Description and accuracy of antibiotic allergy labels at North Shore Hospital

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ABSTRACT

AIMS: Antibiotic allergy labels are common and associated with adverse care. Most people with an antibiotic allergy label are found to be non-allergic on investigation. The aims of this study were to evaluate the burden and accuracy of antibiotic allergy labels at North Shore Hospital and to identify and assess beta-lactam specific allergies, and the potential impact of an inpatient antibiotic allergy service.

METHODS: An evaluation of documented inpatient adverse drug reaction (ADR) labels. Structured assessment of beta-lactam allergies was undertaken using the Austin Health tool.

RESULTS: Three hundred and seven patients were reviewed; 78 patients had an antibiotic allergy label, with 102 individual labels. Fifty-five of these 78 patients underwent structured assessment. Forty-four patients had a beta-lactam-specific antibiotic allergy label. Using the Austin Health tool, 9/44 (20%) of beta-lactam-specific allergy labels could have been removed following a history alone and a further 16/44 (36%) would have been appropriate for direct oral challenge. Antibiotic allergy label accuracy was 64% for beta-lactam antibiotics, and 69% for non-beta-lactams.

CONCLUSIONS: The prevalence of antibiotic specific allergies in our centre was similar to New Zealand and Australian statistics.[1,2] Our study showed that a significant proportion of inpatients with a beta-lactam-specific allergy could be de-labelled on history or with a single dose challenge.

Antibiotic allergies are a very frequently reported adverse drug reaction (ADR) subset in the general population, with an estimated 10% of the general adult population reporting having a penicillin allergy. However, less than 1% of people are confirmed as having an immunoglobulin E (IgE) medicated penicillin allergy when formally tested. Unfortunately, there is both a lack of availability of and awareness of antibiotic allergy testing services in Australia and New Zealand.[3] In hospitals, approximately 25% of patients who require antimicrobial therapy report an allergy to at least one antimicrobial agent.[4] Having an antibiotic allergy "label" is associated with an increased use of less tolerable, more costly alternative "second line" antibiotics, longer hospitalisations, higher total healthcare costs, increased *Clostridioides difficile* infections, increased resistant organism colonisation and increased mortality.[5,6–9]

North Shore Hospital is a 663-bed tertiary care academic centre in Auckland, New Zealand. Each year 46,000 people present to the emergency department, with another 15,000 seen in the Assessment and Diagnostics Unit.[10,11] The use of MedChart Electronic Medication Management version 8.3.1 provided by Dedalus (MedChart) allows for the identification of patients who report having an adverse reaction to any medication once a history has been taken from them by their admitting doctor and pharmacist. Although remote specialist allergy advice is available from another hospital in the Auckland Region, at North Shore Hospital there is currently no mechanism for routine inpatient evaluation and validation of antibiotic allergy labels. The benefit of such a service has already been demonstrated in Auckland: 80% of patients in Middlemore Hospital with a label of "penicillin allergy" safely had their penicillin label removed, including 64% removed by a structured allergy history alone.[12] This study echoes the growing body of international evidence that similarly supports the removal of antibiotic allergy labels by both non-specialist and allergy-specialised services using verified antibiotic assessment tools.[13–16] An adverse drug reaction encompasses all adverse events related to a medication and its administration, while an allergy is restricted specifically to an IgE-mediated reaction. We wanted to identify the accuracy of documented antibiotic allergies and ADRs in inpatients at our institute, and to assess the potential impact of an antibiotic allergy evaluation service on antibiotic allergy labels.

Methods

Medical and surgical staff admitting patients to North Shore Hospital are required to ask about patients' allergies and adverse drug reactions, which are then recorded in the patient's MedChart record. In addition, medication reconciliation is performed for all admitted patients, with the patient's usual medications and any pre-existing allergies and ADRs confirmed and documented by a clinical pharmacist. This information is then uploaded onto the MedChart system. ADRs are uploaded as either an allergy or an intolerance. We documented all antibiotic-specific ADRs and all beta-lactam-specific allergies.

