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ORIGINAL RESEARCH ARTICLE

Diagnosis and Management of Pediatric Chronic Hand Eczema: The PeDRA CACHES Survey

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Abstract

Background Chronic hand eczema (CHE) significantly impacts quality of life. Published literature on pediatric CHE (P-CHE) in North America including knowledge on epidemiology and standard evaluation and management is limited.

Objective Our objective was to assess diagnostic practices when evaluating patients with P-CHE in the US and Canada, produce data on therapeutic agent prescribing practices for the disorder, and lay the foundation for future studies.

Methods We surveyed pediatric dermatologists to collect data on clinician and patient population demographics, diagnostic methods, therapeutic agent selection, among other statistics. From June 2021 to January 2022, a survey was distributed to members of the Pediatric Dermatology Research Alliance (PeDRA).

Results Fifty PeDRA members responded stating that they would be interested in participating, and 21 surveys were completed. For patients with P-CHE, providers most often utilize the diagnoses of irritant contact dermatitis, allergic contact dermatitis, dyshidrotic hand eczema, and atopic dermatitis. Contact allergy patch testing and bacterial hand culture are the most used tests for workup. Nearly all utilize topical corticosteroids as first line therapy. Most responders report that they have treated fewer than six patients with systemic agents and prefer dupilumab as first-line systemic therapy.

Conclusions This is the first characterization of P-CHE among pediatric dermatologists in the United States and Canada. This assessment may prove useful in designing further investigations including prospective studies of P-CHE epidemiology, morphology, nomenclature, and management.

Key Points

This survey of the Pediatric Dermatology Research Alliance members shows that chronic hand eczema is commonly associated with atopic dermatitis and that diagnostic evaluations vary, most commonly including allergic contact dermatitis patch testing or bacterial cultures.

Topical corticosteroids are considered first-line therapy and systemic therapies are rarely utilized.

1 Introduction

Chronic hand eczema (CHE) is defined as hand eczema with symptoms persisting for more than 3 months or with symptoms returning twice or more within a 12-month timeframe [1]. CHE is a term that serves as a diagnosis for a disease process characterized by scaling, erythema, and fissuring,

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among other findings on the skin of the dorsal hands, palms, fingers, and wrists as described by the International Eczema Council in 2021. CHE may be due to a variety of etiologies and have a number of associations including but not limited to atopic dermatitis and contact dermatitis [2]. This disorder has a significant impact on quality of life, with biopsychosocial consequences that include increased healthcare utilization, taking sick leave, job changes, negative self-image, and poor relationships [3–5]. The financial consequences of the disorder can be significant with one review reporting the total cost per year per patient ranging from US$2549 to US$10,883 based on European and US data [5]. Published literature on pediatric chronic hand eczema (P-CHE) is limited, with no published P-CHE management guidelines despite prevalence estimates suggesting that more than 1 in 20 children were affected with this disorder [6–11]. Danish general population data shows that atopic dermatitis (AD) and common filaggrin gene mutations were associated with early onset and persistence of hand eczema [12].

In 2021, the Pediatric Dermatology Research Alliance (PeDRA) initiated the Child and Adolescent Chronic Hand Eczema Study (CACHES) survey to (i) assess diagnostic practices when evaluating patients with P-CHE in the United States and Canada; (ii) evaluate topical and systemic agent prescribing practices for the disorder; and (iii) lay the foundation for future observational and therapeutic studies.

2 Methods

The CACHES survey group developed an anonymous, multiple-choice and case-based online survey using Qualtrics™ to collect data on clinician and patient population demographics, diagnostic methods utilized, topical and systemic agent selection, as well as factors influencing the use of systemic medications for P-CHE. The survey was modeled after the TREatment of severe Atopic eczema in children Taskforce (TREAT) US & CANADA survey and rigorously edited and tested by PeDRA members before deployment [13]. The CACHES survey is detailed in the electronic supplementary material (ESM).

