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ORIGINAL ARTICLE

Serum Concentration of Osteopontin and Interleukin 17 in Psoriatic Patients and Their Relation to Disease Severity

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ABSTRACT

Background*: The pathogenesis of psoriasis vulgaris (PV) appears to be mediated by the interplay between immune cells, and keratinocytes. Osteopontin (OPN) also engaged in the pathogenesis of psoriasis.* ***Objective****: To assess the level of OPN and IL-17 in the serum of psoriatic cases and compare it with their level in healthy people.* ***Methodology****: This case control study was conducted on 50 cases with chronic plaque psoriasis above 18 years old, and matched with age and sex of 40 healthy individuals (control group), dermatologic examination was done by using the Psoriasis Area and Severity Index (PASI) score. Entire cases underwent laboratory tests for their serum concentration of OPN and IL-17.* ***Results****: The mean OPN level was significantly higher in the psoriasis group (21.5±11.7) compared to the control group. The mean IL17 level was significantly increased in the control group (82.6±47.7) compared to the psoriasis group (52.5±54.2). There was a positive significant correlation between IL-17 and PV severity. In discriminating between psoriasis cases and the control group, the AUC for OPN was 0.767, for IL17 it was 0.720, and for the combination of OPN and IL17 it was 0.821. The cut-off value for OPN was greater than 13.3, while for IL17 it was less than 60.9.* ***Conclusion****: the results suggested that OPN and IL17 levels have reasonable discriminative ability in distinguishing psoriasis cases from the control group. Moreover, the combination of OPN and IL17 shows slightly improved performance compared to either parameter alone.*

INTRODUCTION

Psoriasis vulgaris (PV) is a common non-communicable chronic immune-mediated skin condition that could markedly interfere with life quality [1, 2], affecting about 125 million subjects globally [3, 4]. Its pathogenesis appears to be mediated by the interplay between immune cells and keratinocytes (regulated by cytokines which include IL-6, IL-17, and IL-22, interferon (INF), and signalling molecules). This has been demonstrated to be accompanied by an inflammatory condition with raised epidermal proliferation, neoangiogenesis (the development of new blood vessels), and dendritic cell invasion in the skin [5].

Osteopontin (OPN), a protein believed to have a role in PV pathogenesis, has a considerable role in particular physiologic processes and the pathogenesis of inflammatory diseases, malignant tumors, and autoimmune diseases (AIDs) [6]. In recent years, OPN has been considered a multifunctional molecule comprised in the adjustment of Th1 and Th17 responses, proliferation of keratinocytes and apoptosis. In addition, it is thought to have a central function in AID development, as it has the ability to stimulate macrophages to release IL-12 and interact with the CD44 receptor and inhibit IL-10 formation [7].

In addition, OPN triggers Th17 to produce IL-17. Additionally, OPN stimulates the formation of INF gamma by T cells and IL-6 by monocytes, as a result encouraging adhesion and migration of lymphocytes [8]. We aimed to evaluate the level of OPN and IL-17 in the serum of psoriatic cases and compare them to those in healthy individuals. In addition, we determine whether there was a relationship between the severity of PV as determined by the PASI and the levels of OPN and IL-17 in the serum.

METHODOLOGY

Study design

This case-control study was conducted on 50 cases with chronic plaque psoriasis above 18 years old and 40 normal subjects of matched age and sex (control group). They were enrolled from the Dermatology, Andrology & STDs Department, Mansoura University Hospitals.

Exclusion criteria

Cases with an age less than 18 years old, cases that had received systemic therapies for PV throughout the past month prior to the study, cases with other cutaneous disorders such as vitiligo, cases with hepatic or renal dysfunctions, cases with a history of systemic

diseases, pregnancy and breastfeeding women, and smoking patients.

Methods

The entire subjects were subjected to comprehensive history taking regarding age, sex, dietary intake, accompanying psychiatric troubles, associated pathological conditions and drug intake. Comprehensive general examination was conducted and dermatologic evaluation of psoriasis using the PASI score. The body was divided into four areas (head (H) (ten percent); arms (A) (twenty percent); trunk (T) (thirty percent); legs (L) (forty percent)). The final PASI was calculated by adding the four individual scores from each of these areas. The estimated proportion of skin area included in each sector was converted into a grade ranging from zero to six [9].

