



Erken Çocukluk Döneminde Alerji ve Antinükleer Antikorlar Birlikteliği

Coexistence of Allergy and Antinuclear Antibody in Early Childhood

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ABSTRACT

Background: Allergy and autoantibody production are two abnormal conditions of the immune system, resulting from hypersensitivity. It remains unclear whether autoantibodies are also present in association with allergies that begin during early childhood. This study aims to evaluate the presence of antinuclear antibodies (ANA) in allergic children under the age of three. Methods: Allergic children (age < 3 years; n=40) were diagnosed by a specialist based on clinical and laboratory findings. ANA levels were measured using a commercial ELISA test. Demographic data, total and specific (egg, milk) IgE levels, and blood eosinophil percentages were obtained from hospital records. The control group (age 30.5 ± 2.9; n = 40) consisted of healthy individuals without any history of allergy. Results: In the healthy control group, 8 individuals (8/40, 20%) were ANA positive, while 17 allergic children (17/40, 42.5%) tested positive for ANA (p<0.05). ANA positivity was observed in 8 children with an egg allergy, 2 children with a milk allergy, 4 children with both egg and milk allergies, and 3 children with an unknown allergy cause. No significant correlation was found between ANA positivity, IgE levels, and eosinophil percentages (p>0.05). Additionally, no relationship was found between ANA levels and the presence of itching or eczema in allergic children. Conclusions: This study suggests that the relationship between allergies and ANA positivity begins in early childhood and recommends that future studies on the potential interactions of these two conditions should focus on this critical period. Additionally, further research is needed to determine whether both immune anomalies are regulated by similar mechanisms.

Key words: Allergy, Autoantibody, ANA, Children.

ÖZ

Amaç: Alerji ve otoantikor üretimi, aşırı duyarlılık nedeniyle ortaya çıkan bağışıklık sistemi ile ilgili iki anormal durumdur. Erken çocukluk döneminde başlayan alerjilerle otoantikorların ilişkilendirilip ilişkilendirilemeyeceği henüz netlik kazanamamıştır. Bu çalışma, üç yaş altındaki alerjik çocuklarda antinükleer antikorların (ANA) varlığını değerlendirmeyi amaçlamaktadır. Gereç ve yöntem: Alerjik çocuklar (yaş < 3 yıl; n=40), klinik ve laboratuvar bulgularına dayanarak bir uzman tarafından teşhis edilmiştir. ANA düzeyleri, ticari bir ELISA testi ile ölçülmüştür. Demografik veriler, toplam ve spesifik (yumurta, süt) IgE düzeyleri ile kan eozinofil yüzdeleri hastane kayıtlarından elde edilmiştir. Kontrol grubu (yaş 30.5 ± 2.9; n=40), alerjisi olmayan sağlıklı bireylerden oluşturulmuştur. Bulgular: Sağlıklı kontrol grubunda 8 birey (8/40, %20) ANA pozitif çıkarken, 17 alerjik çocuk (17/40, %42.5) ANA pozitif bulunmuştur (p<0.05). ANA pozitifliği, yumurta alerjisi olan 8 çocukta, süt alerjisi olan 2 çocukta, hem yumurta hem de süt alerjisi olan 4 çocukta ve nedeni bilinmeyen alerjisi olan 3 çocukta gözlemlenmiştir. ANA pozitifliği ile IgE düzeyleri ve eozinofil yüzdeleri arasında anlamlı bir ilişki bulunmamıştır (p>0.05). Ayrıca, alerjik çocuklarda ANA düzeyleri ile kaşıntı veya egzama varlığı arasında bir ilişki tespit edilmemiştir. Sonuç: Bu çalışma, alerji ile ANA pozitifliği arasındaki ilişkinin erken çocukluk döneminde başladığını göstermekte ve bu iki durumun potansiyel etkileşimleri üzerine yapılacak gelecekteki araştırmaların bu kritik dönemde odaklanması gerektiğini önermektedir. Ayrıca, her iki bağışıklık anomalisinin benzer mekanizmalarla düzenlenip düzenlenmediğinin belirlenmesi amacıyla daha fazla araştırma yapılması gerektiği sonucuna varılmaktadır.

