Evaluation of the association of Mucosa-Associated Invariant T Cells (MAIT) with childhood asthma

Meral EKŞİ[1,*] ,Huri BULUT[2], Erdem AKALIN[3], Feyza USTABAŞ KAHRAMAN[4], Hakan YAZAN[5], Mebrure YAZICI[6], Mustafa Atilla NURSOY[6], Emin ÖZKAYA[6], Abdürrahim KOÇYİĞİT[7], Erkan ÇAKIR[8]

1Department of Pediatrics, Faculty of Medicine, İstanbul University-Cerrahpaşa, İstanbul, Turkiye

[2]Department of Medical Biochemistry, Faculty of Medicine , Biruni University, İstanbul, Turkiye

[3] Department of Biology, Faculty of Medicine Hospital, Bezmialem Vakıf University, İstanbul, Turkiye

[4]Department of Pediatrics, Faculty of Medicine, Medipol University, İstanbul, Turkiye

[5]Division of Pediatric Pulmonology, Department of Pediatrics, Faculty of Medicine, Bezmialem Vakıf University, İstanbul, Turkiye

[6]Division of Pediatric Immunology and Allergy, Department of Pediatrics, Faculty of Medicine, Bezmialem Vakıf University, İstanbul, Turkiye

[7]Department of Medical Biochemistry, Faculty of Medicine, Bezmialem Vakıf University, İstanbul, Turkiye

[8]Division of Pediatric Pulmonology, Department of Pediatrics, Faculty of Medicine, İstinye University, İstanbul, Turkiye

ORCIDs:

First AUTHOR: https://orcid.org/0000-0003-3077-7729

Second AUTHOR: https://orcid.org/0000-0003-2706-9625

Third AUTHOR:

Fourth AUTHOR: https://orcid.org/0000-0003-3842-7723

Fifth AUTHOR: https://orcid.org/0000-0002-7680-4000

Sixth AUTHOR: https://orcid.org/0000-0003-0444-4584

Seventh AUTHOR: https://orcid.org/0000-0003-0520-1082

Eight AUTHOR: https://orcid.org/0000-0003-453-819X

Ninth AUTHOR: https://orcid.org/0000-0003-2335-412X

Tenth AUTHOR: https://orcid.org/0000-0002-1438-7854

Acknowledgment/disclaimers/conflict of interest

Names of funding organizations: Bezmialem Vakif University BAP coordination unit

There is no conflict of interest in our research.

In our reserch, informed consent was obtained from the families of patients and healthy volunteers.

Evaluation of the association of Mucosa-Associated Invariant T Cells (MAIT) with childhood asthma

Meral EKŞİ[1,*] Huri BULUT[2], Erdem AKALIN[3], Feyza USTABAŞ KAHRAMAN[4], Hakan YAZAN[5], Mebrure YAZICI[6], Mustafa Atilla NURSOY[6], Emin ÖZKAYA[6], Abdürrahim KOÇYİĞİT[7], Erkan ÇAKIR[8]

[1]Department of Pediatrics, Faculty of Medicine, İstanbul University-Cerrahpaşa, İstanbul, Turkiye

[2]Department of Medical Biochemistry, Faculty of Medicine , Biruni University, İstanbul, Turkiye

[3] Department of Biology, Faculty of Medicine Hospital, Bezmialem Vakıf University, İstanbul, Turkiye

[4]Department of Pediatrics, Faculty of Medicine, Medipol University, İstanbul, Turkiye

[5]Division of Pediatric Pulmonology, Department of Pediatrics, Faculty of Medicine, Bezmialem Vakıf University, İstanbul, Turkiye

[6]Division of Pediatric Immunology and Allergy, Department of Pediatrics, Faculty of Medicine, Bezmialem Vakıf University, İstanbul, Turkiye

[7]Department of Medical Biochemistry, Faculty of Medicine, Bezmialem Vakıf University, İstanbul, Turkiye

[8]Division of Pediatric Pulmonology, Department of Pediatrics, Faculty of Medicine, İstinye University, İstanbul, Turkiye

Background/aim: Innate-like T lymphocytes are a recently defined group of T cells that contain mainly Mucosa-Associated Invariant T (MAIT) cells. The relationship between MAIT cells and childhood asthma is controversial. In this study, we aimed to determine the role of MAIT cells in patients with allergic asthma (AA) and non-allergic asthma (NAA). This is the first study to compare the ratios of these cells in patients with AA and NAA.