Between June 2021 and January 2022, the survey was distributed to members of the AD & Psoriasis Focused Study Group of PeDRA, composed of pediatric dermatologists with an interest in CHE. An anonymous survey link was distributed through email with staggered reminder emails. Respondents who practiced outside the United States or Canada were instructed to end the survey and not participate. Participants who continued with the survey were asked about the demographics of their patient population and for estimation of what percentage of their P-CHE patients also had AD. The respondents were queried on their methods of evaluation, diagnostic testing, and therapeutic choices in treating P-CHE in general, as well as the influence of treatment guidelines and perceived barriers to the use of systemic agents. The survey presented four clinical vignettes of children and adolescents with P-CHE and, for each scenario, queried diagnostic categorization, diagnostic testing that would be utilized, and selection of initial therapy and maintenance treatment. Vignettes with representative clinical histories and images were developed by the investigators and reviewed by the survey group. Default options or 'write-in' alternatives were allowed. Participants were given the opportunity to comment on their approach towards P-CHE evaluation and management.

3 Results

3.1 Provider Study Population

A total of 50 survey emails were sent to members of PeDRA's AD & Psoriasis Focused Study Group. The survey was completed by 21 members (42%). Demographic characteristics of respondents are summarized in Table 1. Of the participants, 81.0% completed fellowship training in pediatric dermatology and most (95.2%) practiced in a university teaching hospital/clinic setting. More than 95% of the providers' patients are between the ages of 0 and 20 years old. Survey respondents reported their patient population to be ethnically diverse.

3.2 Estimation of Interrelationship of Pediatric Chronic Hand Eczema (P-CHE) and Atopic Dermatitis (AD)

There was significant variability in the percentage of AD patients reported to have CHE, with 19.0% of respondents reporting < 10% frequency, 52.4% reporting 10–29% frequency, 9.5% reporting 30–49% frequency, and 19.0% reporting ≥ 50% of AD patients with CHE. Consensus was greater regarding the percentage of CHE patients with concurrent AD elsewhere on their body or a history of AD, with 76.2% affirming that 50% or more of their patients with CHE have AD (Table 2).

3.3 Diagnostic Choices

Patients with P-CHE may be given varying diagnostic assignments, reflecting differing clinical manifestations as well as variations in nomenclature use. When queried about terms utilized to describe P-CHE, all respondents reported using the term irritant contact dermatitis (ICD) for P-CHE cases when appropriate (Fig. 1). The terms allergic contact dermatitis (ACD) and dyshidrotic hand eczema were also commonly utilized (each used by

Table 1 Demographic characteristics of survey respondents

Characteristic	*n* (%)
Sex	
Female	17 (81.0)
Male	4 (19.0)
Age (years)	
25–34	3 (14.3)
35–44	9 (42.9)
45–54	6 (28.6)
55–64	1 (4.8)
65–74	2 (9.5)
Highest degree	
MD	17 (81.0)
MD, PhD	3 (14.3)
MD, MSc	1 (4.8)
Residency/Fellowship training completed	
Dermatology and Pediatric Dermatology	12 (57.1)
Pediatrics, Dermatology, and Pediatric Dermatology	4 (19.0)
Pediatrics and Dermatology	2 (9.5)
Only Dermatology	1 (4.8)
Other	2 (9.5)
Country of current employment	
USA	18 (85.7)
Canada	3 (14.3)
Practicing location	
University teaching hospital/clinic	20 (95.2)
Single specialty group practice	1 (4.8)
Years of independent experience	
0–4	7 (33.3)
5–9	2 (9.5)
10–19	7 (33.3)
20+	5 (23.8)

MD Doctor of Medicine, *MSc* Master of Science, *PhD* Doctor of Philosophy, *USA* United States of America

90.5% of respondents), while 76.2% used 'atopic hand eczema' as a label. Other diagnostic labels for P-CHE cases were used in < 25% of queried providers. Most participants report not using any diagnostic tests for patients with P-CHE; Supplementary Figure 1 highlights the frequency of certain diagnostic test utilization (see ESM). Only 19.0% and 14.3% of respondents utilize contact allergy testing and bacterial culture, respectively, over 50% of the time, with 33.3% using contact allergy patch testing over 25% of the time, and 23.8% of those surveyed using bacterial culture over 25% of the time. Other tests such as fungal culture, skin biopsy, IgE testing, and skin prick testing had, respectively, 76.2%, 95.2%, 95.2%, and 95.2% of survey participants using these tests <6% of the time.

