Original

Mindful approaches: Association between atopic dermatitis and autism spectrum disorder and use of visual storyboards

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Abstract

This study compared the prevalence of atopic dermatitis (AD) in pediatric patients with autism spectrum disorder (ASD) versus controls and explored approaches to AD management in children with ASD. We conducted a cross-sectional analysis of the International Business Machines Explorys electronic medical records database in the United States from January 1, 2017, to December 31, 2019. The primary outcome was International Classification of Diseases–10 diagnosis of AD with asthma or allergic rhinitis, a validated algorithm for identifying true AD cases. Logistic regression compared crude prevalence and assessed associations independent of potential confounders. AD prevalence was 5.0% among patients with ASD and 3.6% among controls (crude odds ratio (OR), 1.41; 95% CI, 1.23–1.61). After adjustment for demographics and healthcare visit frequency, the OR attenuated to 1.15 (95% CI, 1.01–1.32; P = .04) and further adjustment for attention-deficit/hyperactivity disorder yielded an OR of 1.09 (95% CI, 0.95–1.25; P = .24). Visual aids and storyboards may support AD management in children with ASD. These findings highlight a modest increase in AD prevalence in this population and underscore the need for tailored strategies to improve dermatologic care in children with ASD.

Introduction

Autism spectrum disorder (ASD) is a neurodevelopmental disorder that typically begins in early childhood and is characterized by restricted behaviors, impaired social skills, and speech delay.[1] Historic terms such as autism, Asperger syndrome, and pervasive developmental disorder not otherwise specified are included under the umbrella term ASD in the *Diagnostic and Statistical Manual of Mental Disorders, 5th edition*.[2] Activities of daily living and language skills may be impaired in children with ASD, which can be further exacerbated by associated comorbidities.[3,4]

Atopic dermatitis (AD) is an atopic skin condition with typical onset in early childhood and significant impact on quality of life.[5] Skin barrier dysfunction in AD results in an aberrant immunologic response that leads to inflammation.[3] AD is marked by dry, red, itchy patches that perpetuate the "itch-scratch cycle." Initial treatment typically includes topical therapies such as barrier ointments and corticosteroids, bleach baths, and gentle skin care regimens. Sensory processing differences and restricted behavior patterns in ASD pose barriers to traditional AD management.[2,6,7]

Studies suggest patients with ASD have higher prevalence of AD than controls, potentially owing to shared immunologic pathways and genetics.[1,5,8] Epidemiologic research shows ASD prevalence has been increasing worldwide.[1,2,6] Despite frequent co-occurrence of ASD and AD, dermatologists may lack confidence in adaptive management strategies. Children with ASD often have higher healthcare utilization and unmet needs, compounded by limited access to dermatologists experienced with ASD.[5,6] Currently, no guidelines exist for treating AD in children with comorbid ASD. Addressing this gap may improve care for this complex population. The aim of this study is to compare AD prevalence in pediatric patients with and without ASD and to share a thoughtful approach to AD management in children with ASD to improve health outcomes.

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Table 1. *ASD and ADHD ICD-9 and ICD-10 Codes.*

ICD Code	Description
ASD	
299.00	Autistic disorder, current or active state
299.01	Autistic disorder, residual state
299.80	Other specified pervasive developmental disorders, current or active state
299.81	Other specified pervasive developmental disorders, residual state
299.90	Unspecified pervasive developmental disorder, current or active state
299.91	Unspecified pervasive developmental disorder, residual state
F84.0	Autistic disorder
F84.5	Asperger's syndrome
F84.8	Other pervasive developmental disorders
F84.9	Pervasive developmental disorder, unspecified
ADHD	
314.00	ADHD, predominantly inattentive
314.01	ADHD, predominantly hyperactive
314.1	ADHD, other type
314.2	ADHD, other type
314.8	ADHD, other type
314.9	ADHD, unspecified type
F90.0	ADHD, predominantly inattentive type
F90.1	ADHD, predominantly hyperactive type.
F90.2	ADHD, combined type
F90.8	ADHD, other type
F90.9	ADHD, unspecified type

Abbreviations: ADHD, attention-deficit/hyperactivity disorder; ASD, autism spectrum disorder; ICD, International Classification of Diseases.

