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Total Serum Immunoglobulin E in patients with psoriasis vulgaris

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ORIGINAL STUDY

Total Serum Immunoglobulin E Levels in Patients with Psoriasis Vulgaris

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Abstract

Background: Psoriasis vulgaris (PV) is a multifactorial disease in which some environmental factors acting on people who have a particular genetic predisposition trigger immune dysregulation and irregular keratinization, inducing typical cutaneous lesions. Serum immunoglobulin E (IgE) levels are low in normal subjects, on the other hand they increase in atopy, parasitic infestation, and particular forms of malignant tumours. The aim of this study was to assess serum levels of total IgE in cases with PV.

Aim: The aim of this study was to evaluate serum concentrations of total IgE in patients with psoriasis vulgaris and compare it with its level in healthy volunteers and it's correlation with disease severity by Psoriasis Area and Severity Index (PASI) score.

Patients and methods: This research was a case−control study and comprised 40 psoriasis cases and matched age and sex 40 healthy subjects. Complete general and dermatological examination comprised a PV evaluation by utilizing the Psoriasis Area and Severity Index score. Serum levels of IgE were quantified in samples using enzyme-linked immunosorbent assay (ELISA) kits.

Results: Higher IgE was considered as risk predictor of Psoriasis vulgaris susceptibility. Higher IgE level was significantly associated with nail psoriasis and psoraitic arthropathy (PsA). Topical and previous systemic treatment was significantly associated with higher IgE, while topical only was significantly associated with lower IgE.

Conclusion: Serum IgE could be used as promising indicator not only to evaluate gravidity of PV but also to follow-up the therapeutic objectives.

Keywords: Immunoglobulin E, Psoriasis area and severity index, Psoriasis vulgaris

1. Introduction

Psoriasis vulgaris (PV) is a frequent chronic auto-inflammatory condition characterized by abnormalities in epidermal proliferation. The global incidence represents ~2%, but differs based on the affected areas (Daniyal et al., 2019). Psoriasis has a lot of variants which include; PV, Palmoplantar psoriasis, Guttate psoriasis, Psoriatic arthritis (PsA), Erythrodermic psoriasis, Inverse psoriasis, Generalized pustular psoriasis. Chronic plaque psoriasis (CPP) the commonest type of the psoriasis is often presented by well-circumscribed erythematous plaques with scales on elbow, knee and the scalp, however any cutaneous area could be affected also (Raychaudhuri et al., 2014).

The actual etiology of PV is not well-identified even though a lot of evidences support the theory that PV is an immune mediated lesion. The T-helper (Th) 1 and Th17 cells play essential role with regard to the inflammation of PV (Rendon and Schäkel, 2019). Even though serum IgE levels are reduced under normal physiological conditions, their levels are increased in atopy and parasitic infestations, as well as in particular forms of malignant tumours. In certain disorders, serum IgE level has a positive correlation with both the activity and the gravidity of lesion, and could be utilized as a reliable indicator. Serum immunoglobulin E

(IgE) levels in dermatological situation (with exception of atopic dermatitis) often were recorded as normal, however elevated serum IgE levels were recorded in cases with allergic dermatitis, bullous pemphigoid and alopecia areata (Kasumagic-Halilovic, 2020).

The potential correlation between serum IgE concentrations and PV was recorded in previous researches (Lotfi et al., 2015; Ünal et al., 2017; Nassar et al., 2021). One study revealed that serum IgE was significantly elevated in 39% of cases with PV and the affected skin comprised

more IgE+ and FcεRI + cells (Yan et al., 2016). Contradictory results were obtained by other authors Who didn't detect an elevation in IgE levels in patients with psoriasis vulgaris (Hosseini et al., 2019). Thus, we aimed to assess serum levels of total IgE in cases with PV and compare it with its level in healthy volunteers and it's correlation with disease severity by Psoriasis Area and Severity Index (PASI) score.

2. Patients and methods

This was a case–control study carried out on a total of 80 patients who were recruited from the Dermatology outpatient clinic of Mansoura University Hospital within the period from January 2022 to July 2022. They were divided into two equal groups; case group that comprised 40 patients suffering from PV and control group that comprised 40 gender and age matched healthy controls. Patients with CPP diagnosed clinically beyond the age of 18 years old. Patients with positive family and personal history of allergy (Atopic dermatitis, Bronchial asthma, Atopic rhinitis, food allergy) were excluded, patients with concomitant disorders including systemic and neoplastic disease, patients with factors affecting IgE levels, and patients with immune dysregulation, polyendocrinopathy, enteropathy, X-linked syndrome (IPEX) syndrome were excluded.