Table 2 Estimation of interrelationship of P-CHE and AD

Characteristic	*n* (%)
Percentage of AD patients reported to have CHE	Number of providers who reported certain frequency
0–5	1 (4.8)
5–9	3 (14.3)
10–19	5 (23.8)
20–29	6 (28.6)
30–49	2 (9.5)
50–74	3 (14.3)
75–84	1 (4.8)
Percentage of CHE patients reported to have either active AD besides on hands or history of AD	Number of providers who reported certain frequency
< 25	1 (4.8)
25–50	4 (19.0)
50–75	8 (38.1)
> 75	8 (38.1)

AD atopic dermatitis, *CHE* chronic hand eczema, *P-CHE* pediatric chronic hand eczema

3.4 Severity Assessment

Regarding severity assessment, 61.9% of participants indicated that they use no scoring systems in clinical practice for pediatric patients with CHE, while 28.6% use a Physician Global Assessment, 14.3% use the Children's Dermatology Life Quality Index (C-DLQI), and 9.5% use the Patient-Oriented Eczema Measure (POEM). None of the respondents reported using the Hand Eczema Severity Index (HECSI), Patient Global Assessment, or Quality of Life in Hand Eczema Questionnaire (QOLHEQ) in clinical practice for P-CHE.

3.5 Topical Therapeutic Choices Based on Clinical Vignettes

Preferences on first-, second-, and third-line topical therapeutics are outlined in Fig. 2. All respondents ($n = 21$) chose topical corticosteroids (TCS) as their first-line topical agent of choice, with 90.5% ($n = 19$) utilizing them as monotherapy. Almost half (42.9%, $n = 9$) preferred using class 2 TCS as first line, 33.3% ($n = 7$) preferred class 3–5, and 19.0% ($n = 4$) preferred class 1. If good disease control was induced with the initial chosen therapy, 71.4% ($n = 15$) would continue the TCS at a decreased frequency of application. With regards to second-line therapeutic choices, providers preferred TCS (28.6%, $n = 6$), topical calcineurin inhibitors (TCI) (28.6%, $n = 6$), and topical phosphodiesterase-4 (PDE4) inhibitors (23.8%, $n = 5$). Two-thirds of those who chose TCI ($n = 4$) and 80.0% ($n = 4$) of those

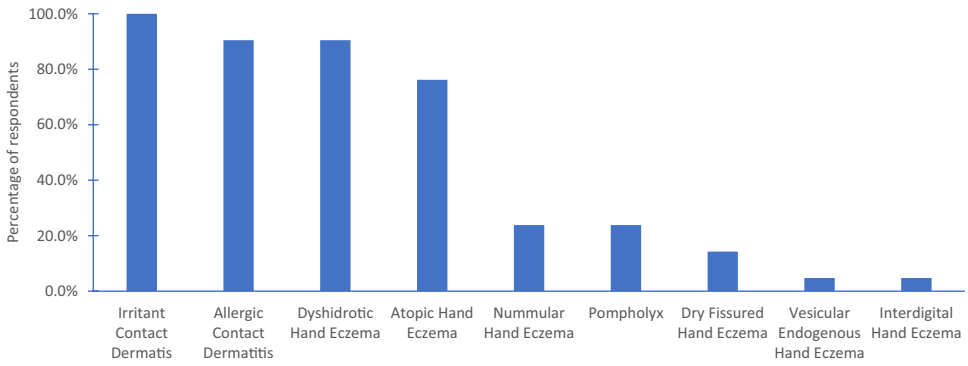

Fig. 1 Pediatric chronic hand eczema (P-CHE) diagnostic assignments ($n = 21$). Providers were asked "Children with CHE may have several diagnostic labels applied. Which of the below diagnoses do you utilize for CHE cases when appropriate?"

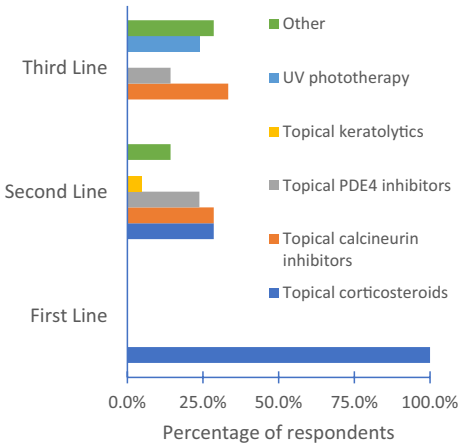

Fig. 2 First-, second-, and third-line topical treatments of choice ($n = 21$). Providers were asked "Imagine a 13 yo with CHE: Besides moisturizers, what is first line topical therapy?" Question was repeated for second-line and third-line therapy