Materials and method: The study included 6-18-year-old children with AA (n = 41), NAA (n = 30), and healthy volunteers (n = 36). The control group consisted of children who came to the outpatient clinic without chronic disease, malnutrition, or acute or chronic infection. The proportions of MAIT, TH17, MAIT-17, and Th17-17 cells were investigated by flow cytometry and compared among AA, NAA, and the control group.

Results: When the AA and NAA patient groups were compared, the mean MAIT cell ratio was significantly lower in NAA patients (median = 0.45, $p < 0.05$). Also, the MAIT cell ratios were substantially lower in NAA patients than in control groups (mean

= 0.504, $p < 0.05$). TH17, MAIT-17, and TH17-17 cells were not statistically significant among the groups.

Conclusion: Our study found that MAIT cell ratios were lower in the NAA patient group compared to the control and AA patients. It has been predicted that MAIT cell depletion may have a role in the development of NAA. Our study is the first on the subject in the literature, and further studies are needed.

Key words: Mucosa-associated invariant T cells, childhood asthma, T helper 17 cell,, innate cells, allergy, interleukin 17

1. Introduction

Asthma is a heterogeneous disease characterized by chronic airway inflammation associated with airway hyperresponsiveness to direct or indirect stimuli. It is defined by respiratory symptoms such as wheezing, shortness of breath, chest tightness and cough, and expiratory airflow limitation [1]. The most substantial risk factor identified in asthma development is the genetic predisposition of the immune system to develop specific IgE antibodies against atopy or common environmental allergens. While atopy has been described in the pathogenesis of asthma, other ways asthma develops without atopy are not clearly defined [2]. Many T cell elements, cytokines, and immune mediators, especially eosinophils and mast cells, play a role in asthma development. Recent studies emphasize the heterogeneity of asthma pathogenesis. This heterogeneity may result from different pathogenic mechanisms such as different patient phenotypes (symptoms, age of onset, atopy, and lung function), airway inflammation, remodeling, and immune and metabolic pathways in a particular microbial environment. Characteristic symptoms such as lung inflammation, mucus secretion, IgE production, and fibrosis, which occur mainly in allergic asthma, were primarily associated with cytokines (IL-4, IL-5, IL-13) produced by Th2 (T helper) cells [3].

In contrast, non-allergic asthma is triggered by the neutrophil-dominant inflammatory response of past viral infections [4]. Neutrophil-dominant asthma form is associated with IL-17 in mice and humans [5-7]. This cytokine has a role in initiating and maintaining neutrophilic inflammation [8]. It also contributes to airway smooth muscle remodeling with TGF- β (Transforming growth factor) [9]. Recently, other potential pathways in which Th17 cells are involved in asthma's pathogenesis have been suggested [10]. It has been reported that interleukin 17 (IL-17) expression in the circulation and airways increases with the severity of asthma in children and adults, and there is also a higher IL-17 in the airways in patients with asthma exacerbations than in patients without asthma exacerbations [11–14]. While IL-17 expression was higher in blood and sputum supernatant taken from children with allergic asthma and rhinitis than healthy controls, no significant difference was reported between children with severe asthma and the control group [15–16]. Although CD4 + T cells (Th17 cells) secreting IL-17 are thought to be the primary source of IL-17 in asthma, cellular sources such as invariant natural killer T (iNKT) and mucosal-associated invariant T cell (MAIT) also

produce IL-17 [17- 18]. Innate-like T lymphocytes (ILT) are relatively recently identified T cells not involved in innate or adaptive immunity [19]. Humans have ILT lymphocyte populations with invariant T cell receptors and α-chain that recognize non-peptide antigens, including iNKT and MAIT cells. There are few studies on iNKT and MAIT cells' role in asthma's pathogenesis [3]. In recent studies, MAIT cells, a subset of ILT lymphocytes, have been reported to have a role in the pathogenesis of asthma because of their presence in the lung and ability to produce Th2 cytokines [10]. However, little is known about the possible effect of MAIT cells on asthma's pathophysiology in childhood.

