Total serum immunoglobulin E in patients with alopecia areata

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ABSTRACT

Context: Alopecia areata (AA) is a common form of localized, non-scarring hair loss. The pathogenesis of the disease is unknown. Previous evidence suggested the involvement of Th2 cytokines in disease pathogenesis. **Aim:** To determine serum level of total IgE, this is mainly influenced by Th2 cytokines, in Egyptian patients with AA. **Materials and Methods:** Fifty subjects with AA (28 males and 22 females) were selected from Dermatology Outpatient Clinic, Menoufiya University Hospital from February 2012 to December 2012. Subjects with other conditions that might elevate serum IgE were excluded from the study. Fifty age- and sex-matched healthy subjects were selected as a control group. Venous blood samples were taken from cases and controls for measurement of total serum IgE by enzyme-linked immunosorbent assay. Skin biopsy was taken from every case from an active area of hair loss. **Results:** Total serum IgE was elevated in 27 (54%) cases. Its values among patients ranged from 13.5 IU/ml to 780 IU/ml. There was a statistically significant difference between cases and controls with regard to mean value of serum IgE ($P < 0.05$). Mean value of IgE did not vary significantly with disease severity, patients' age, patients' gender, disease duration, site of lesions, and positive family history of AA. No correlation was found between serum IgE levels and histopathological changes detected in examined cases. **Conclusions:** Total serum IgE is elevated in AA. This elevation is not related to age, gender, disease duration, disease severity, site of affection or family history of AA.

Key words: Alopecia, IgE, pathogenesis

Access this article online

Website: www.idoj.in

DOI: 10.4103/2229-5178.131076

Quick Response Code:

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INTRODUCTION

Alopecia areata (AA) is a common form of localized, non-scarring hair loss that occurs on any hair bearing skin.[1] The etiopathogenesis of the disease is still unclear. It is suspected to be an autoimmune disease having a genetic predisposition, influenced by environmental and ethnic factors.[2]

Although, the pathogenesis of AA is poorly understood, evidence which suggests that T cells and cytokines play an important role is accumulating. Previous mouse data suggested that the initiation phase of AA is a heavily Th1-based immune response.[3] However, the maintenance of destruction of the hair follicles by cytotoxic cells was suggested to be due to a shift from a Th1 response to a more chronic Th2 immune profile.[4] Thus, AA is a cell-mediated autoimmune disease with late, possibly secondary, humoral response.[5]

Serum IgE concentrations are high in atopy,[6] parasitosis,[7] human immunodeficiency virus infection,[8] systemic lupus erythematosus,[9] and certain types of cancer.[10] The production of IgE is usually Th2 cell determined. The Th2 cytokines, IL (interleukin)-4 and IL-13, are required signals for IgE synthesis. Keratinocytes do not produce IL-4 or IL-13, but are involved in IL-4 or IL-13 induced biological effects.[11] Different studies have measured IgE in AA patients with controversial results.[12-14]

The aim of this work was to evaluate total serum IgE in Egyptian AA patients to investigate the role of Th2 cytokines, which are known to stimulate IgE production, in AA pathogenesis.

MATERIALS AND METHODS

Ethics

Written consent forms approved by the Committee of Human Rights in Research in

Menoufiya University were obtained from studied cases and control subjects. Those were in accordance with the Helsinki Declaration of 1975 (revised in 2000).

Patients

This study included 50 cases with AA and 50 healthy, age- and sex-matched subjects as a control group. Cases were selected from the Dermatology Outpatient Clinic, Menoufiya University Hospital between February 2012 and December 2012.

All studied patients were subjected to complete history taking, general, and dermatological examination. Demographic data (age and gender) and clinical variables (site of lesions, disease severity, disease duration, and family history of AA in first degree relatives of every case) were all documented. Disease duration was calculated from disease onset to time of the first visit.

The severity of AA was graded according to Kavak *et al*.[15] as follows:

- Mild: The presence of three or less patches of alopecia with a widest diameter of 3 cm or less, or the disease is limited to the eyelashes and eyebrows
- Moderate: Existence of more than three patches of alopecia, or a patch greater than 3 cm at the widest diameter without alopecia totalis or alopecia universalis
- Severe: Alopecia totalis or alopecia universalis
- Ophiasis: Snake shaped plaques extending to the scalp border or loss of hair in the shape of a wave at the circumference of the head.

