

# Allergo-immunological characteristics of comorbid passage of allergic rhinitis in children

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**Abstract.** In this article, the clinical and immunological characteristics of the comorbid course of allergic rhinitis with bronchial asthma in children are highlighted. The study was conducted in the children's allergology department of the multidisciplinary clinic of the Tashkent Medical Academy, 50 patients with allergic rhinitis and 100 patients with bronchial asthma were involved. They studied the characteristics of the disease according to clinical symptoms (runny nose, sneezing, rhinorrhea, nasal itching) and immunological (general immunoglobulin E, A, M, G, specific IgE and skin scarification test).

## 1 Introduction

The diagnosis of allergic rhinitis was made according to generally accepted standards, i.e. the clinical presentation of the disease, allergological anamnesis, laboratory data (general blood analysis, total IgE and specific IgE antibodies in blood serum), skin scarification test, rhinoscopy and other tests were performed. The age of the patients in the study was 7 - 12, and the average age was  $4.1 \pm 0.31$ . In group 1, 100 patients with allergic rhinitis comorbid with bronchial asthma, in group 2 50 patients with allergic rhinitis, of which 2a - intermittent AR (IAR) (n=24) and 2b - persistent AR (PAR) (n=26) ) was divided into groups.

Nasal congestion is one of the main symptoms of AR in children [1-3]. In children, various nosological forms of AR were evaluated on a 4-point system according to the severity of nasal congestion (ARIA) scale. The evaluation system was evaluated as follows [4]: 0 points - free breathing through the nose. 1 point - slight difficulty in breathing through the nose. 2 points - a slight runny nose that does not affect the child's activity. 3 points - a significant runny nose without impaired activity. 4 points - from a significant runny nose with impaired activity to the inability to breathe through the nose at all.

## 2 Materials and research methods

During the evaluation, the majority of patients in all three groups had a significant respiratory disorder and impaired patient activity, from significant nasal stuffiness to total inability to breathe through the nose (4 points), i.e.: in patients with AR and BA in group 1 - 72 (72%),

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intermittent AR (IAR) in group 2a - 15 (62.5%) patients, in group 2b with persistent AR (PAR) - 17 (65.3%) patients ( $p < 0.001$ ), (Table 1).

**Table 1.** Assessment of the severity of nasal congestion in patients with different nosological groups and comorbidities of allergic rhinitis.

Points	points 1	point 2	points 3	points 4
1 group (AR +BA), (n=100)	7 (7%)	9 (9%)	12 (12%)	72 (72%)*
2 a group IAR (n=24)	-	4 (16.6%)	5 (20.9%)	15 (62.5%)*
2 b group PAR (n=26)	-	3 (11.5%)	6 (23.2%)	17 (65.3%)*

Note: \* -  $r < 0.001$ . the importance of within-group differences.

Difficulty in nasal breathing in children with various forms of AR causes a significant deterioration in the quality of life of patients and their families [4-6].

When comparing the severity of nasal congestion between the groups with IAR and PAR, patients with PAR had a significantly higher rate of nasal breathing disorder ( $r < 0.01$ ). When comparing patients with comorbid AR with BA with PAR group, almost no differences were found in the severity of nasal congestion ( $r > 0.05$ ).

The second clinical symptom that occurs in various forms of RA in children is rhinorrhea [7, 8]. This symptom was evaluated in a 4-point system as follows (table 2): 1 point - no rhinorrhea; 2 points - rhinorrhea is rarely observed; 3 points - significant rhinorrhea; 4 points - constant rhinorrhea.

**Table 2.** Evaluation of the severity of rhinorrhea in patients with different nosological groups of allergic rhinitis and comorbidities.

