



Clinical-immunological characteristics of family bronchial asthma in Uzbek population

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ABSTRACT

The role of immunological mechanisms in bronchial asthma pathogenesis is widely discussed. Today, among patients with family bronchial asthma, there is no scientific study of the amount of total IgE, IL - 6, and interferon - γ , which is considered a bronchial asthma immunological marker in the bloodstream. The study evaluated the clinical trial characteristics and immune status of the disease in patients with family bronchial asthma in Uzbek populations. The study was conducted on patients with bronchial asthma in 49 families of the Uzbek population. Immunological tests in patients with bronchial asthma in the family have been investigated for general IgE and IL - 6, interferon - γ , which are considered bronchial asthma immunological markers in the bloodstream as part of the IFA method. Among patients with family bronchial asthma in the Uzbek population, an increase in the amount of total IgE and IL-6 among patients with allergic bronchial asthma, a decrease in IFN- γ , an increase in the total amount of IgE in monitored patients, and a reliable increase in IFN γ in unsupervised patients. The Uzbek population shows the important differential-diagnostic and prognostic value of the immune status indicators identified in patients with family bronchial asthma.

Keywords: Family bronchial asthma, immunological indicator, IgE, IL-6, interferon- γ .

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INTRODUCTION

Bronchial asthma (BA) defined as chronic inflammation and hyperreactivity of bronchi which leads to bronchial obstruction. [1,8,17,19,21]. Like other diseases, the characteristics of the clinical manifestation of BA is determined to some extent by the characteristics of the disease pathogenesis. Therefore, the role of immunological mechanisms in the pathogenesis of the disease is widely discussed in the work highlighted [2,3,7,10,15,16,18,20,22,23].

Cytokines, which are part of the immune system, act as the main key to bronchial asthma, participate in the development of chronic inflammatory processes and respond to the character of inflammation. One type of cytokines are interleukins (IL - 6 and interferon - γ), which intensify immune inflammation and anti-inflammatory effects in BA disease [4,5,9,24,28]. In bronchial asthma, IL - 6, interferon - γ , IgE are diagnostically significant [6,11,13,14,29].

So far, little has been done in the Uzbek population in terms of immunological status in patients with family BA. Today, among patients with family BA disease, there is no scientific study of the amount of total IgE, IL-6, and interferon - γ , which is considered an immunological marker in the bloodstream [12, 25,26].

It is intended to study clinical and immunological characteristics in patients with family BA in the Uzbek population. Studying the clinical characteristics and functional characteristics of the disease in Uzbek populations for patients with family bronchial asthma. Evaluation of immune status indicators for patients with family bronchial asthma in Uzbek populations on pathogenetic types of diseases, the severity of passing, and level of disease control.

MATERIAL AND METHODS

The study was conducted in a family of 49 Uzbek populations with bronchial asthma. A clinical-functional and immunological examination was conducted on 131 people infected with bronchial asthma in the family. Their average age is 23.41 [4; 78], with 52 (39.69%) being male and 79 (60.31%) women.

Diagnosis of BA disease was put in accordance with the Global Strategy for Treatment and Prevention of the BA (GINA 2022). 45 applied healthy individuals were examined for the control group.

Evaluation of the external respiratory function of the lungs in patients with family-identified BA was conducted in the "SPIROSIFT SP-5000" apparatus (FUKUDA DENSHI, Japan). Tests were conducted on the basis of the recommendation of the European Respiratory Society for "Standard of Functional Tests of the Lungs." Pharmacological functional testing for the study of obstructive ventilation disorders was conducted in 103 BA patients with β 2-agonists inhalation (Salbutamol, Ventolin, Berotek).

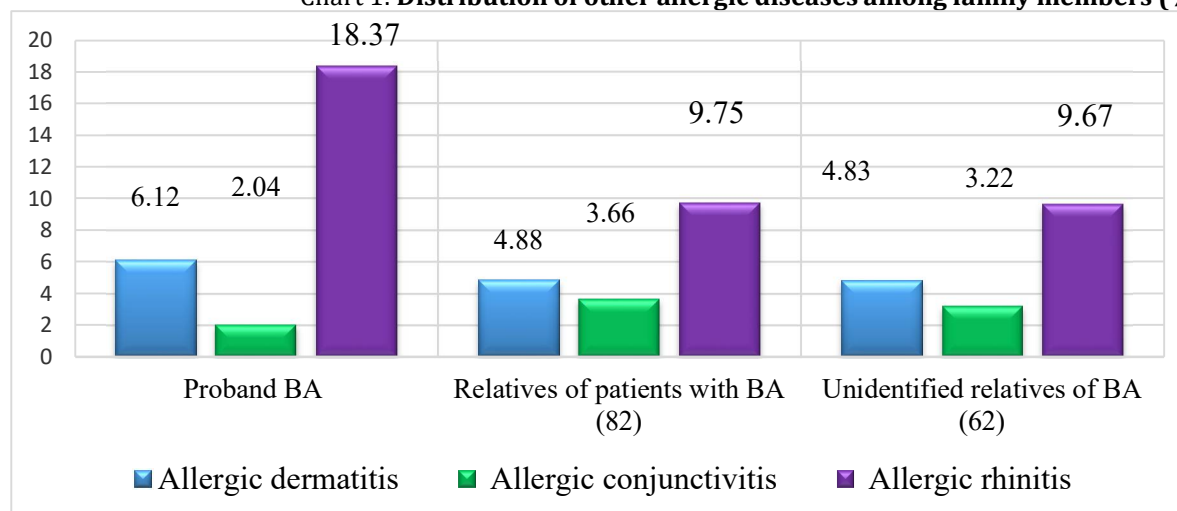
In patients with family BA disease, a general IgE and IL - 6, interferon - γ were examined in the bloodstream using the Vector-Best testing system manufactured in Novosibirsk, Russia. The results of the statistical processing of the data obtained were performed using Microsoft Excel on the Rentum-IV computer. The average arithmetic (M) and the average arithmetic value (m) were calculated for the normal distribution of the selected ones. The difference in reliability between indicators was assessed by the Student t-criterion.

RESULTS AND DISCUSSION

In many studies, it was emphasized that the occurrence of allergic diseases in patients with BA in the family is the effect of heredity. In order to assess the heredity and clinical-functional status of patients in the family, an analysis of the presence of concomitant allergic diseases was conducted in the identified patients in the family. Among 131 patients with BA in the family (49 probands + 82 relatives with BA), 28 (21.36%) had concomitant allergic diseases. Among them, 7 (5.34%) patients had allergic dermatitis, 4 (3.05%) patients had allergic conjunctivitis, and 17 (12.97%) patients had allergic rhinitis.

It was analyzed the occurrence of identified allergic diseases among the persons included in the family examination. Of the 49 probands in the family, 13 (26.53%) had other allergic diseases, of which 3 (6.12%) had allergic dermatitis, 1 (2.04%) had allergic conjunctivitis, and 9 (18.37%) had consisted of allergic rhinitis. 15 (18.29%) of 82 relatives with BA in the family had concomitant allergic diseases, 4 (4.88%) of them had allergic dermatitis, 3 (3.66%) allergic conjunctivitis and 8 (9.75%) and it turned out that one of them had allergic rhinitis. 11 (17.72%) of the 62 relatives in the family without BA identified in the study had concomitant allergic diseases, 3 of them (4.83%) had allergic dermatitis, 2 (3.22%) had allergic conjunctivitis, and 6 had allergic conjunctivitis. 9.67% of them had allergic rhinitis (chart 1).

