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Is the “farm effect” hypothesis still current? Atopy and allergic diseases in rural and urban children in Poland

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ABSTRACT

Objective: The prevalence of allergic diseases has reached epidemic proportions in the Western world. Although farm-living has been associated with a lower prevalence of asthma and atopy, a marked increase in atopy among rural populations after accession to the European Union has been recently reported in Poland. Here, we aimed to investigate the effect of living environment on the prevalence of atopy and allergic diseases in Polish children. **Methods:** 400 schoolchildren aged 10–14 years from the capital city (223) and from traditional rural part of the country (177) were recruited from June to November 2011. Data on allergic diseases and symptoms were collected by means of questionnaire and physical examination. Atopy was assessed based on skin prick tests (SPTs) reactivity to inhalant allergens in 350 children. **Results:** A high discrepancy between the prevalence of allergic symptoms (46.7%) and doctor-diagnosed allergic diseases (25%) was demonstrated ($p < 0.0001$). Urban children had a higher overall prevalence of allergic diseases and atopy than children living in rural areas, 29.3% versus 17.1% ($p = 0.007$) and 33.5% versus 20% ($p = 0.0045$), respectively. However, no significant differences in the rates of particular allergic diseases were noted ($p > 0.05$). There was higher SPT positivity to trees, grass, corn, weeds, animal dander, and molds in urban children ($p < 0.05$). **Conclusions:** Our data support the protective effect of farm-living on the prevalence of atopy and overall allergic diseases, albeit not on particular allergic diseases, in children in Poland. The underlying mechanisms are not identified, but current socioeconomic changes may be responsible.

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Introduction

The increasing incidence of allergic diseases observed over the last 50 years in affluent countries has now reached epidemic proportions worldwide and a further increase is expected in the coming years. Interestingly, there are large variations in the incidence of allergic diseases within a single country or even within the same community (1–5). These differences can be, at least in part, explained by the environment and living conditions.

The first study reporting the protective effect of farm-living on the development of atopy and allergic disease in children by Braun-Fahrlaender et al. in 1999 has fueled an extensive stream of research on this topic. Since then, many studies have repetitively shown a decreased prevalence of allergic sensitization, hay fever, and asthma in children living on a farm, the so called “farm effect” (6–10). According to the hygiene hypothesis, the protective effect of farm-living depends on environmental exposures to non-infectious microbial and non-microbial agents abundantly present in a rural environment (11,12). Interestingly, the potential of farming environment for

disease prevention depends on farming practices and the timing of exposure with early childhood being a critical “time window” (7–13). Early-life contact with a wide range of microbes shapes immune responses by promoting type 1 T-helper (Th) lymphocytes, inhibiting allergic Th2 response, as well as by affecting regulatory T-cells and dendritic cells (13–15). It is the biological diversity of the environment that is believed to play a pivotal role in promoting immune balance and allergy protection (the biodiversity hypothesis) (16). In particular, regular exposure of farm-living children to farm animals and microbes while cattle and poultry breeding, fruit and vegetables cultivation, and unpasteurized farm milk consumption confer the highest protection against allergy (11,15–17). Apparently, this protection seems to extend beyond childhood as it has been recently shown that a farm-upbringing has a beneficial effect on adult lung function and is associated with decreased allergic sensitization and disease in adults (18,19).

The recent global increase in allergic diseases seems to be correlated with lifestyle changes, in particular with

the adoption of a western lifestyle. Rapidly developing second-world countries are now also facing the epidemic of allergic diseases (20). Similarly, the prevalence of atopy and allergic disease in rural western Poland increased after accession to the European Union due to the dramatic decrease in farm-related exposures (21). However, studies assessing changes in allergic sensitization and disease phenotypes during the socioeconomic transformation are scarce.

In this study, we aimed to investigate the prevalence of atopy and allergic diseases in schoolchildren living in urban and one of the most traditional rural areas of eastern Poland and to assess the effect of the living environment on the prevalence of allergy.

Methods

Study population

This cross-sectional study was conducted in Warsaw, the capital city of Poland, and in rural areas of south-eastern Poland (the Lublin province). Participants were recruited among children aged 10–14 years attending schools selected on random basis from the list of schools in the selected region. All children aged 10–14 years attending five public primary and secondary schools in two districts of Warsaw (Wola and Mokotów, 774 students) and four public schools in the Lublin province in the villages of Leopoldów (141 students), Żyrzyn (216 students), Sobieszyn (161 students), and Moszczanka (59 students) were considered eligible for the study.

