

Original Article

Inflammatory Diseases

The impact of meteorological factors on the incidence of infantile atopic dermatitis

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Keywords

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Introduction

Atopic dermatitis (AD, or eczema) is a chronic allergic disease with an onset frequently occurring during the early years of life.^{1,2} Eczema symptoms in children are considered seasonal³ and have complex triggering mechanisms with a critical contribution from environmental conditions.^{4,5} It appears that the harmful effects of various pollutants on children's skin may also act in conjunction with climatic conditions,⁶ or other types of weather.⁷

Different climatic factors influence the postnatal development of skin functional parameters.⁸ Initially, the lowest natural moisturizing factor levels of cheek stratum corneum compared with

Abstract

Background The role of the climate regarding atopic dermatitis (AD) in infants is still unclear. This study aimed to determine the relationship between meteorological conditions and the incidence of early AD.

Methods The study was conducted using a retrospective design. We analyzed children aged 0–24 months with clinically diagnosed AD ($n = 603$), including infantile eczema (IE, $n = 292$), in relation to the mean monthly meteorological data in Minsk. The Mantel–Haenszel method was used to study the association between an AD outcome and meteorological variables, stratifying by potential confounders. Seasons of birth were analyzed in children diagnosed with AD before 6 months of age ($n = 567$) and at 12 months of age ($n = 350$) from 2005 to 2019.

Results The incidence rate of IE was negatively associated with air temperature (adjusted incidence rate ratio = 0.75; 95% confidence interval (CI) 0.59–0.94), precipitation (0.74; 95% CI 0.58–0.93), and positively associated with atmospheric pressure (1.31; 95% CI 1.04–1.66). The highest incidence rate of IE was during spring, and the lowest was during summer. Incidences of AD were less frequent among infants born in the spring (18.1% vs. 29.4%, $P < 0.001$) than among older children. The principal component analysis identified three meteorological combinations where the first one (warm, low humidity) was negatively associated with the incidence rate of AD among children aged 0–24 months (0.77; 95% CI 0.65–0.92), and the third one (rainy, low atmospheric pressure) with IE (0.70; 95% CI 0.54–0.90).

Conclusion Continental seasonal cold-humid weather may influence early AD incidence. Moreover, short-term meteorological factors may play an important role in the onset of IE.

different skin regions in the first year of life were suggested as likely permissiveness for AD development.⁹ Epidemiological studies suggest that common climatic variables are associated with childhood eczema prevalence,^{10,11} but the relationship between climatic conditions and short-term meteorological changes and the first manifestations of AD among infants is scantily known.

In the present work, the incidence rate of early AD or infantile eczema (IE) in a retrospective setting was assessed following monthly meteorological exposure. The analysis was performed on the pediatric population of two climatically similar but ecologically different districts of Minsk to control the impact of air quality on IE incidence.

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Methods

Data sources and definition of diagnoses

We used data from statistical reports of the National Statistical Committee of the Republic of Belarus (NSCRB) and the database of the Minsk City Clinical Dispensary for Skin and Venereal Diseases (MCCDSVD). The database of the MCCDSVD covers children of all ages residing in Minsk in all pediatric outpatient clinic admissions. All the data were anonymized, and study researchers reviewed all the clinical diagnoses. No human subjects were involved in the investigation. Definition of diagnoses: from the MCCDSVD, we obtained the disease-specific ICD-10 (International Classification of Disease, version 10) diagnostic codes to identify outpatients with AD. The diagnosis of AD was ascertained by a specific ICD-10 code – L20.80.¹² We only considered newly diagnosed cases to estimate the incidence rate. Codified AD diagnoses were specified types: “atopic eczema” (flexural, local, or generalized), “neurodermatitis” (local or generalized), and “infantile eczema” (IE).

The cases reported in the MCCDSVD were identified by reviewing records from 12 outpatient clinics in the northern and southern districts of Minsk. All diagnoses of AD were made according to the clinical protocol authorized by the Ministry of Health of the Republic of Belarus,¹³ based on clinical signs (pruritus, with typical morphological elements on the skin and typical localizations), allergy anamnesis (family and patient), and IgE tests. To diagnose AD, at least three major and three minor criteria were used,¹⁴ and a minimal length of time of 6 weeks was observed for the symptoms. Pediatric dermatologists and immunologists determined the clinical and morphological features of inflammation on the skin to confirm the diagnosis. The primary focus was on 603 children aged 0–24 months with diagnoses of AD, of which 292 had IE, reported during the period January 1, 2005, to December 31, 2016. In addition, from 2005 to 2019, we examined 567 children with the first diagnosis of AD before 6 months of age and 350 at 12 months of age to observe the relationship between the season of birth and the incidences of AD.

The study was approved by the Research Ethics Committee of the Belarusian State Medical University, Minsk (22.03.2017 no.14).