Chart 1: Distribution of other allergic diseases among family members (%)

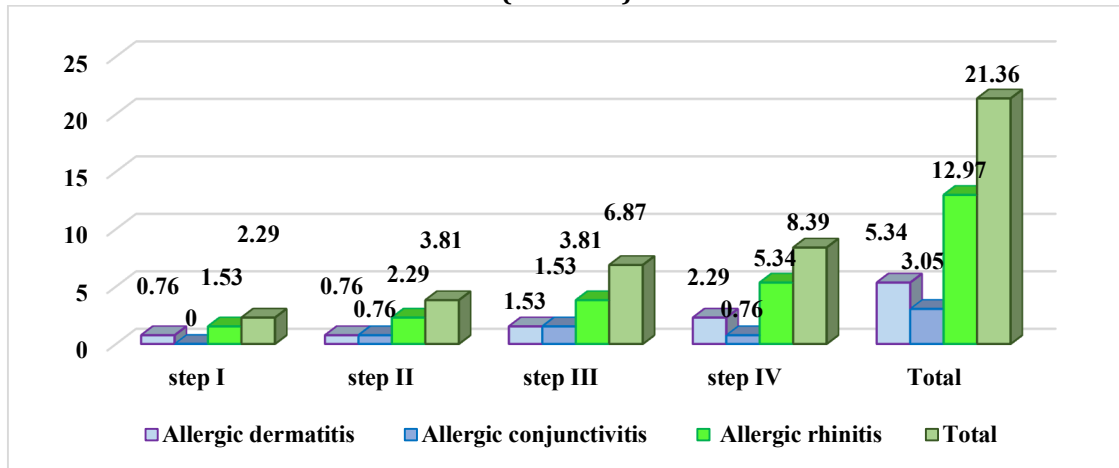


Our research conducted in families of the Uzbek population showed that in patients diagnosed with concomitant allergic diseases, it was observed that the disease often recurred and the disease was not fully controlled. This can be explained by the fact that 26.53% of the probands and 18.29% of the affected relatives had allergic rhinitis. During the research, 24.19% of concomitant allergic diseases were found in individuals without BA in the family, which indicates that they have a genetic background and are risk factors for the development of BA. This is the basis for conducting primary prevention among individuals who have not been diagnosed with BA in the family.

In order to study the relationship of concomitant allergic diseases to the clinical course of familial BA, an analysis of the occurrence of concomitant allergic diseases according to the severity of BA disease was conducted. It was noted that 28 (21.36%) patients with familial BA had concomitant allergic diseases, and 3 (2.29%) patients with step I BA disease had concomitant allergic diseases. 1 of them (0.76%) had

allergic dermatitis and 2 (1.53%) had allergic rhinitis. In the family, 5 (3.81%) patients with step II BA disease were diagnosed with concomitant allergic diseases, including allergic dermatitis 1 (0.76%), allergic conjunctivitis 1 (0.76%) and allergic rhinitis 3 (2.29%) was found in one patient. 9 (6.87%) of patients with step III BA disease in the family had accompanying allergic diseases, including allergic dermatitis 2 (1.53%), allergic conjunctivitis 2 (1.53%) and allergic rhinitis 5 (3.81%) was recorded in one patient. 11 (8.39%) of patients with step IV BA disease in the family had concomitant allergic diseases, including allergic dermatitis 3 (2.29%), allergic conjunctivitis 1 (0.76%) and allergic rhinitis 7 (5.34%) was observed in one patient (chart 2).

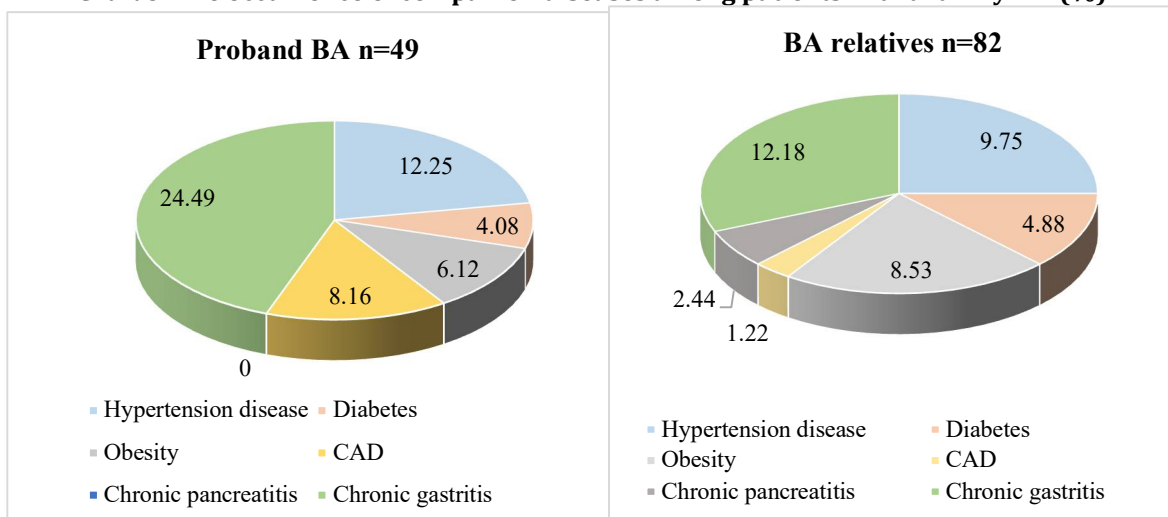
Chart 2: Distribution of allergic diseases identified in the family by the severity of the waiver (numbers)



In patients with familial BA determined in the family, in accordance with the increasing severity of the disease, an increase in the number of concomitant allergic diseases was observed. That is, allergic rhinitis is observed the most, it affects 1.53% of patients with step I disease, 2.29% of patients with step II disease, and 3.81% of patients with step III disease. in, 5.34% of patients with step IV. It has been proven that one of the risk factors for the development of a severe form of the disease in the family is concomitant allergic diseases, and it means the need to take early preventive measures for patients in the family.

59 (45.04%) of patients with familial BA have other accompanying somatic diseases: hypertension 14 (10.69%), diabetes 6 (4.58%), obesity 10 (7.63%), CAD 5 (3.82%) persons, 2 (1.53%) chronic pancreatitis and 22 (16.79%) chronic gastritis were found. Adjacent somatic diseases were identified in 27 (55.10%) of the probands: hypertension in 6 (12.25%), diabetes in 2 (4.08%), obesity in 3 (6.12%), CAD in 4 (8, 16%) and chronic gastritis in 12 (24.49%) and relatives with BA in the family in 32 (39.02%): hypertension 8 (9.75%), diabetes 4 (4.88%), 7 (8.53%) people had obesity, 1 (1.22%) people with obesity, 2 (2.44%) people with chronic pancreatitis, and 10 (12.18%) people with chronic gastritis (chart 3).