Anahtar kelimeler: Alerji, Otoantikor, ANA, Çocuklar

INTRODUCTION

Allergic diseases arise as a result of an abnormal immune response and affect approximately one in every three children worldwide (1). This high prevalence significantly impacts the quality of life for affected children. Associated issues, such as itching, insomnia, and social exclusion, often lead to psychological and social challenges (2,3). Moreover, the time and patience required to manage these conditions also place a burden on families (4). Factors such as dietary restrictions, increased financial burdens, and lifestyle adjustments further strain familial dynamics. Additionally, the unexpectedly high prevalence of allergies in children places considerable pressure on healthcare systems. A study examining the economic impact of childhood food allergies in the United States estimated the total annual cost to be \$24.8 billion (approximately €4,184 per year per child) (5). Furthermore, families incurred indirect costs totaling \$20.5 billion (5).

Autoantibody formation is another example of an abnormal immune response. These autoantibodies target self-antigens, leading to widespread tissue damage and severe complications, including life-threatening blood clots, tissue damage in organs such as the brain and heart, impaired immune system function, and interstitial lung disease (6-8). Among the various types of autoantibodies, antinuclear antibodies (ANA) are the most commonly observed (9). ANA is thought to enter cells and target structures such as the nucleus, DNA, RNA, and centromeres, potentially disrupting cellular function and structure, causing cell death, activating inflammatory responses, and impairing tissue function. ANA plays a significant role in the development of autoimmune diseases, affecting approximately 400 million people globally and contributing to 0.2% of worldwide mortality (10). The rising prevalence of ANA, even among healthy individuals, has raised concerns and underscored the need for a better understanding of the mechanisms behind ANA formation (11).

Both allergies and ANA represent manifestations of an overactive immune response. Although these two conditions may appear distinct, the boundary between them is not clearly defined. Evidence suggests that ANA may coexist with certain allergic conditions (12,13). This co-occurrence may arise from an underlying immune dysregulation that compromises tolerance to both food allergens and self-antigens, though the specific mechanisms remain unclear (14). While existing literature explores the coexistence of these conditions in adults, there is insufficient information regarding the onset of this relationship in early childhood. In particular, it remains unclear whether childhood allergies trigger ANA production. Therefore, the aim of this research is to investigate the coexistence of ANA in children with allergies during early childhood.

MATERIAL and METHOD

Ethical approval for the study was obtained from the Scientific Research and Publication Ethics Committee of İnönü University (protocol no 2023/4721). The study was conducted retrospectively using serum samples from 40 allergic children aged 2 to 32 months (16 female, 24 male). Data regarding demographic information, total IgE levels, allergens, and eosinophil percentages were extracted from hospital records. The control group consisted of healthy individuals without any allergy-related complaints (age 30.5 ± 2.9 ; n = 40, 16 female, 24 male).

Determination of ANA Positivity

ANA were measured using a commercial ELISA test kit (Y ImmunoTek, Türkiye). The procedures were carried out according to the manufacturer's protocol. Serum samples were diluted 1:100 and added to the wells along with negative and positive controls. Subsequently, anti-human IgG conjugated with biotin and streptavidin peroxidase were added sequentially. The plates were washed three times with 0.05% Tween-20 before each solution was added. Finally, a chromogenic substrate (tetramethylbenzidine, TMB) was added, and the reaction was stopped with 11% H₂SO₄. The optical density (OD) of the plates was measured at 450 nm using a spectrophotometer.