Meteorological data, β -activity of radionuclide-associated aerosols and PM10

The source of the meteorological data was the online weather archive.¹⁵ The monthly mean air temperature, relative humidity (RH), wind speed (wind at 10 m above the ground), precipitation, calm, visibility, atmospheric pressure, south-west (SW) wind direction, and ultraviolet (UV) index were limited to 2005–2016.

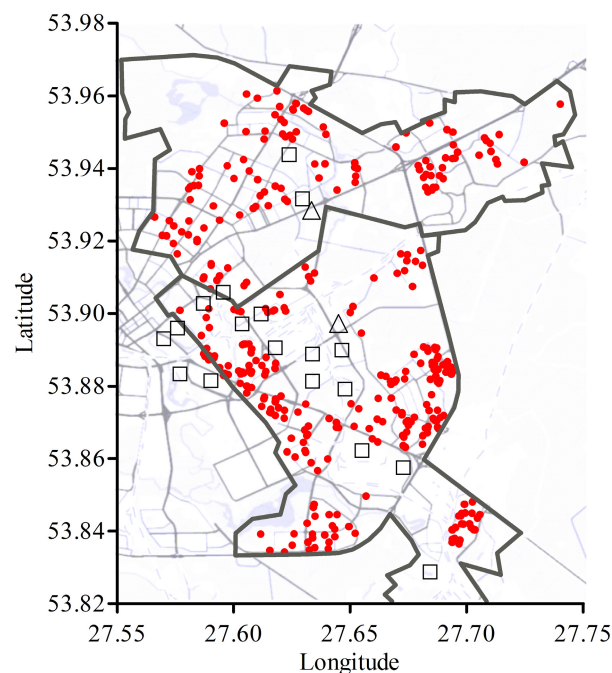


Figure 1 The actual location of the cases of atopic dermatitis (●), industrial sources (□), and two air monitoring stations (△) mapped to two districts of Minsk. Location of the air monitoring stations: in the north residential district—53.928, 27.633; in the south industrial district—53.897, 27.645

As it is known, the variability of natural nuclide levels in the troposphere is seasonal and depends on convectional currents and air mass transfer.^{16,17} We presumed a low dose level of β -activity of radionuclide-associated aerosols (RNAA) as an indicator for the atmospheric state in a polluted urban environment. The levels of β -activity of RNAA were extracted from the online environmental bulletins.¹⁸

Levels of particulate matter with an aerodynamic diameter of $\leq 10 \mu\text{m}$ (PM10) were monitored by two stations located in two neighboring districts in Minsk: the residential, comparably clean north district (59.06 sq km), which contained ~5% of all industrial sources of the city, and the industrial south district (68.06 sq km) which contained more than 60% of all industrial sources (Figure 1). The mean annual atmospheric levels of PM10 were 12–36 $\mu\text{g}/\text{m}^3$ and 21–52 $\mu\text{g}/\text{m}^3$ in residential and industrial districts, respectively. The annual number of days with atmospheric levels of PM10 higher than the upper limit (50 $\mu\text{g}/\text{m}^3$) was 0–40 days and 10–108 days in the residential and industrial districts, respectively.¹⁸

An additional analysis was performed covering the months from April through October, excluding months of central heating use. In Minsk, it is usual practice to keep indoor water heating radiators turned on until the outside temperature gets higher than 8°C.

Table 1 Mean person-years of the population aged 0–2 from 2005 to 2016, the average incidence rate of atopic dermatitis (AD) per 100 person-years, and the number of first-time diagnosed AD, infantile eczema (IE), and AD-IE

	M ± SD	AD		AD-IE n (%)	IE n (%)	Chi-squared (P)
		n (%)	IR (95%CI)			
Total		603 (100)		311 (51)	292 (48)	
Gender						
Boys	7783 ± 589	350 (58)	0.39 (0.23–0.55)	177 (29)	173 (28)	0.33 (0.56)
Girls	6902 ± 522	253 (42)	0.31 (0.21–0.41)	134 (22)	119 (20)	
District of residence						
Residential	7292 ± 529	282 (46)	0.33 (0.18–0.49)	179 (29)	103 (17)	30.03 (<0.001)
Industrial	7393 ± 587	321 (54)	0.37 (0.23–0.50)	132 (22)	189 (31)	
Period						
2005–2010	13,962 ± 1137	422 (69)	0.51 (0.34–0.68)	173 (28)	249 (41)	63.01 (<0.001)
2011–2016	15,411 ± 406	181 (31)	0.19 (0.16–0.22)	138 (23)	43 (7)	

AD, atopic dermatitis; IE, infantile eczema; IR, incidence rate; M, mean person-years; n, number of first-time diagnosed AD and IE; P, the value for Pearson chi-squared test between children with IE and AD-IE; SD, standard deviation.

