Original article

The Association of Allergy and Systemic Lupus Erythematosus as a Single Disease and an Overlapping Syndrome compared to Control Group

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Abstract

Background: Allergic diseases and systemic lupus erythematosus (SLE) sometimes are being connected since both of these diseases are affected by gene-environment processes. SLE can appear coexisting with other autoimmune diseases as an overlapping syndrome. ***Objectives:*** This research was done to investigate the relation of allergic diseases and SLE as a single SLE or overlapping syndrome compared to control. ***Method:*** We collected data from 39 SLE only, 22 overlapping syndrome SLE, and 39 non SLE subjects who had filled an online Score for Allergic Rhinitis (SFAR) questionnaire. ***Results:*** There are significant outcomes of the existence of allergic disease (p=.007), atopic dermatitis (p=.000) and total number of allergies (p=.016) in SLE patients. There is a correlation of the appearance of allergy in SLE as a single or coexisting with other autoimmune disease compared to control group. ***Conclusion:*** Atopic dermatitis and the more number of allergic diseases that the one have, play role in appearing SLE.

Keywords: Allergic disease; systemic lupus erythemathosus; atopic dermatitis

Bangladesh Journal of Medical Science Vol. 22 No. 04 October'23 Page : 916-919
DOI: https://doi.org/10.3329/bjms.v22i4.68680

Introduction:

Allergic diseases are commonly found in the population. This condition is provoked by allergens and appears as recurrent, non-infectious and inflammatory disorder[1]. Some of the allergy presentations are atopic dermatitis, allergic rhinitis, asthma, drug/food allergy, and urticaria[2]. Meanwhile, systemic lupus erythematosus (SLE) is an autoimmune condition triggered by the role of genetic and environmental factors[1]. This disease can appear coexisting with other autoimmune diseases such as Sjögren Syndrome and Rheumatoid Arthritis as an overlapping syndrome. Based on their pathophysiology that is related by gene-environmental process, both allergic diseases and SLE are sometimes being connected[1].

Immune dysregulation with the activation of B cells that leads to the production of immunoglobulins and autoantibodies acts in the development of SLE and allergic diseases[1]. The amplification of autoreactive B cells triggering to high affinity autoantibodies and T cells activation that is a typical condition found in autoimmune diseases such as SLE[2].

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Latest studies report there is a significant association between allergy and SLE. The adjusted incidence rate ratios (aIRRs) of SLE were higher in allergic rhinitis/conjunctivitis (ARC), atopic eczema, and asthma compared to control group in a research performed by Krishna et.al[3]. Study by Hsiao et.al revealed that subjects with atopic dermatitis (OR = 2.13, 95% CI: 1.67–2.70), followed by allergic conjunctivitis and allergic rhinitis (OR = 1.43, 95% CI: 1.26–1.61 and (OR = 1.36, 95% CI: 1.19–1.55) are the most susceptible to develop SLE[4]. Sequeira et.al discovered that drug, skin, and insect allergies were frequently seen in SLE patients and mostly have at least one allergy[5].

Therefore, the relation of SLE with or without overlapping syndrome and allergy is often being studied. This research was done to investigate the relation of allergic diseases and SLE based on its appearance as a single SLE or with other autoimmune diseases compared to non SLE subjects.

Study design:

A retrospective study was done from October 2021 until September 2022. We collected data from 61 Tittari SLE Community members (39 SLE only and 22 overlapping syndrome SLE) and 39 non SLE subjects who had filled an online Score for Allergic Rhinitis (SFAR) questionnaire[6]. The SLE participants who were included in this study were all females and had been diagnosed with SLE previously based on ACR 2019. We excluded subjects with incomplete response to the questionnaire. Before the data were collected, participants had initially filled the informed consents.

Statistical analysis

The results were analysed using SPSS Statistics version 25 by performing Chi Square test to process comparative data between groups. To compare the number of allergic diseases among groups, we performed one way ANOVA test. Then, correlation test was processed using Spearman Rank Correlation Test, the outcomes were significant if $p<0.05$.

Ethical clearance

This research had been ethically accepted by the Research Ethics Committee of Dr. Moewardi General Hospital, Surakarta, Indonesia (No. 372/IV/HREC/2021).

Results:

Table 1 shows significant outcomes of the appearance of allergic disease (p=.007), atopic dermatitis (p=.000) and total number of allergies (p=.016) in SLE-only patients and overlapping syndrome SLE compared to non SLE subjects. There are no significant results for allergic rhinitis and asthma. The occurrence of allergic disease, atopic dermatitis, and total number of allergies in SLE groups are correlated as a one-tailed and two-tailed association (p=.007, p=.014, p=.00 and p=.00, p=.005, p=.010, respectively) that can be seen in Table 2.

Discussion:

The ethiologies of allergy and SLE are various, including genes and environmental factors[1]. Several studies stated significant relationship between SLE and allergy. Krishna et.al found the adjusted incidence rate ratios (aIRRs) of SLE were higher in allergic rhinitis/conjunctivitis (ARC), atopic eczema, and asthma compared to control group[3]. Research by Hsiao et.al revealed that subjects with atopic dermatitis (OR = 2.13, 95% CI: 1.67–2.70), followed by allergic conjunctivitis and allergic rhinitis (OR = 1.43, 95% CI: 1.26–1.61 and (OR = 1.36, 95% CI: 1.19–1.55) are most likely to have risk to develop SLE[3]. Study by Sequeira et.al discovered that drug, skin, and insect allergies were frequently seen in SLE patients and mostly have at least one allergy[5].

