Correlation between Interleukin 22 Serum Level and Severity of Psoriasis

Reham Mohammad Gamal Dewidar[1], Shawky Mahmoud EL Farargy[1] and Naglaa Mohammad Ghanayem[2]

[1]Dermatology and Andrology Department, Faculty of Medicine, Menoufia University, Shebeenelkom, Menoufia, Egypt
[2] Biochemistry Department, Faculty of Medicine, Menoufia University, Shebeenelkom, Menoufia, Egypt
Sameh_khoud2003@yahoo.com

Abstract: Objectives: to study the Correlation between Interleukin 22 serum Level and severity index of Psoriasis **Background**: Interleukin-22 is a member of the IL10 cytokine family, described as having proinflammatory activites on liver, pancreas, intestine and skin. **Material and Methods:** The study was don on 45 subjects. These included 30 cases with chronic plaque psoriasis & 15 age- and sex-matched healthy individuals. All Patients were subjected to history taking and complete medical examination. Serum levels of IL-22 were measured by ELISA technique. Serum levels of IL-22 were statistically analyzed in relation to psoriasis area and severity index (PASI). **Results:** The serum levels of IL-22 was highly elevated in psoriasis patients compared with healthy people The serum IL-22 was significantly higher in patients with severe psoriasis as compared with those with mild and moderate psoriasis. The serum levels of IL-22 was higher in patients with long duration of psoriasis compared with recent psoriatic patients. **Conclusion:** IL-22 is involved in psoriasis. There is significant positive correlation between IL-22 serum levels and each of duration of psoriasis and PASI.
[Reham Mohammad Gamal Dewidar, Shawky Mahmoud EL Farargy and Naglaa Mohammad Ghanayem. **Correlation between Interleukin 22 Serum Level and Severity of Psoriasis.** *Stem Cell* 2017;8(2):19-24]. ISSN: 1945-4570 (print); ISSN: 1945-4732 (online). http://www.sciencepub.net/stem. 4. doi:10.7537/marsscj080217.04.

Keywords: cytokins, inflammation, Psoriasis, skin disease

1. Introduction

Psoriasis is a common cutaneous inflammatory pathology characterized by epidermal hyperplasia, dilated and prominent blood vessels in the dermis, and by an inflammatory infiltrate of leukocytes, predominantly in the dermis affecting 2.5% of the World population that results from genetic predisposition as well as environmental factors (***1*).**

Psoriasis is considered an autoimmune disorder mediated by T cells which, after priming by bacterial antigens, migrate to the skin where they are activated by self-antigens expressed by epithelia and the key participation of dendritic cells that appear also increased in the skin ***(2).***

Soluble biologic mediators produced by activated T cells or by dendritic cells, such as interferon γ (IFN-γ), tumor necrosis factor-α (TNF-α), IL-17, and IL-22, can induce inflammatory molecules and angiogenic factors in keratinocyte and alter their differentiation pathway, These events lead to the cutaneous expression of the disease (3).

A further link between altered immunologic circuitries, lymphocytes infiltration, and epidermal hyperplasia has been provided by recent studies which show that T cells expressing IL-17 may play a major role in psoriasis. This pathological immune circuitry appears driven by interleukin-23. In mice, injection of IL-23 leads to epidermal hyperplasia mediated by IL-22 which, in turn, is produced by IL-17-expressing T cells (4).

IL22 is a member of the IL-10 cytokine family, described as having proinflammatory activities on liver, pancreas, intestine and skin ***(5).***

Th22 cells have been recently described as inflammatory CD4+T cells that produce cytokines such as IL-22, IL-26and IL-13 of which IL-22 is the most important functional cytokine. Th22 cells do not express IL-17A or INF-γ ***(6).***

It is proposed that psoriasis development depends on skin infiltration of Th1/Th17 cells that stimulate macrophages and dermal dendritic cells to release mediators that sustain inflammation and cause abnormal keratinocyte proliferation. The mediators of the Th17 immune system include IL-1, IL-6, IL-23 and transforming growth factor (TGF)-β. Additionally, IL-23 and related interleukins seem to be crucial for psoriasis pathogenesis **(7)**.

IL-22 is the linkage between the infiltrating Th17 cells, driven by IL-23, and keratinocyte hyperplasia and activation. This cytokine is the downstream effector cytokine of IL-23, and can induce many of the pathological features seen in psoriatic skin lesions. The production of IL-22 is up-regulated in psoriatic skin, their levels are high in the peripheral blood, and are correlated with the severity of the disease, suggesting an important role for IL-22 in the pathogenesis of psoriasis **(8)**.

