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Cholinergic Urticaria or Xerosis-Induced Pruritus? A Cross-Sectional Reassessment of Patients Labeled with Cholinergic Urticaria in Iraq

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Abstract
Background. *Cholinergic urticaria (CholU) is a chronic inducible urticaria defined by transient pinpoint wheals that arise within minutes of sweating or a rise in core body temperature. In routine practice the diagnosis is often recorded from a history of heat- or sweat-related itching alone, without the characteristic wheals having been observed.*
Objective. *To estimate how frequently a prior label of CholU was unsupported by objective wheals in an Iraqi specialist cohort, and to characterise xerosis-induced pruritus as a leading alternative explanation.*
Methods. *Cross-sectional reassessment of 60 patients aged 16–50 years previously diagnosed with CholU and with normal baseline laboratory investigations. Reassessment covered lesion morphology, triggers, seasonality, xerosis, and treatment response over one month of standardised skin care. Proportions are reported with Wilson 95% confidence intervals (CIs); the association between xerosis and antihistamine non-response was tested with the chi-square test and expressed as an odds ratio (OR).*
Results. *Only 5/60 patients (8.3%; 95% CI 3.6–18.1) reported the typical transient wheals, and 6/60 (10.0%; 95% CI 4.7–20.1) responded meaningfully to antihistamines. Visible xerosis was present in 44/60 (73.3%; 95% CI 61.0–82.9), winter/cold-season predominance in 48/60 (80.0%), and improvement with emollients in 50/60 (83.3%; 95% CI 72.0–90.7). Within the 54 antihistamine non-responders these proportions were 81.5%, 88.9%, and 92.6%, respectively. Xerosis was strongly associated with antihistamine non-response ($\chi^2 = 32.4$; OR = 12.5; 95% CI 4.2–37.1; $p < 0.001$).*
Conclusions. *In this single-centre cohort, the majority of patients labelled as having CholU lacked objective wheals and instead showed features of xerosis-induced pruritus that improved with emollients. The pattern is consistent with diagnostic anchoring — a history-driven label applied without confirmatory examination. Findings are hypothesis-generating and require confirmation in controlled studies that incorporate standardised provocation testing.*
Keywords: *cholinergic urticaria; xerosis; pruritus; epidermal barrier; alloknesis; diagnostic error; chronic inducible urticaria.*

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I. Introduction

Cholinergic urticaria (CholU) is a well-recognised subtype of chronic inducible urticaria (CIndU). It is characterised by numerous small, transient, intensely pruritic wheals, typically 1–3 mm in diameter and surrounded by a flare of erythema, that appear within minutes of an increase in core body temperature provoked by exercise, passive warming, hot environments, or emotional stress, and that usually resolve spontaneously within one to two hours [1,2]. Among the inducible urticarias, CholU and symptomatic dermographism are the forms most frequently encountered in clinical practice [3].

The diagnosis of CholU is primarily clinical. International guidance emphasises that it should rest on the demonstration of the characteristic wheals — ideally reproduced by a standardised provocation test such as graded exercise or passive warming (for example a hot-bath challenge) — rather than on a compatible history alone [1,2]. In many settings, however, and particularly where provocation testing is not routinely available, the label is assigned on the basis of a patient's account of itching with heat or sweating, without the wheals ever having been observed by a clinician.

This matters because several common dermatoses share the same triggers without sharing the same lesion. Xerosis — a highly prevalent state of impaired epidermal barrier function with reduced filaggrin and ceramide content and increased transepidermal water loss — produces microfissuring of the stratum corneum and

increased exposure of cutaneous sensory nerve endings [5,6]. In barrier-compromised or atopic skin, normally innocuous thermal and mechanical stimuli can activate sensitised itch and pain fibres, producing pricking, stinging, burning, and itching, and rendering ordinarily non-pruritic stimuli capable of provoking itch (alloknesis) [7,8]. When body temperature rises, the skin releases mediators including acetylcholine, histamine, neuropeptides, and cytokines; in normal skin these are barely perceived, but in sensitised skin they may generate symptoms that closely mimic CholU despite the complete absence of wheals [7,9].

The clinical consequence is a genuine differential-diagnostic overlap. In contrast to CholU, xerosis-induced pruritus and the related atopic/xerotic dermatoses typically lack transient wheals, show seasonal (cold, dry weather) exacerbation, respond poorly to antihistamines, and improve with emollient therapy [5,8]. A useful clinical distinction is therefore that CholU is fundamentally a disorder of heat-induced wheal formation, whereas xerotic and atopic skin are disorders of heat-aggravated itch and sensory hypersensitivity.