Study design

The study was conducted in the schools' nurses' or medical office or in other areas indicated by the school headmaster from June to November 2011. The exclusion criteria included: acute infection at the onset of the study, immunization with live attenuated vaccines, infectious diseases (chickenpox, rubella, and scarlet fever) or surgical intervention within the last 8 weeks, immunosuppression and other chronic treatment including antihistamines within the last 7 days (ketotifen within the last 14 days) before the study onset. In another part of this study, we assessed the status of the *Mycobacterium tuberculosis* infection; therefore, we additionally excluded children who had a tuberculin skin test performed within the last 12 months and previous antituberculous treatment.

In the first part of this study, parents were asked to fill in a questionnaire on general health status, received medications, occurrence of allergic diseases as well as symptoms suggestive of allergic disease. Questionnaires were distributed during parent-teacher conferences at schools,

and all classes of the corresponding courses of all the schools were selected. In the second part of the study, children whose parents answered the questionnaire and gave their informed consent were subjected to a routine pediatric examination and skin prick tests (SPTs) performed by a trained allergist. Upon physical examination particular attention was paid to the presence of symptoms suggestive of allergic disease.

SPTs with the following inhalant allergens (Allergopharma Nexter): grass/corn mix, grass mix, hazel, alder, birch, rye, sagebrush, plantain, animal dander mix I, animal dander mix II, *Dermatophagoides farinae*, *Dermatophagoides pteronyssinus*, molds mix I, and molds mix II were performed according to generally accepted standards (22). For the purpose of simplification allergens were classified into trees, grass, corn, weeds, animal dander, house dust mites (HDMs), and molds.

Doctor-diagnosed allergic disease was defined as a combination of an allergic disease reported in a questionnaire and/or an allergic disease diagnosed by the examining clinician based on reported allergic symptoms, physical examination, and SPTs results.

Atopy was defined as a positive SPT result to at least one of the tested allergens. An SPT result was considered positive if the induced mean wheal diameter was 3 mm or greater than the response to saline.

The protocol was approved by the Bioethics Committee of the Medical University of Warsaw, and informed written consent, including consent for SPTs, was obtained from the children's parents or caregivers.

Statistical analysis

All statistical analyses were performed using STATISTICA 12 software. The differences between the groups in continuous variables were computed using the Mann–Whitney *U*-test. The associations between living environment and atopy, allergic symptoms and diseases were analyzed using Chi-square or Fisher exact test and appropriate measures of strength of association – Cramer's *V* and *Phi*. Crude odds ratios (OR) and adjusted odds ratios (aOR) with 95% confidence intervals (95% CI) were calculated using logistic regression analysis, adjusting for age, sex, place of residence (urban versus rural), pet ownership, positive family history of allergic disease, and exposure to tobacco smoke (ETS). Values of $p < 0.05$ were considered statistically significant.

Results

During the study period 1351 children aged 10–14 years were attending the selected schools (577 in Lublin province and 774 in Warsaw). Parents of 965 children

Table 1. Baseline demographic and clinical characteristics.

	urban (n 185)	rural (n 165)	p
Sex:			
Male n/Female n	91/94	86/79	0.58
Age:			
mean (SD)	11.79 (1.26)	12.43 (1.45)	0.00002
Family history of allergic disease n (%)			
positive	53 (28.8)	46 (28.05)	0.98
Exposure to tobacco smoke n (%):			
yes	73 (39.89)	61 (38.13)	0.74
Pet ownership n (%):			
yes	121 (65.76)	101 (61.59)	0.72
≥ 3 pets	12 (6.49)	23 (13.94)	0.009

were present at parent–teacher conferences and received the questionnaires, and 400 (41.5%) of them gave their consent.

To this study, we enrolled 400 children (192 girls and 208 boys, 223 from the city, and 177 from rural areas) aged 10–14 years. The physical examination and SPTs were performed in 350 children – 173 girls and 177 boys, 185 from Warsaw and 165 from rural areas. The remaining 50 children were excluded due to acute infection, introduction of new treatment or consent withdrawal. The baseline demographic and clinical characteristics are presented in Table 1.

