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ORIGINAL RESEARCH

Epidemiology and Burden of Pediatric Atopic Dermatitis in China

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ABSTRACT

Introduction: We aimed to estimate the prevalence, severity, and burden of pediatric atopic dermatitis (AD) in China.

Methods: EPI-CARE China was a cross-sectional online survey that assessed AD in the general pediatric populations (aged 0.5−17 years) between 21 March 2021 and 5 April 2021 in China. Diagnosis of AD prevalence was based on both International Study of Asthma and Allergies in Childhood criteria and self-reported or parent-reported physician confirmation of ever having had AD. Severity (mild, moderate, and severe) in the preceding week was assessed by patient global assessment. Health-related quality of life (HRQoL) was assessed using established dermatology patient-reported outcomes tools (Infant Dermatitis Quality of Life and Children's Dermatology Life Quality Index). Outcomes included type 2 inflammatory comorbidities and itch, skin pain, and sleep disturbance in the previous 24 h (numeric rating scale [NRS]: 0–10 [no symptoms–worst symptoms]), stratified by age group (aged ≤ 5 years, 6–11 years, and 12–17 years).

Results: In 7148 patients, AD prevalence was 3.2% (≤ 5 years, 3.8%; 6–11 years, 4.1%; 12–17 years, 1.7%). Of these, 59.1% (≤ 5 years, 66.1%; 6–11 years, 60.1%; 12–17 years, 39.4%), 38.8% (≤ 5 years, 33.9%; 6–11 years, 38.0%; 12–17 years, 53.1%), and 2.0% (≤ 5 years, 0.0%; 6–11 years, 1.9%; 12–17 years, 7.5%) had mild, moderate, and severe AD, respectively. Patients with moderate AD reported greater impacts on HRQoL than patients with mild AD (too few patients with severe AD provided HRQoL data for comparison). Overall, 90.5% patients reported ≥ 1 atopic comorbid condition. The mean (SD) itch, skin pain, and sleep disturbance NRS values were 5.9 (2.4), 5.6 (2.6), and 5.9 (2.3), respectively.

Conclusions: These results demonstrate that AD is associated with substantial patient burden in pediatric patients in China.

Keywords: Atopic dermatitis; Childhood; Epidemiology; China

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Key Summary Points

There are limited nationally representative data reporting the epidemiology of pediatric atopic dermatitis (AD) prevalence in China.

We aimed to estimate prevalence, severity, and burden of pediatric AD in China using a cross-sectional online survey study (EPI-CARE China).

Pediatric AD prevalence was 3.2% in China, and 90.5% of patients with AD reported ≥ 1 atopic comorbidity.

Pediatric patients with AD experienced substantial disease burden across multiple domains, including type 2 inflammatory comorbidities and AD-related symptoms such as itch, skin pain, and sleep disturbance.

These results demonstrate that AD is associated with substantial patient burden in pediatric patients in China.

INTRODUCTION

Atopic dermatitis (AD), also known as atopic eczema, is a chronic, systemic inflammatory skin condition associated with epithelial, immune, and environmental factors, characterized by intense itch, disruption of the skin barrier, and upregulation of type 2–mediated immune responses in the skin [1, 2]. AD prevalence has increased in the last few decades, particularly in developed countries; multiple environmental, genetic, and immunological factors are thought to be responsible [3]. AD is one of the most common skin disorders worldwide, and recent estimates of AD prevalence have reported rates of 2.1–4.9% in adults in a web-based survey study conducted in 2016 in USA, Canada, France, Germany, Italy, Japan, Spain, and the UK [4]; however, that study did not report data from children or adolescents aged < 18 years.