Chart 3 :The occurrence of companion diseases among patients with a family BA (%)

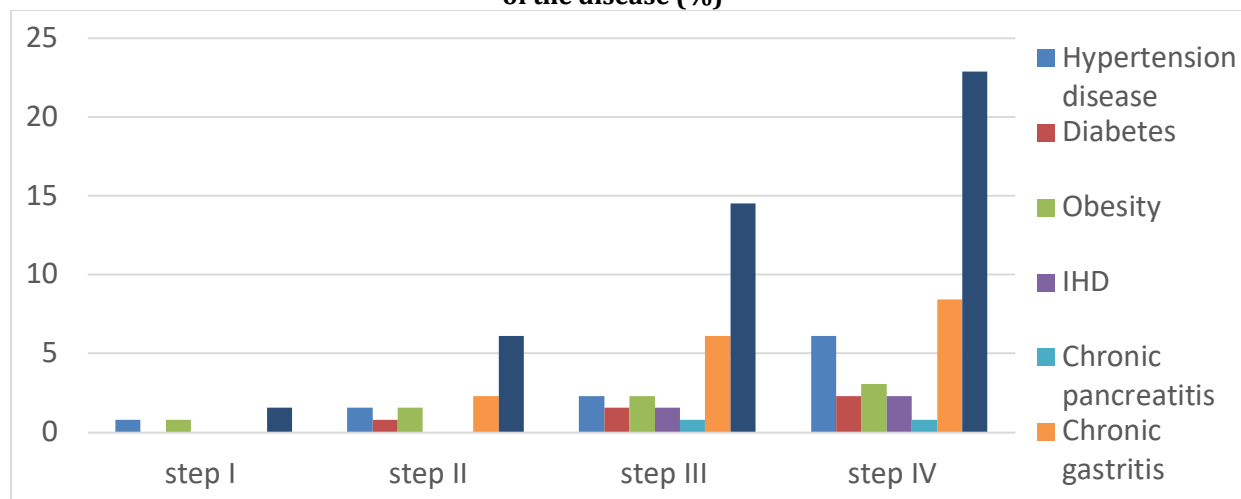


It can be recognized that one of the factors of the failure of standard treatment measures used in patients suffering from severe form of BA in the family and the failure to achieve complete control over the disease are the accompanying somatic diseases. Therefore, it can be explained that there is a need for early treatment in family patients and a method of planning the tactics of the disease.

When analyzing the occurrence of accompanying somatic diseases according to the severity of family BA, 2 (1.53%) patients were diagnosed with BA I step (hypertension 1 (0.76%) and obesity 1 (0.76%) persons), 8 (6.11%) persons diagnosed with step II (hypertension 2 (1.53%), diabetes 1 (0.76%), obesity 2 (1.53%) and chronic gastritis 3 (2.29%) persons), 19 (14.50%) persons diagnosed with step III (hypertension 3 (2.29%), diabetes mellitus 2 (1, 53%), obesity 3 (2.29%), CAD 2 (1.53%), chronic pancreatitis 1 (0.76%), chronic gastritis 8 (6.10%) persons), step III diagnosis 30 (22.90%) patients (hypertension 8 (6.11%), diabetes 3 (2.29%), obesity 4 (3.05%), CAD 3 (2.29%), chronic pancreatitis 1 (0.76%), chronic gastritis 11 (8.4%) patients were diagnosed with concomitant somatic diseases. The distribution of concomitant somatic diseases observed in family members with BA according to the severity of the disease is shown in chart 4.

Thus, with the increase in the severity of the disease in patients with familial BA, the occurrence of concomitant somatic diseases also increases. It can be considered as a basis for expressing the confirmation once again that it is necessary to create a specific treatment tactic.

Chart 4: Distribution of concomitant diseases between the family's BA and patients by the severity of the disease (%)



Based on the anamnesis data collected from the patients, the analysis of the duration of the disease in patients in the family was studied. Out of 131 patients identified in the family, 31 patients (23.7%) have been ill for 5 years. It was found that 9 (6.9%) of them had the disease with step I, 10 (7.6%) with step II and 12 (9.2%) with step III. No patients with IV step of the disease were identified in patients with a duration of illness up to 5 years.

42 (32.0%) had a family history of the disease for 5-10 years, of which 27 (20.6%) had step II disease, 3 (2.2%) had step III. It was found that 12 (9.2%) patients were ill with step IV. 39 (29.8%) patients had a duration of illness of 10-15 years, 14 (10.7%) of them had step II disease, 17 (13.0%) had step III disease, 8 (6.1%) patients were diagnosed with step IV. 19 (14.5%) patients with a disease duration of more than 15 years, 16 (12.2%) of them had the disease III step and 3 (2.3%) had the disease IV step it was found that his mother was ill [table 1].

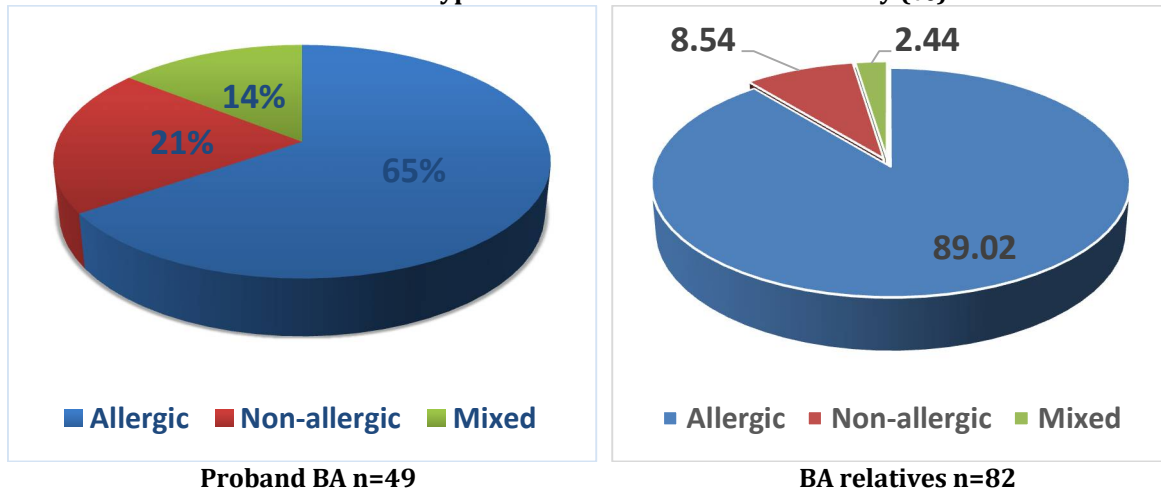
Table 1: Indicators of the severity of the disease according to the duration of BA disease in the family

| Duration of the disease | The degree of severity according to the course of the disease | | | | | | | | Total | |
|-------------------------|---|-----|---------|-----|----------|------|---------|------|-------|------|
| | Step I | | Step II | | Step III | | Step IV | | | |
| | n | % | n | % | n | % | n | % | n | % |
| 0 – 5 years | 9 | 6,8 | 10 | 7,6 | 12 | 9,1 | - | - | 31 | 23,5 |
| 5 – 10 years | - | | 1 | 0,8 | 27 | 20,5 | 15 | 11,4 | 41 | 31,0 |
| 10–15 years | - | | 1 | | 17 | | 8 | | 26 | |
| More than 15 years | - | | - | | 5 | | 11 | | 16 | |
| Total | 9 | 6,8 | 51 | | 48 | | 23 | | 131 | 100 |

The analysis of the duration of the disease in patients with familial BA showed that as the duration of the disease increased, it was expressed by the development of higher steps of the disease, the aggravation of the disease, and the lack of complete control over the disease. This was explained by the low quality of timely diagnosis, treatment and preventive measures of illness in the family.

