



ARTICLE INFO

Qabul qilindi: 25- Oktyabr 2024 yil Ma'qullandi: 28- Oktyabr 2024 yil Nashr qilindi: 31- Oktyabr 2024 yil

KEYWORDS

Chronic purulent rhinosinusitis, obesity, metabolic syndrome, inflammation, comorbidities, exacerbations, immune dysfunction, biochemical markers, upper respiratory tract, treatment outcomes.

CLINICAL CHARACTERISTICS OF CHRONIC PURULENT RHINOSINUSITIS IN PATIENTS WITH OBESITY

Nosirjonov M.A. Profmedservice clinics Republic of Uzbekistan https://doi.org/10.5281/zenodo.14038605

ABSTRACT

Chronic purulent rhinosinusitis (CPRS) is one of the most prevalent upper respiratory tract diseases, with a significant impact on patients, particularly when combined with metabolic disorders such as obesity. Obesity, as part of metabolic syndrome (MS), exacerbates the clinical course of CPRS by promoting systemic inflammation and immune dysfunction. This study aims to analyze the clinical, immunological, and biochemical features of CPRS in patients with and without metabolic syndrome.

A total of 127 patients with CPRS were examined between 2021 and 2023, divided into two groups: patients with CPRS alone (66 patients) and those with CPRS in combination with metabolic syndrome (61 patients). Clinical laboratory, radiological, and functional tests were conducted, with special attention to the duration of the disease, symptom presentation, and associated comorbidities.

The results demonstrated a significantly higher frequency of exacerbations in patients with CPRS and MS, with an average of 8.5 cases per year, compared to 4.63 in patients without MS. Metabolic syndrome was associated with increased systemic inflammation, as reflected by elevated glucose, ALT, and leukocyte levels, as well as the frequency of comorbidities, including bronchopulmonary, gastrointestinal, and endocrine diseases. These findings suggest that MS worsens the progression of CPRS, leading to more frequent relapses, higher rates of inflammation, and a more severe clinical course.

This study underscores the importance of a comprehensive therapeutic approach for patients with CPRS and metabolic syndrome, addressing both inflammation and metabolic dysfunction to improve treatment outcomes

CENTRAL ASIAN JOURNAL OF ACADEMICRESEARCHIF = 5.441

Relevance: Chronic purulent rhinosinusitis (CPRS) is one of the most common diseases of the upper respiratory tract, affecting every eighth patient per year among the adult population. The development of inflammatory diseases of the nose and paranasal sinuses occurs against the background of weakened immune defenses and metabolic disorders [1,5,8,16]. In recent years, special attention has been paid to the study of immunological features in patients with CPRS suffering from metabolic syndrome, which includes such components as obesity, insulin resistance, arterial hypertension and dyslipidemia. These factors have a significant impact on the immune status, potentiating chronic inflammation and changing the immune response [2,7,9,13, 17].

It is necessary to develop new objective methods for diagnosing chronic hepatitis C and determining the severity of the disease. Predicting the severity of the disease is important for determining the volume of personalized medical care [3,6,11,14,18]. In this regard, it seems promising to study the clinical, immunological and biochemical features of this pathology.

Materials and methods of research:To carry out this research work, 127 patients with chronic purulent rhinosinusitis were examined in the period from 2021 to 2023. The following groups were formed to conduct clinical, laboratory and instrumental studies: Group 1 - 66 patients diagnosed with chronic purulent rhinosinusitis; 2nd group – 61 patientsient, with an established diagnosis of chronic purulent rhinosinusitis with metabolic syndrome; 3rd comparison group - 35 patients, conditionally healthy people.

The diagnosis was determined based on clinical and functional data in accordance with the international consensus on the diagnosis and treatment of ENT diseases. (ICD-10). The diagnoses were verified based on a thorough collection of anamnesis, clinical, laboratory (general blood test, urine test) biochemical blood tests, instrumental (X-ray, MSCT, ultrasound). Particular attention was paid to the duration of the pathological process, past and concomitant diseases.