The International Study of Asthma and Allergies in Childhood (ISAAC) previously reported pediatric AD rates ranging from 0.9% (India) to 22.5% (Ecuador) in patients aged 6–7 years and 0.2% (China) to 24.6% (Colombia) in patients aged 13 to 14 years, but these estimates varied widely across geographical regions [5]. As data collection for this study ended in 2004 and AD rates appear to be increasing over time [3], there is a need to update pediatric AD prevalence estimates. Accordingly, the Epidemiology of Children with Atopic Dermatitis Reporting on their Experience (EPI-CARE) study assessed the point prevalence of AD in the pediatric population (0.5–17 years old), including severity distribution and the associated impact on quality of life, in multiple countries across different geographic regions worldwide [6]. EPI-CARE reported prevalence estimates ranging from 2.7% (Israel) to 20.1% (Brazil). However, previous publications based on EPI-CARE did not report prevalence of pediatric AD in China, and there are limited nationally representative data reporting pediatric AD prevalence in China. The EPI-CARE study has since been extended to include China, and here we present prevalence, severity, and burden data.

METHODS

Study Design

EPI-CARE was a multinational, cross-sectional study conducted to assess the prevalence of AD in the pediatric (0.5–17 years) population across various geographic regions worldwide; here we present data from China, collected between 21 March 2021 and 5 April 2021. In line with prior EPI-CARE publications, web-based survey questionnaires were used; this methodology ensured a large sample size representative of the demographic and geographic distribution of the Chinese population, which enabled assessment of multiple baseline variables and facilitated broad comparisons with prior EPI-CARE publications. Participating patients were identified initially by their parents (recruited via online panels), who received web-based invitations to complete a questionnaire to assess eligibility. The first section assessed sociodemographic information to confirm

whether the child met the requirements of the quota algorithm. The presence of AD was then confirmed by (1) ISAAC criteria (presence of an intermittent itchy rash for ≥ 6 months during the previous 12 months, which affected elbows, knees, ankles, buttocks, neck, ears or eyes) and (2) confirmation (either self-reported or parent-reported) of having previously received a diagnosis of AD from a physician (also, children ≤ 5 years of age were required to have reported an itchy rash on the face and also on the elbow–wrist or knee–ankle at any time). Patients who were deemed to have confirmed AD (i.e., meeting both ISAAC criteria and having self-reported or parent-reported physician confirmation) after completing the first part of the questionnaire were then invited to complete the second section, which assessed severity and health-related quality of life (HRQoL) impact of AD. For children aged ≤ 3 years, parents completed this section on their child's behalf using the Infant Dermatitis Quality of Life (IDQoL) scale, which has been validated for parental assessment of the impact of AD on quality of life in infants aged under 4 years [7]. Adolescents (12–17 years) self-completed the Children's Dermatology Life Quality Index (CDLQI) after providing consent for participation. The CDLQI has been validated for assessing the impact of skin disease on quality of life in children and adolescents [8]. A derivative version using images rather than text, the CDLQI Cartoon, has been shown to be equivalent to the CDLQI [9]. For children aged 4–11 years, parents were requested to pass control to their child as much as possible for scales that were validated for completion by younger age groups (using the CDLQI and the CDLQI Cartoon) but retained the right to answer on behalf of their children (using the IDQoL) if they did not feel that their child could accurately use the CDLQI or CDLQI cartoon. Study design and reporting followed Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines where applicable. The data that support the findings of this study are available from the corresponding author upon reasonable request. No personal data were collected from the survey and no medical information was abstracted from the patient medical records; therefore, approval of the study by central and/or local ethical committees in China was not required. The research complied with GDPR and all international/local data protection legislations and Insights Association/EphMRA/BHBIA.

Study Outcomes

Severity in the preceding week was assessed by patient global assessment (PGA), reported as clear/mild, moderate, or severe by the patient or their parents. As a sensitivity analysis, severity in the preceding week was also assessed by the patient-oriented eczema measure (POEM), reported as number of days for seven AD symptoms. Each symptom was scored on a range from 0 to 4 depending on frequency of occurrence in the preceding week, giving a total score range of 0 to 28; a cumulative score of 0–7 was defined as mild, 8–16 as moderate and ≥ 16 as severe. HRQoL was assessed using different patient-reported outcomes (PRO) measures: the IDQoL, which was completed by the parents of children aged 0.5–3 years, and also by the parents of children aged 4–11 years if their parents retained control over completion of the questionnaire; the CDLQI (or CDLQI Cartoon), which was administered to children aged 4–11 years whose parents permitted them to directly complete the questionnaire; and the CDLQI, which was completed by adolescents aged 12–17 years. The presence of type 2 inflammatory comorbidities was reported, and symptoms of itching, skin pain, and sleep disturbance during the previous 24 h were assessed by numeric rating scale (NRS), ranging from 0 (no symptoms) to 10 (worst symptoms possible).

