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# Deficiencies in the Assessment of Penicillin Allergy in Hospitalized Children in Hawai'i, 2021-2023

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## Abstract

*Although claims of penicillin allergy are common, after evaluation they are seldom confirmed and can lead to unnecessary interventions. National recommendations are to thoroughly evaluate potential allergies and, if appropriate, to delabel. This retrospective study reviewed records of children hospitalized at Kapi'olani Medical Center for Women and Children in Honolulu, Hawai'i, between January 1, 2021 and June 30, 2023 to assess the frequency of penicillin allergy claims, the appropriateness of their evaluation, and initiation of interventions. Of 3484 hospitalized children, 97 (2.8%) reported penicillin allergy. Documentation, by the admitting team, of the nature of allergy was incomplete for most (97%) of the hospitalizations, leading to deficient risk stratification, lack of implementation of recommended interventions, and frequent use of second-line antibiotics in 46.8% of those who required antibiotic treatment. While this problem is not unique to Hawai'i, it emphasizes the need for education among local providers to improve outcomes.*

## Abbreviations

**AAAAI:** American Academy of Allergy, Asthma, and Immunology
**EMR** = electronic medical record
**KMCWC** = Kapi'olani Medical Center for Women and Children
**PAL** = penicillin allergy label

## Introduction

In pediatric care, antibiotics are commonly prescribed to treat proven or suspect infections. Given its long, favorable track-record of safety and efficacy, penicillin and its derivatives (eg, amoxicillin) represent some of the most utilized antibiotics. One potential side effect of the penicillins is allergy, which constitutes a relative contraindication for their use. In the United States, data from electronic health records of a large population (411 543 persons) cared for by the Kaiser Permanente Health Care Program in San Diego, CA, detected a cumulative prevalence of self-reported penicillin allergy of 9.0% (95% CI: 8.9-9.1%) for all age groups (0-80+ years); the corresponding pediatric age (0-19 years) prevalence was 5.1% (95% CI: 5.0-5.3%).[1] A smaller (66 419 person), single-center study in Milwaukee, WI, found a 0.9% (95% CI: 0.8-1.0%) prevalence of reported penicillin allergy among pediatric patients seen in the Emergency Department.[2]

Erroneous labeling of penicillin allergy is not innocuous and, by prompting use of alternative second-line antibiotics, can lead to significant adverse health outcomes including increased antibiotic-resistance, higher health care costs, longer hospital stays, adverse side effects, and even mortality.[3] It follows then that, by allowing use of these first-line, less toxic, more effective antibiotics, identifying and safely removing inaccurate labels of penicillin allergy can improve patient care. Yet, data show that fewer than 2% of children are properly evaluated to determine the accuracy of a penicillin allergy label (PAL), and that the management of these labels vary widely across health care settings.[4] In an effort to remediate these deficiencies, the American Academy of Allergy, Asthma, and Immunology (AAAAI) in its most recent 2022 practice parameter update recommends a proactive penicillin allergy delabeling approach, along with education of patients and clinicians on its benefits.[5] The proposed algorithm (shown in **Figure 1**) is based on sequential steps of proper evaluation, risk stratification, and implementation of corrective interventions.

There are no published epidemiological data evaluating the prevalence or management of penicillin allergy in the pediatric population of the state of Hawai'i. This gap is significant given the unique racial, ethnic, and geographic demographics of the state, which may influence allergy prevalence, health care access, and documentation practices. Moreover, the scarcity of access to medical specialists in Hawai'i, including those in allergy and immunology, makes it more challenging to ensure accurate diagnosis and proper management of PALs. The present study aimed to understand the magnitude of the problem at Kapi'olani Medical Center for Women and Children (KMCWC) in Honolulu, HI. The frequency of PALs reported by children hospitalized at KMCWC, the appropriateness of documentation and corresponding risk stratification, the initiation of interventions, and the consequences in the use of second-line antibiotics were assessed. To the study team's knowledge, this is the first epidemiological report addressing PALs in children from Hawai'i, and no Hawai'i-specific data have been previously published in the literature.

