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Validity of Cephalosporin Skin Prick Testing in Children with Self-Reported Cephalosporin Allergy: A Cross-Sectional Study

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ORIGINAL ARTICLE

Validity of Cephalosporin Skin Prick Testing in Children With Self-reported Cephalosporin Allergy: A Cross-sectional Study

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Abstract

Background: **Cephalosporins are a group of antibacterial agents related to the β-lactam group, which are used in the treatment of many types of infections. Cephalosporins are a good choice of cost-effective antibacterial drugs, which are occasionally withheld from treatment strategies because of self-reported clinical histories of cephalosporin and penicillin allergy. Cephalosporin allergies are increasingly reported, with a wide spectrum of reactions. A patient with an allergy to a certain cephalosporin should not use that cephalosporin in the future. The risk of cross-reaction among cephalosporins in patients with a history of sensitivity to certain cephalosporins is unknown.**

Aim of study: **To determine the value of the cephalosporin skin prick test in patients with a self-reported history of cephalosporin allergy and to determine the correlation of cephalosporin skin prick test positive results with some suggested variables.**

Methods: **A cross-sectional study was conducted on patients with a self-reported cephalosporin allergy at Al Fallujah Teaching Hospital for Maternity and Childhood, Iraq, between 1st of November 2022 and 1st of April 2023. Patients' ages ranged from 1 month to 5 years. Patients underwent ceftriaxone skin prick tests. Patients who used antihistamine drugs before the skin prick test were excluded. Erythema and wheal areas >5 × 5 mm were considered positive.**

Results: **The prick test was positive in 60.8 % of children with allergy symptoms and negative in 39.2 % of them. There was a significant association between the cephalosporin-positive prick test and children with a history of self-detected allergy to cephalosporin use ($p = 0.01$). Mothers' educational level was a significant factor ($p = 0.03$). A history of allergy to penicillin use is not significant in the cephalosporin-positive prick test. No significant differences were observed between children with positive prick tests and children with negative prick tests regarding symptoms ($p = 0.6$) and duration ($p = 0.6$). No significant p-value was observed between children with positive prick tests and children with negative prick tests regarding age ($p = 0.9$), gender ($p = 0.9$), residence ($p = 0.9$), and vaccination history ($p = 0.4$). No significant differences were observed between children with positive and negative prick test results regarding family history of penicillin allergy ($p = 0.7$) and other symptoms ($p = 0.5$).**

Conclusions: **Ceftriaxone skin prick test is valuable for assessing ceftriaxone allergy in patients diagnosed based on history alone. Cephalosporins appear to be a safe alternative for most patients with self-reported penicillin allergy; however, further validation is needed. There was a significant relationship between the history described by educated mothers and a positive ceftriaxone prick test.**

Keywords: Cephalosporins allergy, Skin prick test, Penicillin allergy

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Introduction

Cephalosporins are a group of β-lactam antibiotics originally derived from the fungus Cephalosporium acremonium and are widely used to treat various bacterial infections due to their broad-spectrum activity and favorable safety profile (Finberg & Guharoy, 2021).