Calculation of ANA Results

The cut-off value was determined using the cut-off control, as described in the protocol. It was calculated using the formula: average OD of negative controls + 3 standard deviations (SD). The sample OD values were converted to an antibody index (Ab index) using the formula: Ab index = Sample OD / Cut-off OD. Values <1.0 were classified as ANA IgG negative, while values >1.0 were classified as ANA IgG positive. The test was deemed valid if the Ab index of the positive control was >1.1 and the negative control was <0.9.

Statistical Analysis of Data

The normality of the data was assessed using the Shapiro-Wilk test. For correlation analysis, either Pearson or Spearman correlation coefficients were employed, depending on whether the data were parametric (Pearson) or non-parametric (Spearman). In the comparison between the allergic and control groups, a chi-square test was applied to compare the percentage of positivity between the groups.

RESULTS

Demographic Information of the Participants

The demographic characteristics of the allergic children are presented in Table 1, along with their ANA results. The ages of the children ranged from 2 to 32 months, with females constituting 40% of the sample. Seventeen children had an egg allergy, five had a milk allergy, nine had allergies to both egg and milk, and the allergen was unknown in nine cases. Symptoms such as itching, redness, and eczema were observed in 24 children (60%), while 16 children (40%) did not exhibit these symptoms. The total IgE levels were 112 ± 200 kU/L (ranging from 1.1 to 700 kU/L), and the eosinophil percentages averaged $5.3\% \pm 4.4\%$ (ranging from 0.1% to 18%).

Table 1. Demographic and Clinical Characteristics of Allergic Infants and Corresponding ANA Results

Part. no.	Age (month)	Sex	Total IgE (kU/L)	Eozonophil (%)	Itchy skin rash and eczema	Allergen	ANA result
1	4	F	17.4	6.8	Yes	Milk	Negative
2	14	M	32.2	1.8	Yes	Egg	Negative
3	4	M	12.9	4	Yes	Unknown	Negative
4	32	M	246	9	Yes	Egg	Negative
5	12	F	3.2	9	Yes	Unknown	Negative
6	2	F	0.1	6.9	Yes	Unknown	Negative
7	10	F	20.8	8.1	No	Egg	Negative
8	11	M	37.3	N/A	No	Egg	Negative
9	22	M	9.7	2.1	Yes	Egg	Negative
10	9	F	105	8.8	Yes	Egg	Negative
11	17	M	27	1.8	Yes	Egg, Milk	Negative
12	12	M	566	1	Yes	Egg, Milk	Negative
13	5	M	9.3	1	Yes	Unknown	Negative
14	3	M	1.9	2.5	No	Milk	Negative
15	10	F	210	N/A	No	Unknown	Negative
16	12	M	20.4	N/A	No	Unknown	Negative
17	10	F	1429	9.1	No	Egg	Negative
18	9	F	42.1	0.3	Yes	Egg	Negative
19	5	F	2.5	4.3	Yes	Milk	Negative
20	2	M	4.5	7.1	Yes	Egg, Milk	Negative
21	12	M	11.2	6.4	Yes	Egg, Milk	Negative
22	9	F	101	2.8	Yes	Egg, Milk	Negative
23	11	M	1.1	3.6	Yes	Egg	Negative
24	12	M	23.9	2.5	Yes	Egg, Milk	Positive

25	11	M	663	5.1	No	Egg	Positive
26	12	F	92.8	1	No	Milk	Positive
27	12	F	708	2.1	Yes	Egg, Milk	Positive
28	22	F		N/A	No	Egg, Milk	Positive
29	12	M	30.8	5	Yes	Egg	Positive
30	5	M	39.8	18	Yes	Egg	Positive
31	12	M	57.9	N/A	No	Egg	Positive
32	9	M	44.2	3.2	Yes	Unknown	Positive
33	11	M		N/A	No	Unknown	Positive
34	9	M	38.2	11.5	No	Egg	Positive
35	12	F	1.4	0.1	No	Egg	Positive
36	25	M		2.4	No	Unknown	Positive
37	10	F	4.1	1	No	Egg	Positive
38	3	F	1.6	10.3	Yes	Milk	Positive
39	12	M		16.2	No	Egg	Positive
40	10	M	607	N/A	Yes	Egg, Milk	Positive

