

# Allergies in urban versus countryside settings in Poland as part of the Epidemiology of the Allergic Diseases in Poland (ECAP) study – challenge the early differential diagnosis

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## Abstract

**Introduction:** The incidence of allergies depends on a number of factors, including adopting an urban “western” lifestyle, genetic predispositions, and different regions of residence.

**Aim:** To compare the prevalence of allergic conditions (seasonal allergic rhinitis (SAR) and perennial allergic rhinitis (PAR), bronchial asthma (BA), atopic dermatitis (AD)) in a group of countryside versus urban residents in Poland.

**Material and methods:** The prevalence of allergic conditions in urban versus countryside settings was assessed using the translated and approved questionnaire developed for international ECRHS II and ISAAC studies. Respondents were selected via random multistage sampling, with proportionate stratified sampling, and the Polish Resident Identification Number (PESEL) as the basis. A total of 18,617 respondents took part in the study. Subsequently, approximately 25% of the subjects underwent outpatient assessments: skin-prick, lung function, peak nasal inspiratory flow (PNIF) tests, as well as history-taking.

**Results:** Allergic rhinitis (AR) proved to be the most common condition in the entire study population. Children residing in the countryside were twice more likely to be diagnosed with BA (8.33% vs. 4%;  $p < 0.05$ ). Conversely, in the adult subgroup, BA was more commonly observed in urban areas. Whereas reported symptom rates were much higher in AR and AD patients, symptomatic BA was proportionately lower with respect to the official diagnoses (underdiagnosed BA phenomenon). Atopic dermatitis was considerably more common in the metropolitan population. One factor that significantly correlated with allergic diseases was a positive family history.

**Conclusions:** Inhabitants of metropolitan areas are to a greater extent predisposed to allergic conditions. One factor significantly contributing to allergies is genetic predisposition. Given the scale of the problem, there is an urgent need to implement measures for early prevention and diagnosis of allergies to minimize distant health effects.

**Key words:** epidemiology of allergic diseases in Poland, environmental, allergy prevalence, urban versus countryside.

## Introduction

During the current era of diseases of civilization, including allergies, there is an urgent need to fulfil health policies in terms of disease prevention as well as increasing health awareness to reduce the associated risk of complications, including generally low public fitness levels and healthcare system problems. Early diagnosis

of allergies including skin prick tests, sIgE play a fundamental role in the diagnosis of allergic diseases. An extremely interesting phenomenon which is more and more often addressed in the literature on the subject is the local IgE-dependent reaction within the nasal cavity especially in the group of patients with no signs of atopy and having specific IgE antibodies only in the na-

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sal lavage fluid, which are not confirmed by skin tests or sIgE. A nasal challenge test with an allergen, defined as a response of the mucous membrane to environmental factors, which involves the IgE-dependent reaction – is the only method in the group of diagnostic tools enabling tracking the reaction, which frequently in the differential diagnosis scheme, particularly of the allergic rhinitis, allows for the identification of a group of patients with isolated type of IgE-dependent reaction within the nasal mucous membrane. An estimated 35% of the general population in developed countries has been diagnosed with an allergic condition, which makes allergies a modern-day epidemic and the disease of the 21<sup>st</sup> century [1]. The growing incidence of allergies is mostly observed in the urban in comparison to the countryside population. The protective effect seen in the countryside is due to exposure to pathogens from a very young age, drinking raw (unpasteurized) milk, and not striving to achieve “sterile” living conditions. These factors have been included in the hygienic hypothesis that describes a tendency to produce Th2 lymphocytes and allergy development [2, 3]. Conversely, the high level of air pollution, heavy traffic, and urbanization observed in cities significantly contribute to developing allergic conditions.

## Material and methods

The aim of this study was to assess the prevalence of allergic conditions, including allergic rhinitis (AR), bronchial asthma (BA), and atopic dermatitis (AD) in subjects residing in the countryside in comparison to the rates of those conditions in residents of the most urbanized regions in Poland. The results of the Epidemiology of

the Allergic Diseases in Poland (ECAP) study conducted in the period from 2006 to 2008 not only illustrate the current condition of Poles in various regions of Poland and differences in the incidence of allergies to common environmental allergens, but also help predict the epidemiological course of allergies over the next few years.