Two further considerations are relevant to the Iraqi context. First, environmental factors — a dry climate, frequent hot bathing, mechanical irritation, and occlusive clothing — favour xerosis and may inflate the apparent local frequency of "heat-related itch." Second, when a diagnosis is anchored to an initial history, repeated structured questioning may progressively shape a patient's symptom narrative toward the expected pattern, reinforcing a label that was never confirmed by examination. Such mechanisms are well described in the literature on diagnostic error, where anchoring, confirmation bias, and diagnostic momentum perpetuate an early impression [10].

Against this background, the present study reassessed a cohort of patients already carrying a diagnosis of CholU. Its aims were (i) to estimate how often that label was unsupported by objective wheals, (ii) to characterise xerosis-induced pruritus as a leading alternative explanation, and (iii) to examine whether the pattern of findings is consistent with history-driven diagnostic anchoring.

II. Methods

2.1 Study design and setting

This was a single-centre, cross-sectional reassessment conducted during 2025 at the Al-Zahraa Specialized Center for Allergy and Respiratory Diseases, Baghdad, Iraq. Consecutive patients attending with a pre-existing diagnosis of cholinergic urticaria were invited to undergo structured re-evaluation.

2.2 Participants

Sixty patients aged 16–50 years were included. Inclusion required a prior diagnosis of CholU and normal baseline laboratory investigations. Patients with identifiable systemic causes of pruritus or an established alternative dermatological diagnosis were excluded.

2.3 Clinical assessment

Each patient underwent a standardised assessment comprising: (i) lesion morphology, with specific enquiry into, and examination for, transient micropapular wheals, supplemented where possible by patient-supplied photographs of symptomatic episodes; (ii) provoking factors; (iii) seasonality; (iv) signs of xerosis and atopic/xerotic dermatitis (dryness, scaling, flexural eczema, lichenification, excoriations); and (v) prior and subsequent treatment response. All patients were instructed in standardised skin-care measures, including regular emollient use and avoidance of irritants, and were reviewed after one month.

2.4 Statistical analysis

Categorical variables are summarised as counts and percentages. To convey precision, proportions are reported with 95% confidence intervals calculated by the Wilson score method; these intervals were derived from the observed counts and do not represent additional data. The association between visible xerosis and failure to respond to antihistamines was examined using the Pearson chi-square test and expressed as an odds ratio with a 95% confidence interval; a two-sided p-value < 0.05 was considered statistically significant. Analyses were exploratory and no adjustment for multiple comparisons was applied.

Ethical considerations. The study should be conducted in accordance with the Declaration of Helsinki. The institutional review board approval reference and the participant informed-consent statement are required for submission and should be inserted here by the author.

III. Results

3.1 Cohort and lesion morphology

Sixty patients (aged 16–50 years) were reassessed. Typical transient micropapular wheals — the defining lesion of CholU — were identified in only 5 patients (8.3%; 95% CI 3.6–18.1). The remaining 55 patients (91.7%) reported heat- or sweat-related itching, pricking, or stinging without any wheal having been observed on history,

photographs, or examination. A meaningful response to antihistamines was recorded in just 6 patients (10.0%; 95% CI 4.7–20.1). The flow of reassessment and reclassification is summarised in Figure 1.

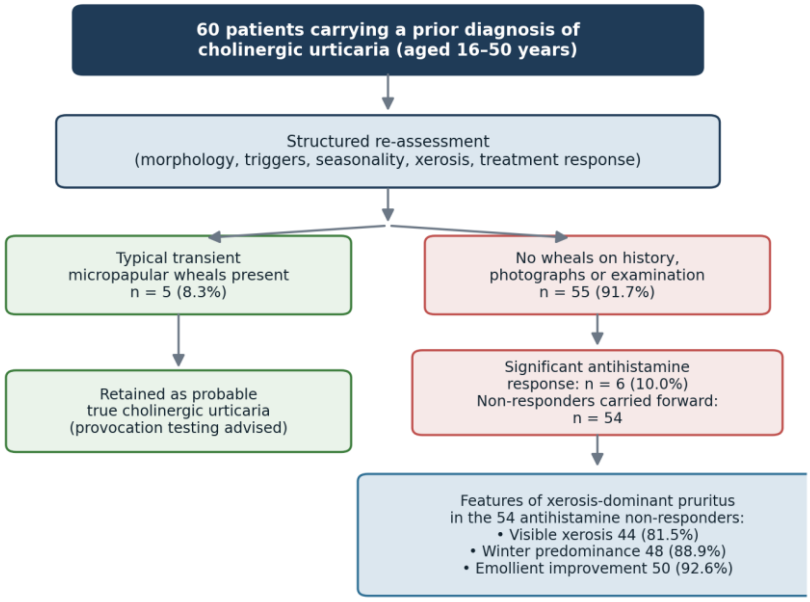
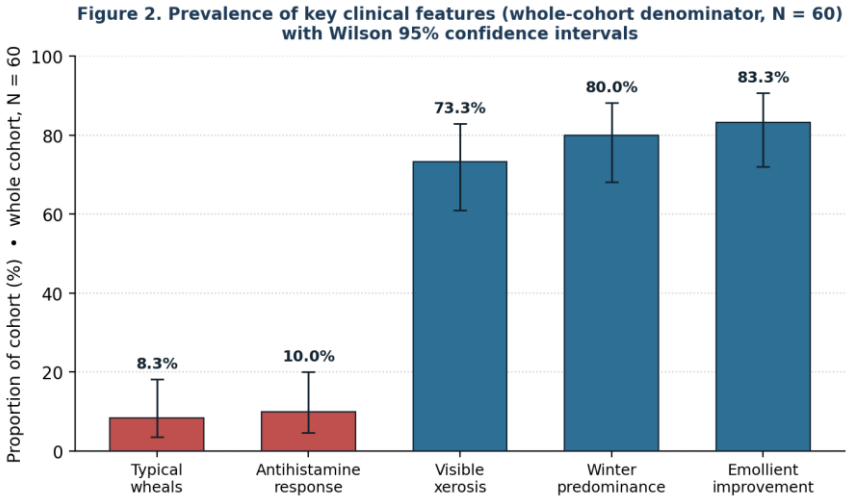