During clinical and radiological examination of patients the following parameters were determined: volume and localization of purulent process; characteristics of the lesion; period of the disease (exacerbation; remission)

Observation of patients was carried out in hospital and consultative dispensary settings.

Statistical processing of the factual material and graphic images were carried out using MS Excel 4.0 software. The reliability of the data was assessed using the reliability criterion (t).

Research results and their discussion:The average age of patients with chronic gastrointestinal reflux without metabolic syndrome was 44.9 ± 2.14 years, patients with chronic gastrointestinal reflux with metabolic syndrome - 51 ± 1.71 years. Age at the time of examination in patients from the studied groups did not reveal reliable differences. When analyzing gender, a reliable prevalence of females in the group of chronic gastrointestinal reflux with metabolic syndrome (62.3%) was revealed by 1.73 times compared to males (36.1%) (P < 0.05). In the group of chronic gastrointestinal reflux without metabolic syndrome, a frequent occurrence of females is also observed.

Data analysis showed differences in the frequency of exacerbations of chronic purulent rhinosinusitis (CPRS) between patients with metabolic syndrome (MS) and without it. The results showed that the average relapse rate in patients of the first group was 4.63±0.18 cases

per year. At the same time, in patients with CPRS and concomitant metabolic syndrome, the relapse rate was significantly higher, amounting to 8.5 ± 0.18 cases per year.

These data suggest that the presence of metabolic syndrome is associated with an increased frequency of relapses of chronic sinusitis. This may be due to the fact that metabolic syndrome, characterized by systemic inflammation and immune dysfunction, worsens the course of rhinosinusitis and increases the risk of recurrent episodes of the disease.

Analysis of complaints of patients with chronic purulent rhinosinusitis (CPRS) depending on the presence of metabolic syndrome (MS) shows differences in the frequency of symptoms. In the group without MS, decreased appetite was noted in 30.1% of patients, while in the group with MS - in 28.3%, which is 1.25 times less often. Sweating, on the contrary, was more common in patients with MS - in 32.3% against 28.5% in the group without MS, which is 1.13 times more. Lethargy was more common in the group without MS (38.2%) compared to the group with MS (43.1%), which is 1.13 times more often. Weakness was observed with almost the same frequency in both groups: 78.8% without MS. and 80.3% with MS, which is only 1.02 times more often in the group with MS. Headaches were more common in the group without MS (90.9%) compared to the group with MS (85.2%), which is 1.07 times more often. Sinus pain was also more common in the group without MS (25.8% versus 19.7%), which is 1.31 times more. Pale skin and fever, on the contrary, were more common in patients with MS. Pale skin was observed in 14.3% of patients with MS and in 15.5% without MS, which is 1.08 times more, and fever was observed in 70.5% of patients with MS and in 77.2% without MS, which is 1.09 times more often. Nasal discharge was observed more often in the group without MS (90.9% versus 85.2%), which is 1.07 times more. Difficulty breathing was noted in 100% of patients in both groups, indicating no differences in this symptom. Summarizing the obtained data on patient complaints in the two groups, it can be said that the presence of metabolic syndrome affects the frequency of some symptoms in patients with CHRS. Some symptoms, such as sweating, pale skin, and fever, are more common in patients with MS, while others, such as decreased appetite, lethargy, and sinus pain, are less common. However, some symptoms, such as weakness and difficulty breathing, remain virtually unchanged in both groups.

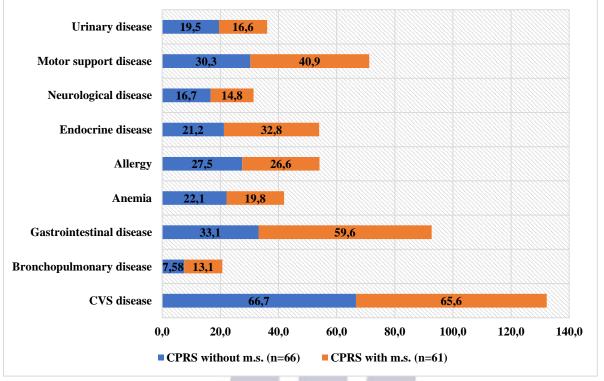


Fig. 1. Associated pathology inexamined groups (%), (P<0.05)

