

Dorota Mrożek-Budzyn^{1,2}, Renata Majewska¹, Agnieszka Kiełtyka¹, Małgorzata Augustyniak¹

THE FREQUENCY AND RISK FACTORS OF ALLERGY AND ASTHMA IN CHILDREN WITH AUTISM - CASE-CONTROL STUDY

¹Chair of Epidemiology and Preventive Medicine Jagiellonian University Medical College

²Regional Sanitary-Epidemiological Station in Mysłenice

ABSTRACT

INTRODUCTION. The evolution of autistic disorders in children depends on many factors, like concomitance of the other diseases, which can escalate the autistic symptoms. One of those groups are allergic diseases, which have one of the highest prevalence rates in children.

OBJECTIVES. The aim of this analysis was to determine the frequency of asthma and allergy in children with autism in comparison to controls and the risk factors of allergic diseases and asthma in both groups.

MATERIAL AND METHODS. Study population included 96 cases diagnosed with childhood or atypical autism and 192 controls matched individually by year of birth, gender and physician's practice. The analysis was performed in each group separately giving possibility to compare the results between study groups.

RESULTS. The frequency of asthma and allergic diseases in both groups has not revealed any statistically significant differences. Children with autism have been affected by asthma in 5,2% and by allergy in 25,0%, controls in 4,7% and 21,9% respectively. All cases of asthma was diagnosed in boys, commonly allergy was also more frequent in boys than girls in both studied groups. However those differences was statistically insignificant. The father's allergy and asthma was revealed as a risk factor of allergy in children with autism. In controls additionally allergy or asthma diagnosed in mother or grandparent increased risk of allergy in children.

CONCLUSIONS. Children with autism were affected by asthma and allergy with similar frequency like children without autistic disorders. Allergy in father was the risk factor of allergic diseases in children with autism.

Key words: *children, autism, allergy, asthma*

INTRODUCTION

The basic objective of the provided studies on children with autism was to establish lack of association between exposure to vaccination (MMR as well as specimens with thimerosal) and the risk to develop autism (1,2). Additional data on children health status, also considering allergy and asthma occurrence were gathered. Developmental disorders in children with autism are changing according to individual way when child is getting older. Evolution of autistic symptoms depends on many factors, also on coexistence of other diseases, which could cause exacerbation of autistic symptoms (3). Allergic diseases are among those with high prevalence in children. Moreover allergic diseases are the most frequent chronic diseases in developmental age - about 20% of children suffer from allergy in

Poland and in some regions it is even 29% (4). The incidence of diseases such as asthma, eczema and allergic rhinitis is recently seen in Western Europe and North America (5,6). Polish studies also indicate rising trend of allergic diseases in children population with significant regional diversity (4,7,8).

Allergic diseases besides its basic symptoms may cause neuropsychiatric disorders, such as hyperactivity or sleep disorders. Those kinds of symptoms can be also related to children with autism, while a discomfort and pain associated with allergy may additionally intensify autistic disorders. That is the reason, why so important is the early diagnosis and proper treatment of coexisting allergy (3).

The aim of this study was to determine the frequency of allergy and asthma in autistic children comparing to control group as well as conclude risk factors of those diseases in both compared children groups.

MATERIAL AND METHODS

The group of cases consisted of children aged up to 14 years living in Malopolska Voivodeship diagnosed with childhood or atypical autism, classified according to ICD 10-criteria as F84.0 or F84.1. The cases were diagnosed by child psychiatrist. Children from control group were matched individually by year of birth, gender and physician's practice in proportion two controls per one child. Detailed description of material and methods of case-control study was presented in earlier publications on lack of associations between exposure to vaccinations (MMR and specimens with thimerosal) and autism in children (1,2). Additionally data on asthma and allergy in children and their families was gathered in both groups (autistic children and control group). Data on children health status and vaccination history were extracted from physician's records. We asked whether child is allergic to any agent and if the sensitivity to allergen was confirmed by skin prick tests. Data on asthma and allergy in family members were based on interview with child's mother (response to question whether allergy or/and asthma was diagnosed by physician in family members).

