**Evaluation of caregiver-reported criteria for diagnosing eczema in young children**

**To the Editor,**

Eczema or atopic dermatitis (AD) is a chronic relapsing inflammatory skin disease with a peak incidence in the first 2 years of life1. Physician diagnosis of AD is still problematic as there is variability in diagnosing AD, especially in young children, and validation studies on diagnostic accuracy and criteria of physician diagnosis of AD are lacking. Furthermore, mild to moderate AD is easily controllable with topical treatment, such as moisturizers and corticosteroids 2, which results in children with AD presenting at the doctor’s office with a normal skin. Epidemiological studies often employ caregiver-reported history of a physician-diagnosed AD as a proxy measure to estimate AD prevalence in children 3,4. When compared to physician diagnosis using Hanifin and Rajka criteria at the clinic visit, a previous study in 0–17-year-old children/adolescents reported sensitivities/specificities of 70%/96% and 83%/89% for caregiver-reported 1-year recall history of AD diagnosis and history of ever having AD, respectively 5. Hence, the present study aimed to evaluate the diagnostic accuracy of life-time caregiver-reported history of physician-diagnosed AD in young children (i.e., life-time prevalence) using the physician diagnosis of AD at clinic visit as the gold standard (i.e., point prevalence, potentially influenced by treatment).

Ethical approval was obtained from Centralized Institutional Review Board (CIRB) of SingHealth (reference 2009/280/D) and Domain Specific Review Board (DSRB) of Singapore National Healthcare Group (reference D/09/021). Data was extracted from The Growing Up in Singapore Towards healthy Outcomes (GUSTO) cohort, which is a mother-offspring cohort where Singapore citizens or permanent residents of Chinese, Malay and Indian ethnicity with homogenous ethnic background were approached for participation 6. Life-time caregiver-reported history of physician-diagnosed AD was derived by asking the following question at 6-, 12-, 18- and 36-month clinic visits, *“Has your child ever been diagnosed with eczema?”*, reflecting life-time prevalence*.* Thereafter, currently active AD diagnosis, reflecting point prevalence, was performed by physicians on the same day using standard Hanifin and Rajka criteria 7 which were used as the reference to evaluate diagnostic accuracy of caregiver-reported history of physician-diagnosed AD. For the main analysis, data from 18- and 36-month clinic visits were used for assessing the diagnostic accuracy of caregiver reported criteria.

Based on the physician diagnosis at clinic visit, 3.42% (31/906) and 4.70% (43/915) children were diagnosed as having active AD at ages 18-months and 36-months, respectively. Using physician-diagnosed AD at 18-months as the gold standard, caregiver-report of physician-diagnosed AD demonstrated high sensitivity (93.3%), specificity (90.4%) and negative predictive value (NPV=99.7%), but a low positive predictive value (PPV=25.2%) (Table 1). Furthermore, at the 36-month visit, caregiver-report of physician-diagnosed AD demonstrated good specificity (86.8%) and NPV (97.5%), but low sensitivity (54.7%) and PPV (16.7%) (Table 1).

An aforementioned cross-sectional study reported reasonable sensitivity/specificity/PPV/NPV (83%/89%/81%/91%) compared to physician diagnosis, with comparable point prevalence (56.0%) and life-time prevalence (58.1%) of AD 5. In this study, a low PPV (16.7% to 25.2%) of the caregiver-reported criteria was observed in our cohort (Table 1), with inflated false-positive cases at both 18-months (74.8%) and 36-months (83.2%). This may be predominantly attributed to the assessment of a different feature of AD, being past prevalence of ever having had AD *versus* having currently active eczema. Differences might be due to the waxing and waning nature of AD in addition to usage of steroids/moisturizers, which are commonly used and very effective in the treatment, and hereby controlling AD. A substantial discrepancy was noted between point prevalence at the clinic visits (3.42% and 4.70% at 18- and 36-month, respectively) and life-time prevalence (12.3% and 15.0% at 18- and 36-month, respectively) in the present study cohort. While the specificity of the caregiver-reported criteria was good at both 18-month (90.4%) and 36-month visits (86.8%) compared to physician diagnosis, its sensitivity dropped substantially from 93.3% at 18month to 54.7%, partially due to higher number of false-negative cases at 36-months compared to 18-months (2.5% vs 0.3%).