With regard to each individual region, the degree of severity was measured by three signs: erythema, induration, and desquamation (scale formation) from zero (no disease) to four (full disease). Following that, the weight of each skin section was multiplied by the area score for that area, and the sum of the three severity parameters was computed for each skin section (the head is 0.1, the arms are 0.2, the body is 0.3, and the legs are 0.4).

Entire subjects underwent laboratory analysis for serum levels of OPN and IL-17. Blood specimens were withdrawn from the two groups. Blood was centrifuged for fifteen minutes at 1000×gram, and serum was immediately separated. Determination of serum levels of OPN and IL-17 was carried out using ELISA kits.

Ethical Consideration

The study design was approved by IRB of Mansoura University (Code number: MS.21.12.1796). A written informed consent was obtained from all subjects. Confidentiality was respected. Collected data weren't used for any purpose other than scientific research.

Statistical Analysis

The collected data were introduced to a PC using SPSS (IBM Corp. Released 2017, Version 25. Armonk, NY). The Shapiro test was conducted to assess the normality of data distribution. Mean±SD, and range were used to define parametric numerical data. Median and range were used for non-parametric numerical data. The student t-test and U test were used to assess the significance of the difference of parametric and non-parametric variables between two study groups, respectively. The Chi-Square test was utilized to assess the correlation between two qualitative variables. The ROC Curve offers a helpful method to assess the validity of the measure for the differentiation between two groups. A p-value is considered significant if <0.05.

RESULTS

Table **(1)** displays that there was insignificant difference observed between the Control and Psoriasis group regarding demographic data (p>0.05). The mean OPN level was significantly increased in the psoriasis group (21.5±11.7) compared with the controls (13.2±6.5) (p<0.001). The mean IL17 level was significantly higher in the controls (82.6±47.7) compared to the psoriasis group (52.5±54.2) (p= 0.007). Table **(2)** shows that the median PASI score was 5.2, with a range of 0.7 to 31.6. The majority of psoriasis cases (39 cases) had a PASI score below 10 (78.0%), while 11 cases had a PASI score above 10 (22.0%).

Table 1: Comparison of demographic data, OPN and IL17 levels between studied groups

		Control n=40		**Psoriasis n=50**		***p***
Age (years)	mean±SD	40.6±11.1		41.8±10.2		0.697
	range	18.0-70.0		18.0-70.0		
Males	N %	14	35.0%	23	46.0%	0.292
Females	N %	26	65.0%	27	54.0%	
OPN	mean±SD	13.2±6.5		21.5±11.7		**<0.001**
	Median	12.1		16.95		
	range	6.3-41.4		8.8-45.3		
IL17	mean±SD	82.6±47.7		52.5±54.2		**0.007**
	Median	68.75		36.5		
	range	25.7-186.9		6.8-245		