Groups	points 1	point 2	points 3	points 4
1 group(AR +BA), (n=100)	6 (6%)	15 (15%)	20 (20%)	59 (59.0%)*
2 a group IAR (n=24)	2 (8.4%)	4 (16.6%)*	6 (25%)	12 (50%)
2 b group PAR (n=26)	4 (15.4%)	15 (57.6%)*	7 (30%)	-

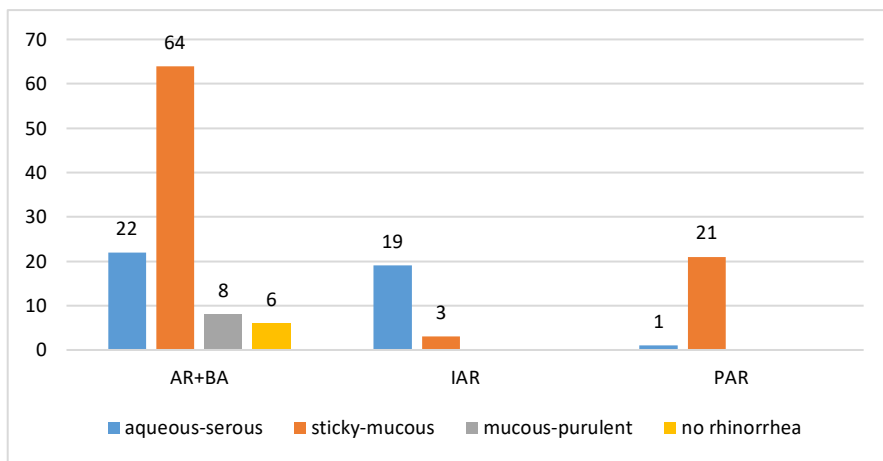
Note: \* -  $p < 0.001$ . the importance of within-group differences.

(59%) of children with AR+BA in group 1 and 12 (50%) patients with IAR in group 2 had rhinorrhea, which was observed constantly during the day and at night (4 points) ( $p < 0.01$ ). In group 2b, 15 (57.6%) of children with PAR had less frequent rhinorrhea (2 points) more often ( $p < 0.01$ ). According to the nature of rhinorrhea, AR+BA is comorbid. In group 1, it differed as follows: watery-serous in 22 (22%), viscous mucus - 64 (64%), mucus purulent nature - 8 (8%) and rhinorrhea was not detected in 6 (6%) patients. In group 2 with IAR, (19) watery-serous discharge was found in 79.1% of cases and (3) sticky mucous discharge in 12.5% of cases ( $r < 0.001$ ). In 2 b-groups with PAR, 21 (80.7%) of children had sticky mucous discharge ( $r < 0.001$ ). In 2 b-groups with PAR, 21 (80.7%) of children had sticky mucous discharge ( $r < 0.001$ ) [2, 5].

Thus, in 50% of cases with IAR, rhinorrhea was of a constant nature, and in 79.1% of cases there was a watery-serous discharge, which is explained by the increased sensitivity of pollen during flowering and characterizes the severe level of AR. Most of the patients with PAR (57.6%) had mild rhinorrhea, and in 80.7% of cases it was observed with discharge of sticky mucus, indicating a chronic course of AR. Continuously observed rhinorrhea in AR+BA in 59.0% of cases, the predominance of sticky mucous discharge over watery-serous and muco-purulent discharge in 64% of cases confirmed that it is chronic against the background of allergic and inflammatory processes. Comparing the 4-point rhinorrhea superiority between groups, higher reliability was confirmed in group 1 with AR+BA ( $r < 0.001$ ), (Figure 1).

The third clinical sign in AR is sneezing [9, 10]. This symptom was evaluated in a 4-point system according to the number of sneezes during the exacerbation of the disease. 1 point -

sneezes up to 5 times a day; 2 points - from 5 to 10 times a day; 3 points - from 10 to 20 times a day; 4 points - 20 or more times a day.



**Fig. 1.** The nature of rhinorrhea in patients with different nosological groups of comorbid and allergic rhinitis.

43 (43%) of patients with AR and BA comorbidity in group 1 had a sneeze grade of 3. In 13 (54.1%) children with IAR in group 2a, sneezing more than 20 times a day (4 points) during the day, at night and in the morning, when the highest concentration of pollen reached its peak, was found to be bothersome ( $r < 0.001$ ). 6 (25.0%) patients were bothered by sneezing up to 20 times (3 points) during the day and evening. 4 (16.6%) patients were observed to sneeze 5 to 10 times a day (2 points) during contact with the allergen. 10 (38.4%) of patients with PAR in group 2b had sneeze grade 3 and 11 (42.3%) children and 39 (39%) patients with AR+BA in group 1 had sneeze grade 4. No differences in sneeze preference (4 and 3 points) were found within the group ( $r > 0.05$ ) (Table 3).

**Table 3.** Assessment of the severity of sneezing in patients with different nosological groups of comorbid and allergic rhinitis.