Target study No. 6 PO5 2005 C/06572 “Initiation of the plan for prevention and early detection of allergic diseases in Poland” (ECAP) involved a population of adults aged 20–44 (standard European Community Respiratory Health Survey, ECRHS) and children aged 6–7 and 13–14 (standard International Study of Asthma and Allergies in Childhood, ISAAC, questionnaire) residing in eight of the largest Polish metropolitan areas (Gdansk, Wroclaw, Poznan, Katowice, Krakow, Lublin, Bialystok and Warsaw), and countryside areas (Zamojski and Krasnostawski counties). Subject distribution in terms of the number of urban and countryside residents was comparable (Table 1). The study design involved two main stages of field research: a survey study based on translated and approved versions of the standard ECRHS and ISAAC questionnaires and clinical (outpatient) assessments conducted according to ECRHS II standards (25% of the respondents completed the ECAP questionnaire). Physicians established the diagnoses based on the standard criteria for the diagnosis of asthma (based on GINA, Global Strategy for Asthma Management and Prevention) and allergic rhinitis (based on ARIA, Allergic Rhinitis and its Impact on Asthma). The ECAP study was conducted in a group of 9,000 children randomly selected via the Polish Resident Identification Number (PESEL) database by the Ministry of Interior and Administration (with ISAAC questionnaires for 6–7 and 13–14 age groups) and a group of 13,500 adults (with ECRHS questionnaires for the 20–44 age

**Table 1.** Study group characteristics

Parameter	6–7 years		13–14 years		Adults	
	n	%	n	%	n	%
<b>Part I: Questionnaire-based study (patient-reported symptoms)</b>						
Urban total	4048	24.44	4177	25.22	8337	50.33
Urban females	1987	49.08	2014	48.21	4936	59.20
Urban males	2061	50.91	2163	51.78	3401	40.79
Countryside total	462	22.48	544	26.47	1049	51.04
Countryside females	231	50	261	47.97	582	55.48
Countryside males	231	50	283	52.02	467	44.51
<b>Part II: Outpatient assessment (physician's diagnosis)</b>						
Urban total	1174	27.70	1149	27.11	1915	45.18
Urban females	575	48.97	559	48.65	1168	60.99
Urban males	599	51.02	590	51.34	747	39.00
Countryside total	156	28.62	172	31.55	217	39.81
Countryside females	82	52.56	80	46.51	143	65.89
Countryside males	74	47.43	92	53.48	74	34.10

group) in 9 regions of Poland (with Warsaw, Lublin, Białystok, Gdansk, Poznan, Wrocław, Katowice, Krakow representing metropolitan areas and Zamojski and Krasnostawski counties representing the countryside). The study design included two main parts. Part I: a questionnaire-based study (22,500 respondents) conducted using the Computer-Assisted Personal Interviewing (CAPI) with Personal Digital Assistant (PDA) devices. Part II: a complementary clinical assessment in 7,000 subjects including: spirometry (EasyOne 2001, Aeromedica, Warszawa) with bronchodilator challenge, skin-prick tests, peak nasal inspiratory flow (PNIF, Clement Clark International, England) before and after nasal decongestant administration, blood sampling for genetic and immune tests according to Clinical Report Form (CRF) instructions and skin-prick tests (Allergopharma; birch, grasses/cereals, wormwood, *Dermatophagoides pteronyssinus* and *Dermatophagoides farinae*), type-I molds (*Botrytis cinerea*, *Cladosporium herbarium*, *Alternaria tenuis*, *Curvularia lunata*, *Fusarium moniliforme*, *Helminthosporium*), type-II molds (*Aspergillus fumigatus*, *Mucor mucedo*, *Penicillium notatum*, *Pullularia pullulans*, *Rhizopus nigricans*, *Serpula lacrymans*), dog, cat, hazel, alder, rye, plantain, *Cladosporium herbarium*, *Alternaria tenuis* as well as negative and positive histamine/negative controls. The following questions were used to assess reported allergy rates: question V 176 “Do you have any nasal allergies, including a runny nose caused by allergy to pollens (hay fever)?” (for AR); question V 160 “Have you ever had asthma?” (for BA); question V 191 “Have you ever had eczema (dermatitis) or any other form of skin allergy?” (for AD). The outpatient-setting diagnosis was based on the patient’s history and included the following diagnoses: seasonal allergic rhinitis (SAR), perennial allergic rhinitis (PAR), atopic BA, and AD. The study was approved by the Ethics Committee of the Medical University of Warsaw and the Inspector General for Personal Data Protection.

### Statistical analysis

In Tables 1–3, the standard statistical analysis for contingency tables has been done. The logistic regression models were used for calculation of the risk factors with the OR risk (Tables 2, 4). For assessing the statistical significance of OR for a considered risk factor, the Wald test has been performed. *P*-value of < 0.05 was considered to be statistically significant.

## Results and discussion

### Part one: Questionnaire-based study (subject-reported symptoms)

The rates of patient-reported symptoms assessed via the questionnaire-based survey showed significant discrepancies versus the rates of the corresponding clinical diagnoses based on a physician-administered questionnaire, skin-prick test results, and spirometric findings. An

analysis of the survey questionnaire showed a markedly higher incidence of allergic conditions in the urban population. Allergic rhinitis was found to affect a significantly (over 1.5 times) greater proportion of the urban population versus the evaluated countryside regions. Although considerably greater proportions of AR and AD patients reported symptoms, symptoms of BA were reported less frequently in comparison to the respective clinical diagnoses, with BA affecting more commonly metropolitan populations. Bronchial asthma was diagnosed considerably more often in adolescents aged 13–14 and adults (Table 2). The highest proportion of reported symptoms was associated with skin lesions, including AD. Moreover, respondents from metropolitan areas, especially children aged 6–7 and 13–14, had a markedly higher risk of AD.

