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Title: Predictive factors of persistent infantile atopic dermatitis up to 6 years old in Taiwan: a prospective birth cohort study.

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Abstract

Background: Atopic dermatitis affects 15-30% of children worldwide. Onset of disease usually occurs within the first year of life, over half of which regress by 6 years old of age. The aim of this study was to investigate the risk factors related to the persistence of infantile atopic dermatitis.

Methods: In this birth cohort study, patients were enrolled prenatally, and followed until 6 years of age; 246 patients had infantile atopic dermatitis at 6 months old. Family history, maternal and paternal total and specific IgE levels and cord blood IgE were recorded. Clinical examination, questionnaire survey and blood samples for total and specific IgE of the children were collected at each follow-up visit.

Results: Of the 246 patients with infantile atopic dermatitis at 6 months of age 48 patients had atopic dermatitis which persisted to 6 years old (19.5%). Risk factors associated with persistent infantile atopic dermatitis after multivariate analysis included: egg white sensitization (odds ratio 3.801, $p = 0.020$), and atopic dermatitis involving two or more areas at 6 months old (odds ratio 2.921, $p = 0.018$) after multivariate analysis with logistic regression. Patients with persistent infantile atopic dermatitis had a higher risk of asthma before 6 years old (39.6% vs. 24.2%, $p = 0.032$).

Conclusion: Egg white sensitization and the initial involvement of two or more areas at six months of age were associated with the persistent infantile atopic dermatitis. Patients with persistent infantile atopic dermatitis are more likely to develop asthma by 6 years of age.

Key words: Atopic dermatitis, birth cohort, persistence, natural history, asthma

Abbreviations: Immunoglobulin E (IgE)

Introduction

Atopic dermatitis is a chronic inflammatory skin disease and a common cause of dermatitis in children.¹ Although reports vary, the overall prevalence of atopic dermatitis is around 15-30% of children worldwide, with higher incidence rates in Western or developed nations.^{2, 3} In general, most patients with atopic dermatitis present within the first few years of life with a decreasing prevalence in older populations.^{4, 5} While all patients with atopic dermatitis exhibit characteristic dry skin with pruritus and associated inflammatory skin changes, infantile atopic

dermatitis is characterized by an early age of onset within the first two years of life, and a predilection over the face and extensor surfaces with sparing of the diaper area.⁶

Longitudinal studies have found that around half of children with infantile atopic dermatitis “outgrow” their disease by six years of age.^{1, 7} Risk factors that lead to the development of atopic dermatitis are relatively well known, and involve interplay of both environmental and hereditary factors, including breakdown of an intact epithelial barrier, allergen sensitization, genetic predisposition and cutaneous infections.⁸ However, less is known about what contributes to the persistence or remission of infantile atopic dermatitis.

In our previous study with a prenatally enrolled birth cohort, we have found that maternal IgE levels were associated with the development of atopic dermatitis by six months of age.⁹ In this longitudinal continuation of our original birth cohort study, children were followed from birth until six years of age. The aim of this study was to examine the allergic features of parents, the natural history of infantile atopic dermatitis, risk factors related to its persistence, and its association with the development of other allergic diseases.

Methods

Subject recruitment and data collection

In total 1812 pregnant women, and 1848 newborns were recruited prenatally for this study from December 1998 to April 2009. Informed consent to the study was obtained from each family after a trained research nurse explained the purpose of this study during their prenatal visit to the Obstetric Clinic at Kaohsiung Chang Gung Memorial Hospital, a large tertiary care center in southern Taiwan, as per our previous reports.¹⁰⁻¹² The study protocol was approved by the Internal Review Board of Chang Gung Memorial Hospital and was compliant with the ethical guidelines for human studies.

Atopic history and blood samples from the mother and father were obtained during the third trimester of pregnancy. The parental atopic history including a history of asthma, allergic rhinitis and atopic dermatitis was obtained using a structured questionnaire. Cord blood samples were obtained immediately after the infant was born. Birth history including gestational age, mode of birth (normal spontaneous delivery or caesarean-section), and gender were collected by chart review.

