Childhood allergy symptoms increase the risk of behavioral problems: A cross-sectional study

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Abstract

Background: Children with allergic symptoms tend to have behavioral or emotional problems. However, previous studies on this association did not control for factors such as parenting stress, demographic characteristics, or allergy presentation. This study aimed to investigate the relationship between childhood allergic symptoms and behavioral problems, adjusted for confounders such as demographic characteristics, parenting stress, and allergy-related variables. Methods: We conducted an online cross-sectional survey among caregivers of children aged 2-6 years (n=633). The Strengths and Difficulties Questionnaire (SDQ) score was used as the primary measure of children's behavioral characteristics. Data on history of wheezing, eczema, and rhinitis were collected from the children's caregivers, using a standardized questionnaire, based on the International Study of Asthma and Allergies in Childhood. Associations were estimated using logistic regression analyses with propensity score to adjust for confounding factors. Results: Univariate analyses showed that history of wheezing was associated with conduct problems, a behavioral component of the SDQ. History of eczema was also associated with hyperactivity. Furthermore, nose symptoms were associated with conduct and emotional problems. After adjusting for potential confounders, history of wheezing (adjusted odds ratio [OR]=1.69, 95% confidence interval [CI]: 1.04-2.75) and nose symptoms (adjusted OR=1.56, 95% CI: 1.05-2.34) remained associated with increased risk of conduct problems. Conclusions: This study revealed that history of wheezing and rhinitis in children are associated with increased risk of behavioral problems, in particular, that of conduct problems. This evidence may inform future research into childhood allergy symptoms and their behavioral problems.

INTRODUCTION

Allergy is a hypersensitivity reaction initiated by immunologic mechanisms.[1] The prevalence of allergic diseases is increasing worldwide, including in Japan. The 1999 International Study of Asthma and Allergies in Childhood (ISAAC) reported that the prevalence of atopic dermatitis ranged from <2% in Iran to >16% in Japan and Sweden among children aged 6-7 years.[2] Phase III of the same study completed 7 years later reported an increase in the prevalence of asthma, rhinoconjunctivitis, and eczema in many countries; a decrease in prevalence was reported only for asthma among adolescents aged 13-14 years.[3]

Previous studies have reported a relationship between childhood attention-deficit hyperactivity disorder (ADHD) as well as other mental health problems and allergy. Studies have shown that children with eczema or atopic dermatitis achieved higher scores on the Strengths and Difficulties Questionnaire (SDQ), indicating that the presence of eczema may be associated with worse mental health.[4-7] Similar findings have been reported for conditions such as ADHD and autism spectrum disorders (ASD) among children with eczema. Children with atopic dermatitis have been shown to be at increased risk of ADHD or ASD. [8-13]

Similar associations have been reported for asthma and rhinitis[5]. A systematic review has found that children with ADHD had a higher rate of asthma than those without ADHD.[14] A separate meta-analysis suggested that patients with asthma, particularly those with severe symptoms, should be considered at higher risk of behavioral difficulties that may necessitate psychosocial interventions.[15] In a nationwide population-based prospective study, Chen suggested that asthma was a risk factor for further development of ADHD. In addition, asthma in very early life has been shown to increase the risk of developing ADHD during school years.[16] Suwan reported increased rates of allergic sensitization in ADHD cases.[17] The prevalence of allergic rhinitis among children with ADHD has also been reported as higher than that among children without ADHD.[17] A study based on the Taiwan National Health Insurance Research Database reported that allergic disorders, in particular, bronchial asthma and allergic rhinitis, but not atopic dermatitis, were risk factors for ADHD[18].

This evidence notwithstanding, previous studies on the relationship between allergic symptoms and childhood behavioral problems often failed to consider the impact of parental factors associated with children's psychosocial development. A study by Tokunaga et al. examined the impact of parenting stress in this context and found that paternal stress was significantly associated with the risk of child hyperactivity/inattention, while maternal stress was significantly associated with difficulties in peer relationships and emotional symptoms.[19] However, it is plausible that parenting stress is the effect, not the cause, of childhood behavioral problems, resulting in poorer SDQ scores.. It is also plausible that this relationship is bi-directional.

This study aimed to investigate the relationship between allergic symptoms and children's behavioral problems, adjusting for potential confounding factors such as demographic characteristics, parenting stress, and allergy-related variables.

