Czech
Journal of Multidisciplinary Innovations
Volume 21 September, 2023.
ISSN (E): 2788-0389
Website: www.peerianjournal.com
Email: editor@peerianjournal.com

Determine Role of IL-5 and Eosinophils in Chronic Bronchial Asthma

Mustafa Hamoodi Jabbar[1], Nasreen Rahman Mohammed[2], Fadhaa Jaber Shinjar[3], Heba Suhail kadhem[4], Zainab Abd Ali Salman[5]
[1,2,3,4,5]University of AL- Qadisiyah, AL-Diwanyia, Iraq.
Corresponding Author: mustafa.hamoudi@qu.edu.iq

Abstract:
Background: Asthma is a chronic inflammatory disease, primarily resulting from interactions between genetic and environmental factors, in which immunological mediators and cells play a key role. This study aimed to determine role IL-5 and eosinophilia in chronic asthma.
Methods: This case-control study was conducted on 70 patients (45 females, 25 males) with chronic bronchial asthma and their age range between 7-88 years. Other 70 healthy subjects (40 females and 30 males) were included as a control group. Optical density of IL-5 in serum was performed by ELISA technique and from which IL-5 was evaluated according to standard carve. Complete blood count was performed for all blood samples to detect eosinophils count (cell/µl) by RUBY system.
Results: The results of the study showed that most patients (24%) were in the age group 36-45 years, also result revealed that 64% of patients were females. Significant association of gender and age for cases and controls not demonstrated ($p > 0.05$). This study detected distinct role of IL-5 mean and eosinophils median in cases of asthma (30.3 pg/ml and 1008 cell/ul respectively) compared to healthy controls (5.3 pg/ml and 199 cell/ul respectively) (P value <0.001) especially in patients with positive family history of asthma and showed the gradually high of IL-5 in serum associated with ordered increase in eosinophil count in peripheral blood.
In conclusion, this study showed that high incidence of bronchial asthma was occur among young adults especially female and immunological markers (IL-5 and eosinophils) significantly associated with acute bronchial asthma.

Keywords: Asthma, Eosinophils, IL-5, ELISA

Introduction

Reversible aviation route check is an indication of asthma, an ongoing provocative illness of the aviation routes with no known reason. No less than 5 to 10 percent of grown-ups experience the ill effects of it, making it one of the most common constant circumstances [1,2]. Asthma can happen whenever in an individual's life, despite the fact that most of cases start before the age of 25. In spite of the fact that asthma has all the earmarks of being a confounded cycle with numerous elaborate qualities and logical quality climate collaborations, it has around 60% heritability, recommending that both hereditary and natural variables assume a part in its etiology [3].

Airborne allergens and viral diseases have all the earmarks of being the main ecological elements. In helpless people, asthma may likewise be welcomed on by diet, smoking, and air

Czech
Journal of Multidisciplinary Innovations
Volume 21 September, 2023. ISSN (E): 2788-0389
Website: www.peerianjournal.com Email: editor@peerianjournal.com

contamination [4,7]. No newfound hereditary variation has expanded risk for the asthma aggregate across all populaces, in spite of this proof for a significant hereditary commitment to the science of asthma and the ID of various competitor qualities. Various hereditary variations might be liable for a singular's asthma heritability and may likewise assume a part in the statement of the aggregate across a populace, as per studies. Also, hereditary variations that impact treatment reaction have been distinguished [5,7,8].

The different clinical indications that favor a fundamentally T helper type 2 (TH2) reaction, with interleukins like interleukin-5 (IL-5) that lead to the development of immunoglobulin E (IgE), supportive of provocative cytokines, and bronchial hyperactivity, as well as the connection among hereditary and natural variables (allergens), are the essential drivers of asthma demeanor [9]. Early asthmatic reactions are set off by Lymphocytes, determined cytokines, IgE, pole cells, and enlistment and actuation of eosinophils, which seem to add to the diligent asthma aggregate with ongoing wind stream block [10] .