## Methods

KMCWC is the main pediatric referral center for Hawai'i and Pacific islands. A retrospective review was conducted of the electronic medical records (EMRs) of patients under 18 years of age hospitalized to KMCWC during the 2-year period July 1, 2021 to June 30, 2023. Patients who reported penicillin allergy were identified and their EMRs thoroughly reviewed. Each hospitalization was treated as a dis-

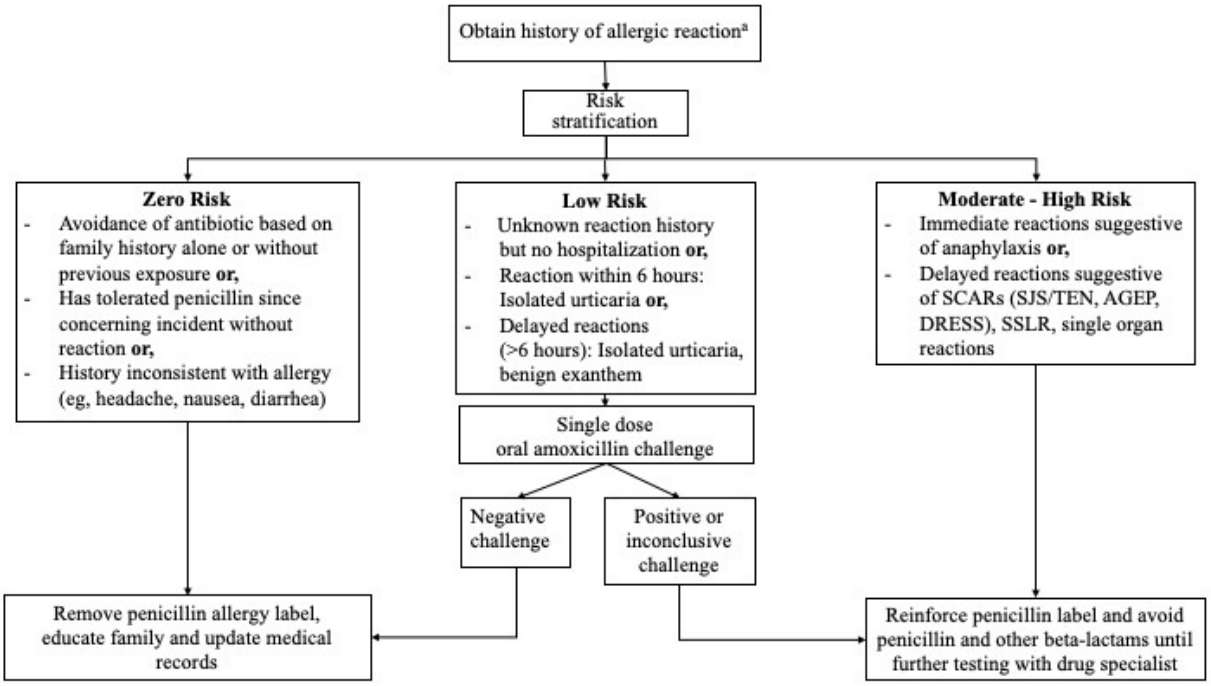


Figure 1. Algorithm for Diagnostic Approach and Decision Making in Pediatric Patients with Suspected Penicillin Allergy According to Risk.[5,6]

[a] Allergy history should include confirming antibiotic name, reaction-associated symptoms, and timing of the reaction. SCARs: severe cutaneous adverse reactions; SJS-TEN: Stevens–Johnson syndrome and toxic epidermal necrolysis; AGEP: acute generalized exanthematous pustulosis; DRESS: drug reaction with eosinophilia and systemic symptoms; SSLR: serum-sickness-like reaction.

tinct encounter, defined as a unique admission to the hospital. As individual patients may have had multiple admissions during the study period, the total number of encounters exceeded the number of unique patients.

Allergy documentation completeness was assessed by examining the 4 fields in the allergy section of the EMR: 1) severity classification, 2) pertinent symptoms, 3) free text comments, and 4) date of occurrence. EMRs with deficiencies were then reviewed by the investigators to further categorize them according to their allergy risk as either zero, low, or moderate-to-high, based on the AAAAI practice parameter (**Figure 1**) with special consideration to the type of reaction and timing in relation to antibiotic administration. Information was also retrieved to identify potential interventions initiated with the aim to clarify the allergy status (such as removal of the PAL, administration of an amoxicillin oral challenge, or referral to an allergist for testing). Finally, in the cases when antibiotics were required for hospitalization, and a penicillin would normally be the drug of choice, it was determined whether instead second-line agents were utilized because of the presence of a PAL.