The study revealed differences in the frequency of comorbidities in patients with chronic rhinosinusitis (CRS) depending on the presence of metabolic syndrome (MS). The analysis showed that cardiovascular diseases (CVD) were almost equally common in patients with CRS both without MS (66.7%) and with MS (65.6%), without significant differences between the groups (p> 0.05). Bronchopulmonary diseases were 1.73 times more common in patients with MS (13.1%) compared to patients without MS (7.58%), which turned out to be statistically significant (p < 0.05). Gastrointestinal tract (GIT) diseases were significantly more common in patients with MS (59.6%) compared to patients without MS. (33.1%), with a difference of 1.80 times (p < 0.01). Anemia was slightly more common in patients without MS (22.1%) compared to patients with MS (19.8%), but this difference was not significant (p > 0.05). The frequency of allergic reactions was similar in both groups (27.5% in patients without MS and 26.6% in patients with MS), and the difference of 1.03 times was also not significant (p > 0.05). Endocrine diseases were 1.55 times more common in patients with MS (32.8%) compared to patients without MS (21.2%), which is a statistically significant difference (p < 0.05). Neurological diseases were slightly more common in patients without MS (16.7%) compared to patients with MS. (14.8%), but this difference of 1.13 times was not significant (p> 0.05). Diseases of the musculoskeletal system were more common in patients with MS (40.9%) compared to patients without MS (30.3%), with a difference of 1.35 times, which is significant (p< 0.05). Diseases of the urinary system were somewhat more common in patients without MS (19.5%) compared to patients with MS (16.6%), but this difference of 1.17 times was also not significant (p > 0.05). (Fig. 1)

Thus, the results show that the presence of metabolic syndrome has a significant impact on the incidence of a number of concomitant pathologies, especially those associated with the bronchopulmonary system, gastrointestinal tract, endocrine system and musculoskeletal system. Among the complications in both groups of those examined with CGRS, orbital processes such as reactive edemas were more common (unilateral sides - 23.9%, and bilateral - 4.79% on average). Nosebleeds were mainly found in the CGRS group with MS. The

incidence of auditory complications was almost the same in the CGRS group with MS and without it.

The accumulation of adipose tissue in the body is the main sign of obesity and is determined by the body mass index (BMI). BMI, in addition to being a diagnostic criterion for obesity, is also an indicator of the relative risk of developing obesity-related diseases, in particular metabolic syndrome. In this regard, we studied anthropometric parameters, which served as one of the criteria for dividing the groups examined.

When studying the BMI in the group of chronic obesity with m.s., a predominance of patients with excess body weight was revealed - 57.4% (n=35), patients with stage I obesity accounted for 32.8% (n=20), with stage II and III obesity accounted for 4.92% (n=3), respectively.

Anterior rhinoscopy revealed: In the CGRS group without MS, pale pink nasal mucosa was found in 32 patients (48.5%), cyanotic nasal mucosa in 9 patients (13.6%), hyperemia and swelling in 15 patients (22.7%), and dryness and atrophy of the nasal mucosa were observed in 9 patients (13.6%). In the CGRS group with MS, pale pink nasal mucosa was found in 29 patients (47.5%), cyanotic nasal mucosa in 16 patients (26.2%), hyperemia and swelling in 11 patients (18.0%), and dryness and atrophy of the nasal mucosa were observed in 5 patients (8.19%).