There is an expansion in eosinophilopoiesis and resulting relocation of eosinophils to the lung in eosinophilic problems like asthma due to: Type 2 cytokines (IL-4 and IL-5) upregulate chemokine creation, including CCL11 (eotaxin 1), CCL24 (eotaxin 2), CCL26 (eotaxin 3), CCL13 (MCP4), and CCL5 (RANTES), which improve chemotaxis for eosinophil dealing from the dissemination to the aviation route [12,13]. Raised degrees of IL-3, IL-5, grip atoms like integrins on the outer layer of blood eosinophils are actuated when these chemokines tie to the chemokine receptor CCR3. Thus, this makes it workable for eosinophils to cooperate with endothelial cells by means of periostin, intracellular attachment particle 1 (ICAM-1), and vascular cell bond atom 1 (VCAM-1), which brings about blood penetration into the aviation route tissue [13,14]. Chemokine knockout mice like CCL11−/− and CCL24−/− show reduced managing of eosinophils to the aeronautics course during allergen challenge [15]. In an Aspergillus fumigatus-activated asthma model, CCR3 knockout mice had lessened eosinophilic flying course exacerbation close by diminished levels of type 2 cytokines, including IL-5 [16,17]. Our study aimed to determine the serum levels of IL-5 and eosinophils in patients with chronic bronchial asthma.

Materials and Methods

Study design: The current research was case- control study included 70 patients (25 males, 45 females) were seen in Al-Diwaniyah Teaching Hospital from January 2022 to Jun 2023. Asthmatic cases were diagnosed clinically by physician as having chronic bronchial asthma. Patients were interviewed directly by using an anonymous questionnaire form which covered name, age, sex, duration of the disease, detail history about occupation, smoking, the frequency of symptoms, any drug use, family history and others. Another group consist of 70 apparently healthy individuals (30 male and 40 female) without any history of systemic disease were clinically considered as healthy also included in this study as a control group. This study was in agreement with ethics of Al-Diwaniyah Teaching Hospital and verbal informed consent was obtained from all participants.

Sample collection: Two ml of blood in other anticoagulant tube use immediately for complete blood count and 2.5 ml of blood in sterile plain tube and allow sample to clot for few minutes at room temperature then followed by separation of serum from the clot by centrifugation for 15

Czech
Journal of Multidisciplinary Innovations
Volume 21 September, 2023.
ISSN (E): 2788-0389
Website: www.peerianjournal.com
Email: editor@peerianjournal.com

minutes at 1000 ×g . Then the serum was divided into sterile plain tubes, labeled and stored at -4 °C one for IL-5 ELISA assay procedure.

Human IL-5 enzyme –linked immunosorbent assay kit: Cusabio (Germany) ELISA kits used for the quantitative determination of IL-5 level in serum and assay procedure carried out according to manufacture's manual.

Eosinophils count: Complete blood count was preformed for each blood test by RUBY framework. Examine strategy for this framework including taking EDTA tube (contain blood test and marked with name and number of patient) in unambiguous rack in RUBY framework. Tests were taken and broke down naturally by this framework. Following 1-5 minutes aftereffect of complete blood count including eosinophils count showed up on PC screen, at last consequence of every patient printed and marked with name and number of patient.

Statistical analysis: results were interned into a computerized database structure. The database was tested for errors using range and logical data cleaning methods, and inconsistencies were remedied. An expert statistical advice was sought for. Statistical analyses were done using SPSS version 20 computer software (Statistical Package for Social Sciences) in corporation with Microsoft Excel 2010.

Results and Discussion.

In this case- control study, 70 patients with chronic bronchial asthma seen in AL-Diwaniya Teaching Hospital (25 males, 45 females), table (1), the age of the patients varied from 7-88 years with a mean age of 33.3 years (SD±17.1), table (2), compared with 70 (30 males, 40 females) apparently healthy subjects with age range from 7 to 85 years, and mean age of 37.4 years (SD±16.3) as a control group. Table (3) showed most of patients are females in percent 64%. Moreover most patients on the age groups 36-45 and > 50 years in prevalence 24% and 21% respectively.