ANA Positivity in Healthy Controls and Allergic Children

Among the 40 healthy individuals, 8 (8/40, 20%) exhibited a positive ANA level (mean index: 0.82 ± 0.36 ; range: 0.39 to 2.51). In contrast, among the allergic children, the ANA test was positive in 17 children (17/40, 42.5%) (mean index: 1.10 ± 0.71 ; range: 0.46 to 4.10) (Fig. 1). The prevalence of ANA positivity in allergic children was significantly higher than that in healthy controls ($p = 0.035$).

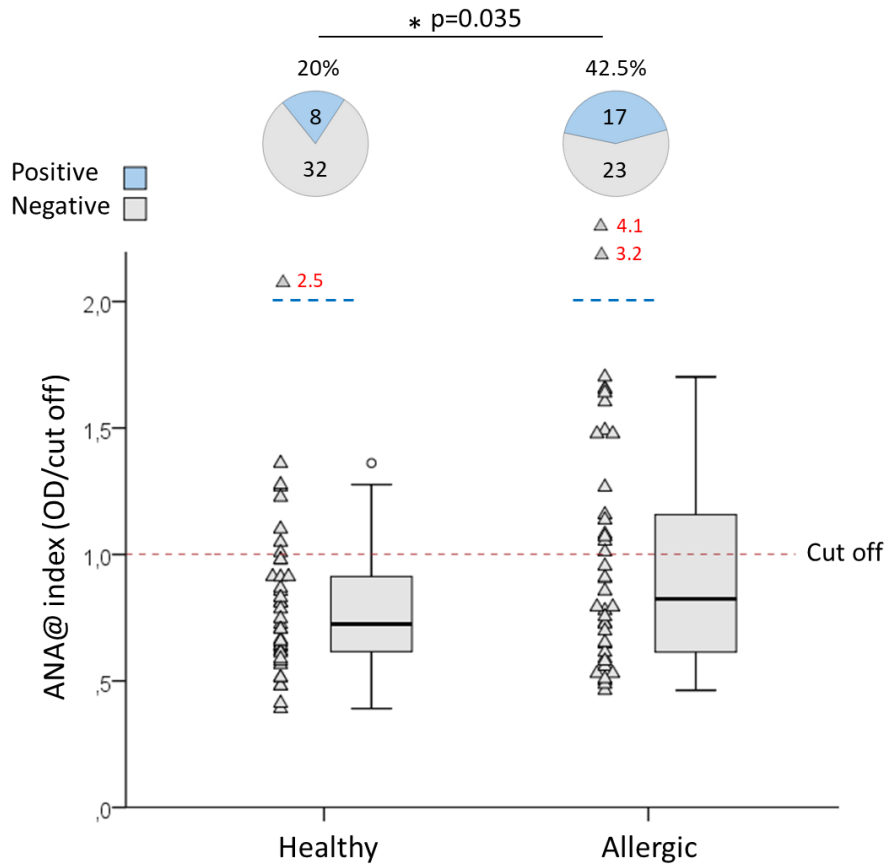


Figure 1. Distribution of ANA positivity and negativity rates in healthy controls and allergic children

Total IgE Levels and Eosinophil Percentages in ANA Positive and Negative Groups

No significant differences were found in total IgE levels (Fig 2A) or eosinophil percentages (Fig 2B) between the ANA positive and ANA negative groups ($p>0.05$).

