



# Antibiotic Allergy Labels in a Liver Transplant Recipient Study

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Patient-reported antibiotic allergies (so-called antibiotic allergy labels [AALs]) are associated with suboptimal prescribing and inferior clinical outcomes, especially in the immunocompromised (1, 2). The prevalence, type, and impact of AALs in liver transplant recipients (LTRs) remain ill defined. We report on AALs and their impact on a cohort of Australian LTRs.

A retrospective matched-cohort study was conducted over a 5-year period (2010 to 2015) at an Australian liver transplant center (Austin Health). Using a departmental liver transplant database, LTRs with an AAL (AAL group) were identified. The same number of matched controls (LTRs without an antibiotic allergy label [non-AAL group]) were randomly selected for comparison. AALs were evaluated and classified as type A adverse drug reactions (ADRs; nonimmune mediated), type B ADRs (immune mediated), or of unknown type (3). Baseline demographics, transplant history, and infection-related admission data were collected. From the time of transplant until 12 months afterward, antibiotics administered during infection-related admissions and their duration of administration were recorded. Readmission, intensive-care unit (ICU) admission, *Clostridium difficile* infection (CDI), multidrug-resistant (MDR) organism isolation, and mortality rate were captured. An MDR organism was defined as a bacterium resistant to at least one agent in three or more antibiotic classes (4).

Of 313 LTRs, 51 (16%) had  $\geq 1$  AAL. Females predominated in the AAL group (75% female versus 25% male;  $P = 0.003$ ), but there was no statistically significant differences in the rates of ICU admission and mortality between males and females (see Table S1 in the supplemental material). Seventy-seven AALs were recorded; of these, 23% (18/77) were type A ADRs, 66% were type B ADRs (51/77), and 10% (8/77) were of unknown type. Of the type A ADRs, 72% (13/18) were gastrointestinal upset, and of the type B ADRs, 6% (3/51) were severe cutaneous ADRs, 55% (28/51) were maculopapular exanthema, 35% (18/51) were anaphylaxis, urticaria, or angioedema, and 4% (2/51) were other reactions. The antibiotics implicated in AALs are demonstrated in Fig. 1.

AAL patients were associated with higher numbers of courses of cephalosporin (107/354 AAL patients [30%] versus 75/328 non-AAL patients [23%];  $P = 0.03$ ) and nitroimidazole (34/354 AAL patients [10%] versus 15/328 non-AAL patients [5%];  $P = 0.02$ ). When the AAL and non-AAL groups were compared, there was a nonsignificant reduction in the number of courses of penicillin V or G or aminopenicillin (26/354 AAL [7%] versus 36/328 non-AAL [11%];  $P = 0.14$ ) and beta-lactam or beta-lactamase

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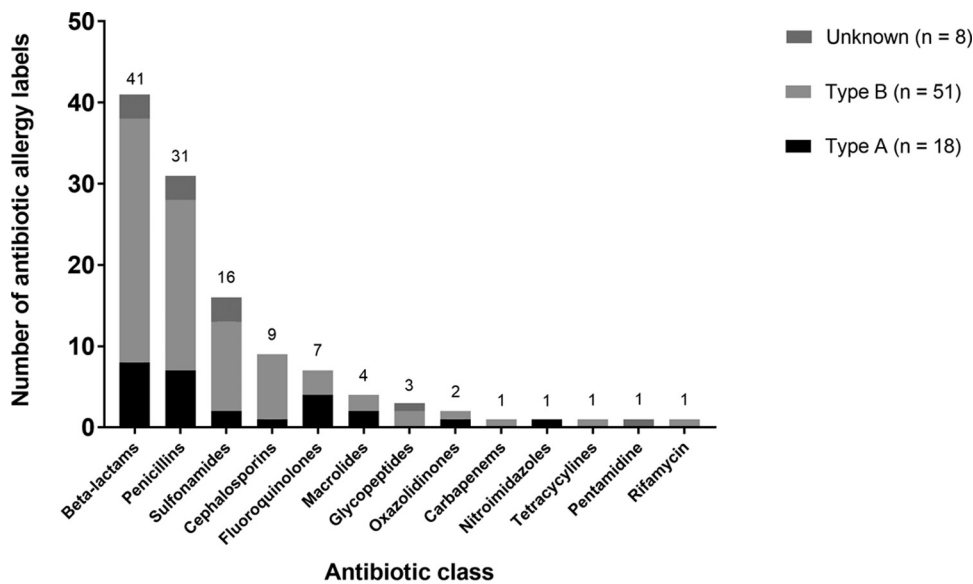


FIG 1 Antibiotic allergy labels per antibiotic class ( $n = 77$ ).

inhibitors (43/354 AAL [12%] versus 49/328 non-AAL [15%];  $P = 0.31$ ). There was also an increasing trend in the number of MDR Gram-negative organisms isolated (4/51 AAL patients [8%] versus 1/52 non-AAL patients [2%];  $P = 0.20$ ) and CDI group (9 AAL patients [18%] versus 3 non-AAL patients [6%];  $P = 0.07$ ).

Sixteen LTRs (31%) in the AAL group had a trimethoprim-sulfamethoxazole (TMP-SMX) ADR history noted, with the majority (11 ADRs [68%]) classified as type B (7 ADRs [43%] were delayed, and 4 [25%] were immediate), 2 (13%) classified as type A, and 3 (19%) classified as unknown. With regard to *Pneumocystis jirovecii* pneumonia prophylaxis, aerosolized pentamidine was employed in 56% (9/16) of these patients with a TMP-SMX ADR history immediately posttransplantation. Only one patient received dapsone, without an ADR. Sixty-three percent (10/16) of the TMP-SMX ADR patients were toxoplasmosis IgG positive, of which 80% (8/10) received no directed toxoplasmosis prophylaxis. In relation to treatment doses, there was a reduction in TMP-SMX usage as a proportion of the total number of antibiotic courses in the AAL group (0/354 AAL versus 9/328 non-AAL [3%];  $P = 0.001$ ).

Although the conclusions are limited by the small cohort size, we identified in LTRs a high prevalence of AALs, predominately AALs to sulfonamides and beta-lactams. Significantly, a large proportion of AALs were type A (23%), amendable to immediate "delabeling." In LTRs with a sulfonamide allergy, TMP-SMX or dapsone may also have been unnecessarily avoided if one considers that antibiotic sulfonamide cross-reactivity is lower than previously thought (5) and TMP-SMX desensitization or rechallenge is often effective (6, 7).

A trend comparable to that shown by nontransplant patients, in whom AALs were found to be associated with increased microbiological resistance and CDI (8), was noted in our cohort. In light of recent increasing cephalosporin resistance (9) and CDI in LTRs (10) and our data demonstrating both, aggressive antibiotic allergy testing and delabeling should be evaluated (11). Use of cephalosporin and other broad-spectrum antibiotics is often a common target for antimicrobial stewardship programs; the addition of antibiotic allergy testing to high-risk antibiotic usage populations, such as transplant recipients, is likely to support antimicrobial stewardship programs by enhancing the use of first-line, narrow-spectrum agents (12). The largest benefit of antibiotic allergy testing is likely to occur pretransplantation, to effectively reduce AAL prevalence and improve antibiotic prescribing in this vulnerable cohort.

**SUPPLEMENTAL MATERIAL**

Supplemental material for this article may be found at <https://doi.org/10.1128/AAC.00078-17>.

**SUPPLEMENTAL FILE 1**, PDF file, 0.4 MB.

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We have no conflicts of interest to declare.

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