2. Material and methods

Study population and selection of patients

This study was don at the Dermatology and Venerology Department, in collaboration with medical biochemistry Department, Faculty of Medicine, Menoufia University during the period from November 2015 and March 2016.

It involved three groups: group II included 15 patients with mild psoriasis (4 males and 11females), group III included 15 patients with sever psoriasis(9males and 6 females) and groupI included 15 age- and sex-matched healthy individuals. (6males and 9 females)

Exclusion criteria for the study sample include:

- Psychological problems, which could influence the study.
- Other skin conditions precluding proper assessment of psoriasis severity.
- Other conditions known to be associated with elevated serum levels of IL-22 as liver disease, rheumatoid arthritis and inflammatory bowel diseases.
- No systemic or topical treatment for three month prior the study.

Informed consent was taken from both the patients and control group subjects before the beginning of the study.

After signing an informed consent patients were subjected to the following:

Every case was subjected to:

I- Complete history taking:

- Personal history which include: name, age and gender.
- Present history of disease including: age of onset, duration, presence of itching
- Family history of psoriasis.
- History of smoking.

II- Examination:

B-Clinical examination:

- General examination was done.
- Cutaneous lesions were clinically evaluated.
- Classificationof psoriasis severity according to the PASI score.

The severity of the disease was assessed by the Psoriasis Area and Severity Index (PASI) score.

For each of 4 body sites (the head and neck, the trunk, the upper extremities, and the lower extremities), 3 components of the psoriatic plaques within it (erythema, induration, and desquamation) are graded from 0 (“complete lack of”) to 4 (“severest possible”). An estimate is then made of the extent of psoriasis in that site by estimating the body surface area with possible scores ranging from 0 to 6. A complex formula is then applied to derive a score which range from 0 to 72 ***(9).***

E=erythema I=induration D=desqumation
0=complete lack of
1=slight 2=moderate 3=severe
4=severest possible
A=percentage skin surface area involved
0= no psoriasis
1= <10% 2= 10<30% 3= 30<50% 4= 50<70%
5= 70<90% 6= 90-100%

The PASI score is calculated by the formula:

PASI = 0.1(Eh + Ih + Dh)Ah + 0.2(Eu + Iu + Du)Au + 0.3(Et + It + Dt) At + 0.4(El + Il + Dl)Al (h=head, u=upper extremities, t=trunk, l=lower extremities)

Chularojanamontri et al., (10) demonstrated that by using the European Medicines Agency definition of psoriasis according to PASI score, it can be classified into:

Mild psoriasis: PASI is <10
Moderate psoriasis: PASI is 10-20
Severe psoriasis: PASI is >20

III- Collection of blood samples

Venous blood samples (5mL) were taken under sterile conditions in a serum separator tube from patients and controls. After clot formation, samples were centrifuged at 1000 x g for 15 minutes. The serum samples were aliquoted and stored at -80°C until further use for IL-22quantification; repeated freeze-thaw cycles were avoided.

Quantification of IL-22 serum levels

Interleukin-22 serum levels were measured by enzyme linke dimmunosorbent assay (ELISA) technique according to the manufacturer's human IL-22 ELISA kits (Boster Biological Technology Co, Ltd, 40459 Encyclopedia Circle, Fremont, CA 94538).

Statistical analysis:

The data collected were tabulated & analyzed by SPSS (statistical package for the social science software) statistical package version 20 on IBM compatible computer.

The results were expressed by applying ranges, means ± S.D., Chi-square test, Mann-Whitney test, T test, Kruskal-Wallis test and P values. P value <0.05 was considered to be significant.

Pearson correlation was used for normally distributed quantitative variables, while Spearman correlation was used for quantitative variables that were not normally distributed or when one of the variables is qualitative.