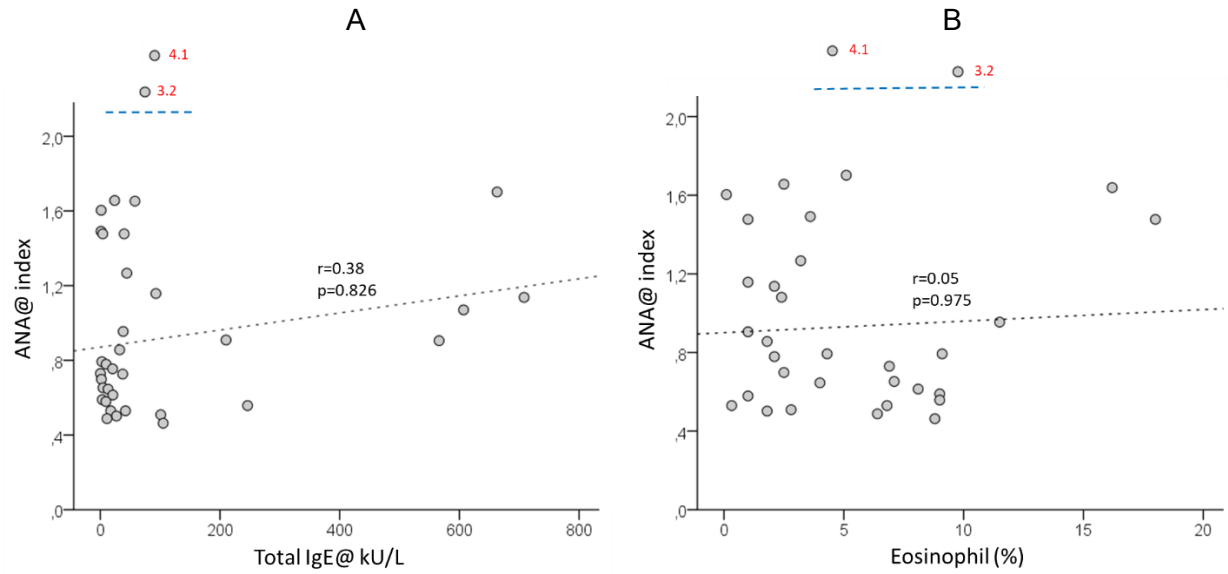


Figure 2. Evaluation of total IgE levels and eosinophil percentages in ANA positive and negative groups (A: comparison of total ige levels and ANA index B: comparison of eosinophil percentages and ANA index)

The Relationship Between the ANA Levels and Itching and Eczema

Allergic children were divided into two groups: those with itching and eczema, and those without. The ANA levels of both groups were compared, and no significant difference was found ($p=0.051$) (Fig 3)

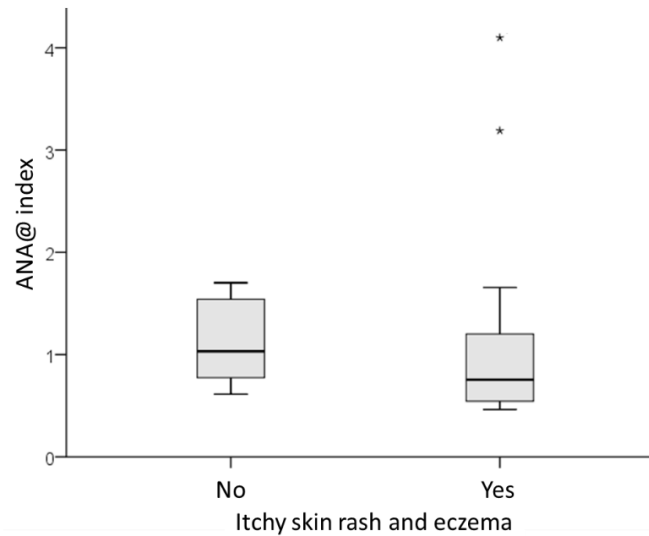


Figure 3. Comparison of ANA levels between allergic children with and without itching and eczema