Table (1): Distribution of patients with bronchial asthma according to age groups and gender

Age Groups/ years	Males No.	Females No.	Total No.(%)
< 15	4	8	12 (17%)
15-25	6	7	13 (19%)
26-35	3	10	13 (19%)
36-45	5	12	17 (24%)
>50	7	8	15 (21%)
Total	25	45	70(100%)

Table (2): The case-control difference in age mean.

Case-control comparison			
	Healthy controls	Cases (Asthma)	P value
Age			

Czech
Journal of Multidisciplinary Innovations
Volume 21 September, 2023.
ISSN (E): 2788-0389
Website: www.peerianjournal.com
Email: editor@peerianjournal.com

(years)			
Range	(7 - 85)	(7 - 88)	
Mean	33.3	37.4	0.509 [NS]
SD	17.1	16.3	
SE	2.04	1.95	
N	70	70	

❖ NS= No Significant, SD= Standard Deviation, SE= Standard Error, N= Number

Table (3): The case-control difference in gender distribution.

Case-control comparison					
	Healthy controls		Cases (Asthma)		
Gender	N.	%	N.	%	P value
Female	40	57	45	64	0.341[NS]
Male	30	43	25	36	
Total	70	100.0	70	100.0	

The mean serum IL-5 and median eosinophil count were significantly higher among cases with asthma 30.3 pg/ml and 1008 cell/µL respectively compared to healthy controls 5.3 pg/ml and 199 cell/µL respectively, table (4).

Table(4): The case-control difference in mean serum IL-5 and blood eosinophil count.

Serum IL-5 conc. pg/ml	Case-control comparison		P Value
	Healthy controls	Cases (Asthma)	
Range	(3.6 – 8.7)	(10.2 - 80)	< 0.001
Mean	5.3	30.3	
SD	1.09	9	
SE	0.27	1.1	
N	70	70	

Czech
Journal of Multidisciplinary Innovations
Volume 21 September, 2023.
ISSN (E): 2788-0389
Website: www.peerianjournal.com
Email: editor@peerianjournal.com

Eosinophil count (cell/uL)			**< 0.001**
Range	**(50 - 300)**	**(650 - 4100)**	
Median	**199**	**1008**	
Inter-quartile range	**(130 - 260)**	**(150 - 1500)**	
N	**70**	**70**	

Table (5) showed the lowest range of IL-5 was 12.4 - 55.3 (mean ± SD=19.3 ± 4.4) associated with lowest quartile of eosinophil (<800 cell/uL), high range of IL-5 is 23.7 – 64.21(mean ± SD = 28.8± 7.2) associated with increased number of eosinophil (interquartile range = 934 - 1279 cell/uL) and higher range of IL-5 is 35.2 – 77.5 (mean ± SD = 41.9± 9.8) associated with highest quartile of eosinophil (> 1566 cell/uL). A very strong and statistically significant positive (direct) linear correlation of IL-5 level with eosinophil count (r=0.8223) also showed in this results.

Table (5): link of eosinophil count and serum IL-5 concentration in asthma cases

	Eosinophil count (cell/uL)-quartiles			**P(ANOVA) trend**
	First (lowest) quartile (< 800)	**Average-inter-quartile range (150 - 1500)**	**Fourth(highest) quartile (>1566)**	
Serum IL-5 conc. pg/ml				**< 0.001**
Range	**(12.4 - 55.3)**	**(23.7 – 64.21)**	**(35.2 – 77.5)**	
Mean	**19.3**	**28.8**	**41.9**	
SD	**4.4**	**7.2**	**9.8**	
SE	**1.22**	**0.74**	**2.19**	
N	**13**	**37**	**20**	
r=0.8223				

Table (6) showed increase eosinophil count and high serum level of IL-5 in asthmatic patients with positive family history (IL-5 mean ± SD=48.9±8.3 and eosinophil median =2348) whereas decrease eosinophil count and low level of IL-5 in serum of asthmatic patients with negative family history with asthma (IL-5 mean ± SD=26.2 ±9.5, eosinophil median =950).

Czech
Journal of Multidisciplinary Innovations
Volume 21 September, 2023.
ISSN (E): 2788-0389
Website: www.peerianjournal.com
Email: editor@peerianjournal.com

Table (6): The mean and median of studied markers by family history of asthma.

