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Association of Severe Atopic Dermatitis with month of birth in Armenian pediatric patients

To the editor,

Atopic dermatitis (AD) is a chronic relapsing skin disease which affects 15%-20% of children worldwide.¹ It is also considered as a major risk factor for developing other atopic diseases including food allergy, asthma, and allergic rhinitis later in life—a phenomenon known as the “atopic march.” Multiple factors, including season of birth and associated perinatal environmental conditions, have been known to play important roles in the manifestation of AD.² Moreover, about 20% of patients with AD have moderate-to-severe disease, which is associated with significantly lower quality of life, imposing considerable burden on the nation's health-care resources.³ Therefore, studying severe AD patients might be very important in managing overall AD-related disease burden. The objective of the present study was to identify potential birth season(s) associated with severe AD in Armenian pediatric patients, which would be helpful for the country's health-care researchers working toward identifying potential factors associated with severe pediatric AD in Armenia.

To evaluate the association between birth season and future development of severe AD, we analyzed de-identified data obtained from the patients' data cards (containing month of birth and AD severity levels of pediatric AD patients) of Arabkir Medical Center (AMC), Institute of Child and Adolescent Health, Yerevan, Armenia. All children diagnosed with AD between years 2008 and 2012 were included in this study (as the data were available). In the AMC hospital, severity was clinically graded into mild, moderate, and severe (SCORAD or EASI values were not available from the data cards) depending on dryness, redness, scratch marks, presence/absence of skin thickening (lichenification). Our final dataset consisted of de-identified information on age (in years), gender, month of birth, home-city, clinically determined severity and age at disease onset of 342 children. The mean age of the study cohort was 2.5 years, with 57% of the children being males. About 63.2% had disease onset before 1 year, whereas 19% had onset after 1 but before 2 years and 17.8% after 2 years. About 86.8% of the children had mild-to-moderate disease and 13.2% had severe disease. In logistic regression models, disease severity (severe vs mild/moderate) was treated as the

outcome variable, while gender, age at onset, month/season of birth were treated as predictor variables. Season was defined as follows: winter = December, January, and February; spring = March, April, and May; summer = June, July, and August; and fall = September, October, and November. All *P*-values below .05 were considered statistically significant. All analyses were carried out using the SAS statistical package (SAS Version 9.1, SAS Inc., NC, USA). Tables 1 and 2 show the results demonstrating the associations between season of birth and the severity of AD with spring (Table 1) and summer (Table 2) as reference seasons. Analysis adjusted for gender and age of onset that explored the association between birth season and AD severity with spring as reference season showed that being born in winter was associated with a lower risk of developing severe AD when compared to spring (OR = 0.2, 95% CI = 0.06, 0.64; *P*-value = .007). Gender was significantly associated with AD severity, with females having a lower risk of developing severe AD compared with males (OR = 0.32, 95% CI = 0.15, 0.68; *P*-value = .003). When the reference season was changed to summer, the results were similar, with winter births having a lower risk of developing severe AD when compared to summer (OR = 0.29, 95% CI = 0.09, 0.93; *P*-value = .04).

Existing data suggested strong relationships between the season of birth, perinatal exposure, and development of diseases including AD.^{2,4} Pediatric AD is a growing health problem in the republic of Armenia as indicated by steady increase in the number of registered pediatric AD cases nationwide, and in the capital city of Yerevan (Source: National Institute of Health of the Republic of Armenia; data not shown). However, there are no/very limited data currently available that could explain the connection between environmental exposure and severe AD manifestation in Armenian children. Characterizing the perinatal exposure, which is linked to birth season, could be very helpful in identifying the seasonal environmental risk factors associated with severe AD later in life. The present study indicates that being born in spring might be significantly associated with clinical manifestation of severe AD. Interestingly, previous authors have demonstrated the association between IgE-mediated aeroallergen sensitization and AD disease severity in German school children.⁵ Further studies are required to understand the mechanistic

TABLE 1 Association between season of birth and the severity of AD (severe disease [n = 45] vs mild/moderate disease [n = 297]) with spring as the reference season

Birth Season	Odds ratio (95% Confidence Intervals)	P-value
Autumn	0.7 (0.3, 1.63)	.41
Spring (reference)	1.0	
Summer	0.68 (0.29, 1.62)	.39
Winter	0.2 (0.06, 0.64)	.007*

Results from logistic regression were adjusted for gender and age at onset.

*Statistically significant.

TABLE 2 Association between season of birth and the severity of AD (severe disease [n = 45] vs mild/moderate disease [n = 297]) with summer as the reference season

Birth Season	Odds ratio (95% Confidence Intervals)	P-value
Autumn	1.03 (0.45, 2.34)	.95
Spring	1.47 (0.62, 3.48)	.39
Summer (reference)	1.0	
Winter	0.29 (0.09, 0.93)	.038*

Results from logistic regression were adjusted for gender and age at onset.

*Statistically significant.

relationship between birth season and severe AD in Armenia. A previous research among suspected atopic children showed that grass pollen was the most significant allergen in Armenia, followed by mite, pet, *Alternaria*, and tree pollen types.⁶ Interestingly, aerobiological studies confirmed the presence of allergenic pollen load in the flowering seasons starting in March-April, the months of birth associated with higher number of severe pediatric AD.⁶ Apart from pollen, exposure to dust mite, low sunlight/vitamin D, maternal tobacco smoke, pets/animals, and extreme dry/cold weather might play critical roles. Future studies have been designed to examine the roles of multiple juvenile and perinatal environmental factors (eg, allergen and pollutant exposure and sensitization, fluctuations in temperature and humidity), on the manifestation

of severe AD among Armenian children. The results could be helpful for the country's policymakers and health-care providers.

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