3. Results

Patient characteristics

The patients group included 30 psoriatic patients. 15 patients with mild psoriasis (groupI) They were 11 females (73.3%) and 4 males (26.7%), their ages with a mean (30.13±7.3). there were 3smokers (20%) and 12 non smokers (80%) there were 6 with positive family history (40%) and 9 with negative family history(60%) there were 6 with itching(40%) and 9 without itching (60%) their BMI with Mean ± SD 25.6±2.4, theirPASI score with Mean ± SD 4.40±1.4,

their Age of disease onset27.7±7.3 Years, their Duration of disease with Mean ± SD 2.47±1.2 Years.15 patients with sever psoriasis (groupII). They were 6 females (60%) and 9 males (40%), their ages with a mean (37.9±7.6). there were 6smokers (40%) and 9 non smokers (60%) there were 7 with positive family history (46.7%) and 8 with negative family history (53.3%) there were 10 with itching (66.7%) and 5 without itching (33.3%) their BMI with Mean ± SD 29.5±4.8, their PASI score with Mean ± SD 22.8±8.1, their Age of disease onset30.6±5.4Years, the Duration of disease with Mean ± SD 7.53±2.5Years.

The control group included 15 normal individuals (groupIII). They were 9 females (60%) and 6 males (40%), their ages with a mean (32.20±5.5).

There is no statistically significant differences between groups as regard gender.

There is statistically significant differences between group I and III & IIand III regards to Age whereas non significant statistical difference existed between groupI and II.

The serum level of IL-22 in group II was ranged from (320.5-510) pg/ml with a mean of (430.36±114.9). The serum level of IL-22 in group III was ranged from (550-1055) pg/ml with a mean of (804.4±154.2). There is statistically significant differences between studied groups as regards toIL22 serum level.

BMI in group I was ranged from (18.2-32.8) with a mean of (24.73±4.7), in group I I was ranged from (22-29.9) with a mean of (23.3-37.7) and in group III was ranged from (23.3-37.7) with a mean of (29.5±4.8). There is statistically significant differences between groups as regarding BMI.

Table 1: comparison between studied groups regarding their demographic data Table (1): groups regarding their demographic data

variables	Group 1 No= 15		Group II No =15		Group III No=15		Test of sig.	P value	Post.hoc
Gender	**NO**	**%**	**NO**	**%**	**NO**	**%**			
Male	**6**	**40**	**4**	**26.7**	**9**	**60**	χ^2		
Female	**9**	**60**	**11**	**73.3**	**6**	**40**	**3.4**	**>0.05**	
Age (Years) Mean ± SD	**32.20±5.5**		**30.13±7.3**		**37.9±7.6**		**F 5.12**	**<0.05**	**P1=0.14 P2=0.02* P3=0.004***

P > 0.05 (Insignificant P ≤0.05 (Significant) F (One way ANOVA test) χ^2 chi-square test
P1 = (Group I vs. Group II) P2= (Group I vs. Group III) P2= (Group II vs. Group III) Group I=Control Group II= Mild psoriasis Group III= Sever psoriasis

Table (2): Clinical data of studied Psoriatic patients (NO=30)

	Group II No =15		Group III No=15		Test of sig.	P value
	NO	**%**	**NO**	**%**		
Gender					χ^2	
Male	**4**	**26.7**	**9**	**60**		
Female	**11**	**73.3**	**6**	**40**	**3.3**	**>0.05**
Smoking					χ^2	
Yes	**3**	**20**	**6**	**40**		
No	**12**	**80**	**9**	**60**	**1.4**	**>0.05**
Family history					χ^2	
Positive	**6**	**40**	**7**	**46.7**		
Negative	**9**	**60**	**8**	**53.3**	**0.36**	**>0.05**
Itching					χ^2	
Present	**6**	**40**	**10**	**66.7**		
Absent	**9**	**60**	**5**	**33.3**	**2.14**	**>0.05**
BMI(kg/m2) Mean ± SD	**25.6±2.4**		**29.5±4.8**		**t 2.80**	**<0.05**
PASI score Mean ± SD	**4.40±1.4**		**22.8±8.1**		**U 4.9**	**<0.05**
Age of disease onset(years) Mean ± SD	**27.7±7.3**		**30.6±5.4**		**1.2**	**>0.05**
Duration of disease(years) Mean ± SD	**2.47±1.2**		**7.53±2.5**		**U 4.5**	**<0.05**

χ^2 chi-square test U= Mann- whiteny test t=student t test; Group II= Mild psoriasis Group III= Sever psoriasis
P > 0.05 (Insignificant P ≤0.05 Significant)