DISCUSSION and CONCLUSION

The present study examining the interaction between allergies and ANA observed a relatively high prevalence of ANA positivity in allergic children under three years of age. The coexistence of these two conditions may suggest potential common pathways that could contribute to the development of both ANA and allergies. A review of the literature revealed a limited number of studies addressing the coexistence of food allergies and autoantibodies in children. However, several studies in adults have proposed hypotheses linking these conditions, which may involve genetic predisposition, inflammation, and the homology of food proteins with human tissue antigens (15,16). Although the control group consisted of healthy adults, this is not considered a major limitation, as previous studies have shown that ANA positivity rates are similar in healthy adults and healthy children (17,18).

Genetic Factors and Molecular Mimicry in the Coexistence of Allergies and ANA

This study provides early evidence that the coexistence of food allergies and ANA may begin in early childhood, which could indicate that similar genetic factors might contribute to the development of both conditions. Kreiner et al (19). reported that 48% of genetic loci associated with autoimmune diseases also correlated with allergies. Moreover, variants in genes regulating T cell function might influence both allergy and ANA formation by affecting immune cell activity and cytokine production (20). Gonzalez et al. investigated the FOXP3 gene, which is essential for regulatory T cell function, in a cohort of 255 children, finding that mutations in the FOXP3 gene were more prevalent among children with both allergic and autoimmune diseases (21). A meta-analysis has shown that the incidence of allergy and autoimmunity is higher in individuals with these conditions compared to healthy controls (22). Additionally, a study on the coexistence of ANA and asthma in adults found an ANA positivity rate of 22% among asthma patients (23). The current study's findings indicate that the coexistence of allergies and ANA begins in childhood; however, further research is needed to confirm whether this coexistence persists into adulthood.

Role of Inflammation in the Coexistence of Allergies and Autoantibody Formation

Inflammation may also play a significant role in the coexistence of allergies and autoantibody formation. Excessive secretion of inflammatory mediators by mast cells has been linked to both allergic and autoimmune conditions (20). Pro-inflammatory cytokines released during allergic reactions have been associated with autoimmune diseases (24). Inflammation can lead to hypersensitivity of the immune system, promoting the production of antibodies against self-antigens (25). While our study did not measure inflammatory cytokines directly, we assessed total IgE levels and eosinophil counts (26,27). Our results did not indicate a direct relationship between ANA positivity and IgE or eosinophil levels, suggesting that other inflammatory mediators might be involved in ANA formation.

Molecular Mimicry and Autoantibody Formation

Molecular mimicry between food allergens and human tissue could also contribute to autoantibody formation. Common childhood food allergens, such as cow's milk and eggs, are believed to share molecular similarities with human tissues (10). Thus, antibodies generated against food allergens like milk and eggs may inadvertently stimulate autoantibody production in allergic individuals. Krishma et al. conducted a large-scale study and found that the incidence of autoimmune diseases was higher in allergic individuals compared to healthy controls (22). Vojdani et al. demonstrated that milk-specific antibodies could cross-react with neural structures, potentially triggering neuroimmune responses (28). Additionally, a study found molecular similarities between egg proteins and Langerhans islet cell proteins, suggesting that egg consumption could be linked to the development of type 1 diabetes (29). These findings support the notion that allergies and autoantibodies may interact more strongly during early childhood, warranting further investigation into the underlying mechanisms of this coexistence.

The present study revealed an incidence of ANA positivity of 42.5% in a cohort of 40 allergic infants, suggesting that the mechanisms underlying allergies may also be linked to autoantibody production. Although early childhood is a critical period for the development of immunological diseases, there is surprisingly limited information available regarding the interplay between these two conditions. Given the significant burden associated with both allergies and autoantibody-related diseases, this study highlights the urgent need for further research to elucidate the mechanisms that lead to the development of allergies and autoantibody formation in early life.