Pathogenetic types of the disease were studied in 131 familial BA patients included in the study. In this case, 32 (65.31%) of the 49 probands in the family had an allergic disease, 10 (20.41%) had a non-allergic disease, and 7 (14.28%) had a mixed type of the disease, 73 (89.02%) of the 82 sick relatives) allergic, 7 (8.54%) non-allergic, and 2 (2.44%) with a mixed type [chart 5].

Chart 5: Clinical type of bronchial asthma in the family (%)



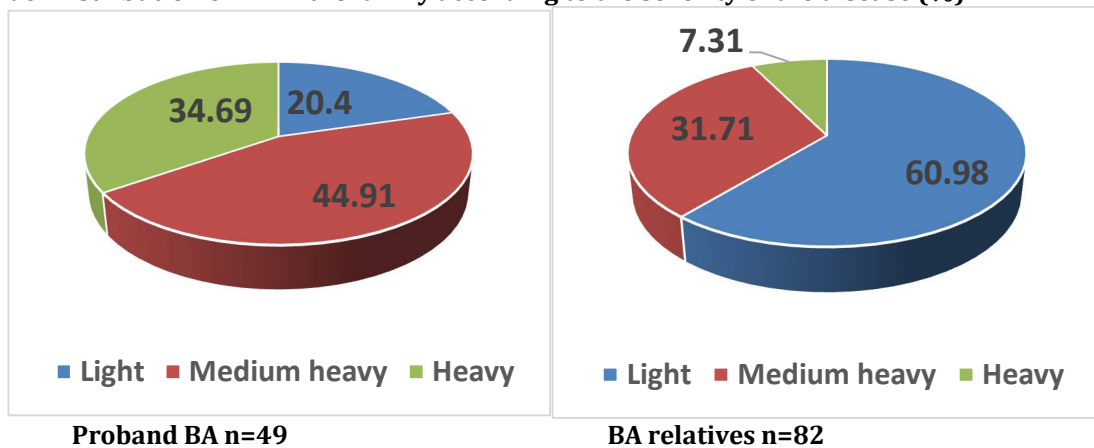
Thus, it was found that 65.31% of the probands and 89.02% of their relatives had an allergic type of the disease in the family, which indicates that the allergic type of the disease is inherited from generation to generation in patients with familial BA.

As a result of clinical and functional tests conducted in the family, the level of severity of the disease was assessed in 131 familial BA patients included in the study. Accordingly, 10 (20.40%) of the probands with BA in the family had mild disease, 22 (44.91%) had moderate disease, and 17 (34.69%) had severe disease. it was noted that he was infected with

Among family relatives, 50 (60.98%) patients had a mild degree of BA, 26 (31.71%) patients had a moderate degree, and 6 (7.31%) patients had a severe degree of the disease. was found to be infected [chart 6].

Based on the data in the picture, it should be noted that moderate (44.91%) and severe (34.69%) levels of the disease were more common in probands in the family, and more disease in relatives with BA. it was noted that he was infected with a light level (60.98%). This can be explained by insufficient control, treatment and preventive measures of the disease in the family.

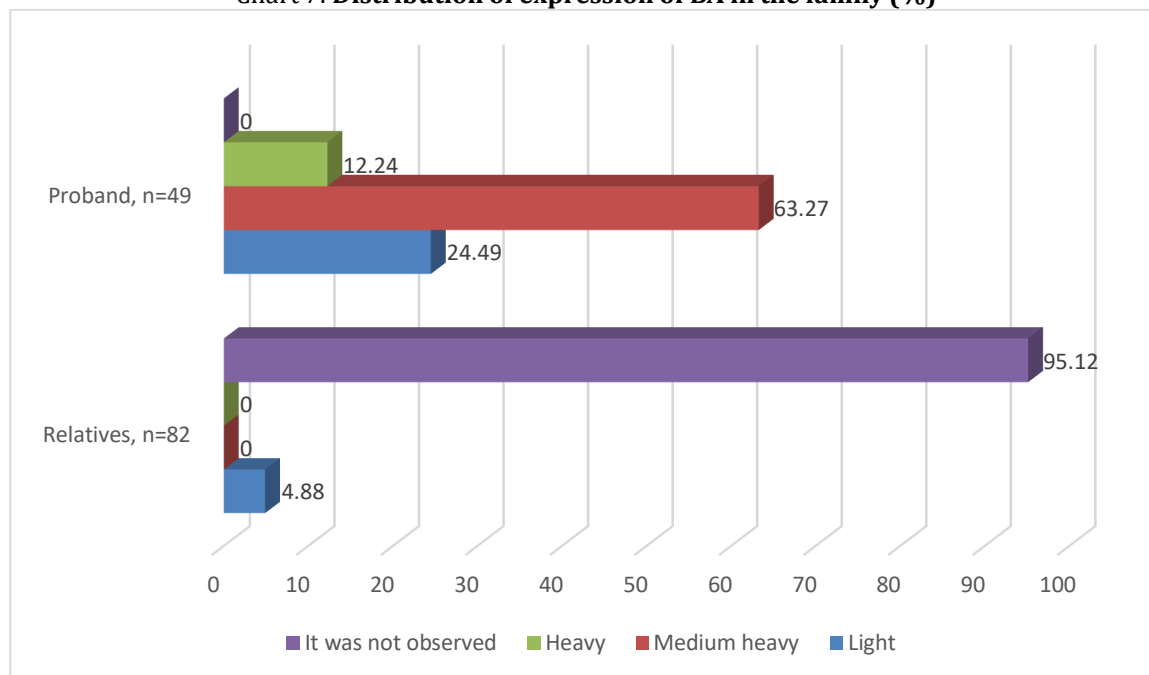
Chart 6: Distribution of BA in the family according to the severity of the disease (%)



When studying the degree of manifestation of the disease in family patients with BA, it was found that at the time of the study, 12 (24.49%) probands had mild BA disease, 31 (63.27%) probands had a mild disease. It was noted that the disease was moderately severe and 6 (12.24%) probands had a severe disease.

It was found that only 4 (4.88%) patients from family relatives had mild BA disease. It was noted that 78 (95.12%) of the relatives in the family with BA did not develop the disease at the time of the study. However, these patients are in the period of remission of the disease, and the diagnosis of the disease was made as a result of clinical and functional examination methods. The distribution of expression of BA disease in the family is shown in chart 7.

