and nonimmune cells like keratinocytes and fibroblast in the skin , IL-6 has also been shown to affect the function of cells in the skin (Lee, *et al*., 2013; Oleiwi,2020).

For example, IL-6 promotes keratinocyte proliferation and migration and increases fibroblast proliferation. It's exerting multiple biologic actions on different types of target cells with a wide range of biological effects, such as promoting cells proliferation and differentiation, promoting-cells growth and cytotoxic T-cells differentiation .

It cooperates with IL-3,G-CSFandGM-CSFtopromotehematopoieticstemcellsgeneration2(Gallucci *et al*., 2004).

Irritant Contact Dermatitis (ICD) is an inflammatory response of the skin to chemical or physical irritants and is characterized by epidermal hyperplasia, inflammatory cell in flux into lesional skin, and inflammatory cytokine release including IL-6, While it is known that IL-6 confers a protective effect to the skin during ICD (Lee *et al.*, 2013).

The protective role of IL-6 in the context of the skin has been reported . In fact, during skin inflammation and wound healing, IL-6 has been shown to promote skin repair and regeneration (McFarland-Mancini *et al*., 2010) . The effect of IL-6 on keratinocyte function has also been well reported where IL-6 has been shown to promote migration and proliferation (Hernández-Quintero *et al.*, 2006) . IL-6 has been reported to confer aprotective effect on the skin during inflammation (Frempah *et al*., 2019).

Intended use Immunoassay for in vitro quantitative determination of Interleukin-6 (IL-6) in human serum and plasma. This assay can be used to aid in the management of critically ill patient sasanearly indicator of acute inflammation IL-6 is asingle peptide chain composed of 212 amino acids,which is cleaved at the N-terminus to produce a 184 amino acid peptide with a molecular weight between22~27kDal.Usually,IL-6 is few in the serum. But it can be rapidly raised in the course of acute inflammatory reactions associated with injury, trauma, stress, infection, brain death, neoplasia, and other situations. Naturally, it has been widely used in clinical diagnosis of acute or chronic inflammation.

In addition, sequential measurements of IL-6 in serum or plasma of patients admitted to the ICU (intensive care unit) showed to be use full in evaluating the severity of (Systemic Inflammatory Response Syndrome) SIRS (Israeli *et al*., 2022).

In addition, IL-6 exerts stimulatory effects on T-and B-cells ,thus favoring chronic inflammatory responses .Gharagozlou *et al.*(2013) indicated that IL-6 in the serum or stimulated cultured peripheral blood mononuclear cells of patients with AD, might increase the clinical significance of the results. Strategies targeting IL-6 and signalling led to effective prevention and treatment of models of rheumatoid arthritis and other chronic inflammatory diseases such as atopic dermatitis disease (Gabay, 2006) .The study was designed to measure serum levels of IL-6 in atopic dermatitis and to compare them with healthy subjects.

II. METERALS AND METHODS

The study included 90 members (50 males and 40 females with an average age of 28 years and arrange of age (less than1year to 63 years). Forty five Patients who were diagnosed with Atopic dermatitis over the period of study from November-2021 to March-2022 were eligible for this study. They were diagnosed clinically by a dermatology consultant at Al-Nasiriyah Teaching Hospital and the Doctor's clinic. And 45 subjects were healthy group. The personal information for each member was collected through direct interviews with the patient and healthy people. Only patients who fulfilled the criteria of Hanifan and Rajka (1980), and who had not used topical or systemic antimicrobial drugs, corticosteroids or antihistamines for at least 2weeks before investigation, were included in the study.

Blood samples (4-5 ml) were collected from each participant by vein puncture using plastic disposable 5ml syringes , from all patients and control groups, sample was allowed to clot at room temperature in clot activator gel tubes before centrifuging , then centrifuged for 15 minutes at approximately 5000 rpm to obtain unhemolyzed cell-free serum. The samples were then labeled with a reference code, gender, and time of collection Sera were frozen and stored at -20ºC until the (IL-6 measurement by standard curve). The concentrations were quantitatively determined in sera of patients and healthy control subjects by means± SD .IL-6 ECLIA kit(Nipigon Health Corp-Canada) is used to measure the levels of IL-6 using technique Electro-chemi lumenescence Immunoassay

III. RESULTAND DISCUSSION

Patients with AD have shown an elevated mean sera levels of IL-6 (12.26pg/ml), as compared with the healthy control (4.05pg/ml), there was a high significant difference between the healthy control group and patients ($p < 0.01$).Which was three-fold higher in the total AD group compared to the healthy control group as seen in Table (1).