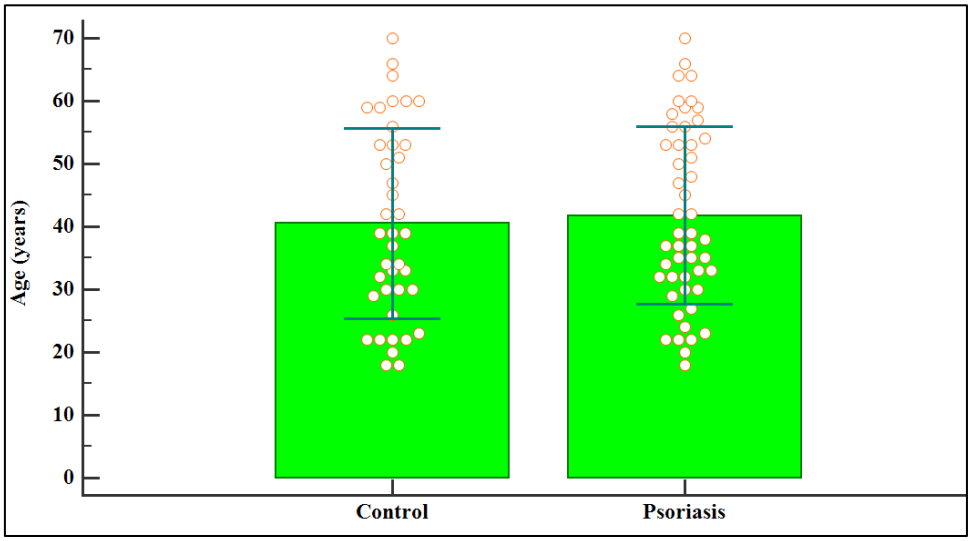
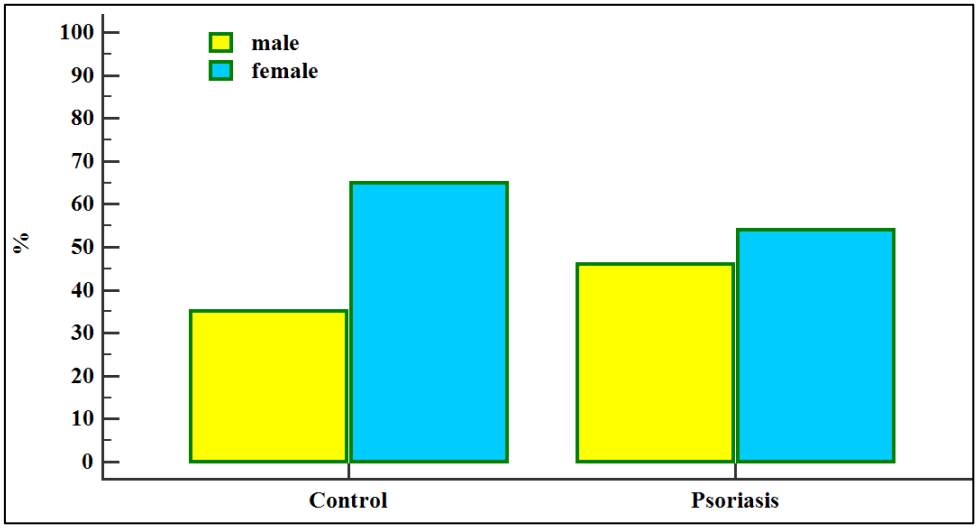


Fig. 1: Age among studied groups. Columns represent means, error bars represent SD, circles represent values.



Fig/ 2: Gender frequency among studied groups. Columns represent percentages.

Table 2: PASI score among all studied psoriasis cases

		Psoriasis n=50	
PASI	Median (range)	5.2	(0.7-31.6)
PASI <10	N, %	39	78.0
PASI >10	N, %	11	22.0

Table **(3)** displays that the AUC for OPN was 0.767, for IL17 it was 0.720, and for the combination of OPN and IL17 it was 0.821 regarding validity of OPN and IL17 levels in discriminating between the psoriasis cases and the control group. The cut-off value for OPN was greater than 13.3, while for IL17 it was less than 60.9. Performance characteristics are shown. Overall, the results suggest that OPN and IL17 levels have reasonable discriminative ability in distinguishing psoriasis cases from the control group. Moreover, the combination of OPN and IL17 shows slightly improved performance compared to either parameter alone.

Table **(4)** shows the validity of OPN and IL17 levels in discriminating between psoriasis cases with PASI scores below 10 and above 10. The AUC for OPN was 0.596, for IL17 it was 0.720, and for the combination of OPN and IL17 it was 0.725. The cut-off values were determined as greater than 17.8 for OPN and greater than 46.6 for IL17. These values indicated moderate discriminatory power for IL17. While OPN had poor AUC. The combination of IL17 and OPN showed better AUC than each parameter alone, with non-statistically significant differences between each parameter or combination. Overall, the results suggest that OPN level alone has limited discriminative ability in distinguishing psoriasis cases with PASI scores below 10 from those with PASI scores above 10.

