Prevalence of Atopic Dermatitis in Chinese Children aged 1–7 ys

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Prevalence of atopic dermatitis (AD) is increasing worldwide. Up to date, there has been no face-to-face nation-wide study in China. We aim to explore the prevalence of clinical diagnosed AD in children aged 1–7 ys in China. Twelve metropolises were chosen from different areas of China. In each region, we selected 4–10 kindergartens and 2–5 vaccination clinics randomly. A complete history-taking and skin examination were performed by dermatologists. The definite diagnosis of AD and the severity were determined by two or three dermatologists. All criteria concerned in UK diagnosis criteria, characteristic presentation of AD and atypical manifestations were recorded in detail. A total of 13998 children from 84 kindergartens and 40 vaccination clinics were included. The prevalence of AD was 12.94% by clinical diagnosis of dermatologists overall, with 74.6% of mild AD. Comparatively, prevalence of AD based on UK diagnostic criteria was 4.76%. This is the first face-to-face nation-wide study in Chinese children aged 1–7 ys, revealing that the prevalence of AD in children is closer to that of wealthier nations.

Atopic dermatitis (AD) is a common, highly pruritic chronic inflammatory skin disorder in children, which is often associated with other atopic diseases such as asthma and allergic rhinitis. Previous study of AD in a hospital-based setting in China revealed that the average onset of AD is 0.86 ± 3.87 years, with 94.6% of them developing AD less than 2 years old. Although not life threatening, intense itching and sleep loss can significantly impact on the quality of life of the individual and his/her family. As a consequence, more than one thousand epidemiological studies related to the prevalence and environmental risk and protective factors of AD were published during the past decades. A systematic review of epidemiological Studies showed the international time trends in the incidence and prevalence of atopic eczema from 1990 to 2010 were increasing in Africa, eastern Asia, western Europe and parts of northern Europe (i.e. the UK). In Europe, East Germany saw a rise in the number of newly diagnosed AD cases in children up to the age of 6 years from 16.0% in 1991 to 23.4% in 1997, however, the incidence of AD was stable among preschool children in West Germany after the country’s reunification. Prevalence of atopic eczema in 6 to 7-year-old schoolchildren in Spain using ISAAC Phase III in 2010 was 5.92%. In the contrast, another similar study Brazilian schoolchildren show the prevalence ranged from 3.3% to 7.3%.
The epidemiological result. In the current study, we intended to perform a nation-wide face-to-face study conducted by dermatologists in Chinese children aged 1–7 yrs. Of the 15,000 children surveyed, 14478 (96.52%) finished questionnaire and were examined by dermatologists. 480 individuals were excluded by data analysis due to overage or incomplete information. 335 individuals were less than 1-year-old and 22 individuals were over 7-year-old. Another 123 cases didn’t give full information. Finally, a total of 13998 preschool children were included in this study.

**Population characteristics.** The epidemiological study was performed in 84 kindergartens and 40 vaccination clinics in 12 metropolises throughout China. The characteristics of 13998 children are listed in Table 1. There were no significant differences in these characteristics between the AD and non-AD groups.

**Prevalence of AD.** The point prevalence of AD based on clinical diagnosis by dermatologists was 12.94% overall (1811 of 13998), ranging from 9.00% to 24.69% between metropolises for preschool children in China (Fig. 1 and Table 2). The proportion of mild, moderate and severe AD is 74.60%, 23.96%, and 1.44% respectively (Table 3). Of all 1531 mild AD, 780 cases presented with xerosis. The highest district prevalence values were reported in inland area of China, such as Chengdu (24.69%), Hefei (20.31%) and Taiyuan (19.73%). The lowest prevalence values were in the north and east part of the country (Fig. 1 and Table 2). The prevalence is decreasing along with the growth of age on the whole (Table 4). The Cohen’s kappa coefficient for total subjects was 0.69 and it varies between 0.5 and 0.8 in 12 metropolises (Table 2). Pearson correlation test indicated that no correlation was detected between the kappa coefficients and the AD prevalence by the clinical diagnosis (r = 0.03, p = 0.925). Comparatively, the prevalence of AD based on UK diagnostic criteria for children aged 1–7 yrs was 4.76% (667/13998). The sensitivity, specificity, positive predictive value and negative predictive value were 36.27%, 99.91%, 98.5%, and 91.34% for UK diagnostic criteria. In addition, 2 psoriasis vulgaris and 106 contact dermatitis were diagnosed. No scabies, hereditary metabolic disease or lymphoma were found.