2.1. Methods

All cases were subjected to complete history taking with regard to age, sex, occupation, marital condition, dietary intake, accompanying psychiatric troubles, accompanying medical or surgical conditions and drug intake, general examination and comprehensive dermatologic examination that comprised a clinical evaluation of PV. Lesions were scored according to PASI score which is the commonest approach utilized to evaluate disease severity in cases with PV (Langley and Ellis, 2004). The included cases were also classified based on PASI score into:

(1) Mild PV (PASI less than or equal to 10),

(2) Moderate PV (PASI more than 10 and less than 20), Severe PV (PASI more than or equal to 20).

2.2. Laboratory investigations

Three ml of venous blood were withdrawn from subjects and serum were undergone centrifugation for 15 min at $2000 \times g$ within one hour of collection. Harvested serum were stored at -20 till analysis. Serum concentrations of IgE were quantified in samples by utilizing ELISA kits ((Invitrogen, USA, Catalog # BMS2097), based on the user manufacturer. Assay range is 7.8–500 ng/ml.

2.3. Test principle

The IgE Quantitative Test Kit was mainly depending on a solid phase ELISA which uses one anti-IgE antibody (Ab) for solid phase immobilization and another anti-IgE Ab in the Ab-enzyme conjugate solution. The test serum was added to the IgE Ab coated microtiter wells followed by incubation with the Zero Buffer. The human IgE in the specimen combined with the Ab on the well. The well was after that washed to withdraw the remaining specimens, and IgE Ab labeled with horseradish peroxidase was added. The conjugate was connected by immunological method to the IgE on the well, which ultimately ends in the IgE molecules. Following incubation at 22C, the wells were washed to discard unbound Abs. A solution of TMB was added followed by incubation for 20 min which ultimately changed into bluish coloration. The color formation was stopped by adding 2 N HCl, and the colour was altered to yellow and evaluated by using spectrophotometrical method at 450 nm. The IgE level has a direct correlation with the colour intensity.

2.4. Specimen collection

The serum was obtained from the blood sample using EDTA-free sterile tube. The material and components comprised Ab-coated microtiter wells, zero Buffer (11 ml), enzyme conjugate reagent (6 ml), Tetramethylbenzidine Substrate (11 ml), stop Solution (11 ml), reference standards, comprising 0, 10, 50, 100, 400, and 800 IU/ml of IgE, in liquid.

2.5. Procedure

(1) The required numbers of coated wells was secured.
(2) About 100 μl of Zero Buffer was dispensed into all wells.

(3) Then, 20 µl of standard, samples, and controls were added into proper wells.

(4) Adequate mixing for 5—10 s was done.

(5) Incubation at 37 °C for 30 min.

(6) The incubation mixture was discarded by flicking plate content into a waste container.

(7) Rinsing and flicking of the microtiter wells five times with distilled H2O were performed.

(8) Striking the wells in a sharp manner was performed into absorbent paper to discard the remaining water drops.

(9) About 50 µl of Enzyme Conjugate Reagent was dispensed into all wells.

(10) Gentle rocking was done for 5 s.

(11) Incubation at 37 C for half an hour.

(12) Discard the mixture via flicking plate contents into sink.

(13) Rinsing followed by flicking of the microtiter wells were done for 5 times by using distilled H$_2$O.

(14) Sharp striking of the wells onto absorbent paper was done to discard the remaining water drops.

(15) Dispense 100 µl TMB solution into all wells. Gentle mixing for five sec was done.

(16) Incubation at 37 °C was performed in the dark for fifteen minutes.

(17) The reaction was stopped via the addition of 100 µl of stop Solution to all wells.

(18) Gentle mixing for 30 s.

(19) The OD was read at 450 nm by using a microtiter reader.

2.6. Calculations

The mean absorbance value was calculated (A450) for standards, specimens, controls and patient samples. Construct a standard curve via plotting the mean absorbance acquired from all reference standard against its level in IU/ml, in which the absorbance value on the Y axis and levels on the X axis. The mean absorbance values were used for all specimens to detect the matching level of IgE.

2.7. Ethical consideration

The Mansoura Faculty of Medicine, IRB approved the current study (MS.22.03.1900). An informed consent was taken before their participation. Privacy was guaranteed at all levels. Entire data were utilized only for scientific aims.