Our aim in this study is to reveal the role of MAIT cells associated with the pathogenesis of asthma in the development of asthma in line with very new data by comparing it with the AA, NAA, and control groups. Our study is the first study comparing MAIT cell rates in this group of patients.

2. Materials and Methods

2.1 Patient and control groups

Seventy one patients aged 6 - 18 years who applied to the Bezmialem Vakif University Pediatric Chest Diseases Outpatient Clinic between January and December 2019 had three or more lifelong reactive airway attacks, typical asthma symptoms, and confirmed variable expiratory airflow limitations and were diagnosed with asthma according to GINA 2018 criteria, were included in our study.

Thirty-six patients between the ages of 6 and 18 without any chronic disease were included in the control group. Seventy-one children, 31 of whom were girls, and 36 healthy volunteers, 23 of whom were girls between the ages of 6 and 18, diagnosed with asthma according to the 2018 GINA criteria, were included in the study.

Patients with chronic upper airway cough syndrome, inhaled foreign body, bronchiectasis, primary ciliary dyskinesia, congenital heart disease, bronchopulmonary dysplasia, cystic fibrosis, immunodeficiency syndromes, neuromuscular disease, gastroesophageal reflux disease, etc. causing recurrent reactive airway attacks and those with other chronic diseases were excluded from the study.

The patient group was classified as allergic (n = 41) and non-allergic (n = 30) based on the GINA 2018 guideline. Patients with at least one inhaler allergen sensitivity (dust, pollen, feather, etc.) and a history and family history of doctor-diagnosed eczema, allergic rhinitis, and food allergy were included in the allergic asthma (AA) group. In the non-allergic asthma (NAA) group, patients with no allergen sensitivity and no doctor-diagnosed allergic disease history and/or family history were included (2). The control group consisted of healthy volunteer children brought to the Pediatric Outpatient Clinic for routine control and did not have a history of reactive airway attack, malnutrition, and acute and/or chronic disease.

2.2 Flow cytometry

Peripheral venous blood samples from AA, NAA, and control groups were collected in heparin tubes. Then, into 12 x 75 mm 5 ml PS tubes, 20 ul CD3 FITC (BD Cat no: 345763, USA), 20 ul CD161 APC (BD Cat no: 550968, USA), and 5 ul TCR V alpha 7.2 PE (Biolegend Cat no: 351706, USA) antibodies were placed and 100 ul of peripheral blood samples were added on each. After incubation in the dark at room temperature, FACS lysing solution (BD ref: 349202, USA) was added to the tubes and vortexed and incubated in the dark at room temperature for 5 minutes. After the incubation, the tubes were centrifuged at 400 x g for 4 minutes, and the supernatants were removed. Cell wash (BD ref: 349524, USA) was added to the pellets obtained, and a vortex was performed. All samples were centrifuged at 400 x g for 4 minutes, and the supernatants were removed again, then vortexed with FACS permeabilizing solution (BD ref: 340973, USA) and incubated in the dark at room temperature for 10 minutes. All supernatants were removed from the samples and subjected to a re-centrifugation and washing process as described above. IL-17A PerCP 5.5 (BD Cat no: 560799) was then added to the tubes and incubated at room temperature in the dark for 3 - 40 minutes. All supernatants were removed after all samples were centrifuged and washed as above. 200 ul cell wash (BD ref: 349524, USA) was added to the tubes, and the reading was done within 10 minutes. Analyzes were performed on a BD Facscanto II (4 - 2 - 2, USA) device using the BD FacsDiva program.

2.3 Statistical Analysis

For statistical analysis, the IBM SPSS Statistics v. 22.0 program has been used. The distribution of the data was analyzed using the Shapiro-Wilk test. Mann-Whitney U test was used to compare two groups that did not have a normal distribution. The Kruskal-Wallis test was used in the comparisons of three groups that did not have a normal distribution. Post-hoc comparison of significant results was made with Dunn's test. Descriptive statistics of the data are given as a median, interquartile range, and mean ± standard deviation. $P < 0.05$ was accepted as significant.

