

Research Article

What Drives Diagnostic Testing in Pediatric Acute Urticaria? A Real-World Cohort Study

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Abstract

Objectives: Pediatric acute urticaria (AU) is a common reason for visits to emergency and outpatient clinics. Although international guidelines recommend against routine diagnostic testing for AU, such tests remain frequently performed in clinical practice. We aimed to evaluate diagnostic test use in pediatric AU, identify factors associated with test ordering, and assess the impact of testing on clinical management.

Methods: This retrospective observational cohort study included children aged 0-18 who presented to the pediatric emergency department or outpatient clinics at a tertiary care hospital with AU (with or without angioedema) over a 2-year period. Demographic and clinical data, including diagnostic test details, management strategies and referral patterns, were extracted from electronic medical records. The primary outcome was whether diagnostic testing was performed during the clinical course. The secondary outcome was whether diagnostic tests influenced clinical management. To identify independent predictors of diagnostic test use, we used multivariable logistic regression.

Results: Of the 300 children included (median age 6.1 years), 214 (71.3%) underwent diagnostic testing. Testing was more common among patients who did not receive pharmacological treatment at first contact than among those who did (85.5% vs 67.2%, $p=0.006$). In multivariable analysis, referral before starting treatment was the strongest predictor of diagnostic testing (adjusted odds ratio [aOR], 3.21; 95% CI, 1.98-5.22). Conversely, initiating treatment at first contact (aOR 0.48; 95% CI 0.29-0.79) and being managed by pediatric allergy-immunology specialists (aOR 0.39; 95% CI 0.21-0.71) were associated with lower testing rates. Despite the common use of testing, it led to a documented change in clinical management in only 7 cases (2.3%). Confirmed IgE-mediated food allergy was identified in five children (1.7%), all of whom had a clear history of immediate reactions triggered by suspected food allergens.

Conclusion: In pediatric AU, diagnostic testing is frequently performed, but it rarely alters patient management. The way tests are ordered appears to be influenced more by care pathways and treatment timing than by specific clinical signs. Starting treatment early based on symptoms and making targeted referrals might help reduce unnecessary tests in routine pediatric care.

Keywords: Acute urticaria, care pathways, diagnostic testing

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Acute urticaria (AU), which presents as the sudden appearance of wheals with or without angioedema, is one of the most common allergic presentations in children. It often prompts families to seek care in emergency departments or outpatient clinics.^[1,2] Most episodes resolve spontaneously and are triggered by infections. However, because the symptoms appear suddenly and are highly noticeable, they often cause concern for both parents and healthcare providers, particularly regarding the possibility of food or drug allergies.^[1,3,4] Studies and guidelines consistently show that broad, non-targeted diagnostic testing in children with AU rarely yields useful information or alters management. False-positive results from such tests can lead to unnecessary dietary restrictions, increased anxiety for families, and more healthcare visits.^[3,5-8] Despite this, testing remains common in practice, with limited clinical benefit.^[9] In busy emergency and outpatient settings, unnecessary testing can add costs, delay treatment, and divert resources without improving patient outcomes.^[10] A key unresolved issue is why diagnostic testing in AU remains so widespread despite evidence that it offers no significant clinical advantage.^[4,8] While caregivers' expectations and the desire for reassurance are acknowledged to play a role, physicians' decision-making may also be affected by aspects of the healthcare system and care pathways, though these influences are not well characterized in existing research.^[11] Therefore, we conducted a real-world cohort study to evaluate diagnostic testing practices among children with AU. Our objective was to move beyond reporting diagnostic yield and to identify modifiable care-pathway factors that influence diagnostic testing in real-world pediatric practice, with the aim of informing strategies to reduce low-value testing while maintaining safe and effective care.

