

**Ministry of Health of the Republic of Uzbekistan
Tashkent Medical Academy**



Central Asian Journal of Medicine

№ 3 / 2022

Tashkent



1083

certificate

EDITORIAL BOARD

Editor-in-Chief

Alisher K. Shadmanov, DSc, M.D., Tashkent Medical Academy

Deputy Chief Editor

Oktyabr R. Teshaev, DSc, M.D., Tashkent Medical Academy

Executive Editor

Feruza Khidoyatova, DSc, M.D., Tashkent Medical Academy

Editorial Team

Anis L. Alyavi, Academician, DSc, M.D., The Republican Specialized Scientific and Practical Medical Center for Therapy and Medical Rehabilitation, Uzbekistan

Feruz G. Nazirov, Academician, DSc, M.D., The Republican Specialized Center of Surgery named after Academician V.Vakhidov, Uzbekistan

Ravshan D. Kurbanov, Academician, DSc, M.D., The Republican Specialized Cardiology Center, Uzbekistan

Shavkat I. Karimov, Academician, DSc, M.D., Tashkent Medical Academy, Uzbekistan

Turgunpulat A. Daminov, Academician, DSc, M.D., Tashkent Medical Academy, Uzbekistan

Laziz N. Tuychiev, DSc, M.D., Tashkent Medical Academy, Uzbekistan

Abdugaffar G. Gadaev, DSc, M.D., Tashkent Medical Academy, Uzbekistan

Dilbar K. Najmutdinova, DSc, M.D., Tashkent Medical Academy, Uzbekistan

Jae Wook Choi, DSc, M.D., Korea University, South Korea

Farkhad O. Akilov, DSc, M.D., Republican Specialized Center of Urology, Uzbekistan

Bakhtiyor U. Iriskulov, DSc, M.D., Tashkent Medical Academy, Uzbekistan

Nargiza N. Parpieva, DSc, M.D., Republican Specialized Scientific and Practical
Medical Center Of Tuberculosis And Pulmonology, Uzbekistan

Rikhsi A. Sabirova, DSc, M.D., Tashkent Medical Academy, Uzbekistan

Feruza L. Azizova, DSc, M.D., Tashkent Medical Academy, Uzbekistan

Barno T. Kholmatova, DSc, M.D., Tashkent Medical Academy, Uzbekistan

Raisa I. Shalina, DSc, M.D., Department of Obstetrics and Gynecology, Pediatric
Faculty, Russian National Research Medical University named after N.I. Pirogov,
Russian Federation

Antanas Vaitkus, DSc, M.D., Hospital of Lithuanian University of Health Sciences
Kaunas Clinics Academy of Medicine, Lithuania

Briko I. Nikolay, DSc, M.D., Honored Scientist of the Russian Federation,
Academician of the Russian Academy of Sciences, Professor, Chief Epidemiologist
of the Ministry of Health of the Russian Federation, Head of the Department of
Epidemiology and Evidence-Based Medicine, Sechenov University, Russian
Federation

Galina V. Yarovenko, DSc, M.D., Professor of Surgery Department, Samara State
Medical University, Russian Federation

Alisher O. Okhunov, DSc, M.D., Tashkent Medical Academy, Uzbekistan

Nargiza M. Nurillaeva, DSc, M.D., Tashkent Medical Academy, Uzbekistan

Assistant Editor

Abror Musakhonov, Tashkent Medical Academy, Uzbekistan

Jakhongir Khamdamov, Tashkent Medical Academy, Uzbekistan

Journal edited and printed in the computer of
Tashkent Medical Academy editorial department

Editorial board of Tashkent Medical Academy

Head of the department: M.N. Aslonov

English language editor: A.Kh. Juraev

Designer corrector: S.R. Sultonova

Organizer: Tashkent Medical Academy



FREQUENCY OF IL 12B GENE POLYMORPHISM AMONG PATIENTS WITH CHRONIC RHINOSINUSITIS POLYPOSIS

Ulugbek S. Khasanov ¹, Ulugbek N. Vokhidov ², Jamolbek A. Djuraev ³

1 MD, Professor, Head of the department of Otolaryngology and stomatology, Tashkent medical academy, Uzbekistan
E-mail: ukhasanov@yahoo.com