Ethics committee approval for our study was obtained from Bezmialem Vakif University Clinical Research Ethics Committee.

3. Results

3.1 Patient and control groups

The mean age of 41 AA patients (48.7% female) was 10.5 ± 3.1 years, while the mean age of 30 patients (40% female) diagnosed with NAA was 8.2 ± 2.3 years. All of the AA group had positive allergy skin tests, while the entire NAA group's allergy skin test was negative. 63.9% of the control group was recorded as girls and 36.1% as boys. The mean age of 36 patients (63.8% girls) in the control group was 10.9 ± 3.2 years. There was no significant difference between all groups in terms of mean age and gender. The

demographic and clinical data of all patient and control groups are summarized in Table 1. The comparison of MAIT cell ratios with AA, NAA and control groups is evaluated graphically in Figure.

3.2 Flow cytometry results and comparisons

When all patient and control groups were compared, the MAIT cell ratio was significantly lower in NAA patients ($p = 0.011$) (Table 2). When the means of Th17, MAIT + IL-17A +, and CD3 + IL17A + cell ratios were evaluated, it was not found significant among all groups ($p = 0.319$, $p = 0.568$, $p = 0.467$) (Table 2). When NAA and control patient groups were compared within themselves, the mean MAIT cell ratio was significantly lower in NAA patients. ($p = 0.011$). No significant difference was found when the mean of Th17, MAIT + IL-17A +, and CD3 + IL17A + cell ratios were compared between NAA and control patients. ($p > 0.05$). When the AA and control groups were compared, an important difference was not found between the groups in the mean of Th17, MAIT, MAIT + IL17A +, and CD3 + IL17A + cell ratios ($p > 0.05$) (Table 2). Finally, when comparing the mean of Th17, MAIT, MAIT + IL17A +, and CD3 + IL17A + cell ratios of all patient groups (AA + NAA) and the control group, no significant difference was found ($p > 0.05$).

4. Discussion

Although asthma is a prevalent disease in children, there is little information about MAIT cells' role in childhood asthma's pathophysiology, and these are not clear. Our study compared the MAIT cells, Th17 cells, and IL-17 levels produced from them in allergic and non-allergic patient groups and control groups in school-age children.

In our non-allergic patient group, the MAIT cells were significantly lower than the other groups. When we compared the mean ratios of IL-17-producing MAIT cells (MAIT + 17 A +) between the groups, we could not find a significant difference.

MAIT cells have been identified in recent years, and their association with bacterial, fungal, and mycobacterial infections and autoimmune diseases has been demonstrated [20]. Asthma pathogenesis is very heterogeneous, and many cytokines and cell groups have been associated with asthma in recent years. It has been shown in the literature that iNKT and MAIT cells are associated with asthma [21]. A study suggested that high circulating MAIT cells at 1 reduce the risk of developing asthma at 7. High circulating MAIT cells are highly correlated with IFN-γ-producing CD4 + T cells and were thought to be protective against asthma development [22]. In the study by Lezmi et al., asthmatic patients with and without attacks were evaluated in school-age children, and it was found that MAIT-17 cells showed a positive correlation with asthma severity. It is thought that this is most likely caused by MAIT-17, causing asthma symptoms [10]. In a study conducted by the same team on children with severe asthma in 2019, MAIT 17 and TH 17 were evaluated in BAL fluid, and it was shown that the amount of these cells in BAL increased more than in blood [23]. In our study, MAIT cells were low in the

NAA group, but the relationship between disease severity and MAIT cells was not evaluated.

Likewise, regardless of the patient's severity, there was no significant difference between the MAIT 17 and TH 17 numbers in AA, NAA, and control groups. IL 17 levels were evaluated in the nasal/bronchial mucosa of patients with severe and mild asthma in adults, and it was shown that IL 17 expression was higher in severe asthma. Also, it was established in this study that IL 17 is associated with bronchial neutrophilia, attack, and FEV 1 [24]. In our study, plasma sampling was performed instead of the nasal mucosa, and we showed no significant difference in the number of IL-17-producing MAIT cells in the AA, NAA, and control groups. A study by Ashmore et al. in adults showed that MAIT cells were negatively correlated with airway limitation in patients with asthma [25].