Interestingly, when only the caregiver-reported criteria, suggesting life-time prevalence of “ever having eczema” was compared across different follow-up visits, 25.9% (28/108) of children with a positive caregiver history of ever having AD diagnosis by 18-months, subsequently reported a negative history of ever being diagnosed with AD at 36-months (Table 2). Additionally, the agreement between the caregiver-reported eczema across the two assessments was poor (Cohen’s kappa = 0.62), which possibly explains the difference observed in the sensitivities between 18-months and 36-months. This discrepancy was slightly higher with a longer follow up period (28.7% and 27.9% between 12-to 36-months and 6- to 36-months, respectively), suggesting that the caregiver-report of previous physician-diagnosed AD may potentially be prone to recall bias, although this cannot be unequivocally proven. While lack of clarity and/or interpretation of the question asked can also possibly mislead the caregivers to report only active/ongoing eczema, future studies are warranted for critical evaluation of recall bias during history taking of AD in epidemiological settings, especially when using caregiver reported measures in young children. Our findings nonetheless suggest that information bias (misreporting) at 18-months is less likely than at 36-months.

A strength of the study is its longitudinal study design which may have partially prevented missed cases arising from waxing and waning of AD over time, since 58.7% (18/31) of children diagnosed with AD at 18-months did not present AD symptoms at 36-month visit. A major limitation of using physician-diagnosis at the clinic visit as the gold standard is that it may be suggestive of point prevalence at the time of clinic visit but not of the actual life-time prevalence, owing to the relapsing/remitting nature of AD, and/or the effect of its treatment. We did not have information from questions that have higher specificity for AD, such as an itchy rash affecting usual locations. Furthermore, the study was limited by the logistic constraint in assessing inter- and intra-examiner reliability among physicians for AD assessment, although Hanifin-Rajka criteria have been shown to exhibit high inter-rater agreement (ICC>0.80) among physicians/dermatologists.8 Another confounder to consider in the future study is the role of symptomatic treatment in AD, which can suppress active AD, mainly in children with mild to moderate AD.

In conclusion, the study findings indicate the significant, yet unexplored, influence of recall bias when using caregiver-report in estimating life-time AD prevalence in young children, potentially leading to underestimation of actual AD cases, which may be especially critical in populations with low disease prevalence rates.

**Acknowledgements**

We thank Dr Rahul Nair and Dr Pui Ling for their help in dental examination. We also acknowledge Dr Nisha Subash Chandran Suyien and Dr Chng Chai Kiat for providing useful comments to revise the manuscript draft.

The continuous and skillful help of the home visitors and the clinical team from the National University Hospital and the K.K Women’s and Children’s Hospital, as well as the database and biostatistics teams, is deeply appreciated.

**Funding statement**: This research is supported by the Singapore National Research Foundation under its Translational and Clinical Research (TCR) Flagship Programme and administered by the Singapore Ministry of Health’s National Medical Research Council (NMRC), Singapore (grant no. NMRC/TCR/004-NUS/2008; NMRC/TCR/012-NUHS/2014). Additional funding is provided by the Singapore Institute for Clinical Sciences, Agency for Science Technology and Research (A\*STAR), Singapore. KMG is supported by the UK Medical Research Council (MC\_UU\_12011/4), the National Institute for Health Research (NIHR Senior Investigator (NF-SI-0515-10042) and the NIHR Southampton Biomedical Research Centre) and the European Union (Erasmus+ Programme Early Nutrition eAcademy Southeast Asia-573651-EPP-1-2016-1-DE-EPPKA2-CBHE-JP). This study was also funded by Singapore’s NMRC (grant nos. NMRC/CIRG/1341/2012: R-221-000-059- 511 and NMRC/CSA/022/2010), NRF370062-HUJ-NUS and NUHS Bridging Funds 02/FY16 (R-221-000-110-733).