Table 3: Validity of OPN and IL17 level for discrimination between psoriasis cases and control groups

	OPN	IL17	OPN+IL17
AUC	0.767	0.720	0.821
95% CI	0.670 to 0.865	0.614 to 0.825	0.733 to 0.908
Cut off (%)	>13.3	<60.9	-
Sensitivity (%)	78	82	82
Specificity (%)	65	57.5	65
PPV (%)	73.6	70.7	74.5
NPV (%)	70.3	71.9	74.3
Accuracy (%)	72.2	71.1	74.4
P1	-	0.492	0.048
P2	-	-	0.043

P1, comparison of AUCs vs. AUC of OPN
P2, comparison of AUCs vs. AUC of IL17

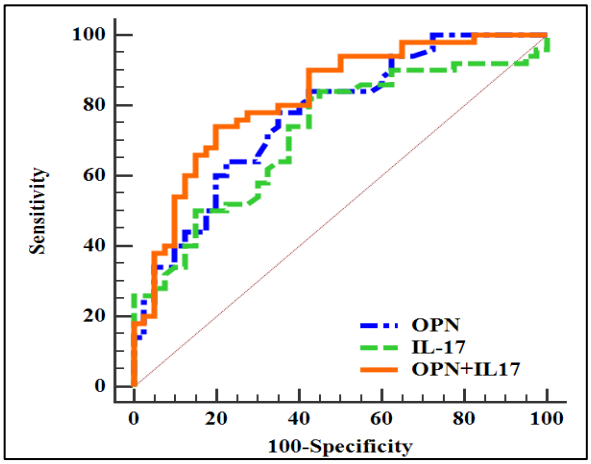


Fig. 3: ROC curve of OPN and IL17 level for discrimination between psoriasis cases and control groups.

Table 4: Validity of OPN and IL17 level for discrimination between PASI<10 and PASI>10 psoriasis cases

	OPN	IL17	OPN+IL17
AUC	0.596	0.720	0.725
95% CI	0.428 to 0.763	0.561 to 0.889	0.555 to 0.885
Cut off (%)	>17.8	>46.6	-
Sensitivity (%)	54.5	63.6	63.6
Specificity (%)	61.5	71.8	71.8
PPV (%)	28.5	38.9	38.9
NPV (%)	82.7	87.5	87.5
Accuracy (%)	60.0	70.0	70.0
P1	-	0.265	0.289
P2	-	-	0.380

P1, comparison of AUCs vs. AUC of OPN
P2, comparison of AUCs vs. AUC of IL17

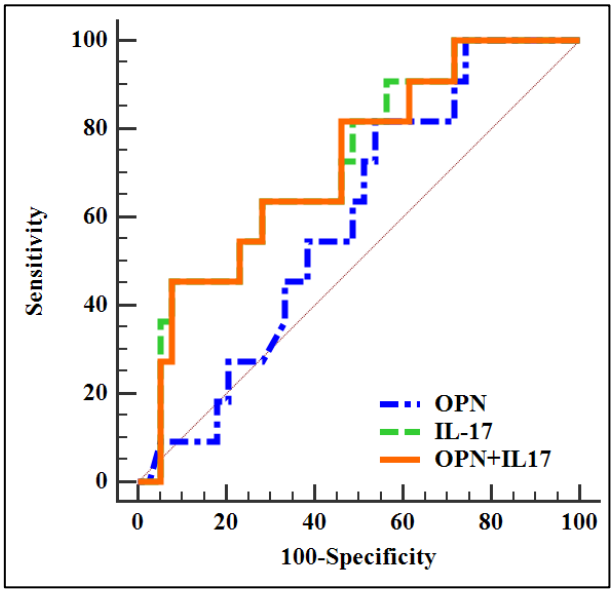


Fig. 4: ROC Curve of OPN and IL17 level for discrimination between PASI<10 and PASI>10 psoriasis cases.