Data was summarized as frequency (percent) for categorical data and analyzed using Pearson's $\chi^2$ (chi-square) test, 2-sided, using GraphPad Prism version 5 (GraphPad Software, San Diego, California). This research study was deemed exempt from Institutional Review Board by the Hawaii Pacific Health Research Institute (HPRI Study Number: 2023-083).

## Results

In the 24-month period from July 1, 2021 to June 30, 2023, 3484 unique children were hospitalized to KMCWC for a total of 4552 hospitalizations; their median age at hospitalization was 10 years (range: 5 months to 17 years). Of them, 97 children (2.8%; 95% CI: 2.2-3.3%), accounting for 149 (3.3%; 95% CI: 2.8-3.8%) hospitalizations, were identified with a PAL; amoxicillin (110 hospitalizations) was most implicated, followed by amoxicillin-clavulanate (12 hospitalizations), ampicillin (3 hospitalizations), and piperacillin-tazobactam (2 hospitalizations). In 22 hospitalizations, the type of penicillin was not specified. Of the total unique patients, 1944 (55.8%) were male and 1540 (44.2%) female, of whom 61 (3.1%) and 36 (2.3%), respectively, had a PAL. Patient self-identified race showed that 1503 (43.1%) were Native Hawaiian or Pacific Islander, 996 (28.6%) were Asian, 626 (18.0%) were White, 228 (6.5%) were mixed race, 65 (1.9%) were Black, 66 (1.9%) were unknown. Of the aforementioned racial categories, 35 (2.3%), 24 (2.4%), 23 (3.7%), 11 (4.8%), 3 (4.6%) and 1 (1.5%), respectively, had a PAL. Statistical comparisons of PAL frequencies by sex and race did not yield significant differences ($P$>.05, $\chi^2$ test, **Table 1**).

Allergy documentation was mostly incomplete, with only 5 out of 149 hospitalizations (3.3%) having all 4 required fields completed. Severity classification was the most neglected field, missing in 117 (78.5%) hospitalizations. On further EMR review, 39 of these cases (26.2%) could be classified as zero risk, 108 (72.5%) as low risk, and

Table 1. Patient Demographics and Reported Penicillin Allergy Status, Kapi'olani Medical Center for Women and Children, July 1, 2021 to June 30, 2023.

| | Unique patients No. (%)[b] | Reported penicillin allergy No. (%)[b] | *P*-value[a] |
|---|---|---|---|
| **Total** | 3,484 (100)[b] | 97 (2.8)[c] | |
| **Sex** | | | .2 |
| Male | 1944 (55.8) | 61 (3.1) | |
| Female | 1540 (44.2) | 36 (2.3) | |
| **Race** | | | .2 |
| Native Hawaiian/ Pacific islander | 1503 (43.1) | 35 (2.3) | |
| Asian | 996 (28.6) | 24 (2.4) | |
| White | 626 (18) | 23 (3.7) | |
| Black | 65 (1.9) | 3 (4.6) | |
| Unknown | 66 (1.9) | 1 (1.5) | |
| More than one | 228 (6.5) | 11 (4.8) | |

[a] $\chi 2$ (chi-square) test, two-sided, compares distributions within subgroups
[b] percent of grand total

2 (1.3%) as moderate-to-high risk for penicillin allergy. Inpatient interventions in response to the PAL were rare and noted in only 8 patients (5.4%): 7 received an oral amoxicillin challenge and 1 was referred to an allergist; none was delabeled, despite 39 qualifying as low risk. Furthermore, in subsequent hospitalizations, 32 children were found to have received a beta-lactam antibiotic without an adverse reaction, but none had their PAL removed. More than half of the patients (79, 53.0%) required antibiotics during their hospital stay, with 37 (46.8%) of the 79 given second-line antibiotics (in decreasing order of use: clindamycin, ceftriaxone, azithromycin, ciprofloxacin, vancomycin, meropenem, or linezolid) due to their PAL.