2 MD, Docent of the department of Otolaryngology, Tashkent State Dental Institute, Uzbekistan
E-mail: dr_ulugbek@list.ru

3 MD, Docent of the department of Otolaryngology and stomatology, Tashkent medical academy, Uzbekistan
E-mail: drdjuraev@mail.ru

ABSTRACT

Analyzing the prevalence of genotypic variants of this polymorphism, we revealed a direct association of the C/C monogenotype of the A1188C rs3212227 polymorphism in the IL12B gene with the development of polyposis processes. In addition, these data emphasize the prognostic significance of the C/C genotype of the rs1800896 polymorphism of the IL-12B gene in the development of CPMS. In carriers of this genotype, the relative risk of developing CPMS increases by more than 3 times, compared with carriers of other genotypic variants of the rs3212227 polymorphism of the IL12B gene.

Key words: paranasal sinuses, polyp, allele, genotyping.

INTRODUCTION

Diseases of the paranasal sinuses are among the most common pathologies in otorhinolaryngology, which is facilitated by the current environmental situation, the prevalence of allergic and viral respiratory diseases, and a decrease in local and general immunity. All researchers agree that in recent years there has been a tendency in the world to increase the incidence of chronic sinusitis, including chronic polypous rhinosinusitis (CPRS) [1,2,3].

Epidemiological studies of CPRS in Russia, which were conducted with an interval of 5 years, indicate that the prevalence of the disease does not change

significantly in selected time intervals in each specific region. Due to a number of reasons (environmental situation, social and drug load, changes in the functional parameters of the most important homeostatic systems of the human body, etc.), it is not necessary to expect a decrease in the incidence of CPRS. Leading otolaryngologists consider the stability of CPRS incidence rates, regardless of regional characteristics or other external factors, to be the basis for a more detailed study of the causes of this nosology [4], primarily the genetic predisposition to the development of CPRS. Many facts speak in favor of the genetic hypothesis of the development of CPRS. It has been proven that the risk of developing CPRS in the presence of polypous heredity is 25 times higher, with a heterozygous carrier of the MZ phenotype (deficiency of alpha-1 antitrypsinase) - 4 times, with a dry type of earwax - 3 times [5]; changes in karyotypes of peripheral blood cells in patients with CPRS were found [6]. Since chromosomal polymorphism can determine individual sensitivity to the occurrence of any disease, i.e. the individual response of the body to a damaging factor, persons with karyotype variants that differ from the norm are at risk of developing certain diseases depending on hypo-, hyper-, or normosensitivity of the hereditary apparatus [7,8,9,10].

Numerous studies of the last decade have demonstrated the dependence of the immune response on the allelic polymorphism of cytokine genes. The result of such work in vitro is the identification of individual alleles of genes associated with increased or decreased production of the corresponding cytokine [11]. The data obtained to date suggest that polymorphic cytokine genes are able to take an active part in the formation of a specific immune response to human pathological conditions. Individual allelic variants may be associated with the level of production of the corresponding protein, which also affects the course of the disease and the development of a number of complications. However, it remains unclear which mutations and which cytokines are of decisive importance in the development of individual diseases. Therefore, a promising direction of molecular genetic research is the study of the contribution of specific alleles to the tendency to infection in the development of pathology [12,13,14,15,16].

The current stage in the development of cytology, histology, and clinical anatomy, as well as progress in diagnostic technologies, has led to the concept of the nasal cavity as a complex morphofunctional system [17]. The modern knowledge of anatomy, histology and physiology, as well as the morphogenesis of various pathological processes in the nasal cavity and paranasal sinuses, obtained in the course of scientific research, has significantly expanded the understanding of the functional significance of these structures in the adaptive capabilities of the

nasal cavity to respiratory conditions, their role in the respiratory system in general [18,19].

Modern histological and clinical-functional studies have made it possible to ascertain the growth of chronic diseases of the mucous membrane of the nasal cavity and paranasal sinuses, the formation of various endonasal formations [20]. This is due to the deterioration of the ecological and social situation, increased virulence of the microbial flora, changes in its composition and resistance to antibacterial drugs. In the pathogenesis of diseases of the ENT organs, in addition to the infectious agent, the leading role belongs to the immune system of the mucous membranes of the nose and pharynx, as well as the general reactions of humoral and cellular immunity [21].

The body's resistance to exogenous and endogenous pathological factors is largely associated with the ability to quickly adapt to changing environmental conditions. The mucous membrane of the nasal cavity serves as the first protective barrier where local immunity reactions take place.