With reference to the *Ethical Guidelines for Observational Studies: Observational research, audits and related activities* (NEAC 2012), this study did not meet the threshold of requiring review by a Health & Disability Ethics Committee. The study was granted Waitematā District Health Board Locality Authorisation (ref: RM14304)

We conducted a study of adult medical and surgical inpatients in North Shore Hospital between October and September 2019. Prior to the study, the interviewing investigator received training in antibiotic allergy assessment by experienced clinicians. The beta-lactam antibiotic allergy assessment tool (AAAT) developed at Austin Health, Melbourne, Australia was utilised for this project. This is a validated tool developed to aid non-allergists in the assessment and management of all patients with reported beta-lactam allergies. Using patient-reported signs and symptoms, the tool phenotypes the reaction according to what system is affected, when and for how long, and what the reaction was. An appropriate management strategy is then recommended. After training, the interviewing investigator was assessed for their ability to correctly determine an antibiotic allergy phenotype and make a recommendation on the appropriate management strategy for the identified phenotype using a series of published clinical scenarios specifically designed for this purpose. In choosing to utilise the Austin Health AAAT, we focussed our investigation on beta-lactam specific allergies. This AAAT was selected as it is a point-of-care tool that can be easily used by a spectrum of non-allergist healthcare professionals.[15]

The interviewing investigator alternated between medical and surgical wards throughout the study. Every week, using MedChart, the ADR histories of all patients on the chosen ward were reviewed. Patients' age, gender and ethnicity data were collected. The total number of medication allergies and ADRs were recorded, with specific recording of culprit antibiotics (by antibiotic class). Patients without an ADR history were excluded. Patients with a documented antibiotic specific allergy were approached for a detailed allergy interview, during which they were asked to describe the documented allergy and to quantify when the reaction had occurred. The Austin Health tool enabled us to phenotype each reported reaction to beta-lactam antibiotics.[15] This allowed us to identify which patients could have their label removed by history alone (direct de-labelling), those who were appropriate for a supervised oral penicillin challenge, those who were suitable for skin testing followed by oral rechallenging and those who required further specialist assessment. The accuracy of pre-existing antibiotics ADRs and allergies was assessed by comparing the medication and information documented in MedChart with the history given by the patients.

Inclusion criteria were adults aged 18 years and above who were admitted under the general medical, orthopaedic or general surgical services, and who had at least one ADR label recorded on MedChart. Patients were not approached for a detailed allergy history if they were physiologically unstable at the time of interview, declined an interview or were unable to provide an accurate history, including those with significant cognitive impairment where no collateral could be obtained, or if there was a language barrier where no interpreter was available to accurately interview the patient.

Interpretation and statistical analysis

The outcomes of interest were the proportion of inpatients with antibiotic ADR labels, the amount of beta-lactam-specific antibiotic allergy labels, the accuracy of these beta-lactam antibiotic allergy labels and the proportion of patients with beta-lactam antibiotic allergy labels that might be appropriate for "direct de-labelling" or direct oral antibiotic challenge. Descriptive and comparative statistical analyses were performed using IBM SPSS version 25 (IBM Corporation, Armonk, NY). Inter-group differences between patients with "any ADR label", patients with antibiotic ADR labels who were interviewed and patients with antibiotic ADR labels who were not interviewed were analysed using ANOVA (age) and Fisher's exact tests (sex, ethnicity).

Results

A total of 307 patients were reviewed. One hundred and sixty-nine out of 307 (55%) of these patients had a recorded ADR. Seventy-eight out of 169 (25%) had an antibiotic-specific allergy. Of these 78 patients, 55/78 (71%) did not meet any of the exclusion criteria so were interviewed (Figure 1).

There were 102 antibiotic allergy labels in total recorded for the 78 inpatients. Penicillins were the most frequently recorded antibiotic allergy class with 54/102 (53%), followed by macrolides with 11/102 (11%), sulphonamides with 10/102 (10%), and cephalosporins with 6/102 (6%). There were 21/102 (20%) antibiotic-specific allergies from other classes.

Beta-lactam phenotypes and recommended management

In the interviewed cohort of 55 patients, we identified and phenotyped 47 beta-lactam-specific antibiotic allergies (41 penicillin and 6 cephalosporin) in 44 patients. The most described beta-lactam allergy phenotypes were dermatological (n=27, 57%) (Table 2). There were four (9%) respiratory or systemic reactions, two (4%) were haematological, eight (17%) were gastrointestinal and six (13%) were unknown. There were two patients (4%) with beta-lactam-specific allergies that were not covered by the Austin Health Tool: one had a report of bradycardia associated with amoxicillin-clavulanate, and one reported myalgia associated with penicillin use. Neither of these reactions were assessed as likely to be mediated by drug allergy, and therefore would also be appropriate for supervised direct oral challenge.