Statistical Analysis

All baseline characteristics were reported descriptively. AD prevalence data were weighted by age, sex, and region to ensure that the sample was representative of the general pediatric population of China; representativeness was assessed by Quota Methods of Apportionment [10]. A minor weighting adjustment was applied to ensure that the participant group was highly

representative of the general population; the urban versus rural quota was not considered, as the sample size in rural areas was too low. All outcomes were stratified by age group (aged ≤ 5 years, 6–11 years, 12–17 years). Student *t* tests were used to compare continuous variables, and *z* tests were used to describe the association between categorical variables. Informed consent was obtained for all participants before completing the survey; parents were asked to confirm voluntary participation after reading a statement of informed consent, and parents of participants aged 12–17 years were asked to let their child confirm their voluntary participation.

RESULTS

A total of 7148 respondents were included in the analysis. Baseline sociodemographic data for this group before and after weighting are shown in Supplementary Table 1. After weighting, the sample remained similar in terms of age, sex, and region; over half of the participants (53.9%) were male, and 35.0% ($n=2502$), 33.2% ($n=2374$), and 31.8% ($n=2272$) were included in the ≤ 5 years, 6–11 years and 12–17 years groups, respectively (Table 1).

Prevalence and Severity of AD

Prevalence of self-reported or parent-reported, physician-confirmed AD (17.2–21.9%) was substantially higher than ISAAC-defined AD (3.5–7.0%). Using both definitions (self-report or parent report of physician confirmation and ISAAC criteria) to determine AD, weighted prevalence was 3.2% overall and was 3.8%, 4.1%, and 1.7% in the ≤ 5 years, 6–11 years, and 12–17 years groups, respectively (Fig. 1); prevalence was largely driven by suburban/urban regions and was very rarely seen in rural settings. Prevalence of AD was significantly ($P<0.01$) higher in patients aged ≤ 5 years residing in an urban (versus suburban) setting, in patients in all age groups who had a current or occasional smoker in the household (versus those who did not have a smoker in the household), and in patients in all age groups who had a domestic pet (versus no pet) at home (Supplementary Table 2).

The majority of patients had mild (59.1%) AD, as measured by PGA, and the prevalence of mild AD appeared to progressively decrease with age (66.1%, 60.1%, and 39.4% of patients in the ≤ 5 years, 6–11 years and 12–17 years groups, respectively) in parallel with an increase in the prevalence of severe AD (0%, 1.9%, and 7.5% in the ≤ 5 years, 6–11 years, and 12–17 years groups, respectively). (Fig. 2A). Severity assessed by POEM provided comparable scores (Fig. 2B).

Comorbidities and Symptoms

The majority of patients with a qualifying AD diagnosis ($n=233$) reported at least one type 2 inflammatory comorbidity (90.5%), and the proportion of patients reporting at least one type 2 inflammatory comorbidity appeared to increase with age (Fig. 3A). The most frequently reported comorbidities in pediatric and adolescent patients with AD were hay fever, asthma, seasonal allergies, and allergic rhinitis, which were reported by over 40% of all patients with AD across all age groups (Fig. 3B; Supplementary Table 3).

Mean NRS scores for itch (5.9), skin pain (5.6), and sleep disturbance (5.9) were consistent across age groups (Fig. 4). Among patients aged ≤ 5 years who completed the IDQoL, 36.6% of patients with mild AD ($n=15/41$) reported a "very large" or "extremely large" impact on their HRQoL, compared with 81.8% of patients with moderate AD ($n=18/22$); no patients aged ≤ 5 years with severe AD completed the IDQoL (Supplementary Table 4). HRQoL results were similar among patients who completed the CDLQI; across age groups, the proportion of patients reporting a "very large" or "extremely large" impact on HRQoL ranged from 33.3 to 41.8% of patients with mild AD and 61.9 to 81.1% of patients with moderate AD (Supplementary Table 5); only