Figure 1. Flow of patient re-classification. Percentages for the lower box are expressed relative to the 54 antihistamine non-responders; whole-cohort values are given in Table 2.

3.2 Features of xerosis-induced pruritus

Features pointing to xerosis-induced pruritus predominated. Across the whole cohort, visible xerosis was present in 44/60 patients (73.3%; 95% CI 61.0–82.9), a winter/cold-season predominance was reported by 48/60 (80.0%; 95% CI 68.2–88.2), and improvement with emollient therapy occurred in 50/60 (83.3%; 95% CI 72.0–90.7). Because antihistamine non-responders are the group of principal interest, the same features are also expressed within that subgroup of 54 patients, where they reached 81.5%, 88.9%, and 92.6%, respectively (Table 2). The dual denominators are presented explicitly to avoid ambiguity; both describe the same underlying observations. Whole-cohort proportions with their confidence intervals are shown in Figure 2.



3.3 Association between xerosis and antihistamine non-response

Visible xerosis was strongly associated with failure to respond to antihistamines ($\chi^2 = 32.4$; odds ratio 12.5; 95% CI 4.2–37.1; $p < 0.001$). This association is reported as originally analysed; the underlying 2×2 contingency table should accompany the manuscript so that readers can verify the cell counts and the derivation of the odds ratio (see the editorial report).

Tables

Table 1. Cohort and study characteristics.

Characteristic	Value
Patients reassessed, n	60
Age range, years	16–50
Setting	Single specialist centre, Baghdad, Iraq
Study design	Cross-sectional reassessment, 2025
Baseline laboratory investigations	Normal (inclusion criterion)
Follow-up duration	1 month

All values as supplied; baseline laboratory normality was an inclusion criterion.

Table 2. Frequency of key clinical features, with Wilson 95% confidence intervals, expressed against both the whole cohort (N = 60) and the antihistamine non-responder subgroup (n = 54).

Clinical feature	n / N	%	95% CI
Typical transient wheals	5 / 60	8.3	3.6–18.1
Response to antihistamines	6 / 60	10.0	4.7–20.1
Visible xerosis (whole cohort)	44 / 60	73.3	61.0–82.9
Winter predominance (whole cohort)	48 / 60	80.0	68.2–88.2
Emollient improvement (whole cohort)	50 / 60	83.3	72.0–90.7
Visible xerosis (non-responders)	44 / 54	81.5	69.2–89.6
Winter predominance (non-responders)	48 / 54	88.9	77.8–94.8
Emollient improvement (non-responders)	50 / 54	92.6	82.4–97.1

Confidence intervals are derived from the reported counts and add no new data. The two denominators describe the same observations and are shown to remove ambiguity present in the original abstract.

Table 3. Clinical features distinguishing cholinergic urticaria from xerotic/atopic pruritus (synthesised from the supporting teaching material).

Feature	Cholinergic urticaria	Xerotic / atopic pruritus
Primary lesion	Transient pinpoint wheals (1–3 mm) with surrounding erythema	No wheals; dry skin, scaling, eczema, lichenification, excoriations
Onset after heat/exercise	Within minutes	Itch worsens with heat; no transient wheal
Lesion duration	Individual lesions resolve in 1–2 hours	Skin changes persist for days to weeks
Antihistamine response	Usually significant	Poor or only partial
Emollient response	Not the mainstay	Marked improvement
Seasonality	Often perennial; heat-related	Cold, dry season predominance
Provocation testing	Exercise / passive warming reproduces wheals	Provocation mainly increases itch; no wheals

The distinction is not absolute: the conditions can coexist, and cholinergic urticaria is reported more frequently in atopic individuals than in the general population.