Chart 7: Distribution of expression of BA in the family (%)



In the Uzbek population, clinical and functional examinations of the families of patients with familial BA showed that in order to detect BA disease in family members early and express its severity level, TNF was checked, and obstructive ventilation disorders in the respiratory tract were the severity of the disease. changes corresponding to their levels were detected. In patients with familial BA, accompanying allergic diseases were observed, which indicated that there is a risk of developing the disease in the family. This situation showed the necessity of early preventive measures for patients in the family. In addition, concomitant somatic diseases were noted in patients with familial BA, which indicated that this disease is severe and requires specific treatment tactics.

In patients with familial BA, as the duration of the disease increases, the development of the course of the disease, the lack of complete control over the disease, and the worsening of the disease are observed. Allergic type of the disease was more common in the family (65.31% of probands, 89.02% of relatives), which indicated heredity with this allergic type. The severity of the disease was high in the family, and this was explained by the lack of control, treatment and preventive measures for the disease in the family. It can be said that these are the basis for early diagnosis, timely control of the disease, treatment and preventive measures in a family with familial BA.

In order to detect BA early in the family and to express its severity, the external respiratory function was investigated in those suspected of having BA in the family. The family analyzed the rates of external respiratory function in terms of severity of the disease in probands with BA. At the lightweight level of family BA, the average value of FEV1 was $84.51 \pm 1.94\%$, the average value of FVC was $89.22 \pm 2.04\%$, The average value of FEF25 was $85.22 \pm 1.39\%$, the average value of FEF25 was $80.27 \pm 2.31\%$, and the average value of FEF50 was $83 \pm 23 \pm 1.94\%$, and the average value of FEF75 was $90.34 \pm 3.11\%$.

At the moderately severe level of family BA, the average value of FEV1 was $74.28 \pm 1.87\%$, the average value of FVC was $80.49 \pm 2.89\%$, the PEF morning value was $77.49 \pm 1.81\%$, The average value of FEF25 was $76.31 \pm 1.89\%$, the average value of FEF50 was $72.90 \pm 5.66\%$, and the average value of FEF75 was $86.69 \pm 6.12\%$.

At a severe level, the average value of FEV1 was $58.87 \pm 2.29\%$, the average value of FVC was $78.24 \pm 3.20\%$, the PEF morning value was $58.59 \pm 2.63\%$, The average value of FEF25 was $63.20 \pm 6.47\%$, the average value of FEF50 was $60.16 \pm 5.12\%$, and the average value of FEF75 was $80.3 \pm 4.48\%$ [Table 2].

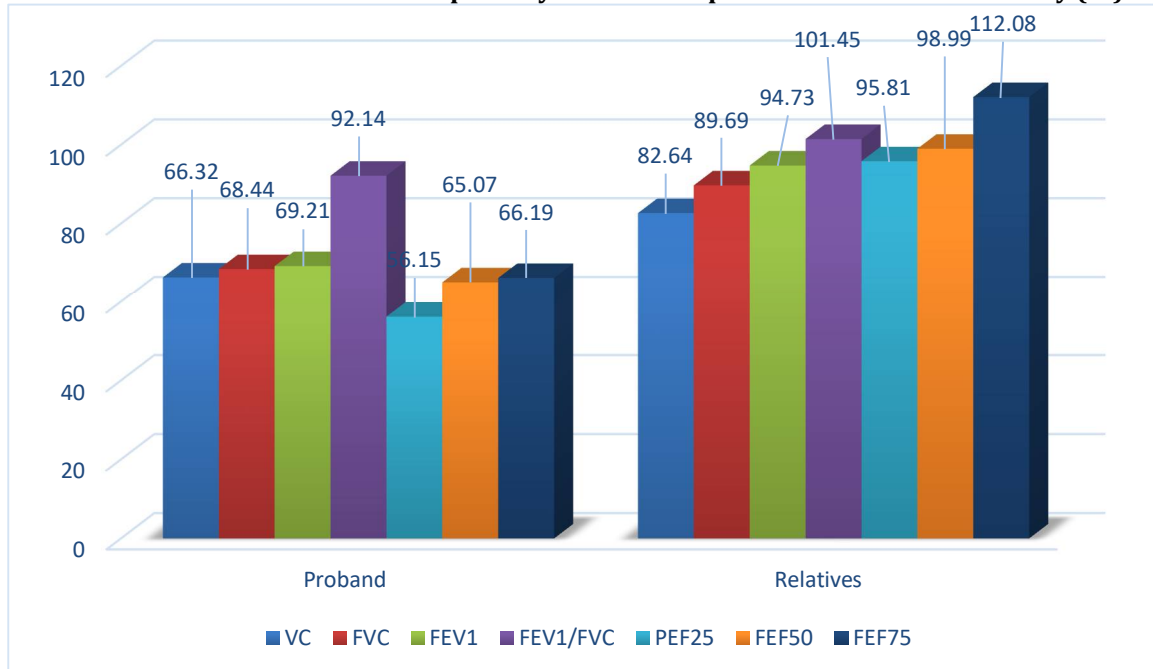
Table 2: Functional characteristics of the proband by weight level of BA

| External respiratory indicators | Severity of BA | | | P ₁₋₂ | P ₁₋₃ | P ₂₋₃ |
|---------------------------------|----------------|-------------------|------------|------------------|------------------|------------------|
| | Light n=10 | Medium heavy n=22 | Heavy n=17 | | | |
| FEV1, mean % | 84,51±1,94 | 74,28±1,87 | 58,87±2,29 | 0,017 | 0,036 | 0,186 |
| FVC, mean % | 89,22±2,04 | 80,49±2,89 | 78,24±3,20 | 0,04 | 0,002 | 0,02 |
| PEF morning value, % | 85,22±1,39 | 77,49±1,81 | 58,59±2,63 | 0,364 | 0,04 | 0,007 |
| FEF 25, % | 80,27±2,31 | 76,31±1,89 | 63,20±6,47 | 0,04 | 0,002 | 0,02 |
| FEF 50, % | 83,23±1,94 | 72,90±5,66 | 60,16±5,12 | 0,002 | 0,007 | 0,186 |
| FEF 75, % | 90,34±3,11 | 86,69±6,12 | 80,3±4,48 | 0,001 | 0,039 | 0,298 |

Thus, when we evaluated the rates of external respiratory function for probands with a determined family BA in the family, changes were made to match the severity of the disease. Checking the function of external breathing in these patients is one of the most advanced diagnostic methods, and family BA helps to make an early and timely diagnosis.

While the study was conducted, the external respiratory function was studied in patients diagnosed with family BA. Of the external respiratory conditions in the family, the average value of the VC is 66.32%, and the average value of FVC is 68.44%, The average value of FEV1 was 69.21%, the FEV1/FVC ratio was 92.14%, the average value of FEF5 was 56.15%, the average value of FEF50 was 65.07%, and the average value of FEF75 was 66.19%. Patients with family relatives, the average value of the VC is 82.64%, the average value of FVC is 89.69%, and the average value of FEV1 is 94.73%, The ratio to FEV1/FVC was 101.45%, the average value of FEF5 was 95.81%, the average value of FEF50 was 98.99%, and the average value of FEF75 was 112.08%[Chart 8].

Chart 8: Indicators of external respiratory function for patients with BA in the family (%)



Thus, it was found that the rates of external respiratory function in the family were considered diagnostic criteria for family BA, and they decreased reliably significantly compared to the rate of relatives infected with BA in probands. These indicators indicate a pronounced violation of the obstructive type of lung ventilation in probands, which indicates that the BA's disease is severe.