**Risk factors for AD.** Residence in rural and an older age are both protective factors for AD. Exposed to passive smoking (especially exposed to also during pregnancy), premature birth, and choosy in food are risk factors for AD. Pet ownership, delivery pattern and feeding pattern in the first 6 months after birth are not shown to be associated with AD prevalence in logistic regression analysis (Table 5).

**Discussion**

AD is a global public health concern considering its increasing prevalence and impact on life quality of patient and family. The ISAAC (International Study of Asthma and Allergies in Childhood) revealed that AD affects children across the globe, although the disease prevalence varies substantially between countries. The prevalence of AD is also increasing, especially in developing countries. The current study is the first face-to-face nation-wide study conducted by dermatologists in Chinese children aged 1–7 yrs.

AD prevalence at 12.94% in Chinese children aged 1–7 yrs is very close to that of Japan and Korea, but it is much higher than two previous Chinese studies of AD prevalence, both of which used UK diagnostic criteria. The first study was conducted in 2002 by distributing 49241 questionnaires to 10 provincial capitals, including 6 cities in our study, and showed that the prevalence of AD in children aged 1–7 yrs was 3.07% in 2002. The second study was conducted in 8 communities of Shanghai in 2010 by questionnaire, and showed that prevalence of AD was 8.3% in children aged 3 to 6 in Shanghai. Except for sample variance and fluctuation of prevalence with time, another

| Characteristics | AD group (n = 1811) | Non-AD group (n = 12187) |
|-----------------|--------------------|--------------------------|
| Age, mean ± SD (ys) | 3.15 ± 1.70 | 3.62 ± 3.26 |
| Range (ys) | 1–6.83 | 1–6.83 |
| Gender (%) | | |
| Male | 6461 (46.16%) | 869 (47.98%) |
| Female | 7537 (53.84%) | 6333 (52.02%) |

Table 1. Demographic characteristics of study population. SD, standard deviation; ys, years.
two factors, the way of data collection and selection of different diagnostic standards, also lead to discrepancy of our study and previous ones. There have been numerous epidemiological studies of AD using questionnaires, but few studies have been performed by dermatologists’ physical examinations owing to much time and cost involved. Secondly, we used clinical diagnosis by experience dermatologists, which is in general considered

Figure 1. AD prevalence of children aged 1–7 ys in China (The figure is created using mapinfo made in China http://www.downxia.com/downinfo/50308.html and Adobe PhotoShop CS6 softwares http://rj.baidu.com/soft/detail/23675.html).

| Metropolis  | Children surveyed | Diagnosis of AD | Prevalence (%) | Cohen’s kappa coefficient |
|-------------|-------------------|-----------------|----------------|--------------------------|
| Chengdu     | 482               | 119             | 24.69          | 0.69                     |
| Hefei       | 517               | 105             | 20.31          | 0.73                     |
| Taiyuan     | 603               | 119             | 19.73          | 0.70                     |
| Chongqing   | 556               | 98              | 17.63          | 0.51                     |
| Wuhan       | 764               | 129             | 16.88          | 0.72                     |
| Dalian      | 679               | 102             | 15.02          | 0.80                     |
| Changsha    | 1260              | 176             | 13.97          | 0.66                     |
| Shenyang    | 1037              | 123             | 11.86          | 0.59                     |
| Shenzhen    | 1504              | 178             | 11.84          | 0.75                     |
| Nanjing     | 1026              | 117             | 11.40          | 0.65                     |
| Shanghai    | 2547              | 273             | 10.72          | 0.71                     |
| Beijing     | 3023              | 272             | 9.00           | 0.68                     |
| Total       | 13998             | 1811            | 12.94          | 0.69                     |