After birth, follow-up clinic visits were arranged at 6 months and 6 years of age. History of atopic disease including asthma, atopic dermatitis, and rhinitis was obtained using a questionnaire at each visit. A diagnosis of atopic dermatitis was made by a clinician using the suggested universal criteria for atopic dermatitis proposed by the American Academy of Dermatology.¹³ In brief, the diagnosis of atopic dermatitis was made in any child who fulfilled all three of the following criteria: pruritus, eczematous changes in an age-specific pattern (facial neck and extensor involvement in infants with sparing of the diaper-area; flexural lesions in older children), and a chronic relapsing clinical course. Infantile atopic dermatitis was defined as physician-confirmed atopic dermatitis as determined by the 6 months old visit. Persistent infantile atopic dermatitis was defined as physician-confirmed atopic dermatitis determined by both the 6 month old and 6 year old visit.

- Initial severity of atopic dermatitis at 6 months of age was determined by factors modified from the Eczema Area and Severity Index.¹⁴ Physicians assessed for areas of involvement (face, neck, trunk or limbs), the presence of cutaneous characteristics (papule formation, erythema and induration, weeping and lichenification), and duration of the lesions. Moderate to severe atopic dermatitis was defined as the presence of any of the following: involvement of more than two areas of the body, duration of a single lesion for more than 8

weeks, and the presence of weeping or lichenification. Atopic dermatitis involving two or more areas was defined as involvement of the face and one other area including the neck, trunk or extremities. (Figure 1)

Detection of Total IgE and Specific IgE levels

Levels of total IgE and specific IgE were determined using the Pharmacia CAP system (Pharmacia & Upjohn Diagnostic AB, Uppsala Sweden).¹⁵ All blood samples were centrifuged at 3000 rpm for 15 minutes, and the resulting sera were collected and stored at -70°C until analysis. Cord blood total IgE levels were assessed using a low-range total IgE detection system; maternal and paternal total IgE levels, and the IgE levels obtained at the 6 month and 6 year follow up visits were determined using a full-range total IgE detection system. A pilot study including 100 random samples was performed, and four common specific IgEs were identified in the general population : *Dermatophagoides pteronyssinus* (35.0%), cockroach (17.6%), shrimp (14.6%), and peanut (7%).⁹ A review of the literature revealed that the most common types of food allergen sensitization in Asian children were milk protein and egg white.¹⁶ Parental samples were tested for three common specific IgEs against *Dermatophagoides pteronyssinus*, cockroach and shrimp.⁹ Blood samples obtained after 6 months and 6 years of follow-up were tested for specific IgEs against *Dermatophagoides pteronyssinus*, cockroach, milk, egg white, peanut and shrimp. Elevated cord blood IgE levels were defined as any level more than 0.5 KU/L (corresponding to the 80th percentile) according to previous reports.^{9, 17} Sensitization to aeroallergens including *Dermatophagoides pteronyssinus* and cockroach was defined as a specific IgE level of more than 0.35 KU/L. Because no food challenge testing was performed, a higher specific IgE level cut-off point of more than 0.7 KU/L was chosen for food allergens including milk, egg white, peanut

and shrimp.¹⁸ According to our routine clinical practice, parents were advised to avoid allergens when a specific IgE level was more than 0.35 KU/L for aeroallergens (i.e. mite and cockroach) and more than 0.7 KU/L for food allergens (i.e. egg white, milk, peanut, shrimp), but were not given strict instructions to eliminate certain foods from the infant's or the mother's diet.

Data analysis

We initially estimated the final sample size to be 183 based on a study power of 0.8, with significance of less than 0.05 for a two-sided alternative hypothesis, the 15-30% effective rate of atopic dermatitis, a 40% follow-up rate from birth to 6 years of age using PASS 2008 Statistical Software (Utah, USA). In total, 246 children with infantile atopic dermatitis were included in this study, which exceeded our original estimate.