Our study found that there are significant correlation of the appearance of allergic diseases, atopic dermatitis, and total number of allergies (p=.007; p=.00; and p=.016) in SLE patients both in SLE and overlapping syndrome compared to the control group. Allergic diseases such as allergic rhinitis, atopic dermatitis, asthma, food allergy, drug allergy, and urticaria were observed in our subjects. The most frequent type of allergy we found to be related to SLE was atopic dermatitis. The more number of allergies that a person have, significantly related to the development of SLE. Therefore, our results supported the previous researches.

Dysregulation of immunity and increased mediators of inflammation are commonly found in allergy and autoimmune disease. IgE is having a role in autoimmune disease by stimulating both type 1 (Th1) and type 2 (Th2) helper T cells and leading to persistent inflammation and autoantibody generation. IgE is also having a main feature in allergy mechanism. Since allergy and SLE may have similar pathogenesis, the appearance of allergy and SLE is

Table 1. Comparative Analyses Results

Variables	Category	Cases (n%)		Controls (n%)	Total (n%)	P
Allergic disease	Non SLE	17 (43,5)		22 (56,5)	39 (100)	**.007**
	SLE only	25 (86,2)		4 (13,8)	29 (100)	
	SLE with other autoimmune	12 (70,5)		5 (29,5)	17 (100)	
Atopic Dermatitis	Non SLE	9 (23,1)		30 (76,9)	39 (100)	**.000**
	SLE only	23 (79,3)		6 (20,7)	29 (100)	
	SLE with other autoimmune	11 (64,7)		6 (35,2)	17 (100)	
Allergic Rhinitis	Non SLE	13 (33,3)		26 (66,6)	39 (100)	.502
	SLE only	10 (34,4)		19 (65,6)	29 (100)	
	SLE with other autoimmune	8 (47)		9 (53)	17 (100)	
Asthma	Non SLE	5 (12,8)		34 (87,2)	39 (100)	.460
	SLE only	6 (20,7)		23 (79,3)	29 (100)	
	SLE with other autoimmune	5 (29,4)		12 (70,6)	17 (100)	
Total number of allergic disease		No allergy	1 allergy	2 or more allergies		**.016**
	Non SLE	22 (56,5)	9 (23)	8 (20,5)	39 (100)	
	SLE only	18 (62)	11 (37)	0	29 (100)	
	SLE with other autoimmune	8 (47)	9 (53)	0	17 (100)	

Note: CI = confidence interval; NA = not available; AR = allergic rhinitis; AD = atopic dermatitis.

Table 2. Spearman's Correlation Test Results

Clinical Manifestation				
	One tailed		*Two tailed*	
	Spearman's r	P-value	Spearman's r	P-value
Allergic diseases	.246	.007	.246	.014
Atopic dermatitis	.366	.000	.366	.000
Allergic Rhinitis	.074	.231	.074	.462
Asthma	.113	.132	.113	.265
Total number of allergic disease	.257	.005	.257	.010

Note: CI = confidence interval; NA = not available; AR = allergic rhinitis; AD = atopic dermatitis.

probable to develop both diseases[7].

Our research showed that there was a correlation between atopic dermatitis and SLE as a single or coexisting with other autoimmune. Atopic dermatitis and SLE appeared to have increasing Th2 and Th17 cytokines, meanwhile decreasing Th1. In SLE patients with active disease, increased level of IgE was found, similar to allergic patients. As a result, it is probable that increased level Th2 and IgE production seen in atopic dermatitis could lead to autoimmunity, such as SLE with or without any other autoimmune disease[8].

Confino-Cohen et al found that individuals with atopic dermatitis had a higher risk of SLE, and the high incidence of autoantibodies suggested a pathogenic mechanism that could be autoimmune in nature[9]. IgE autoantibodies against proteins from keratinocytes and endothelial cells were found in 25% of atopic dermatitis subjects in Hsiao et.al study[4]. Autoreactivity was found based on the mechanisms of chronic relapsing remitting pattern of atopic dermatitis and the immediate hypersensitive reaction

elicited by autologous and human components. The number of atopic dermatitis and asthma is higher in childhood and decreased in adulthood, in the other hand, SLE has its peak coincidence in adulthood and minimum number in child age. This may indicate that children with allergy can develop autoimmunity in the future[10,11].

The limitations of our study are we did not measure the disease activity of SLE and patient's allergic status was only investigated from the questionnaire, therefore some confounding factors could not be fully ignored.

Conclusion:

There is a significant relation of allergy in SLE as a single or coexisting with other autoimmune disease compared to the control. Atopic dermatitis and the more number of allergic diseases that the one have, play role in appearing this autoimmune disease. Further study observing the relation of SLE based on its disease activity and allergy with advanced diagnosis is suggested.

Source of fund (if any)

This study was not supported with any fundings.

Conflict of interest

Authors stated there is no conflict of interest exist.

Authors' contribution

KP performed the study, analysed the datas, and wrote the manuscript. YW, DP, and ND conceived the idea and supervised the research. AM contributed in the data collection and manuscript.

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