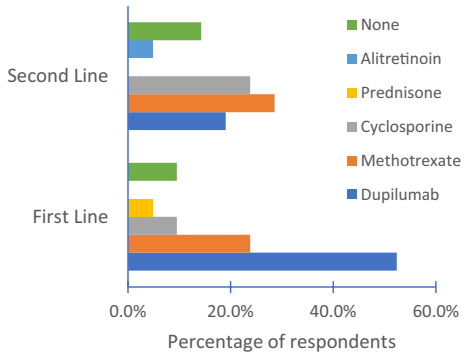

Fig. 3 First- and second-line systemic treatments of choice ($n = 21$). Providers were asked "What is your first line systemic therapy for a pediatric patient with chronic hand eczema where the primary indication is for CHE?" Question was repeated for second-line therapy

who chose topical PDE4 inhibitors as preferred second-line agents would combine these agents with TCS in their second-line management. Third-line topical agents of choice included TCI (33.3%, $n = 7$) and ultraviolet (UV) phototherapy (23.8%, $n = 5$), with 85.7% ($n = 6$) of those who chose TCI and 80.0% ($n = 4$) of those who chose UV phototherapy reporting that they would combine these agents with TCS as well.

3.6 Consideration of Systemic Medications

The majority (57.1%, $n = 12$) of participants stated that they have only treated one to five pediatric patients with systemic therapy for the primary indication of CHE. Lack of perceived clinical need (66.7%, $n = 14$), patient/family views (66.7%, $n = 14$), side-effect profiles (52.4%, $n = 11$), and need for blood monitoring (52.4%, $n = 11$) were major factors that discouraged the use of systemic agents (Supplementary Table 1, see ESM). The most favored first-line systemic therapy for P-CHE was dupilumab (52.4%, $n = 11$) followed by methotrexate (23.8%, $n = 5$) (Fig. 3). Second-line agents of choice were methotrexate (28.6%, $n = 6$), cyclosporine (23.8%, $n = 5$), and dupilumab (19.0%, $n = 4$). Most (76.2%) denied following any guidelines or protocols to direct their use of systemic therapy.

3.7 Patient Vignettes

Vignette 1 presented a 16-year-old male with thick hyperkeratotic plaques of the bilateral palms and fingers. Most respondents (71.4%) chose to pursue contact allergy patch testing and almost half (47.6%) opted to obtain bacterial culture and/or fungal culture or potassium hydroxide (KOH) preparation of the affected areas of the hands for diagnostic testing. Diagnostic labelling showed great variation; atopic hand eczema (19.0%), hyperkeratotic endogenous hand eczema (19.0%), ACD (14.3%), and nummular hand eczema (14.3%) were the most recorded diagnoses. Hyperkeratotic hand eczema is defined as hand eczema characterized by hyperkeratosis of the palmar hands while endogenous hand eczema is defined as hand eczema arising secondary to auto-antigens or an exaggerated response to external factors, likely due to a defective cutaneous barrier [14].

Vignette 2 presented a 5-year-old female with vesicles of the bilateral palms and fingers. Most participants (76.2%) chose to not obtain any diagnostic testing. All respondents characterized the disease presentation as either dyshidrotic hand eczema (90.5%) or pompholyx (9.5%).

Vignette 3 presented a 9-year-old female with erythematous papules and plaques of the hands and fingers in the setting of wet-work exposure. Respondents were largely split on obtaining contact allergy patch testing (52.4%) versus no diagnostic testing (42.9%). Most respondents (61.9%) described the presentation as ICD while 28.6% described it as ACD.

Vignette 4 presented a 13-year-old male with lichenified erythematous scaly plaques of the hands and wrists in the setting of a history of AD. The most popular forms of diagnostic testing respondents chose included contact allergy patch testing (47.6%) and bacterial culture of the affected areas of the hands (28.6%) while 42.9% opted not to obtain any diagnostic testing. Most (76.2%) considered this disease process as atopic hand eczema.