Data processing

All data were analyzed using STATA version 14.2. The incidence rate of AD was computed as the number of new AD cases expressed as a percentage of the total number of children aged 0–24 months at risk. Analysis of the first diagnosed AD per month was performed in relation to the monthly mean values of the meteorological variables individually tested. Patients were grouped for each meteorological variable by median cut-off point into ranges of two intervals, low and high, in order to calculate the change in incidence rate for interval change in a particular meteorological variable. Thus, the diagnosed cases were grouped for each meteorological variable in order to calculate the incidence rate ratio (IRR), which was the relative risk of the first diagnosis of AD with increasing values of the meteorological variables. Since the meteorological variables were individually dichotomized, the lower half of each set of the dichotomized data was used as the reference group, and the higher half-exposure as one.

All data were arranged in 2 × 2 tables where AD cases represented outcome variables. Crude IRR of AD with 95% confidence intervals (CIs) were calculated between referent meteorological conditions and exposed ones. We used the Mantel–Haenszel method to study the association between an AD outcome and meteorological variables, stratifying by potential confounder, that is, according to gender, two districts, or two periods. In particular, we considered that trends of some environmental variables in Minsk¹⁹ and uneven levels of air pollutants (e.g., PM10) because of unequally distributed industrial sources in the city (Figure 1) could be potential confounding conditions. On this basis, the incidence rate of AD was calculated for two periods (2005–2010 and 2011–2016) and two districts (northern residential and southern industrial) using person-years at risk (Table 1). Next, we adjusted the

IRRs (aIRR) by the period and the district. Before estimating IRR, we checked whether the IRRs were homogeneous. The homogeneity of effect between strata was determined with chi-squared tests. The confounding was excluded if the aIRR differed from the crude IRR by <5%.

Principal component analysis (PCA) was used to reveal components with the best mutually correlated meteorological variables. The components were selected if their eigenvalue was >1 and their loading value was >0.5. After the varimax method, the components represented dominant combinations of the meteorological variables. Monthly component scores were split at the median into low (reference) and high values to determine the IRR of AD under one of the dominant meteorological combinations.

A two-sided $P < 0.05$ indicated statistical significance for all estimates.

Results

Pediatric population characteristics

The descriptive statistics for first-time AD diagnosis are shown in Table 1. The results of the reported monthly diagnoses of AD were weighted to represent the populations of children aged 0–24 months in two districts of Minsk. AD cases showed a predominance of boys (58% boys vs. 42% girls). A higher frequency of IE (189 cases) was observed in the southern industrial district of the city than (103 cases) in the northern residential district. The incidence rate of AD and IE was higher during the 2005–2010 period than in 2011–2016.

Association between air temperature and incidence rate of AD and IE

The analysis revealed that higher mean monthly air temperatures between 7.4 and 26.6°C were associated with a

Table 2 Association between mean monthly meteorological variables and incidence rates of atopic dermatitis (AD) among children aged 0–24 months