In the group with chronic respiratory distress syndrome without m.s., difficulty breathing due to nasal septum deviation was observed in 7 patients (10.6%), without respiratory distress - in 6 patients (9.1%), hypertrophy of the inferior turbinates - in 10 patients (15.1%), hypertrophy of the middle turbinates was detected in 4 patients (6.06%), and polyposis of the nasal passages - in 13 patients (19.7%). And in the group with chronic respiratory distress syndrome with m.s., nasal septum deviation was observed in 9 patients (14.7%), without respiratory distress - in 4 patients (6.55%), and hypertrophy of the inferior turbinates - in 15 patients (24.5%). hypertrophy of the middle turbinates was detected in 2 patients (3.27%), and polyposis of the nasal passages - in 9 patients (14.7%).

The presence of purulent discharge in the middle nasal passage in the group of chronic respiratory syndrome without m.s. was observed in 28 patients (42.4%), in the upper nasal passages - in 17 patients (25.7%). Purulent discharge from the lower nasal passages was observed in 13 patients (19.7%). Purulent discharge from the posterior wall of the larynx was observed in 8 patients (12.1%).

In the group of chronic respiratory distress syndrome with MS, purulent discharge in the middle nasal passage was observed in 25 patients (40.9%), in the upper nasal passages - in 15 patients (24.5%). Purulent discharge from the lower nasal passages was observed in 16 patients (26.2%). Purulent discharge from the posterior wall of the larynx was observed in 5 patients (8.19%).

When analyzing the functional methods of research, no reliable difference was found between the studied parameters, the data obtained indicate the presence of minor but potentially significant changes in blood pressure in patients with chronic heart failure and metabolic syndrome, which may reflect the negative impact of metabolic syndrome on the cardiovascular system. At the same time, differences in respiratory rate and pulse between the groups were minimal.

In patients with chronic purulent rhinosinusitis (CPRS) and metabolic syndrome (MS), specific changes in the general blood test are observed, reflecting a combination of the inflammatory process and metabolic disorders.

In the group of patients with chronic hepatitis C without MS, grade I anemia was more common (7.58% versus 6.56%), which is a difference of 1.02 times. And grade II anemia was observed in 3.03% of patients, which is higher compared to 1.64% in the group with MS. Grade III anemia had similar rates in both groups (1.52% versus 1.64%, respectively).

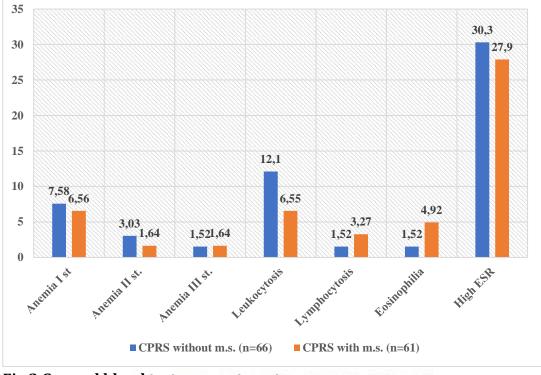


Fig.2.General blood test parametersat examined groups, (P<0.05)

Leukocytosis was significantly more pronounced in the CGRS group without MS (12.1% vs. 6.55%), with a difference of 5.55 times (P \leq 0.05). However, lymphocytosis and eosinophilia were more common in CGRS patients with metabolic syndrome: lymphocytosis was recorded in 3.27% vs. 1.52%, and eosinophilia in 4.92% vs. 1.52%, respectively. (Fig. 2)

High erythrocyte sedimentation rate (ESR), indicating the presence of an inflammatory process, was slightly lower in the group of chronic erythrocyte sedimentation with MS (27.9% versus 30.3%, respectively). Increased levels of eosinophils and lymphocytes reflect systemic inflammation, while more pronounced leukocytosis in patients without MS may be due to local inflammation in the sinuses. High ESR, despite chronic inflammation, is slightly lower in patients with MS, which may be associated with the body's adaptation to a long-term inflammatory process.

Thus, metabolic syndrome in combination with chronic hepatitis C increases lymphocytic and eosinophilic inflammation, while simultaneously reducing the severity of leukocytosis and ESR, which indicates a complex interaction of inflammatory and metabolic processes in these patients.