Table 1 Baseline sociodemographic data and AD diagnosis in the ≤ 5 years, 6–11 years, and 12–17 years groups

	≤ 5 years	6–11 years	12–17 years
Age, years	(*n* = 2502)	(*n* = 2374)	(*n* = 2272)
Mean (SD)	3.70 (1.65)	8.94 (1.66)	14.68 (1.57)
Median (range)	3.83 (0.50–5.92)	8.83 (6.00–11.92)	14.75 (12.00–17.92)
Sex, *n* (%)	(*n* = 2502)	(*n* = 2374)	(*n* = 2272)
Female	1140 (45.6%)	1041 (43.9%)	1114 (49.0%)
Male	1361 (54.4%)	1332 (56.1%)	1160 (51.0%)
Number of siblings	(*n* = 2502)	(*n* = 2374)	(*n* = 2272)
Mean (SD)	0.06 (0.26)	0.07 (0.29)	0.05 (0.30)
Median (range)	0.00 (0.00–5.00)	0.00 (0.00–5.00)	0.00 (0.00–7.00)
Height, cm	(*n* = 2489)	(*n* = 2374)	(*n* = 2253)
Mean (SD)	1.00 (0.20)	1.34 (0.15)	1.59 (0.12)
Median (range)	1.00 (0.40–1.50)	1.35 (0.80–1.80)	1.60 (1.00–1.86)
Weight, kg	(*n* = 2293)	(*n* = 2342)	(*n* = 2238)
Mean (SD)	17.86 (5.34)	33.77 (9.59)	50.98 (12.42)
Median (range)	18.0 (3.0–30.0)	32.0 (15.0–80.0)	50.0 (25.0–175.0)
Smoker at home, *n* (%)	(*n* = 2493)	(*n* = 2365)	(*n* = 2263)
Yes	1559 (62.3%)	1359 (57.3%)	1279 (56.3%)
No	934 (37.3%)	1005 (42.3%)	985 (43.3%)
Domestic animal at home, *n* (%)	(*n* = 2502)	(*n* = 2373)	(*n* = 2272)
Yes	1166 (46.6%)	1271 (53.6%)	1216 (53.5%)
No	1336 (53.4%)	1102 (46.4%)	1058 (46.5%)
Residence, *n* (%)	(*n* = 2502)	(*n* = 2373)	(*n* = 2272)
Urban	1309 (52.3%)	1672 (70.5%)	851 (37.4%)
Suburban	208 (8.3%)	166 (7.0%)	198 (8.7%)
Rural	985 (39.4%)	535 (22.6%)	1225 (53.9%)
AD diagnosis, *n* (%)	(*n* = 2502)	(*n* = 2374)	(*n* = 2272)
(1) ISAAC	176 (7.0%)	160 (6.7%)	79 (3.5%)
(2) Self-reported or parent-reported, physician-confirmed AD	548 (21.9%)	407 (17.2%)	403 (17.7%)
Prevalence of AD (1 + 2)	96 (3.8%)	96 (4.1%)	38 (1.7%)

Owing to the prevalence weighting adjustment, the sum of n for individual category variables may not match the overall n for each category