Our study had some limitations: The patients' clinical grade, attack status, and asthma scores were not evaluated. In future studies, it will be beneficial to investigate the MAIT cell at the tissue level (sputum or BAL fluid) and during acute attacks. Detailed analyses of the frequency and functional subgroups of these cells in the context of different asthma endotypes could be crucial for the development of new therapeutic approaches.

In conclusion, this study found that MAIT cells were lower in patients with non-allergic asthma than in AA and control groups. This is the first study in the literature to compare MAIT cells in children with allergic and non-allergic asthma.

REFERENCES

1. Sagmen SB, Ceyhan B. Severe asthma. Kocatepe Medical Journal; 19 (4): 157-163. https://doi.org/10.18229/kocatepetip.475027
2. National Asthma Education and Prevention Program: Expert panel report II: Guidelines for the diagnosis and management of asthma. National Heart, Lung, and Blood Institute (NIH publication no. 97-4051), Bethesda, MD 1997.
3. Lezmi G. Leite-de-Moraes M. Invariant Natural Killer T and Mucosal-Associated Invariant T Cells in Asthmatic Patients. Frontiers in Immunology 2018; 9: 1766. https://doi.org/10.3389/fimmu.2018.01766
4. Wenzel SE, Schwartz LB, Langmack EL, Halliday JL, Trudeau JB, Gibbs RL, Chu HW. Evidence that severe asthma can be divided pathologically into two inflammatory subtypes with distinct physiologic and clinical characteristics. American Journal of Respiratory and Critical Care Medicine;160 (3): 1001–1008. https://doi.org/10.1164/ajrccm.160. 3.9812110
5. Wilson RH, Whitehead GS, Nakano H, Free ME, Kolls JK, Cook DN. Allergic sensitization through the air way primes Th17 dependent neutrophilia and airway hyperresponsiveness. American Journal of Respiratory and Critical Care Medicine; 180 (8): 720–730. https://doi.org/10.1164/ rccm.200904-0573OC