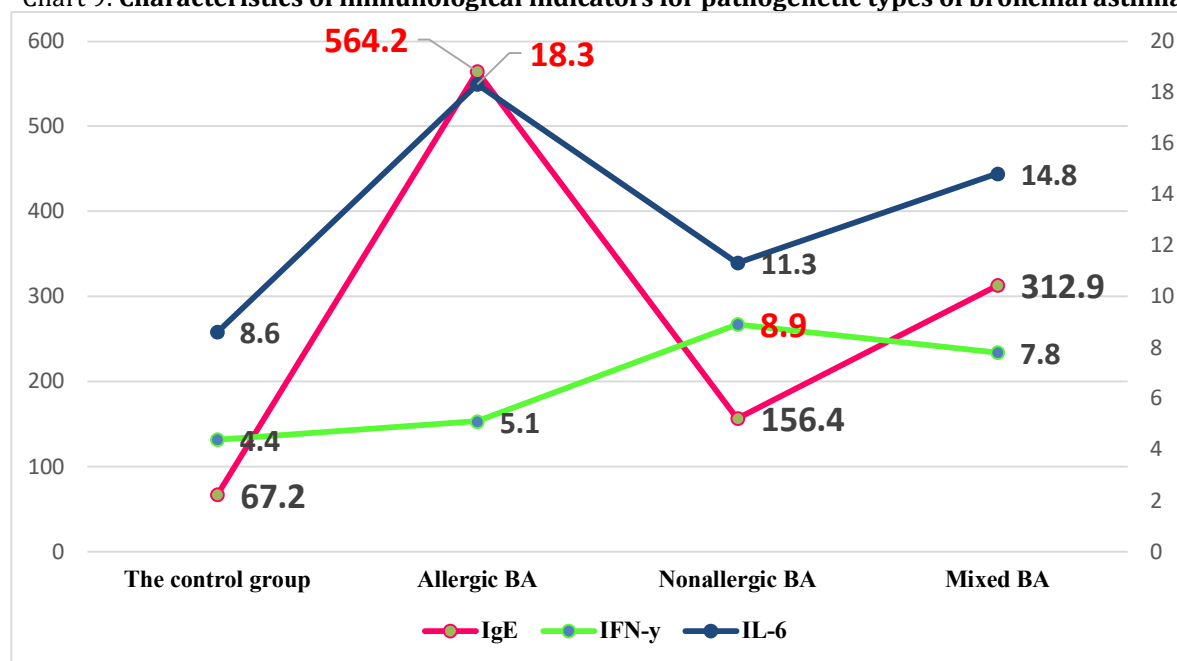
Based on the results of examination of patients, the level of production of total IgE, IL-6 and interferon-g detected in the peripheral blood serum of patients with pathogenetic types of familial BA was studied. The amount of total IgE, IL-6 and IFN-γ in peripheral blood serum of patients with allergic type of familial BA, respectively (564.2 ± 72.04 ME/ml; 18.3 ± 1.3 pg/ml; 5.1 ± 0.12 pg/ml) statistically reliable from the

indicator of practical healthy individuals (67.2±16.44 ME/ml; 8.6±2.4 pg/ml; 4.4±0.8pg/ml) increased (r<0.001, r<0.05).

The amount of total IgE, IL-6 and IFN-g in peripheral blood serum of patients with nonallergic type of familial BA, respectively (156.4±21.5 ME/ml; 11.3±1.06 pg/ml; 8.9 ±1.08 pg/ml) reliably exceeded the value of healthy individuals (67.2±16.44 ME/ml; 8.6±2.4 pg/ml; 4.4±0.8pg/ml) was noted (r<0.01, r<0.05).

Total IgE, IL-6 and IFN-γ levels in peripheral blood serum of patients with mixed type of familial BA, respectively (312.9±44.23 ME/ml; 14.8±1.23; 7.87±1, 28 pg/ml) was found to be reliably higher than the indicator of practically healthy individuals (67.2 ±16.44 ME/ml; 8.6±2.4; 4.4±0.8 pg/ml) (r<0.001 , r<0.05)[chart 9].

Chart 9: Characteristics of immunological indicators for pathogenetic types of bronchial asthma



The study of the level of IgE, IL-6 and IFN-γ products in patients with familial BA showed that the amount of inflammatory IgE and cytokines in the peripheral blood was high, regardless of the pathogenetic types of the disease. The amount of IgE, IL-6 and IFN-γ in peripheral blood serum was allergic (564.2±72.04 ME/ml; 18.3±1.3 pg/ml; 5.1±0.12 pg/ml) , nonallergic (156.4±21.5 ME/ml; 11.3±1.06 pg/ml; 8.9±1.08 pg/ml) and mixed (312.9±44.23 ME/ml; 14.8±1.23; 7.87±1.28 pg/ml) it was noted that a statistically reliable difference (p<0.001, p<0.01, p<0.05) was observed in pathogenetic types. This information about the immunological mechanisms in the pathogenesis of familial BA can be the basis for recommending a new differentiated approach to diagnosis and pathogenetic treatment that stops the development of inflammatory diseases of the respiratory tract. The highest index of total IgE detected in peripheral blood serum in the allergic type of the disease (564.2±72.04 ME/ml) confirms that it is a diagnostic immunological marker. Compared with other types of the disease in the family BA allergic type, it was shown that the increase in the amount of IL-6 in the peripheral blood serum of patients, and the decrease in the amount of interferon-g are comparative diagnostic markers for distinguishing pathogenetic types of the disease.

The immunological indicators of patients with BA in the family were evaluated according to the steps of the disease. Total IgE, IL-6 and IFN-γ levels in peripheral blood serum were significantly increased in patients with all steps of the disease according to the severity of familial BA. In step I of the disease, respectively (311.1±32.4 ME/ml; 18.2±2.9 pg/ml; 7.2±1.1 pg/ml) in the control group (67.2 ±16.44 ME/ml; 8.6±2.4; 4.4±0.8 pg/ml), respectively in step II (262.6±21.3 ME/ml; 17.7±2.1 pg/ml; 7.8±0.9 pg/ml) in the control group (67.2 ±16.44 ME/ml; 8.6±2.4; 4.4±0.8 pg/ml), III – pog in the mother, respectively (171.6±18.6 ME/ml; 14.5±2.7 pg/ml; 8.9±1.4 pg/ml) in the control group (67.2 ±16.44 ME/ml; 8.6±2.4; 4.4±0.8 pg/ml), respectively in IV step (132.3±12.7 ME/ml; 12.3±1.9 pg/ml; 9.6±1.2 pg/ml) in the control group (67.2±16.44 ME/ml; 8.6±2.4; 4.4±0.8 pg/ml) (p<0.001, p <0.01, p<0.02, p<0.05) [table 3].