Patients with one or more of the following were excluded:

1. Atopy or any form of allergy, including first degree relatives. This was carried out by:
   - History taking (past or current history of atopic dermatitis, asthma and/or allergic rhinoconjunctivitis in cases and/or relatives)
   - Clinical examination (dermatological, ophthalmic, chest and ear, nose, and throat examination)
   - Skin prick test to a panel of allergens.
2. Bacterial, viral infection and/or parasitic infestations
3. Smokers
4. Use of any form of topical or systemic treatment
5. Sessions of Psoralen + UVA (PUVA), for at least 6 months before this study
6. Hyper IgE syndrome and acute phase of acute coronary syndromes
7. Past or present history of malignancy.

Measurement of serum total IgE

Cases and control subjects were subjected to determination of total serum IgE level by enzyme-linked immunosorbent assay using the enzyme immunoassay for the quantitative determination of IgE concentration in human serum, Immunospec Corporation, Canoga Park CA.

Skin biopsy taking

Skin biopsy samples were taken under local anesthesia from every case from an active area of hair loss. All specimens were fixed in 10% neutral-buffered formalin and subjected to routine tissue processing that ended with paraffin-embedded blocks ready for sectioning.

Statistical procedure

Results were collected, tabulated, statistically analyzed using statistical package SPSS version 11. Data were statistically described in terms of range, mean ± standard deviation (±SD), frequencies (number of cases) and relative frequencies (percentages) when appropriate. Kruskal-Wallis test was used for comparison between three or more groups not normally distributed having quantitative variables. Comparison of quantitative variables was carried out using Mann-Whitney test for independent samples. Associations between inflammatory cell infiltration and laboratory values were analyzed using the Pearson's correlation test. A $P < 0.05$ was considered statistically significant.

RESULTS

Studied population

Cases included 28 males (56%) and 22 females (44%). Patients' ages ranged from 10 years to 53 years with a mean ± SD age of 28.38 ± 11.52 years. Disease duration ranged from 1 month to 26 months with a mean ±SD duration of 4.39 ± 4.74 months [Table 1].

Control group included 25 males (50%) and 25 females (50%). Their ages ranged from 12 years to 50 years with a mean ±SD ageof 27.54 ± 10.36 years.

Thirty cases (60%) had scalp AA, 10 cases (20%) had beard AA and 10 cases (20%) had alopecia universalis [Table 1].

Regarding disease severity, 17 cases (34%) had mild AA, 18 cases (36%) had moderate AA, 10 cases (20%) had severe AA and 5 cases (10%) had ophiasis. Family history was positive in 12 (24%) cases [Table 1].

Histopathological examination

Examination of hematoxylin and eosin-stained sections showed increased proportion of catagen and telogen hair follicles, and perifollicular mononuclear inflammatory infiltration. Lesional mononuclear cell count around hair follicles has a mean ± SD value of 25.38 ± 12.69 cell. Slight perivascular inflammatory cell infiltration comprised mainly of mononuclear cells was also

noted. Eosinophilic infiltration around lower hair follicles was found in 25 patients (50%) (5 cases with mild, 8 cases with moderate, 10 cases with severe AA and 2 cases with ophiasis). Lesional eosinophilic count around hair follicles has a mean ± SD value of 2.15 ± 1.68.

Serum IgE in studied population

Serum IgE level in studied cases ranged from 13.5 IU/ml to 780 IU/ml with a mean ± SD value of 187.92 ± 242.51 (IU/ml). IgE was elevated in 27 cases (54%). There was a statistically significant difference between cases and controls regarding mean value of total IgE ($P < 0.05$) [Table 2].

There were insignificant differences in mean values of IgE among AA cases regarding disease severity ($P > 0.05$), Patients' ages ($P > 0.05$), patients gender ($P > 0.05$), disease duration ($P > 0.05$), and site of affection and positive family history of AA [Table 3].