Cephalosporins are a good choice of cost-effective antibacterial drugs, which are occasionally withheld from treatment strategies due to self-assessment of allergy based on skin manifestations for cephalosporin and penicillin (Louden et al., 2021; Norton et al., 2022). This will cause not only caution with cephalosporin but even with certain penicillin antibiotics due to the presence of cross-reactivity between them (Chiron et al., 2020). Current accurate statistics indicate that 10 % of patients complain of penicillin allergy. Immunological investigations indicate that only a small number of patients have a true allergy to penicillin (Luintel et al., 2025). Allergic reactions to cephalosporins are becoming increasingly common, with a wide spectrum of immunological mechanisms. Cephalosporins are one of the leading causes of perioperative severe allergy that can lead to anaphylaxis and severe skin side effects. Patients allergic to cephalosporins may tolerate cephalosporins with other R1 side chains but may react to other beta-lactams with common R1 side chains. Skin prick tests for cephalosporins have not been reliable but appear to have a good negative predictive value for other antibiotics in the same family with disparate R1 side chains (Choi, 2019). A patient who has had an allergy to a certain cephalosporin should not use that cephalosporin in the future. The probability of a drug allergic reaction when different cephalosporins are used in patients with a history of sensitivity to certain cephalosporins is unknown. Some researchers have mentioned that the rate of cross-reactivity among cephalosporins is not significant (Chaabane et al., 2009). A detailed history of suspected drugs and allergies, supported with an accurate review of medical records, may be valuable in guiding therapeutic options. Patients with a history of penicillin allergy may experience reactions to cephalosporins. A skin prick test for an allergy to penicillin might be helpful in persons with a history of such an allergy who are treated with cephalosporins (The Journal of Allergy and, 2019). Overestimation of B-lactam "allergy" may lead to withholding of penicillin and cephalosporin antimicrobials and change to drugs that have many non-preferred clinical consequences, including therapy failures, increased rates of toxicity for the alternative drugs, and, of course, the costs (Macy, 2014).

The aim of this study

1. To determine the value of cephalosporin skin prick tests in patients with self-reported cephalosporin and penicillin allergies.
2. To determine the correlation of cephalosporin skin prick test results with some suggested variables.

Materials and methods

A cross-sectional study was conducted at Al Fallujah Teaching Hospital for Maternity and Childhood between 1st of November 2022 and 1st of April 2023.

This study was approved by the Scientific Committee of the College of Medicine, University of Fallujah, and the Ethics Board of Al-Fallujah Teaching Hospital for Maternity and Childhood under approval number 4/133, dated 11/8/2023.

The patient group used for this research involved patients from Al Fallujah Teaching Hospital for Maternity and Childhood who were admitted to the emergency unit. Patients ages ranged from 1 month to 5 years old. The questionnaire was prepared after reviewing many papers on this subject. Clinical history was obtained from the mothers, and it included age at onset of reaction, name of drug, details of the side effect (type of reaction: anaphylaxis, urticaria, angioedema, or maculopapular rash), family history of cephalosporin allergy, and mother education.

Inclusion criteria: Any child that needs admission to the department of emergency with suspicion of penicillin and cephalosporin hypersensitivity by the family description, depending on the history of previous use of these groups of drugs with apparent allergic symptoms.

Exclusion criteria: Any patient that uses antihistamine drugs before the skin prick test.

Patients attended the inpatient clinic where they underwent a ceftriaxone skin prick test. The penicillin prick test was not done. The prick test was done by paramedical staff and observed by resident doctors, who decided whether the test was positive or negative. The skin test was done on the forearm by the prick (puncture) technique. If both the erythema and wheal reaction appeared to the antibiotic materials (at 15 min) and the reaction area was greater than 5 × 5 mm (>25 mm^2), the patient was considered to be allergic to the antibiotic.

Statistical analysis: The children's information was entered into and interpreted statistically by SPSS program 26. Suitable tables were implemented accordingly. The chi-square and Fisher's exact tests were used for categorical variables. A p-value of ≤ 0.05 was regarded as significant.

Results

This study included fifty-one children with allergy symptoms with a mean age of 20.4 months; 39.2 % of them were less than 12 months' old, 51 % of them were in the age group of 12–36 months, and 9.8 % of them were in the age group of 37–60 months. Male children were more than females (51 % vs. 49 %). The residence of studied children was commonly rural (54.9 %). The mothers' educational level was distributed as follows: primary level (31.4 %), secondary level (25.5 %), and college level (43.1 %). The vaccination history was positive in 66.7 % of children (Table 1).

Common allergy symptoms were wheel (37.3 %), rash (15.7 %), edema (9.8 %), dyspnea (7.8 %), itching (5.9 %), rash & wheel (5.9 %), wheel & dyspnea (5.9 %), etc. The allergy was immediate after antibiotics in 37.3 % of children, after 1 min in 39.2 % of children, and after 1 h in 23.5 % of them. The allergy was to penicillin in 58.8 % of children and to cephalosporin in 41.2 % of them (Table 2).