Prevalence of atopy, allergic symptoms, and doctor-diagnosed allergic disorders in the study population

Atopy was diagnosed in 101 (27.6%) children with HDMs being the most common allergens. 37.9% of all atopic children were monosensitized, 45.3% of them were allergic to 2–4 allergens and 16.8% to ≥5 allergens. The prevalence of allergic symptoms was 46.7%. However, the

overall prevalence of allergic disease defined as at least one doctor-diagnosed allergic disorder was significantly lower and did not reach 25% ($p < 0.0001$). The juxtaposition of the prevalence of specific allergic symptoms along with the prevalence of associated allergic disorders renders this discrepancy even more pronounced (Figure 1).

Prevalence of atopy, allergic symptoms, and doctor-diagnosed allergic disorders in urban versus rural children

Urban children had significantly higher SPT positivity rate than children living on farms, 33.5% versus 20% ($p < 0.05$), respectively. There was a weak correlation between living in a city and the prevalence of atopy ($p = 0.0045$, $Fi = 0.152$, $df = 1$). Also, the prevalence of polyvalent sensitization was much higher in urban (25.95%) versus rural (6.66%) children ($p = 0.00000$, $Fi = 0.257$, $df = 1$). Yet, the development of monovalent sensitization showed the opposite tendency, although not statistically significant (Figure 2). Furthermore, we observed higher SPT positivity to all inhalant allergens in children living in a city versus children from rural areas and apart from HDMs all the differences reached statistical significance (Figure 3).

Moreover, the overall prevalence of a doctor-diagnosed allergic disease was higher in children living in Warsaw (29.3% versus 17.1%, $p = 0.007$), but the calculated correlation was rather weak ($p = 0.007$, Cramer's $V = 0.144$, $df = 2$). In contrast, no differences between the groups were shown in rates of particular allergic diseases. Similarly, no significant differences in the prevalence of allergic symptoms were noted between the groups, with the exception of food allergy symptoms that were more frequently reported by urban children ($p < 0.05$). Although there was an age difference

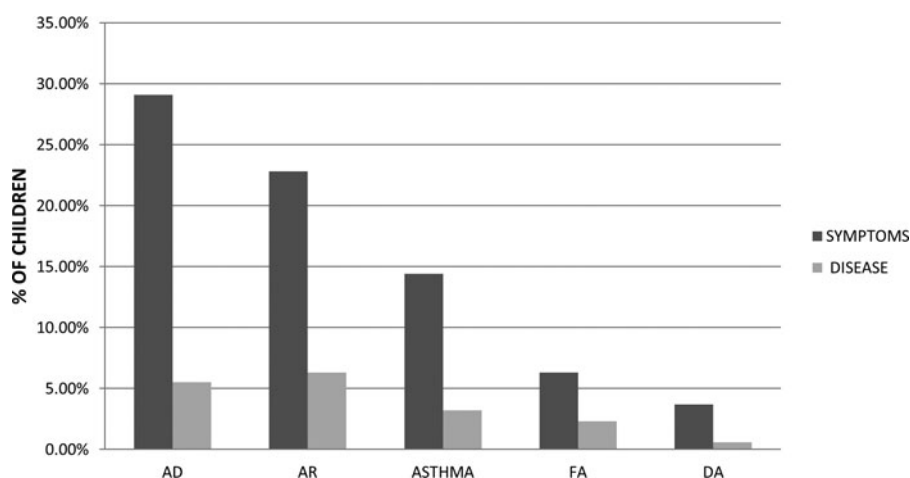


Figure 1. Prevalence of reported allergic symptoms and associated doctor-diagnosed allergic diseases in the study population. All the differences are statistically significant ($p < 0.05$). AD – atopic dermatitis; AR – allergic rhinitis; FA – food allergy; DA – drug allergy.