For all four vignettes, nearly all responders chose TCS as first-line therapy, with nearly all selecting TCS as monotherapy. If a provider induced good disease control with their chosen therapy, over 70% would continue this treatment regimen at a decreased frequency.

4 Discussion

Our investigation reveals that pediatric dermatologists report a strong association of CHE with AD in line with epidemiological evidence [12]. These providers utilize the diagnostic labels ICD, ACD, dyshidrotic hand eczema, and AD for P-CHE, and, when prompted, associate such diagnoses with clinical vignettes of P-CHE. While such outcomes parallel data from prior publications which found the most common diagnoses among patients with P-CHE to include AD, ACD, and ICD [15–17], our study showed tremendous variability in diagnostic assignments, reflecting problems with nomenclature. In vignette 1, even though all providers were presented with the same clinical vignette with an associated image, four different diagnoses were almost evenly chosen, demonstrating the need for greater consensus on nomenclature and diagnosis. Although those surveyed agree that P-CHE is associated with AD, in vignette 4, almost 25% of providers did not choose atopic hand eczema as the underlying etiology, demonstrating that it is not well defined when hand dermatitis should be associated with AD versus other diagnoses. Furthermore, there was inconsistency in providers' perception on the percentage of AD patients with CHE. In the recent European guidelines, classification of CHE did not include dyshidrotic eczema, emphasizing that harmonization is needed at a global level [18]. Moreover, use of the term dyshidrotic eczema has been argued against for more than a decade, similar to pompholyx, yet the label is still used by many clinicians [19]. In addition, the different terms that are associated with CHE have different uses. Hyperkeratotic hand eczema and pompholyx serve more as clinical descriptors while ICD, ACD, and AD point to underlying etiologies. In AD, harmonization efforts have led to more articles being published using the term AD rather than atopic eczema or eczema, in turn showing that it may be possible to standardize terminology [20].

Diagnostic testing is used on a limited basis, with providers considering ACD patch testing, though with great variation by clinical scenario. Toledo et al. found the clinical relevance of patch testing in P-CHE to be 78% and four investigations reported that > 14.5% of children referred for patch testing had hand eczema [16, 17, 21, 22]. This can be compared with guidelines based on adult population data which are mixed on their expert recommendations for patch testing in patients with CHE, as the International Eczema Council (IEC) failed to come to an agreement on the use of patch testing for CHE while the European Society of Contact Dermatitis (ESCD) recommended patch testing of all CHE patients [2, 14]. Interestingly, in this survey, culture of the affected areas of the hands was also commonly considered for P-CHE, which reflects P-CHE's association with AD and *Staphylococcus aureus* colonization and infection [9, 11, 23–25]. However, it may also represent consideration of bacterial infection as part of their differential diagnosis for P-CHE [26].

Despite the absence of guidelines for the management of P-CHE, providers generally agreed with the use of TCS as first-line monotherapy for the disorder, both in general and for each of the vignettes, with most opting to continue such therapy at decreased frequency if disease control was achieved. When faced with second- and third-line topical choices, there was greater variability in preferences, including TCI, topical PDE4 inhibitors, and UV phototherapy, yet most still opted to combine other topicals with TCS. Systemic therapy is rarely used by the survey participants, due mostly to a lack of perceived clinical need and patient/family views of such therapies, instead of a lack of guidelines or age of the patient. If systemic therapy was considered, dupilumab, a systemic medication reserved for the management of moderate-to-severe atopic dermatitis poorly controlled with topical agents alone in the United States and Canada, was noted as first line [27, 28]. This may relate to the sense of high rates of overlap of P-CHE with AD. The preference for dupilumab by both American and Canadian providers as a first-line systemic treatment may reflect changes in use patterns over time, but contrasts with the adult CHE guidelines of the Guideline Development Group of the ESCD published in 2022 which recommend the use of alitretinoin or cyclosporine

for systemic therapy, but not dupilumab [18]. Alitretinoin and cyclosporine may be less attractive to the pediatric dermatologists surveyed given the adverse event profiles in children. These include premature epiphyseal closure with alitretinoin as seen in reports of children using systemic retinoids long-term including isotretinoin and etretinate [29, 30]; and nephrotoxicity and hypertension with cyclosporine use. Additionally, alitretinoin is not available in the United States and its efficacy is most pronounced in hyperkeratotic CHE [18]. It should be noted that the topical PDE4 inhibitor, crisaborole, is available in the United States and Canada as a non-steroidal agent for the management of atopic dermatitis and guidelines recommend its use in adult AD management [31].