Serum IgE level was not correlated with the perifollicular mononuclear cell infiltrate or esinophilic count ($P > 0.05$) [Table 4].

Table 1: Demographic and clinical data of studied patients

Demographic data	Studied group	
	Mean±SD	Range
Age years	28.38±11.52	10-53
Disease duration (months)	4.39±4.74	1-20
Clinical data	No.	%
Sex		
Male	28	56
Female	22	44
Site		
Scalp	30	60
Bread	10	20
Alopecia universalis	10	20
Severity		
Mild	17	34
Moderate	18	36
Severe	10	20
Ophiasis	5	10
Family history		
Positive	12	24
Negative	38	76

SD: Standard deviation

Table 2: Comparison between cases and control group regarding mean values of serum IgE

IgE	Patient group	Control group	U test	*P* value
Mean±SD	187.92±242.51	68.38±91.27	2.84	0.043*

U test: Mann-Whitney test, *: Significant, IgE: Immunoglobulin E

DISCUSSION

Immunoglobulin E plays a crucial role in the pathogenesis of allergic disorders. The process involved in IgE production by B cells include germline ε transcript expression, IgE class switching, clonal expansion of B cells, and differentiation into IgE-secreting plasma cells.[16]

It is believed that AA is an organ-specific autoimmune disease, targeting anagen-stage follicles which leads to disruption of hair follicle growth.[17]

Although, increased levels of Th1 cytokines (interferon-γ (IFN-γ) and IL-2) in lesional AA skin have been reported,[18] Th2 immune response was also incriminated in the pathogenesis of AA.[19,20]

Table 3: Association between IgE levels and clinical parameters of AA cases

Clinical parameters	Mean+SD	Test of significance	*P* value
Severity			
Mild	277.4±288.94	K test	0.062
Moderate	168.56±155.39	3.77	
Severe	109.75±120.33		
Ophiasis	132.25±115.63		
Age			
≤18 years	185.42±276.01	*U* test	0.078
>18 years	188.8±233.78	0.59	
Sex			
Male	281.52±288.07	*U* test	0.081
Female	68.8±63.19	1.72	
Duration			
≤1 year	155.65±222.26	*U* test	0.09
>1 year	201.76±252.51	0.14	
Site			
Beard	129.65±14.11	*U* test	0.08
Scalp	126.80±7.77	0.32	
Whole body	172.28±7.62		
Family history of AA			
Positive	123.44±13.17	*U* test	0.61
Negative	176.52±6.78	2.15	

U test: Mann-Whitney test, K test: Kruskal-Wallis test, AA: Alopecia areata, IgE: Immunoglobulin E

Table 4: Pearson's correlation between IgE values and histopathological changes in AA cases

Histopathological changes	Total serum IgE	
	r	*P* value
Perifollicular esinophilic infiltration	0.447	0.19
Perifollicular mononuclear cell infiltration	0.64	0.24

r: Correlation coefficient, AA: Alopecia areata, IgE: Immunoglobulin E

The aim of this work was to evaluate total serum IgE in Egyptian AA patients to investigate the role of Th2 cytokines, which are known to stimulate IgE production, in AA pathogenesis.

In the current study, total serum IgE was elevated in 27 (54%) cases with significant difference in its mean values between cases and controls.

The association of serum IgE levels and AA has been previously investigated with varying results. Przybilla *et al*.[21] found elevated total IgE in 19.7% of studied AA patients**.** Later on, O'Loughlin *et al*.[22] found elevated total serum IgE in 30% of AA patients. Kasumagić-Halilović and Prohić[14] also found elevated total IgE in 37% of AA patients. Attia *et al*.[5] found elevated total IgE in 48.3% of Egyptian AA cases. Zuel Fakkar *et al*.[23] found elevated total IgE in 50% of studied Egyptian cases. Zhao *et al*.[24] demonstrated significant elevation of IgE in patchy AA than healthy control. Bork *et al*.[25] also recorded a significant increase in serum IgE (32%) in children with AA.

However, in contrast to these results, the total serum IgE levels were not elevated in AA patients than normal population in other previous similar studies.[26-28] This discrepancy could be attributed the different numbers of patients involved, and to the different environmental factors, which may affect IgE level.