Metabolic syndrome has a significant impact on the frequency of elevated biochemical

CENTRAL ASIAN JOURNAL OF ACADEMIC RESEARCH IF = 5.441

www.in-academy.uz

parameters in patients with chronic suppurative rhinosinusitis (CPRS). The study found that in the group of patients with CPRS and metabolic syndrome, 16.4% had elevated alanine aminotransferase (ALT) levels, while in the group without metabolic syndrome, this figure was 9.09%. This difference indicates an almost twofold increase (1.8 times) in the probability of elevated ALT in patients with metabolic syndrome, which may be associated with the development of non-alcoholic fatty liver disease and insulin resistance (P < 0.05).

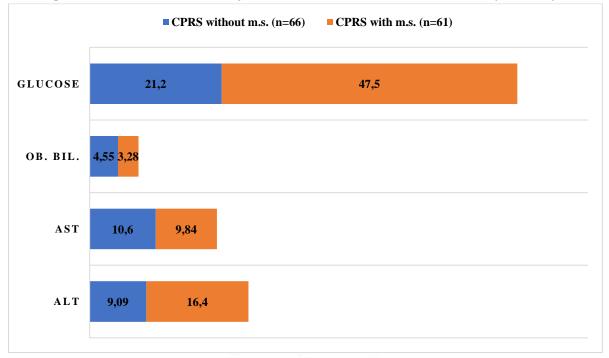


Fig.3.Blood biochemistry parameters, (P<0.05)

Aspartate aminotransferase (AST) levels remained relatively stable: 9.84% of patients with metabolic syndrome and 10.6% without it had elevated levels of this enzyme, indicating a slight decrease in the likelihood of elevated AST (by 1.07 times) in the presence of metabolic syndrome (P > 0.05). (Fig. 3)

The decrease in the frequency of increased total bilirubin in patients with metabolic syndrome is also noticeable: 3.28% versus 4.55% in the group without metabolic syndrome, indicating a probability of a decrease in the indicator by almost 1.4 times (P < 0.05). This may be due to impaired liver function in metabolic syndrome.

The most significant difference was observed in glucose levels, where 47.5% of patients with metabolic syndrome had elevated levels, compared to 21.2% in the group without metabolic syndrome. This indicates a more than twofold increase (2.24 times) in the likelihood of elevated glucose levels in patients with metabolic syndrome, confirming the presence of insulin resistance (P < 0.01).

These data highlight the importance of considering the metabolic status of patients when assessing biochemical parameters in the context of chronic rhinosinusitis.

The discovery of vitamins is a breakthrough in understanding the relationship between disease and health. Vitamin D, also known as the sunshine vitamin, was first identified in the early 20th century and was associated with research into rickets [4, 15]. In addition to its effects on calcium and phosphorus homeostasis, vitamin D is also involved in providing immunity against microbial pathogens. It has been shown toparticipation in the formation of local immunity of the musculoskeletal system, by actively influencing the biological functions

Table 1.

of bone cells, cartilage tissue and joint capsule, various processes and regulatory systems, including inflammation, immunity and response to therapy[10, 12].

Vitamin D in rheumatism has direct and indirect mechanisms of influence.Serum vitamin D levels vary significantly between populations and are influenced by many geographic and cultural factors [3, 11]. Although people living in Uzbekistan have a higher chance of exposure to sunlight; which is the main source of vitamin D, rheumatic pathologies remain one of the main causes of morbidity and mortality in the country. Since juvenile rheumatoid arthritis is a controversial and multifaceted pathological process, studying the concentration of vitamin D as one of the factors leading to the development of a vicious circle is relevant.

In the studied groups, the vitamin content in the blood serum was determined in all patients (Table 1).

Parameters	KHRS without MS (n=66)	HGR with m.s. (n=61)
Severe deficit < 10	25.75% (17)	34.4 (21)
Deficit 10 - 20	33.3% (22)	37.7 (23)
Failure 10 - 30	40.9% (27)	27.8 (17)

Vitamin D level in examined patients, ng/ml (p<0.05)

Analysis of the distribution of patients with different levels of parameter deficits in chronic purulent rhinosinusitis (CPRS) showed that metabolic syndrome has a significant impact on the level of these deficits. In the group of patients with metabolic syndrome, 34.4% had a pronounced parameter deficit (below 10), which is 8.65% (1.34 times) higher than in the group without metabolic syndrome. Parameter deficits in the range of 10-20% were recorded in 37.7% of patients with MS, which is 4.4% (1.13 times) higher than in patients without MS.