Maternal and paternal total IgE levels in and the total IgE levels of children at 6 months and 6 years of follow-up were log-transformed into a normal distribution, and compared using the Student's *t*-test. Total IgE values were presented as mean and standard error. Categorical data were compared using Chi-square and Fisher's exact test was used for categorical data with an expected count of less than 5. A stepwise multiple logistic regression analysis of parental, birth and data collected after 6 months of follow-up was performed using forward Wald analysis to determine factors that potentially predicted the persistence of infantile atopic dermatitis. A *p*-value of less than 0.05 was considered to be statistically significant. All statistical calculations were performed using SPSS for Windows, version 14.0 (Chicago, Ill) (SPSS Inc., Chicago, IL, USA).

Results

Study population

Of the 1848 children enrolled in this study, 219 who were not born in our hospital were excluded due to insufficient birth data. A further 83 did not return for the 6 month follow-up visit, and 790 did not return for the 6 year follow-up visit, and 32 did not have adequate data regarding atopic dermatitis history. In total, 724 patients had adequate data regarding atopic dermatitis from birth to 6 years of age.. There were no significant differences in parental allergic history, parental total IgE and specific IgE, cord blood IgE , birth history, 6 month old atopic dermatitis history, and 6 month old total and specific IgE between the 724 patients with adequate follow-up at 6 years of age, and those who did not (Table 1).Of the 724 patients with adequate follow-up data, 246 (33.9%) children with confirmed infantile atopic dermatitis at 6 months old were selected for analysis. Of these 246 patients, 48 had atopic dermatitis that persisted to 6 years of age (19.5%), and in the other 198 atopic dermatitis resolved (80.5%). (Figure 2)

Parental and birth factors associated with persistent infantile atopic dermatitis

We found that persistent infantile atopic dermatitis was associated with maternal mite sensitization (50.0% vs. 26.5%, $p = 0.002$), but not with maternal total IgE, cockroach or shrimp sensitization, or allergic history. Paternal factors including levels of paternal total IgE, paternal mite, cockroach or shrimp sensitization or history of paternal allergic disease were similar between those with persistent infantile atopic dermatitis and those with infantile atopic dermatitis that resolved before 6 years of age. In addition, persistent infantile atopic dermatitis was not associated with differences in cord blood IgE, gestational age, mode of delivery or gender. (Table 2)

Factors at 6 months old associated with persistent infantile atopic dermatitis

The patients with persistent infantile atopic dermatitis had higher levels of total IgE at 6 months of age when compared to those with infantile atopic dermatitis that resolved (log-normalized, mean $\pm$ SE, 1.414 ± 0.086 vs. 1.214 ± 0.039 , $p = 0.028$). In addition, persistent infantile atopic dermatitis was also associated with higher rates of egg white sensitization at 6 months old (25.0% vs. 9.5%, $p = 0.008$). However, there were no statistically significant differences in mite, cockroach, milk, peanut and shrimp sensitization at 6 months old between the patients with persistent atopic infantile atopic dermatitis and those in whom infantile atopic dermatitis resolved.

Because our original questionnaire did not include a comprehensive review of diet prior to 6 months old, it was unclear whether the patients with egg white sensitization were exposed to solids or other food allergens at an earlier age. Of note, the rate of exclusive breastfeeding was very low in our study. Of the 246 patients with atopic dermatitis at 6 months old, only 19 were exclusively breastfed for 4 months, and 13 were exclusively breast fed until 6 months old.

However, exclusive breastfeeding for either 4 or 6 months was not associated with the persistence of infantile atopic dermatitis (6.1% vs. 14.6%, $p = 0.067$; 4% vs. 10.2%, $p = 0.140$ respectively), although this finding may have been affected by the low rates of exclusive breastfeeding in our cohort.