The mechanism of IgE elevation in AA is not exactly known. A variety of cytokines control IgE production. IL-4, IL-6, IL-7, IL-9 and IL-13, enhance IgE production. In contrast, IFN-γ and IL-10 inhibit IgE synthesis.[11]

Arps and Kölsch[29] reported that IL-10 deficient mice showed elevated ratios of $CD4^+$: $CD8^+$ T cells, indicating a higher capacity to provide B cell activation, which results in a strongly elevated IgE response. In accordance with this observation, intralesional under-expression of IL-10 mRNA, was demonstrated in patients with AA.[18] Thus, elevated serum IgE in AA patients may reflect IL-10 deficiency-associated B cell stimulation. Further studies on a larger scale are required to prove this observation.

Another possible explanation can be introduced based on the observation of Katagiri *et al*.[20] who reported lower levels of IFN-γ, and TGF-ß1 mRNA in non-atopic patients with AA than those in healthy controls. Decreased levels of IFN-γ and Transforming growth factor ß1 (TGF-ß1) were also shown in patients with atopic dermatitis. These results indicated a similarity between atopic dermatitis and AA based on their cytokine profile. Decreased levels of these cytokines lead to enhanced IgE production. Going with that, experiments carried out by Deeths *et al*.[30] showed that antigen specific T-cells from AA patients appear to have some intrinsic defect towards the production of IFN-γ, possibly suggesting a state of partial tolerance in the skin of these patients.

Contrary to these results, Teraki *et al*.[19] reported that serum levels of IFN-γ were significantly elevated in patients with extensive AA. However, Gregoriou *et al*.[31] concluded that, the elevated serum levels of IFN-γ in AA patients may reflect the state of inflammation, especially in the extensive forms of the disease, and the measurement of serum IFN-γ may be useful in discriminating those who are likely to develop alopecia universalis from the remaining local disease, or as a prognostic indicator.

Elevated serum IgE in AA cases may also due to increased tumor necrosis factor (TNF)- α that is known to play a key role in the pathogenesis of AA. TNF-α is synthesized in epidermal keratinocytes along with several other cytokines[32] and is a very potent inhibitor of proliferation.[33] TNF-α may enhance IgE levels by creating a micro-environment rich in the Th2 cytokines, IL-4 and IL-13, stimulating IgE class switching.[34]

In addition, the sera of patients with AA have been found to contain extremely high levels of B cell activating factor (BAFF) that belongs to the TNF family, produced by myeloid lineage cells.[35] It is considered that the production of BAFF is stimulated by IFN-γ that is known to be increased in severe AA patients.[36,37]

Previous studies reported higher serum levels of IL-4 in AA cases than in normal subjects.[5,20] IL-4 is a stimulant of IgE production.[11]

Another possible mechanism of IgE elevation in AA patients may be also due to over-expression of CD40. It is a member of a family of surface molecules with homology to the nerve growth factor receptor and is expressed on B cells.[38] Zhang *et al*.[39] suggested that CD40 stimulation alone could enhance IgE production from *in vivo* - driven, IgE-producing cells. CD40 was also found to be expressed in the hair structures including the dermal papilla of AA lesions confirming a possible role in elevated serum IgE in some AA patients.[40]

Another possible explanation for elevated IgE in AA is supported by genetic linkage. Many genetic loci and defined genes have been associated with the etiology of allergic disorders.[41] The atopic disorders have been reported to occur with an incidence that varies from 1% to 52% in patients with AA.[42] It has also been observed that AA pursues a severe course in the presence of atopy and has an early onset and longer duration, with poor response to treatment.[43]

Association between atopy and 11q13 genetic locus was discovered by Young *et al*.[44] Subsequent research revealed that 11q13 genetic locus contains among other genes the FCεRIβ gene, encoding for the high affinity IgE receptor β chain (FCεRIβ).[45] Genes for Ig heavy (Gm) and light (Km) chain genotypes, discovered on human chromosome 14, have also been implicated in AA susceptibility.[46] Attia *et al*.[5] reported that

elevated serum IgE in patients with AA may be related to their HLA profile. Elevated IL-4 and IgE were observed in patients with DRB1*07 and DRB1*11.