Limitations of the Study

The observation of the coexistence of allergy and ANA in children under the age of three provides important evidence suggesting that this relationship begins in early childhood. Despite the small sample size (n=40), significant data have been obtained that provide valuable insights into this topic. Although the control group consisted of healthy adults, this did not substantially limit the comparison, as the prevalence of ANA positivity is known to be similar in healthy adults and healthy infants.

Ethical Approval: Ethical approval for the study was obtained from the Scientific Research and Publication Ethics Committee of İnönü University (protocol no. 2023/4721).

Conflict of Interest: The authors declare that there is no conflict of interest to disclose.

Author Contributions: Concept: FD, Design: FD, YY, EY, YD, Supervision: SY, Resources: FD, SY

Materials: EY, YD, Data Collection and Processing: YY, EY, YD, Analysis and Interpretation: FD, SY, Literature Review: FD, YY, SY, Writing: FD, Review: SY

Financial Support: The authors declare that the study received no funding.

REFERENCES

1. Chad Z. Allergies in children. PCH. 2001;6(8):555-66. <http://dx.doi.org/10.4038/sljch.v46i4.8386>
2. Ridolo E, Caffarelli C, Olivieri E, et al. Quality of sleep in allergic children and their parents. Allergol. Immunopathol. 2015;43(2):180-4. <https://doi.org/10.1016/j.aller.2014.01.004>
3. Jarosz M, Syed S, Blachut M, Badura Brzoza K. Emotional distress and quality of life in allergic diseases. Wiad Lek. 2020;73(2):370-3. doi: 10.36740/WLek20200213
4. Antolín-Amérigo D, Manso L, Caminati M, et al. Quality of life in patients with food allergy. Clin. Mol. Allergy. 2016;14:1-10. <https://doi.org/10.1186/s12948-016-0041-4>
5. Gupta R, Holdford D, Bilaver L, Dyer A, Holl JL, Meltzer D. The economic impact of childhood food allergy in the United States. JAMA pediatrics. 2013;167(11):1026-31. doi:10.1001/jamapediatrics.2013.2376
6. Taha M., Samavati L. Antiphospholipid antibodies in COVID-19: a meta-analysis and systematic review. RMD open, 2021; 7(2), e001580. <https://doi.org/10.1136/rmdopen-2021-001580>
7. Goncalves D, Mezidi M, Bastard P, et al. Antibodies against type I interferon: detection and association with severe clinical outcome in COVID-19 patients. CTI, 2021 10(8), e1327. <https://doi.org/10.1002/cti2.1327>
8. Fagyas M, Nagy Jr B, Ráduly A.P., Mányiné I. S., et al. The majority of severe COVID-19 patients develop anti-cardiac autoantibodies. Geroscience, 2022; 44(5):2347-2360. <https://doi.org/10.1007/s11357-022-00649-6>
9. Pascolini S, Vannini A, Deleonardi G, et al. COVID-19 and immunological dysregulation: can autoantibodies be useful? CTI. 2021;14(2):502-8. <https://doi.org/10.1111/cts.12908>
10. Mitratza M, Klijs B, Hak A.E, Kardaun J.W., Kunst, A.E. Systemic autoimmune disease as a cause of death: mortality burden and comorbidities. Rheumatology, 2021;60(3), 1321-1330. <https://doi.org/10.1093/rheumatology/keaa537>
11. Dinse G.E., Parks C.G., Weinberg C.R. et al. Increasing prevalence of antinuclear antibodies in the United States. A&R. 2020; 72(6):1026. doi: 10.1002/art.41214
12. Grygiel-Górniak B, Rogacka N, Rogacki M, Puszczewicz M. Antinuclear antibodies in autoimmune and allergic diseases. Reumatologia. 2017;55(6):298-304. <https://doi.org/10.5114/reum.2017.72627>
13. Maurer M, Altrichter S, Schmetzer O, Scheffel J, Church MK, Metz M. Immunoglobulin E-mediated autoimmunity. Front. immunol. 2018;9:359991. <https://doi.org/10.3389/fimmu.2018.00689>
14. Vojdani A, Gushgari LR, Vojdani E. Interaction between food antigens and the immune system: Association with autoimmune disorders. Autoimmun. Rev. 2020;19(3):102459. <https://doi.org/10.1016/j.autrev.2020.102459>