Interestingly, the failure rate in the 10-30% range was higher in the group without MS, amounting to 40.9% versus 27.8% in the group with MS, which is 13.1% (1.47 times) more.

The results highlight the need for more careful monitoring and correction of metabolic disorders in patients with metabolic syndrome to prevent the development of severe forms of deficiency and maintain overall health.

When collecting anamnesis, it was revealed that most of those examined were taking medications containing vitamin D. But, unfortunately,, Most people find it difficult to reach recommended intake levels of vitamin D, even if they consume a healthy and balanced diet, because rich food sources of vitamin D are rare.

X-ray examination revealed unilateral horizontal fluid level in the maxillary sinuses in 6 patients in the 1st group and in 8 patients in the second group, bilateral - in 5 patients in the 1st group and in 4 patients in the second group, in the frontal bone cavity - in 3 patients in the 1st group and in 4 patients in the second group. Reduction of unilateral homogeneous pneumatization in the maxillary sinuses - in 3 patients in the 1st group and in 5 patients in the second group, in the 1st group and in 5 patients in the

CENTRAL ASIAN JOURNAL OF ACADEMIC RESEARCH IF = 5.441

second group, in the ethmoid bone cavity - in 12 patients in the 1st group and in 15 patients in the second group. Bilateral decrease in homogeneous pneumatization of the maxillary cavity - in 2 patients in the 1st group and in 1 patient in the second group, in the ethmoid bone cavity - in 7 patients in the 1st group and in 9 patients in the second group. Decrease in homogeneous pneumatization of the maxilla and ethmoid cavities on one side - in 15 patients in the 1st group and in 5 patients in the second group, on both sides - in 7 patients in the 1st group and in 5 patients in the second group. Unilateral decrease in pneumatization intensity of all cavities was observed in 19 patients in the 1st group and in 20 patients in the second group and decrease in intense pneumatization of all cavities on both sides - in 4 patients in the 1st group and in 3 patients in the second group.

To exclude the presence of polyps in the paranasal sinuses, contrast radiography with iodolipol or urografin was performed. Radiographic contrast visualization of the nasal cavity provided information not only on pathological processes in the mucous membrane, but also on productive inflammatory changes in the mucous membrane, as well as on its effective inflammation, polyp formation, its shape, size and quantity.

Thus, the presence of metabolic syndrome significantly aggravates the clinical course of chronic purulent rhinosinusitis, increasing the frequency of exacerbations of the disease. In this group, concomitant pathologies are more often observed, such as diseases of the bronchopulmonary system, gastrointestinal tract and other endocrine pathologies, which requires a comprehensive approach to treatment taking into account these factors. Adding vitamin D to the standard of therapy in the treatment of patients with CHRS contributes to a more rapid restoration of metabolic disorders and strengthening of local immunity.

References:

1. Alieva V.Sh. Clinical and molecular genetic aspects of allergic rhinitis in Uzbekistan: dis. ... Doctor of Medicine: 14.00.36 /; Ministry of Health of the Republic of Uzbekistan, TMA. - T, 2012. - P.211.

2. Abdukayumov A. A. Main aspects of the relationship between clinical data and structural changes in patients with rhinosinusitis combined with chronic glomerulonephritis / A. A. Abdukayumov // Pediatrics. - Tashkent, 2016. - No. 4. - P. 9-13.

3. Boyko N. V., Lodochkina O. E., Stagnieva I. V. Prospects for the treatment of chronic rhinosinusitis // Russian Rhinology: scientific and practical journal / Russian Society of Rhinologists. - Moscow: Media Sfera Publishing House. - 2020. - Vol. 28 No. 4. - P. 235-240.