Table 2. AD prevalence of children aged 1–7 ys by metropolis.

| AD severity (Objective SCORAD) | NO. | %   |
|--------------------------------|-----|-----|
| Mild (<15)                     | 1351| 74.60|
| Moderate (15–40)               | 434 | 23.97|
| Severe (>40)                   | 26  | 1.44 |

Table 3. Severity of atopic dermatitis.
as gold standard\textsuperscript{12}, as the standard but not any criteria in the epidemiological survey. In order to guarantee uniformity of subjective diagnosis, a panel of experienced dermatologists enrolled in skin examination. In addition, every single diagnosis of AD was made by 2 or 3 dermatologists to avoid fallibility and guarantee accuracy of data. The total Cohen's kappa coefficient at 0.69 showed a relatively good consistency. A relatively higher proportion of mild AD in Chongqing patients can partly explain the relatively low kappa coefficient at 0.51. No correlation between the kappa coefficient and the AD prevalence based on clinical diagnosis indicated low possibility of over-diagnosis by the third dermatologist. Two patients with psoriasis vulgaris and 106 patients with contact dermatitis, whereas no scabies, hereditary metabolic disease or lymphoma was found. All subjects diagnosed with contact dermatitis had the skin lesion only localized to perioral or perianal region for no more than 3 months. All authors regard the dermatologists' diagnosis as correct and trustable in the present study. When UK diagnostic criteria used, the prevalence of AD in children aged 1–7 ys according to data collected by dermatologists in our study seems quite close to that from questionnaires 10 years ago (4.76% compared to 3.07%). However, if clinical diagnosis of dermatologists adopted, the prevalence of AD in the current study is much higher than previous data using UK diagnostic criteria (12.94% compared to 3.07%).

Little is known about the distribution of AD severity in Chinese population and abroad. Current study showed that about 74.60% affecters presented with mild lesions. 23.96% of AD is moderate and 1.44% of AD is severe. In epidemiology of 0–17 childhood atopic dermatitis in US, 67% of children had mild, 26% had moderate, and

| Metropolis | 1–2 yrs | 2–3 yrs | 3–4 yrs | 4–5 yrs | 5–6 yrs | 6–7 yrs |
|------------|---------|---------|---------|---------|---------|---------|
| Chengdu    | 62      | 24 (38.71) | 28 | 10 (35.71) | 77 | 28 (36.36) | 84 | 19 (22.62) | 117 | 13 (11.10) | 114 | 25 (21.93) |
| Hefei      | 84      | 24 (28.57) | 51 | 17 (33.33) | 73 | 10 (13.70) | 129 | 25 (19.38) | 140 | 25 (17.86) | 40 | 4 (10.00) |
| Taiyuan    | 108     | 31 (28.70) | 81 | 16 (19.75) | 113 | 25 (22.12) | 129 | 20 (15.50) | 125 | 18 (14.40) | 47 | 9 (19.15) |
| Chongqing  | 130     | 39 (30.00) | 63 | 14 (22.22) | 113 | 16 (14.16) | 97 | 13 (13.40) | 108 | 10 (9.26) | 45 | 6 (13.33) |
| Wuhan      | 98      | 29 (29.59) | 56 | 9 (16.07) | 180 | 28 (15.56) | 190 | 32 (16.84) | 167 | 25 (14.97) | 73 | 6 (8.22) |
| Dalian     | 152     | 31 (20.39) | 84 | 13 (15.48) | 171 | 14 (8.19) | 140 | 25 (19.38) | 69 | 13 (18.84) | 63 | 8 (12.70) |
| Changsha   | 240     | 18 (7.50) | 198 | 20 (10.10) | 218 | 34 (15.60) | 236 | 47 (19.92) | 270 | 44 (16.30) | 116 | 17 (14.66) |
| Shenyang   | 196     | 27 (13.64) | 115 | 12 (10.43) | 214 | 28 (13.08) | 257 | 29 (11.28) | 149 | 16 (10.74) | 106 | 11 (10.38) |
| Shenzhen   | 282     | 61 (21.63) | 168 | 17 (10.12) | 225 | 22 (9.78) | 334 | 32 (9.58) | 382 | 37 (9.69) | 98 | 13 (13.27) |
| Nanjing    | 117     | 37 (31.62) | 91 | 16 (17.58) | 207 | 19 (9.18) | 226 | 11 (4.87) | 252 | 25 (9.92) | 133 | 9 (6.77) |
| Shanghai   | 449     | 82 (18.26) | 271 | 26 (9.59) | 352 | 32 (9.09) | 562 | 56 (9.96) | 579 | 52 (8.98) | 334 | 25 (7.49) |
| Beijing    | 593     | 98 (16.53) | 295 | 37 (12.54) | 519 | 43 (8.29) | 720 | 30 (4.17) | 559 | 33 (5.90) | 337 | 31 (9.20) |
| Total      | 2513    | 501 (19.94) | 1501 | 207 (13.79) | 2462 | 299 (12.14) | 3104 | 337 (10.86) | 2917 | 311 (10.66) | 1501 | 156 (10.39) |