It is known that in many organs and tissues, including the nasal mucosa of the human body, there are neuroendocrine cells that belong to the link of autonomic regulation of organs. Moreover, the structural and functional features of neuroendocrine cells and their bioamine profile in patients with signs of polypous rhinosinusitis are practically not studied. Therefore, the study of the morphophysiological organization of the nasal mucosa in humans is an urgent problem of modern cytology, histology, and cell biology.

Given the above, we conducted a study of the genetic polymorphism of cytokine genes in patients with CPRS, the results of which demonstrate genetically determined features of the immune response that contribute to the development of CPRS, as well as determining some of the clinical features of the disease.

Material and methods:

In accordance with the purpose of the study and to fulfill the tasks set, clinical studies were conducted in 140 patients with CPRS and chronic rhinosinusitis, who were examined and treated in the ENT department of the multidisciplinary clinic of the Tashkent Medical Academy in 2017-2019. The examined patients met the following criteria: the presence of polypous tissue in the nasal cavity, wiping the common nasal passage completely or not less than 50%; complaints of prolonged difficulty in nasal breathing; according to the patient, the disease significantly reduces the quality of his life; absence of acute inflammatory pathology; written informed consent for surgical treatment and morphological examination of the surgical material (attached to the medical history).

To study the diallelic polymorphism of the promoter regions of the genes of the studied interleukins, 50 healthy (without CPRS) donors, men and women, were examined. The average age of the examined donors was 51.3 ± 1.44 years.

For real-time PCR, a commercial kit with SYBRGreen I dye (Litekh, Russia) was used. Polymorphism of five positions of the IL10 gene rs1800895 592C>A was studied. Genotyping of samples was carried out using real-time allele-specific polymerase chain reaction (PCR) on a DT-96 device (DNA-Technology) using SYBR Green I intercalating dye. The reaction mixture corresponded to the manufacturer's recommendations.

The reaction started with the activation phase of Taq polymerase (93°C , 1 min.). The next 35 PCR cycles consisted of denaturation (93°C , 10 sec), annealing (64°C , 15 sec), and elongation (72°C , 20 sec) phases. The signal was read at the elongation stage.

Results and discussion.

The values of the distribution of alleles and genotypes of the A1188C rs3212227 polymorphism in the IL 12B gene in the 1-2 group and control presented in table 1.

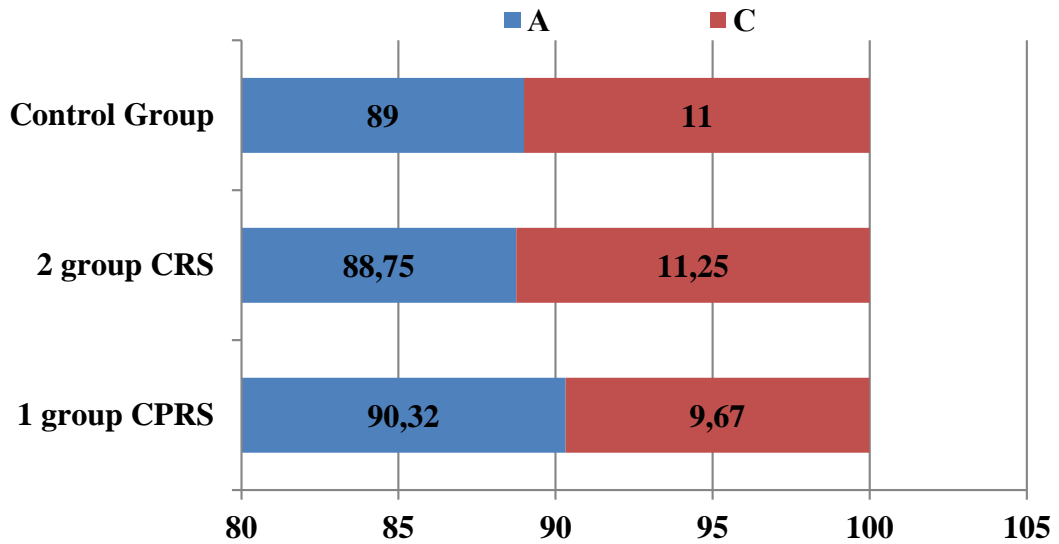
Table 1

The frequency of distribution of alleles and genotypes of the A1188C rs3212227 polymorphism in the IL 12B gene in groups of patients and controls