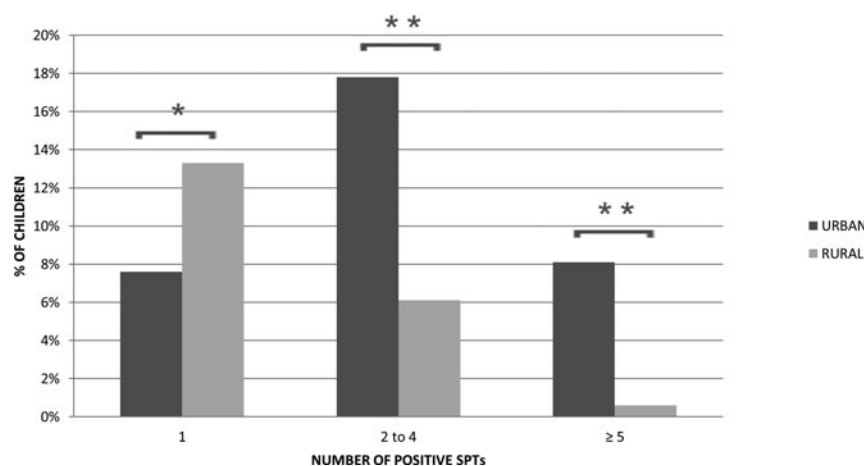


Figure 2. Percentage of children with one, two to four and five or more positive skin prick tests to inhalant allergens among urban and rural children. SPTs – skin prick tests. * $p < 0.05$; ** $p = 0.0008$.

between rural and urban children, no association between age and the prevalence of any allergic symptom, disease or sensitization was noted ($p > 0.05$). Table 2 summarizes current allergic symptoms, allergic diseases, and sensitization in urban and rural children.

Other risk factors of atopy and allergy

Among other studied potential risk factors of atopy and allergy only pet ownership, ETS and positive family history of allergic disease showed associations with the studied outcomes in univariate analysis (data not shown).

Logistic regression analysis proved the protective effect of pet ownership on the prevalence of sensitization to one (OR = 0.40; 0.19–0.83) and five or more (OR = 0.31; 0.10–0.91) allergens, but not on polyvalent sensitization or atopy in general. Children from families having three or more pets had lower prevalence of allergic disease ($p = 0.037$, $Fi = -0.166$, $df = 1$) and atopy ($p = 0.045$, $Fi = -0.159$, $df = 1$) than children owing only one pet. In particular, having ≥ 3 pets was associated with

lower prevalence of polyvalent sensitization ($p = 0.032$, $Fi = -0.156$, $df = 1$), sensitization to trees ($p = 0.029$, $Fi = -0.17$, $df = 1$), and grass pollen ($p = 0.047$, $Fi = -0.159$, $df = 1$). Although owing ≥ 3 pets decreased the odds of having allergic disease in univariate analysis, it was not confirmed in a multivariate model.

Positive family history of allergic disease was negatively associated with doctor-diagnosed allergic disease (OR = 2.15; 1.25–3.72), namely with asthma (OR = 3.53; 1.02–12.25), and allergic rhinitis (AR) (OR = 7.18; 2.63–19.64) as well as with non-infectious rhinitis symptoms (OR = 2.44; 1.41–4.22).

Surprisingly, ETS was inversely related to SPT positivity to HDMs (OR = 0.49; 0.25–0.95), polyvalent sensitization (OR = 0.48; 0.25–0.94), and doctor-diagnosed allergic disease (OR = 0.49; 0.28–0.88) (Table 3).

Discussion

This cross-sectional study showed a high prevalence of atopy, allergic diseases, and allergic symptoms in

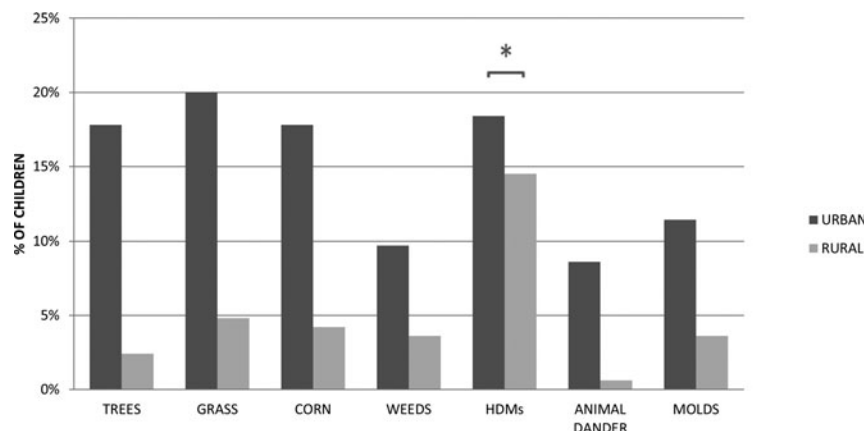


Figure 3. Distribution of positive skin prick tests to specific inhalant allergens among urban and rural children. Apart from house dust mites allergens, all the differences are statistically significant ($p < 0.05$). HDMs – house dust mites. * $p < 0.05$.