METHODS

Study design and settings

This cross-sectional study was conducted in June 2019 as an online survey of 2,215 candidates, registered at a private online research firm, who raised preschool children; among them, 1,030 completed the questionnaire (response rate 46.5%). Participants were primary caregivers of children aged 2-6 years.

Prior to answering the questionnaire, the website administrator provided consent forms to respondents and informed them that completing the questionnaire was equivalent to their agreement to study participation. This study adhered to the Declaration of Helsinki, and was approved by the ethics committee of Nagoya City University Graduate School of Nursing (Approval No. 19014-2).

Outcomes, exposures, and covariates

The questionnaire collected data on SDQ domains used as a measure of children's behavioral problems, demographic characteristics of children and their caregivers, Parenting Stress Index short form (PSI-SF), and ISAAC scores. SDQ is an instrument used to evaluate both positive and negative infant, child, and adolescent behavior.[20] It includes 25 items scored on a 3-point Likert-type scale across 5 domains; emotional problems, conduct problems, hyperactivity, peer problems, and prosocial behavior. The total difficulties score as assessed in this study consisted of the 4 domains excluding prosocial score, as that domain alone had a positive value. [20]The total difficulties score was used as an outcome in this study. The Japanese SDQ, translated from the original version developed in the United Kingdom, has been validated and is considered applicable to children in Japan.[21]

The PSI is a self-reported measure of stress associated with childcare.[22] The PSI-SF, which is an abbreviated version of PSI, consists of 19 items scored on a 5-point Likert-type scale. The Japanese PSI-SF has been validated and applied in this study.[23,24] Parenting stress was divided into parent- and child-associated domains, and assessed comprehensively based on the total score. Higher scores indicated higher stress levels.

Statistical Analysis

The primary outcome was total difficulties score for SDQ in each domain: hyperactivity, emotional symptoms, conduct problems, and peer problems. Each score can be interpreted as "normal," "borderline," and "clinical," on a scale from the lowest to highest score. Matsuishi proposed the total difficulties score classification as "normal," "borderline," and "clinical," corresponding to 0-12, 13-15, and 16-40 points, respectively. Matsuishi sets the ranges for the domains of emotional problems, conduct problems, and peer problems as 0-3 for "normal," 4 for "borderline," and 5-10 for "clinical". The ranges for the hyperactivity domain were defined as 0-5 for "normal," 6 for "borderline," and 7-10 for "clinical". In cases where the outcomes were divided into binary results corresponding to non-occurrence or occurrence, it is generally recommended that "borderline" results are included in occurrence when high sensitivity is desired(normal vs. borderline and clinical) , and excluded when high specificity is desired(normal and borderline vs. clinical). [20] We have used the recommended borderline and clinical cutoff scores as criteria for dichotomizing primary outcome variables.

Exposure variables used in this study were history of allergic symptoms such as wheezing, eczema, and nose symptoms since birth. The potential confounding variables were age and sex (demographic characteristics), PSI-SF scores (parents' psychological aspect), doctor's diagnosis, and family history of allergic diseases such as atopic dermatitis, food allergy, asthma, rhinoconjunctivitis, and hay fever, as well as other items of the ISAAC.

We performed logistic regression analyses to estimate crude and adjusted odds ratios (OR), accounting for propensity scores yielded by all confounding variables. The items used to determine propensity scores are shown in Supplementary Table 1. When integrating all confounders into one variable as a propensity score and determining the propensity score variables for each exposure, the variables relevant to the simultaneous factors inducing collinearity, such as a history of diseases or period prevalence, were excluded. The analyses applied a complete case analysis. As the online survey prevented responders from submitting their forms with missing values, the dataset involved no missing values. All statistical analyses were performed using SPSS version 22.0.

RESULTS

Data from a total of 633 surveys were included in the analysis (valid rate 61.5%) (Figure 1). Participants were 633 primary caregivers. Of these, 52.4% were parents of boys, and 35.2% had children with physician-diagnosed atopic dermatitis (11.7%), food allergy (9.6%), asthma (10.7%), rhinoconjunctivitis (12.8%), and hay fever (8.7%). A total of 221 children had general behavioral problems as measured by the total difficulties score; 187(29.5%) had conduct problems, 148(23.4%) had hyperactivity, 113(17.9%) had emotional problems, and 171(27.0%) had peer problems. Participant characteristics and their SDQ scores are presented in Table 1.