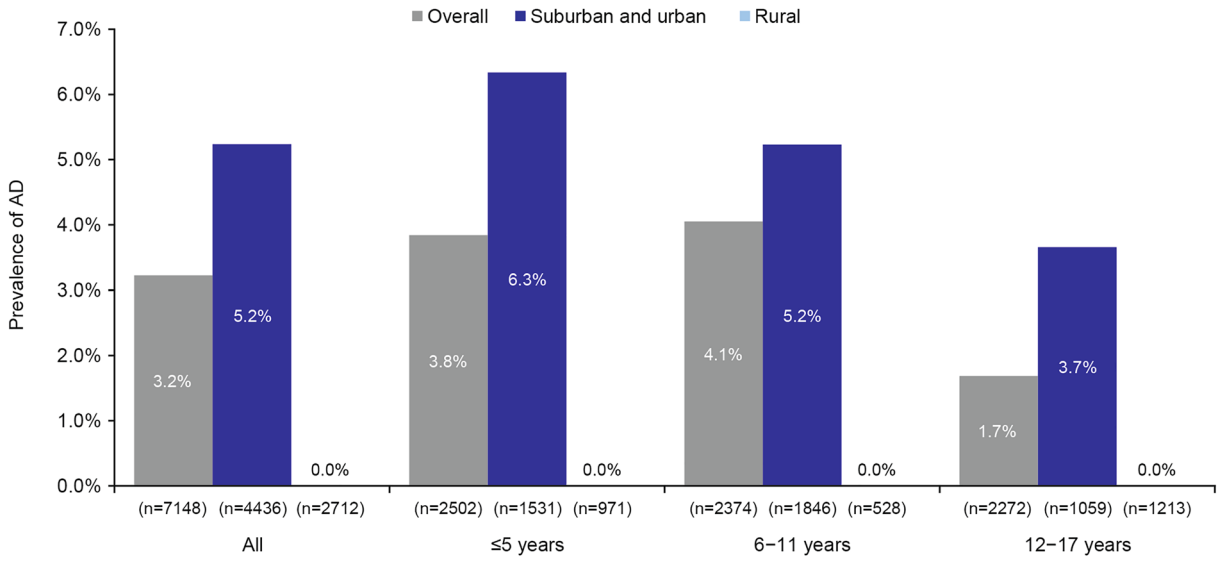

Fig. 1 Prevalence of AD diagnosis (per International Study of Asthma and Allergies in Childhood criteria) within cohort ($n = 7148$), and stratified by residential area

five patients with severe AD (6–11 years, $n = 2$; 12–17 years, $n = 3$) completed the CDLQI.

DISCUSSION

This survey demonstrated that approximately 3% of the pediatric population in China were affected by AD, and those patients experience a substantial disease burden across multiple domains, including type 2 inflammatory comorbidities and AD-related symptoms, such as itch, skin pain, and sleep disturbance. Additionally, although sample sizes were small, dermatology PRO tools (the IDQoL and the CDLQI) suggested that the presence of AD was associated with substantial impact on HRQoL and that this impact was greater in patients with moderate versus mild AD (too few patients with severe AD completed the IDQoL and CDLQI to enable meaningful analysis).

These data extend previous reports across multiple geographical locations from the EPI-CARE study. Prevalence estimates in China were generally lower than those seen in corresponding EPI-CARE studies in other geographical regions, despite comparable methodology; in a previous multinational report from the EPI-CARE study, only Israel (2.7% in children aged 0.5–17 years) had a lower prevalence of pediatric AD [6]. The reason for such wide geographical variation in AD prevalence is currently unclear but is likely to relate to a combination of ethnic, racial, and/or socioeconomic factors [11]. These results are also broadly in line with prior assessments of pediatric AD in China. A large-scale multicenter face-to-face dermatology assessment reported a prevalence of 4.8–12.9% in children aged 1–7 years [12]. Similarly, in a 2010 prior cross-sectional study in preschool children aged 3–6 years in Shanghai, China, the prevalence of AD diagnosed according to UK working group criteria [13] was 8.3% [14]. The slightly lower AD prevalence observed in our study may be attributable to the use of ISAAC criteria and to our conservative AD definition, whereby AD cases were also required to have a self-reported or parent-reported confirmation of a physician diagnosis of AD. Indeed, although we employed a dual-factor identification (both self-reported ISAAC criteria and self-reported or parent-reported physician-confirmed diagnosis) in this study, self/parent-reported physician-confirmed AD rates were much higher than ISAAC-based AD rates, which aligns with previous studies.