Table 4. AD prevalence stratified by age subgroup.

| Risk factor | Classification | AD prevalence by the presence of the risk factor | P value | OR (95%CI) |
|-------------|----------------|-----------------------------------------------|---------|------------|
| Increasing of age | — | — | <0.001** | 0.829 (0.802–0.857) |
| Residence status (rural) | urban | 8738 (62.42%) | — | <0.001** | 0.886 (0.071–0.105) |
| | rural | 5260 (37.58%) | | | |
| Exposed to passive smoking | not exposed to | 7384 (52.75%) | | | |
| | exposed to but not during pregnancy | 3485 (24.90%) | | 0.023* | 1.076 (1.010–1.145) |
| | exposed also including pregnancy time | 3129 (22.35%) | | | |
| Pet ownership | not exposed to | 12692 (90.67%) | | | |
| | exposed to but not during pregnancy | 570 (4.07%) | | 0.75 | 0.983 (0.887–1.091) |
| | exposed also including pregnancy time | 736 (5.26%) | | | |
| Delivery pattern | vaginal delivery | 6857 (48.99%) | | 0.21 | 1.077 (0.971–1.194) |
| | cesarean section | 7141 (51.01%) | | | |
| Premature birth | No | 12836 (91.70%) | | 0.001** | 1.334 (1.124–1.584) |
| | Yes | 1162 (8.30%) | | | |
| Giving up exclusive breast-feeding during first 6 months of life | exclusive breast-feeding | 8491 (60.66%) | | 0.083 | 0.941 (0.881–1.004) |
| | mixed feeding | 2613 (18.67%) | | | |
| | powdered milk | 2894 (20.67%) | | | |
| Choosy in food | No | 10293 (73.53%) | | <0.001** | 1.272 (1.135–1.425) |
| | Yes | 3705 (26.47%) | | | |

Table 5. Logistic regression of factors associated with AD. *P < 0.05, **P < 0.01. All the risk factors were included in a single formula.
7% had severe disease throughout the country. Another study of 290 children aged 1–5 year preschool children show that 82% had mild, 12% moderate, and 6% severe disease of AD in 2000. Also a study using clinician assessment of severity found 84% mild, 14% moderate and 2% severe in 1760 children aged 1–5 year in 1998. The distribution of AD severity in China seems similar to that in abroad.

Prevalence of AD ranges from 9.00% to 24.69% among cities. A general geographic trend of higher disease prevalence in inland area of China was found. It is noted that inland cities accelerate industrialization in the past year. Shenzhen and Hong Kong are two cities next to each other geographically. Prevalence of AD in Shenzhen aged 1–7 ys is currently 11.84%, compared with 14% in children aged 6–12.5 ys in Hong Kong in 2000. In another aspect, the prevalence of AD is highest among 1–2 year old children and descends with age in general, which is in accordance with natural advance of AD. Prevalence of AD fluctuates with age, indicating that multiple factors play a role in AD development.