15. Valenta R, Mittermann I, Werfel T, Garn H, Renz H. Linking allergy to autoimmune disease. *Trends Immunol.* 2009;30(3):109-16. doi: 10.1016/j.it.2008.12.004
16. Charles N, Rivera J. Basophils and IgE: Linking the Allergic Environment to Autoimmunity. *The Open Allergy Journal.* 2010;3(1). doi: 10.2174/1874838401003010081
17. Wananukul S, Voramethkul W, Kaewopas Y, et al. Prevalence of positive antinuclear antibodies in healthy children. *Asian Pac J Allergy Immunol.* 2005;23(2-3):153-7. doi: 10.1177/101053950502300306
18. Sperotto F, Brachi S, Seguso M, et al. Prevalence of antinuclear antibodies in a general pediatric cohort from the Veneto region. *Pediatric Rheumatology.* 2013;11(Suppl 2):P18. doi: 10.1186/1546-0096-11-S2-P18
19. Kreiner E, Waage J, Standl M, et al. Shared genetic variants suggest common pathways in allergy and autoimmune diseases. *J Allergy Clin Immunol.* 2017;140(3):771-81. <https://doi.org/10.1016/j.jaci.2016.10.055>
20. Rottem M, Gershwin ME, Shoenfeld Y. Allergic disease and autoimmune effectors pathways. *J. Immunol. Res.* 2002;9:161-7. <https://doi.org/10.1080/1044667031000137638>
21. Pacheco-Gonzalez R, Avila C, Dávila I, et al. Analysis of FOXP3 gene in children with allergy and autoimmune diseases. *Allergol Immunopath.* 2016;44(1):32-40. <https://doi.org/10.1016/j.aller.2015.01.012>
22. Krishna MT, Subramanian A, Adderley NJ, Zemedikun DT, Gkoutos GV, Nirantharakumar K. Allergic diseases and long-term risk of autoimmune disorders: longitudinal cohort study and cluster analysis. *Eur. Respir. J.* 2019;54(5).
23. Agache I, Duca L, Anghel M, Pamfil G. Antinuclear antibodies in asthma patients- a special asthma phenotype? *IJAAI.* 2009;8(1):49-52.
24. Valenta R, Mittermann I, Werfel T. et al. Linking allergy to autoimmune disease. *Trends Immunol.* 2009; 30(3):109-116. doi: 10.1016/j.it.2008.12.004
25. Abbas AK, Lichtman AH, Pillai S. *Basic Immunology: Functions and Disorders of the Immune System*, 6th ed: Elsevier India; 2019.
26. Yazıcı D. Assessment of inflammatory biomarkers, total IgE levels, SNOT-22 scores in allergic rhinitis patients. *ENT Updates.* 2019;9(2):128-32. doi: 10.32448/entupdates.581445
27. Nagata M, Nakagome K, Soma T. Mechanisms of eosinophilic inflammation. *Asia Pac. Allergy.* 2020;10(2):e14. doi: 10.5415/apallergy.2020.10.e14
28. Vojdani A, Kharrazian D, Mukherjee PS. The prevalence of antibodies against wheat and milk proteins in blood donors and their contribution to neuroimmune reactivities. *Nutrients.* 2014;6(1):15-36. <https://doi.org/10.3390/nu6010015>
29. Vojdani A, O'Bryan T, Green J, et al. Immune response to dietary proteins, gliadin and cerebellar peptides in children with autism. *Nutr. Neurosci.* 2004;7(3):151-61. <https://doi.org/10.1080/10284150400004155>