In crude logistic regression models, a higher risk of conduct problems was observed among children with history of wheezing than among those without (OR= 1.48, 95% confidence interval [CI]: 1.01-2.16). A similar association was observed between nose symptoms and conduct problems, indicating a higher risk of conduct problems among children with nose symptoms than among those without (OR=1.65, 95% CI: 1.16-2.33). Additional associations were observed between history of wheezing and peer problems (OR=0.59, 95% CI: 0.38-0.91), that of rash and hyperactivity (OR=1.62, 95% CI: 1.02-2.57), and that of nose symptoms and emotional problems (OR=1.62, 95% CI: 1.06-2.45) (Table 2).

Adjusted ORs indicated that only history of wheezing (adjusted OR=1.69, 95% CI: 1.04-2.75) and nose symptoms (adjusted OR=1.56, 95% CI: 1.05-2.34) affected the risk of conduct problems. No other associations between childhood allergic symptoms and behavioral problems were detected after adjusting for propensity scores.

DISCUSSION

This study found that history of wheezing and rhinitis in children were associated with increased risk of developmental problems, in particular, that of conduct problems. Previous studies have investigated the

relationship between the presence of allergies and behavioral characteristics of children. However, unlike previous studies, the present study analyses included adjustments for potential confounding factors such as demographic characteristics, parenting stress, and allergy-related variables. Allergy-related variables included ISAAC items, clinician's diagnosis of allergies, and family history of allergies. To control for the impact of collinearity, which was likely between the variables that represent similar concepts, we performed adjustments using propensity scores.

Adjusted estimates indicated an association between history of wheezing and that of nose symptoms and childhood conduct problems. This result is consistent with that of previous studies, reporting that rhinitis and asthma, but not eczema, were associated with increased risk of ADHD.[18] A separate cross-sectional study using SDQ as an outcome measure and logistic regression analyses adjusted for gender, age, and primary caregiver's educational level has shown that children with current asthma symptoms were more likely to present with conduct problems than those without.[5] This study differed from ours in that no significant association between conduct problems and history of asthma or hay fever were observed. This discrepancy might be due to between-study differences in definition of outcomes and associated cutoff scores. For example, Hammer-Helmich et al. adopted the "clinical" value as a cutoff score, whereas we adopted the "borderline" value as the cutoff score. Goodman suggested that the "borderline" cutoff score be used in studies of high-risk samples where false positives are not a major concern[20]; however, we believe that using a highly sensitive threshold is appropriate to reduce the danger of overlooking an association. Another possible reason for between-study differences in findings is use of different confounders for adjustment during analysis. The present study adjusted for different types of confounders, using the propensity score technique. Following these adjustments, our results indicate an association between history of wheezing and/or nose symptoms in children and conduct problems; this finding may inform selection of confounders and support new perspectives in future studies.

Biologically, allergy-sensitized children have elevated levels of inflammatory cytokines. Studies in clinical psychiatry have shown that levels of specific cytokines play a role in signaling the brain to produce neurochemical, neuroendocrine, and neuroimmune responses that correspond to behavioral changes. These responses may affect important brain activities such as sleep, appetite, and neuroendocrine regulation.[25] Depending on the rate and amount at which cytokines cross the blood brain barrier, diverse neuropsychiatric symptoms may emerge, including low or depressed mood, anxiety, or psychosis.[26] This is not the case with eczema-related findings; this study's findings were consistent with those of previous studies on allergic symptoms[25,26] and behavioral problems in children.

In the present study, history of wheezing and rhinitis affected the risk of conduct problems in children after adjustment for potential confounders. Both wheezing and rhinitis cause respiratory symptoms, which may lead to sleep disorders. Poor sleep quality can adversely affect the behavior of children.[27] In addition, a previous systematic review revealed the presence of sleep disorders in children with ADHD[28]; a separate review reported that associations between sleep and psychopathology are complex and likely bidirectional.[29] Therefore, additional studies are needed to elucidate the association between ADHD-like behavioral characteristics and sleep.

That is to say, given these findings, we believe that high impulsiveness can be attributed in part to the psychological effect of elevated levels of inflammatory cytokines that are triggered by allergic sensitization; in addition, low quality of sleep is likely to play a role in tendency toward behavioral irritation. However, further studies are needed to confirm these associations.