Methods

Study Design and Population

We conducted a retrospective, real-world cohort study of children presenting with AU, either alone or with angioedema, to the pediatric emergency department or to the outpatient clinics of family medicine, general pediatrics, and pediatric allergy-immunology at a single tertiary care hospital. Between December 2023 and December 2025, 347 children with AU and/or angioedema were identified through a hospital-wide electronic medical record (EMR) search using ICD-10 diagnostic codes. Children aged 0-18 years with AU, defined as wheals with or without angioedema lasting less than 6 weeks, were eligible for inclusion. Patients with isolated angioedema were also included if available clinical documentation supported a histamin-

ergic phenotype (a reported response to antihistamine therapy and the absence of features suggestive of bradykinin-mediated disease, such as lack of response to antihistamines). Patients were excluded if they had chronic urticaria, anaphylaxis at presentation, hereditary angioedema, primary immunodeficiency, autoimmune disease, or systemic inflammatory or infectious conditions requiring extended evaluation, as well as those with insufficient documentation to permit reliable assessment of diagnosis, treatment timing, or outcomes. All records were manually reviewed to reduce diagnostic errors and prevent information bias. After applying these criteria, 300 children were included in the final analysis (Fig. 1).

Data Collection

Demographic, clinical, treatment, diagnostic testing, and outcome data were extracted from the electronic medical record using a predefined, standardized abstraction form and data dictionary. Collected variables included age, sex, clinical phenotype, suspected trigger as recorded by the treating physician, history of atopic disease, previous episodes of urticaria or angioedema, care pathway and referral patterns, treatment characteristics, diagnostic testing, and clinical outcomes. Care-pathway variables comprised the point of first medical contact, physician specialty, referral patterns during the episode, and referral timing relative to initiation of oral H1-antihistamine therapy. Treatment variables included whether an oral H1-antihistamine, the guideline-recommended first-line therapy for AU^[5], was prescribed at first medical contact or at discharge, as well as treatment setting, medication class, route of administration, and the specialty of the physician initiating therapy.

Diagnostic testing was categorized as either laboratory testing or allergy-focused testing. Laboratory testing could be performed at any level of care and included non-allergy-related investigations ordered specifically to evaluate AU and/or angioedema during the index episode. Allergy-focused testing, including skin prick testing (SPT) and/or serum-specific IgE (sIgE) measurement, was performed exclusively by pediatric allergy-immunology specialists after referral, either during the acute episode or within a 6-week follow-up period, consistent with the conventional definition of AU. The timing of test ordering relative to referral and treatment initiation was also recorded.

Study Outcomes

The primary outcome was whether diagnostic testing was performed during the clinical course. The secondary outcome was whether diagnostic testing influenced clinical management, defined as a documented change in management based on test results. Clinically relevant man-

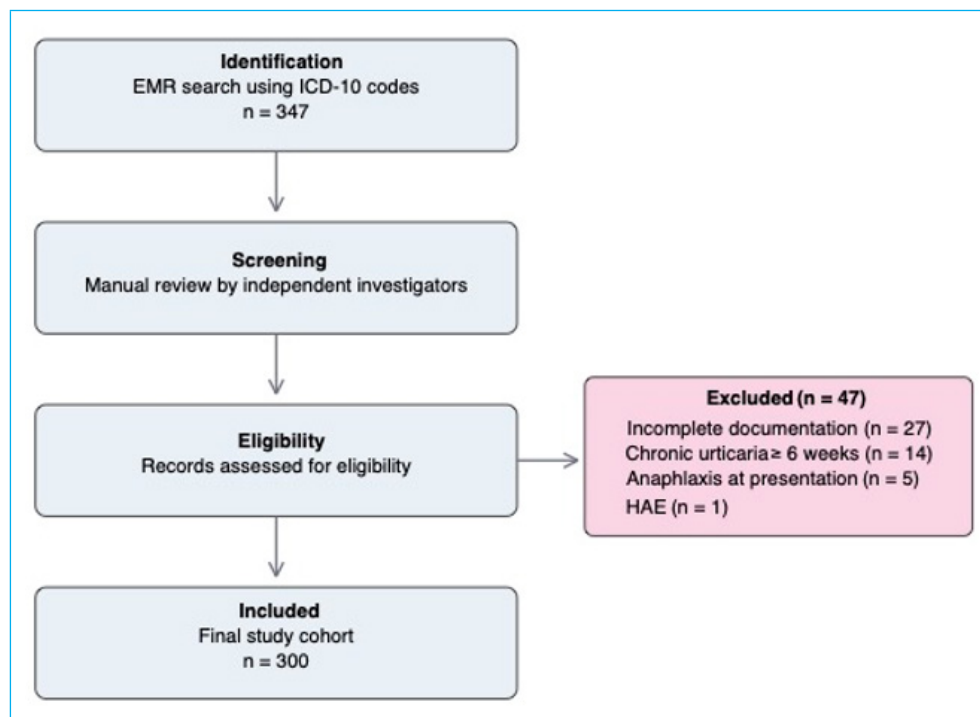


Figure 1. Flow diagram of patient selection.