### Part two: Outpatient assessment (clinical diagnosis)

The study, conducted in accordance with the ECRHS and ISAAC standards, revealed the greatest proportion of subjects to be affected by AR. The age groups characterized by the highest AR prevalence were adolescents (aged 13–14) and adults (aged 22–44). Interestingly, perennial AR was shown to be most prevalent in urban populations, whereas countryside residents, apart from 13–14-year-old adolescents, most often suffered from SAR. The second most prevalent allergic condition in the Polish population was BA. It was twice as prevalent in 6–7-year-olds and slightly more in 13–14-year-olds residing in the countryside versus their urban counterparts. Conversely, in the adult population, BA was more common in urban residents. Atopic disease was markedly more common in populations from urban areas. In fact, AD affected over 3.5 times more 6–7-year-old children and two times more 13–14-year-old adolescents in cities, in comparison with their peers living in the countryside. Any region-related differences in AD symptom rates in adults were not statistically significant.

### Positive skin-prick test rates

The subpopulation in which skin-prick tests were conducted most often and yielded most pronounced reactions were residents of metropolitan areas (Table 3). Seasonal allergens were the cause of more cases of allergy than perennial ones. The youngest evaluated age group tested positive mostly for the following allergens: grass/cereals, house dust mites, rye, birch, and cat, with these allergens also producing the most pronounced skin reactions. Positive skin-prick tests in the group aged 13–14 in cities were mostly due to the same allergens as in the youngest evaluated group and additionally included wormwood, birch, and dog allergens. The number of allergens producing a positive reaction increased with age (with ribleaf, alder, and hazel, yielding highly positive skin-prick tests). Conversely, the most prevalent allergies

**Table 2.** Allergy prevalence stratified by region

**Part I: Questionnaire-based study (patient-reported symptoms)**

Parameter	6–7 years		13–14 years		Adults	
	n	%	n	%	n	%
Urban AR	980	24.30	1051	25.20	1833	22.02
Countryside AR	85	18.39	109	20.03	134	12.77
Urban BA	163	4.04	255	6.13	331	3.98
Countryside BA	14	3.05	18	3.32	20	1.90
Urban AD	1932	47.78	2907	40.92	2907	34.91
Countryside AD	134	29.06	136	25	252	24.06

Parameter	6–7 years			13–14 years			Adults					
	OR	95% CI	P-value	OR	95% CI	P-value	OR	95% CI	P-value			
AR	1.438596	1.124761	1.84	< 0.05	1.333333	1.068663	1.663554	< 0.05	1.887574	1.563195	2.279265	< 0.05
BA	1.347222	0.773689	2.345913	< 0.05	2.06383	1.268632	3.357471	< 0.05	2.041667	1.294081	3.221129	< 0.05
AD	2.259947	1.831333	2.788875	< 0.05	2.084746	1.700623	2.555631	< 0.05	1.705128	1.469549	1.978473	< 0.05

**Part II: Outpatient assessment (physician’s diagnosis)**

Parameter	6–7 years		13–14 years		Adults	
	n	%	n	%	n	%
Urban SAR	125	10.64	167	14.53	284	14.83
Countryside SAR	26	16.66	22	12.79	36	16.58
Urban PAR	157	13.37	194	16.88	303	15.82
Countryside PAR	16	10.25	26	15.11	29	13.36
Urban BA	47	4.00	61	5.30	89	4.64
Countryside BA	13	8.33	11	6.39	6	2.764
Urban AD	112	9.54	111	9.66	68	3.55
Countryside AD	4	2.56	8	4.65	8	3.68

Parameter	6–7 years			13–14 years			Adults					
	OR	95% CI	P-value	OR	95% CI	P-value	OR	95% CI	P-value			
SAR	0.603437	0.38089	0.955992	< 0.05	1.180995	0.74388	1.902092	> 0.05	0.861592	0.589662	1.258926	> 0.05
PAR	1.344828	0.780675	2.316664	> 0.05	1.160643	1.268632	3.357471	< 0.05	1.274725	0.846111	1.920462	> 0.05
BA	0.479167	0.253073	0.907251	< 0.05	0.824561	0.424887	1.600192	> 0.05	1.701754	0.735479	3.937526	> 0.05
AD	3.592593	1.306233	9.880873	< 0.05	2.111111	1.011114	4.407803	< 0.05	1	0.474057	2.109452	> 0.05

AD – atopic dermatitis, AR – allergic rhinitis, BA – bronchial asthma, PAR – perennial allergic rhinitis, SAR – seasonal allergic rhinitis.

were those to non-seasonal allergens, i.e. *D. pteronyssinus*, *D. farinae*, and dog. Moreover, an increased rate of allergies to wormwood and grasses/cereals was observed in adult residents of the countryside/urban areas.