The family history of penicillin allergy was positive in 62.7 % of children. Other family histories were commonly eczema (17.6 %), food allergy (15.7 %), asthma (11.8 %), rhinitis (11.8 %), bronchitis (9.8 %), etc. Other symptoms of allergy were respiratory symptoms (39.2 %), fever (29.4 %), GIT symptoms (23.5 %), insect bite (3.9 %), insect bite & fever (2 %), and GIT symptoms with fever (2 %) (Table 3).

The ceftriaxone prick test was positive in 60.8 % of children with allergy symptoms, while negative in 39.2 % of them (Fig. 1).

No significant differences were observed between children with positive ceftriaxone prick tests and children with negative prick tests regarding age ($p = 0.9$), gender ($p = 0.9$), residence ($p = 0.9$), and vaccination history ($p = 0.4$). Mother's educational level was a significant factor ($p = 0.03$) (Table 4).

Table 1. General characteristics of children with allergy symptoms.

Variable	No.	%
Age: mean ± SD (20.4 ± 14.1 months)		
Less than 12 months	20	39.2
12–36 months	26	51.0
37–60 months	5	9.8
Gender		
Male	26	51.0
Female	25	49.0
Residence		
Urban	23	45.1
Rural	28	54.9
Mother's educational level		
Primary level	16	31.4
Secondary level	13	25.5
College-level	22	43.1
Vaccination history		
Positive	34	66.7
Negative	17	33.3
Total	**51**	**100.0**

Table 2. Clinical characteristics of children with allergy symptoms.

Variable	No.	%
Symptoms		
Rash	8	15.7
Wheel	19	37.3
Dyspnea	4	7.8
Rash & wheel	3	5.9
Wheel & dyspnea	3	5.9
Dyspnea & itching	1	2.0
Dyspnea & rash	2	3.9
Wheel & itching	2	3.9
Itching	3	5.9
Oedema	5	9.8
Rash & itching	1	2.0
Duration		
Immediate	19	37.3
After 1 min	20	39.2
After 1 h	12	23.5
Antibiotics		
Cephalosporin	21	41.2
Penicillin	30	58.8
Total	**51**	**100.0**

Table 3. Family history of children with allergy symptoms.

Variable	No.	%
Family history of penicillin allergy		
Positive	32	62.7
Negative	19	37.3
Other family histories		
Asthma	6	11.8
Eczema & allergy	4	7.8
Bronchitis	5	9.8
Rhinitis	6	11.8
Eczema & bronchitis	4	7.8
Asthma & bronchitis	4	7.8
Eczema & food allergy	2	3.9
Eczema & rhinitis	3	5.9
Eczema	9	17.6
Food allergy	8	15.7
Other symptoms		
GIT symptoms	12	23.5
Fever	15	29.4
Respiratory symptoms	20	39.2
Insect bite	2	3.9
Insect bite & fever	1	2.0
GIT & fever	1	2.0
Total	**51**	**100.0**