Table 2. Prevalence of allergic symptoms, allergic diseases and sensitization in urban and rural children.

	urban <i>n</i> (%)	Rural <i>n</i> (%)	p-value	crude OR (95% CI)	aOR (95% CI)*
<i>Allergic symptoms</i>					
asthma symptoms	26 (14.1)	26 (16)	0.88	1.01 (0.29–3.55)	1.15 (0.61–2.16)
Non-infectious rhinitis	45 (24.5)	32 (19.6)	0.19	1.37 (0.82–2.29)	1.35 (0.78–2.31)
Eczema	56 (30.4)	44 (27)	0.41	1.21 (0.76–1.94)	1.11 (0.68–1.81)
Food allergy	18 (9.8)	4 (2.5)	0.0052	4.31 (1.42–13.06)	3.90 (1.26–12.09)
Conjunctivitis symptoms	3 (1.6)	1 (0.6)	0.036	2.69 (0.27–26.28)	2.41 (0.24–24.21)
Drug allergy	6 (3.3)	7 (4.3)	0.61	0.75 (0.25–2.29)	0.82 (0.26–2.61)
Any allergic symptom	101 (54.89)	84 (51.53)	0.47	1.17 (0.77–1.79)	1.20 (0.77–1.87)
<i>Doctor-diagnosed allergic disease</i>					
asthma	6 (3.3)	5 (3.1)	0.92	1.07 (0.32–3.60)	1.04 (0.30–3.62)
AR	16 (8.7)	6 (3.7)	0.06	2.49 (0.95–6.55)	2.35 (0.85–6.51)
AD	14 (7.6)	5 (3.1)	0.06	2.60 (0.91–7.42)	2.37 (0.80–7.02)
FA	6 (3.3)	2 (1.2)	0.18	2.71 (0.54–13.71)	3.04 (0.53–17.44)
Conjunctivitis	4 (2.2)	1 (0.6)	0.23	3.60 (0.40–32.79)	2.94 (0.31–27.63)
DA	0	2 (1.2)	0.22	—	—
Venom allergy	3 (1.6)	0	0.15	—	—
Any allergic disease	54 (29.3)	28 (17.1)	0.0071	2.02 (1.20–3.39)	2.22 (1.28–3.85)
<i>Allergic sensitization (SPT)</i>					
at least 1 positive SPT	62 (33.5)	33 (20)	0.0045	2.02 (1.23–3.29)	2.18 (1.30–3.68)
Monovalent	14 (7.6)	22 (13.3)	0.08	0.53 (0.26–1.08)	0.57 (0.27–1.196)
Polyvalent	48 (26.0)	11 (6.6)	0.0000	4.91 (2.44–9.85)	5.05 (2.46–10.35)
2–4 allergens	33 (17.8)	10 (6.1)	0.0008	3.37 (1.60–7.09)	3.29 (1.53–7.07)
≥5 allergens	15 (8.1)	1 (0.6)	0.0008	14.47 (1.88–111.58)	16.42 (2.08–129.79)
Trees	33 (17.8)	4 (2.42)	0.0000	8.74 (3.01–25.34)	8.31 (2.81–24.53)
Grass	37 (20)	8 (4.8)	0.0000	5.07 (2.28–11.26)	5.14 (2.26–11.66)
Corn	33 (17.8)	7 (4.2)	0.0001	4.90 (2.10–11.45)	4.92 (2.06–11.73)
Weeds	18 (9.7)	6 (3.6)	0.0243	2.86 (1.10–7.40)	2.83 (1.07–7.52)
Mites	34 (18.4)	9 (14.5)	0.3357	1.32 (0.75–2.35)	1.46 (0.80–2.66)
Animal dander	16 (8.6)	1 (0.6)	0.0005	15.53 (2.02–119.25)	15.85 (2.03–123.58)
Molds	21 (11.4)	6 (3.6)	0.0069	3.39 (1.33–8.66)	3.84 (1.46–10.11)

AR-allergic rhinitis; AD – atopic dermatitis, FA – food allergy, DA – drug allergy, aOR- adjusted odds ratio; 95% CI – 95% confidence intervals.

*Adjusted for age, sex, pet ownership, family history of allergic disease, and exposure to tobacco smoke.