Table 3: Characteristics of immunological indicators for the severity of bronchial asthma in the family

| Group | Immunological indicators | | |
|---------------|--------------------------|-------------------|------------------------|
| | IgE (ME/ ml) | IL-6 (pg/ ml) | IFN- γ (pg/ ml) |
| Control n=21 | 67,2 \pm 16,44 | 8,6 \pm 2,4 | 4,4 \pm 0,8 |
| Step I n=3 | 311,1 \pm 32,4**** | 18,2 \pm 2,9** | 7,2 \pm 0,9* |
| Step II n=16 | 262,6 \pm 21,3**** | 17,7 \pm 2,1*** | 7,8 \pm 0,7*** |
| Step III n=15 | 171,6 \pm 18,6**** | 14,5 \pm 1,2* | 8,9 \pm 1,4*** |
| Step IV n=8 | 132,3 \pm 12,7*** | 12,3 \pm 1,9 | 9,6 \pm 1,2*** |

Note: *-differences are significant compared to the indicators of the control group (*- $p < 0.05$, **- $p < 0.02$, ***- $p < 0.01$, ****- $p < 0.001$).

Thus, in patients with familial BA, with increasing steps of the disease, the amount of total IgE and IL-6 in the patient's blood serum decreased, but the amount of IFN- γ increased. Such changes in the amount of total IgE, pro-inflammatory and anti-inflammatory cytokines, which are criteria for allergic inflammation, can be evaluated as markers of the level of the inflammatory process in familial BA. In familial BA, it can be explained that as a result of deficiencies in the immune system, it causes the development and severity of the disease. This shows that it is a criterion for timely diagnosis of the disease and determining treatment tactics.

In patients with familial BA, the amount of total IgE in the peripheral blood serum of the duration of the disease up to 5 years - 304.2 \pm 24.9 ME/ml, up to 5-10 years - 271.6 \pm 26.7 ME/ml, up to 10-15 years - 189.4 \pm 25.8 ME/ml, over 15 years - 172.7 \pm 22.4 ME/ml, compared to the control group - 67.2 \pm 16.44 ME/ml, it was observed a reliable increase ($p < 0.001$).

In patients with familial BA, the amount of IL-6 in peripheral blood serum up to 5 years - 16.2 \pm 1.9 pg/ml, 5-10 years - 15.4 \pm 2.1 pg/ml, 10-15 years - 14, 6 \pm 1.3 pg/ml, over 15 years - 13.1 \pm 2.9 pg/ml, compared with the control group - 8.6 \pm 2.4 pg/ml, a statistically significant difference was observed ($p < 0.02$, $p < 0.05$).

In patients with familial BA, the amount of IFN-g in the peripheral blood serum of disease duration up to 5 years - 6.0 \pm 0.9 pg/ml, 5-10 years - 6.4 \pm 1.2 pg/ml, 10-15 years - 7, There was a significant difference in the values of 2 \pm 0.7 pg/ml, compared to the control group - 4.4 \pm 0.8 pg/ml. Only in the period of more than 15 years - 8.4 \pm 1.4 pg/ml, a reliable difference was noted ($p < 0.05$) [table 4].

Table 4: Immunological status of familial bronchial asthma according to disease duration

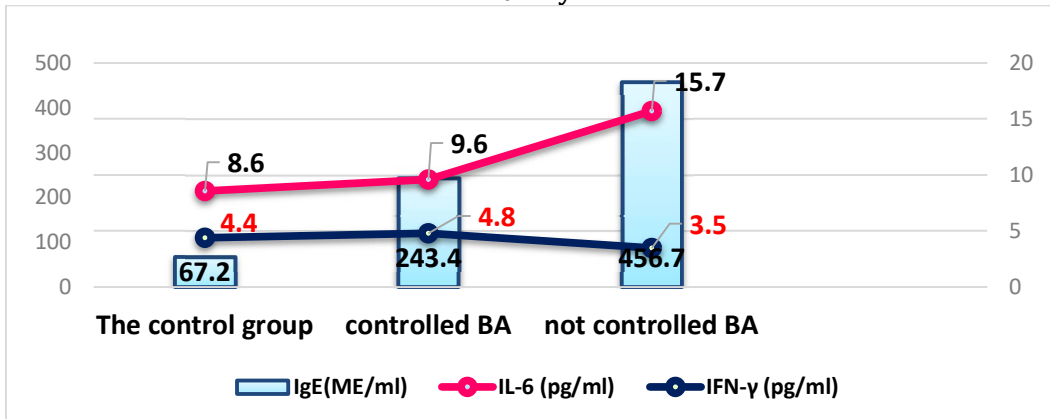
| Group | Control n=21 | 1-5 years n=10 | 5-10 years n=14 | 10-15 years n=12 | >15 years n=6 |
|---------------------|------------------|---------------------|---------------------|---------------------|---------------------|
| IgE ME/мл | 67,2 \pm 16,44 | 304,2 \pm 24,9*** | 271,6 \pm 26,7*** | 189,4 \pm 25,8*** | 172,7 \pm 22,4*** |
| IL-6 пг/мл | 8,6 \pm 2,4 | 16,2 \pm 1,9** | 15,4 \pm 2,1* | 14,6 \pm 1,3* | 13,1 \pm 2,9 |
| IFN- γ пг/мл | 4,4 \pm 0,8 | 6,0 \pm 0,9 | 6,4 \pm 1,2 | 7,2 \pm 0,7** | 8,4 \pm 1,4* |

Izoh: *-farqlar nazorat guruhi ko'rsatkichlariga nisbatan ahamiyatli (*- $p < 0,05$, **- $p < 0,02$, ***- $p < 0,001$).

The obtained results revealed that the study of immunological mechanisms in the pathogenesis of familial BA, i.e. the role of general IgE, IL-6 and IFN- γ is of great importance in the development and continuation of the inflammatory process of the respiratory tract in this pathology.

Immunological parameters determined in patients with familial BA were evaluated according to the level of disease control. The amount of total IgE in peripheral blood serum was significantly increased in patients with familial BA who did not reach control (456.7 \pm 32.8 ME/ml) compared to control patients (243.4 \pm 29.3 ME/ml) ($p < 0.001$). . Compared to the control group, the total IgE content (67.2 \pm 16.44 ME/ml) was found to be significantly different in both groups ($p < 0.001$). The amount of IL-6 in peripheral blood serum was significantly increased in patients with familial BA who did not achieve control (15.7 \pm 2.3 pg/ml) compared to control patients (9.6 \pm 1.9 pg/ml) ($p < 0.05$). The amount of IL-6 in the control group (8.6 \pm 2.4 pg/ml) was reliably increased compared to the control group ($p < 0.05$). It was noted that the amount of IFN-g in peripheral blood serum was significantly decreased in patients with familial BA who did not achieve control (3.5 \pm 0.8 pg/ml) compared to patients who achieved control (4.8 \pm 0.9 pg/ml). The amount of IFN- γ in the control group was 4.4 \pm 0.8 pg/ml [chart 10].