Table(1):Sera LevelsofIL-6 in Patients and Healthy

Groups	No	IL-6Mean±SD
Patient	45	12.26±6.26
Control	45	4.05±2.5
P value	0.000	
T-test value	8.170	

*

(P<0.01) High significant difference

T cells from the peripheral blood of patients with atopic dermatitis produce more IL-6 than T cells from healthy people, which could be due to the higher stimulation status of T cells in atopic dermatitis (Toshitani *et al.*, 1993). Thus, it is normal for interleukin-6 levels to be high in current study patients. Interrupting IL6–receptor signaling improves atopic dermatitis but associates with bacterial super infection .Atopic dermatitis is a multifactorial disorder associated with Th2-polarized CD-41 T cells that can over produce IL-6, IL-5 , IL-4,and IL-13. IL-6 is secreted by activated T cells and macrophages. It regulates the immune response , inflammation and pathogen responses, bone metabolism, and hematopoietic. The role of IL-6 in eliciting atopic dermatitis remains undefined . It is released in the cutaneous response to allergen challenges in atopic individuals and can be over produced by dendritic cells from atopic patients (Navarini *et al*., 2011).The relationship between sera means levels of IL-6 in AD patients with severity of disease showed highly significant increased mean levels of IL-6 (24.52pg/ml) in patients with severe AD as compared with patients with mild AD(9.35pg/ml, $p < 0.05$), and there was also highly significant difference in mean levels of IL-6 between AD patients with moderate and severe disease (12.58pg/ml,24.52pg/ml, respectively $P<0.05$). In addition, there was a significant difference in mean levels of IL-6 between mild and moderate AD patients ($p=0.013$)(Table 2).

Table(2): Sera levels of IL-6 in patients'groups

Groups	No	Mean ±SD	Comp.	P.V.	T-test value
Mild	23	9.35±4.5	Mild-Moderate	0.013*	-2.610
Moderate	17	12.58±3.3	Moderate-Severe	0.00*	-5.757
Severe	5	24.52±6.2	Mild-Sever	0.00*	-6.400

The results revealed an increase in the levels of IL-6 in severe AD patientscompared with others groups with statistically significant . This result relatively agree with data recorded by Ilves and Harvima (2015) .

IV. CONCLUSION

IL6 play a critical role in the pathogenesis of dermatitis, and their elevated levels related with the clinical severity of the disease .

ACKNOWLEDGMENT

We thank the dermatologists at Al-Hussein Teaching Hospital for providing us with Atopic Dermatitis samples. We are also grateful to the Department of Pathological Analysis in the College of Science - Thi-Qar University

REFERENCES

Frempah, B., Luckett-Chastain, L. R., andGallucci, R. M. (2019). IL-6 NegativelyRegulates IL-22Rα Expression on Epidermal Keratinocytes: Implications for Irritant Contact Dermatitis. Journal of Immunology Research,2019(2019):1-9.

Gabay,C.(2006).Interleukin-6 and chronic inflammation .Arthritis Research &Therapy,8(2), 1–6.

Gallucci, R. M., Sloan, D. K., Heck, J. M., Murray, A. R., and O'Dell, S. J. (2004). Interleukin6 in directly induces keratinocyte migration. Journal of Investigative Dermatology,122(3), 764-772.

Gharagozlou, M, Farhadi E, Khaledi M, Behniafard N, Sotoudeh S, Salari R, Darabi B, Fathi SM, Mahmoudi M,Aghamohammadi A, AmirzargarAA, and Rezae N (2013). Association Between the Interleukin 6 Genotype at Position –174 and Atopic Dermatitis . J InvestigAllergolClinImmunol , 23(2): 89-93 .

Hernández-Quintero,M.,Kuri-Harcuch,W., GonzálezRobles A.,and Castro-Muñozledo,F . (2006). Interleukin-6 promotes human epidermal keratinocyte proliferation and keratincytoskeleton reorganization in culture. Cell and tissue research,325(1), 77-90.

Ilves, T., andHarvima, I. T. (2015). Decrease in chymase activity is associated withincreaseinIL-6 expression in mast cells in atopic dermatitis. Act aDermato-Venereologica,95(4).

Israeli, E., Okura, H., Kreutz, B., Piktel, R., Hadji, A., Tu, B., ... andHemken, P. M.(2022). Development of a new automated IL-6 immunoassay. Journal of ImmunologicalMethods,504, 113262.

Lee, E. G., Mickle-Kawar, B. M., andGallucci, R. M. (2013). IL-6 deficiency exacerbates skininflammationinamurinemodelofirritantdermatitis. Journalofimmunotoxicology,10(2), 192-200.

McFarland-Mancini, M. M., Funk, H. M., Paluch, A. M., Zhou, M., Giridhar, P. V.,Mercer, C. A., .. and Drew, A. F. (2010). Differences in wound healing in mice withdeficiency of IL-6 versus IL-6 receptor. The journal of immunology, 184(12), 7219-7228.

Navarini, A.A., French,L.E., and Hofbauer,G.F.L. (2011).InterruptingIL-6-receptor signaling improves atopic dermatitis but associates with bacterial superinfection. Journal of Allergy and Clinical Immunology,128(5),1128–1130.

Oleiwi, A. H. (2020). Some Cytokines Levels (IL-6 and IL-10) in Sera Patients with Cutaneous Leismanasisin Nassiriya Province. University of Thi-Qar Journal of Science, 7(2), 4-6.

Schaper, F., and Rose-John, S. (2015). Interleukin-6: biology, signalling and strategiesofblockade. Cytokine& growth factorreviews,26(5),475-487.

Tanaka, T., Narazaki, M., andKishimoto, T. (2014). IL-6 in inflammation, immunity, and disease.ColdSpring Harborperspectivesinbiology,6(10),a016295.

Toshitani, A., Ansel, J. C., Chan, S. C., Li, S. H., andHanifin, J. M. (1993). Increased interleukin 6 production by T cells derived from patients with atopic dermatitis. Journal of Investigative Dermatology, 100 (3) , 299–304.