10–14-year-old schoolchildren in Poland. We observed higher prevalence of atopy and overall allergic disease in urban children. In particular, we demonstrated significant differences in SPT positivity to the majority of inhalant allergens and in the prevalence of polyvalent sensitization between the groups. However, no significant differences in rates of particular diseases between farm-living and urban children were shown. Strikingly, in our study, ETS was inversely related to allergic-diseases and polyvalent allergic sensitization.

Soaring rates of childhood atopy and allergic disease have been repeatedly reported over the last decades in affluent countries. The high prevalence of allergic conditions in children taking part in our study stays in agreement with previous global and Polish reports (3,4,23–26). Although we observed a smaller prevalence of atopy (27.1%), asthma (3.2%), and AR (6.34%) in

our study than had been previously reported in Polish children, the prevalence of eczema and atopic dermatitis (AD) in our study corresponded to that observed in ECAP study- the most extensive epidemiological study on the prevalence of allergic diseases in Poland (3).

A lower prevalence of doctor-diagnosed allergic disease than that of patient-reported symptoms indicated in our study has also been demonstrated, e.g., in ECAP study (4). There are two possible scenarios leading to such a discrepancy – either allergic disease was underdiagnosed in children with actual allergic symptoms or allergic symptoms were overdiagnosed in children without an allergic disease. According to our data, the difference was particularly evident in rural children. One could possibly attribute such a finding to diminished access to health care in non-urban regions of the country and subsequent underdiagnoses of allergic diseases. Alternatively, parents

Table 3. Adjusted associations of risk factors with allergic symptoms, diseases, and atopy.

	Allergic symptoms aOR (95% CI)	Allergic disease aOR (95% CI)	Atopy aOR (95% CI)
Pet ownership*	0.96 (0.61–1.53)	0.91 (0.52–1.58)	0.63 (0.37–1.05)
≥ 3 pets*	0.91 (0.42–1.98)	0.26 (0.06–1.20)	0.49 (0.16–1.54)
positive family history of allergic disease†	1.28 (0.79–2.10)	2.20 (1.27–3.83)	1.52 (0.89–2.59)
ETS‡	0.90 (0.574–1.41)	0.49 (0.28–0.87)	0.60 (0.35–1.03)

*aORs with 95% CIs adjusted for age, sex, living environment (urban/rural), positive family history of allergic disease, and ETS.

†aORs with 95% CIs adjusted for age, sex, living environment (urban/rural), pet ownership, and ETS.

‡aORs with 95% CIs adjusted for age, sex, living environment (urban/rural), positive family history of allergic disease, and pet ownership.

of undiagnosed children could possibly be unaware of certain symptoms and their relation to allergic diseases, and thus do not seek help from specialists. Another possible explanation, however, might be parents' tendency to attribute non-specific symptoms of their children to a non-existent allergy, which, in turn, may have led to overestimation of the prevalence of allergic symptoms. Since the diagnosis of allergic disease in our study was verified by a clinician, we consider the latter to be the most probable.

The results of our study further support the protective farm-effect. We observed a higher prevalence of atopy and overall doctor-diagnosed allergic disease in urban children. Similarly to previous report, the majority (66.6%) of rural allergic children were monosensitized, although the proportion in our study was much higher (25). Additionally, we demonstrated significantly higher SPT positivity to all but one inhalant allergens in urban versus rural children. The only allergens against which sensitization was comparable in both groups were, not surprisingly, HDMs. At the same time, urban children were more frequently sensitized against allergens traditionally associated with rural environment, e.g., trees, grass, corn, weeds, animal dander, and molds. These results are in agreement with a recent meta-analysis by Campbell et al. who showed a significant protective effect of farm exposure during early childhood on allergic sensitization (OR = 0.60 (0.52 – 0.70)) and, in particular, on sensitization to cat and timothy (OR = 0.60 (0.51 – 0.70); OR = 0.46 (0.41 – 0.51)) (27).