2.8. Statistical analysis

Data were analyzed by using SPSS software, version 18. Qualitative data were defined by utilizing number and percentage. Quantitative data were defined by utilizing mean ± SD. Significance of the acquired results was judged at the (≤ 0.05) level. χ^2, MC tests were utilized for comparison of qualitative data between groups. Kruskal Wallis and Mann Whitney U test were utilized for comparison between two studied groups and more than two studied groups, respectively for nonnormal distribution of the data. One Way ANOVA test was utilized for comparison between at least 2 independent groups with Post Hoc test.

3. Results

The current study was carried out on 40 psoriasis vulgaris patients with matched age and sex 40 normal control individuals. The mean age of studied patients 40.6 ± 12.4. The case group comprised 19 (47.5%) males and 21 (52.5%) females. Mean ± SD PASI score was 1.7 ± 2 among all studied cases, 48.8% of the cases had mild grade psoriasis and 1.3% had moderate grade psoriasis. Among all studied psoriasis cases, 17.5% had Nail psoriasis and 2.5% had psoraitic arthropathy (Fig. 1). Table 1.

Among all studied cases, 10% received topical and biologic treatment, 22.5% received topical and previous systemic treatment, 27.5% received topical and NB-UVB and 20% received topical treatment only (Table 2). The level of Ig-E was significantly higher in cases in comparison with control group (median = 25.5 (0.6_1323) versus 6.9 (0.3_76) respectively, $P < 0.001$)) (Table 3). Higher IgE level was significantly associated with nail psoriasis with mean (695.1 ± 489.5) and psoriatic arthropathy (262). Table 4.

Topical and previous systemic treatment was significantly associated with higher IgE level with mean (632.1 ± 465.6 SD) while topical treatment only was significantly associated with lower IgE level with mean (8.1 ± 7 SD). While IgE was not affected by topical and biological treatment as well as topical and NB-UVB treatment (Table 5).

ROC curve of IgE was carried out for discrimination between PV group and control group for evaluation of diagnostic validity of this marker. IgE showed moderate accuracy area under the ROC curve (AUC) (AUC = 0.765). At best cutoff value of 8.7, sensitivity (Sn) was 70%, specificity (Sp) was 75%, positive predictive value (PPV) was 73.7%, negative predictive value (NPV) was 71.4%, accuracy was 72.5% (Table 6). ROC curve of IgE was carried out for prediction of nail Psoriasis susceptibility. IgE demonstrated high accuracy AUC (AUC = 0.935). At best instead of value of 130, Sn was 100%, Sp was
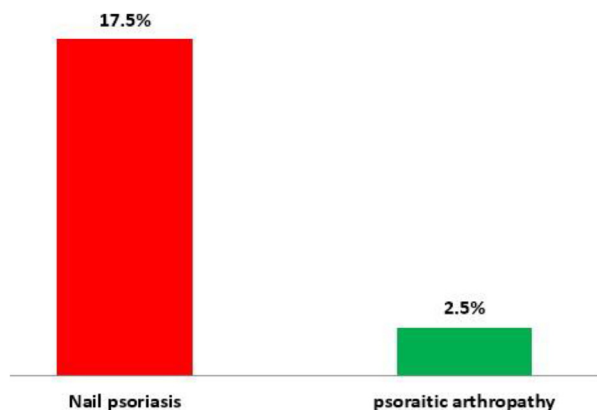
Fig. 1. Clinical findings among all studied psoriasis cases.

84.8%, PPV was 58.3%, NPV was 100%, accuracy was 87.5% (Tables 7 and 8).

4. Discussion

PV is an inflammatory dermal lesion in which the cells and molecules of the innate and adaptive immune systems play an essential role. Of note, the immune pathways which become stimulated in PV represent amplifications of immune circuits that exist as inducible pathways in normal skin Lowes and colleagues (Lowes et al., 2014).

Cases with PV were demonstrated to be associated with overproduction of IgE. Greater concentrations of IgE were reported in blood of PV cases in comparison with PV healthy subjects. In addition, cases with a prolonged history of dermal lesions had an increase in total IgE level Kasumagic-Halilovic (2020).

Hence, the present study aimed to assess values of total IgE in cases with PV in comparison with PV healthy subjects and its correlation with disease severity. The current study comprised 40 PV cases and matched age and sex 40 healthy controls.

In the current study, the mean age of PV cases was 40.6 ± 12.4 years.