After phenotyping the 44 patients with beta-lactam-specific allergies, the Austin Health Tool recommended the following management: nine patients (20%) were appropriate for direct de-labelling, 16 patients (36%) were appropriate for a supervised direct oral challenge, 14 patients (32%) were appropriate for inpatient skin testing before oral challenge and three patients (7%) were deemed appropriate for outpatient specialist antibiotic allergy assessment and/or testing.

Figure 1: Patient selection process.

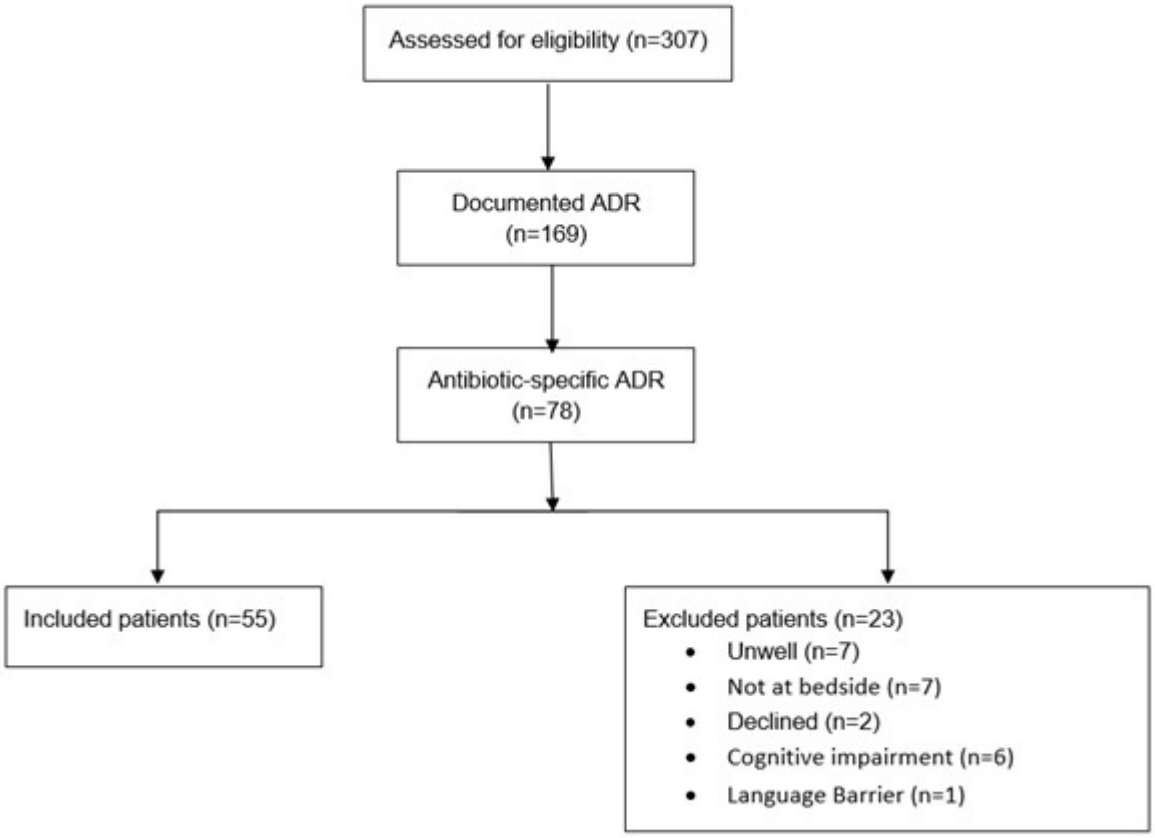

Table 1: Comparative demographics between patients with any adverse drug reaction label and both interviewed and non-interviewed patients with antibiotic-allergy labels.

Demographics	Any ADR label (n=169)	Antibiotic specific allergy interviewed (n=55)	P-value
Median age, years (IQR)	76 (64–86)	77 (63–88)	0.22
Female	100 (60%)	35 (64%)	0.89
Ethnicity			
NZ European	117 (69%)	38 (69%)	0.97
Other European	31 (18%)	11 (20%)	
Pacific Islands	9 (5%)	2 (4%)	
Māori	6 (4%)	2 (4%)	
Asian	6 (4%)	2 (4%)	

Table 2: Austin Health Tool dermatological phenotypes in patients with beta-lactam adverse drug reactions.