Methods

This was a cross-sectional study of the International Business Machines Explorys database. Explorys is a multihealth system research platform comprising electronic medical record (EMR) data from over 40 integrated healthcare systems, 400 000 healthcare providers, and approximately 53 million unique patients across all United States census regions.[9] The source population for the present analysis was a 15% random sample of database participants. Subjects aged 2–17 years with at least 1 encounter in the database between January 1, 2017, and December 31, 2019, were included if they had at least 1 year of total activity in the database (to allow adequate time for comorbidities to be recorded in the EMR) and at least 6 months of activity in the database during the study period. Comparison groups included subjects with ASD and those without. Patients with ASD were defined as having at least 1 occurrence of any of the International Classification of Diseases (ICD)–9 or ICD-10 codes found in **Table 1** prior to December 31, 2019.[10] Positive predictive value (PPV) for this definition (based on ICD-9 codes only) was 81% (682/845). The control group was composed of all patients satisfying the inclusion/exclusion criteria without any of the above diagnosis codes for ASD in their medical record.

The primary outcome was AD, defined as at least 1 ICD-10 code for AD in addition to at least 1 code for asthma or allergic rhinitis (**Table 2**).[11] This case definition displayed a PPV of 81% and 88% based on 2 independent EMR samples in the United States. The case definition included diagnosis of asthma or allergic rhinitis because a diagnosis of AD alone has been shown to have poor validity.[11,12] Covariates included age (years 2–4, 5–9, 10–14, 15–17), sex, race/ethnicity (White, Black, Asian, other/multiracial), number of inpatient, outpatient, and emergency department encounters during the study period (proxy for healthcare utilization, to account for detection bias), Medicaid status (proxy for socioeconomic status), and attention-deficit/hyperactivity disorder (ADHD) diagnosis as defined by ICD-9 or ICD-10 code.[13]

Statistical analysis included descriptive statistics comparing demographic characteristics between groups. Crude (unadjusted) prevalence of AD was compared in patients with and without ASD. Logistic regression was used to compare prevalence of AD while adjusting for

Table 2. *AD, Asthma, and Allergic Rhinitis ICD-10 Codes.*

ICD-10 Code	Description
AD	
L20.89	Other atopic dermatitis
L20.9	Atopic dermatitis, unspecified
L20.84	Intrinsic (allergic) eczema
Asthma	
J45.20	Mild intermittent asthma, uncomplicated
J45.21	Mild intermittent asthma with (acute) exacerbation
J45.22	Mild intermittent asthma with status asthmaticus
J45.30	Mild persistent asthma, uncomplicated
J45.31	Mild persistent asthma with (acute) exacerbation
J45.32	Mild persistent asthma with status asthmaticus
J45.40	Moderate persistent asthma, uncomplicated
J45.41	Moderate persistent asthma with (acute) exacerbation
J45.42	Moderate persistent asthma with status asthmaticus
J45.50	Severe persistent asthma, uncomplicated
J45.51	Severe persistent asthma with (acute) exacerbation
J45.52	Severe persistent asthma with status asthmaticus
J45.901	Unspecified asthma with (acute) exacerbation
J45.902	Unspecified asthma with status asthmaticus
J45.909	Unspecified asthma, uncomplicated
J45.990	Exercise induced bronchospasm
J45.991	Cough variant asthma
J45.998	Other asthma
Allergic rhinitis	
J30.1	Allergic rhinitis due to pollen
J30.2	Other seasonal allergic rhinitis
J30.5	Allergic rhinitis due to food
J30.81	Allergic rhinitis due to animal hair and dander (cat, dog)
J30.89	Other allergic rhinitis
J30.9	Allergic rhinitis, unspecified