In terms of disease severity, the patients with atopic dermatitis involving two or more areas had a higher risk of developing persistent infantile atopic dermatitis (56.3% vs. 36.4%, $p = 0.012$), whereas atopic dermatitis duration for more than 8 weeks and the presence of weeping or lichenification were similar between the patients with persistent infantile atopic dermatitis and those in whom infantile atopic dermatitis resolved. (Table 3)

Factors that may predict persistence of infantile atopic dermatitis

To identify the potential parental, birth and factors present at 6 months of age that may predict the persistence of infantile atopic dermatitis, multiple logistic regression analysis was performed in a step-wise manner. According to our regression model, egg white sensitization at 6 months old (odds ratio 3.801, 95% confidence interval 1.237-11.678, $p = 0.020$), and atopic dermatitis involving two or more areas (odds ratio 2.921, 95% confidence interval 1.206-7.070, $p = 0.018$) were associated with the persistence of infantile atopic dermatitis. Other parental, birth or factors at 6 months old were not significant enough to be included in the regression model.

(Table 4)

Persistent infantile atopic dermatitis and risk of allergic disease at 6 years old

In both groups of patients, we found that the rates of egg white sensitization decreased from 6 months to 6 years of age (25% vs. 10.4%, and 9.5% vs. 2.5% in persistent and resolved AD groups, respectively), and that rates of mite sensitization increased from 6 months to 6 years of age (2.5% vs. 68.8% and 1.8% vs. 47.7% in the persistent and resolved AD groups, respectively). This is consistent with previous studies which reported that food allergen sensitization are more prevalent in infancy, with aeroallergen sensitization occurring later in childhood,^{19, 20} In addition, we also found that persistent infantile atopic dermatitis was associated with higher levels of total IgE (log-normalized, mean $\pm$ SE, 2.257 ± 0.087 vs. 1.888 ± 0.046 , $p < 0.001$), mite allergen sensitization (68.8% vs. 47.7%, $p = 0.009$), and egg white sensitization (10.4% vs. 2.5%, $p = 0.027$) at 6 years old. Persistent infantile atopic dermatitis was not associated with cockroach, milk, peanut or shrimp sensitization. In addition, patients with persistent infantile atopic dermatitis were more likely to be diagnosed with asthma before 6 years

of age (39.6% vs. 24.2%, $p = 0.032$), but had similar rates of allergic rhinitis and urticaria compared with the patients in whom infantile atopic dermatitis resolved. Rates of maternal and paternal smoking, smoking within the home, and living near heavy traffic (defined as living near a road with more than 4 traffic lanes) did not differ between the patients with persistent or resolved atopic dermatitis at 6 years of age. (Table 3)

Discussion

Our results showed that egg white sensitization at 6 months of age and atopic dermatitis initially involving more than two areas of the body were predictive factors associated with persistent infantile atopic dermatitis up to 6 years of age. In addition, the patients with persistent infantile atopic dermatitis had higher levels of total IgE at 6 months and 6 years old, and were more likely to be diagnosed with asthma before 6 years old.

To date, only a few other studies have examined the risk factors associated with the persistence of atopic dermatitis, with similar results. In a study of 177 children aged 5 to 18 years, persistence of atopic dermatitis into school age was associated with peanut, egg and dust mite allergy.²¹ Two other studies reported that the duration of atopic dermatitis in young children was associated with the initial severity although different scoring systems were used.^{22, 23} Despite varying ages at initial enrollment and differences in the duration of follow-up in these three studies, in general, the persistence of atopic dermatitis appears to be associated with higher initial severity scores, and mite and food allergen sensitization. This has also been reported in another birth cohort study of 1314 children followed from birth to 7 years old.⁷