This study has several strengths and limitations. This study is the first to adjust for confounding factors, including participant demographic characteristics, parenting stress, and allergy-related variables. Study limitations are as follows. First, while we adjusted for multifaceted confounders, we did not control for unmeasured or residual confounding by factors such as sleep and psychopathological characteristics. Second, as this was a cross-sectional study, the presented findings preclude meaningful discussions of causality. Further studies are warranted to confirm our findings; such studies should involve a longitudinal design and a representative sample. Third, we did not control for the impact of medication that could affect sleepiness

or mental health, such as antihistamines. Finally, caregivers may have reported increased parenting stress due duties associated with care of children with allergies; however, we could not account for this factor in this study.

In conclusion, this study revealed that history of wheezing and rhinitis in children is associated with increased risk of behavioral problems, in particular, that of conduct problems.

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Key message: This study revealed an association between childhood history of wheezing and rhinitis and conduct problems. The strength of this study is that it adjusted for confounding factors, including demographic characteristics, parenting stress, and allergy-related variables. In addition, to control for the impact of collinearity, we adjusted for these factors using propensity scores, increasing the reliability and validity of our findings.

REFERENCES

1. Johansson SG, Hourihane JO, Bousquet J, et al. A revised nomenclature for allergy. An EAACI position statement from the EAACI nomenclature task force. *Allergy.* 2001;56(9):813-824.

2. Williams H, Robertson C, Stewart A, et al. Worldwide variations in the prevalence of symptoms of atopic eczema in the International Study of Asthma and Allergies in Childhood. *J Allergy Clin Immunol.*1999;103(1 Pt 1):125-138.

3. Asher MI, Montefort S, Björksten B, et al. Worldwide time trends in the prevalence of symptoms of asthma, allergic rhinoconjunctivitis, and eczema in childhood: ISAAC Phases One and Three repeat multicountry cross-sectional surveys. *Lancet.* 2006;368(9537):733-743.

4. Ballardini N, Kramer MS, Oken E, et al. Associations of atopic dermatitis and asthma with child behaviour: Results from the PROBIT cohort. *Clinical & Experimental Allergy.* 2019;49(9):1235-1244.

5. Hammer-Helmich L, Linneberg A, Obel C, Thomsen SF, Tang Møllehave L, Glümer C. Mental health associations with eczema, asthma and hay fever in children: a cross-sectional survey. *BMJ Open.*2016;6(10):e012637.

6. Kuniyoshi Y, Kikuya M, Miyashita M, et al. Severity of eczema and mental health problems in Japanese schoolchildren: The ToMMo Child Health Study. *Allergology International.* 2018;67(4):481-486.

7. Schmitt J, Apfelbacher C, Chen C-M, et al. Infant-onset eczema in relation to mental health problems at age 10 years: Results from a prospective birth cohort study (German Infant Nutrition Intervention plus). *Journal of Allergy and Clinical Immunology.*2010;125(2):404-410.

8. Lee C-Y, Chen M-H, Jeng M-J, et al. Longitudinal association between early atopic dermatitis and subsequent attention-deficit or autistic disorder: A population-based case-control study. *Medicine.*2016;95(39):e5005-e5005.

9. Strom MA, Fishbein AB, Paller AS, Silverberg JI. Association between atopic dermatitis and attention deficit hyperactivity disorder in U.S. children and adults. *The British Journal Of Dermatology.*2016;175(5):920-929.

10. Yaghmaie P, Koudelka CW, Simpson EL. Mental health comorbidity in patients with atopic dermatitis. *Journal of Allergy and Clinical Immunology.* 2013;131(2):428-433.

11. Liao T-C, Lien Y-T, Wang S, Huang S-L, Chen C-Y. Comorbidity of Atopic Disorders with Autism Spectrum Disorder and Attention Deficit/Hyperactivity Disorder. *The Journal of Pediatrics.*2016;171:248-255.

12. Schmitt J, Romanos M, Schmitt NM, Meurer M, Kirch W. Atopic eczema and attention-deficit/hyperactivity disorder in a population-based sample of children and adolescents. *JAMA.* 2009;301(7):724-726.

13. Chen MH, Su TP, Chen YS, et al. Is atopy in early childhood a risk factor for ADHD and ASD? a longitudinal study. *Journal of psychosomatic research.* 2014;77(4):316-321.

14. Miyazaki C, Koyama M, Ota E, et al. Allergic diseases in children with attention deficit hyperactivity disorder: a systematic review and meta-analysis. *BMC Psychiatry.* 2017;17(1):120-120.