Abbreviations: AD, atopic dermatitis; ICD, International Classification of Diseases.

age, sex, race, Medicaid status, and healthcare utilization (adjusted model 1). A second logistic regression (adjusted model 2) was performed adjusting for ADHD diagnosis in addition to all variables included in adjusted model 1. Missing data were handled using multiple imputation by chained equations with m = 20 imputations. Regression coefficients were pooled using Rubin's rules. Two sensitivity analyses were performed: (1) complete-case analysis in the subset of patients with no missing data for any of the analysis variables, and (2) using a less restrictive AD case definition requiring only 1 AD diagnosis.

A storyboard is a visual aid designed to help explain new experiences to children with ASD.[14] To aid in managing AD in patients with ASD, visual storyboards were developed by Nika Finelt, MD, and Silvija P. Gottesman, MD, board-certified dermatologists, in collaboration with Mehreen Kakwan, MA, CCC-SLP, a speech-language pathologist, illustrator, and published book author (**Figure 1** and **Figure 2**).

Results

Subjects who fulfilled the inclusion criteria are shown in **Table 3**. Of these, 4727 had a diagnosis of ASD, while 220 446 did not. Thus, approximately 2.1% of the study population had a formal ASD diagnosis. Characteristics of patients with and without ASD are described in **Table 4**. The ASD group tended to be somewhat older (86.5% aged 5-17 years versus 77.1% among controls) and were more likely to be male (78.1% versus 50.5%). Racial distribution was similar between groups. Patients with ASD

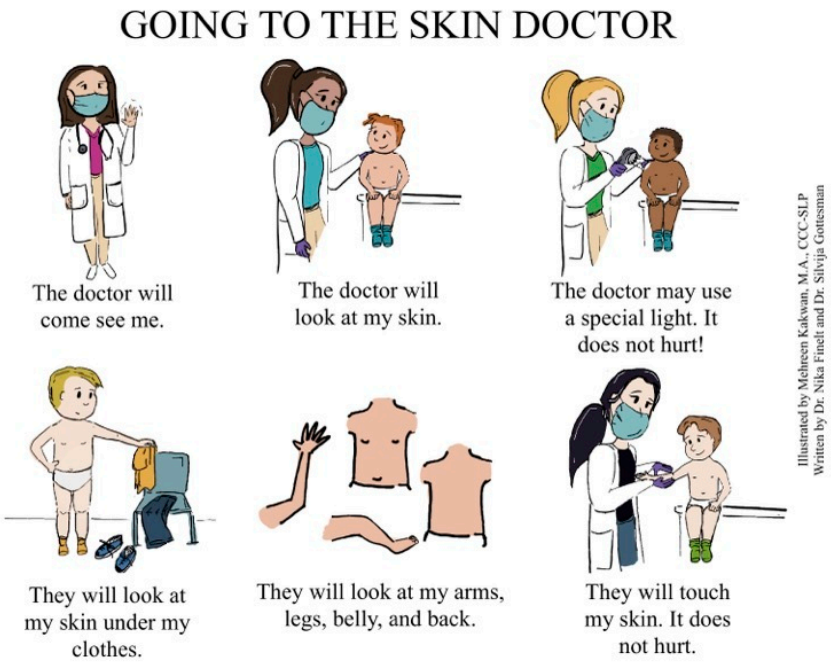

Figure 1. *A visual story with cartoons and simple phrases to help children with autism spectrum disorder understand what happens when going to the dermatologist for a skin evaluation.*