A series factors including age, residence status, exposed to passive smoking, premature birth, breast-feeding, pet ownership, delivery pattern and choosy in food were previously considered to be associated with AD prevalence and evaluated in multiple studies. AD prevalence is generally considered declined with age and to be lowered in rural areas, which is consistent with current study. For breast-feeding, there is strong evidence to support that breast-feeding during the first 4 months of life causes a reduction in incidence and severity of atopic disease in patients at high risk, however, the risk reduction from breast-feeding only applies to children at high risk. Besides, there were conflicts on the impact of passive smoking on AD (both as risk and protective factors), premature birth (decreased risk for severe atopic dermatitis), pet ownership (protective influence being under investigation), delivery pattern and choosy in food. In our study, passive smoking, premature birth, and choosy in food are risk factors for AD. Pet ownership, delivery pattern and feeding pattern in the first 6 months of life are not influence factors for AD development, which somewhat enrich the information on controversial risk factors for Chinese pediatric AD, and indicated that more studies are required.

One of the earliest and most recognized sets of diagnostic criteria is the 1980 Hanifin and Rajka criteria. While widely used in clinical trials, it is not convenient for use in clinical practice because of comprehensive criteria. Several international groups have proposed modifications to address limitations (eg, Kang and Tian criteria, International Study of Asthma and Allergies in Childhood [ISAAC] criteria). The United Kingdom (UK) Working Party, in particular, systematically distilled the Hanifin and Rajka criteria down to a core set that is suitable for epidemiologic/population-based studies and that can be used by non-dermatologists. It consists of 1 mandatory and 5 major criteria and does not require any laboratory testing. The UK Working Party diagnostic schemes have been validated in studies and tested in different populations. It is noted that there is a huge discrepancy in the AD prevalence between the dermatologists’ diagnosis (12.94%) and the UK diagnostic criteria (4.76%). Using clinical diagnosis as gold standard, the sensitivity, specificity, positive predictive value and negative predictive value were 36.27%, 99.91%, 98.5%, and 91.34% for UK diagnostic criteria. Compared to previous studies, a relatively low sensitivity was also shown. The cause for the low sensitivity can be explained as following. In the current study, it is noted that AD patients at an early age with mild phenotype are easy to be omitted when diagnosed by UK diagnosis criteria. For example, 63.17% AD patients diagnosed by dermatologists were not approved when UK diagnosis criteria worked. Among them, 84.97% were mild AD with the objective SCORAD value less than 14.8 while other 15.03% of them show that their objective SCORAD value was between 15 and 53.5. Among missed diagnosed patients, 43.33% of them didn’t report persistent pruritis over 12 months, which is a mandatory criterion in UK diagnosis criteria. 51.29% of them denied a generally dry skin in the last year. Both were not easy for carers to judge and reply accurately in practice, especially for children less than 1 year old. 98.10% denied personal asthma or hay fever, which is rarely seen or diagnosed in children less than 3 year old. 89.80% of them did not show rash in the skin creases. 6.94% were normal before 2 years old. Therefore, it was also speculated that all above made missed diagnosis when UK diagnosis criteria adopted.

In conclusion, this is the first face-to-face nation-wide study in Chinese preschool children conducted by dermatologists to evaluate the prevalence of AD, revealing that the prevalence of AD in children aged 1–7 ys is close to that of wealthier nations.

Methods

Study population. This epidemiologic study used a population-based stratified random sample of 15000 individuals. The target population consisted of preschool children with age range 1–7 years in kindergartens (age 4–7 years) and vaccination clinics (age 1–3 years), considering that the rate of kindergarten attendance is over 90% according to data from local Bureau of education while vaccination rate is over 95% according to data from local center for disease control and prevention among 1–7 year old children in metropolises. For nation-wide study, 12 metropolises were chosen from different areas of China: Shenyang, Beijing, Dalian, Taiyuan, Nanjing, Hefei, Shanghai, Wuhan, Chengdu, Chongqing, Changsha and Shenzhen, respectively, throughout China (Fig.1). In each region, we randomly selected 4–10 kindergartens and 2–5 vaccination clinics. The precise numbers of kindergartens, vaccination clinics and samples enrolled in epidemiological survey were decided statistically according to demographic data of children among 1–7 years in each city when prevalence of AD was estimated in multiple studies.