With respect to histopathological changes, our study showed perifollicular esinophilic infiltration in 50% of examined cases. Zhao *et al*.[24] reported the presence of esinophilic infiltration around hair follicles in patchy AA. Elston *et al*.[47] detected eosinophils in all stages of AA. Peckham *et al*.[48] detected the presence of eosinophils in fibrous tracts and in peribulbar infiltrates in 44% of examined AA biopsies and concluded that eosinophilic infiltration in fibrous tracts and near hair bulbs is a helpful diagnostic feature of AA, especially when biopsy specimens lack the peribulbar lymphocytic infiltrate.

It was postulated that activated eosinophils may underlie an increased total serum IgE level in patients with eosinophilic pneumonia.[49] Further studies are required to confirm whether this is true for AA or not.

In the present study, there was insignificant difference in mean IgE levels among AA cases with different disease severities. This was in line with Kasumagić-Halilović and Prohić[14] and Zuel Fakkar *et al*.[23] However, contrary to our finding, Attia *et al*.[5] reported significant elevation of IgE in alopecia universalis than patchy AA and alopecia totalis. This conflict may be due to different proportions of severe and localized cases in the two studies.

In the present work, there was insignificant variation in mean IgE levels among AA cases with with different disease durations. This was at variance with the report of Zuel Fakkar *et al*.[23] and Attia *et al*.[5] who found a significant association between elevated IgE and long disease duration. Higher values were reported among patients having disease for more than one year. This controversy may be attributed to different clinical characteristics of studied cases in each study.

Insignificant differences in IgE levels among cases, regarding their ages and gender in our study were similar to the findings of Zuel Fakkar *et al*.[23]

In the current work, no correlation was detected between IgE values and lesional esinophilic count. Similar result was obtained by Zhao *et al*.[24] in their studied population of patchy AA.

In summary, IgE elevation in AA cases suggests a shift from a Th1 response in early AA to a more chronic Th2 immune profile, with secondary B-cell stimulation and possible IgE class switching. However, esinophilic infiltration and/or genetic factors may be also responsible for such elevation. Further studies on a larger scale and on different AA presentations are required for firmer conclusions.