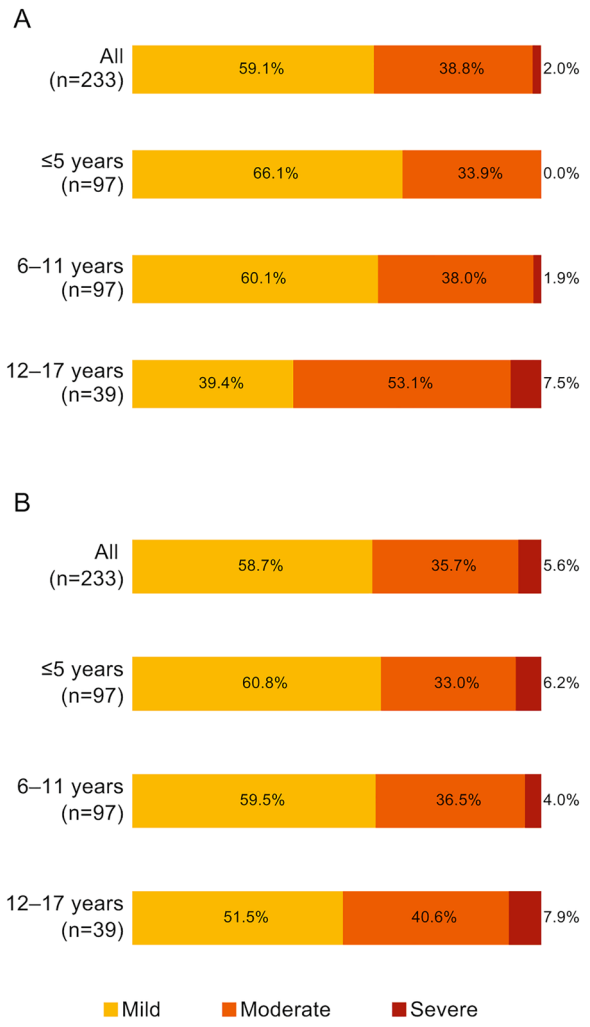

Fig. 2 Severity of AD assessed by **A** PGA and **B** POEM, overall and by age group

The studies reported by Guo et al. (2016) and Xu et al. (2012) also reported that the prevalence of pediatric AD was higher in urban than in rural areas in China. Xu et al. (2012) noted industrial manufacturing, pollution, exposure to animals, maternal age, overcrowding in an apartment, differences in diet (e.g., processed versus fresh food), socioeconomic factors, and time spent indoors as potential factors leading to higher pediatric AD prevalence in urban areas. The association between AD prevalence and urbanization has also been observed in other countries; a systematic review of AD prevalence in children and adolescents reported that this link was particularly strong in developing countries [15]. Potential contributing factors noted in the systematic review broadly match those highlighted in the Xu 2012 study, but additional factors mentioned were water intake (e.g., spring versus chlorinated water), increased vehicular traffic, and differences in climate.

The majority of patients across all age groups assessed experienced mild or moderate AD, which is in line with previous reports in adult AD populations [4] and were broadly comparable with scores reported for these age groups in other geographical locations [6]. We assessed severity primarily by PGA, which we assume to represent a more precise and holistic measure of severity than other symptom-based measures, such as POEM. Our sensitivity analysis using POEM to assess severity demonstrated similar findings to PGA. The observations that the prevalence of severe AD increases with age, with a parallel decrease in mild AD, may indicate a progression of severity in patients with AD (i.e., patients with mild AD at a young age may develop more severe AD by the time they reach 11–17 years of age). Similarly, another population-based study from the UK also reported a decrease in the prevalence of mild AD concurrent with an apparent increase in the prevalence of severe AD [16]. Similarly, the proportion of patients reporting more than one comorbidity and also the rates of specific type 2 inflammatory comorbidities, such as food allergies and allergic rhinitis, appeared to be more frequently reported with increasing age. The link between AD and allergic rhinitis has previously been demonstrated [17, 18]. Taken collectively, these observations of increasing severity and prevalence are in line with the "atopic-march" concept of AD and subsequent type 2 inflammatory comorbidities [19]. Appropriate longitudinal studies would be required to conclusively demonstrate this atopic-march concept in the pediatric AD population in China.