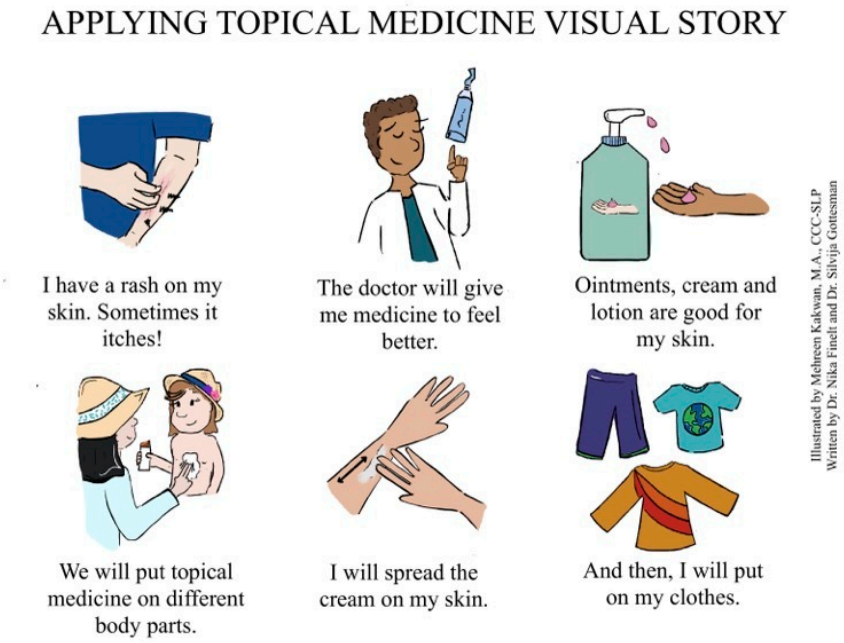

Figure 2. *A visual story with cartoons and simple phrases to help children with autism spectrum disorder understand the application process of topical products for treatment of skin disorders.*

were more likely to have Medicaid insurance (50.8% versus 34.0%) and a diagnosis of ADHD (37.0% versus 7.9%). They also had more healthcare encounters during the study period (median, 3.0 versus 2.0).

Prevalence of AD was 5.0% (234/4727) in patients with ASD and 3.6% (7848/220 446) in controls (crude odds ratio [OR], 1.41; 95% CI, 1.23–1.61) (Table 5). After adjusting for demographic variables and healthcare encounters, odds of AD were 15% higher among patients with ASD (OR, 1.15; 95% CI, 1.01–1.32; *P* = .04). Additional adjustment for ADHD attenuated the OR to 1.09 (95% CI, 0.95–1.25; *P* = .24).

In complete-case sensitivity analysis, AD prevalence was 4.4% in patients with ASD and 2.9% in controls. Un-

Table 3. *Study Eligibility Criteria and Patient Flowchart.*

Criteria	Patients Not Meeting Criteria, n	Remaining, n
At least 1 encounter at a participating Explorys institution between January 1, 2017, and December 31, 2019	–	2 582 476
Age data available	1050	2 581 426
Aged 2–17 years during study period	2 113 850	467 576
At least 1 year of observable person-time in database	134 006	333 570
At least 6 months of observable person-time during study period	108 397	225 173
With ASD diagnosis	–	4727
Without ASD diagnosis	–	220 446

Abbreviations: ASD, autism spectrum disorder.

adjusted and adjusted ORs ratios were similar to those in the primary multiple imputation analysis (Table 6). In a second sensitivity analysis using at least 1 AD diagnosis only, prevalence was 8.4% in ASD patients and 7.2% in controls. The crude OR for AD diagnosis alone was 1.17 (95% CI, 1.05–1.30). Adjusted ORs were similar to those from the primary analysis (Table 6).