Table (3): comparison between studied groups regarding IL22 serum level

	Group 1 No= 15	Group II No =15	Group III No=15	Test of sig.	Post.hoc
IL22level(pg/ml)				**F**	**P1=0.229**
Mean ± SD	**8.48±2.6**	**43.36±4.9**	**804.4±154.2**		**P2=<0.001**
Range	**3.8-14.5**	**32.5-51**	**550-1055**	**382.2**	**P3=<0.001**

F (One way ANOVA test) P > 0.05 (Insignificant P ≤0.05 Significant <0.001 highly significant)
P1 = (Group I vs. Group II) P2= (Group I vs. Group III) P2= (Group II vs. Group III)
Group I=Control Group II= Mild psoriasis Group III= Sever psoriasis

Table (4): comparison between studied groups regarding BMI

variables	Group 1 No= 15	Group II No =15	Group III No=15	Test of sig.	
BMI(kg/m2)				**F**	**P1=0.565**
Mean ± SD	**24.73±4.7**	**25.6±2.4**	**29.5±4.8**	**5.64**	**P2=0.003**
Range	**18.2-32.8**	**22-29.9**	**23.3-37.7**		**p3=0.014**

F (One way ANOVA test) P > 0.05 (Insignificant P ≤0.05 Significant) P1 = (Group I vs. Group II)
P2= (Group I vs. Group III) P2= (Group II vs. Group III) Group I=Control Group II= Mild psoriasis
Group III= Sever psoriasis

Table (5): Effect of family history, itching and smoking on PASI score in studied patients:

Family history	**Mean ±SD**	**U**	**P value**
Positive (No=13)	**4.78±1.2**		
Negative **(No=17)**	**3.83±1.7**	**1.0**	**0.31**
Itching			
Present(N= 16)	**4.17±1.3**		
Absent(N=14)	**4.56±1.5**	**0.75**	**0.45**
Smoking			
Yes(N=9)	**3.33±2.3**	**0.92**	
NO(N=21)	**4.67±1.1**		**0.35**

Group II=Mild psoriasis Group III=sever psoriasis U= Mann- whiteny test

4. Discussion

The present study included 45 subjects. they were classified in to three groups:-15 age & gender matched healthy controls(groupI),15 patients with mild psoriasis (groupII) and15 patients with sever psoriasis (groupIII), all patients and controls were clinically evaluated and blood samples were collected for detection of serum IL-22 by ELISA technique. In the patient group, patients with mild psoriasis (groupI) 11 were females (73.3%) and 4 males (26.7%), with a mean age (30.13±7.3), patients with sever psoriasis (groupII) 6 were females (60%) and 9 males (40%) with a mean of age (37.9±7.6), while in the control group 9 were females (60%) and 6 males (40%), their ages with a mean (32.20±5.5). In The present study, females were more affected than males this was in agreement with the result of **Huerta et al., (**11**)** who reported that, psoriasis affects adult female more than males**,** While this result differed from the results of **Ozer et al., (**12**), Icen et al., (**13**) and Tollefson et al., (14)** who founded that psoriasis affect male more than female**,** But **Almakhzangy and Gaballa (**15**)** reported equal incidence in both sexes. Recently**, Parisi et al., (16)** found no clear conclusions about whether the disease varied according to gender.

In the present study the age of onset of the disease in psoriatic patients (GroupII: ranged between19 years to 42 years with a mean (27.7 ±7.3) and Group III ranged between 26 years to 53years with a mean (30.6±5.4) it is different from ***Sommer* et al., *(17)*** who reported that the age of onset ranged from 8 to 42 years with a mean ±SD 29.4 ±9.9, **Anne et al., (**18**)** who reported that the disease started at age ranged between 9 years and 65 years with a mean value of (39 ± 15.2). It is also different from ***Almakhzangy and Gaballa (*15*)*** who reported that the disease started at age ranged between 26 years and 59 years with a mean value of (40.4 ± 9.9). In the present study serum levels of IL-22 in psoriatic patients were significantly higher than controls. That result was in agreement with the study done by ***Choe et al.,*(19*)* meephansan et al., *(*20*)* *Coimbra et al*.,(21*)* they found higher levels of serum IL-22 in psoriasis patients than in healthy controls. A finding that goes

with **Stoma *et al.*,*(*22*)** *suggested that th22 response may contribute to the skin and systemic inflammatory disease in psoriasis. early identification of soluble biomarkers and initiation of well. matched treatment may prevent exacerbation and progression of psoriasis.*

In the present study there was statistical significant correlation between serumlevel of IL-22 and duration of psoriasis These results were in agreee with that of Stoma ***et al., (***22***) and Almakhzangy and Gaballa(***15***).***

In the present studythere is significant positive correlation between serum level of IL-22 and psoriasis area and severity index (PASI) with (R = 0.153, *P* = 0.03 with mild psoriasis and R = 0.45, *P* = 0.02 with severe psoriasis).