**Factors contributing to allergic conditions in a given population**

Genetic relations were found to be one of the significant environmental-social risk factors for allergy development (Table 4). The observed risk of developing both AR and BA was nearly two times higher in subjects whose

siblings and/or father were affected. Moreover, the risk of AD in subjects whose paternal grandfather was affected was over two-fold higher in metropolitan residents and over 5-fold higher in the countryside. Income below €1,000 in urban areas was also associated with a higher risk of developing PAR, in comparison to that in the countryside.

The currently observed increase in the incidence of allergic conditions raises concern; there are an estimated 4 million Poles suffering from BA, and one in four residents has an allergic condition, with approximately 20% of the study population receiving inadequate treatment (based on the ECAP Report). A number of single-center

**Table 3.** Proportion of positive skin-prick tests stratified by the region of residence

Parameter	6–7 years						13–14 years						Adults					
	≥ 3 mm		3–5 mm		≥ 6 mm		≥ 3 mm		3–5 mm		≥ 6 mm		≥ 3 mm		3–5 mm		≥ 6 mm	
	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
Urban areas:																		
Birch	117	9.9	85	7.2	32	2.7	192	16.7	123	10.7	69	6.0	327	17.0	159	8.3	168	8.7
Grasses/cereals	188	16.0	121	10.3	67	5.7	299	26.0	148	12.8	151	13.1	436	22.7	199	10.3	237	12.3
Wormwood	89	7.5	76	6.4	13	1.1	202	17.5	164	14.2	38	3.3	388	20.2	268	13.9	120	6.2
<i>Dermatophagoides pteronyssinus</i>	177	15.0	121	10.3	56	4.7	312	27.1	163	14.1	149	12.9	475	24.8	285	14.8	190	9.9
Type I molds	73	6.2	51	4.3	22	1.8	141	12.2	103	8.9	38	3.3	162	8.4	128	6.6	34	1.7
Type II molds	48	4.0	47	4.0	1	0.1	63	5.4	59	5.1	4	0.3	149	7.7	134	6.9	15	0.7
Dog	68	5.7	65	5.5	3	0.2	85	7.3	76	6.6	9	0.7	203	10.6	189	9.8	14	0.7
Cat	96	8.1	73	6.2	23	1.9	181	15.7	128	11.1	53	4.6	281	14.6	185	9.6	96	5.0
<i>Dermatophagoides farinae</i>	168	14.3	114	9.7	54	4.5	280	24.3	154	13.4	126	10.9	427	22.2	278	14.5	149	7.7
Hazel	78	6.6	51	4.3	27	2.2	142	12.3	94	8.1	48	4.1	278	14.5	156	8.1	122	6.3
Alder	72	6.1	53	4.5	19	1.6	132	11.4	96	8.3	36	3.1	275	14.3	179	9.3	96	5.0
Rye	127	10.8	79	6.7	48	4.0	216	18.7	126	10.9	90	7.8	364	19.0	184	9.6	180	9.3
Ribleaf	49	4.1	47	4.0	2	0.1	98	8.5	80	6.9	18	1.5	207	10.8	186	9.7	21	1.0
<i>Cladosporium herbarum</i>	34	2.8	30	2.5	4	0.3	53	4.6	51	4.4	2	0.1	121	6.3	113	5.9	8	0.4
<i>Alternaria tenuis</i>	98	8.3	70	5.9	28	2.3	123	10.7	77	6.7	46	4.0	130	6.7	98	5.1	32	1.6
Countryside:																		
Birch	25	16.0	24	15.3	1	0.6	20	11.6	19	11.0	1	0.5	32	14.7	32	14.7	0	0
Grasses/cereals	29	18.5	28	17.9	1	0.6	26	15.1	23	13.3	3	1.7	43	19.8	36	16.5	7	3.2
Wormwood	28	17.9	28	17.9	0	0	25	14.5	25	14.5	0	0	40	18.4	38	17.5	2	0.9
<i>Dermatophagoides pteronyssinus</i>	35	22.4	31	19.8	4	2.5	52	30.2	41	23.8	11	6.3	66	30.4	57	26.2	9	4.1
Type I molds	18	11.5	17	10.8	1	0.6	14	8.1	14	8.1	0	0	27	12.4	27	12.4	0	0
Type II molds	23	4.0	23	4.0	0	0.1	17	5.4	17	5.1	0	0.3	30	7.7	30	6.9	0	0.7
Dog	33	21.1	33	21.1	0	0	23	13.3	23	13.3	0	0	29	13.3	29	13.3	0	0
Cat	21	13.4	20	12.8	1	0.6	13	7.5	11	6.3	2	1.1	22	10.1	20	9.2	2	0.9
<i>Dermatophagoides farinae</i>	31	14.3	29	9.7	2	4.5	32	24.3	28	13.4	4	10.9	51	22.2	44	14.5	7	7.7
Hazel	18	11.5	18	11.5	0	0	20	11.6	19	11.0	1	0.5	21	9.6	20	9.2	1	0.4
Alder	19	12.1	19	12.1	0	0	16	9.3	15	8.7	1	0.5	18	8.2	17	7.8	1	0.4
Rye	22	14.1	22	14.1	0	0	20	11.6	19	11.0	1	0.5	26	11.9	20	10.1	4	1.8
Ribleaf	18	11.5	18	11.5	0	0	18	10.4	18	10.4	0	0	22	10.1	21	9.6	1	0.4
<i>Cladosporium herbarum</i>	16	10.2	16	10.2	0	0	14	8.1	14	8.1	0	0	15	6.9	15	6.9	0	0
<i>Alternaria tenuis</i>	19	12.1	18	11.5	1	0.6	10	5.8	9	5.2	1	0.5	14	6.4	14	6.4	0	0

