Mental Health Comorbidity in Atopic Dermatitis

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Abstract

Background—Recent data, primarily from Europe, suggest children with atopic dermatitis may be at increased risk of developing mental health disorders.

Objective—We aimed to quantify the mental health burden associated with pediatric atopic dermatitis in the United States.

Methods—A cross-sectional study design was used analyzing data from the 2007 National Survey of Children's Health – a survey reporting on the health status of 92,642 non-institutionalized children ages 0-17. The lifetime prevalence of various provider-diagnosed mental health conditions was calculated for those with and without a history of atopic dermatitis.

Results—The odds of having attention-deficit/hyperactivity disorder was significantly increased in children with atopic dermatitis compared to non-atopic dermatitis controls, OR 1.87 (95% CI 1.54, 2.27) even after controlling for known confounders. The adjusted odds ratios for depression, anxiety, conduct disorder, and autism were 1.81 (95% CI 1.33,2.46) , 1.77 (95% CI 1.36, 2.29), 1.87 (1.46, 2.39), and 3.04 (95% CI 2.13, 4.34), respectively, and these estimates were all statistically significant. A clear dose-dependent relationship was observed between the prevalence of a mental health disorder and the reported severity of the skin disease.

Conclusions—Our data reveal a striking association between mental health disorders and atopic dermatitis in the U.S. pediatric population. The severity of the skin disease alters the strength of the association. Prospective cohort studies are needed to verify these associations and to explore underlying mechanisms. Strategies to prevent atopic dermatitis or to aggressively treat early skin inflammation may modify the risk of developing mental health disorders in at-risk children.

Keywords

Atopic dermatitis; Comorbidities; Attention-deficit/hyperactivity disorder; Anxiety; Depression; Autism; Prevalence

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Introduction

Atopic dermatitis (AD) is the most prevalent chronic condition in children, with a U.S. prevalence of 10%-17% and similar estimates in Europe and Asia.[1-3] It is a global public health concern considering its increasing prevalence and mounting financial costs to health systems.[4-6] Patients with AD experience unrelenting pruritus – the primary source of morbidity in this disorder. Even mild disease negatively impacts a child's life quality and more generalized disease can impact a child and family to a similar degree as having type I diabetes.[7-9] Additionally, children frequently suffer the negative effects of various comorbid conditions associated with AD.

Well-recognized comorbidities associated with AD include asthma, food allergy, allergic rhinitis, and a predisposition to cutaneous infections.[10] Children with AD also experience significant psychosocial and behavioral issues compared to their peers.[11,12] Parents of children with AD report increased fussiness, irritability, and crying in their child, especially during scratching episodes.[13] Daud and colleagues found children with severe eczema, when compared to unaffected children, had difficulty with psychosocial adjustments and displayed more clinginess and fearfulness.[14] Hashizume found both state and trait anxiety to be elevated in adults with AD.[15]

More recently, AD has been linked to more well-defined mental health disorders including attention-deficit/hyperactivity disorder, depression, and autism.[16-19] Although adding important information, these studies need confirmation due to their inherent limitations. Studies of ADHD and depression in AD have been cross-sectional in nature and have not used strict disease definitions.[16,18] Studies examining the relationship between autism and AD have involved only small patient samples and did not examine AD separately from other atopic disorders.[19,20] There are no studies examining the association between AD and mental health conditions in a large population of U.S. children. The objective of this current study was to perform a comprehensive evaluation of mental health disorders in children with AD utilizing a large population-based survey of children in the U.S.

Methods

Data source

We used data from the 2007 National Survey of Children's Health (NSCH) survey of 91,642 households, which was designed to estimate the prevalence of various child health issues including physical, emotional, and behavioral factors. The NSCH was sponsored by the Maternal and Child Health Bureau and the U.S. Department of Health and Human Services. The National Center for Health Statistics conducted a total of 91,642 interviews using the State and Local Area Integrated Telephone Survey (SLAITS) program with a 51.2% completion rate. The telephone numbers were chosen at random, followed by identification of the households with one or more children under the age of 18. Subsequently, one child was randomly selected for interview. The survey results were weighted to represent the population of non-institutionalized children nationally and in each state. Using the data from U.S. Bureau of the Census, weights were adjusted for age, sex, race, ethnicity, household size, and educational attainment of the most educated household member to provide a dataset that was more representative of each state's population of non-institutionalized children less than 18 years of age. The National Center for Health Statistics of Center for Diseases Control and Prevention oversaw sampling and telephone interviews. More detailed information on the survey procedure can be found at the Center for Disease Control and Prevention website.[21]