Limitations of our investigation include a small sample size of 21 providers as well as the response rate to the survey of 42%, which may constrain the generalizability of the data. Additionally, we did not include vignettes with children of younger ages including toddlers, nor did we ask about factors discouraging use of other diagnostic tools or treatments besides systemics due to the length of the survey. Furthermore, it should be noted that although moisturizer use, avoidance of water work, use of protective gloves, as well as other preventative factors are recommended for patients with hand eczema, we did not include queries on such in our investigation [18]. Recall bias is inherent in a survey study of this type, and providers may have had difficulty estimating the prevalence of P-CHE, its relationship to AD or other inflammatory cutaneous conditions, or history of response previously to certain therapies without contemporaneous observation and assessment. Similarly, assessing diagnostic choices and treatment selection for case scenarios may not reflect historic practice. Additionally, topical ruxolitinib was not included as a choice for possible topical therapeutics as such medication was not FDA approved by survey deployment. Systemic JAK inhibitors, however, were included as options for systemic agents in our survey.

To our knowledge, this is the first published investigation that attempts to assess the epidemiology, diagnosis, and management of P-CHE among pediatric dermatologists in the United States and Canada. Currently, there is no published consensus data on clinical characteristics, biopsychosocial consequences, testing methods, or treatment guidelines for the pediatric population. Many questions remain regarding P-CHE's domains: What percentage of affected patients have active AD or a history of AD? What percentage of those with P-CHE have other inflammatory skin conditions, or relevant ACD? What are the course and phenotypic findings of hand dermatitis in pediatric patients? How will newer systemic and topical medications being utilized and developed for AD and other inflammatory conditions be used to address this disorder? What are the specific biopsychosocial consequences of this disorder in the pediatric population? This study displays the need for more precise data which might be gained from a cross-sectional study or prospective registry, which may be utilized to increase our understanding of P-CHE and assist in further research and guideline development. Furthermore, such data can only be collected if nomenclature regarding the underlying diagnoses of CHE and P-CHE are harmonized.

5 Conclusion

Despite the limited data on P-CHE, providers from the United States and Canada maintain some agreement on the disorder, with most associating P-CHE with AD, preferring TCS as first-line therapy, and considering dupilumab as its first-line systemic treatment. However, many questions remain regarding P-CHE's associations, course, and future management, as well as nomenclature used to determine its etiology. This investigation demonstrates the need and serves as a foundation for future large-scale investigations with the ultimate objective of developing much-needed guidelines into this debilitating pediatric eczematous condition.

Supplementary Information The online version contains supplementary material available at https://doi.org/10.1007/s40272-023-00574-x.

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Declarations

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Ethics approval Reviewed and approved by University of California, San Diego Investigational Review Board; approval #210154. The study was performed in accordance with the ethical standards as laid down in the 1964 Declaration of Helsinki and its later amendments or comparable ethical standards.

Consent to participate Informed consent was obtained from all individual participants included in the study.

Consent to publish Informed consent was obtained to publish anonymous survey data. For the photo associated with vignette 1 in the supplementary materials: Image used with permission from VisualDx. For the photo associated with vignette 2 in the supplementary materials: Image by Raimo Suhonen, MD courtesy of DermNetNZ (https://dermnetnz.org/). Image used with permission from Raimo Suhonen, MD and DermNetNZ. For the photo associated with vignette 3 in the supplementary materials: Human hand with dermatitis.jpg by James Heilman, MD courtesy of Wikimedia Commons licensed under CC BY-SA 3.0. Go to https://creativecommons.org/licenses/by-sa/3.0/ to read the full license text. For the photo associated with vignette 4 in the supplementary materials: Image by BSIP SA courtesy of Alamy Inc. is licensed under the Alamy License Agreement purchased for use in magazines and books in perpetuity worldwide. Go to https://www.alamy.com/terms/us.aspx to read the full license text.

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

Code availability Not applicable.

Author contributions All authors contributed to the study conception and design. Material preparation, data collection and analysis were performed by MAH. The first draft of the manuscript was written by MAH and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

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