15. MCQUAID EL, KOPEL SJ, NASSAU JH. Behavioral Adjustment in Children with Asthma: A Meta-Analysis. *Journal of Developmental & Behavioral Pediatrics.* 2001;22(6):430-439.

16. Chen M-H, Su T-P, Chen Y-S, et al. Asthma and attention-deficit/hyperactivity disorder: a nationwide population-based prospective cohort study. *Journal of child psychology and psychiatry, and allied disciplines.* 2013;54(11):1208-1214.

17. Suwan P, Akaramethathip D, Noipayak P. Association between allergic sensitization and attention deficit hyperactivity disorder (ADHD).*Asian Pacific journal of allergy and immunology.*2011;29(1):57-65.

18. Shyu C-S, Lin H-K, Lin C-H, Fu L-S. Prevalence of attention-deficit/hyperactivity disorder in patients with pediatric allergic disorders: A nationwide, population-based study. *Journal of Microbiology, Immunology and Infection.* 2012;45(3):237-242.

19. Tokunaga A, Iwanaga R, Yamanishi Y, et al. Relationship between parenting stress and children's behavioral characteristics in Japan.*Pediatrics International.* 2019;61(7):652-657.

20. Goodman R. The Strengths and Difficulties Questionnaire: A Research Note. *Journal of Child Psychology and Psychiatry.*1997;38(5):581-586.

21. Matsuishi T, Nagano M, Araki Y, et al. Scale properties of the Japanese version of the Strengths and Difficulties Questionnaire (SDQ): A study of infant and school children in community samples. *Brain and Development.* 2008;30(6):410-415.

22. Abidin RR. *Parenting Stress Index: Manual (PSI).* Pediatric Psychology Press; 1990.

23. Narama M, Kanematsu Y, Araki A, et al. Validity and Reliability of the Japanese Version of the Parenting Stress lndex. *Pediatric health research.* 1999;58(5):610-616.

24. Araki A, Kanematsu Y, Yokosawa S, Arayashiki A, Aizumi I, Hujishima K. A Study for Developing Parenting Stress-Short Form Scale.*Pediatric health research.* 2005;64(3):408-416.

25. Kronfol Z, Remick DG. Cytokines and the brain: implications for clinical psychiatry. *The American journal of psychiatry.*2000;157(5):683-694.

26. Yarlagadda A, Alfson E, Clayton AH. The blood brain barrier and the role of cytokines in neuropsychiatry. *Psychiatry (Edgmont (Pa : Township)).* 2009;6(11):18-22.

27. Dahl RE. The impact of inadequate sleep on children's daytime cognitive function. *Seminars in Pediatric Neurology.*1996;3(1):44-50.

28. Cortese S, Faraone SV, Konofal E, Lecendreux M. Sleep in Children With Attention-Deficit/Hyperactivity Disorder: Meta-Analysis of Subjective and Objective Studies. *Journal of the American Academy of Child & Adolescent Psychiatry.* 2009;48(9):894-908.

29. Gregory AM, Sadeh A. Sleep, emotional and behavioral difficulties in children and adolescents. *Sleep Medicine Reviews.*2012;16(2):129-136.