Flow diagram illustrating identification of eligible patients through ICD-10-based electronic medical record screening, independent manual review, application of exclusion criteria, and inclusion in the final study cohort of children with acute urticaria and/or angioedema, including key exclusion reasons

agement changes included initiation, discontinuation, or modification of treatment; establishment of a specific diagnosis requiring disease-specific management (e.g., confirmed IgE-mediated food allergy or probable drug hypersensitivity); implementation of allergen or drug avoidance measures; or other documented changes in follow-up or management decisions based on the test results.

Statistical Analysis

The distribution of continuous variables was assessed using the Shapiro–Wilk test. Normally distributed continuous variables are presented as means with standard deviations (SD), whereas non-normally distributed continuous variables are reported as medians with interquartile ranges (IQR). Categorical variables are presented as counts and percentages. Group comparisons were conducted using chi-square or Fisher’s exact tests, as appropriate.

Multivariable logistic regression was used to identify independent predictors of diagnostic testing. Covariates were selected a priori for clinical relevance and included presence of angioedema, atopic history, point of first contact, prescription of oral H1-antihistamine therapy at the first visit, physician specialty, and referral status. Referral status was coded as a categorical variable reflecting the timing of

referral relative to treatment initiation (no referral, referral before treatment initiation, and referral after treatment initiation). All predefined covariates were entered simultaneously into the multivariable model using a forced-entry approach. Complete data were available for the outcome and all prespecified covariates included in the model; therefore, no imputation or other missing-data handling procedure was required. Multicollinearity among the included predictors was assessed using variance inflation factors (VIFs) and tolerance values, and potentially influential observations were evaluated using Cook’s distance. Improvement in model fit relative to the intercept-only model was assessed using the likelihood-ratio test. Model calibration was evaluated using the Hosmer–Lemeshow goodness-of-fit test, whereas discrimination was assessed using the area under the receiver operating characteristic curve (AUC), with its corresponding 95% confidence interval (CI). Results are reported as adjusted odds ratios (ORs) with 95% CIs. A two-sided $p < 0.05$ was considered statistically significant.

Statistical analyses were conducted in Jamovi (v2.2.26, The Jamovi Project, Sydney, Australia), and figures were created using GraphPad Prism (v9.5.1, GraphPad Software, Boston, MA, USA) and Adobe Illustrator 2023 (v27.9.0, Adobe Inc., CA, USA). The authors used an artificial intelligence (AI)-as-

sisted language-editing tool, Grammarly (v1.162.2.0, Grammarly Inc., San Francisco, CA, USA), solely for minor grammatical and language corrections. No artificial intelligence tools were used for data analysis, interpretation, or the generation of scientific content.

Ethical Considerations

The study was conducted in accordance with the Declaration of Helsinki and approved by the Recep Tayyip Erdogan University Non-Interventional Clinical Research Ethics Committee (no: 2026/223, date: 04.06.2026); informed consent was waived due to the retrospective design. This study was not a clinical trial; therefore, clinical trial registration was not applicable.

Results

Among the 300 children in the cohort, the median age was 6.1 years (IQR 3.3–9.6), and 159 (53.0%) were male. Most children presented with isolated AU (n=274, 91.3%). AU with angioedema was observed in 24 patients (8.0%), whereas two patients (0.7%) presented with isolated angioedema. A personal history of atopic disease was documented in 38 patients (12.7%), and a family history of atopy in 44 patients (14.7%). 104 patients (34.7%) had experienced at least one previous episode of urticaria. Baseline demographic and clinical characteristics of the study population are summarized in Table 1.

The initial evaluation was most commonly performed by general practitioners in the pediatric emergency department (n=138, 46.0%), followed by general pediatricians in outpatient clinics (n=114, 38.0%) and family medicine physicians in the family medicine outpatient clinic (n=48, 16.0%).