(min, max)	<i>n</i>	AD IR (95% CI)	Crude IRR (95% CI)	aIRR [†] (95% CI)	aIRR [‡] (95% CI)
Temperature (°C)					
Low (−11.1, 7.2)	342	0.40 (0.31–0.48)	Reference	Reference	Reference
High (7.4, 26.6)	261	0.31 (0.24–0.37)	0.76 (0.65–0.90)**	0.76 (0.65–0.89) ^a	0.75 (0.63–0.88) ^a
Relative humidity (%)					
Low (52, 77)	265	0.31 (0.24–0.37)	Reference	Reference	Reference
High (77, 93)	338	0.39 (0.31–0.48)	1.29 (1.09–1.52)*	1.28 (1.09–1.51) ^a	1.13 (0.96–1.33) ^a
Wind speed (m/s)					
Low (0.9, 1.7)	229	0.26 (0.20–0.31)	Reference	Reference	Reference
High (1.7, 3.1)	374	0.45 (0.36–0.53)	1.76 (1.49–2.07)***	1.75 (1.48–2.06) ^a	1.44 (1.21–2.70)
Calm (%)					
Low (1.2–15.8)	350	0.41 (0.32–0.50)	Reference	Reference	Reference
High (16.5–38.8)	253	0.29 (0.23–0.35)	0.71 (0.60–0.84)***	0.71 (0.60–0.83) ^a	0.76 (0.65–0.90) ^a
SW wind direction (%)					
Low (0.4, 6.9)	237	0.27 (0.21–0.34)	Reference	Reference	Reference
High (6.9, 28.0)	366	0.42 (0.35–0.51)	1.53 (1.29–1.80)***	1.52 (1.30–1.80) ^a	1.26 (1.06–1.49)
Precipitation (mm)					
Low (6.2, 51)	327	0.38 (0.30–0.46)	Reference	Reference	Reference
High (52, 249)	276	0.32 (0.25–0.39)	0.83 (0.70–0.98)*	0.83 (0.71–0.98) ^a	0.80 (0.68–0.94) ^a
AP (mmHg)					
Low (731.6, 740.9)	264	0.30 (0.23–0.37)	Reference	Reference	Reference
High (740.9, 750.7)	339	0.40 (0.32–0.48)	1.28 (1.09–1.50)**	1.28 (1.09–1.51) ^a	1.31 (1.11–1.54)
UV-index					
Low (0.2, 2.1)	353	0.41 (0.33–0.49)	Reference	Reference	Reference
High (3.2, 6.6)	250	0.29 (0.23–0.35)	0.70 (0.59–0.83)***	0.70 (0.60–0.83) ^a	0.70 (0.60–0.83) ^a
Visibility (km)					
Low (5.3, 11.9)	342	0.40 (0.31–0.48)	Reference	Reference	Reference
High (11.9, 17.7)	261	0.31 (0.24–0.37)	0.75 (0.64–0.89)**	0.75 (0.64–0.88) ^a	0.86 (0.73–1.01) ^a
βRNA (10 ^{−5} Bq/m ³)					
Low (3, 17.7)	298	0.38 (0.30–0.47)	Reference	Reference	Reference
High (18, 22.9)	222	0.27 (0.21–0.33)	0.71 (0.60–0.85)***	0.71 (0.60–0.85) ^a	0.95 (0.79–1.15) ^a
Seasons					
Spring	162	0.38 (0.27–0.48)	1.50 (1.17–1.91)**	1.50 (1.16–1.93) ^a	1.50 (1.17–1.91)
Summer	108	0.25 (0.17–0.33)	Reference	Reference	Reference
Autumn	160	0.37 (0.28–0.46)	1.49 (1.16–1.92)**	1.48 (1.16–1.90)	1.48 (1.16–1.89) ^a
Winter	173	0.41 (0.27–0.54)	1.61 (1.26–2.07)***	1.61 (1.26–2.05) ^a	1.60 (1.25–2.03)

aIRR[†] and aIRR[‡]—the combined Mantel–Haenszel estimates where district (northern residential vs. southern industrial) and period category (2005–2010 vs. 2011–2016) are potential confounders, respectively.

n, number of first-time diagnosed atopic dermatitis; IR, incidence rate; IRR, incidence rate ratio; aIRR, adjusted incidence rate ratio;

SW-wind, south-west wind direction; AP, atmospheric pressure; βRNA, β-activity of RNA; AD, atopic dermatitis; CI, confidence interval.

^aThere is homogeneity across the category strata ($P > 0.1$).

* $P < 0.05$.

** $P < 0.01$.

*** $P < 0.001$.

decreased incidence rate of AD (aIRR 0.75, 95% CI: 0.63–0.88) (Table 2) in comparison with AD incidence at lower temperatures (−11.1–7.2°C). The higher mean monthly air temperatures (aIRR 0.75, 95% CI: 0.59–0.94) were also associated with a decreased incidence rate of IE (Table 3).

Precipitation, atmospheric pressure, UV-index

Higher mean monthly precipitation was associated with a decreased incidence rate of AD or IE (aIRR 0.80, 95% CI: 0.68–0.94, and 0.74, 95% CI: 0.58–0.93, respectively), and

atmospheric pressure, with an increased incidence rate of AD or IE (aIRR 1.28, 95% CI: 1.09–1.51, and 1.31, 95% CI: 1.04–1.66, respectively; Tables 2 and 3).

A higher mean monthly UV-index (3.2–6.6) was associated with a decreased incidence rate of AD (aIRR 0.70, 95% CI: 0.60–0.83; Table 2).

Seasons of AD incidence and seasons of birth

We found that the highest incidence rate of IE was observed during the winter (aIRR 1.80, 95% CI: 1.26–2.56) and spring

Table 3 Association between mean monthly meteorological variables and incidence rate of infantile eczema (IE)