	Family history of Asthma		
	Negative	Positive	P
Serum IL13conc. pg/ml			0.04
Range	(14.8 - 50.3)	(13.8 - 80)	
Mean	26.2	48.9	
SD	9.5	8.3	
SE	2.14	1.19	
N	24	46	
Eosinophil count (cell/uL)			0.002
Range	(598 - 3111)	(720 - 4100)	
Median	950	2348	
Inter-quartile range	(970 - 2499)	(1274 - 4100)	
N	24	46	

Discussion

Adult patients in our study with chronic bronchial asthma have the highest age and gender characteristics, with a prevalence of 24% among those aged 36 to 45 and 21% among those older than 50 years. These differences may be attributable to high life activities like work and exercise, which increase sensitivity to allergens, as well as hormonal changes in females (such as during pregnancy and menstruation), which may also increase asthma frequency [18].

This results agreed with eventual outcomes of Mishra (2004), who focused on 70 occurrences of bronchial asthma at age 10-70 years, found high prevalence of asthmatic patients during age 21-40 years, followed by age 10-20 years and decrease with age [19]. According to Choi (2021), the prevalence of asthma was highest in children aged 6 to 17 years old (15.3%), and it decreased with age for both older men and women. This was due to the connection between atopy and a raised eosinophil level in asthmatic cases, which was a strength for especially children but was absent in the most established adult class until it was absent in adults aged 55 years [20].

Mishra (2004) (19) tracked down that the mean time of asthmatic patients (36.2 and 30.78 individually) and controls (32.3 and 29.23 separately) was $P > 0.05$, and Vergara et al (2010) [21]. who considered 429 nonrelated grown-up asthmatics and 401 controls (mean age 36.15 and 34.98 years, separately) observed that this was predictable with our discoveries Li and others, In certain populaces (especially metropolitan ones), it was guessed that the predominance of bronchial asthma in more established asthmatics might be the aftereffect of lacking asthma treatment or medical care, an expansion in smoking or openness to air contamination, and an expansion in other aspiratory sicknesses or microbial diseases in the aviation routes [22].

Czech
Journal of Multidisciplinary Innovations
Volume 21 September, 2023. ISSN (E): 2788-0389
Website: www.peerianjournal.com Email: editor@peerianjournal.com

The current investigation discovered that grown-up ladies had a higher commonness of asthma (64%) than men (36%). This recommends that grown-up females were especially impacted by asthma since there is a more noteworthy possibility that sex-related hormonal or biochemical contrasts might assume a part in asthma's pathophysiology. A different study found that adult women are more likely than men to have asthma because female sex hormones increase the secretion of IL-5 and total IgE. Progesterone, then again, keeps pole cells from delivering receptor, and estrogen invigorates FoxP3+ administrative T (Treg) cells [23-25]. This results agreed with most examinations that saw sex as a bet factors of bronchial asthma. The authors claim that adult women are more likely than men to have asthma because they are less clinically and immunologically responsive to hormonal changes. In addition, a difference in hormonal status may play a role in the relationship between age and asthma prevalence in both sexes. This could have an impact on airway size, inflammatory conditions, and smooth muscle and vascular functions. Despite the fact that Choi (2021) referenced these distinctions on the grounds that the aviation route type and lung capability of grown-up guys are more prominent than those of grown-up females, a more modest [20].

This outcome noticed a huge relationship between centralization of IL-5 and intense bronchial asthma (P <0.001), this might be because of its significant job in pathophysiology of bronchial asthma. IL-5 assume significant part in eosinophil gathering and considered as a critical figure IgE combination by B cells, separation of guileless Immune system microorganisms into Th2 effector cells, AHR and aviation route irritation [26].

As per the ongoing review, asthmatic patients had a fundamentally more significant level of eosinophils in their fringe blood (p=0.001). The focal effector cell eosinophil, which is liable for progressing aviation route irritation, may assume a part in the pathology of asthma by causing an expansion in the quantity of these cells in asthma. As a consequence of this, the cell might cause damage to the nerves and mucosa of the airway [27,28].