Atopic type 2 inflammatory comorbidities were widely reported, with over 90% of patients reporting at least one type 2 inflammatory comorbidity; this was generally consistent across age groups (85–98%). The most frequently reported comorbidities were hay fever, asthma, seasonal allergies, and allergic rhinitis, which

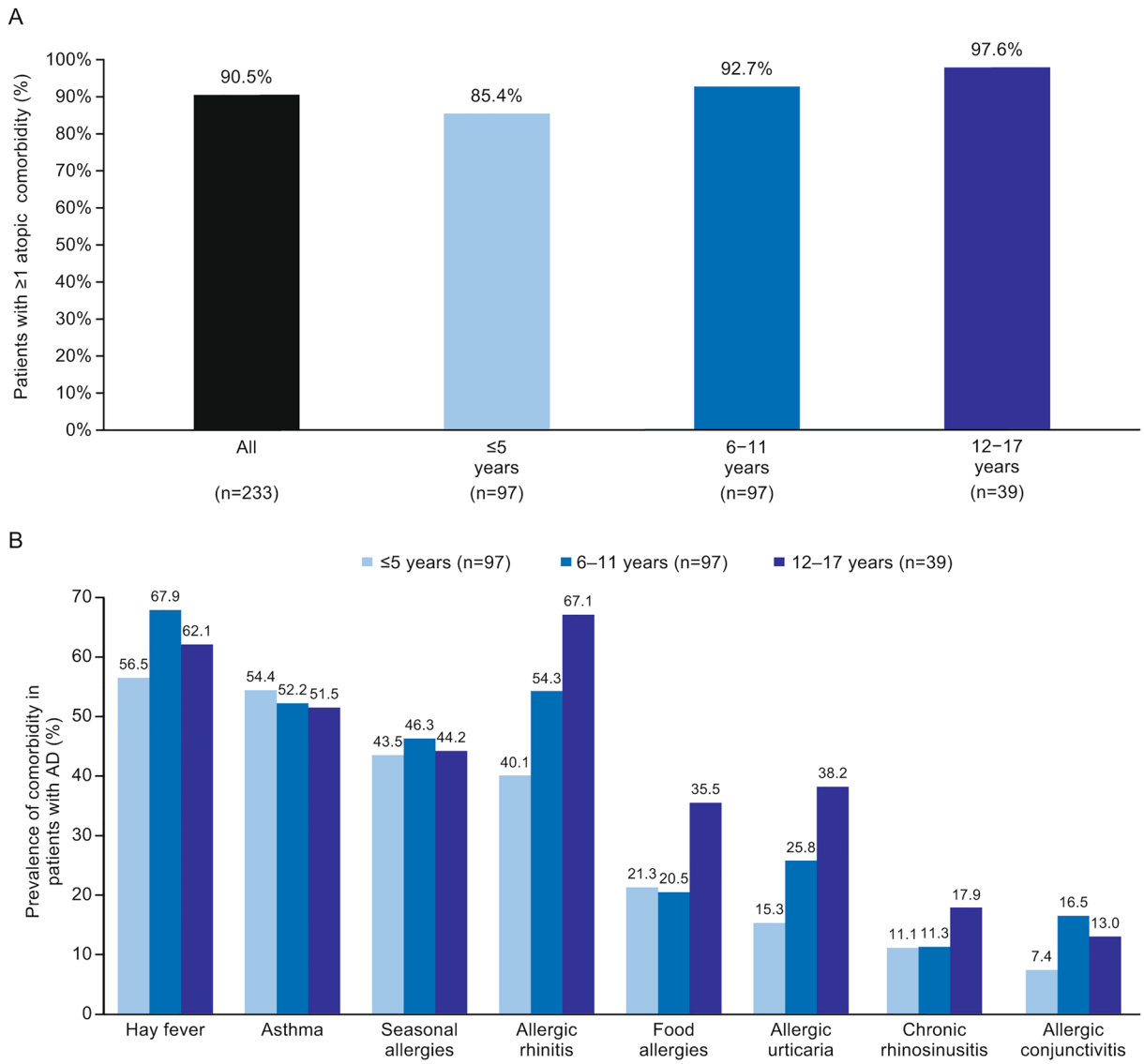

Fig. 3 **A** Presence of ≥ 1 atopic type 2 inflammatory comorbidity; **B** prevalence rates for individual type 2 inflammatory comorbidities (only comorbidities reported in > 10% of patients are shown)