(min, max)	<i>n</i>	IE IR (95% CI)	Crude IRR (95% CI)	aIRR [†] (95% CI)	aIRR _‡ (95% CI)
Temperature (°C)					
Low (−11.1, 7.2)	165	0.19 (0.13–0.26)	Reference	Reference	Reference
High (7.4, 26.6)	127	0.15 (0.10–0.20)	0.77 (0.61–0.97)*	0.77 (0.61–0.97) ^a	0.75 (0.59–0.94) ^a
Relative humidity (%)					
Low (52, 77)	136	0.16 (0.11–0.21)	Reference	Reference	Reference
High (77, 93)	156	0.18 (0.12–0.25)	1.15 (0.91–1.45)	1.15 (0.91–1.44) ^a	0.92 (0.73–1.16) ^a
Wind speed (m/s)					
Low (0.9, 1.7)	81	0.09 (0.05–0.13)	Reference	Reference	Reference
High (1.7, 3.1)	211	0.26 (0.18–0.33)	3.14 (2.41–4.09)***	3.07 (2.36–4.00)	2.27 (1.72–2.99)
Calm (%)					
1.2–15.8	178	0.21 (0.14–0.28)	Reference	Reference	Reference
16.5–38.8	114	0.13 (0.09–0.18)	0.63 (0.49–0.80)***	0.63 (0.50–0.80) ^a	0.71 (0.56–0.90) ^a
SW wind direction (%)					
Low (0.4, 6.9)	104	0.12 (0.07–0.17)	Reference	Reference	Reference
High (6.9, 28.0)	188	0.22 (0.16–0.29)	1.79 (1.41–2.30)***	1.79 (1.41–2.30)	1.28 (1.00–1.63) ^a
Precipitation (mm)					
Low (6.2, 51)	167	0.20 (0.13–0.27)	Reference	Reference	Reference
High (52, 249)	125	0.15 (0.10–0.20)	0.74 (0.58–0.93)*	0.74 (0.58–0.93) ^a	0.72 (0.57–0.91) ^a
AP (mm Hg)					
Low (731.6, 740.9)	129	0.15 (0.10–0.20)	Reference	Reference	Reference
High (740.9, 750.7)	163	0.20 (0.13–0.26)	1.27 (1.01–1.61)*	1.27 (1.01–1.60) ^a	1.31 (1.04–1.66) ^a
UV-index					
Low (0.2, 2.1)	166	0.20 (0.13–0.26)	Reference	Reference	Reference
High (3.2, 6.6)	126	0.15 (0.10–0.20)	0.75 (0.59–0.96)*	0.75 (0.60–0.95) ^a	0.75 (0.60–0.95)
Visibility (km)					
Low (5.3, 11.9)	155	0.18 (0.12–0.25)	Reference	Reference	Reference
High (11.9, 17.7)	137	0.16 (0.11–0.22)	0.87 (0.68–1.10)	0.86 (0.68–1.08) ^a	1.08 (0.85–1.36) ^a
βRNAA (10 ^{−5} Bq/m ³)					
Low (3, 17.7)	161	0.21 (0.14–0.28)	Reference	Reference	Reference
High (18, 22.9)	77	0.09 (0.06–0.13)	0.46 (0.34–0.60)***	0.46 (0.35–0.60)	0.77 (0.67–1.03) ^a
Seasons					
Spring	97	0.23 (0.14–0.31)	2.03 (1.42–2.94)***	2.03 (1.44–2.88) ^a	2.02 (1.42–2.85) ^a
Summer	48	0.11 (0.05–0.17)	Reference	Reference	Reference
Autumn	61	0.15 (0.07–0.22)	1.27 (0.86–1.90)	1.27 (0.87–1.86) ^a	1.27 (0.87–1.85)
Winter	86	0.21 (0.10–0.31)	1.80 (1.25–2.62)**	1.80 (1.26–2.56) ^a	1.79 (1.25–2.55)

aIRR[†] and aIRR_‡—the combined Mantel–Haenszel estimates where district (north residential vs. south industrial) and period category (2005–2010 vs. 2011–2016) are potential confounders, respectively.

aIRR, adjusted incidence rate ratio; AP, atmospheric pressure; IR, incidence rate; IRR, incidence rate ratio; *n*, number of first-time diagnosed infantile eczema; SW-wind, south-west wind direction; βRNAA, β-activity of RNAA.

^aThere is homogeneity across the category strata ($P > 0.1$).

* $P < 0.05$.

** $P < 0.01$.

*** $P < 0.001$.

(aIRR 2.02, 95% CI: 1.42–2.85), compared with the lowest incidence rate during the summer (Table 3).

Children with AD incidence before 6 months of age were more likely to be born in the summer ($P = 0.016$) and less in the spring ($P < 0.001$) than children with AD incidence at 12 months of age (Table 4).

RH, wind speed, calm, wind direction, and β-activity of RNAA

The analysis showed that the associations between the incidence rate of AD or IE and RH, wind speed, wind direction, and

monthly days with calm, atmospheric β-activity of the RNAA were significant but substantially confounded by the period of collected data (Tables 2 and 3).