Our birth cohort study of 246 patients with infantile atopic dermatitis showed similar results. Persistent infantile atopic dermatitis was associated with egg white, but not peanut or

shrimp allergen sensitization, and involvement of more than two areas of the body at 6 months old. In addition, due to our study design with we were able to evaluate the ability of maternal, paternal and birth factors to predict the persistence of atopic dermatitis. We previously found that maternal but not paternal IgE levels were associated with infant eczema.⁹ The results of the current study further showed that maternal mite sensitization was associated with persistence of infantile atopic dermatitis up to 6 years of age. Of note, maternal allergic history, paternal allergen sensitization and allergic history did not seem to contribute to the development of persistent infantile atopic dermatitis. This seems to suggest that the prenatal environment, and particularly maternal mite sensitization, may be an independent risk factor contributing to the persistence of infantile atopic dermatitis. Several previous studies have shown that dust mite exposure during pregnancy is associated with a lower percentage of interferon-gamma producing CD4 (+) T cells in cord blood²⁴ and increased development of atopic dermatitis in the first year of life.²⁵ Reduction of mite exposure in the prenatal environment may therefore help to reduce the incidence of persistent of infantile atopic dermatitis.

Patients with atopic dermatitis can be delineated into two populations; those with IgE-mediated disease which involves around 70% to 80% of patients, and those without IgE-mediated disease which constitute the remaining 20% to 30%.²⁶ In patients with IgE-mediated disease, memory T-cells induce Th2 immunity by increasing the production of Th2 related cytokines such as IL-4 and IL-13 which results in increased IgE production.²⁶ In a similar birth cohort study of 144 children followed from 6 months to 14 months of age, persistent infantile atopic dermatitis was associated with higher levels of total IgE and increased Th2 and phytohemagglutinin-induced IL-4 production,²⁷ providing further evidence that persistent infantile atopic dermatitis is associated with increased Th2 polarization early in life. In our study,

we found that persistent infantile atopic dermatitis was associated with higher levels of total IgE at both 6 months and 6 years old on univariate analysis. (Table 3) However, after further multivariate analysis, total IgE at 6 months old was not significant enough to be included in the regression model. (Table 4) It is possible that higher total IgE levels at six months of age in patients with persistent atopic dermatitis may be associated with a greater degree of skin involvement. Nonetheless, the results of our study seem to suggest that persistent infantile atopic dermatitis may be associated with IgE-mediated disease.

The strengths of this study include its large sample size of 246 patients with infantile atopic dermatitis, and also the study design. As a prospective birth cohort study, we were able to include parental and perinatal factors, and observe the natural history of atopic dermatitis from birth to 6 years of age. There are a few limitations of this study. First, the incidence of atopic dermatitis was higher than in previous reports,³ which may be due to the urban location of our hospital or a greater willingness of parents with an allergic history to enroll in this study initially. In addition, the relatively low rate of retention in our study may also be a limitation. It is possible that patients with a parental history of allergy or those with infantile atopic dermatitis would have been more motivated to return for follow-up. However, analysis of possible participation bias showed that there were no significant differences in parental allergic history, total or specific IgE, or cord blood IgE between the patients with and without loss of follow-up. (Table 1). In addition, patients with intermittent symptoms of atopic dermatitis between 6 months and 6 years old were not identified in our study, although the rates of persistence and remission in our study (19.5% and 80.5%, respectively) are similar to the rates reported in a recent Taiwanese nationwide survey of early onset atopic dermatitis.²⁸

In conclusion, in our prospective birth cohort study we identified risk factors predicting persistent infantile atopic dermatitis including egg white sensitization and initial involvement of two or more areas of the body at six months of age. We also found that patients with persistent infantile atopic dermatitis were more likely to develop asthma by 6 years old. Further studies are needed to validate our findings in a different population.

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Table 1: Participation Bias: Comparison of patients with and without loss of follow-up by 6 years old