## Discussion

This study reveals significant deficiencies in the documentation and management of PALs among hospitalized children in Hawai'i, starting with incomplete documentation, especially regarding severity classification, which hindered appropriate interventions. Despite most PALs qualifying as low (72.5%) or zero (26.2%) risk, few patients received recommended interventions (either an oral amoxicillin challenge, or removal of the allergy label, respectively). These findings are consistent with national data that shows that only a minority of subjects with a PAL are properly evaluated despite strong recommendation from many national groups, and highlights the fact that there remains a substantial discrepancy between clinical evidence and actual practice when it comes to penicillin allergy delabeling.[7,8] Furthermore, the authors found that even when some patients received and tolerated beta-lactam antibiotics, their allergy labels remained unchanged. The frequent use of second-line antibiotics due to allergy labels highlights the clinical consequences of inadequate allergy evaluation.

Correcting the deficient evaluations and lack of interventions for PALs at KMCWC will require a multidisciplinary approach at many levels. Suggestions outlined in the literature include implementing standardized protocols for documenting drug allergies in EMRs; optimizing EMRs to be user-friendly, educating health care providers on proper classification and management of drug allergies, developing allergy delabeling programs, and quality improvement initiatives.[3,9] Locally, the authors, in cooperation with KMCWC, propose a multi-level approach, starting with provider-focused interventions such as incorporating penicillin allergy education into residency and hospitalist training, hosting grand rounds or other educational sessions for primary care providers, and promoting delabeling in younger children to address unconfirmed PALs before they become perpetuated into adolescence. Institutionally, the authors propose to incorporate penicillin allergy evaluation into medical checklists and implement an in-hospital standardized low-risk amoxicillin oral challenge protocol, following the successful experience described by Ray et al[9] Systemically, the EMR platform should be modified to incorporate electronic prompts and prevent entry of incomplete allergy histories – which is especially important given that 97% of current penicillin allergy labels in the KMCWC system lack complete documentation.

Of note, the prevalence of PALs in the present study (2.8%; 95% CI: 2.2-3.3%) is lower than the prevalence found by the Kaiser Permanente group (5.1%; 95% CI: 5.0-5.3%),[1] but higher than the study in Milwaukee (0.9%; 95% CI: 0.8-1.0%).[2] The authors believe several factors may contribute to the discrepant results between the studies. First, the present data is based on hospitalized children rather than the general pediatric population, which may lead to inherent differences in health care access and documentation practices. Second, the unique geographic and health care context of Hawai'i may impact health care utilization or continuity of care, hence affecting opportunities for antibiotic exposure or allergy labeling. Third, KMCWC patient demographics differ from national trends. A prior study by Taylor et al[10] suggests that non-Hispanic White children have the highest rates of PALs, whereas this group com-

prised a minority of the current study's population. Similarly, PALs seem to vary by sex and age-composition of the study population.[1] Fourth, differences in clinician practices could also contribute, as rates of PALs are known to vary across providers and clinics.[11,12] Lastly, this study was conducted during a time of increasing national awareness, following the 2022 AAAAI practice parameter update, which may have influenced provider behavior and documentation.

The main limitations of this study include its retrospective nature and its data source from a single-center only, which may limit generalizability. Still, many hospital-based practices may relate to this study's findings.

## Conclusion

Penicillin allergy labeling remains a common but often inaccurate diagnosis among hospitalized children in the state of Hawai'i. In as much as the study population here included is a good reflection of the general population, close to 3% of children in Hawai'i may be labeled as penicillin allergic, many of them erroneously, and potentially not receive the recommended first-line treatments. This study highlights deficiencies in documentation completeness, risk stratification, and follow-up interventions, despite most allergy labels qualifying as low or zero risk. These gaps contribute to unnecessary use of second-line antibiotics and missed opportunities for safe delabeling. Given the unique patient demographics of Hawai'i and health care environment, tailored approaches are needed to address these issues effectively. To improve patient outcomes, focused efforts including provider education, standardized allergy documentation protocols, integration of penicillin allergy evaluation into clinical workflows, and implementation of active delabeling protocols are essential. The study findings underscore the need for institutional and systemic changes to reduce inaccurate penicillin allergy labels, optimize antibiotic stewardship, and enhance pediatric care in Hawai'i.

### *Conflicts of Interest*

The authors have no conflicts of interest relevant to this article to disclose


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