Table 1. Baseline characteristics and clinical presentation of the study population (n=300)

Characteristic	Value
Age, median (IQR 25-75%), years	6.1 (3.3-9.6)
Male sex, n (%)	159 (53.0)
Clinical presentation, n (%)	
Isolated acute urticaria	274 (91.3)
Acute urticaria with angioedema	24 (8.0)
Isolated angioedema	2 (0.7)
Personal history of atopic disease, n (%)	38 (12.7)
Family history of atopy, n (%)	44 (14.7)
Previous episodes of urticaria, n (%)	104 (34.7)

Data are presented as median (interquartile range, IQR) or number (percentage), as appropriate. IQR: Interquartile range; n: number.

Pharmacological treatment for acute symptom control was initiated at first medical contact in 238 patients (79.3%). Of these, 168 received second-generation oral H1-antihistamines alone, 24 received parenteral first-generation H1-antihistamines without systemic corticosteroids, and 46 received parenteral first-generation H1-antihistamines with systemic corticosteroids. Among the 70 patients who received parenteral first-generation H1-antihistamines with or without systemic corticosteroids, oral H1-antihistamine therapy was prescribed in 44 (62.9%), whereas 26 (37.1%) were discharged without an oral H1-antihistamine prescription.

During the clinical course, 120 of 186 patients (64.5%) initially evaluated by general practitioners in the pediatric emergency department or by family medicine physicians in the family medicine outpatient clinic were referred to general pediatricians. Of these, 70 of 120 (58.3%) were subsequently referred to pediatric allergy-immunology specialists. By contrast, only 22 of 114 patients (19.3%) initially evaluated by general pediatricians were referred to pediatric allergy-immunology specialists. With respect to treatment timing, 89 patients (29.7%) were referred before initiation of oral H1-antihistamine therapy, whereas 53 (17.7%) were referred after initiation of oral H1-antihistamine therapy.

Diagnostic testing was performed in 214 patients (71.3%) (Fig. 2a). The clinical indication for testing was explicitly documented in 126 patients (58.9%). Among these, testing was most frequently prompted by systemic symptoms such as fever or fatigue (42.0%), followed by caregiver request or parental concern (30.0%), personal or family history of atopy (16.0%), suspicion of food or drug allergy (8.0%), and recurrent AU episodes (4%). In the remaining patients, diagnostic testing was performed for non-specific or undocumented reasons. A total of 80 patients were referred primarily for allergy testing by physicians other than pediatric allergy-immunology specialists. Following clinical reassessment by pediatric allergy-immunology specialists, testing was not considered clinically indicated in 60 of these patients (75.0%). Allergy testing was ultimately performed in only 20 of these referred cases.

Patterns of diagnostic testing and their clinical yield are shown in Table 2. At least one abnormal laboratory or allergy test result was identified in 64 patients (21.3% of the overall cohort; 29.9% of tested patients). In most cases, these abnormalities were non-specific and did not clarify the aetiology, initiate specific treatment, identify an alternative diagnosis, or escalate therapy. Despite this diagnostic burden, test results led to a documented change in clinical management in only 7 patients (2.3% of the overall cohort;