4. Boev V. I., Kokorina O. V. Effect of vitamin D3 level in blood serum and lactase gene polymorphism on the development of chronic rhinosinusitis with polyps // Bulletin of Otorhinolaryngology. - M., 2018. - Vol. 83 No. 5. - P. 49-54.

5. Dzhuraev Zh.A. Polyposis rhinosinusitlarining rivozhlanishida clinical geneticist omillarning ahamiyati va davolash samaradorligini oshirish : Tibbiyot fanlari daktori (DSe) dis. abstract: 14.00.04 / TMA / Zh. A. Juraev. - Tashkent, 2021. - 68 b.

6. Davydova A. P. Features of the practice of using fusafungine (bioparox) in the treatment of chronic rhinosinusitis in adolescents // Pediatrics. Journal named after G. N. Speransky. - M., 2014. - Vol. 93 No. 1. - P. 22.

7. Karpova E. P., Vagina E. E., Emelyanova M. P. Chronic rhinosinusitis in children // Pediatrics. Journal named after G. N. Speransky. - M., 2016. - Vol. 95 No. 2. - P. 110-113.

8. Kapustina T. A., Parilova O. V., Markina A. N. / Enzymatic activity of lymphocytes in chronic rhinosinusitis associated with chlamydial infection / Russian Rhinology. - M., 2013. - No. 1. - P. 16-18.

9. Agnieszka Gibała. Monika Pobiega Exacerbations of Chronic Rhinosinusitis—Microbiology and Perspectives of Phage Therapy Joanna Szaleniec 1, , October 2019.-R.987.

10.Allbegger KW Pathophysiology 0f acute rhinosinusitis //Wien. mesh Wschr.- 2018. -Vol. 104, N5.-P. 58-61.

11.Brook I. Vocum p., Frazier EH Bacteriology and beta - lactamase activity in acute and chronic maxillary sinusitis //Arch. Otolaryngol Heck. Surg•. -vol. 122, N4. -P. 418-422.

12. Fayzullaeva N.Ya. Raufov A.A./Clinical aspects of bronchial asthma and chronic obstructive pulmonary disease in adults /Academica: An international Multidisciplinary Research Journal-Vol. 11, Issue 2, February 2021; 297(1704) ; 297-235; doi:10.5958/2249-7137.2021.00486.9

13. Raufov A.A., Fayzullaeva N.Ya., Tairova S.F., Atajanova N.M. The relationship between vitamin D levels and obesity in patients with overlapping bronchial asthma and COPD. /中华

劳动卫生职业病杂志2021年月第39卷第7期Chin J Ind Hyg Occup Dis, 2021, Vol.39No.7/383/DOI10.5281/zenodo.5517628

14. Raufov A.A. ; Fayzullaeva N.Ya. / Clinical case of late detection of cftr gene mutation / \oplus \oplus

劳动卫生职业病杂志2021年月第39卷第7期Chin J Ind Hyg Occup Dis, 2021, Vol.39,

No.7/396/DOI10.5281/zenodo.5517738

15. Hoggard., Brett Wagner Mackenzie Chronic Rhinosinusitis and the Evolving Understanding of Microbial Ecology in Chronic Inflammatory Mucosal Disease Michael. January. 2017. Volume 30 Issue.-R.754-758.

16. Jae-Sung Nam. , Yun Ho Roh., Wasan Almazouq Fahad. Association between obesity and chronic rhinosinusitis with nasal polyps: a national population-based study. 2016.-R.1232-1236.

17.Van Cauwenberge PG, Vander Mijnsbrugge AM The microbiolog of acute and chronic sinusitis and otitis media: a review //Eur. Arch. Otorhinolaryngol. -2003. -Vol.250, suppl. 1. -P. 3-6.

18. Yao Liu. Head and Neck Surgery, Faculty of Medicine, Chulalongkorn University and King Chulalongkorn Memorial Hospital, Bangkok, Thailand.2020.No.1.-R.456