**Conflicts of interest:** Lynette Pei-chi Shek has consultant arrangements with Mead Johnson and Nestle; has received payment for lectures from Danone and Nestle; and has received research funding from Danone. Yap Seng Chong have received research collaborations and funding from Abbott, Danone, and Nestec. Bee Wah Lee has received honoraria for serving on an advisory board for Nestle Nutrition, has received payment for lectures from Danone Nutrition, and has received travel support from the Asia Pacific Association of Allergy Asthma and Immunology. Keith Godfrey has received reimbursement for speaking at conferences sponsored by companies selling nutritional products and is part of an academic consortium that has received research funding from Abbott Nutrition, Nestec, Benevolent AI Bio Ltd. and Danone; he has patents issued for phenotype prediction and predictive use of CpG methylation; and has a patent pending for maternal nutrition composition. The authors have no conflicts of interest relevant to this article to disclose.

**Authors’ contributions**

Tosha Ashish Kalhan conducted the data analyses, drafted, and critically reviewed for important intellectual content. Evelyn Xiu Ling Loo and Carolina Un Lam assisted in obtaining grants/resources for the study, collected data and critically reviewed the manuscript for important intellectual content. Lynette Pei-chi Shek, Michael Kramer, Hugo Van Bever, Anne Goh, Yap Seng Chong, Bee Wah Lee, Kok Hian Tan, Seang-Mei Saw and Keith M Godfrey obtained grants/resources for the study, conceptualized and designed the study and critically reviewed the manuscript for important intellectual content. Bindu Karunakaran collected data and critically reviewed the manuscript for important intellectual content. Chin-Ying Stephen Hsu obtained grants/resources, conceptualized, and designed the study, conducted the analyses, drafted and revised the manuscript and critically reviewed the manuscript for important intellectual content. All authors approved the final manuscript as submitted and agree to be accountable for all aspects of the work.

Author list with affiliations

Tosha Ashish Kalhan1, Evelyn Xiu Ling Loo2, Lynette Pei-chi Shek2,3, Michael S Kramer4,5, Carolina Un Lam6, Bindu Karunakaran1, Hugo Van Bever 3,7, Anne Goh8, Yap Seng Chong9, Bee Wah Lee3,10, Kok Hian Tan11, Seang Mei Saw12, Keith M Godfrey13,14, Chin-Ying Stephen Hsu1#

Affiliations

1Faculty of Dentistry, National University of Singapore, Singapore

2Singapore Institute of Clinical Sciences, Agency for Science, Technology and Research (A\*STAR), Singapore

3Department of Paediatrics, Yong Loo Lin School of Medicine, National University of Singapore, Singapore.

4Departments of Pediatrics and of Epidemiology and Biostatistics at McGill University Faculty of Medicine, Montreal, Quebec

5Dept. of Epidemiology, Biostatistics & Occupational Health, The Montreal Children's Hospital

6Chief Dental Officer’s Office, Ministry of Health, College of Medicine Building, Singapore

7Khoo Teck Puat-National University Children’s Medical Institute, National University Hospital, Singapore

8Allergy Service, Department of Pediatrics, KK Women’s and Children’s Hospital, Singapore

9Department of Obstetrics and Gynecology, Yong Loo Lin School of Medicine, Singapore

10Mount Elizabeth Medical Centre, Singapore

11Department of Maternal Fetal Medicine, KK Women’s and Children’s Hospital, Singapore

12Saw Swee Hock School of Public Health, National University of Singapore

13NIHR Southampton Biomedical Research Centre, University of Southampton and University Hospital Southampton NHS Foundation Trust, Southampton, UK

14Medical Research Council Lifecourse Epidemiology Unit, University of Southampton, Southampton, UK

#Correspondence:

Chin-Ying Stephen Hsu, DDS MS PhD

Faculty of Dentistry, National University of Singapore,

9 Lower Kent Ridge Rd, Singapore 119085

Email: denhsus@nus.edu.sg

Keywords: Eczema, atopic dermatitis, diagnosis, prevalence, accuracy

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