Table **(5)** displays insignificant association between OPN & IL17 and gender among all cases. Table **(6)** shows insignificant association between OPN levels and the PASI scores among all the psoriasis cases. The median IL17 level was 32.00 (range 6.76-245.00) in cases with PASI scores below 10 and 53.50 (range21.80-186.30) in cases with PASI scores above 10. The difference was a significant (p=0.024), indicating a potential correlation between IL17 levels and psoriasis severity.

Table **(7)** presents the associations of OPN levels and IL17 levels with age and PASI score in the psoriasis group. There was a non-significant association observed between OPN levels and age (rs=0.025, p=0.818) or between OPN levels and PASI score (rs=0.065, p=0.655). There was no significant association observed between IL17 levels and age (rs=-0.137, p=0.198). In contrast, there was a significant positive association between IL17 levels and PASI score (rs=0.320, p=0.023), indicating a potential association between IL17 levels and psoriasis severity.

Table 5: Association of OPN and IL17 with gender among all studied subjects (psoriasis cases and control group)

		Subjects N=90					
		OPN		*p*	*IL17*		*p*
		median	range		median	range	
Gender	**Males**	15.7	6.3-45	0.176	40.8	6.76-186.9	0.288
	Females	14.2	7.4-45.3		54.5	6.78-245	

Mann Whitney test was used

Table 6: Association of OPN and IL17 with PASI among all studied psoriasis cases

		psoriasis N=50					
		OPN		*p*			*p*
		median	range		median	range	
PASI	**<10**	16.7	8.8-45.3	0.337	32.00	6.76-245.00	***0.024***
	>10	17.9	13-45		53.50	21.80-186.30	

Mann Whitney test was used

Table 7: Correlations of OPN and IL17 levels with age, and PASI score in psoriasis group

	psoriasis N=50			
	OPN		IL17	
	rs	*p*	*rs*	*p*
Age	0.025	0.818	-0.137	0.198
PASI	0.065	0.655	0.320	***0.023***

rs, correlation coefficient

DISCUSSION

Our study was conducted on 50 psoriasis vulgaris patients; also, 40 healthy subjects of matched age and sex were in the control group.

Regarding the demographic data between the control group and the psoriasis group. The mean of the age was similar between the two groups (control group was 40.6±11.1 years versus psoriasis group was 41.8±10.2 years), there was a non-significant difference observed regarding gender between both groups (table 1) . While, Aalemi et al. [14] revealed that the mean age of psoriatic cases was 33.4±13.1 years versus 41.1±15.4 years for controls. Both groups demonstrated insignificant differences regarding sex which agreed with our results.

The present study revealed that the median PASI score was 5.2, with a range of 0.7 to 31.6. The majority of psoriasis cases (39 cases) had a PASI score below 10 (78.0%), while 11 cases had a PASI score above 10 (22.0%).(table 2) In another study by Chen et al. [15] 4230 psoriasis cases were mainly male (64.6%), with an average age of 38.6 years. The PASI score for cases with PV was more than 7.2.

Our study displayed that there was a significant elevation in the average OPN value in the PV group (21.5±11.7) compared to healthy controls (13.2±6.5).(table 1) These findings were in the same line with Kyriakou et al. [16] who recorded that cases with PV were asssoiated with a significant increase in OPN levels compared to placebos.

A study by Abdel-Mawla et al. [17] recorded a significant difference in OPN expression in the dermal inflammatory infiltrate of lesional and nonlesional (NL) skin of psoriatic cases vs. controls in terms of dermal inflammatory infiltrate density. Also the study found a significant difference in epidermal OPN expression of lesional and NL skin of psoriatic cases versus controls.

In the same line, El-Eishi et al. [18] displayed that lesional skin of psoriatic cases revealed a significant increase in OPN values compared to controls.

In the same line, Buommino et al. [19] found that OPN amount in psoriatic patients' lesional and NL skin was substantially higher compated to controls' normal skin. This cytokine was discovered in 75% of lesional skin samples and 25% of NL skin samples. These findings may suggest that in certain psoriatic patients, NL skin may be prone to developing the disease, secondary to higher OPN expression.