were reported by over 40% of patients across all age groups. These observations in the Chinese pediatric AD population align closely with previous findings from a US cross-sectional study reporting that rates of asthma and allergic rhinitis were over 30% in the pediatric AD population and that over 70% of pediatric patients with AD reported at least one type 2 inflammatory comorbidity [20]. In addition to these comorbidities, across all age categories, approximately one-third of patients with mild AD and the majority of patients with moderate AD reported at least a "very large" impact on their HRQoL. Taken collectively these observations suggest that even mild and moderate AD cases may be associated with a substantial HRQoL burden for patients.

Strengths of this study include its conservative AD definition (requiring diagnosis according to ISAAC criteria and also a report of physician confirmation of AD) and the large and nationally representative sample size in China. Unweighted

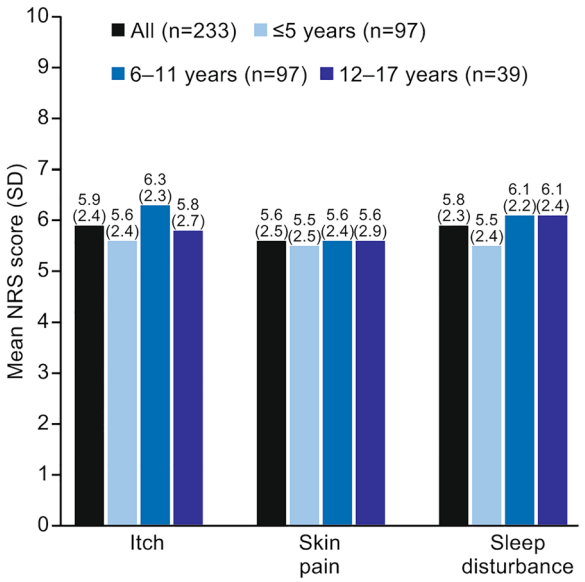

Fig. 4 Mean (SD) NRS symptom scores, overall and by age group

and weighted data remained similar, indicating that the original sample was unbiased and representative of the population. Limitations include those inherent to similar survey-based studies, namely recall biases and self-selection biases (i.e., patients more likely to participate may inherently be more likely to have AD). More specifically, one may hypothesize that parents of children with more severe AD may have been more inclined to complete the online survey than parents of children with mild AD; additionally, socioeconomically disadvantaged families may have been less likely to have internet access and/or be computer-literate. However, as the methodology used is consistent with previous EPI-CARE reports, the data reported provide compelling evidence for comparison with similar data drawn from other countries. Lastly, it should be noted that the HRQoL findings are based on small sample sizes.

CONCLUSIONS

This cross-sectional online survey study showed that in China, 3.2% of the pediatric population were reported to have AD, which was associated with substantial symptom, comorbidity, and HRQoL burden. There remains a substantial unmet need for comprehensive disease management in combination with novel therapies to alleviate the clinical and HRQoL burden in pediatric patients with AD in China.

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Author Contributions. Chien-Chia Chuang carried out study conceptualization, funding acquisition, methodology, supervision, and writing—review and editing; Lydia Braham-Chaouche carried out data curation, formal analysis, methodology, resources, software, and writing—review and editing; Tarek Mnif carried out data curation, formal analysis, methodology, resources, software, and writing—review and editing; Ryan Thomas carried out study conceptualization, methodology, and writing—review and editing.

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Data Availability. The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

Declarations

Conflict of Interest. Chien-Chia Chuang is an employee and stockholder of Sanofi. Lydia Braham-Chaouche and Tarek Mnif are employees of Cerner Enviza, which received funding for this analysis from Sanofi and Regeneron Pharmaceuticals Inc. Ryan Thomas is an employee and stockholder of Regeneron Pharmaceuticals Inc.

Ethical Approval. No personal data were collected from the survey and no medical information was abstracted from the patient medical records; therefore, approval of the study by central and/or local ethical committees in China was not required. The research complied with GDPR and all international/local data protection legislations and Insights Association/EphMRA/BHBIA.

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