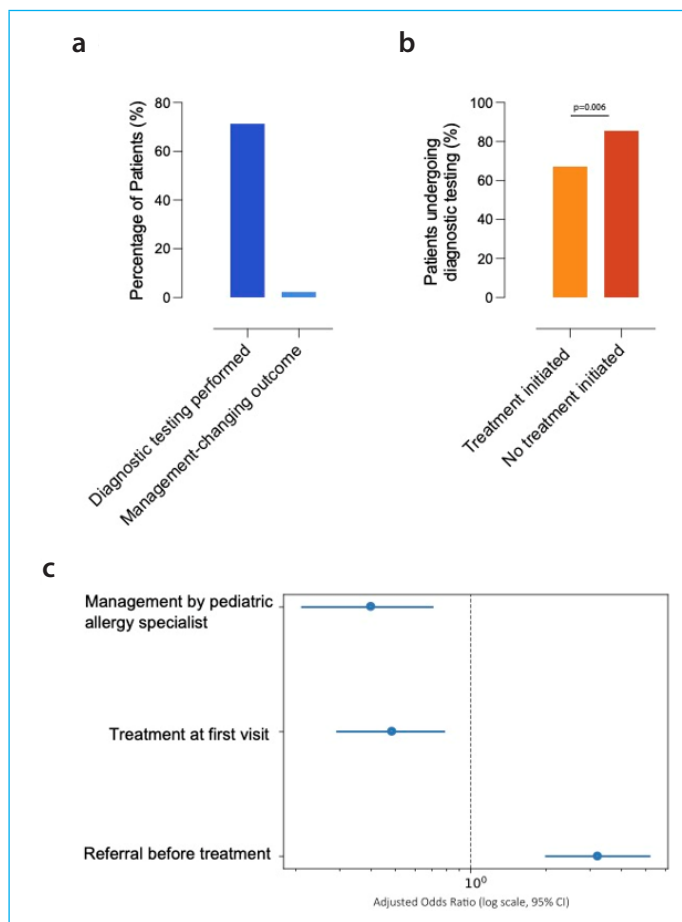


Figure 2. Diagnostic testing burden and care-pathway determinants in pediatric acute urticaria. **(a)** Proportion of patients undergoing diagnostic testing and those with testing-related changes in clinical management. **(b)** Diagnostic testing rates stratified by initiation of oral antihistaminic treatment at the first visit. **(c)** Forest plot of adjusted odds ratios (aORs) with 95% confidence intervals from multivariable logistic regression analysis identifying care-pathway predictors of diagnostic testing. Odds ratios are presented on a logarithmic scale; the dashed vertical line indicates an odds ratio of 1. Referral before treatment initiation refers to referral before initiation of guideline-recommended second-generation oral H1-antihistamine therapy. Treatment at first visit was defined as initiation of any pharmacologic therapy for acute symptom relief

3.3% of tested patients) (Fig. 2a). Confirmed IgE-mediated food allergy was identified in 5 patients (1.7% of the overall cohort; 2.3% of tested patients), all of whom had a clearly documented history compatible with immediate-type urticarial reactions before diagnostic testing. Two additional patients (0.7% of the overall cohort; 0.9% of tested patients) were considered to have probable drug hypersensitivity, based on a consistent temporal relationship and compatible clinical features. Overall, diagnostic investigations did not lead to any change in diagnosis, treatment, or follow-up strategy in 207 of 214 tested patients (96.7%).

Table 2. Patterns and clinical yield of diagnostic testing in children with acute urticaria

Diagnostic testing variable	n (%)
Any diagnostic testing performed*	214 (71.3)
Laboratory investigations	202 (94.4)
Allergy-focused testing	20 (9.3)
Any abnormal test result	64 (29.9)
Clinical impact of testing	7 (3.3)
Specific diagnoses identified	
Confirmed IgE-mediated food allergy	5 (2.3)
Drug hypersensitivity	2 (0.9)

*Categories are not mutually exclusive; 8 patients underwent both laboratory and allergy-focused testing. Percentages are calculated based on the number of patients who underwent diagnostic testing (n=214).

Diagnostic testing was significantly associated with both referral timing and treatment status at first medical contact. It was significantly more frequent in patients referred before initiation of oral antihistamine therapy than in those referred after treatment initiation (88.8% vs. 54.7%, $p<0.001$) and more frequent among patients who did not receive pharmacological treatment at first medical contact than among those who did (85.5% vs 67.2%, $p=0.006$) (Fig. 2b).

In multivariable logistic regression analysis, referral before initiation of oral antihistamine therapy emerged as the most prominent independent predictor of diagnostic testing (adjusted OR [aOR] 3.21, 95% CI 1.98-5.22). A history of AU episodes was also independently associated with increased odds of diagnostic testing (aOR 1.56, 95% CI 1.01-2.41). In contrast, initiation of treatment at the first visit was associated with lower odds of diagnostic testing (aOR 0.48, 95% CI 0.29-0.79). Management by pediatric allergy-immunology specialists was similarly associated with reduced testing (aOR 0.39, 95% CI 0.21-0.71) (Fig. 2c). Neither the presence of angioedema nor a personal history of atopy independently predicted diagnostic testing. The independent predictors of diagnostic testing identified in multivariable logistic regression analysis are presented in Table 3. The likelihood-ratio test indicated that the fitted model provided a significantly better fit than the intercept-only model ($\chi^2 = 27.60$, $df = 6$, $p<0.001$). The Hosmer–Lemeshow goodness-of-fit test showed no evidence of substantial lack of fit ($\chi^2 = 3.73$, $df = 8$, $p=0.881$). Model discrimination was modest, with an AUC of 0.670 (95% CI, 0.607–0.733). Multicollinearity diagnostics showed VIF values ranging from 1.04 to 2.24 and tolerance values ranging from 0.45 to 0.97, indicating no evidence of problematic multicollinearity. The maximum Cook’s distance was 0.039, suggesting that no individual observation exerted undue influence on the fitted model.