**Table 4.** Allergy provoking factors stratified by regions

Variable	SAR			PAR			Asthma			AD		
	OR	95% CI	P-value	OR	95% CI	P-value	OR	95% CI	P-value	OR	95% CI	P-value
<b>Urban areas:</b>												
Gender:												
Females	0.99	0.83–1.18	> 0.05	0.70	0.59–0.83	< 0.05	0.59	0.44–0.79	< 0.05	1.14	0.89–1.45	> 0.05
Males reference												
Income:												
Below €275 reference level:												
€275–€1000	0.96	0.68–1.38	> 0.05	1.45	0.99–2.12	> 0.05	1.61	0.80–3.23	> 0.05	0.74	0.47–1.16	> 0.05
> €1000	1.43	0.96–2.12	> 0.05	1.57	1.03–2.40	< 0.05	1.98	0.92–4.23	> 0.05	1.07	0.64–1.78	> 0.05
Education:												
Primary school reference level:												
High school	1.42	0.55–3.66	> 0.05	0.70	0.33–1.44	> 0.05	2.66	0.35–19.73	> 0.05	1.40	0.18–10.58	> 0.05
University/college	1.62	0.62–4.19	> 0.05	0.64	0.31–1.34	> 0.05	1.83	0.24–13.80	> 0.05	1.76	0.23–13.31	> 0.05
Allergies in the family:												
Mother	1.17	0.92–1.48	> 0.05	1.41	1.13–1.75	< 0.05	1.26	0.87–1.83	> 0.05	2.27	1.73–2.98	< 0.05
Father	1.68	1.31–2.17	< 0.05	1.71	1.34–2.18	< 0.05	1.54	1.02–2.31	< 0.05	2.29	1.68–3.12	< 0.05
Siblings	1.59	1.29–1.96	< 0.05	1.11	0.90–1.37	> 0.05	1.46	1.04–2.04	< 0.05	1.45	1.09–1.92	< 0.05
Maternal grandparents	1.19	0.83–1.68	> 0.05	1.11	0.79–1.56	> 0.05	1.29	0.75–2.23	> 0.05	No data		
Paternal grandparents	1.17	0.73–1.89	> 0.05	1.45	0.95–2.22	> 0.05	3.13	1.84–5.33	< 0.05	2.45	1.50–4.01	< 0.05
<b>Countryside:</b>												
Gender:												
Females	1.12	0.69–1.79	> 0.05	0.68	0.41–1.13	> 0.05	0.43	0.20–0.93	< 0.05	No data		
Males reference												
Income:												
Below €275 reference level:												
€275–€1000	0.89	0.52–1.51	> 0.05	0.82	0.46–1.44	> 0.05	0.51	0.21–1.20	> 0.05	1.81	0.68–4.76	> 0.05
> €1000	1.37	0.14–12.65	> 0.05	1.57	0.17–14.57	> 0.05	Sample size too small		Sample size too small			
Education:												
Primary school reference												
High school	4.14	0.52–32.92	> 0.05	0.93	0.24–3.57	> 0.05	Sample size too small		Sample size too small			
University/college	7	0.78–62.52	> 0.05	0.47	0.07–3.13	> 0.05	Sample size too small		Sample size too small			
Allergies in the family:												
Mother	0.45	0.13–1.50	> 0.05	0.45	0.13–1.50	> 0.05	0.78	0.18–3.40	> 0.05	No data		
Father	1.22	0.41–3.66	> 0.05	1.22	0.41–3.66	> 0.05	1.46	0.32–6.49	> 0.05	2.31	0.50–10.57	> 0.05
Siblings	1.24	0.60–2.57	> 0.05	1.24	0.60–2.57	> 0.05	1.51	0.55–4.11	> 0.05	No data		
Maternal grandparents	0.83	0.10–6.75	> 0.05	0.83	0.10–6.75	> 0.05	2.18	0.26–18.06	> 0.05	No data		
Paternal grandparents	0.55	0.07–4.29	> 0.05	0.55	0.07–4.29	> 0.05	1.44	0.18–11.50	> 0.05	5.19	1.07–25.16	< 0.05