Such mean age was in agreement with González-Álvarez and colleagues, Aryanian and colleagues studies in which the mean age was 42.6 and 41.56 ± 16.20 years (González-Álvarez et al., 2019; Aryanian et al., 2021).

Table 1. Severity of psoriasis cases.

		Psoriasis Vulgaris n = 40	
PASI score	Mean ± SD	1.7 ± 2	
	Median, range	1.2 (0.6–12)	
Mild	N, %	39	97.5%
Moderate	N, %	1	2.5%

Table 2. Received treatment among studied cases.

	Psoriasis Vulgaris n = 40
	N (%)
Topical and biological treatment	4 (10.0%)
Topical and previous systemic treatment	9 (22.5%)
Topical and NB-UVB	11 (27.5%)
Topical treatment only	16 (20%)

Table 3. Comparison of IgE level among studied groups.

		Control n = 40	Psoriasis Vulgaris n = 40	P
IgE IU/mL	Mean, SD	11.4 ± 16.7	190.9 ± 337.8	<0.001
	Median, Mini - Max	6.9 (0.3–1323)	25.5 (0.6–1323)	

Comparison by Mann Whitney test.

Table 4. Comparison of IgE level among psoriatic cases according to clinical data.

	IgE level (IU/mL) Mean ± SD	Median	Minimum – Maximum	P
Nail psoriasis				
Absent	84.0 ± 163.4	17.0	(0.6–667.0)	0.027
Present	695.1 ± 489.5	449.0	(189.0–1323.0)	
Psoraitic arthropathy				
Absent	189.1 ± 342.0	24.6	(0.6–1323.0)	<0.001
Present	262.0±	262.0	(262.0–262.0)	

In our study, the prevalence of psoriasis in males was 47.5% vs. 52.5% in female. As regard other studies, Male sex was a factor accompanied by a higher possibility of PV (1.88% males versus 1.56% females, OR: 1.21, 95% IC: 1.151.27) (Fernández-Armenteros et al., 2019). In addition, this higher ratio of males was detected in previous European researches which include (2.4 females % versus 1.9%

Table 5. Comparison of IgE level among psoriatic cases according to received treatment.

	IgE level (IU/mL) Mean (SD)	Median	Mini - Max	P
Topical and biological				
Absent	171.2 ± 350.1	19.9	(0.6–1323.0)	0.988
Present	368.2 ± 81.4	380.8	(262.0–449.0)	
Topical and previous systemic				
Absent	62.8 ± 123.2	16.4	(0.6–449.0)	<0.001
Present	632.1 ± 465.6	482.0	(72.8–1323.0)	
Topical and NB-UVB				
Absent	251.4 ± 380.8	17.3	(0.6–1323.00)	0.988
Present	31.4 ± 16.9	32.7	(6.2–54.4)	
Topical only				
Absent	312.8 ± 393.3	130.9	(6.2–1323.0)	<0.001
Present	8.1 ± 7.0	6.3	(0.6–26.4)	

Table 6. Validity of IgE for discrimination between the studied groups.

	IgE
AUC	0.765
Cutoff	8.7
Sensitivity (%)	70
Specificity (%)	75
PPV (%)	73.7
NPV (%)	71.4
Accuracy (%)	72.5

Table 7. Validity of IgE for prediction of nail Psoriasis susceptibility.

	IgE
AUC	0.935
Cutoff	130
Sensitivity (%)	100
Specificity (%)	84.88
PPV (%)	58.3
NPV (%)	100
Accuracy (%)	87.5

Table 8. Correlations of IgE with age and PASI score.

	IgE		P
	rs		
Age	−0.004	0.982	
PASI score	0.834	<0.001	

rs, correlation coefficient.

males) Ferrándiz and colleagues (Ferrándiz et al., 2014), and (2.90% males vs. 2.59% females) Radtke and colleagues (Radtke et al., 2017). Additional researches demonstrated a greater incidence of PV in females, which include (2.5% in females vs. 1.9% in males) Stern and colleagues (Stern et al., 2004), in the Unites States, on the other hand two Unites Kingdom researches demonstrated no significant difference between genders Gelfand and colleagues, Seminara and colleagues (Gelfand et al., 2005; Seminara et al., 2011).

In our study, the Mean PASI score was 1.7, among all studied cases, 48.8% had mild grade psoriasis and 1.3% had moderate grade psoriasis. In the present study, serum IgE showed significantly higher concentration in cases in comparison with the control group (median, minimum–maximum = 25.5 (0.61323) versus 6.9 (0.3–76), respectively, $P < 0.001$).