Statistical analysis. Differences between two groups in nominal variables were studied using χ^2 test or exact Fisher test (if expected cell count less than 5). Parameters measured on continuous scale were compared by Mann-Whitney test. Estimation of allergy and asthma risk associated with potential risk factors was provided using logistic regression.

RESULTS

Studied group consisted on 96 autistic children and 192 children from control group with mean age of 7.5 ± 2.6 years, 81.2% boys and 19.8% girls. Groups characteristic was presented in table I. The frequency of asthma and allergy was not statistically significantly different in both groups. In the group of children with autism, asthma occurred in 5.2% and allergy in 25.0%, while in control group 4.7% and 21.9%, respectively (tab. I). All asthma cases were among boys, both in autistic and control group (6.3% and 5.8% in boys, respectively) (tab. II). Autistic boys had allergy 4 times more frequent than girls (respectively), however that difference was not statistically significant and might be the result of small number of girls in study group. In control group also boys had allergy more frequent than girls as well, however difference was lower (tab. II).

Skin prick tests in children with allergy symptoms were administrated to 33.3% autistic children and

81% of children from control group. Difference was statistically significant ($p=0.001$). All skin prick tests performed in autistic children were positive, while in control group 2 children had negative tests outcomes. At the time of interview over half of the children with allergy among controls were treated, as only 25% of autistic one ($p=0.019$) (tab. I).

Table I. Groups characteristics and frequency of asthma and allergy in children with and without autism

	Control group (N=192)		Autistic children (N=96)		p
	N	%	N	%	
Maternal age > 35 years	14	7.0	12	12.9	ns
Maternal higher education	70	34.8	29	30.5	ns
Gestational age < 38 weeks	22	11.0	21	21.9	0.021
Taking medication during pregnancy	55	27.2	43	43.8	0.004
Birth injury	9	4.7	13	13.5	0.008
Apgar score < 9	21	10.4	17	17.7	0.094
Children with asthma	9	4.7	5	5.2	ns
Children with allergy	42	21.9	24	25.0	ns
Skin prick tests administrated	34	81.0*	8	33.3*	0.001*
Positive skin prick tests	32	94.1**	8	100**	ns **
Children treated on allergy	23	57.1*	6	25.0*	0.019*

* among children with allergy symptoms; ** among children with administrated skin prick tests

In the group of children with autism we did not observed any statistically significant differences in presence of asthma in family (regardless of percentage diversity) among children who had or had not asthma. Lack of statistical significance is mainly associated with small number of asthma cases in that group. On the other hand, in children from control group asthma was more frequent among family members (in every considered level of relationship) of children with that disease compared to others. Analyzing family burden of allergic diseases among children with allergy, it was more frequent in allergic ones in both autistic and control group. Statistical significance was reached for all considered relatives in control group but only for mother and father in autistic group (tab. III). Analyses stratified to child gender were conducted as well. Among boys with allergy, allergic diseases were more frequent in their parents, than in non-allergic group in both studied groups.

Food allergy in infancy period was more frequent in allergic children. In autistic group food allergy was present in 66.7% of allergic children and in 20.8% in non-allergic ones. In control group percentages were equal 42.9% and 23.3%, respectively (differences sta-

Table II. Characteristic of study group according to allergy and asthma

	Control group				p	Autistic children				p
	without asthma		with asthma			without asthma		with asthma		
	N	%	N	%		N	%	N	%	
boys*	145	94.2	9	5.8	ns	75	93.8	5	6.3	ns
girls*	38	100	0	-		16	100	0	-	
Asthma diagnosed in relatives										
grandparents	21	11.7	5	55.6	0.028	13	15.1	2	40.0	ns
mother	4	2.2	1	11.1	0.032	3	3.3	1	20.0	ns
father	2	1.1	3	33.3	0.001	1	1.1	0	0.0	ns
siblings**	6	3.3	3	33.3	<0.001	4	4.8	1	25.0	ns
parent	6	3.3	4	44.4	<0.001	4	4.4	1	20.0	ns
	without allergy		with allergy		p	without allergy		with allergy		p
	N	%	N	%		N	%	N	%	
	boys*	118	76.6	36		23.4	ns	57	71.3	
girls*	32	84.2	6	15.8	15	93.8		1	6.3	
Allergy diagnosed in relatives										
grandparents	7	4.9	8	20.0	0.005	9	14.1	5	22.7	ns
mother	9	6.0	10	23.8	0.002	8	11.1	9	37.5	0.010
father	8	5.4	6	14.6	0.083	2	2.9	7	29.2	0.001
siblings**	19	12.8	11	26.2	0.053	13	18.6	7	30.4	ns
parent	17	11.5	15	35.7	<0.001	10	14.3	12	50.0	<0.001
Food allergy in neonatal period	35	23.3	18	42.9	0.012	15	20.8	16	66.7	<0.001