Through the arrival of lipid go between, receptive oxygen species, and granule-related fundamental proteins, which cause bronchoconstriction and bodily fluid hypersecretion and harm nerves and epithelial cells [29]. Although tissue eosinophilia and eosinophil degranulation have been linked to a number of fibrotic syndromes, and the eosinophil is the source of a number of fibrogenic and growth factors like TGF-, TGF-, fibroblast growth factor-2, VEGF, matrix metalloproteinase-9, IL-5, IL-4, and IL-17, the possibility that the eosinophil is the source of these

The impact of IL-4 on TH2 to create IL-3, IL-5, IL-9, and GM-CSF, which animated bone marrow to blend of new eosinophils, as well as IL-4's job in upgraded adhesiveness of the endothelium for eosinophils, was answerable for the progressive expansion in eosinophil include in fringe blood and the particular job that IL-5 played in asthma. Eosinophil cells moreover mix, store and conveyance IL-5 during provocative response to go over its abilities (for example eosinophils assortment) [30-32]. Eosinophils, which are leukocytes that come from the bone marrow, are uncommon in healthy people; Be that as it may, type 2 cytokines — interleukins (IL)-4, - 5, and - 13 can accelerate eosinophilopoiesis, broaden eosinophil endurance, and transport to the injury site during sickness. Eosinophilia, tissue harm, and aviation route pathology are the consequences of an unusual fiery reaction in conditions like unfavorably susceptible asthma. It has been exhibited that the pleiotropic type 2 cytokine IL-5 assumes a urgent part in the improvement of asthma and other eosinophilic circumstances [33,34]. IL-5 levels are brought up in animal

Czech
Journal of Multidisciplinary Innovations
Volume 21 September, 2023. ISSN (E): 2788-0389
Website: www.peerianjournal.com Email: editor@peerianjournal.com

models of eosinophilic disturbance and in the blood and tissue still up in the air to have eosinophilic issues. Eosinophil endurance, initiation, and dealing are only a couple of the numerous pathogenic instruments that are set off by IL-5 flagging. Preclinical models and clinical trials of IL-5 inhibitors in patients have revealed robotic experiences into the role of this cytokine in eosinophilia-producing cells. According to the findings of clinical trials [33-35], IL-5 plays a significant mechanistic role in asthma and other eosinophilic disorders. As a result, the cytokine IL-5 and its receptor are key molecular targets for current biological therapies aimed at improving the management of severe and difficult-to-treat eosinophilic disease because of their central role in the pathophysiology of T2-high asthma (36).

Conclusion

Our results showed that the concentration of IL-5 and eosinophils count increased in chronic bronchial asthma compared with healthy subjects, and an increase in these immunological markers was seen in patients with a positive family history. It also correlated a positive linear relationship between IL-5 and the number of those cells.

References

1. Amruta N., Kandikattu H. K. (2018). Apoptosis of inflammatory cells in asthma. Int. J. Cell Biol. Physiol. 1, 1–6.
2. Anderson W. C., III., Szefler S. J. (2019). Cost-effectiveness and comparative effectiveness of biologic therapy for asthma. Ann. Allergy Asthma Immunol. 122, 367–372.
3. Bagnasco D., Ferrando M., Varricchi G., Puggioni F., Passalacqua G., Canonica G. W., *et al.* (2017). Anti-interleukin 5 (IL-5) and IL-5Rα biological drugs: efficacy, safety, and future perspectives in severe eosinophilic asthma. Front. Med. 4:135.
4. Bel E. H., Wenzel S. E., Thompson P. J., Prazma C. M., Keene O. N., Yancey S. W., *et al.* (2014). Oral glucocorticoid-sparing effect of mepolizumab in eosinophilic asthma. N. Engl. J. Med. 371, 1189–1197.
5. Khadhim M.M., AL-Damerchi A.T., Kazaal M.A. (2015). Evaluation of A Disintegrin and Metalloprotein33 Gene Polymorphism in Bronchial Asthma. AL-Qadisiya Medical Journal. 11(19), 1-9.
6. Bhalla A., Mukherjee M., Nair P. (2018). Airway eosinophilopoietic and autoimmune mechanisms of eosinophilia in severe asthma. Immunol. Allergy Clin. N. Am. 38, 639–654.
7. Shaheed O.S., Kazaal M.A. (2017). Association of a Disintegrin and Metalloproteinase 33 Gene Polymorphisms with Chronic Obstructive Pulmonary Disease in Iraqi Population. J. Pharm. Sci. & Res. 9(10), 2240-2243.
8. Mukherjee M., Nair P. (2018). Autoimmune responses in severe asthma. Allergy Asthma Immunol Res. 10, 428- 447.
9. Broughton S. E., Dhagat U., Hercus T. R., Nero T. L., Grimbaldeston M. A., Bonder C. S., *et al.* (2012). The GM-CSF/IL-3/IL-5 cytokine receptor family: from ligand recognition to initiation of signaling. Immunol. Rev. 250, 277–302.
10. Bochner B. S., Gleich G. J. (2010). What targeting eosinophils has taught us about their role in diseases. J. Allergy Clin. Immunol. 126, 16–25.