Discussion

Our study suggests that AD has a higher prevalence in individuals with ASD compared to those without ASD, with a crude OR of 1.41. This corroborates prior literature proposing a correlation between ASD and AD.[2,3,5,6,15-19] A recent meta-analysis found significantly higher prevalence of AD in patients with ASD than in controls (overall OR, 1.49; 95% CI, 1.20–1.83).[1] The cause of this association has not been fully elucidated and is likely multifactorial, involving genetic, immunologic, and environmental factors. Several genes, including *ADRB2*, *GATA-3*, and brain-derived neurotrophic factor genes, have been associated with both conditions. It has also been hypothesized that the pro-inflammatory state in AD, characterized by increased mast cells and cytokines such as interleukin-6 and tumor necrosis factor-alpha, may compromise the blood-brain barrier, potentially contributing to neurobehavioral effects and explaining why ASD prevalence may increase with AD severity.[1,16,19-23] Stress and vitamin D deficiency have also been implicated in both conditions.[1,24] Further studies are needed to elucidate the relationship between ASD and AD. Among study participants, the association between ASD and AD was attenuated after adjusting for demographic factors and healthcare encounters but remained positive (OR, 1.15; 95% CI, 1.01–1.32).

Regardless of the underlying cause, the frequent co-occurrence of ASD and AD highlights the need for pediatric dermatologists to be familiar with ASD and understand that managing AD in these patients requires a tailored approach.[17] Patients with ASD often have sensory processing differences, which may complicate AD management.[2,6] These atypical responses may present as hypersensitivities, hyposensitivities, or sensory-seeking behaviors. Hypersensitivities may include amplified reactions to stimuli, such as certain textiles, making dermatologic exams and topical therapies challenging. Sensory-seeking behaviors may manifest as skin-picking or scratching, sometimes causing bleeding, particularly in those with hyposensitivity.[2] Intolerance of topical therapies and repetitive skin-picking can hinder adherence to standard AD regimens. Additionally, patients with ASD frequently have complex medical and social needs that may be difficult to address in fast-paced dermatology settings, with many parents reporting that providers do not fully address their concerns.[6] Educating dermatologists on the unique needs of patients with ASD and providing modified management strategies for providers and caregivers could help close this practice gap and improve care.

Visual aids and storyboards are effective tools for communication with children with ASD and other developmental disabilities. They can introduce topics ranging from handwashing and dressing to school tasks and emotional awareness. Visual stories have also been successfully applied to sun safety and procedural preparation in patients with ASD.[2,4] We hope the storyboards will increase comfort during dermatologic exams and topical therapy management, while providing dermatologists a practical tool to guide care and support parental involvement at home.

One limitation of this study is potential detection bias, as greater interaction with healthcare systems may increase AD documentation in patients with ASD.[25] We attempted to mitigate this bias by adjusting for healthcare utilization. Another potential confounder is ADHD diagnosis, which several prior studies have accounted for when examining the ASD–AD association. In our analysis, the independent association between ASD and AD was weaker after adjustment for ADHD. Strengths of this study include a large, heterogeneous population, use of a validated AD case definition, and adjustment for demographic and comorbid factors.

Table 4. *Characteristics of Patients With and Without ASD.*

Characteristic		Patients With ASD (n = 4727)	Control Patients (n = 220 446)
Age, y			
	Mean ± SD	9.64 ± 4.28	9.06 ± 4.74
	Median (Quartile 1, Quartile 3)	9.00 (6.00, 13.00)	9.00 (5.00, 13.00)
Age group, y, n (%)			
	2–4	639 (13.5)	50 373 (22.9)
	5–9	1754 (37.1)	68 234 (31.0)
	10–14	1517 (32.1)	63 264 (28.7)
	15–17	817 (17.3)	38 575 (17.5)
Sex, n (%)			
	Female	1036 (21.9)	108 866 (49.5)
	Male	3688 (78.1)	111 223 (50.5)
	Missing	3 (0.1)	357 (0.2)
Race, n (%)			
	White	1916 (72.7)	93 007 (69.4)
	Black	351 (13.3)	21 652 (16.2)
	Asian	64 (2.4)	3315 (2.5)
	Other/multiracial	306 (11.6)	15 956 (11.9)
	Missing	2090 (44.2)	86 516 (39.2)
Census region, n (%)			
	Midwest	1348 (28.6)	67 456 (30.7)
	Northeast	223 (4.73)	9766 (4.45)
	Puerto Rico	0 (0.0)	2 (< 0.01)
	South	2645 (56.1)	119 546 (54.4)
	West	502 (10.6)	22 906 (10.4)
	Missing	9 (0.2)	770 (0.3)
Medicaid insurance, n (%)		1963 (50.8)	57 792 (34.0)
	Missing	863 (18.3)	50 334 (22.8)
ADHD, n (%)		1750 (37.0)	17 513 (7.9)
Healthcare encounters during study period, n			
	Mean ± SD	2.77 ± 1.44	2.46 ± 1.27
	Median (Quartile 1, Quartile 3)	3.00 (2.00, 4.00)	2.00 (2.00, 3.00)