Table 3. Multivariable logistic regression analysis of factors associated with diagnostic testing

Predictor	Adjusted OR	95% CI	p
Referral before treatment initiation*	3.21	1.98–5.22	<0.001
Previous episodes of urticaria	1.56	1.01–2.41	0.04
Treatment at first visit†	0.48	0.29–0.79	0.004
Management by pediatric allergy specialists	0.39	0.21–0.71	0.002
Presence of angioedema	1.12	0.54–2.31	0.76
Personal or family history of atopy	1.09	0.62–1.92	0.77

OR: Odds Ratio; CI: confidence interval. Multivariable logistic regression analysis was performed to identify independent factors associated with diagnostic testing. Variables were selected a priori based on clinical relevance and study hypotheses. All predictors listed were entered simultaneously into the model. Referral status was categorized according to timing relative to treatment initiation (no referral, referral before treatment, referral after treatment). Multicollinearity was assessed prior to model construction and was not detected. Results are presented as adjusted odds ratios (ORs) with 95% confidence intervals (CI). A two-sided $p < 0.05$ was considered statistically significant. * Referral before treatment initiation refers to referral before initiation of guideline-recommended second-generation oral H1-antihistamine therapy

† Treatment at first visit was defined as initiation of any pharmacologic therapy for acute symptom relief

Discussion

In this real-world cohort of children with AU, our results reveal a clear mismatch between guideline recommendations and clinical practice. Nearly three-quarters of patients underwent diagnostic testing, yet only 2.3% had their care changed as a result. This low impact aligns with earlier research indicating that routine diagnostic workups in pediatric AU rarely yield useful, actionable results.^[3,5,12,13] For comparison, Santa et al.^[13] reported a similarly high testing rate in a Portuguese pediatric cohort, with a diagnostic yield of less than 5%. Our cohort likewise showed a low rate of management-changing findings, highlighting that this pattern is consistent across various healthcare systems.

The low incidence of confirmed IgE-mediated allergy in our cohort supports this interpretation. Almost all cases with confirmed IgE-mediated allergy had a documented clinical history suggestive of immediate-type hypersensitivity before testing. This aligns with previous studies showing that broad laboratory and allergy testing in unselected AU populations rarely identifies a meaningful trigger^[1,7,14] and reinforces current guidelines that diagnostic evaluation should be based on clinical history rather than routine testing.^[3,5,6]

A key finding of this study is that testing behavior appears to be influenced more by how care is delivered than by patient phenotype. In multivariable analysis, neither accompanying angioedema nor a personal history of atopy independently predicted the likelihood of diagnostic testing. Instead, testing was more closely associated with the care pathway, particularly referral before starting treatment. This suggests that, in pediatric acute urticaria, overuse of diagnostic tests may be driven by workflow-related decisions rather than by specific clinical risk factors.^[15,16] The link between the timing of treatment initiation and the frequency of diagnostic testing is clinically sensible. When symptoms are not addressed early, tests may be used instead of direct

treatment, especially in cases that appear severe but typically resolve on their own. In such situations, ordering tests can provide reassurance or maintain clinical momentum, even if the likelihood of obtaining useful information is low. Our results imply that starting guideline-recommended antihistamine treatment promptly could do more than just alleviate symptoms; it might also reduce uncertainty and help avoid unnecessary tests.^[10,11,17] Another notable observation was that systemic symptoms were the most documented reason for diagnostic testing, yet none of the tests performed for this purpose led to an alternative diagnosis or a significant change in management. In our cohort, these symptoms did not appear to be reliable indicators of clinically important underlying disease. This might explain why broad laboratory workups often add little value in typical cases of AU.^[3,5,6,18,19] We also observed frequent use of systemic corticosteroids, sometimes prescribed without concurrent oral antihistamines. This approach is difficult to justify under current guidelines and likely reflects an effort to quickly suppress visible symptoms rather than adhering to an evidence-based treatment plan for AU.^[6,20,21] While clinical urgency or caregiver expectations may influence this practice, it also underscores that AU management is sometimes driven more by immediate symptom relief than by a well-considered therapeutic plan.