Strikingly, as opposed to most recent studies, we were unable to show any significant differences between urban and rural children in the prevalence of particular allergic diseases, despite the fact, that the prevalence of, e.g., atopic dermatitis, AR or food allergy in urban children was at least two-fold higher. This can result either from low prevalence of allergic diseases in our study or from the actual increase in the prevalence of allergic disease among Polish villagers, which some associate with recent socio-economic changes. Lately, Sozanska et al. noted the almost complete disappearance of the previously evident contrast between town and village people in western Poland in the prevalence of atopy and some allergic diseases over just a 9-years period (21). The authors attribute this phenomenon to the socioeconomic transformation that took place after Poland's accession to the European Union and its significant impact on local farming practices. The most evident changes affecting animal husbandry resulted in a spectacular decrease in the number of cows and other large animals. This reduction of farm-related exposures might lie at the root of the observed substantial increase in atopy and AR among the villagers. Although the study by Sozanska et al. was conducted in 2012 in lower Silesia, whereas our patients were examined in 2011 in the

culturally and historically distinct middle-east region of Poland where traditional farming is still prevalent, some conclusions can still be reached. We argue that the lack of significant differences in the prevalence of particular allergic diseases with the still present difference in the prevalence of atopy between urban and rural children in our study could be possibly attributed to the same socio-economic changes observed in Silesia, albeit advanced to a lesser extent. Unfortunately, we could not have verified it, since data on farm-related exposures in our study were not available. Future research should focus on describing the observed process of transition from non-allergic to allergic status in a step-by-step manner.

The protective effect of a farm-upbringing on atopy, asthma, wheezing, and hay fever has been vastly, albeit inconclusively, documented (28–35). Of note, the majority of studies demonstrating this protective effect were conducted in Western Europe, where dairy-based farming is predominant. However, the majority of farms in Poland are small, family-run, and with farming practices that differ from those in other countries. Therefore, the protective effect of farm-living in Europe cannot be directly extrapolated to Polish villages (36). This issue notwithstanding, the protective effect of rural environment against the development of allergy had been previously demonstrated in Polish children (4,25–36). Worthy of note, the protection provided by farm-living depends on farming practices, which differ around the world, Europe and even within a single community. Recently, it has been suggested that it is rather the type of farming that determines the protective effect against atopy and allergies, with cattle breeding and unpasteurized farm milk consumption playing a pivotal role in this process (37). The time of exposure also seems to be important. It has been shown, that children living on a farm during the first year of life were protected against atopy and allergic disease to a greater extent than those exposed later. Similarly, children of full-time farmers were more protected than those of part-time farmers (38,39).

What remains elusive is how exactly a farm-upbringing modifies the risk of allergy. Recent research addressing this issue has concentrated on the biodiversity hypothesis (16,40,41). In aggregate, regular early exposure of rural children to natural environmental factors may interfere with their microbiome and may set a direction in immune cell lineage commitment towards Th1 response, and thus protect them from allergic disorders. Support for this concept comes from a study indicating a lower prevalence of asthma and atopy in Russian Karelians than in Finnish Karelians living in geographically adjacent regions (42). Of note, Russian Karelians have been shown to be exposed to a higher bacterial load in the environment and to have higher skin and nasal microbial composition and diversity (41,42). Similar conclusions

can be drawn from a study comparing asthma prevalence in Amish and Hutterite farm children – two United States agricultural populations with distinct farming practices. Low asthma prevalence in Amish children has been attributed to traditional farming practices modulating the microbial composition of the community environment (43). Although biodiversity was out of the scope of the present study, the results of studies like ours are essential in furthering our understanding of how the changing environment protects children against allergies in countries under socioeconomic transformation.

Apart from farm-living, several other studied risk factors, such as positive family history of allergic disease, pet ownership, and ETS were associated with atopy or allergic disease development in our study. Surprisingly, all of these parameters were similarly distributed among urban and rural children.

It is particularly difficult to explain why a positive family history of allergic disease was reported by a similar proportion of participants in both settings. In light of hygiene hypothesis, a high prevalence of allergic disease in the families of farm-living children seems to be questionable, although it is not implausible. Indeed, recent study by Sozanska et al. indicated a significant increase in the prevalence of atopy among Polish villagers, and the prevalence of atopy was very similar in the village and town populations (21). Alternatively, since this parameter was based solely on questionnaire data and was not verified by a clinician, it might have been overstated, as it had been suggested for a high prevalence of reported allergic symptoms. If the latter is true, the arising question is to what extent in each setting – however, we have no data on this subject, nor are we aware of such data from other studies conducted among Polish children.