Abbreviations: ASD, autism spectrum disorder; ADHD, attention-deficit/hyperactivity disorder.

Conclusion

These findings highlight the high crude prevalence and frequent co-occurrence of ASD and AD. They underscore the importance of employing thoughtful, tailored management strategies to improve care for this unique patient population.

Potential conflicts of interest

Nika Finelt, MD, serves on the advisory board for Verrica and is a contributor to Elsevier. The remaining authors declare no conflicts of interest.

Table 5. *Prevalence of AD in Patients With and Without ASD.*

Outcome	Patients With ASD (n = 4727)	Control Patients (n = 220 446)	*P* Value
AD cases, n	234	7848	–
AD prevalence, %	5.0	3.6	–
Crude OR (95% CI)	1.41 (1.23–1.61)	Ref	< .001
Demographic-adjusted OR (95% CI)[a]	1.15 (1.01–1.32)	Ref	.04
Demographic plus ADHD-adjusted OR (95% CI)[b]	1.09 (0.95–1.25)	Ref	.24

Abbreviations: AD, atopic dermatitis; ADHD, attention-deficit/hyperactivity disorder; ASD, autism spectrum disorder; CI, confidence interval; OR, odds ratio.
[a] Adjusted for age group, sex, race, Medicaid insurance (yes/no), and number of healthcare encounters.
[b] Adjusted for age group, sex, race, Medicaid insurance (yes/no), number of healthcare encounters, and ADHD diagnosis.

Table 6. *Sensitivity Analyses for AD Outcome in Patients With and Without ASD.*

Outcome	Patients With ASD	Control Patients	*P* Value
Complete case analysis			
AD cases, n (total sample)	82 (1868)	2573 (89 673)	–
AD prevalence, %	4.4	2.9	–
Crude OR (95% CI)	1.55 (1.24–1.95)	Ref	< .001
Demographic-adjusted OR (95% CI)[a]	1.26 (1.00–1.58)	Ref	.049
Demographic plus ADHD-adjusted OR (95% CI)[b]	1.12 (0.89–1.41)	Ref	.34
Less restrictive AD case definition (multiple imputation)			
AD cases, n (total sample)	395 (4727)	15 928 (220 446)	–
AD prevalence, %	8.4	7.2	–
Crude OR (95% CI)	1.17 (1.05–1.30)	Ref	.003
Demographic-adjusted OR (95% CI)[b]	1.13 (1.02–1.26)	Ref	.02
Demographic plus ADHD-adjusted OR (95% CI)[c]	1.09 (0.98–1.22)	Ref	.11

Abbreviations: AD, atopic dermatitis; ADHD, attention-deficit/hyperactivity disorder; ASD, autism spectrum disorder; CI, confidence interval; OR, odds ratio.
[a] Adjusted for age group, sex, race, Medicaid insurance (yes/no), and number of healthcare encounters.
[b] Adjusted for age group, sex, race, Medicaid insurance (yes/no), number of healthcare encounters, and ADHD diagnosis.
[c] AD case definition was based on at least 1 International Classification of Diseases–10 diagnosis code for AD, regardless of additional diagnosis of asthma or allergic rhinitis.

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