	Group	Allele frequency				Frequency distribution of genotypes					
		A		C		A\A		A\C		C\C	
		n	%	n	%	n	%	n	%	n	%
	CPRS n=31	56	90.32	6	9.67	25	80.64	6	19.35	0	0
	CRS n=40	71	88.75	9	11.25	31	77.5	9	22.5	0	0
	Control group n=73	130	89.0	16	11.0	57	78.1	16	21.9	0	0

Taking into account the fact that the detection of allele A prevailed in all groups of the study. It should be taken into account that in the frequency of detection of allele A in the 1st group slightly prevailed, relative to its values in the 2nd and control groups. The frequency of allele C, on the contrary, was slightly higher among patients of group 2, relative to its frequency in group 1 and the population sample.

The study of the distribution of genotypes showed that the homozygous A/A genotype was slightly, almost 1.2 times more often detected in group 1 (80.64%), while the frequency of detection of the heterozygous A/C genotype was insignificantly 1.1 times higher among patients with HRS 2 groups. The reverse situation could be observed in the study of the homozygous C/C genotype, which was not detected among all study groups (Figure 1.2).



Pic.1. The frequency of distribution of alleles of the A1188C rs3212227 polymorphism in the IL 12B gene in groups of patients and controls

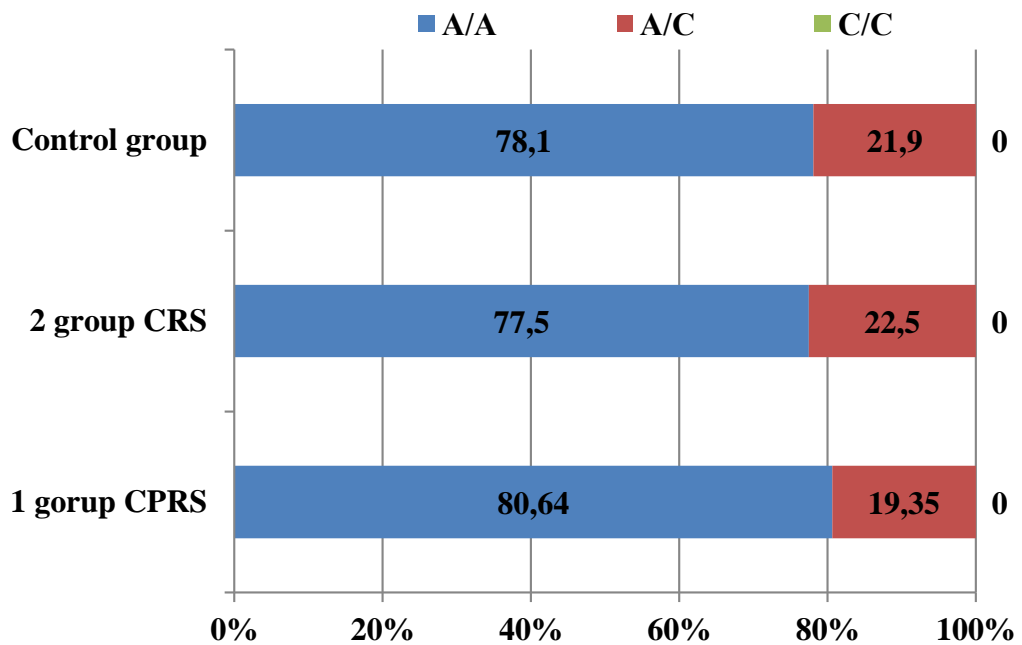


Fig. 2. Distribution frequency of A1188C rs3212227 polymorphism genotypes in IL 12B gene groups and subgroups of patients and controls

In table 2 presents the results of the analysis of the distribution of alleles and genotypes among representatives of the population sample and patients in groups 1-2.