Meanwhile, another study found a non-significant difference in tissue OPN expression between lesional and NL skin in cases with PV. Furthermore, tissue OPN didn't correlate with circulatry OPN, despite the fact that significant differences in tissue OPN were documented between lesional skin of psoriatic cases and NL skin of controls [20].

Our study displayed that the mean IL17 level was significantly increased in the control group (82.6±47.7)

compared with the psoriasis group (52.5±54.2). The median IL17 level was lower in the psoriasis group (36.5) compared with the controls (68.75). (table 1)

These findings contradicted those of Michalak-Stoma et al. [21] who discovered that serum IL-17 values in psoriatic cases (4.24 3.69 pg/ml) were increased compared to the controls (3.06 1.19 pg/ml), but there were non-significant differences. When compared to IL-17 serum levels (4.24 3.69 pg/ml), psoriatic plaques had a greater level of IL-17 (68.32 51.68 pg/ml). Significant differences were recorded in serum IL-17A value among cases with PV compared to the controls in certain researches [22, 23].

In differentiating psoriasis sufferers from the controls in our study, the AUC for OPN was 0.767, for IL17 it was 0.720, and for the combination of OPN and IL17 it was 0.821. The cut-off value for OPN was larger than 13.3, while the cut-off value for IL17 was less than 60.9, implying that OPN and IL17 levels have reasonable discriminative power. Furthermore, the combination of OPN and IL17 performs somewhat better than each parameter alone. (table 3)

For distinguishing between psoriasis cases with PASI scores below 10 and above 10 in the current study, the AUC for OPN was 0.596, for IL17 it was 0.720, and for the combination of OPN and IL17 it was 0.725. The cut-off values for OPN were greater than 17.8 and larger than 46.6 for IL17. These data imply that IL17 has a modest discriminating power. OPN, on the other hand, showed a low AUC, that both OPN levels have limited discriminative ability in distinguishing psoriasis cases with PASI scores less than 10 from those with PASI scores greater than 10 .(table 4)

Similarly, Przepiórka-Kosińska et al. [6] discovered no link between OPN serum levels and psoriasis severity as evaluated by PASI. IL-17 serum levels, on the other hand, linked favorably with psoriasis severity as determined by PASI, BSA, and DLQI. This suggests that the greater the patients' IL-17 serum content, the worse their psoriasis was on average.

The current investigation found non-significant variations in the correlation of OPN with gender and age among all subjects investigated(table 5,7). Furthermore, there were non-significant differences between OPN concetrations and PASI scores in any psoriasis cases.(table 6)

On the other hand, Abdel-Mawla et al. [17] displayed a significant relationship between epidermal OPN expression and dermal inflammatory infiltration in cases with PV and PASI score. Also, El-Eishi et al. [18] recommended a potential role of OPN in terms of PV pathogenesis as well as PV severity.

Our study reported a non-significant relationship between IL17 levels and gender or age, with the median IL17 level being 32 in cases with PASI scores less than 10 and 53.5 in instances with PASI scores greater than 10.(table 6) The difference was significant, showing a possible link between IL17 levels and the severity of psoriasis.

Limitations of the present study included the small sample size, no tissue biopsy taken and examined from psoriasis cases and control, and no more recent studies evaluating levels of both osteopontine and IL 17 in psoriasis patients in the same study, so further studies have to be conducted to confirm the presenting results.

CONCLUSION

Our study concluded that osteopontin level was markedly increased in psoriasis cases than controls, but the level of IL-17 was lower in cases than controls. There was no significant association between OPN levels and the PASI scores among all the psoriasis cases, while IL-17 serum level correlated positively with PV severity assessed by PASI.

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Author Contributions
The authors participated in the design and drafting of the article. This article is approved by authors.

Conflicts Of Interest
None.

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List of Abbreviations
AIDs: Autoimmune disease
AUC: Area under curve
IL-17: Interlukin-17
INF: Interferon
NL: Non lesional
OPN: Osteopontin
PASI: The Psoriasis Area and Severity Index
PV: Psoriasis vulgaris
ROC Curve: Receiver operating characteristic curve
rs: Correlation coefficient
SD: Standard deviation

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