Diagnostic criteria of AD. All dermatologists involved in study have rich clinical experience in AD and have been trained to unify their recognition of AD in advance. In this study, clinical diagnosis made by experienced dermatologists was considered as gold standard. The clinical diagnosis is essentially following the definition of AD, a chronic, relapsing, highly pruritic, inflammatory skin disease that frequently predate the development of allergic rhinitis or asthma, moreover, other allergic, pruritic, or erythematousquamous dermatosis, contact dermatitis, psoriasis, scabies, or hereditary metabolic disease and lymphoma have been carefully excluded by history inquiring (Questions included “when were the skin disorder developed and how long it has been existing’
“when was the disease most severe” “what do you consider as the predisposing factors” “Has family members affected by same disease!” and physical examination (all positive signs of skin were recorded). No laboratorial test was performed for dermatologist to make the diagnosis.

Data collection. The study and related questionnaire were approved by the Ethical Committee of Xinhua Hospital affiliated to Shanghai Jiaotong University School of Medicine. Permission was also obtained from Center for Disease Control and Prevention (CDC) and school principals. Written Informed consent was provided by all children's parents. Data collection was carried out in accordance with the principles of the Declaration of Helsinki and approved guidelines. From December 2013 to February 2014, dermatologists visited schools or vaccination clinics and independently evaluated whether or not the child had AD and the severity. Each subject was inspected by 2 dermatologists independently at first. Each dermatologist was given an equal and independent authority to make their own diagnosis after a 10–15 minutes' dermato logical physical examination. One dermatologist did not know another dermatologist’s diagnosis, whether each subject met the UK Criteria, or other physician's idea in advance. If inconsistency exists between 2 dermatologists, the idea of another senior dermatologist will be adopted after examining the patient again. Afterwards, two dermatologists evaluated the severity of each AD patients according to “SCORing Atopic Dermatitis” (SCORAD), a clinical tool for assessing the severity of atopic dermatitis objectively, independently and the average score would be the final result. The severity of AD is evaluated and classified as mild (<15), moderate (15–40) or severe (>40) according to the objective components of the SCORAD index (clinical signs and disease extent, total score 83). All diagnostic criteria mentioned in UK diagnostic criteria as well as personal and family history of atopic diseases including infantile eczema were investigated and recorded in detail for determination of AD incidence based on UK diagnosis criteria (Parents or guardians filled the relevant forms). All characteristic presentation of AD as well as atypical clinical manifestations were also inspected and recorded in detail for all subjects. General information, personal and family history of skin diseases including allergic/atopic disorders and the subjective symptom of pruritus were collected from parents or other family members by dermatologists on the examination day in vaccination clinics or one week ahead for children in kindergartens.

Risk factor. Possible risk factors19–29 for AD included age, residence status (urban or rural district), passive smoking (not exposed to, exposed but not during pregnancy, exposed also including pregnancy time), pet ownership (not exposed to, exposed to but not during pregnancy, exposed also including pregnancy time), delivery pattern (vaginal delivery or caesarean), premature birth or not, feeding pattern during the first 6 month after birth (exclusive breast-feeding, mixed feeding, powdered milk), and choosy or not in food. So we evaluated the factors in the epidemiological study.

Statistical analysis. The prevalence of AD in various age groups and cities, as well as the severity of AD was calculated separately. The consistency between the diagnosis of two dermatologists was examined by Cohen's kappa coefficient. Pearson correlation test was used to evaluate the correlation of Cohen's kappa coefficients and AD prevalence of various cities diagnosed by clinical dermatologists. Logistic regression using the forward likelihood ratio was performed to explore risk factors of AD by data from dermatological examination and questionnaire survey. A p-value at less than 0.05 is considered statistically significant. Compared to dermatologist diagnosis, the sensitivity, specificity, positive predictive value and negative predictive value were calculated for UK diagnostic criteria.

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**Additional Information**

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