studies in highly industrialized countries show that SAR sufferers constitute approximately 32.7% of the population aged 18–22 years in Japan, 42% of 9-year-old children in the USA, and an estimated 29% of respondents in the 5–59-year age range in the UK [4–6]. This trend of growing allergy rates can be mostly attributed to air pollution and higher prevalence of contact allergens, especially in the case of AD. Factors such as infections or exposure to endotoxins may have a protective effect or provoke the development of AD. The increased incidence of allergies in urban areas is associated with a number of factors responsible for the significant differences versus the countryside. The influence of environmental factors is mixed (complex, overlapping effects). Typically, the human body is exposed to multiple factors of various concentrations or intensities. Effects of such exposure depend not only on qualitative and quantitative composition of these factors, but also on the potential for their interaction.

Attempts to determine the significance of the individual factors have often yielded inconclusive results and effects of a certain factor confirmed in one study have not been confirmed in another. These discrepancies may be due to divergent criteria for diagnosing allergies used by different authors, as well as different study designs. There are many environmental factors that contribute to developing allergies, including the phenomenon of thermal inversion (air temperature increases with increasing altitude, which leads to a high concentration of pollens and airborne chemical compounds), different seasons (spring and summer are the periods of most intense pollen emissions), changes in weather during the pollen season (thunderstorms may induce hydration of pollen grains and fragmentation of various pollen particles, which increases the frequency of asthma attacks), humidity, temperature, and wind speed.

There are a number of epidemiology studies demonstrating a close association between the incidence of allergies and the concentration of air pollutants [7–11] due to energy consumption and exhaust emissions [12, 13]. Air pollution is a serious environmental problem both in the developed and developing countries [11]. The most dangerous pollutants include coarse particulate matter (PM<sub>10</sub>), fine particulate matter (PM<sub>2.5</sub>), nitrogen oxides (NO<sub>x</sub>), ozone, and sulfur oxides (SO<sub>x</sub>) [11, 12, 14]. Exposure of a grass pollen to higher NO<sub>2</sub> and ozone levels leads to increased release of allergen-laden pollen grains, thus raising the pollen's proinflammatory potential. Exposure to NO<sub>x</sub>, SO<sub>x</sub>, and ozone may damage the respiratory mucosa and disrupt the mucociliary apparatus, which increases the risk of asthmatic or allergic rhinitis exacerbations. Additional factors, i.e. cigarette smoke or Diesel exhaust fumes, may aggravate allergic reactions [2, 3].

Polish studies conducted as part of the ECAP project demonstrated that AR is an allergic condition that shows