	Patients with loss of follow-up before 6 y/o Mean $\pm$ SE	Patients with complete follow-up at 6 y/o Mean $\pm$ SE	p-value
Patient Data at Birth			
Cesarean section	233/787 (29.6%)	182/660 (27.6%)	0.395
Gestational Age ≥ 37 weeks	850/905 (93.9%)	674/724 (93.1%)	0.499
Male Gender	482/905 (53.3%)	385/724 (53.2%)	0.973
Cord blood total IgE > 0.5 KU/L	161/799 (20.2%)	128/626 (20.4%)	0.890
Smoking within the home	158/793 (19.9%)	185/718 (25.8%)	0.007
Living near street with > 4 lanes	123/673 (18.3%)	121/669 (18.1%)	0.928
Maternal Data			
Total IgE (KU/L)*	1.631 $\pm$ 0.019 (N=864)	1.626 $\pm$ 0.022(N=719)	0.880
Mite Sensitization	269/862 (31.2%)	210/716 (29.3%)	0.419
Cockroach Sensitization	97/862 (11.3%)	88/718 (12.3%)	0.537
Shrimp Sensitization	40/861 (4.6%)	49/717 (6.8%)	0.061
History of allergic disease	493/903 (54.6%)	392/724 (54.1%)	0.856
Maternal smoking	1/795 (0.1%)	0/718 (0%)	1.000
Paternal Data			
Total IgE (KU/L)*	1.803 $\pm$ 0.019 (N=863)	1.822 $\pm$ 0.021(N=712)	0.501
Mite Sensitization	322 / 861 (37.4%)	286/710 (40.3%)	0.243
Cockroach Sensitization	179/860 (20.8%)	171/710 (24.1%)	0.121
Shrimp Sensitization	94/859 (10.9%)	96/708 (13.6%)	0.114
History of allergic disease	388/901 (43.1%)	326/724 (45.0%)	0.428
Paternal smoking	234/795(29.4%)	235/718 (32.7%)	0.166
6 month old Total and Specific IgE			
Total IgE (KU/L)*	1.136 $\pm$ 0.025(N=434)	1.179 $\pm$ 0.022(N=588)	0.197
Mite Sensitization	5/435 (1.1%)	9/589 (1.5%)	0.606
Cockroach Sensitization	0/432 (0%)	3/586 (5%)	0.266
Egg White Sensitization	25/426 (5.9%)	49/587 (8.3%)	0.134
Milk Sensitization	7/426 (1.6%)	12/587 (2%)	0.642
Peanut Sensitization	4/425 (0.9%)	4/587 (0.7%)	0.727
Shrimp Sensitization	0/423(0%)	1/584(0.2%)	1.000
6 month old questionnaire data			
Exclusive breast feeding for ≥ 6 months	64/821 (7.8%)	50/720 (6.9%)	0.524
Atopic dermatitis	244/822 (29.7%)	246/724 (34.0%)	0.070
Atopic dermatitis involving $\geq$ two areas	102/822 (12.4%)	99/724 (13.7%)	0.460
Atopic dermatitis lasting for ≥ 8 weeks	45/743 (6.1%)	54/656 (8.2%)	0.113
Atopic dermatitis with weeping or lichenification	7/744 (0.9%)	9/657(1.4%)	0.451

*Total IgE levels were log transformed into a normal distribution, and presented as mean $\pm$ standard error.

Table 2: : Comparison of patients with resolving or persistent infant atopic dermatitis (Birth and parental factors)

	No AD at 6 y/o (N=198) Mean $\pm$ SE	Persistent AD at 6 y/o (N=48) Mean $\pm$ SE	p-value
Patient Data at Birth			
Cesarean section	47/176 (26.7%)	6/40 (15.0%)	0.120
Gestational Age $\geq$ 37 weeks	188/198 (94.9%)	45/48 (93.8%)	0.722
Male Gender	120/198 (60.6%)	23/48 (47.9%)	0.110
Cord blood total IgE > 0.5 KU/L	45/168 (26.8%)	15/44 (34.1%)	0.338
Smoking within the home	45/194 (23.2%)	11/48 (22.9%)	0.967
Living near street with > 4 lanes	32/184 (17.4%)	11/45 (32.9%)	0.277
Maternal Data			
Total IgE (KU/L)*	1.632 $\pm$ 0.044 (N=196)	1.798 $\pm$ 0.087 (N=48)	0.095
Mite Sensitization	52/196 (26.5%)	24/48 (50.0%)	0.002
Cockroach Sensitization	25/196 (12.8%)	11/48 (22.9%)	0.075
Shrimp Sensitization	12/195 (6.2%)	5/48 (10.4%)	0.341
History of allergic disease	112/198 (56.6%)	32/48 (66.7%)	0.203
Maternal smoking	0/194 (0%)	0/48 (0%)	N/A
Paternal Data			
Total IgE (KU/L)*	1.822 $\pm$ 0.039 (N=196)	1.843 $\pm$ 0.081 (N=48)	0.817
Mite Sensitization	82/194 (42.3%)	24/48 (50%)	0.334
Cockroach Sensitization	39/194 (20.1%)	15/48 (31.3%)	0.097
Shrimp Sensitization	23/194 (11.9%)	8/48 (16.7%)	0.372
History of allergic disease	98/198 (49.5%)	19/48 (39.6%)	0.217
Paternal smoking	62/194 (32.0%)	18/48 (22.5%)	0.465