Tables

Table 1. Demographic characteristics of participating children and their parents

Children		n	%
Diagnosis of allergic disease	Allergy	223	35.2
	Atopic dermatitis	74	11.7
	Food allergy	61	9.6
	Asthma	68	10.7
	Rhinoconjunctivitis	81	12.8
	Hay fever	55	8.7
Age(y)	2	153	24.2
	3	145	22.9
	4	148	23.4
	5	143	22.6
	6	44	7.0
Sex	Boy	332	52.4
	Girl	301	47.6
Primary daytime caregiver	kindergarten	237	37.4
	nursery school	176	27.8
	authorized child institution	76	12.0
	none	144	22.7
Caregivers		n	%
	Age of father	35.8	6.3
Father's employment status	full-time employment	560	88.5
	part-time employment	2	0.3
	self-employed	37	5.8
	unemployed	2	0.3
	other	3	0.5
	absence of father	29	4.6
Father's academic background	junior high school	42	6.6
	high school	174	27.5
	junior college /vocational school	110	17.4
	university or above	278	43.9
	Age of mother	33.4	6.1
Mother's employment status	full-time employment	85	13.4
	part-time employment	152	24.0
	self-employed	8	1.3
	side job at home	19	3.0
	unemployed	315	49.8
	absence from work	32	5.1
	other	20	3.2
	absence of mother	2	0.3
Mother's academic background	junior high school	22	3.5
	high school	181	28.6
	junior college /vocational school	213	33.6
	university or above	212	33.5
	other	3	0.5
Parental marital status	married/common-law marriage	595	94.0
	divorced/separated	31	4.9
	unmarried /single	7	1.1
Family income	<2 million yen	18	2.8
	2 to less than 4 million yen	125	19.7
	4 to less than 6 million yen	178	28.1
	6 to less than 8 million yen	82	13.0
	8 to less than 10 million yen	32	5.1
	10 to less than 12 million yen	10	1.6
	12 to less than 15 million yen	4	0.6
	15 to less than 20 million yen	3	0.5
	>20 million yen	2	0.3
	other	52	8.2
Strengths and difficulties questionnaire score		n	%
Total difficulties score	Normal	412	65.1
	Borderline, Clinical	221	34.9
Conduct problems	Normal	446	70.5
	Borderline, Clinical	187	29.5
Hyperactivity	Normal	485	76.6
	Borderline, Clinical	148	23.4
Emotional symptoms	Normal	520	82.1
	Borderline, Clinical	113	17.9
Peer problems	Normal	462	73.0
	Borderline, Clinical	171	27.0

Table 2. Logistic regression of associations between children's characteristics(Strengths and Difficulties Questionnaire) and history of allergic symptoms

	Strengths and difficulties questionnaire components									
	total difficulty score		conduct problems		hyperactivity		emotional symptoms		peer problems	
	crude model OR (95% CI)	adjusted model OR (95% CI)	crude model OR (95% CI)	adjusted model OR (95% CI)	crude model OR (95% CI)	adjusted model OR (95% CI)	crude model OR (95% CI)	adjusted model OR (95% CI)	crude model OR (95% CI)	adjusted model OR (95% CI)
wheeze ever	1.26 (0.87-1.82)	1.48 (0.93-2.37)	**1.48 (1.01-2.16)**	**1.69 (1.04-2.75)**	1.32 (0.87-1.98)	1.24 (0.73-2.10)	1.54 (0.99-2.39)	1.50 (0.85-2.63)	**0.59 (0.38-0.91)**	0.69 (0.40-1.18)
rash ever	1.34 (0.87-2.05)	1.06 (0.63-1.77)	1.15 (0.74-1.81)	0.87 (0.50-1.50)	**1.62 (1.02-2.57)**	1.21 (0.69-2.13)	1.01 (0.58-1.73)	0.87 (0.45-1.67)	1.08 (0.68-1.72)	1.11 (0.63-1.93)
nose symptoms ever	1.27 (0.91-1.76)	1.40 (0.96-2.05)	**1.65 (1.16-2.33)**	**1.56 (1.05-2.34)**	1.22 (0.84-1.77)	1.23 (0.80-1.89)	**1.62 (1.06-2.45)**	1.45 (0.89-2.35)	0.84 (0.59-1.19)	1.09 (0.73-1.63)

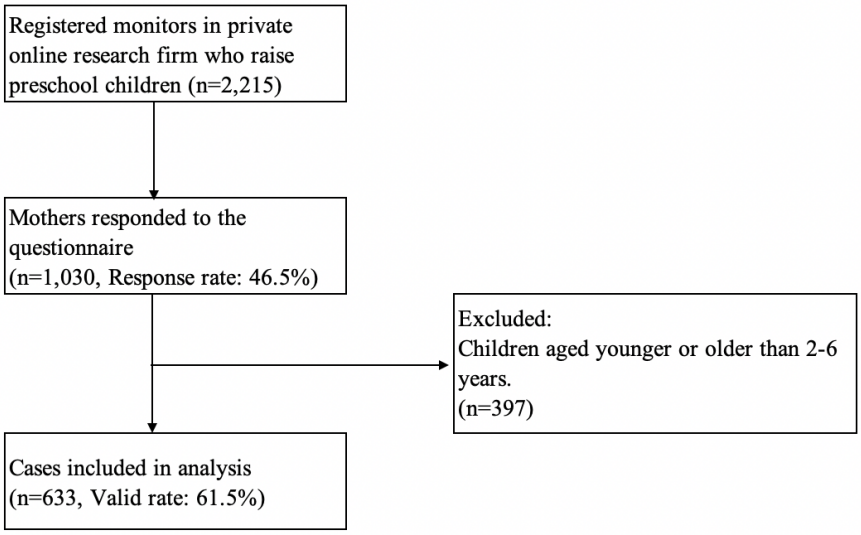
Dependent variable: Strength and difficulties Questionnaire (Conduct problems, Hyperactivity, Emotional symptoms, Peer problems, and Total difficulty score)