Czech
Journal of Multidisciplinary Innovations
Volume 21 September, 2023. ISSN (E): 2788-0389
Website: www.peerianjournal.com Email: editor@peerianjournal.com

11. Brusselle G., Germinaro M., Weiss S., Zangrilli J. (2017). Reslizumab in patients with inadequately controlled late-onset asthma and elevated blood eosinophils. Pulm. Pharmacol. Ther. 43, 39–45
12. Chipps B. E., Newbold P., Hirsch I., Trudo F., Goldman M. (2018). Benralizumab efficacy by atopy status and serum immunoglobulin E for patients with severe, uncontrolled asthma. Ann. Allergy Asthma Immunol. 120, 504–511.
13. Devos R., Guisez Y., Plaetinck G., Cornelis S., Tavernier J., van der Heyden J., *et al.* (1994). Covalent modification of the interleukin-5 receptor by isothiazolones leads to inhibition of the binding of interleukin-5. Eur. J. Biochem. 225, 635–640.
14. Dorman S. C., Efthimiadis A., Babirad I., Watson R. M., Denburg J. A., Hargreave F. E., *et al.* (2004). Sputum CD34+ IL-5Rα+ cells increase after allergen: evidence for in situ eosinophilopoiesis. Am. J. Respir. Crit. Care Med. 169, 573–577.
15. Pelaia, C., Paoletti, G., Puggioni, F., Racca, F., Pelaia, G., Canonica, G. W., & Heffler, E. (2019). Interleukin-5 in the Pathophysiology of Severe Asthma. Frontiers in physiology, 10, 1514.
16. Flood-Page P., Menzies-Gow A., Phipps S., Ying S., Wangoo A., Ludwig M. S., *et al.* (2003). Anti-IL-5 treatment reduces deposition of ECM proteins in the bronchial subepithelial basement membrane of mild atopic asthmatics. J. Clin. Invest. 112, 1029–1036.
17. Ghazi A., Trikha A., Calhoun W. J. (2012). Benralizumab – a humanized mAb to IL-5Rα with enhanced antibody-dependent cell-mediated cytotoxicity – a novel approach for the treatment of asthma. Expert. Opin. Biol. Ther. 12, 113–118.
18. Kazaal M.A., Habeeb A.A., Hasan H.N. (2023). Evaluation Role of IL-13 and Eosinophils in Adult Asthmatic Patients. Journal of Biomedicine and Biochemistry, 2 (2), 17-24.
19. Mishra V. (2004). Effect of obesity on asthma among adult Indian women. Int J Obesity. 28, 1048–1058.
20. Choi BS. (2021). Eosinophils and childhood asthma. Clin Exp Pediatr. 64(2),60-67.
21. Vergara CI., Acevedo N., Jiménez S., Martínez B., Mercado D., Gusmão L., Barnes K.C., Caraballo L. (2010). A Six-SNP haplotype of ADAM33 is associated with asthma in a population of Cartagena, Colombia. Int Arch Allergy Immunol.152(1), 32-40.
22. Gonzalez D., Benitez M., Quirce S. (2019). Benralizumab: a new approach for the treatment of severe eosinophilic asthma. J. Investig. Allergol. Clin. Immunol. 29, 84–93.
23. Greenfeder S., Umland S. P., Cuss F. M., Chapman R. W., Egan R. W. (2001). Th2 cytokines and asthma. The role of interleukin-5 in allergic eosinophilic disease. Respir. Res. 2, 71–79.
24. Hakonarson H., Maskeri N., Carter C., Chuang S., Grunstein M. M. (1999). Autocrine interaction between IL-5 and IL-1beta mediates altered responsiveness of atopic asthmatic sensitized airway smooth muscle. J. Clin. Invest. 104, 657–667.
25. Haldar P. (2017). Patient profiles and clinical utility of mepolizumab in severe eosinophilic asthma. Biol. Ther. Dent. 11, 81–95.
26. Hart T. K., Cook R. M., Zia-Amirhosseini P., Minthorm E., Sellers T. S., Maleeff B. E., *et al.* (2001). Preclinical efficacy and safety of mepolizumab (SB-240563), a humanized monoclonal antibody to IL-5, in cynomolgus monkeys. J. Allergy Clin. Immunol. 108, 250–257.