Table 2

Differences in the frequency of occurrence of alleles and genotypes of the A1188C rs3212227 polymorphism in the IL 12B gene in the 1st and control groups

Alleles and genotypes	Number of examined alleles and genotypes				Xi ²	p	RR	+95%CI	OR	+95% CI
	CPRS		Control							
	n	%	n	%						
A	56	90,32	130	89,04	0,076	0,273	1,014	4,130	1,149	3,093
C	6	9,68	16	10,96	0,076	0,727	0,986	1,683	0,871	2,332
A/A	25	80,65	57	78,08	0,086	0,273	1,033	4,550	1,170	3,347
A/C	6	19,35	16	21,92	0,086	0,305	0,883	3,890	0,855	2,440

The analysis showed that if the frequency of allele A detection did not have statistically significant differences in detection in groups 1 and control, however, there was a tendency to increase its detection among patients with CPRS ($\chi^2 = 0.07$; $P = 0.2$; $RR = 1.01$; $OR = 1.14$; $95\% CI: 4.13-3.09$), while allele C, on the contrary, was characterized by a tendency to increase its occurrence among conditionally healthy individuals ($\chi^2=0.07$; $P=0.7$; $RR=0.98$; $OR=0.87$; $95\% CI: 1.68-2.33$).

An analysis of the frequencies of detection of the A/A genotype showed that among patients with CPRS this genotype was detected statistically insignificant less than 1.1 times more often than in the group of conditionally healthy individuals ($\chi^2=0.08$; $P=0.2$; $RR=1.03$; $OR=1.17$; $95\% CI: 4.55-3.34$). The study of the distribution of the A/C genotype showed the same picture, according to which a slight and statistically insignificant prevalence was found - 1.1 times the frequency of its detection in the control group of conditionally healthy individuals, relative to the detection values of this genotype in patients of group 1 with CRRS ($\chi^2=0.08$; $P=0.3$; $RR=0.88$; $OR=0.85$; $95\% CI: 3.890-2.44$).

The results of the analysis of the distribution of alleles and genotypes of the A1188C rs3212227 polymorphism in the IL 12B gene presented in Table 3 demonstrate the same indicators in patients with CRS and among conditionally healthy individuals.

Analysis of the distribution of A and C alleles showed a slight less than 1.0 times and statistically insignificant predominance of the A allele in the control

sample ($\chi^2=0.004$; $P= 0.36$; $RR=0.99$; $OR=0.97$; 95% CI: 2.95-2.30), and there was also a statistically insignificant, less than 1.0 times, predominance of the allele C among patients with CRS ($\chi^2=0.04$; $P=0.6$; $RR=1.0$; $OR=1.03$; 95% CI: 1.84-2.45).

It was found that the A/A genotype among conditionally healthy individuals is insignificant, less than 1.0 times higher than its frequency of detection among patients with CRS ($\chi^2 = 0.005$; $P = 0.35$; $RR = 0.99$; $OR = 0.96$; 95% CI: 3.18-2.43).

Table 3

Differences in the frequency of occurrence of alleles and genotypes of the A1188C rs3212227 polymorphism in the IL 12B gene in the 2nd and control groups

Alleles and genotypes	Number of examined alleles and genotypes				Xi ²	p	RR	+95%CI	OR	+95%CI
	CRS		Control							
	n	%	n	%						
A	71	88,75	130	89,04	0,004	0,360	0,997	2,959	0,971	2,305
C	9	11,25	16	10,96	0,004	0,640	1,003	1,846	1,030	2,454
A/A	31	77,5	57	78,08	0,005	0,360	0,993	3,184	0,967	2,432
A/C	9	22,5	16	21,92	0,005	0,352	1,027	3,293	1,034	2,592

It was also found that the heterozygous A/C genotype of the A1188C rs3212227 polymorphic locus in the IL 12B gene was evenly distributed in group 2 and in the control group, and its detection frequency was practically the same in both studied samples, with extremely low and statistically insignificant prevalence in the subgroup of patients with CRS ($\chi^2 =0.005$; $P=0.3$; $RR=1.02$; $OR=1.03$; 95% CI: 3.29-2.59).

The results of the analysis of the distribution of alleles and genotypes of the A1188C rs3212227 polymorphic locus in the IL 12B gene among patients with CPMS in comparison with group 2 are presented in table 4.

Analysis of the distribution of alleles A and G did not reveal statistically significant differences in the frequency of their detection in the 1b subgroup and in the control sample. Thus, the G genotype did not have significant and statistically significant differences in both studied groups, being practically at the same level in them, only slightly prevailing among conditionally healthy individuals.