Of note, the possible correlation of serum IgE levels and PV is formerly recorded. This agree with the previous study of Kasumagic-Halilovic, Lotfi and colleagues, Nassar and colleagues, Yan and colleagues and Chen et al. recorded a significant elevation in serum IgE levels in cases with PV compared with controls ($P < 0.05$) (Kasumagic-Halilovic, 2020; Lotfi et al., 2015).

Kasumagic-Halilovic (2020) revealed that serum IgE was associated with a significant increase in cases with PV (46.7%) compared with normal individuals (control group) (10%).

Our results demonstrated that, higher IgE level was significantly associated with nail psoriasis and psoraitic arthropathy (PsA). Topical and previous systemic treatment was significantly associated with higher IgE, while topical treatment only was significantly associated with lower IgE. While IgE was not affected by topical and biological treatment as well as topical and NB- UVB treatment.

Preceding research demonstrated that IL-8 suppressed IL-4-induced IgE formation and endogenous TNF-α and IL-6 are important in the context of IgE formation in atopic cases Cruse and colleagues (Cruse et al., 2008).

ROC curve of IgE was carried out by us for differentiation between PV group and control group for evaluation of diagnostic validity of this marker. IgE showed moderate accuracy (AUC = 0.765). At best cutoff value of 8.7, Sn was 70%, Sp was 75%, PPV was 73.7%, NPV was 71.4%, accuracy was 72.5%.

ROC curve of IgE was carried out for prediction of nail Psoriasis susceptibility, IgE demonstrated high accuracy (AUC = 0.935). At best cutoff value of 130, Sn was 100%, Sp was 84.8%, PPV was 58.3%, NPV was 100%, accuracy was 87.5%.

In the present study, serum IgE demonstrated significant positive correlation with PASI score ($P < 0.001$, r = 0.834), but not with age ($P = 0.982$, r = −0.004). Nassar and colleagues (Nassar et al., 2021) observed a significant positive association between serum IgE concentration and PASI scores in cases with PV. In contrast, Lotfi and colleagues (Lotfi et al., 2015) have demonstrated a statistically significant close correlation between serum levels of IgE and PASI score in cases with erythrodermic psoriasis, however cases with CPP not. This discrepancy may be due to changes in the clinical features of the evaluated patients.

A significant association between IgE level and disease severity by utilizing.

PASI score did not achieve, ($P = 0.11$) neither significant correlation between IgE level and disease duration ($P = 0.46$) or age ($P = 0.6$) or sex of the cases ($P = 0.99$).

There are only restricted and debated records in the literatures in terms of detection of serum IgE levels with regard to clinical manifestations of PV Hajdarbegovic and colleagues (Hajdarbegovic et al., 2013). A Th1/Th17 immune response has been considered the main pathogenesis in the context of PV. On the other hand, elevated IgE levels, a

prototypical predictor of Th2-predominant immune processes Skaaby and colleagues (Skaaby et al., 2015), has been also demonstrated in cases with PV Voulgari and colleagues (Voulgari et al., 2016), in particular in those with the generalized pustular form, in which they were considered a biomarker of inflammation burden Paparo and colleagues (Paparo et al., 2014). In contrast, Hajdarbegovic and colleagues (Hajdarbegovic et al., 2013) have reported that co-manifestation of atopy, a state associated with elevated serum IgE concentrations, could even protect cases with PV from developing PsA and reducing its gravidity.

Even though limited by its retrospective nature and the comparatively small sample size, the recorded observations were supported by the reproduction of the confirmed association of nail and joint affection in cases with PV Langenbruch and colleagues (Langenbruch et al., 2014). Voulgari and colleagues (Voulgari et al., 2016) speculated that elevated serum IgE concentrations among cases with PV could indicate the stimulation of a regulatory Th1overcoming Th2 immune response. Additional researches are required to elucidate the actual roles with regard to the IgE level alteration in the pathogenesis and gravidity of PV and PsA.

4.1. Conclusion

These data demonstrated that serum IgE was significantly expressed in PV, especially in nail psoriasis and PsA, which indicate that the high serum IgE level could be a frequent feature in cases with PV. Correlation analysis showed significant association between IgE level and disease severity. So, serum IgE could be used as promising indicator not only to evaluate gravidity of PV but also to follow-up the therapeutic objectives.

Conflicts of interest

No conflicts of interest.

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