Independent variable: History of allergic symptoms(Wheeze ever, Rash ever, and Nose symptoms ever)

Propensity score: Age, Sex, Parenting Stress, International Study of Asthma and Allergies in Childhood (ISAAC), Diagnosis by clinician, and Family history

SDQ, strengths and difficulties questionnaire; OR, odds ratio; 95% CI, 95% conficence interval

Figure legends: Flow diagram of study data selection



Appendix: Items used to estimate propensity scores

Supplementary table 1. Items used to estimate propensity scores

	Wheeze ever		Rash ever		Nose symptoms ever	
	OR	95% CI	OR	95% CI	OR	95% CI
Age (y)						
2	ref.		ref.		ref.	
3	1.93	0.98-3.83	0.40	0.18-0.87	1.47	0.87-2.48
4	1.30	0.63-2.69	0.46	0.22-0.99	1.37	0.80-2.34
5	1.48	0.73-2.99	0.87	0.43-1.78	1.58	0.91-2.74
6	1.86	0.68-5.11	0.27	0.07-1.04	1.15	0.50-2.66
Female	0.79	0.49-1.26	1.11	0.67-1.85	0.80	0.55-1.15
Total PSI-SF score	1.01	0.99-1.03	1.00	0.98-1.03	1.01	0.99-1.03
ISAAC						
Wheeze ever			0.95	0.42-2.16	1.07	0.59-1.97
Wheeze in the past 12 months			1.40	0.56-3.48	1.15	0.53-2.48
Asthma ever	13.39	3.85-46.63	0.27	0.05-1.41	0.40	0.10-1.53
Wheeze during or after exercise in the past 12 months	6.16	1.07-35.41	2.64	0.79-8.85	3.05	0.57-16.44
Night cough in the past 12 months	1.78	0.87-3.62	1.31	0.61-2.84	2.51	1.22-5.15
Rash ever	1.12	0.32-3.94			2.37	0.89-6.32
Rash in the past 12 months	0.99	0.31-3.24			0.73	0.29-1.87
Eczema ever	0.47	0.11-2.04	2.56	0.90-7.34	3.53	1.04-12.01
Symptoms of dry skin in the past 12 months	1.21	0.73-2.03	2.57	1.47-4.50	1.57	1.04-2.37
Nose symptoms ever	0.75	0.32-1.72	2.22	0.84-5.82		
Nose symptoms in the past 12 months	1.80	0.79-4.10	0.88	0.35-2.25		
Hay fever ever	0.57	0.19-1.70	0.40	0.10-1.61	8.32	2.52-27.49
Diagnosis by clinician						
Atopic dermatitis	1.23	0.27-5.62	2.90	0.99-8.49	0.28	0.08-1.02
Food allergy	1.93	0.85-4.38	3.56	1.71-7.40	0.63	0.31-1.28
Asthma	3.40	0.77-15.08	2.44	0.46-12.91	4.32	1.02-18.32
Rhinoconjunctivitis	2.32	1.12-4.83	1.08	0.48-2.45	7.85	3.08-19.99
Hay fever	0.89	0.25-3.21	1.66	0.36-7.56	0.65	0.15-2.79
Family history						
Atopic dermatitis	1.56	0.90-2.71	1.28	0.72-2.28	1.61	1.03-2.52
Food allergy	0.95	0.52-1.75	0.63	0.32-1.24	1.00	0.61-1.63
Asthma	2.20	1.28-3.78	2.29	1.28-4.07	1.00	0.62-1.59
Rhinoconjunctivitis	0.93	0.56-1.54	1.05	0.60-1.84	1.86	1.26-2.74
Hay fever	1.31	0.77-2.21	1.29	0.71-2.34	0.75	0.51-1.11
Cox & Snell R-square value of each model	0.311		0.229		0.256	
Nagelkerke R-square value of each model	0.458		0.386		0.342	

OR, odds ratio; CI, confidence interval; ISAAC, International Study of Asthma and Allergies in Childhood; PSI-SF, parenting stress index short form