Table 4

Differences in the frequency of occurrence of alleles and genotypes of polymorphism A1188C rs3212227 in the IL 12B gene in the 1- and 2-groups

Alleles and genotypes	Number of examined alleles and genotypes				Xi ²	p	RR	+95%CI	OR	+95%CI
	CPRS		CRS							
	n	%	n	%						
A	56	90,32	71	88,75	0,091	0,400	1,018	3,639	1,183	3,516
C	6	9,68	9	11,25	0,091	0,600	0,983	2,333	0,845	2,517
A/A	25	80,65	31	77,5	0,104	0,400	1,041	3,985	1,210	3,861
A/C	6	19,35	9	22,5	0,104	0,446	0,860	3,292	0,827	2,628

However, it was noted that the A genotype, which also had no significant and significant differences in the frequency of its distribution, slightly prevailed among patients with CPRS ($\chi^2=0.09$; $P=0.4$; $RR=1.01$; $OR=1.18$; 95% CI: 3.63-3.51).

The frequency of the A/A genotype was statistically insignificant, less than 1.0 times, prevailed among patients with CPRS relative to patients with CRS ($\chi^2=0.1$; $P=0.40$; $RR=1.04$; $OR=1.21$; 95% CI: 3.985 -3.86).

The A/C genotype, on the contrary, was insignificantly 1.1 times more likely to be detected among patients with CRS ($\chi^2 =0.1$; $P=0.44$; $RR=0.86$; $OR=0.82$; 95% CI: 3.292-2.62).

Conclusion

Thus, our data confirm the complexity of the genetic mechanism for the development of polyposis processes in patients with CPRS and indicate the need and importance of understanding complex gene interactions in the analysis of the development and clinical stage of the pathology under study. Analyzing the prevalence of genotypic variants of this polymorphism, we revealed a direct association of the C/C monogenotype of the A1188C rs3212227 polymorphism in the IL12B gene with the development of polyposis processes.

In addition, these data emphasize the prognostic significance of the C/C genotype of the rs1800896 polymorphism of the IL-12B gene in the development of CPRS. In carriers of this genotype, the relative risk of developing CPMS increases by more than 3 times compared with carriers of other genotypic variants of the rs3212227 polymorphism of the IL12B gene.

The absence of significant differences in the prevalence of IL12B gene genotypes among conditionally healthy donors and CRS patients may be due to the fact that the presence of an unfavorable polymorphism, in itself, is not enough for the development of this disease. In genetically predisposed persons, CPRS will develop according to the scheme of interaction in the "genotype-phenotype"

system (gene-environment). At the same time, the presence of unfavorable genotypic variants can influence the clinical course of the disease.

REFERENCES

1. Ayumi Fukuoka, Tomohiro Yoshimoto. Barrier dysfunction in the nasal allergy, *Allergology International*, Volume 67, Issue 1, 2018, Pages 18-23.
2. Blazej Grzeskowiak, Malgorzata Wierzchowska, Rafal Walorek, Malgorzata Seredyka-Burduk, Katarzyna Wawrzyniak, Pawel Krzysztof Burduk. Steroid vs. antibiotic impregnated absorbable nasal packing for wound healing after endoscopic sinus surgery: a randomized, double blind, placebo-controlled study. *Brazilian Journal of Otorhinolaryngology*. Volume 85, Issue 4, 2019, Pages 473-480
3. Chia-Yu Chiu, Gurchetan Randhawa, Khaled Nada, Ewa Tomczak, Addi Feinstein, Karen Hennessey. A nasal hypertrophic lesion as a presentation of herpes simplex virus, *IDCases*, Volume 15, 2019
4. Claus Bachert, Peter W. Hellings, Joaquim Mullol, Robert M. Naclerio, Jingdong Chao, Nikhil Amin, Annette Grabher, Brian N. Swanson, Jennifer D. Hamilton, Sophie Guillonneau, Christine Taniou, Donghui Zhang, Gianluca Pirozzi, Neil M.H. Graham, Heribert Staudinger, Leda P. Mannent, Asif Khan. Dupilumab improves patient-reported outcomes in patients with chronic rhinosinusitis with nasal polyps and comorbid asthma, *The Journal of Allergy and Clinical Immunology: In Practice*, Volume 7, Issue 7, 2019, Pages 2447-2449
5. Donald A. Leopold, David Elkayam, John C. Messina, Colette Kosik-Gonzalez, Per G. Djupesland, Ramy A. Mahmoud. NAVIGATE II: Randomized, double-blind trial of the exhalation delivery system with fluticasone for nasal polyposis, *Journal of Allergy and Clinical Immunology*, Volume 143, Issue 1, 2019, Pages 126-134
6. FR Ernst, R Imhoff, M Minshall, AS DeConde, RP Manes. PMD35 - Steroid-Eluting Sinus Implant Versus Revision Surgery for Patients with Recurrent Chronic Rhinosinusitis with Nasal Polyps (CRSWNP): An Economic Evaluation Model. *Value in Health*, Volume 21, Supplement 1, 2018, Page S165
7. G. Mortuaire, I. Gengler, M. Balden, M. Capron, G. Lefèvre. Impact of allergy on phenotypic and endotypic profiles of nasal polyposis, *European Annals of Otorhinolaryngology, Head and Neck Diseases*, Volume 135, Issue 3, 2018, Pages 159-162
8. K. Siva Balaji, B.N. Ashwini. 12. Shrinkage and non-recurrence of Ethmoidal Nasal Polyp with ayurvedic treatment – Case report. *Journal of*