REFERENCES

1. Kasumagić-Halilović E. Thyroid autoimmunity in patients with alopecia areata. Acta Dermatovenerol Croat 2008;16:123-5.
2. Gilhar A, Ullmann Y, Berkutzki T, Assy B, Kalish RS. Autoimmune hair loss (alopecia areata) transferred by T lymphocytes to human scalp explants on SCID mice. J Clin Invest 1998;101:62-7.
3. Carroll JM, McElwee KJ, E King L, Byrne MC, Sundberg JP. Gene array profiling and immunomodulation studies define a cell-mediated immune response underlying the pathogenesis of alopecia areata in a mouse model and humans. J Invest Dermatol 2002;119:392-402.
4. HogenEsch H, Torregrosa SE, Boggess D, Sundberg BA, Carroll J, Sundberg JP. Increased expression of type 2 cytokines in chronic proliferative dermatitis (cpdm) mutant mice and resolution of inflammation following treatment with IL-12. Eur J Immunol 2001;31:734-42.
5. Attia EA, El Shennawy D, Sefin A. Serum interleukin-4 and total immunoglobulin E in nonatopic alopecia areata patients and HLA-DRB1 typing. Dermatol Res Pract 2010;2010:503587.
6. Gurevitch AW, Heiner DC, Reisner RM. IgE in atopic dermatitis and other common dermatoses. Arch Dermatol 1973;107:712-5.
7. Sutton BJ, Gould HJ. The human IgE network. Nature 1993;366:421-8.
8. Park JH, Shin BC, Do BH, Oh JT, Lee JM, Kim SW, *et al*. Serum IgE levels in Korean patients with human immunodeficiency virus infection. Korean J Intern Med 2002;17:88-93.
9. Mikecz K, Sonkoly I, Mészáros C, Szegedi G. Serum IgE level in systemic lupus erythematosus. Acta Med Hung 1985;42:59-65.
10. Ovcina-Kurtovic N, Kasumagic-Halilovic E. Serum levels of total immunoglobulin E in patients with psoriasis: Relationship with clinical type of disease. Med Arh 2010;64:28-9.
11. Yssel H, Abbal C, Pène J, Bousquet J. The role of IgE in asthma. Clin Exp Allergy 1998;28:104-9.
12. Ledesma GN, York KK. Suppressor cell decrease in alopecia areata. Arch Dermatol Res 1982;274:1-8.
13. Wüthrich B, Grob PJ, Zisiadis S. Immunological study of alopecia areata. Hautarzt 1980;31:495-501.
14. Kasumagić-Halilović E, Prohić A. Serum levels of total immunoglobulin E in patients with alopecia areata: Relationship with clinical type of the disease. Acta Dermatovenerol Croat 2006;14:149-52.
15. Kavak A, Baykal C, Ozarmağan G, Akar U. HLA in alopecia areata. Int J Dermatol 2000;39:589-92.
16. Geha RS, Jabara HH, Brodeur SR. The regulation of immunoglobulin E class-switch recombination. Nat Rev Immunol 2003;3:721-32.
17. Gilhar A, Kalish RS. Alopecia areata: A tissue specific autoimmune disease of the hair follicle. Autoimmun Rev 2006;5:64-9.
18. Hoffmann R, Wenzel E, Huth A, van der Steen P, Schäufele M, Henninger HP, *et al*. Cytokine mRNA levels in alopecia areata before and after treatment with the contact allergen diphenylcyclopropenone. J Invest Dermatol 1994;103:530-3.
19. Teraki Y, Imanishi K, Shiohara T. Cytokines in alopecia areata: Contrasting cytokine profiles in localized form and extensive form (alopecia universalis). Acta Derm Venereol 1996;76:421-3.
20. Katagiri K, Arakawa S, Hatano Y. *In vivo* levels of IL-4, IL-10, TGF-beta1 and IFN-gamma mRNA of the peripheral blood mononuclear cells in patients with alopecia areata in comparison to those in patients with atopic dermatitis. Arch Dermatol Res 2007;298:397-401.
21. Przybilla B, Ring J, Völk M. Total IgE levels in the serum in dermatologic diseases. Hautarzt 1986;37:77-82.
22. O'Loughlin S, Diaz-Perez JL, Gleich GJ, Winkelmann RK. Serum IgE in dermatitis and dermatosis: An analysis of 497 cases. Arch Dermatol 1977;113:309-15.
23. Zuel Fakkar NM, Attia EA, Moussa MS. Evaluation of total serum immunoglobulin E in alopecia areata. Egypt Dermatol Online J 2010;6:1-9.