Czech
Journal of Multidisciplinary Innovations
Volume 21 September, 2023.
ISSN (E): 2788-0389
Website: www.peerianjournal.com
Email: editor@peerianjournal.com

27. Ip W. K., Wong C. K., Wang C. B., Tian Y. P., Lam C. W. (2005). Interleukin-3, -5, and granulocyte macrophage colony-stimulating factor induce adhesion and chemotaxis of human eosinophils via p38 mitogen-activated protein kinase and nuclear factor kappaB. Immunopharmacol. Immunotoxicol. 27, 371–393.
28. Kips J. C., O'Connor B. J., Langley S. J., Woodcock A., Kerstjens H. A., Postma D. S., *et al.* (2003). Effects of SCH55700, a humanized anti-human interleukin-5 antibody, in severe persistent asthma: a pilot study. Am. J. Respir. Crit. Care Med. 167, 1655–1659.
29. Koike M., Nakamura K., Furuya A., Iida A., Anazawa H., Takatsu K., *et al.* (2009). Establishment of humanized anti-interelukin-5 receptor α chain monoclonal antibodies having a potent neutralizing activity. Hum. Antibodies 18, 17–27.
30. Lambrecht B. N., Hammad H. (2015). The immunology of asthma. Nat. Immunol. 16, 45–56.
31. McGregor M. C., Krings J. G., Nair P., Castro M. (2019). Role of biologics in asthma. Am. J. Respir. Crit. Care Med. 199, 433–445.
32. Nair P., Wenzel S., Rabe K. F., Bourdin A., Lugogo N. L., Kuna P., *et al.* (2017). Oral glucocorticoid-sparing effect of benralizumab in severe asthma. N. Engl. J. Med. 376, 2448–2458.
33. Ortega H. G., Liu M. C., Pavord I. D., Brusselle G. G., FitzGerald J. M., Chetta A., *et al.* (2014). Mepolizumab treatment in patients with severe eosinophilic asthma. N. Engl. J. Med. 371, 1198–1207.
34. Park S. W., Kim D., Chang H. S., Park S. J., Lee Y. M., Park J. S., *et al.* (2003). Association of interleukin-5 and eotaxin with acute exacerbation of asthma. Int. Arch. Allergy Immunol. 131, 283–290.
35. Pelaia G., Vatrella A., Busceti M. T., Gallelli L., Calabrese C., Terracciano R., *et al.* (2015). Cellular mechanisms underlying eosinophilic and neutrophilic airway inflammation in asthma. Mediat. Inflamm. 2015:879783.
36. Pelaia, C., Paoletti, G., Puggioni, F., Racca, F., Pelaia, G., Canonica, G. W., & Heffler, E. (2019). Interleukin-5 in the Pathophysiology of Severe Asthma. Frontiers in physiology, 10, 1514.