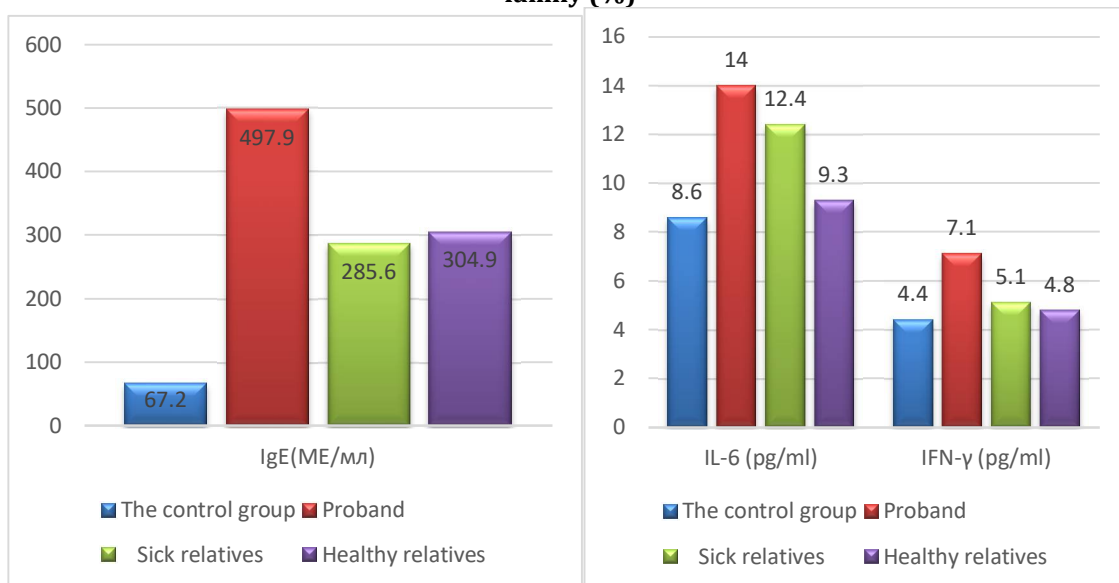
Chart 10: Characteristics of immunological indicators for controlling bronchial asthma in the family



The study of the level of total IgE and IL-6 showed that their content in the peripheral blood was high regardless of the period of disease control and uncontrolled ($p < 0.001$). It was noted that the amount of IFN-g was significantly reduced in those who did not achieve disease control. Thus, these indicators of cytokine products in the control of the disease were explained as the basis for a new approach to diagnosis.

It is known from the literature that the change in the immunological state of the body is one of the main causes of BA pathogenesis. IgE and cytokines, which are immunological markers of inflammation, depend on the level of expression, the step of the disease and the severity of the disease. It is of great importance in studying the immunological condition of the persons in the family, diagnosis, treatment and prevention. The amount of total IgE, IL-6 and IFN-g was analyzed in the control group (proband, relatives with familial BA and healthy people). In this case, the amount of total IgE in the peripheral blood serum was 304.2 ± 24.9 ME/ml in family probands, 271.6 ± 26.7 ME/ml in relatives with BA, and 189.4 ± 25.8 ME/ml in relatives without BA. made ml. When comparing these groups in the family with the value of immune indicators - 67.2 ± 16.44 ME/ml, it was statistically reliably higher ($p < 0.001$). The amount of IL-6 in peripheral blood serum in probands - 16.2 ± 1 , 9 pg/ml, in relatives with BA - 15.4 ± 2.1 pg/ml, in relatives without BA - 14.6 ± 1.7 pg/ml. In comparison with the indicator of the control group - 8.6 ± 2.4 pg/ml, it was expressed as a reliable increase in all the above groups ($p < 0.02$, $p < 0.05$). The amount of IFN-γ in peripheral blood serum was 7.1 ± 1.2 pg/ml in probands, 5.1 ± 0.9 pg/ml in relatives with BA, and 4.8 ± 0.8 pg/ml in relatives without BA. organized. In the control group, this indicator was recorded - 4.4 ± 0.8 pg/ml [chart 11].

Chart 11: Characteristics of immunological indicators in those who are divided into groups in the family (%)



Thus, total serum IgE levels were reliably elevated in all family groups examined, including probands, relatives with BA, and relatives without BA ($p < 0.001$). These sources confirm that the development of IgE-mediated mechanism plays a key role in the development of allergic inflammation in familial BA, and indicate the presence of an allergic background in relatives without BA. The levels of IL-6 and IFN- γ detected in the blood serum of patients in the family also showed that they correspond to the periods of the disease and are inflammatory biomarkers.

The correlation between IgE, IL-6 and IFN γ in groups studied in the family is shown in Table 5. In patients with familial BA, there is a statistically correct relationship between the pathogenetic types of the disease and the concentration level of IgE-IL-6 in all groups of patients, in the general group $r = 0.64$; $p < 0.01$, $r = 0.74$ in allergic type; $p < 0.01$ has a positive correlation, in non-allergic type $r = 0.11$; $p < 0.05$, $r = 0.25$ in mixed type; It was found that $p < 0.05$ has a weak positive correlation.

In patients with familial BA, there is a statistically inverse relationship between the pathogenetic types of the disease and the concentration level of IL-6-IFN- γ in all groups of patients, $r = -0.33$ in the general group; $p < 0.02$, $r = -0.21$ in allergic type; $p < 0.05$, $r = -0.41$ in non-allergic type; $p < 0.02$, it was found that there is a negative weakly expressed correlation relationship, no correlation relationship was observed in the mixed type.

In patients with familial BA, there is a statistically inverse relationship between the pathogenetic types of the disease and the level of IgE - IFN- γ concentration in all groups of patients, $r = -0.34$ in the general group; $p < 0.02$, $r = -0.30$ in allergic type; $p < 0.02$, the presence of a weakly expressed correlation relationship, in the mixed type $r = 0.22$; It was noted that $p < 0.05$ had a weak positive correlation, and no correlation was observed in the non-allergic type.

Table 5 : **Correlation of IgE , IL-6, and IFN γ in the groups studied**

| Patient group | Correlation indicators | | |
|----------------|------------------------|-------------------|-------------------|
| | IgE-IL-6 | IL-6-IFN γ | IgE- IFN γ |
| General group | 0,64 | -0,33 | -0,34 |
| p | <0,01 | <0,02 | <0,02 |
| Allergic BA | 0,74 | -0,21 | -0,30 |
| p | <0,01 | <0,05 | <0,02 |
| Nonallergic BA | 0,11 | -0,41 | 0,04 |
| p | <0,05 | <0,02 | >0,05 |
| Mixed BA | 0,25 | 0,04 | 0,22 |
| p | <0,05 | >0,05 | <0,05 |

The results of the conducted correlation analysis show that the development of cytokines in different pathogenetic forms of BA is unique. Table 4.4 shows that interleukins are more involved in the types of pathology, IgE-IL-6, IL-6-IFN- γ and IgE-IFN- γ are slightly less involved in patients with all types of the disease.

CONCLUSIONS

1. The presence of other allergic diseases in individuals with BA in the Uzbek population indicates that there are risk factors in the development of the disease and that the presence of concomitant diseases is one of the factors that do not adequately achieve the level of control of the disease
2. The resulting embryo was allowed to nutrients and then inserted into her womb, where it was implanted. This indicates the need for timely treatment and a preventive plan.
3. The high amount of general IgE identified in healthy relatives in the family indicates the need for primary prevention, indicating that they have other allergic diseases and are hereditary to the disease. Thus, the immune status indicators identified in patients with family bronchial asthma in the Uzbek population have important differential-diagnostic and prognostic implications.

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