Study variables

The diagnosis of AD was derived from an affirmative response to the following question: "During the past 12 months, have you been told by a doctor or other health care provider that [S.C.] had eczema or any kind of skin allergy?" AD disease severity was based on the parent/guardian assessment of the skin disease with the following question, "Would you describe [his/her] eczema or skin allergy as mild, moderate, or severe?" The lifetime prevalence of the mental health disorders was assessed by the following root question, "Has a doctor or other health care provider ever told you that [S.C.] had _____," followed by the following phrases:

- "attention-deficit disorder or attention-deficit/hyperactive disorder, that is, ADD or ADHD?"

- "depression?"

- "anxiety problems?"

- "behavioral or conduct problems, such as Oppositional Defiant Disorder or Conduct Disorder?"

- "Autism, Asperger's Disorder, Pervasive Developmental Disorder, or other Autism Spectrum Disorder?"

These diagnoses were chosen because they had previously been reported as associated with AD. There were no other mental health conditions included in the survey.

Statistical Methods

The survey question defining AD was dependent on whether the child had seen a provider in the last 12 months. Thus, we limited the analyses only to those children who had seen a provider in the past year. All analyses were performed using SURVEY procedures in SAS version 9.2. Univariate associations were tested by Rao-Scott Chi-square method. Multivariate results were obtained by logistic regression for domains of weighted survey data.

Regression Models

Main-effects logistic regression models were developed to determine the association between eczema status and a diagnosis of psychiatric conditions adjusted for various potential confounders. Covariates in each of the models included eczema severity category (mild, moderate, severe), gender, age category, ethnicity/race composite variable (defined as Hispanic, non-Hispanic White, non-Hispanic Black, non-Hispanic multiracial and non-Hispanic other), household income (0-99% FPL vs. 100%+ FPL), highest educational level for the household (less than HS, HS diploma, greater than HS), family size (1-2 children vs. 3 or more children), residence in metropolitan area, number of nights per week of enough sleep, presence of a tobacco smoker in the household, and current asthma. Because depression, anxiety, conduct disorder, and autism can be associated with ADHD, we included ADHD as a covariate in all models in order to evaluate whether these conditions are associated with eczema *independent* of ADHD.[22] Covariates with Chi-square p-values greater than 0.05 were removed from the model to simplify models, and to increase sample size available for modeling. In addition, for each outcome a separate model was run using a binary eczema variable comparing the effect of any eczema vs. no eczema. Models were created *with and without* a number of adequate night's sleep variable. We separated out these models because data for the sleep variable were only available for children 6 years of age and older. The addition of the sleep variable did not significantly alter any of the associations between the mental health comorbidities and AD, thus only the models without the sleep variable were reported.

Results

Overall, 91,642 children were represented in the survey. 79,667 had seen a provider in the previous year and were included in the analyses. Characteristics of the overall population and AD population are shown in Table 1. The prevalence of the classic atopic comorbidities – asthma, hayfever, and food allergy – were all increased in the AD population compared to the non-AD population, as would be expected. The overall 12-month period prevalence of AD for 2007 was 12.98% (12.43, 13.54), a significant increase from the 2003 estimate of 10.69% (10.3, 11.0) (p<0.0001) we previously reported.[1] The majority of children with AD had mild disease (66.98%), while 26.00% and 7.02% of children had moderate and severe disease, respectively. The state-by-state AD prevalence ranged between a low of 8.51% in California to a high of 20.09% in the District of Columbia.

The prevalence of AD was highest in the youngest age category and decreased with age consistent with the natural history of the disease (Table 1). The highest prevalence of AD was found in children of black race (Table 2).