This study not only highlights the low diagnostic yield but also explains why unnecessary testing remains common in routine practice. Earlier research has mainly focused on causes, triggers, or the frequency of abnormal results.^[1,2,4,12,19,22] In contrast, our findings suggest that the key question may not be which patients undergo testing, but rather what prompts testing in the first place. From this perspective, unnecessary testing in AU should not be viewed solely as a knowledge gap but as an issue related to how care is delivered.

Another important takeaway from our research is that pediatric allergy-immunology specialists can play a crucial role in reducing unnecessary testing. This observation also emphasizes the high number of unnecessary referrals in our cohort and suggests that initial assessment and management by non-specialist care providers may influence the appropriate use and cost-effectiveness of healthcare, beyond the issue of unnecessary testing in pediatric AU.

Taken together, these findings support a treatment-first, response-guided approach to pediatric AU. Early antihistamine therapy, brief clinical reassessment, and selective referral based on history and symptom evolution may reduce low-value testing without compromising patient safety. Based on these observations, we propose a pragmatic, study-informed care pathway (Appendix) to support more rational diagnostic decision-making in routine pediatric practice.

The key strength of this study is its comprehensive coverage of the initial care process for pediatric AU, spanning frontline and specialist healthcare settings within a single integrated system. This approach enabled us to assess testing behaviors across the entire early care pathway, from initial contact to specialist consultation, and to distinguish abnormal test results from those that actually influenced patient care.

This study has several limitations. Its retrospective design and reliance on medical record documentation introduce a risk of information bias, and the reassurance value of diagnostic testing could not be reliably assessed from the records. In addition, the exclusion of patients with incomplete records may have introduced selection bias if these patients differed systematically from those included in the final cohort. The single-center setting may limit generalizability to other healthcare systems or resource settings, and ICD-10-based EMR searches, though supplemented by detailed manual review, carry a residual risk of diagnostic misclassification. Future prospective multicenter studies are needed to confirm these findings and to explore caregiver- and physician-level determinants of testing in greater depth.

Conclusion

In conclusion, diagnostic testing in pediatric AU is common but rarely alters clinical management. More importantly, testing behavior appears to be shaped less by clinical features suggestive of IgE-mediated disease than by referral patterns, treatment timing, and care-pathway structure. These findings suggest that low-value testing in AU may persist despite existing recommendations and that reducing it may therefore require changes in frontline clinical decision-making rather than guideline awareness alone.

Disclosures

Ethics Committee Approval: The study was approved by the Recep Tayyip Erdogan University Non-Interventional Clinical Research Ethics Committee (no: 2026/223, date: 04.06.2026).

Informed Consent: Informed consent was waived due to the retrospective design of the study.

Conflicts of Interest: The authors declared no conflict of interest.

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Authorship Contributions: Concept – MYA, APS; Design – MYA, APS; Supervision – APS; Data Collection or Processing: APS, SB, EYG; Analysis or Interpretation: MYA, APS, SB, EYG; Literature Search: MYA, SB, EYG; Writing: MYA; Critical Review: APS.

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Appendix. Practical care pathway for children with acute urticaria

Initial clinical assessment

- Make a clinical diagnosis based on history and physical examination
- Exclude anaphylaxis and non-histaminergic (bradykinin-mediated) angioedema

First medical contact

- Initiate second-generation oral H1-antihistamine therapy
- Reassure caregivers about the self-limited nature of acute urticaria
- Do not request routine laboratory or allergy tests

Early response assessment (24-72 hours):

Adequate clinical response

- Symptom resolution or marked improvement
 - No routine laboratory or allergy testing
 - No referral required

Inadequate response or red flags

- Persistent symptoms despite appropriate antihistamine therapy
- Systemic symptoms (e.g., persistent fever, impaired general condition)
- History suggestive of immediate-type hypersensitivity
 - Targeted evaluation guided by clinical history

Referral to pediatric allergy-immunology

- Consider referral for recurrent or persistent AU, atypical presentations, or a convincing history of IgE-mediated allergy
- Referral is not routinely indicated for uncomplicated first episodes responding to treatment