Principal component analysis

The PCA identified three components: first, warm, less humid (52%–77%), clear, sunny, and calm weather; second, low wind speed and high β-activity of RNAA; third, rainy weather and low atmospheric pressure (Table 5). The first component was associated with a decrease in the incidence rate of AD (aIRR = 0.77, 95% CI: 0.65–0.92). The third component was

Table 4 Seasons of birth among children with AD incidence before 6 months of age ($n = 567$) and at 12 months of age ($n = 350$)

Season of birth	Total			Boys			Girls		
	6 months <i>n</i> (%)	12 months <i>n</i> (%)	<i>P</i>	6 months <i>n</i> (%)	12 months <i>n</i> (%)	<i>P</i>	6 months <i>n</i> (%)	12 months <i>n</i> (%)	<i>P</i>
Winter	136 (23.9)	82 (23.4)	0.67	80 (24.0)	52 (28.8)	0.23	56 (23.8)	30 (28)	0.13
Spring	103 (18.1)	103 (29.4)	<0.001***	57 (17.1)	47 (26.4)	0.016*	46 (19.5)	56 (20)	0.005**
Summer	169 (29.8)	79 (22.5)	0.016*	96 (28.9)	42 (23.3)	0.17	73 (31.0)	37 (17)	0.038*
Autumn	159 (28.0)	86 (24.5)	0.24	99 (29.8)	39 (21.6)	0.047*	60 (25.5)	47 (31)	0.63

P—the Pearson Chi-squared test value between children with AD incidence before 6 months of age and at 12 months of age.

**P* < 0.05.

***P* < 0.01.

****P* < 0.001.

Table 5 Principal component analysis of the association between meteorological variables and incidence rate of atopic dermatitis (AD) among children aged 0–24 months, and infantile eczema (IE)

	Components		
	First	Second	Third
RH (%)	−0.908*	−0.079	0.132
Visibility (km)	0.905*	0.124	−0.056
UV-index	0.903*	0.183	0.291
Temperature (°C)	0.860*	0.163	0.295
Calm (%)	0.639*	0.571	0.096
βRNAA (10 ^{−5} Bq/m ³)	−0.119	0.809*	−0.186
SW-wind (%)	−0.300	−0.680*	0.079
Wind speed (m/s)	−0.526	−0.667*	−0.159
Precipitation (mm)	0.146	0.070	0.868*
Atmospheric pressure	0.009	0.221	−0.771*
Eigenvalues (percent variance)	4.75 (47.59)	1.78 (17.86)	1.10 (11.04)
Component description	Dry, clear, sunny, warm, calm	High βRNAA, less windy	Rainy, low air pressure
AD			
Crude IRR (95% CI)	0.73 (0.61–0.87)***	0.58 (0.49–0.70)***	0.78 (0.65–0.93)**
Gender aIRR (95% CI)	0.73 (0.61–0.87) ^a	—	0.78 (0.65–0.93) ^a
District aIRR (95% CI)	0.73 (0.61–0.87) ^a	—	0.78 (0.65–0.93) ^a
Period aIRR (95% CI)	0.77 (0.65–0.92) ^a	0.77 (0.63–0.94) ^a	0.76 (0.64–0.91) ^a
IE			
Crude IRR (95% CI)	0.76 (0.59–1.00)*	0.25 (0.18–0.34)***	0.72 (0.55–0.94)*
Gender aIRR (95% CI)	—	—	0.72 (0.56–0.94) ^a
District aIRR (95% CI)	—	—	0.72 (0.56–0.94) ^a
Period aIRR (95% CI)	0.86 (0.66–1.11) ^a	0.41 (0.29–0.57) ^a	0.70 (0.54–0.90) ^a

aIRR, adjusted incidence rate ratio, the combined Mantel-Haenszel estimate where gender, district, or period category are potential confounders.

IRR, incidence rate ratio; RH, relative humidity; SW-wind, south-west wind direction; βRNAA, β-activity of RNAA; AD, atopic dermatitis; IE, infantile eczema; RH, relative humidity.

^aThere is homogeneity across the category strata ($P > 0.1$).

**P* < 0.05.

***P* < 0.01.

****P* < 0.001.

Table 6 Association between mean monthly meteorological variables and incidence rate of infantile eczema (IE) in the absence of central heating use

(min, max)	<i>n</i>	IE IR (95% CI)	Crude IRR (95% CI)	aIRR [†] (95% CI)	aIRR _‡ (95% CI)
Temperature (°C)					
Low (4.4, 14.4)	91	0.19 (0.12–0.26)	Reference	Reference	Reference
High (14.5, 22.6)	56	0.11 (0.05–0.17)	0.62 (0.44–0.88)**	0.61 (0.44–0.86) ^a	0.63 (0.45–0.88) ^a
Relative humidity (%)					
Low (52, 72)	89	0.18 (0.11–0.28)	Reference	Reference	Reference
High (72, 87)	58	0.12 (0.06–0.18)	0.65 (0.45–0.91)*	0.65 (0.47–0.91) ^a	0.65 (0.46–0.90) ^a
Precipitation (mm)					
Low (6.2, 59)	80	0.17 (0.09–0.24)	Reference	—	—
High (60, 249)	67	0.13 (0.06–0.19)	0.83 (0.59–1.16)	—	—
AP (mmHg)					
Low (735.1, 741.1)	66	0.13 (0.07–0.19)	Reference	—	—
High (741.2, 748.4)	81	0.17 (0.10–0.24)	1.24 (0.88–1.74)	—	—
UV-index					
Low (1.5, 5.1)	82	0.17 (0.10–0.24)	Reference	—	—
High (5.1, 6.6)	65	0.13 (0.07–0.19)	0.79 (0.56–1.11)	—	—

aIRR[†] and aIRR_‡ – the combined Mantel-Haenszel estimates where district (north residential vs. south industrial) and period category (2005–2010 vs. 2011–2016) are potential confounders, respectively.