To broadly address the question whether AD increases one's risk for any mental health disorders, we first examined mental health care utilization (Table 3). Children with AD see mental health care providers more often and receive more mental health therapy than their peers without AD. Parents of children with eczema were significantly more concerned about their child's behavior compared to parents without children with AD.

We then examined specific doctor-diagnosed mental health disorders and found the prevalence of ADHD, anxiety, depression, conduct disorders, and autism to be significantly increased in children with AD (Table 4). The associations were strong and consistent for both a lifetime prevalence of the mental health disorder (e.g., ADHD ever) and for a point prevalence of the disorders (e.g., ADHD now). The prevalence of each mental health disorder also strongly correlated with disease severity in univariate analyses (Table 5). Because sleep loss has been previously proposed as a potential mechanism explaining the relationship between pediatric AD and mental health conditions, we evaluated the number of nights of adequate sleep stratified by AD severity. The mean number of reported nights of adequate sleep decreases with the child's eczema severity. The mean number of adequate nights of sleep was 6.09 (95% CI: 6.06, 6.12) for children without eczema and 5.22 (4.59, 5.86) for those reporting severe eczema. The percent of parents reporting their child gets seven nights of adequate sleep decreases as the child's eczema severity increases. Similarly, the percent of parent reporting their child gets zero nights of adequate sleep increases with eczema severity (Table 6).

Logistic regression models were created for each mental health outcome in order to control for known confounders that may influence the relationship between AD and each mental health outcome. Because adding in the sleep variable eliminated all children 6 and under from the analyses, we only report the results without the sleep variable included. Separate analyses were performed that included the sleep variable. The results of the two models were very similar and the significance of the results did not change (data not shown). Dose-dependent relationships between eczema severity and the mental health outcome remained significant for ADHD, conduct disorder and autism (Table 7). Lastly, an interaction between the number of nights of adequate sleep X eczema was found to be significant for the ADHD outcome, but was not significant for any of the other models (data not shown).

Discussion

Our study examining data from the 2007 National Survey of Children's Health found strong associations between AD and several mental health disorders in the U.S. pediatric

population. These data represent the first comprehensive evaluation of the mental health burden associated with pediatric AD in the United States. We found children with AD have an increased prevalence of ADHD, depression, anxiety, conduct disorder, and autism compared to their unaffected peers. The probability of having these mental health disorders directly correlated with the reported severity of the eczema. All associations between the mental health disorders and AD remained significant after confounding factors were taken into consideration, such as socioeconomic factors and the presence of asthma. These data confirm and expand upon previous findings showing an association between various mental health conditions and AD. The link between psychological disturbances and atopic disease has been recognized since the early 1900's.[23] The first population-based study examining the link was performed by Schmitt and colleagues in 2009, who found a strong association between ADHD and AD.[16] Since that initial study, a systematic review of six subsequent studies confirmed the link between AD and ADHD and estimated that up to 9% of all ADHD cases may be due to AD alone.[24] The results from our study agree with these findings and represent the first data examining the link between AD and ADHD in a non-European population. Similar to previous studies, our data are cross-sectional, so no conclusions regarding temporal relationships, and thus causality, can be drawn.

The results of our study also revealed that AD is associated with other mental health disorders including depression, anxiety, conduct disorder and autism. Taurines and colleagues recently found many of these mental health disorders may actually be ADHD comorbidities.[25] In order to evaluate whether AD was directly related to the other mental health disorders, we included ADHD in our adjusted models. The associations remained strong in the adjusted models, suggesting the associations between AD and other mental health disorders do not occur via the development of ADHD. Our data are in agreement with previous reports of these associations found in the literature. For example, a family-based study found a higher prevalence of anxiety disorders in families with an atopic history, including AD.[26] A controlled study from Germany found increased rates of anxiety, depression, and suicidal ideation in adults with AD.[27] Three recent studies found an increased risk of autism in children with atopic diseases.[19,20,28] These studies of autism and AD were limited by the lumping of all atopic disease into one category, however. The strength of our current study, as compared to these previous studies, lies in the population-based nature of the survey, the number of families surveyed, and the ability to examine AD separately from other atopic conditions.