We were unable to show a protective effect of pet ownership against the development of atopy and allergic disease. In a further analysis, we observed decreased prevalence of atopy and allergic disease in children from families having three or more pets compared with their peers owing only one pet. Not surprisingly, having three or more pets was more common among families from rural areas than among families living in Warsaw (13.94% vs 6.49%). Although some protection of having ≥ 3 pets against atopy and allergy was shown in univariate analysis, we were unable to confirm it in a multivariate model, possibly due to relatively small number of children owing ≥ 3 pets (35 children).

The surprising negative association of ETS with the development of polyvalent sensitization and allergic disease indicated in our study stands in opposition to the generally accepted negative impact of ETS on atopy and allergy (44). However, similar results have been already reported (25). The possible explanation can lay in a too small sample size or, alternatively, in parents' tendency

to quit smoking when they become aware of their child's allergy.

Our present study has several advantages. First of all, our study was completed by 87.5% of included patients, which allowed us to reduce selection bias to the greatest possible extent, taking into account small sample size and participation rate. Furthermore, unlike other cross-sectional studies, our study's outcomes were objectified by a clinician with experience in allergic diseases. In many previous studies, the outcome definitions were based on single variables such as parent-reported symptoms or doctor's-diagnosed disease, which may have led to over- or under-estimation of the actual prevalence of allergic disease. According to the protocol of our study, the physical examination and SPTs in all of the included children were conducted by a trained allergist rendering our outcome definition more rigorous. Moreover, we used SPTs as an objective marker of allergic sensitization. Thus, the outcome definitions were based on combined data from a questionnaire, physical examination, and SPT results. This helped us minimize the effects of "recall bias" in comparison with studies relying solely on questionnaire data and avoid a potential over-estimation of the prevalence of allergic disease.

The main limitations of our study encompass a relatively small sample size and small participation rate rendering our results subject to a selection bias. To this study, we enrolled 400 schoolchildren representing 41.5% of approached potential participants and 29.61% of all eligible students attending the selected schools in Warsaw and the Lublin province. Warsaw is the capital city of Poland, whereas the Lublin province is a middle-east region of Poland, which maintains the most traditional farming practices in the country with scarce industry related mainly to farming (agricultural and the food industry). In 2011, Warsaw had a population of 1.7 million residents, including 59,000 children aged 10–14 years, whereas the rural areas of Lublin province were inhabited by 1.1 million people with approximately 52,500 children aged 10–14 years. Thus, our sample size represents 0.00031% of all children aged 10–14 years in both settings.

Considering the potential explanations for a low participation rate we concentrated on the methodology of our study. On the one hand, due to limited resources, the examiner visited the selected schools only twice – once to present the study and distribute the questionnaires during parent–teacher conferences, and once to examine the students and administer the SPT. On the other hand, the participation rate in parent–teacher conferences was moderate to high and varied between the schools and courses between 60% and 90% allowing us to approach the parents of 71.4% of all eligible students. Therefore, we conclude that the most possible explanations for the low-participation rate include parents' lack of time to fill in the

questionnaire or their unwillingness to take part in the study. Importantly, although the participation rate was a bit higher among rural children, the difference between the groups was not significant (33.64% versus 39.76%). When we analyzed both groups according to age (10–12-year-olds and 13–14-year-olds), we noted distinctively high participation rate among older rural children. This discrepancy might have been partly responsible for the observed age difference between urban and rural children (mean age 11.79 years vs 12.43 years, respectively; $p < 0.001$). Potential factors responsible for such an age difference include the number of students in each course in the selected schools, the number of approached parents attending parent-teacher conferences and the aforementioned participation rate, which was the highest among older rural children. Additionally, this study was conducted before and after summer school holidays, which in Poland last for 2 months (July and August). Due to logistical reasons, we managed to enroll 38% of urban children and only 15% of rural children before the holidays, which also might have contributed to the age difference between the groups.

Another possible limitation of our study is the lack of total or specific IgE level measurements as additional markers of atopy. We did, however, perform SPTs in all included children, which allowed us to objectively assess the atopic status of the participants.

Conclusions

In this study, we demonstrate that the protective effect of farm-living on the prevalence of atopy and overall allergic diseases is still present, albeit not on the prevalence of particular allergic diseases in children in Poland. This trend can be possibly attributed to significant changes in local farming practices after Poland's accession to the European Union. While current studies are far from conclusive in determining the exact mechanisms behind the farming effect, determining the impact of the rural environment across populations is an important piece of the puzzle that will likely help us understand current trends in the epidemiology of allergic diseases.

Declaration of interest

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

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