* % from gender; * among those having siblings

Table III. Allergy and asthma in family members of children with and without autism stratified by gender.

	Control group				p	Autistic children				p
	without allergy		with allergy			without allergy		with allergy		
	N	%	N	%		N	%	N	%	
Boys										
Allergy diagnosed in relatives										
grandparents	5	4.5	7	20.6	0.007	8	15.7	5	23.8	ns
mother	8	6.8	9	25.0	0.005	4	7.0	9	39.1	0.001
father	5	4.3	5	14.3	0.052	2	3.6	7	30.4	0.002
siblings	14	12.0	9	25.0	0.056	10	18.2	7	31.8	ns
Asthma diagnosed in relatives										
grandparents	11	9.5	11	30.6	0.002	9	16.7	3	13.6	ns
mother	2	1.7	2	5.6	ns	1	1.8	3	13.0	0.069
father	0	0.0	3	8.3	0.012	1	1.8	0	0.0	ns
siblings	3	2.5	2	5.6	ns	4	7.0	1	4.5	ns
Girls										
Allergy diagnosed in relatives										
grandparents	2	6.5	1	16.7	ns	1	7.7	0	-	ns
mother	1	3.1	1	16.7	ns	4	26.7	0	-	-
father	3	9.4	1	16.7	ns	0	-	0	-	-
siblings	5	16.1	2	33.3	ns	3	20.0	0	-	ns
Asthma diagnosed in relatives										
grandparents	3	9.7	1	16.7	ns	3	21.4	0	-	ns
mother	0	0.0	1	16.7	ns	0	-	0	-	-
father	2	6.3	0	0.0	ns	0	-	0	-	-
siblings	2	6.5	2	33.3	ns	0	-	0	-	-

tistically significant) (tab. III). Other factors taken into consideration, such as pregnancy and delivery course, child health status in neonatal period as well as endured diseases and selected environmental condition were not differentiate studied groups. Hence, they were not presented and omitted in further analysis.

First multivariable model presents odds ratios for asthma according to family burden of that disease. In control group risk of allergy was higher if asthma was diagnosed at family member - for grandparents OR=3.8, for mother OR=6.0 and for father OR=7.1 (results statistically significant for grandparents and father and

Table IV. Risk of allergy in the study groups

	Odds Ratios of allergic diseases in studied groups							
	Asthma diagnosed in relatives				Allergy diagnosed in relatives			
	Control group		Autistic children		Control group		Autistic children	
	OR (95%CI)	P	OR (95% CI)	P	OR (95% CI)	P	OR (95% CI)	P
grandparents	3.8 (1.5 – 9.2)	0.003	0.6 (0.1 – 2.7)	ns	5.1 (1.4 – 17.2)	0.010	1.3 (0.3-5.6)	ns
mother	6.0 (0.9 – 37.9)	0.057	8.7 (0.8 – 90.9)	0.070	5.1 (1.7 – 15.7)	0.004	3.7 (0.9 - 14.9)	0.062
father	7.1 (1.02 – 49.3)	0.047	0	ns	4.2 (1.3 – 13.5)	0.018	9.3 (1.6-52.9)	0.012
parent	6.7 (1.7-25.4)	0.006	4.1 (0.6-26.1)	ns	4.6 (2.1 – 10.3)	<0.001	7.0 (2.3 - 21.4)	0.001

borderline significant for mother). In autistic children only asthma at mother was associated with higher risk of allergy (OR=8.7), however it was also borderline statistically significant ($p=0.07$)

Next multivariable model shows odds ratios for allergy according to family burden of that disease. Results were similar to above presented for asthma. Allergy at grandparents, mother and father were significantly higher the allergy risk at child (OR=5.1, OR=5.1 and OR=4.2 respectively) from non-autistic group. In autistic one only allergy at father was the factor that higher the risk of allergy at child (OR = 9.3, $p<0,05$).