Clinical manifestations		Number (%) of patients (n=27)
Childhood exanthem[&]		1 (4)
Immediate diffuse rash [%]		1 (4)
Diffuse rash or localised rash with no other symptoms [#]	Within the last 10 years	2 (8)
	Over 10 years ago	12 (48)
Rash and mucosal ulceration		1 (4)
Pustular, blistering or desquamating rash		2 (8)
Angioedema		8 (32)

[&] Details of rash timing with antibiotic course unknown, with no severe features or hospitalisation.
[%] Immediate considered to be within 2 hours of first dose.
[#] Onset after first 24 hours of beginning the antibiotic course.

Accuracy of recorded antibiotic labels

From the interviewed cohort of 55 patients, we compared all antibiotic specific allergies (n=73) recorded on MedChart against the allergy description obtained by structured allergy history. The accuracy of beta-lactam-specific allergies was 30/47 (64%), the accuracy of non-beta-lactam antibiotic allergy labels was 18/26 (69%). Overall, the accuracy of antibiotic allergy labels was 48/73 (66%).

Discussion

Our study shows that antibiotic-specific allergy labels are common in the adult inpatient population at North Shore Hospital, with 25% of the overall inpatients having one or more antibiotic allergy MedChart label. This compares similarly with other international centres, with the National Antimicrobial Prescribing Survey in Australia finding a rate of 25% in their population.[2] Consistent with other literature, we found that

beta-lactams (penicillins 53%, cephalosporins 6%) were the class of antibiotic most commonly associated with antibiotic allergy labels.[4] Following a structured allergy assessment, a third of these beta-lactam allergies were found to be inaccurate.

While specialist allergist services are critical for the formal evaluation of complex patients or potentially life-threatening allergic reactions, there is increasing evidence to support the role of appropriately trained non-allergists in the identification, assessment and evaluation of patients with antibiotic allergies.[17] Such services have demonstrated that select, low-risk patients can safely undergo an oral beta-lactam challenge without prior skin testing and have found that over 90% of challenged patients tolerate penicillins.[18] In our study, we found that 39 (71%) beta-lactam-specific allergies would have been appropriate for assessment by a trained non-allergist: nine reactions could be de-labelled by history alone, and a further 30 reactions would have been suitable for either an oral antibiotic challenge or a skin test in order to be de-labelled. Incorporating a validated, reproducible tool such as the Austin Health tool in the routine evaluation and potential removal of allergy labels could be associated with benefits for patients (reduced morbidity and mortality), for the hospital (reduced cost and duration of inpatient stays) and for wider society (by avoidance of unnecessarily broad-spectrum antibiotic use).[13–16,19]

Together, these findings support the introduction of a service to undertake routine evaluation of beta-lactam allergy labels at North Shore Hospital. The training of front-line staff who undertake the initial medication history and medication reconciliation (medical, surgical, and pharmacy staff) in the routine use of an AAAT would be beneficial in terms of antibiotic stewardship and patient outcomes. Inequalities exist nationwide with regards to access to specialist allergy services. Routine use of an AAAT would aid to reduce the amount of people who are referred to these oversubscribed services. Looking more broadly, our study, as well as the Middlemore study, show that the regular use of an AAAT in hospitalised patients in New Zealand hospitals by non-allergy specialists is beneficial.[12] A national guideline outlining their role and use across New Zealand is lacking. The authors hope that studies such as ours will aid to change this.

This study is limited by its relatively small size from one hospital, which may skew our findings. North Shore Hospital has a lower proportion of Māori, Pacific Island and Asian ethnic groups than the general New Zealand population.[20] Our small sample size and differing ethnic breakdown could be factors that led to the discrepancy between the proportion of Middlemore patients who can be de-labelled by interview alone (64%) and of North Shore patients (20%). Recall bias of our participants must also be assumed in the description of ADRs, especially those from more than 10 years ago; however, this is not unique to our study, and other challenge studies have shown that such historic reactions can frequently be challenged safely.

Conclusion

We have shown that at our centre, recorded antibiotic allergies are very common, and frequently inaccurate. The introduction of a service for the routine evaluation of antibiotic allergies would be expected to significantly improve the delivery of best practice medicine to our clients. Importantly, the bulk of this service could be offered by staff that are already present and seeing these patients without the need for specialist intervention or referrals.

COMPETING INTERESTS
Nil.

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