*Total IgE levels were log transformed into a normal distribution, and presented as mean $\pm$ standard error. AD : atopic dermatitis

Table 3: Comparison of patients with resolving or persistent infant atopic dermatitis (6 month old and 6 year old data)

	No AD at 6 y/o (N=198) Mean $\pm$ SE	Persistent AD at 6 y/o (N=48) Mean $\pm$ SE	p-value
6 month old Total and Specific IgE			
Total IgE (KU/L)*	1.214 $\pm$ 0.039 (N=168)	1.414 $\pm$ 0.086 (N=40)	0.028
Mite Sensitization	3/169 (1.8%)	1/40 (2.5%)	0.575
Cockroach Sensitization	2/168 (1.2%)	0/40 (0%)	1.000
Egg White Sensitization	16/168 (9.5%)	10/40 (25%)	0.008
Milk Sensitization	3/168 (1.8%)	2/40 (5%)	0.246
Peanut Sensitization	2/168 (1.2%)	1/40 (2.5%)	0.475
Shrimp Sensitization	1/166 (0.6%)	0/40 (0%)	1.000
6 month old questionnaire data			
Exclusive breast feeding for $\geq$ 6 months	8/198 (4.0%)	5/48 (10.2%)	0.140
Atopic dermatitis involving $\geq$ two areas	72/198 (36.4%)	27/48 (56.3%)	0.012
Atopic dermatitis lasting for $\geq$ 8 weeks	44/171 (25.7%)	10/43 (23.3%)	0.738
Atopic dermatitis with weeping or lichenification	8/172 (4.7%)	1/43 (2.3%)	0.691
6 year old Total and Specific IgE			
Total IgE (KU/L)*	1.888 $\pm$ 0.046 (N=197)	2.257 $\pm$ 0.087 (N=48)	<0.001
Mite Sensitization	94/197 (47.7%)	33/48 (68.8%)	0.009
Cockroach Sensitization	24/197 (12.2%)	11/48 (22.9%)	0.057
Egg White Sensitization	5/197 (2.5%)	5/48 (10.4%)	0.027
Milk Sensitization	4/197 (2.0%)	1/48 (2.1%)	1.000
Peanut Sensitization	3/197 (1.5%)	1/48 (2.1%)	0.584
Shrimp Sensitization	18/197 (9.1%)	5/48 (10.4%)	0.784
6 year old questionnaire data			
History of asthma	48/198 (24.2%)	19/48 (39.6%)	0.032
History of allergic rhinitis	121/198 (61.1%)	34/48 (70.8%)	0.211
History of urticaria	43/198 (21.7%)	14/48 (29.2%)	0.272

*Total IgE levels were log transformed into a normal distribution, and presented as mean $\pm$ standard error.
AD : Atopic dermatitis.

Table 4: Factors predicting persistent infantile atopic dermatitis

	Odds Ratio	95% Confidence Interval	p-value
Egg White Sensitization at 6 months old	3.801	1.237-11.678	0.020
Atopic dermatitis ≥ 2 areas at 6 months old	2.921	1.206-7.070	0.018

Figure legends

Figure 1: Schematic representation of areas of atopic dermatitis involvement. 1 : Face, 2 : Neck, 3: Trunk, 4: Extremities. Involvement of more than two areas was defined as involvement of the face and one other area including the neck, trunk or limbs.