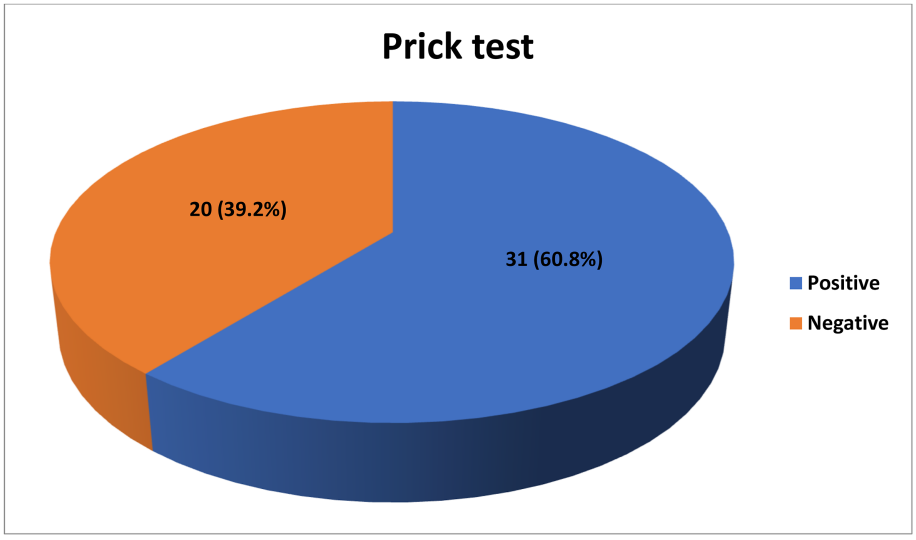

Fig. 1. Prick test result in children with allergy symptoms.

No significant differences were observed between children with positive ceftriaxone prick tests and children with negative prick tests regarding symptoms (p = 0.6) and duration (p = 0.6). There was a significant association between a ceftriaxone-positive prick test and children with a history of cephalosporin use (p = 0.01) more than penicillin use (Table 5).

No significant differences were observed between children with ceftriaxone-positive prick tests and children with negative prick tests regarding family history of penicillin allergy (p = 0.7), other family histories (p = 0.3), and other symptoms (p = 0.5) (Table 6).

Table 4. Distribution of general characteristics according to prick test results.

Variable	Prick test				P
	Positive		Negative		
	No.	%	No.	%	
Age					0.9^{NS}
Less than 12 months	12	38.7	8	40.0	
12–36 months	16	51.6	10	50.0	
37–60 months	3	9.7	2	10.0	
Gender					0.9^{NS}
Male	16	51.6	10	50.0	
Female	15	48.4	10	50.0	
Residence					0.9^{NS}
Urban	14	45.2	9	45.0	
Rural	17	54.8	11	55.0	
Mother's educational level					0.03^{S}
Primary level	6	19.4	10	50.0	
Secondary level	10	32.3	3	15.0	
College-level	15	48.4	7	35.0	
Vaccination history					0.4^{NS}
Positive	22	71.0	12	60.0	
Negative	9	29.0	8	40.0	

S = Significant; NS = Not significant.

Discussion

The ceftriaxone skin prick test demonstrated a high positive rate (60.8 %) compared to the negative rate (39.2 %), emphasizing its critical role in identifying immediate hypersensitivity reactions in emergency settings. These findings align with prior studies in pediatric populations (Antonino et al.), reinforcing the test's reliability as a diagnostic tool. However, the notable proportion of negative test results (39.2 %) warrants further exploration. This discrepancy may stem from several factors: families

Table 5. Distribution of clinical characteristics according to prick test results.

Variable	Prick test				P
	Positive		Negative		
	No.	%	No.	%	
Symptoms					0.6^{NS}
Rash	4	12.9	4	20.0	
Wheel	11	35.5	8	40.0	
Dyspnea	3	9.7	1	5.0	
Rash & wheel	3	9.7	0	–	
Wheel & dyspnea	2	6.5	1	5.0	
Dyspnea & itching	0	–	1	5.0	
Dyspnea & rash	1	3.2	1	5.0	
Wheel & itching	1	3.2	1	5.0	
Itching	3	9.7	0	–	
Oedema	3	9.7	2	10.0	
Rash & itching	0	–	1	5.0	
Duration					0.6^{NS}
Immediate	12	38.7	7	35.0	
After 1 min	13	41.9	7	35.0	
After 1 h	6	19.4	6	30.0	
Antibiotics					0.01^{S}
Cephalosporin	17	54.8	4	20.0	
Penicillin	14	45.2	16	80.0	

NS = Not significant, S = Significant.

Table 6. Distribution of family history according to prick test results.