The mechanisms underlying mental health disorders and AD are unknown. The sleep disturbance that accompanies AD may be one mechanism by which children with AD could theoretically be predisposed to concomitant mental health conditions. Romanos and colleagues found the association between AD and ADHD to be much stronger if sleep disturbance was present.[29] Disrupted sleep patterns have well-known negative effects on the mental state of children, including effects on behavior, school functioning, attention, and mood.[30-32] In agreement with the Romanos study, we found the presence of sleep loss modified the relationship between AD and ADHD, although the relationship remained significant even in children without reported sleep loss. Inadequate sleep did not appear to significantly influence the relationships between AD and other mental health disorders. Another theoretical mechanism explaining the association between mental health and AD could be the wide-ranging effects of inflammation. As in AD, clinical investigations have linked depression, anxiety, and autism to elevated levels of pro-inflammatory cytokines.[33-35] Therefore, AD and mental conditions may result, in part, from shared disturbances in inflammatory pathways. Lastly, the link between AD and mental health disorders may be explained by the chronic nature of the skin disease. Blackman and colleagues found that children with any chronic illness of childhood, such as diabetes, arthritis, or heart problems, had an increased risk of emotional and behavioral problems including ADHD.[36] Therefore,

mental health disturbances could be a common end result of many chronic disorders of childhood with AD being but one of these.

Our study had several limitations and these associations need further corroboration. The most important limitations of our study are its cross-sectional design and the use of disease definitions with minimal validation. By using cross-sectional data, we are unable to establish a temporal relationship between AD and the development of mental health disorders thus limiting our ability to establish causality. Our study relied on parental reporting of health provider-diagnosed conditions for both exposures and outcomes. The validity of these definitions has not been completely established. Two previous studies found that parental report of doctor-diagnosed "eczema" to have acceptable sensitivity and specificity.[2,37] In addition, the increased prevalence of asthma and hayfever among children we identified as having AD, along with a decrease in AD prevalence observed in older age groups, lends support that the parental report of provider-diagnosed eczema was actually AD in our study. We have no such verification with the mental health diagnoses and misclassification bias is a possibility. The children in our study with concomitant AD and ADHD or anxiety may not truly have these mental health disorders, but may be merely displaying symptoms of their chronic pruritic skin disease. Nevertheless, the fact these children have received these diagnoses from their providers, whether accurate or not, reflects the significant psychological burden associated with AD. Prospective cohort studies using validated criteria will be needed to address these issues. Future work should also examine the effect of therapy may have on the development or severity of these mental health disorders.

In conclusion, our data reveal a striking association between mental health disorders and AD in the U.S. pediatric population. The severity of the skin disease appears to alter the strength of the association. Prospective cohort studies are needed to verify these associations. Strategies to prevent AD or to aggressively treat early skin inflammation may modify the risk of developing mental health disorders in at-risk children.

Acknowledgments

Abbreviations

AD	Atopic dermatitis
ADHD	Attention-deficit/hyperactivity disorder
NSCH survey	2007 National Survey of Children's Health
SLAITS program	State and Local Area Integrated Telephone Survey
FPL	Federal Poverty Level

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Clinical Implications

Atopic dermatitis may increase a child's risk of developing mental health disorders. Children with more severe skin disease appear to be at greatest risk. Longitudinal and mechanistic studies are needed.

Capsule Summary

Several mental health disorders, including attention-deficit/hyperactivity disorder and autism, were associated with atopic dermatitis using a large population-based survey of children's health in the United States. The strength of the associations correlated with the severity of the skin disease.