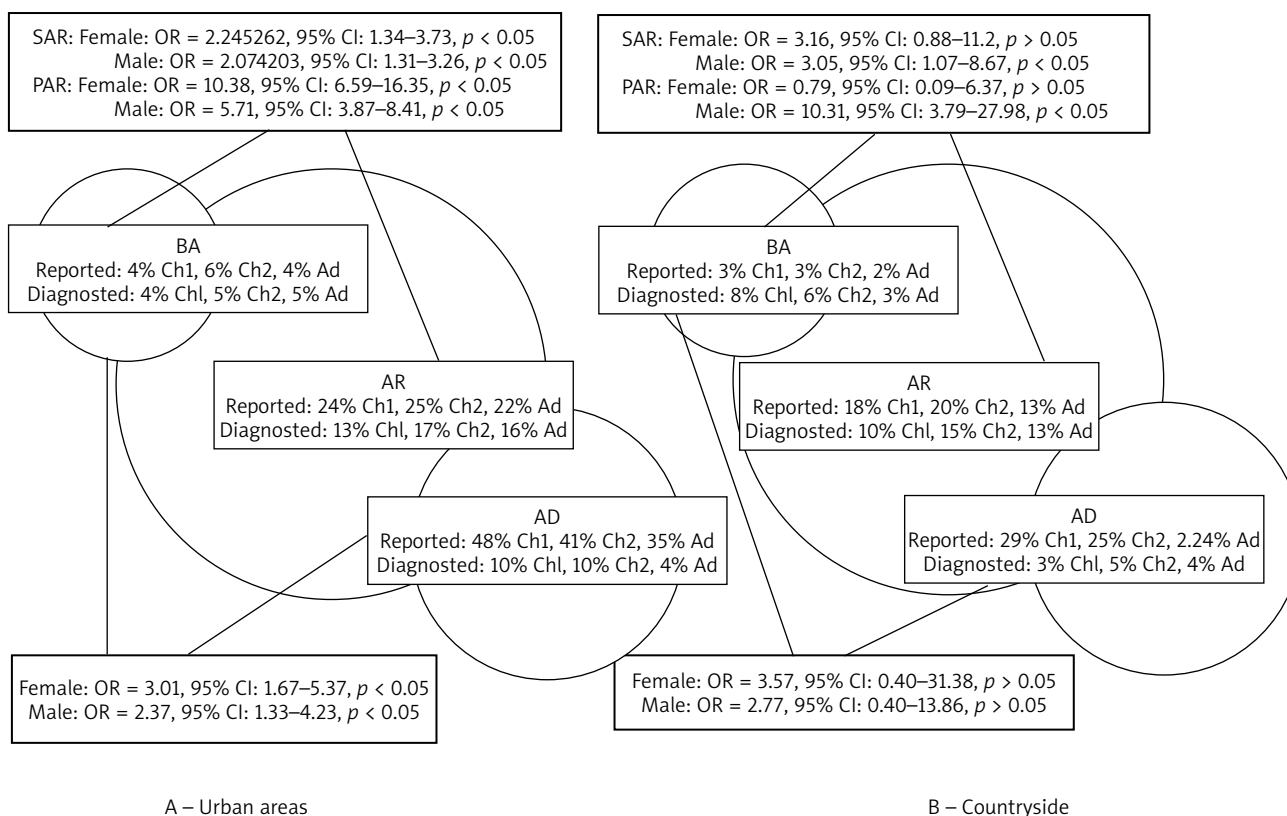
most significant differences by region (city vs. countryside). The most common allergies to environmental and contact factors in the order of decreasing prevalence are as follows: AR, BA, and AD. Seasonal allergic rhinitis in the 6–7-year-old children was diagnosed in the order of decreasing prevalence in Warsaw (20.8%), Poznan (17%), Gdansk (15.3%), Bialystok (10.7%), Krakow (9.2%), and Wroclaw (6.1%). Perennial allergic rhinitis in this age group was diagnosed in the order of decreasing prevalence in Poznan (22.6%), Warsaw (16.7%), Gdansk (13%), Wroclaw (11.4%), Bialystok (10%), and Krakow (2.7%); in comparison to its 16.0% diagnosis rate in the countryside [1]. One analysis by Tomaszewska *et al.* conducted (as part of the ECAP study) in a smaller population of one voivodship, the city of Lublin ( $n = 2,422$ ) and the countryside represented by the Zamojski and Krasnostawski counties ( $n = 2,055$ ) revealed 27.9% of the evaluated countryside population and 30.4% of the metropolitan population to be suffering from AR (SAR and PAR) ( $p < 0.05$ ). Bronchial asthma was found in 14.5% of urban residents and in 10.1% of countryside residents ( $p < 0.05$ ) [15, 16]. These findings are similar to those reported by Komorowski in a study on the incidence of BA in the Polish population, which showed clear differences between the evaluated regions. Physician-diagnosed BA was observed in the following proportions of the study population: 19.5% in Poznan, 14.5% in Lublin, 12% in Gdansk, 10.6% in Krakow, 9.1% in Warsaw, 8.1% in Katowice, and 6.0% in Bialystok [17]. Interestingly, the rates of patient-reported symptoms of AR or AD proved to be higher than the rates of these conditions confirmed with an official diagnosis. Moreover, as much as 66.9% of the patients had been unaware of their disease (underdiagnosed BA). Kupryś-Lipińska *et al.* showed significantly higher rates of BA in the population of children in the evaluated urban ( $n = 482$ ) and countryside ( $n = 469$ ) regions, of 18.4% and 6%, respectively [18]. Seasonal allergic rhinitis was diagnosed in 16.1% and 6.7% of the general population in the urban and countryside regions, respectively. The proportion of AD diagnoses was much higher in the countryside than in the city (11.9% vs. 10.2%). The proportions of BA and SAR diagnoses were equal at approximately 13.2% in the group of evaluated adults in urban areas [6]. The extent of the problem is illustrated by the increasing trend in BA incidence observed in children participating in the ISAAC study in large metropolitan areas in Indonesia (4.1–2.1% of children aged 6–7 and 13–14), in Costa Rica (32.1% of 6–7-year-olds), in the UK (32.2% of 13–14-year-olds). The ECRHS study additionally demonstrated the development of AD in adult populations [18].