Variable	Prick test				P
	Positive		Negative		
	No.	%	No.	%	
Family history of ceftriaxone allergy					0.7[NS]
Positive	20	64.5	12	60.0	
Negative	11	35.5	8	40.0	
Other family histories					0.3[NS]
Asthma	4	12.9	2	10.0	
Eczema & allergy	3	9.7	1	5.0	
Bronchitis	5	16.1	0	–	
Rhinitis	5	16.1	1	5.0	
Eczema & bronchitis	2	6.5	2	10.0	
Asthma & bronchitis	1	3.2	3	15.0	
Eczema & food allergy	1	3.2	1	5.0	
Eczema & rhinitis	1	3.2	2	10.0	
Eczema	6	19.4	3	15.0	
Food allergy	3	9.7	5	25.0	
Other symptoms					0.5[NS]
GIT symptoms	5	16.1	7	35.0	
Fever	9	29.0	6	30.0	
Respiratory	14	45.2	6	30.0	
Insect bite	1	3.2	1	5.0	
Insect bite & fever	1	3.2	0	–	
GIT & fever	1	3.2	0	–	

NS = Not significant.

might overreport allergic symptoms, attributing non-specific manifestations (e.g., rashes) to ceftriaxone when alternative causes exist. Additionally, suboptimal technique during test administration or inherent limitations in the test's sensitivity could contribute to false-negative outcomes.

Statistical analysis revealed no significant differences between ceftriaxone-positive and ceftriaxone-negative prick test groups regarding age ($p = 0.9$), gender ($p = 0.9$), residence ($p = 0.9$), vaccination history ($p = 0.4$), or the timing of local reaction onset ($p = 0.6$). These findings suggest that demographic and clinical variables do not independently influence test outcomes. In contrast, maternal education level showed a significant association with ceftriaxone-positive prick tests ($p = 0.03$). Educated mothers may provide more accurate descriptions of allergy symptoms, highlighting the role of caregiver knowledge in diagnostic reliability (Kostecka et al., 2022).

Notably, the cephalosporin prick test yielded significant results in patients with prior cephalosporin exposure but not in those with a history of penicillin allergy. This supports existing evidence, such as the study by Zagursky et al. (Zagursky & Pichichero, 2018), indicating the safety of cephalosporin use in penicillin-allergic patients. Furthermore, no significant associations were observed between ceftriaxone prick test results and other symptoms ($p = 0.6$) or family history of allergies ($p = 0.7$), corroborating findings from Sagar & Katelaris (2013) that these factors may not strongly predict ceftriaxone hypersensitivity.

Conclusions

1. The ceftriaxone skin prick test demonstrates substantial diagnostic value in confirming ceftriaxone allergy, particularly in cases where clinical history alone is inconclusive.
2. Maternal education level significantly correlates with accurate reporting of allergy symptoms and positive prick test results, underscoring the importance of caregiver literacy in allergy diagnosis.
3. Cephalosporins appear to be a viable and safe alternative for most patients with self-reported penicillin allergy, though larger-scale studies are needed to validate this conclusion.

Limitations: This study's small sample size ($n = 51$) limits the generalizability of findings and may reduce statistical power to detect subtle associations. Future research with expanded cohorts is warranted to confirm these observations and explore additional confounding variables.

Ethics information

This study was approved by the Scientific Committee of the College of Medicine, University of Fallujah, and the Ethics Board of Al-Fallujah Teaching Hospital for Maternity and Childhood (Approval No. 4/133, dated 11/8/2023). Informed consent was obtained from the mothers of all participating children.

Authors contribution

Bashar T. Huweidy: Conceptualization, Methodology, Data Collection, Writing – Original Draft. **Bashar I. Mohammed**: Supervision, Critical Review, Writing – Review & Editing. **Jessar S. Hasan**: Data Collection, Clinical Supervision. **Ghaith W. Hamdoon**: Statistical Analysis, Data Interpretation.

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Conflict of interest

The authors declare no conflict of interest.

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