6. Bullens DM, Truyen E, Coteur L, Dilissen E, Hellings PW, Dupont LJ, Ceuppens JL. IL-17 mRNA in sputum of asthmatic patients:linking T cell driven inflammation and granulocytic influx? Respiratory Research; 7 (1): 135. https://doi.org/10.1186/1465-9921-7135
7. Chesné J, Braza F, Chadeuf G, Mahay G, Cheminant MA, Loy J, Brouard S, Sauzeau V ,Loirand G, Magnan A. Prime role of IL-17A in neutrophilia and airway smooth muscle contraction in a house dust mite-induced allergic asthma model. The Journal of Allergy and Clinical Immunology; 135 (6): 1643-1645.E5. https://doi.org/10.1016/j.jaci.2014.12.1872
8. Lindén A. Role of interleukin-17 and the neutrophil in asthma. International Archives of Allergy and Immunology; 126 (3): 179–184. https://doi.org/10.1159/000049511
9. Evasovic JM, Singer CA. Regulation of IL-17A and implications for TGF-β1 comodulation of airway smooth muscle remodeling in severe asthma. American Journal of Physiology Lung Cellular and Molecular Physiology; 316 (5): L843–L868. https://doi.org/10.1152/ajplung.00416.2018
10. Lezmi G. Taam R. A. Dietrich C. Chatenoud L. Blic J. Leite-de-Moraes M. Circulating IL-17-producing mucosal-associated invariant T cells (MAIT) are associated with symptoms in children with asthma. Clinical Immunology 2018; 188 (7): 7-11. https://doi.org/10.1016/j.clim.2017.11.009
11. Al-Ramli W, Prefontaine D, Chouiali F, Martin J.G, Olivenstein R, Lemiere C, Hamid Q. T(H)17-associated cytokines (IL-17A and IL-17F) in severe asthma. The Journal of Allergy and Clinical Immunology; 123 (5): 1185–1187. https://doi.org/10.1016/j.jaci.2009.02.024
12. Agache I, Ciobanu C, Agache C, Anghel M. Increased serum IL-17 is an independent risk factor for severe asthma. Respiratory Medicine; 104 (8): 1131–1137. https://doi.org/10.1016/j.rmed.2010.02.018
13. Ricciardolo F.L, Sorbello V, Folino A, Gallo F, Massaglia G.M, Favata G, Conticello S, Vallese D, Gani F, M, Malerba M, Folkerts G, Rolla G, Profita M, Mauad T, Di Stefano A, Ciprandi G. Identification of IL-17F/frequent exacerbator endotype in asthma. The Journal of Allergy and Clinical Immunology; 140 (2): 395–406. https://doi.org/10.1016/j.jaci.2016.10.034
14. Sorbello V, Ciprandi G, Di Stefano A, Massaglia G.M, Favata G, Conticello S, Malerba M, Folkerts G, Profita M, Rolla G, Ricciardolo F.L. Nasal IL-17F is related to bronchial IL-17F/neutrophilia and exacerbations in stable atopic severe asthma. Allergy; 70 (2): 236–240. https://doi.org/10.1111/all.12547
15. Albano G.D, Di Sano C, Bonanno A, Riccobono L, Gagliardo R, Chanez P, Gjomarkaj M, Montalbano A.M, Anzalone G, La Grutta S, Ricciardolo F.L, Profita M. Th17 immunity in children with allergic asthma and rhinitis: a pharmacological approach. Plos One; 8 (4): e58892.
16. Andersson C.K, Adams A, Nagakumar P, Bossley C, Gupta A, De Vries D, Adnan A, Bush A, Saglani S, Lloyd C.M. Intraepithelial neutrophils in pediatric severe asthma are associated with better lung function. The Journal of Allergy

and Clinical Immunology;139 (6): 1819–1829. https://doi.org/10.1016/j.jaci.2016.09.02

17. Michel M.L, Keller A.C, Paget C, Fujio M, Trottein F, Savage P.B, Wong C.H, Schneider E, Dy M, Leite-de-Moraes M.C. Identification of an IL-17-producing NK1.1(neg) iNKT cell population involved in airway neutrophilia. Journal of Experimental Medicine; 204 (5): 995–1001.
18. Dusseaux M, Martin E, Serriari N, Peguillet I, Premel V, Louis D, Milder M, Le Bourhis L, Soudais C, Treiner E, Lantz O. Human MAIT cells are xenobiotic-resistant, tissue-targeted, CD161hi IL-17-secreting T cells. Blood; 117 (4): 1250–1259. https://doi.org/10.1182/blood-2010-08-303339
19. Iwamura C. Nakayama T. Role of CD1d- and MR1-Restricted T Cells in Asthma.Frontiers in Immunology; 28:9:1942. https://doi.org/10.3389/fimmu.2018.01942
20. Hinks, T. S. C. (2016). Mucosal-associated invariant T cells in autoimmunity, immune-mediated diseases and airways disease. Immunology; 148 (1): 1–12. https://doi.org/10.1111/imm.12582
21. Victor J. R, Lezmi G, Leite-de-Moraes M. New Insights into Asthma Inflammation: Focus on iNKT, MAIT, and γδT Cells. Clinical Reviews in Allergy and Immunology; 59 (3): 371–381. doi: 10.1007/s12016-020-08784-8
22. Chandra S, Wingender G, Greenbaum J. A, Khurana A, Gholami A. M, Ganesan, A.P, Rosenbach M, Jaffee K, Gern J. E, Wood R, O'Connor G, Sandel M, Kattan M, Bacharier L, Togias A, Horner A.A, Kronenberg M. (2018). Development of Asthma in Inner-City Children: Possible Roles of MAIT Cells and Variation in the Home Environment. The Journal of Immunology; 200 (6): 1995–2003. https://doi.org/10.4049/jimmunol.1701525
23. Lezmi G, Abou-Taam R, Garcelon N, Dietrich C, Machavoine F, Delacourt C, Adel-Patient K, Leite-de-Moraes M. (2019). Evidence for a MAIT-17–high phenotype in children with severe asthma. Journal of Allergy and Clinical Immunology; 144 (6): 1714-1716.e6. https://doi.org/10.1016/j.jaci.2019.08.003
24. Ricciardolo F. L. M, Sorbello V, Folino A, Gallo F, Massaglia G. M, Favatà G, Conticello S, Vallese D, Gani F, Malerba M, Folkerts G, Rolla G, Profita M, Mauad T, Di Stefano A, Ciprandi G. (2017). Identification of IL-17F/frequent exacerbator endotype in asthma. Journal of Allergy and Clinical Immunology; 140 (2): 395–406. https://doi.org/10.1016/j.jaci.2016.10.034
25. Ishimori A, Harada N, Chiba A, Harada S, Matsuno K, Makino F, Ito J, Ohta S, Ono J, Atsuta R, Izuhara K, Takahashi K, & Miyake S. (2017). Circulating activated innate lymphoid cells and mucosal-associated invariant T cells are associated with airflow limitation in patients with asthma. Allergology International; 66 (2): 302–309. https://doi.org/10.1016/j.alit.2016.07.005