Groups	points 1	point 2	points 3	points 4
1 group(AR +BA), (n=100)	3 (3%)	15 (15%)	43 (43%)	39 (39%)
2 a group IAR (n=24)	1 (4.1%)	4 (16.6%)	6 (25%)	13 (54.1%) *
2 b group PAR (n=26)	-	5(19.3%)	10 (38.4%)	11 (42.3%)

Note: \* -  $r < 0.001$ . the importance of within-group differences.

Thus, sneezing was found to be a mandatory symptom of AR in all groups of patients ( $r > 0.05$ ). In 43% of patients with AR+BA, moderate and in 39% of cases significant sneezing was accompanied by the disease, the intensity corresponds to the PAR group, which was explained that the increased allergic sensitivity of the respiratory organs is also associated with the presence of an inflammatory process. Sneezing of varying intensity occurred in 16.6%–54.1% of patients with IAR, and the observation of more than 20 times during the day and night was evident in this form of rhinitis compared to other forms. It was observed that PAR patients sneeze up to 20 times a day (38.4%) and more (42.3% of cases), which occurred more frequently throughout the year, day and night, especially during periods when sensitization to pollens and household allergens was noted. which aggravated the course of the underlying disease [11].

In children with different nosological forms of AR, the fourth symptom is itching in the nasal cavity during the exacerbation of the disease, which also played an important role in

the clinical presentation of the disease [4, 7, 11]. This sign was also evaluated on a 4-point scale: 1 point - does not bother; 2 points - rare; 3 points - average 4 points - constant (Table 4).

**Table 4.** Assessment of the severity of nasal itching in patients with different nosological groups of comorbid and allergic rhinitis.

Groups \ Points	points 1	point 2	points 3	points 4
1 group (AR+BA), (n=100)	3 (3.0%)	15 (15%)	19 (19%)	63 (63%) *
2 a group IAR (n=24)	-	5 (20.8%)	5 (20.8%)	14 (58.4%) *
2 b group PAR (n=26)	-	1(3.8%)	4 (15.4%)	21 (80.8%) **

Note: \* -  $r < 0.001$ , significance of intra-group differences; \*\*  $r < 0.05$ , significance of differences between groups.

Constant itching in the nose (4 points) was observed in 63 (63%) patients in group 1 with AR+BA, 14 (58.4%) in group 2a with IAR, and 21 (80.8%) in group 2b PAR ( $p < 0.01$ ). In group 2a patients with IAR, this process was explained by constant pollen sensitization and cross-reactivity caused by consumption of high- and medium-obligated foods. In group 1 and group 2b, nasal itching was observed during the day and evening as a result of sensitivity to pollen, household and house dust, and the presence of obligate allergens in food [10, 12].

Thus, persistent itching of the nasal cavity was observed in all three groups (63.0%, 58.4%, 80.8%), of which it was noted that patients with PAR were high (80.8%) and present throughout the year ( $p < 0.05$ ). In IAR, persistent itching (58.4%) was caused by pollen sensitization. In AR+BA patients, this sign (63.0%) was observed in the presence of the inflammatory process together with sensitization to pollen.

Humoral immunity was studied in children with different nosological forms of AR. The functional state of B-lymphocytes was evaluated by the level of immunoglobulins of class A, M, G in children with different nosological forms of AR and in healthy children (control group). The total immunoglobulin E level was determined.

Immunoglobulin class A (IgA) is synthesized by lymphocytes of the nasal mucosa and causes local immunity. In group 2 with AR aged 7 to 12 years, 65% of patients had increased IgA ( $2.4 \pm 0.41$  g/l) compared to healthy children ( $1.40 \pm 0.23$  g/l) ( $p < 0.01$ ). In children of AR+BA group 1, 39.3% of patients had increased IgA by  $2.9 \pm 0.53$  g/l ( $r < 0.001$ ). In group 2 of patients with AR, a decrease in IgA concentration was observed in 35.9% of patients ( $1.2 \pm 0.5$ g/l) (Table 5).