Table 1

Characteristics of the population in those with and without eczema

Variable	Strata	Frequency (Percent) in Category of Total Population	Frequency (Percent) in Category of AD Population	Frequency (Percent) in Category of Non-AD Population	Chi square p-value for correlation
Age	0-3	17367 (23.76)	2868 (28.59)	14499 (23.04)	<.0001
	4-8	20113 (28.18)	2942 (30.13)	17171 (27.89)	
	9-12	15975 (20.81)	1954 (19.99)	14021 (20.93)	
	13-18	26133 (27.25)	2644 (21.30)	23489 (28.14)	
Gender	Female	38181 (48.56)	5016 (49.81)	33165 (48.38)	0.2537
	Male	41315 (51.44)	5385 (50.19)	35930 (51.62)	
Ethnicity/Race	White	53103 (56.49)	6326 (52.49)	46777 (57.09)	<.0001
	Black	8113 (14.65)	1618 (22.18)	6495 (13.52)	
	Hispanic	9797 (19.76)	1215 (15.62)	8582 (20.38)	
	Multiracial	3824 (4.35)	613 (5.39)	3211 (4.20)	
	Other	3441 (4.75)	466 (4.31)	2975 (4.81)	
Household income	0-99% FPL	9276 (18.11)	1253 (17.49)	8023 (18.21)	0.4719
	100% FPL and above	70312 (81.89)	9155 (82.51)	61157 (81.79)	
	0-99% FPL	9276 (18.11)	1253 (17.49)	8023 (18.21)	0.7581
	100-199% FPL	13112 (20.36)	1756 (20.35)	11356 (20.36)	
	200-399% FPL	26444 (31.05)	3478 (32.04)	22966 (30.90)	
	400% FPL and above	30756 (30.48)	3921 (30.12)	26835 (30.53)	
History of asthma	Yes	10811 (14.03)	2431 (25.24)	8380 (12.35)	<.0001
	No	68679 (85.97)	7952 (74.76)	60727 (87.65)	
History of hayfever	Yes	14735 (16.93)	3513 (34.45)	11222 (14.31)	<.0001
	No	64706 (83.07)	6874 (65.55)	57832 (85.69)	
History of food allergy	Yes	4307 (5.11)	1600 (15.10)	2707 (3.62)	<.0001
	No	75172 (94.89)	8781 (84.90)	66391 (96.38)	

Table 2

Prevalence of AD stratified by age, gender, race, and household income

Variable	Strata	Frequency, (Percent) of AD	Chi square p-value
Age	0-3	2868 (15.62)	<0.0001
	4-8	2942 (13.88)	
	9-12	1954 (12.47)	
	13-18	2644 (10.15)	
Gender	Female	5016 (13.33)	0.26
	Male	5385 (12.68)	
Ethnicity / Race	White	6326 (12.09)	<0.0001
	Black	1618 (19.69)	
	Hispanic	1215 (10.29)	
	Multiracial	613 (16.11)	
	Other	466 (11.82)	
Household income	0-99% FPL	1253 (12.54)	0.76
	100-199% FPL	1756 (12.98)	
	200-399% FPL	3478 (13.40)	
	400% FPL and above	3921 (12.83)	

Table 3

Prevalence of mental health care utilization and mental health concern according to eczema status in the 2007 National Survey of Children Health (NSCH)

Variable	Group Without Eczema, Frequency (%)	Group With Eczema, Frequency (%)	Chi-square p-value
Seen a mental health care provider	5423 (7.89)	1033 (12.12)	<.0001
Received treatment for behavior	4640 (6.61)	1043 (11.31)	<.0001
Parent concerned about child's behavior			
None	16647 (79.93)	3174 (75.42)	
A little	2809 (13.82)	698 (16.59) [4]	
A lot	991 (6.25)	252 (7.99)	0.0470

Table 4

Prevalence of mental health disorders in children according to eczema status in the 2007 National Survey of Children Health (NSCH)

	Group Without Eczema, Frequency (%)	Group With Eczema, Frequency (%)	Odds Ratio	95% CI of OR	Chi-square p-value
ADHD					
Ever	5501 (8.19)	959 (12.60)	1.62	(1.35, 1.93)	<.0001
Current	4233 (6.37)	747 (9.57)	1.55	(1.29, 1.87)	<.0001
Medicated	3009 (4.31)	483 (6.27)	1.49	(1.17, 1.88)	0.0009
Depression					
Ever	2226 (3.37)	492 (6.52)	2.00	(1.49, 2.69)	<.0001
Current	1218 (1.76)	274 (3.93)	2.28	(1.55, 3.35)	<.0001
Anxiety					
Ever	3072 (4.13)	681 (7.25)	1.81	(1.43, 2.29)	<.0001
Current	1921 (2.59)	474 (5.09)	2.02	(1.59, 2.56)	<.0001
Conduct Disorder					
Ever	2356 (3.97)	546 (7.74)	2.03	(1.63, 2.52)	<.0001
Current	1693 (2.85)	434 (6.51)	2.37	(1.86, 3.02)	<.0001
Autism					
Ever	994 (1.49)	283 (3.97)	2.73	(1.94, 3.84)	<.0001
Current	642 (0.89)	176 (2.19)	2.51	(1.67, 3.77)	<.0001