aIRR, adjusted incidence rate ratio; AP, atmospheric pressure; IR, incidence rate; IRR, incidence rate ratio; *n*, number of first-time diagnosed infantile eczema; IE, infantile eczema.

^aThere is homogeneity across the category strata ($P > 0.1$).

* $P < 0.05$.

** $P < 0.01$.

associated with decreased AD and IE incidence (aIRR 0.76, 95% CI: 0.64–0.91 and 0.70, 95% CI: 0.54–0.90, respectively).

Meteorological variables and incidence rate of IE in the absence of central heating use

Higher mean monthly air temperature and RH throughout April–October were associated with a decreased incidence rate of IE (aIRR 0.63, 95% CI: 0.45–0.88, and 0.65, 95% CI: 0.46–0.90, respectively; Table 6).

Discussion

In this study, we stressed the importance of meteorological factors as likely affecting the clinical start of IE in continental climates. An association was found between meteorological changes and the incidence rate of AD or IE among children aged 0–24 months.

Air temperature, RH, UV-index

We determined the association of meteorological values like higher mean monthly air temperature (7.4–26.6°C) with a decrease in IE incidence. The lowest incidence rate of IE was observed during the summer period, for which warm air temperature, comparably high UV-index, precipitation, and good visibility were typical in Minsk. In contrast, the highest incidence rate of IE was observed during spring.

We interpret the results of the present study regarding the humid continental climate in Minsk, which is located in subzone “Dfb” according to the Köppen-Geiger climate classification,²⁰ with cold, humid winters and mild summers. They determined that the work’s negative association between the mean monthly air temperature and the incidence rate of AD is consistent with a negative association between the mean annual air temperature and the prevalence of atopic eczema symptoms estimated in school children of different climatic areas of Western Europe.²¹

The higher IE or AD incidence in cold, humid weather could imply its disrupting effects on the barrier function of infant skin. However, the differences in barrier function between healthy and AD-predisposed infant skin are not well-known. Investigations showed that infant skin has larger trans-epidermal water loss values than seen in adults²² and a slower decrease of trans-epidermal water loss in preterm infants at high RH, suggesting delayed epidermal barrier maturation at comparably more humid conditions.²³ To the contrary, in a prospective study conducted in neonates who developed AD, an increased trans-epidermal water loss was observed only after the development of skin lesions, and it was suggested that the decreased barrier function of AD infants is not inherent.²⁴ In addition, it has been shown that cold airflow alters skin pH and epidermal filaggrin degradation products in children with AD.²⁵ In our study, the association between RH and AD incidence was not

obvious, while the association with cold temperature was definite. Inborn infant skin vulnerability to cold, humid weather could likely be related to an aggravation of already developing eczematous lesions rather than its initiation during the first years of age.

Our finding of the highest mean monthly UV-index association with the lowest incidence rate of AD aligns with the study where more significant direct UV light exposures in early infancy were associated with a lower incidence of eczema and proinflammatory immune markers by 6 months of age.²⁶ It is known that UV stimulates cutaneous synthesis of pre-vitamin D, but findings indicate that UV light exposure appears to be more beneficial than vitamin D supplementation in early life.^{26–28} Here, we may only theorize that seasonal UV irradiation contributes to infant AD by involving vitamin D metabolism.

The protective effect of warm, moderately dry (RH 52%–77%) and sunny weather against the incidence of AD was confirmed in the present research by the PCA. An increased onset of IE can result from seasonally cold-humid weather in the continental conditions of Minsk. This is in agreement with the results of the other researchers who point to the seasonality of early eczema. For instance, a Norwegian study showed that the seasons of infant AD onset were winter and spring.²⁹ In Leeds, more frequent incidence of “infant eczema” was noticed between February and April and it was comparably rare in the summer.³⁰ Seasonal types of eczema among children were stated in the temperate climate of Augsburg.³ It was reported that climatic factors exerted influence at the biochemical and ultrastructural levels in normal adult skin on the cheeks and the hands.³¹ However, climatic or seasonal roles in epidermal barrier functions in healthy or AD-predisposed infants require further investigation.