There is statistically significant differences between groups as regarding BMI. These results were in agree with that of **Armstrong et al.,*(***23***)*** found that psoriasis patients had higher incidence and prevelance of obesity compared with those without psoriasis. Patients with more severe psoriasis were at higher odds of obesity compared with those with mild psoriasis. In patients with preexisting psoriasis, their likelihood of developing new-onset obesity was higher than those without psoriasis. Also **Naldi et al***.(*24*)*, demonstrated that the risk of psoriasis was directly related to elevated BMI. The risk of psoriasis was higher in obese patients compared with overweight patients.

Murray et al.,*(*25*)* found that psoriasis patients were more likely to have a higher BMI, using same gender siblings as genetic controls. In disagreement with our study.

Zindanci et al.,*(*26*)* did not find that BMI and waist circumference significantly higher in psoriasis patients.

There was significant positive correlation between serum level of IL-22 and psoriasis area and severity index (PASI) with (R = 0.153, *P* = 0.03 with mild psoriasis and R = 0.45, *P* = 0.02 with severe psoriasis). These results were in agree with that of ***Nakajima et al***. (27***) Meephansanet al. (***20***).*** Also ***Lo et al.,*** **[17]**who studied correlation between serum IL-22, IL-17 and IL-6 and (PASI), they found that Pearson's correlation test revealed that serum IL-22 concentration in psoriasis patients correlated well with psoriasis area and severity index (PASI) but not IL-17 indicating that the serum IL-22 is a good marker of clinical severity of psoriasis.

In the present study there was statistical significant correlation between duration of psoriasis and severity of psoriasis measured by (PASI) in agree with **Ali Al Raddadi *et al.* (**28).

References

1. Boniface K, Diveu C, Morel F, et al(2007): Oncostatin M secreted by skin infilterating T lymphocytes is a potent keratinocyte activator involved in skin inflammation. J Immunnol;178:46150-22.
2. W. R. Swindell, A. Johnston, J. J. Voorhees, J. T. Elder, and J. E. Gudjonsson (2013): "Dissecting the psoriasis transcriptome: inflammatory- and cytokine-driven gene expression in lesions from 163 patients," BMC Genomics, vol. 14, no. 1, article 527.
3. Guttman-Yassky K. E. Nograles, L. C. Zaba, E. et al (2008): "Th17 cytokines interleukin (IL)-17 and IL-22 modulate distinct inflammatory and keratinocyte-response pathways," British Journal of Dermatology, vol. 159, no. 5, pp. 1092–1102.
4. Ma, H. L. S. Liang, J. Li et al(2008): "IL-22 is required for Th17 cell-mediated pathology in a mouse model of psoriasis-like skin inflammation," Journal of Clinical Investigation, vol. 118, no. 2, pp. 597–607.
5. Cella M, Fuchs A, Vermi W, et al(2009): human natural killer subset provides an innate source of IL-22 for mucosal immunity. Naturee;457(7230): 722-725.
6. Sabat R and Wolk K. Research in practice (2011): IL-22 and IL-20: Significance for epithelial homeostasis and psoriasis pathogenesis. Journal der Deutschen Dermatologischen Gesellschaft.;9(7): 518-523.
7. Blauvelt A. (2008): T-helper 17 cells in psoriatic plaques and additional genetic links between IL-23 and psoriasis. J Invest Dermatol; 128:1064-1067.
8. Shimauchi T, Hirakawa S, Suzuki T, Yasuma A, Majima Y, Tatsuno K, Yagi H, Ito T and Tokura Y (2013): Serum interleukin-22 and vascular endothelial growth factor serve as sensitive biomarkers but not as predictors of therapeutic response to biologics in patients with psoriasis. J Dermatol.;40:805-812.
9. Robert JGC (2015): Assessing Psoriasis Severity and Outcomes for Clinical Trials and Routine Clincal Practice. Dermatol Clin; 33: 57-71.
10. Chularojanamontri L, Christopher E, Grriffiths M et al (2014): Responsiveness to Change and Interpretability of the Simplified Psoriasis Index. J Dermatol; 134: 351-358.
11. Huerta C, Rivero E, and Garcia Rodriguez LA. (2007): Incidence and risk factors for psoriasis in the general population. *Arch Dermatol;*143:1559–1565.
12. Ozer Arican, Murat Aral, Sezai Sasmaz, et al., (2005): Serum Levels of TNF-α, IFN-γ, IL-6, IL-8, IL-12, IL-17, and IL-18 in Patients with