**Table 5.** Level of immunoglobulin IgA (g/l) in blood serum in patients and healthy children.

Groups	Healthy n=30	AR n=40	BA n=39	AR+BA n=33
	M±m	M±m	M±m	M±m
Young				
7-12 years old	$1.40 \pm 0.23$	$2.4 \pm 0.41$ **	$1.2 \pm 0.5$ **	$2.9 \pm 0.53$ ***

Note: \*  $r < 0.05$ ; \*\*  $r < 0.01$ ; \*\*\*  $r < 0.001$  - the reliability of the differences between the parameters of the groups of children whose indicators of the control group were examined. Thus, in the study of humoral immunity, an increase in IgA was noted in patients with AR and AR+BA ( $r < 0.01$ ;  $r < 0.001$ ), which concluded that immunological mechanisms are imperfect at this age and immunological processes are activated in response to allergen exposure.

Immunoglobulins of the M class (IgM) are produced in response to an acute infection, carry out antibacterial immunity. The change in IgM concentration was close to those in the control group (healthy children) ( $r > 0.05$ ), (Table 6).

**Table 6.** Level of immunoglobulin IgM (g/l) in blood serum in patients and healthy children.

Groups	Healthy n=30	AR n=35	BA n=36	AR+BA n=35
	M±m	M±m	M±m	M±m
Young 7-12 years old	1.31±0.12	1.39±0.2	1.30±0.24	1.40±0.31

Note: \*r < 0.05; reliability of differences between groups' indicators;

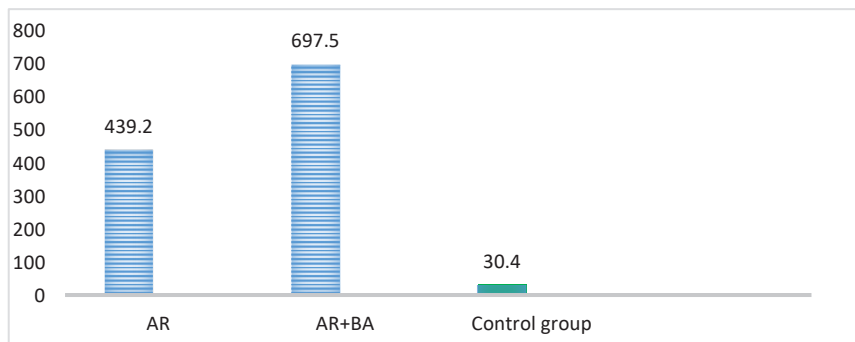
Immunoglobulins of the G class are the most important effectors of humoral immunity, which are characterized by a decrease or suppression of the humoral immune response. Based on the analyzes conducted between healthy children and patients with different nosological forms, certain changes were noted in all three groups. In group 1 (AR+BA), IgG (5.7±0.98\*\*g/l) decreased (p < 0.001). A decrease in the humoral part of the immune system is associated with the continuous and recurrent continuation of the allergic process in the mucous membrane of the nasal cavity (Table 7). In the AR and BA groups (10.2±1.27 g/l and 10.9±1.9 g/l), an increase of IgG was noted compared to the healthy group (9.8±2.08 g/l) (r < 0.01).

**Table 7.** Level of immunoglobulin IgG (g/l) in blood serum in patients and healthy children.

Groups	Healthy n=30	AR n=50	BA n=36	AR+BA n=100
	M±m	M±m	M±m	M±m
Young 7-12 years old	9.8±2.08	10.2±1.27	10.9±1.9*	5.7±0.98 **

Note: \*\* r < 0.01; \*r<0.001; the reliability of the differences between the background indicator and the indicators of the control group.