Ayurveda and Integrative Medicine, Volume 9, Issue 2, Supplement 1, 2018, Page S2

9. Kanako Yoshida, Tetsuji Takabayashi, Yoshimasa Imoto, Masafumi Sakashita, Norihiko Narita, Shigeharu Fujieda. Reduced nasal nitric oxide levels in patients with eosinophilic chronic rhinosinusitis, *Allergology International*, Volume 68, Issue 2, 2019, Pages 225-232

10. Martin Desrosiers. Brave New (Microbial) World: implications for nasal and sinus disorders, *Brazilian Journal of Otorhinolaryngology*, 2019

11. Matthew Szymaszek, Gentian Toshkesi. Mount Fuji sign following nasal polypectomy: Conservative management of pneumocephalus, *Interdisciplinary Neurosurgery*, 2019

12. Philippe Lavigne, Stella E. Lee. Immunomodulators in chronic rhinosinusitis, *World Journal of Otorhinolaryngology - Head and Neck Surgery*, Volume 4, Issue 3, 2018, Pages 186-192

13. R. Jankowski, C. Rumeau, P. Gallet, D.T. Nguyen. Nasal polyposis (or chronic olfactory rhinitis), *European Annals of Otorhinolaryngology, Head and Neck Diseases*, Volume 135, Issue 3, 2018, Pages 191-196

14. R. Jankowski, D.T. Nguyen, A. Russel, B. Toussaint, P. Gallet, C. Rumeau. Chronic nasal dysfunction, *European Annals of Otorhinolaryngology, Head and Neck Diseases*, Volume 135, Issue 1, 2018, Pages 41-49

15. Shigeharu Fujieda, Yoshimasa Imoto, Yukinori Kato, Takahiro Ninomiya, Takahiro Tokunaga, Toshiki Tsutsumiuchi, Kanano Yoshida, Masanori Kidoguchi, Tetsuji Takabayashi. Eosinophilic chronic rhinosinusitis, *Allergology International*, 2019

16. Takahisa Koyama, Shin Kariya, Yasuharu Sato, Yuka Gion, Takaya Higaki, Takenori Haruna, Tazuko Fujiwara, Akira Minoura, Soshi Takao, Yorihisa Orita, Kengo Kanai, Masami Taniguchi, Kazunori Nishizaki, Mitsuhiro Okano. Significance of IgG4-positive cells in severe eosinophilic chronic rhinosinusitis, *Allergology International*, Volume 68, Issue 2, 2019, Pages 216-224

17. Taku Ito, Satoshi Ikeda, Tomoaki Asamori, Keiji Honda, Yoshiyuki Kawashima, Ken Kitamura, Keiko Suzuki, Takeshi Tsutsumi. Increased expression of pendrin in eosinophilic chronic rhinosinusitis with nasal polyps, *Brazilian Journal of Otorhinolaryngology*, 2018

18. Tsuguhisa Nakayama, Tomomitsu Hirota, Daiya Asaka, Masafumi Sakashita, Takahiro Ninomiya, Taiyo Morikawa, Mitsuhiro Okano, Shinichi Haruna, Naohiro Yoshida, Sachio Takeno, Yasuhiro Tanaka, Mamoru Yoshikawa, Junichi Ishitoya, Nobuyuki Hizawa, Sumito Isogai, Chihiro Mitsui, Masami Taniguchi, Hiromi Kojima, Shigeharu Fujieda, Mayumi Tamari. A genetic variant

near TSLP is associated with chronic rhinosinusitis with nasal polyps and aspirin-exacerbated respiratory disease in Japanese populations, *Allergology International*, 2019