Moreover, multicenter epidemiological studies (e.g. by Blair and Settignano) showed a higher incidence of AR symptoms in patients with BA (28–78%) than in individuals without BA symptoms (5–20%) [19, 20]. A breakthrough in AR and BA co-occurrence came with the ECRHS-questionnaire-based study conducted by Ley-

naert *et al.* in 90,478 subjects in Spain, the UK, Australia, France, the US, Italy, and the Benelux countries. The authors demonstrated BA without AR in 1–6% of respondents, BA co-occurring with AR symptoms in 7.6–22.6% of respondents, AR without BA in 10.5–36.2%, and AR co-occurring with BA symptoms in 50.0–77.1% of respondents (OR = 8) [21]. The presented study results (Figure 1) clearly show that the risk of BA co-occurrence in AR patients, especially those with PAR, both in the countryside and in urban areas is ten times higher in the evaluated groups and over three times higher in patients (especially female patients) with AD. A review of the available literature demonstrated that children diagnosed with AD are 2.14-fold more prone to BA than children without AD. Moreover, AD in conjunction with allergies to common environmental allergens is a significant marker of the allergic march.

The highest prevalence of AD has been observed in the Scandinavian countries (15.6–22.3%) followed by the UK (10.6–16%), Lithuania (1.8–3%), and Albania (2–3.7%) [22]. In adult respondents, the highest rates of AD were found in Estonia (17.6%), followed by the Scandinavian countries (8–9%), the UK (8.1%), and Switzerland (2.2%)

[23]. Polish studies show 2.0–22.6% (mean 9%) of respondents diagnosed with AD, with considerably more 6–7-year-olds and 13–14-year-olds affected (3.5-fold and 2-fold, respectively) [24]. There were no statistically significant differences in terms of the region of residence in adults with AD. Different regions of Poland showed different AD diagnosis rates (Hanifin and Rajka criteria): in Poznan 16.76%, in Katowice 7.18%, in Lublin 6.98%, in Wroclaw 6.38%, in Warsaw 6.31%, in Gdansk 5.95%, in Bialystok 4.42%, and in Krakow 2.02%. In the countryside, 3.67% of subjects were diagnosed with AD. Interestingly, the rates of patient-reported AD symptoms were significantly higher in urban areas, with over 40% of children aged 6–7 and 14–15 affected (the symptoms were reported by the children’s legal guardians). The proportion of patient-reported AD symptoms in the adult group was 34.91% [25]. The patient-reported rates illustrate the scale of the problem of dermatoses, especially in the population of younger children. The main causes of skin problems are parabens (esters of 4-hydroxybenzoic acid). These compounds are considered to be among the most common preservatives used in cosmetic products



AD – atopic dermatitis, Ad – adults, AR – allergic rhinitis, BA – bronchial asthma, Ch1 – children 6–7 years old, Ch2 – children 13–14 years old, PAR – perennial allergic rhinitis, SAR – seasonal allergic rhinitis.

**Figure 1.** The prevalence of allergic conditions in the questionnaire-based study in urban areas (A) vs. countryside (B)



(they are found in 22,000 cosmetic products approved for everyday use), food products, and medications [26].

Positive skin tests were observed considerably more often in residents of metropolitan areas. The dominant allergens were seasonal and included grasses/cereals, birch, wormwood, and *D. farinae*. The group of young children living in the countryside was found to be most commonly affected by house dust mite and dog allergens. In adults, co-allergens were grasses/cereals and wormwood. The phenomenon of patient-reported allergies to house dust mites despite negative skin tests is common among countryside residents [2]. These findings were similar to those obtained by Bousquet *et al.* in ECRHS I study conducted in 35 centers around the world, Nicolai and von Mutius in Germany, and Sożanska *et al.* in Poland [27–29].

Genetic etiology of allergic conditions has been confirmed in a number of studies; the risk of a co-occurring atopic condition is 25–35% in individuals whose sibling has been diagnosed with allergy, 30–50% when one or both parents are affected by allergies, and 70% when both parents suffer from the same allergic condition [30]. These findings are consistent with the observed incidence of BA and AR [1]. The last decade saw identification of various human leukocyte antigens (HLA) that play a crucial role in AR [1]. Moreover, based on the presence of filaggrin loss-of-function mutations 2282del4 and R501X (typically predisposing to AD in the Caucasian populations by disrupting keratin fiber binding in the late stages of differentiation and affecting the cornified envelope), Ponińska *et al.* (ECAP study) estimated a high risk of developing co-occurring allergies in a group of 3,802 subjects with AD (OR = 2.01, 95% CI: 1.20–3.36,  $p = 0.007$ ), AR (OR = 1.69, 95% CI: 1.12–2.54,  $p = 0.011$ ), and BA (OR = 2.22, 95% CI: 1.24–3.96,  $p = 0.006$ ). This suggests that efforts to restore the epidermal barrier may play an important role in BA prevention and treatment [31].

The observed region-dependent increase in the incidence of allergic diseases within the last decade (western lifestyle, increased use of agricultural chemicals in Poland, gradual obliteration of the typical features of the Polish countryside) calls for introducing measures of primary prophylaxis, as well as prevention of complications and secondary allergies. In light of the significant problem of asthma underdiagnosis and the findings of this study, there is a need to initiate preventive measures and implement early diagnosis of rhinologic and allergic disorders.

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### Conflict of interest

The authors declare no conflict of interest.

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