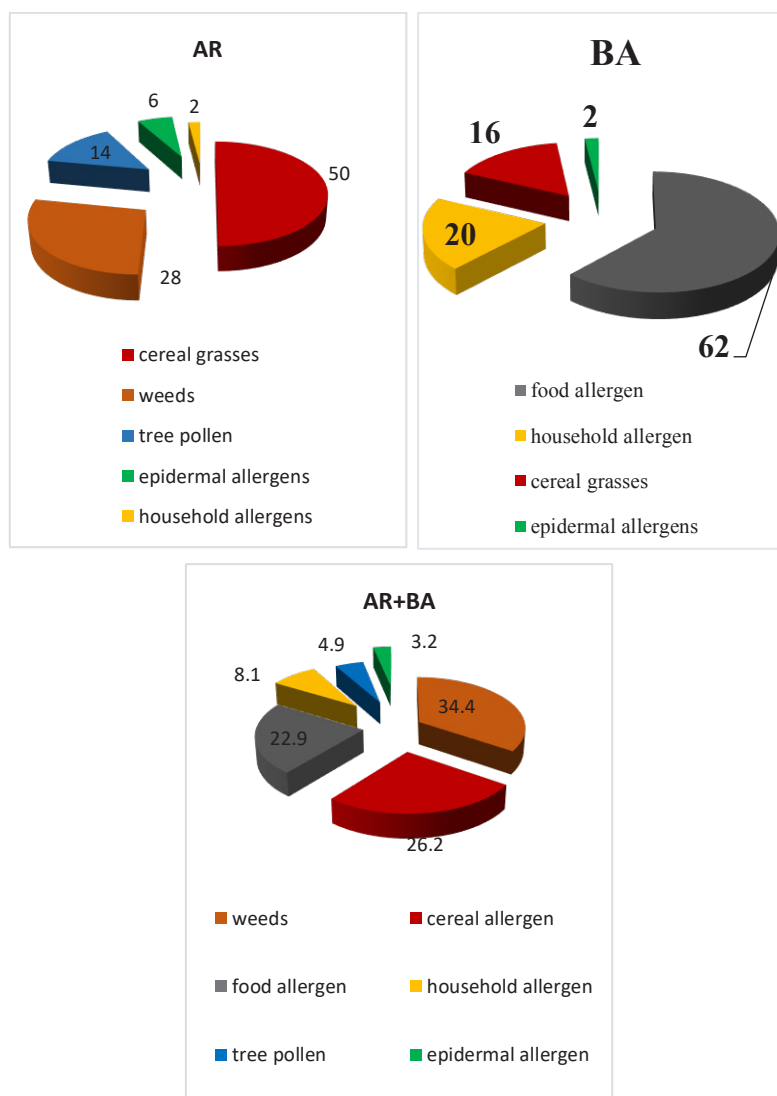
In all three groups, it was found that the amount of total IgE increased compared to the norm in all groups (r < 0.001). The mean value of total IgE was 439.2±43.1 HB/ml in AR group patients, 697.5±39.6 HB/ml in AR+BA patients compared to 30.4±2.3 HB/ml in the control group (figure 2).



**Fig. 2.** The amount of total IgE in the test groups.

When we studied the amount of specific IgE in the patients in the study, the following were found. In children with AR, the number of patients with the highest sensitivity to allergens of causative importance was recorded for cereals - 25 (50.0%) and weeds - 14 (28.0%) (r < 0.001). In this group of patients, cases of exacerbation of the disease prevailed from June to October, but the period of exacerbation of the disease did not last more than a month. Sensitivity to tree pollen was noted in 7 (14.0%) patients, the period of exacerbation

of the disease was observed from March to May, the lowest sensitivity to epidermal allergens - 3 (6.0%) and household allergens - 1 (2.0%) sensitization in patients was determined (fig. 3).



**Fig. 3.** Distribution of patients with different nosological forms of the disease depending on the nature of sensitization.

In patients with AR+BA (n=61), mainly weeds - 21 (34.4), grain allergens - 16 (26.2), food allergens - 14 (22.9), less household allergens - 5 (8.1%), sensitization to tree pollen - 3 (4.9%) and epidermal allergens - 2 (3.2%) was detected ( $r < 0.001$ ).

### 3 Conclusions

The clinical presentation of all forms of AR is characterized by a set of main and additional symptoms, their intensity and duration reflect the severity of the disease and the

characteristics of different forms of AR, which allows them to belong to different forms of AR. When analyzing the humoral state, the activation of the local immunological system in patients with AR and BA, due to increased sensitization by allergens, an increase in IgA was noted ( $r < 0.001$ ). Immunodeficiency in school-age and adolescent children with AR+BA was manifested by decreased levels of IgA and IgJ as a result of long-term contact with allergens ( $r < 0.001$ ). In the group with AR, sensitization to weed (72.5%), spiky grass (60.0%) allergens prevailed, followed by susceptibility to tree pollen (17.5%). In the AR+BA comorbid group, sensitization to weed allergens was 57.6%, cereal allergens - 51.5%, household allergens - 18.6%, and observation of epidermal allergens together with tree pollen was 9.1%. The number and seasonality of outbreaks depended on the type of allergen that was etiologically important in each case.

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