19. Ugo Consolo, Pierantonio Bellini, Giuseppe Lizio. Trans-nasal endoscopic marsupialization of a voluminous radicular cyst involving maxillary sinus and nasal cavity: A case report and a literature review on this surgical approach, *Oral and Maxillofacial Surgery Cases*, Volume 4, Issue 3, 2018, Pages 91-96

20. Wejdan Alrasheed, Ali Almomen, Abdulrahman Alkhatib. A rare case of nasal septal schwannoma: Case report and literature review, *International Journal of Surgery Case Reports*, Volume 55, 2019, Pages 149-151

21. Yong Won Lee, Yong Min Kim. Antrochoanal polyp concomitant with turbinoethmoidal osteoma: A case report, *International Journal of Surgery Case Reports*, Volume 43, 2018, Pages 1-3

Contents

FREQUENCY OF IL 12B GENE POLYMORPHISM AMONG PATIENTS WITH CHRONIC RHINOSINUSITIS POLYPOSIS Ulugbek S. Khasanov, Ulugbek N. Vokhidov, Jamolbek A. Djuraev	5
GENDER AND AGE CHARACTERISTICS OF CHILDREN HOSPITALIZED WITH CORONAVIRUS INFECTION IN UZBEKISTAN Laziz N. Tuychiev, Umid E. Eraliev, Gulnara K. Khudaykulova Nilufar K. Djuraeva.....	16
AUTOIMMUNE DIATHESIS END RHEUMATOID ARTHRITIS IN CHILDREN Lola K. Rakhmanova, Akramjon M. Rakhmanov	22
PATHOPHYSIOLOGICAL SUBSTANTIATION OF THE USE OF A NEW DRUG BASED ON G. LUCIDUM AND ALKHADIA IN THE TREATMENT OF CORONAVIRUS INFECTION CAUSED BY SARS COV-2. Pulat M. Abilov, Bakhtiyor U. Iriskulov, Zukhra N. Boboeva	36
ASSESSMENT OF COGNITIVE FUNCTIONS IN PATIENTS WITH POST-COVIDAL CEREBROASTENIC SYNDROME Ulugbek D. Shadiev, G.S. Rakhimbaeva.....	45
ULINASTATIN IN THE CONSERVATIVE THERAPY OF CHRONIC PANCREATITIS Mirvosit M. Karimov, Pulat S. Zufarov, Go'zal N. Sobirova, Pulatova I. Nargiza, Shahlo S. Aripdjanova	54
TREATMENT OF ACUTE EROSIVE-ULCERATIVE GASTRODUODENAL BLEEDING M.Sh. Khakimov, U.I. Matkuliev, Sh.E. Ashurov, O.T. Sattarov, J.K. Dekhkonov.....	62
TREATMENT PROCEDURES FOR ANEMIA IN EXPERIMENTAL ANIMALS WITH LOCAL VEGETABLE PROTEIN PRODUCTS Mavlonjon Nasirdinov, Nizom Ermatov	72
NURSES' ROLE IN CARRYING OUT REHABILITATION ACTIVITIES IN HYPERTENSIVE PATIENTS Zarifa T. Usmanova, Mutabar A. Mirpayzieva, Barno H. Abdullaeva	80
EFFECT OF PLANT PHOTOSENSITIZER PSORALEN ON MITOCHONDRIAL STRUCTURES IN INFLAMMATORY PROCESSES Nigora F. Abdukhalikova, Bakhtiyor U. Iriskulov	88
COMPARATIVE ANALYSIS OF TREATMENT RESULTS IN PATIENTS WITH DAMAGE TO DUENUM IN DIFFERENT SURGICAL TACTICS S.A. Ruziboev, Kh.R. Amonov	99
MONITORING OF WATER POLLUTION IN HOT CLIMATES Guzal T. Iskandarova, Aziza M. Yusupxo'jaeva	109



MUHARRIRIYAT VA NASHRIYOT BO'LIMI

Volume – 13,62 usl. printer. Circulation – 100. Format 60x84. 1/8.
Listening means «Times New Roman». Printed in TMA editorial and publisher department.
100109. St. Farabi 2, Tel.: (998 71)214-90-64, e-mail: rio-tma@mail.ru