Seasons of birth are particularly important in the development of AD in infants,^{32,33} and most likely involve both the role of outside meteorological conditions and indoor microclimate, especially during the cold months. In the present work, we could not exclude the possible role of the season of birth in the risk of early AD. Nevertheless, we revealed that infants born in spring had a decreased risk of AD during the first 6 months of life when compared with the risk of AD diagnosed 12 months after birth. These results are consistent with previous studies that showed a negative association between infant atopic eczema and spring birth in Slovakia.³⁴ It is appropriate to suggest that the decrease in IE incidence in the summer may be connected to the decrease of AD in infants born in the spring. However, we did not reveal a changed risk of AD in infants born during winter, and there was no increase of IE during autumn despite the risk of AD in infants born in the summer. Nevertheless, it is unclear whether or not winter birth plays a role in the higher incidence rate of IE in the continental climate of Minsk. There is a need for more detailed monthly studies to estimate the effects of the weather and indoor conditions during the postnatal period on the risk of AD in infants.

Precipitation and air pressure

The PCA revealed the association of lower IE incidence with the third combination—higher precipitation and lower atmospheric pressure, which were also individually associated with the incidence rate of IE. These results show some consistency with a positive correlation between the relative risk of daily outpatients with eczema and barometric pressure in subtropical climate subzones of Turkey and China.^{35,36} However, there are contradictions with studies from Spain¹⁰ and the United States,¹¹ where a higher mean annual or seasonal precipitation was positively associated with a statewide estimated prevalence of childhood eczema. Taking into account that the prevalence of childhood AD symptoms is positively associated with latitude,²¹ while different authors used climatic conditions of different latitudes for the analysis of the prevalence of childhood eczema, we presume that meteorological changes used for the analysis of IE incidence in a single climatic subzone may be part of the reason for the contradictions.

Lower IE incidence in meteorological conditions with higher precipitation and lower air pressure may be related to a warm, sunny summer at the latitude of Minsk. In addition, the incidence of IE could also depend on environmental conditions, including some that are strictly related to harmful weather components. For example, cold-humid weather can reflect an air temperature inversion in urban districts during winter, resulting in an accumulation of air pollutants,³⁷ while urban air can be comparably cleared out by precipitation during summer.

In order to assess the actual role of climate or meteorological conditions in the development of IE, other environmental variables, mainly seasonal traits, should be considered possible confounders. In the present study, we assumed that home heating conditions and probable temperature inversion in the city during the cold-humid season (November–March) might cause biased estimates of IRR. Thus, we additionally analyzed the incidence rate of IE after excluding months of central heating use. A negative association was revealed between air temperature or outdoor RH and IE incidence throughout April–October (Table 6). Despite the consistency of these results with studies demonstrating inverse associations of childhood AD with temperature and humidity,^{11,21} further research should be conducted to uncover the contribution of outdoor and indoor climate conditions in the development of infantile AD.

This study has several strengths, including the analysis of monthly meteorological data corresponding to individual children, the uniformity of the meteorological variables within one climatic subzone, the use of PCA to examine patterns of meteorological variables, and the estimation of the season of birth. The study also accounted for potential confounders caused by the ecological conditions in two urban districts. The results might represent similar climatic areas.

This research also has limitations. First, we used established diagnoses of AD, and the criteria for eczema could be different from the criteria usually used for the trials in other publications,

e.g., the minimal length of symptoms for diagnosis was 6 weeks while other researchers classified rashes as eczema if they lasted at least 2 weeks, showing a comparably higher percentage of eczema among infants in Belarus.³⁸ Second, the estimated meteorological conditions in the present study were restricted by the variables of only one geographical place. Therefore, it should be interpreted at the level representing the singularity of the urban area of Minsk. Further studies are needed to analyze the role of short-term environmental changes in eczema onset in children under 2 years of age in climatically identical urban conditions. Third, our study lacks data on family history of atopy, and no detailed measurements of the individual exposure of the patients to pets or maternal smoking were included. Such indoor factors as humidity at home, exposure to pets, and occasional maternal smoking, which are known to be associated with AD development in infancy,^{39,40} should not be ignored for a better estimation of their role as potential confounders. Furthermore, facts on the important role of familial or genetic predisposing factors for AD in early infancy^{40–42} ought to be accounted for in the future. In this regard, it remains to be seen whether the season of onset in early onset AD-predisposed infants depicts a particular risk of IE manifestation as a result of the meteorological changes.

Conclusion

In conclusion, this study showed that seasonal cold-humid conditions in continental climates were associated with a higher incidence of AD among children aged 0–24 months. Particularly, short-term meteorological changes might impact the onset of IE. Further investigations related to forecasting and AD monitoring systems could help understand the relationship between meteorological variability, microclimate, and early skin atopic reactions, and thus improve the management of IE.

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