IV. Discussion

In this single-centre cohort, only a small minority of patients carrying a diagnosis of CholU had the lesion that defines the condition. Transient micropapular wheals were documented in 8.3% of patients, and a meaningful antihistamine response — expected in genuine, histamine-driven CholU — occurred in only 10%. Conversely, features of xerosis-induced pruritus were common: visible xerosis in roughly three-quarters of the cohort, a cold-season predominance in four-fifths, and emollient-responsive symptoms in the large majority. Taken together, these observations suggest that a substantial proportion of the CholU label in this setting reflected xerosis-induced pruritus rather than true inducible urticaria.

The pattern is internally coherent. The poor antihistamine response argues against a predominantly histaminergic, mast-cell–driven mechanism, while the strong emollient response points to epidermal barrier dysfunction as the central problem [5,6]. A defective barrier increases transepidermal water loss and exposes and sensitises cutaneous nerve endings; sensitised fibres then translate the thermal and mediator changes that

accompany sweating — including acetylcholine and neuropeptide release — into pricking, stinging, and itch, and lower the threshold at which ordinarily innocuous stimuli evoke itch (alloknesis) [7,8,9]. This neurobiology explains how a patient with no wheals can nonetheless describe symptoms that map convincingly onto the textbook trigger profile of CholU.

Environmental factors plausibly amplify the effect locally. A dry climate, frequent hot bathing, mechanical irritation, and occlusive clothing all promote xerosis and heat-related itch, and may help explain why local clinical impressions can diverge from international epidemiological expectations. The practical implication is the clinical rule that emerges from the supporting material: cholinergic urticaria is a disease of reproducible heat-induced wheals, whereas xerotic and atopic skin are diseases of reproducible heat-induced itch. Where wheals cannot be demonstrated — by direct observation, patient photographs, or provocation testing — and dry skin or an atopic background is present, xerosis-induced pruritus deserves primary consideration [1,2].

A second theme concerns how the original label may have been formed and sustained. When a diagnosis is anchored to an initial history of "itching when I sweat," subsequent structured questioning can progressively shape the patient's account toward the anticipated pattern, while confirmatory examination is omitted. This is not a novel cognitive mechanism but a recognised family of diagnostic errors — anchoring, confirmation bias, and diagnostic momentum — in which an early impression is reinforced rather than tested [10]. Framing the present findings in these established terms is more defensible than proposing a wholly new entity; the data here are consistent with such anchoring but cannot, by design, demonstrate it. The remedy is the same remedy advocated for diagnostic error generally: deliberately seek disconfirming evidence — in this case, objective wheals — before the label is retained.

These results align with the broader understanding of CIndU and pruritus. Contemporary classifications stress objective confirmation and provocation testing for inducible urticarias [1,3], and the itch literature establishes barrier dysfunction and peripheral/central sensitisation as sufficient to generate heat- and touch-evoked itch without urticaria [7,8]. The contribution of the present study is to quantify, in a real-world specialist cohort, how often the CholU label may rest on history alone, and to direct attention to a common, treatable alternative.

4.1 Limitations

Several limitations temper interpretation. The design is cross-sectional and single-centre, without a comparison group, so the findings describe this cohort rather than a general population and the odds ratio cannot establish causation. Crucially, standardised provocation testing (graded exercise or passive warming) was not performed; because such testing is the reference standard for confirming CholU, its absence means that true CholU cannot be formally excluded and that reclassification rests on clinical features and treatment response. The one-month emollient follow-up is short, and an open, unblinded response to emollients is vulnerable to placebo effects, regression to the mean, and confounding by seasonal change. Reliance on patient-reported wheals and recalled seasonality introduces recall and reporting bias, and the proposed contribution of diagnostic anchoring was inferred rather than measured. Xerosis severity was assessed clinically without a validated scale. Finally, the association between xerosis and antihistamine non-response is partly bound up with the classification under examination, so it should be read as descriptive rather than confirmatory, and the underlying contingency table should be made available.

V. Conclusions

In this specialist Iraqi cohort, most patients labelled with cholinergic urticaria lacked the defining transient wheals and instead displayed emollient-responsive features of xerosis-induced pruritus. The findings indicate that xerosis is a major and treatable contributor to symptoms commonly misclassified as CholU, and that the misclassification is plausibly sustained by well-described diagnostic anchoring. Greater reliance on objective findings — demonstration of wheals through examination, photographs, or provocation testing — should improve diagnostic accuracy. Because the study is cross-sectional, uncontrolled, and conducted without formal provocation testing, these conclusions are hypothesis-generating and warrant confirmation in controlled studies that incorporate standardised provocation and longer follow-up.

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