To conclude, analyzed models considering risks of asthma and allergy associated with its family burden confirmed increased risk if above diseases was diagnosed in grandparents or parents in group of children from control group. In autistic children results were mostly statistically insignificant, what can be a result of small number of asthma cases in that group.

DISCUSSION

Provided study did not reveal statistically significant differences in frequency of asthma and allergy in autistic children compared to control group, however autistic ones suffered from these diseases a little bit more frequent. Our results are consistent with other published studies, nevertheless most of them considered whole spectrum of autistic disorders, not only autism (9,10). It has to be pointed out that children from control group are mostly from general population, but they do not represent it proper way, as number of boys 4 times exceeds the number girls. That is a reason why analysis of prevalence in studied diseases should be stratified by child gender. According to asthma there were too few cases in both analyzed groups to compare results between boys and girls and all of them were among boys with only a slightly higher prevalence in autistic ones compared to control group. Considering the fact that all asthma cases were among boys, the prevalence of

asthma for all children in our study population is higher than the one we could expect among children representing children population of Malopolska Voivodeship. Obtained outcomes are situated in a range of asthma prevalence published on the basis of other researches in Poland (4,7,11).

According to allergy, we observed significant diversity in its prevalence in a group of autistic children, with higher allergy prevalence in boys compared to girls. In control group the difference was also statistically significant with proportion of boys 1.5 to 1 in girls. It may suggest a rightness/validity more frequently lifted hypothesis on incidence of some gene interactions present in autistic children, which causes changes in immune system, rising e.g. risk of allergy (10).

It should be pointed that only 33% autistic children with allergic disease had skin prick tests done. Rest of them was diagnosed on the basis of clinical symptoms, what may influence on possible error in comparison frequency of a disease according to child gender. Many publications are rising a problem of diagnostic difficulties in recognizing chronic diseases if they coexist with autism. It is also a problem in diagnosing allergic ones. The fact, that 3-fold lower percentage of autistic children compared to control group with allergy symptoms had skin prick tests administrated, is a confirmation that it is difficult to provide routine diagnostic when there is no cooperation from child, and practitioners often quit it. From the other sight clinical diagnosis is also difficult because of problems in proper communication with patient or habitude attribute allergic symptoms to those associated with autism. Appropriate early allergy diagnosis in autistic children is very important, as those symptoms could escalate autistic disorders (9).

At children with autism higher risk of allergy was associated with allergy disease in their fathers. In control group allergy or asthma in all considered relatives increased the risk of allergy at child, but maternal allergy was higher risk factor than paternal. Analysis of risk factors of asthma was impossible due to small number of asthma cases among children.

Family conditionings of prevalence of asthma and allergy in general population were studied recursively/frequently, however their results are inconsistent. Most of them indicated similar associations like our study, but there were also those which showed higher weight to paternal than maternal asthma or allergy in risk of burden offspring those diseases (12), what was similar to our results in a group of autistic children. In such a studies where there are considered possible hereditary conditionings it is important to perform analyses stratified by gender, because mechanism of inheritance may be different in both cases (13). The study weaknesses are connected with small number of girls. The only outcome in control group is, that paternal was more frequent in boys with disease, what is consistent with other studies (12). We found difficulties in comparing results on asthma and allergy in our autistic group with other publications, as those found in different databases cover whole spectrum of autism disorders, not with childhood or atypical autism, which are in our study.

SUMMARY

Prevalence of asthma and allergy in children with autism were similar to those present in control group. None significant differences was also observed between autistic and non-autistic boys. Risk of allergy in autistic children was higher if allergy was diagnosed in their fathers.

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Received: 10.12.2012

Accepted for publication: 20.06.2013

Address for correspondence:

Dorota Mrozek-Budzyn

Chair of Epidemiology and Preventive Medicine

Jagiellonian University Medical College

ul. Kopernika 7a, 31-034 Kraków

tel. +48 12 423 10 03

e-mail: dorota.mrozek-budzyna@uj.edu.pl