Table 5

Prevalence of mental health disorders in children with eczema according to parental report of eczema severity.[*]

Outcome	Eczema Status	Frequency (%) of Mental Health Outcome	Chi-square p-value[*]
ADHD	None	5501 (8.19)	<.0001
	Mild	563 (10.68)	
	Moderate	280 (13.21)	
	Severe	116 (27.70)	
Depression	None	2226 (3.37)	0.0101
	Mild	266 (5.40)	
	Moderate	150 (7.20)	
	Severe	75 (14.11)	
Anxiety	None	3072 (4.13)	0.0002
	Mild	384 (5.47)	
	Moderate	211 (9.11)	
	Severe	85 (16.26)	
Conduct Disorder	None	2356 (3.97)	<.0001
	Mild	298 (5.91)	
	Moderate	176 (8.07)	
	Severe	V2 (22.89)	
Autism	None	994 (1.49)	<.0001
	Mild	156 (2.55)	
	Moderate	88 (5.00)	
	Severe	39 (12.85)	

[*] Chi-squared tests were in this table were performed for only disease severities mild, moderate, and severe. The "none" category was included for reference only.

Table 6

Parental report of number of nights of adequate sleep stratified by eczema status. Values are the percent of parents reporting the average number of nights of adequate sleep.

Eczema severity category	Nights of adequate sleep per week (% of subjects per eczema severity category)								Chi square p-value
	0	1	2	3	4	5	6	7	
None	1181 (2.03)	369 (0.70)	1109 (2.23)	1520 (2.74)	2504 (4.98)	6976 (13.18)	5148 (9.16)	28199 (64.98)	<0.0001
Mild	133 (3.05)	39 (0.87)	97 (2.06)	136 (4.10)	282 (7.51)	619 (13.26)	482 (10.66)	2336 (58.49)	
Moderate	62 (3.71)	15 (1.73)	43 (1.79)	64 (3.05)	111 (7.11)	274 (16.69)	151 (7.21)	916 (58.72)	
Severe	23 (8.26)	4 (2.52)	19 (9.33)	16 (2.57)	25 (8.68)	44 (8.95)	28 (3.84)	229 (55.85)	

Table 7

Odds of mental health conditions in children according to eczema status after adjusting for potential confounders.[*]

Mental Health Condition	No Eczema	Eczema							
	Reference	Mild aOR (95%CI)	p-value	Moderate aOR (95%CI)	p-value	Severe aOR (95% CI)	p-value
ADHD	1.00	1.66 (1.28, 2.15)	<.0001	1.76 (1.30, 2.38)	0.0004	4.35 (2.73, 6.93)	<.0001
Anxiety	1.00	1.44 (1.01, 2.05)	0.09	2.18 (1.47, 3.23)	0.0006	2.81 (1.28, 6.17)	0.03
Depression	1.00	1.64 (1.06, 2.53)	0.08	2.02 (1.31, 3.14)	<0.0097	2.12 (1.00, 4.48)	0.22
Conduct Disorder	1.00	1.59 (1.17, 2.18)	0.0068	1.82 (1.22, 2.72)	0.0159	3.90 (1.88, 8.09)	0.0016
Autism	1.00	1.78 (1.14, 2.77)	0.0159	3.25 (1.79, 5.90)	0.0003	7.41 (3.82, 14.36)	<.0001

[*] Covariates in each of the models included eczema severity category (mild, moderate, severe), gender, age category, ethnicity/race composite variable, household income, highest educational level for the household, family size, residence in metropolitan area, presence of a tobacco smoker in the household, and current asthma. ADHD was added to all models except for the one describing ADHD. Covariates with Chi-square p-values greater than 0.05 were removed from the final models. All p-values are FDR-adjusted.