24. Zhao Y, Zhang B, Caulloo S, Chen X, Li Y, Zhang X. Diffuse alopecia areata is associated with intense inflammatory infiltration and CD8+ T cells in hair loss regions and an increase in serum IgE level. Indian J Dermatol Venereol Leprol 2012;78:709-14.
25. Bork J, Dallaire M, Lewis S, Boeck C, Hordinsky M. Childhood alopecia areata and atopy: A significant disease association. Am J Hum Genet 1995;57:619-28.
26. Tan E, Tay YK, Goh CL, Chin Giam Y. The pattern and profile of alopecia areata in Singapore – A study of 219 Asians. Int J Dermatol 2002;41:748-53.
27. Roselino AM, Almeida AM, Hippolito MA, Cerqueira BC, Maffei CM, Menezes JB, *et al*. Clinical-epidemiologic study of alopecia areata. Int J Dermatol 1996;35:181-4.
28. Whitmont KJ, Cooper AJ. PUVA treatment of alopecia areata totalis and universalis: A retrospective study. Australas J Dermatol 2003;44:106-9.
29. Arps V, Kölsch E. The role of interleukin-10 in the generation of CD4+ and CD8+ memory T cells (expressing a CD44+, CD62L-phenotype) and their contribution to the regulation of immunoglobulin E antibody formation. Int Arch Allergy Immunol 2002;127:198-207.
30. Deeths MJ, Endrizzi BT, Irvin ML, Steiner LP, Ericson ME, Hordinsky MK. Phenotypic analysis of T-cells in extensive alopecia areata scalp suggests partial tolerance. J Invest Dermatol 2006;126:366-73.
31. Gregoriou S, Papafragkaki D, Kontochristopoulos G, Rallis E, Kalogeromitros D, Rigopoulos D. Cytokines and other mediators in alopecia areata. Mediators Inflamm 2010;2010:928030.
32. Ansel J, Perry P, Brown J, Damm D, Phan T, Hart C, *et al*. Cytokine modulation of keratinocyte cytokines. J Invest Dermatol 1990;94:101S-107S.
33. Symington FW. Lymphotoxin, tumor necrosis factor, and gamma interferon are cytostatic for normal human keratinocytes. J Invest Dermatol 1989;92:798-805.
34. Altin J, Shen C, Liston A. Understanding the genetic regulation of IgE production. Blood Rev 2010;24:163-9.
35. Kuwano Y, Fujimoto M, Watanabe R, Ishiura N, Nakashima H, Ohno Y, *et al*. Serum BAFF and APRIL levels in patients with alopecia areata. J Dermatol Sci 2008;50:236-9.
36. Mackay F, Schneider P, Rennert P, Browning J. BAFF AND APRIL: A tutorial on B cell survival. Annu Rev Immunol 2003;21:231-64.
37. Mackay F, Leung H. The role of the BAFF/APRIL system on T cell function. Semin Immunol 2006;18:284-9.
38. Splawski JB, Fu SM, Lipsky PE. Immunoregulatory role of CD40 in human B cell differentiation. J Immunol 1993;150:1276-85.
39. Zhang L, Weetman AP, Friedmann PS, Oliveira DB. HLA associations with alopecia areata. Tissue Antigens 1991;38:89-91.
40. Sato-Kawamura M, Aiba S, Tagami H. Strong expression of CD40, CD54 and HLA-DR antigen and lack of evidence for direct cellular cytotoxicity are unique immunohistopathological features in alopecia areata. Arch Dermatol Res 2003;294:536-43.
41. Cookson W. Genetics and genomics of asthma and allergic diseases. Immunol Rev 2002;190:195-206.
42. Kaur S, Sharma VK, Kumar L, Kumar B. Atopy and alopecia areata in North Indians. Indian J Dermatol Venereol Leprol 2002;68:267-9.
43. Shellow WV, Edwards JE, Koo JY. Profile of alopecia areata: A questionnaire analysis of patient and family. Int J Dermatol 1992;31:186-9.
44. Young RP, Sharp PA, Lynch JR, Faux JA, Lathrop GM, Cookson WO, *et al*. Confirmation of genetic linkage between atopic IgE responses and chromosome 11q13. J Med Genet 1992;29:236-8.
45. Cox HE, Moffatt MF, Faux JA, Walley AJ, Coleman R, Trembath RC, *et al*. Association of atopic dermatitis to the beta subunit of the high affinity immunoglobulin E receptor. Br J Dermatol 1998;138:182-7.
46. Galbraith GM, Pandey JP. Km1 allotype association with one subgroup of alopecia areata. Am J Hum Genet 1989;44:426-8.
47. Elston DM, McCollough ML, Bergfeld WF, Liranzo MO, Heibel M. Eosinophils in fibrous tracts and near hair bulbs: A helpful diagnostic feature of alopecia areata. J Am Acad Dermatol 1997;37:101-6.
48. Peckham SJ, Sloan SB, Elston DM. Histologic features of alopecia areata other than peribulbar lymphocytic infiltrates. J Am Acad Dermatol 2011;65:615-20.
49. Hattori T, Hizawa N, Takahashi D, Isada A, Takahashi A, Maeda Y, *et al*. Total serum IgE levels in eosinophilic lung diseases. Arerugi 2006;55:647-54.

Cite this article as: Bakry OA, El Shazly RA, Basha MA, Mostafa H. Total serum immunoglobulin E in patients with alopecia areata. Indian Dermatol Online J 2014;5:122-7.

Source of Support: Nil, **Conflict of Interest:** None declared.