Figure 2: Study flow chart

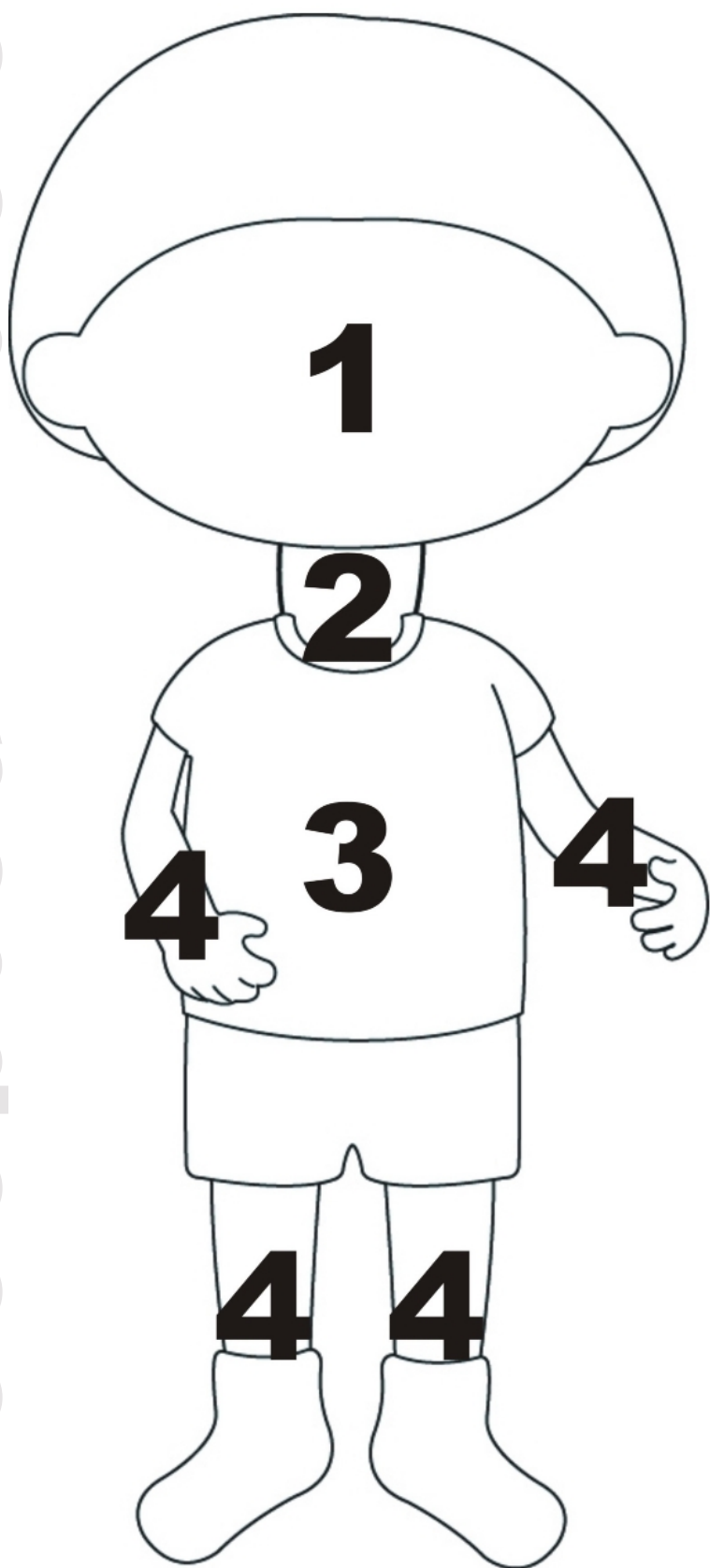


Figure 2