Active Psoriasis and Correlation With Disease Severity Mediators Inflamm; 273-279.
13. Icen M, Crowson CS, McEvoy MT, et al. (2009): Trends in incidence of adult-onset psoriasis over three decades: a population-based study. *J Am Acad Dermatol; 60(3):394-401*.
14. Tollefson MM, Crowson CS, McEvoy MT et al.,(2010): Incidence of psoriasis in children: a population-based study. J Am Acad Dermatol;62(6):979-987.
15. Almakhzangy I. and Gaballa A. (2009): Serum Level OF IL-17, IL-22, IFN- γ in patients with psoriasis. *Egyptian Dermatology Online Journal;*5:1- 4.
16. Parisi R, Symmons DP, Griffths CE et al. (2013): Global epidemiology of psoriasis: asystematic review of incidence and prevalence. *J Invest Dermatol;133(2):377-385.*
17. Sommer DM, Jenisch S, Suchan M, et al. (2006): Increased prevalence of the metabolic syndrome in patients with moderate to severe psoriasis. *Arch Dermatol Res;* 298: 321–328.
18. Anne M, Raychaudhuri SP, and Fber EM. (2003): The prevalence of psoriasis in the world. *J Eur Acad Dermatol Venerol;*15:16-19.
19. Choe YB, Hwang YJ, Hahn HJ, Jung JW, Jung HJ, Lee YW, Ahn KJ and Youn JI: A comparison of serum inflammatory cytokines according to phenotype in patients with psoriasis. Br J Dermatol. (2012);167(4):762-7.
20. Meephansan J, Ruchusatsawat K, Sindhupak W, Thorner PS and Wongpiyabovorn J. Effect of methotrexate on serumlevels of IL-22 in patients with psoriasis. Eur J Dermatol. (2011);21(4):501-4.
21. Coimbra S, Oliveira H, Reis F, Belo L, Rocha S, Quintanilha A, Figueiredo A, Teixeira F, Castro E, Rocha-Pereira P andSantos-Silva A. Interleukin (IL)-22, IL-17, IL-23, IL-8, vascular endothelial growth factor and tumour necrosis factor-α levels in patients with psoriasis before, during and after psoralen-ultraviolet A and narrowband ultraviolet B therapy. Br J Dermatol. (2010); 163(6):1282-90.
22. Michalak-Stoma A, Bartosińska J, Kowal M, et al., (2013): Serum levels of selected Th17 and Th22 cytokines in psoriatic patients;35(6):625-31.
23. Armstrong, A.W., Harskamp, C.T., Dhillon, J.S.et al., (2014): Psoriasis and smoking: a systematic review and meta-analysis. British Journal of Dermatology, 170: 304–314.
24. Naldi L, Peli L and Parazzini F. (1999): Association of early-stage psoriasis with smoking and male alcohol consumption: evidence from an Italian case-control study. Arch Dermatol; 135(12):1479-84.
25. Murray ML, Bergstresser PR, Adams-Huet B, Cohen JB. Relationship of psoriasis severity to obesity using same gender siblings as controls for obesity. Clin Exp Dermatol 2008; 34:140-4.
26. Zindancı I, Albayrak O, Kavala M, Kocaturk E, Can B, Sudogan S, et al. Prevalence of Metabolic Syndrome in Patients with Psoriasis. Scientific World J 2012; 2012: 1-5.
27. Nakajima H, Nakajima K, Tarutani M, Morishige R and Sano S. Kinetics of circulating Th17 cytokines and adipokines in psoriasis patients. Arch Dermatol Res.(2011); 303(6):451-5.
28. Ali Al Raddadi, Abdulhadi Jfri and Sahal Samarghandi. et al.,(2016): Psoriasis: Correlation between severity index (PASI) and quality of life index (DLQI) based on the type of treatment. Journal of Dermatology & Dermatologic Surgery. Volume 20, Pages 15–18.

4/5/2017