Table 1: Demographic and clinical characteristics of the patient and control groups.

	AA (n: 41)	NAA (n : 30)	Control (n : 36)	p
Age, y	10.5 ± 3.1	8.2 ± 2.3	10.9 ± 3.2	> 0.05*
Girls (n, %)	20, 48.7%	12, 40%	23, 63.9 %	>0.05*
Typical asthma symptoms (n, %)	41, 100%	30, 100%	0	>0.05*
Confirmed variable expiratory airflow limitation (n,%)	41, 100%	30, 100%	0	>0.05*
Skin prick test positivity (n, %)	41, 100%	0	0	>0.05*
Family history of atopy	35, 87.5%	0	0	
Total IgE height (n, %)	36, 90%	0	0	
Eosinophilia (n, %)	25, 62.5%	0	0	

* Pearson Chi-square test, AA: Allergic asthma, NAA: Non-allergic asthma

Table 2: Comparison of the results of allergic asthma, non-allergic asthma and control group.

	MAIT*	**MAIT + IL 17 A +***	**TH17***	**CD3+IL17A+***
Allergic asthma (mean):	0.80 ± 0.52	0.018 ± 0.012	22.68 ± 6.22	0.19 ± 0.14
Allergic asthma Median (IQR):	0.68 (0.06 - 2.42)	0.02 (0.005 - 0.05)		0.15 (0.03 - 0.74)
Non-allergic asthma (mean)	0.50 ± 0.33	0.016 ± 0.011	22.16 ± 6.73	0.14 ± 0.07
Median (IQR)	0.45 (0.05 - 1.4)	0.015 (0-0.04)		0.13 (0.02 - 0.34)
Control (mean):	0.82 ± 1.00	0.024 ± 0.020	23.96 ± 8.39	0.25 ± 0.42
Median (IQR)	0.64 (0.22 - 6.3)	0.02 (0 - 0.09)		0.15 (0.02 - 2.46)
P* value	0.027	0.319	0.568	0.467
Post hoc p value**	$p^{a,n} = 0.011$	$p^{a,n} = 0.66$	$p^{a,n} = 0.736$	$p^{a,n} = 0.99$
	$p^{a,c} = 0.526$	$p^{a,c} = 0.264$	$p^{a,c} = 0.451$	$p^{a,c} = 0.787$
	$p^{n,c} = 0.039$	$p^{n,c} = 0.145$	$p^{n,c} = 0.594$	$p^{n,c} = 0.779$

MAIT: Mucosa associated invariant T cell, MAIT + IL17A+: Interleukin 17 A producing MAIT, TH17: T helper 17, CD3+IL17A+: Interleukin 17 A producing CD 3 lymphocyte, *Kruskal Wallis test, a: Atopic asthma, n: non-atopic asthma, c: control

Figure : Comparison of MAIT results of AA, NAA, and control group.