Disparities in Drug Allergy Labeling in China: Half of All Labels Are Attributed to ß-Lactams

Shi W[1,2], Low MCH[3], To JCL[3], Kan AKC[1], Liu N[2], Huang J-X[2], Pai P[1,2], Li PH[1,2]

[1]*Division of Rheumatology and Clinical Immunology, Department of Medicine, Queen Mary Hospital, The University of Hong Kong, Hong Kong SAR, China*

[2]*Department of Medicine, University of Hong Kong-Shenzhen Hospital, Shenzhen, Guangdong, China*

[3]*Department of Pharmacology and Pharmacy, The University of Hong Kong, Hong Kong SAR, China*

J Investig Allergol Clin Immunol 2025; Vol. 35(6)
doi: 10.18176/jiaci.1106

Key words: Allergy. ß-Lactam. Drug. China. Disparities.

Palabras clave: Alergia. Betalactámicos. Medicamentos. China. Disparidades.

ß-Lactams, particularly penicillins, are among the most widely prescribed medications but also the most commonly reported culprits of drug allergy [1-3]. Global differences in health care policies, infrastructures, and allergy resources contribute to varying approaches in drug allergy (de) abeling [4,5]. However, non–evidence-based approaches to drug allergy diagnosis may inadvertently increase mislabeling, leading to unnecessary avoidance of first-line antibiotics and compromising antimicrobial stewardship efforts.

Since the 1950s, Mainland China has mandated pre-emptive penicillin skin testing (PST) before prescription, regardless of exposure or history. These practices often diverge from international standards in that they omit prick testing, use large-volume intradermal injections at lower concentrations, lack key reagents or controls, and apply nonstandard interpretations of results [6]. Such practices result in a high rate of false positive skin test results and lead to mislabeling of patients as penicillin-allergic, even in cases where there is no history of exposure or reactions to penicillin. Previous studies in Mainland China have demonstrated that penicillin allergy labels lead to inappropriate antibiotic prescriptions, longer hospital stays, and a greater need to consult infectious disease specialists [7]. Moreover, subsequent re-evaluation of these penicillin allergy labels established through pre-emptive PST revealed a false-positive rate exceeding 97% [8]. In contrast, Hong Kong, a Special Administrative Region of China, follows its own guidelines without pre-emptive PST, aligning with international standards [9,10]. This study aimed to compare the prevalence of ß-lactam allergy labels between 2 regions in China with differing clinical practices and to explore their underlying causes and implications.

The prevalence of allergy labels was compared between the Hong Kong general population (HK cohort) and all patients attending Hong Kong University-Shenzhen (HKU-SZH) in Mainland China (SZ cohort) between January 2018 and December 2022. The primary outcome was prevalence of all drug allergy labels; the secondary outcomes included prevalence of ß-lactam and penicillin allergy labels. For the HK cohort, all drug allergy data from the Hospital Authority (the sole public health care provider) were anonymized and analyzed, as detailed in a previous publication [2]. These were compared with the demographic and drug allergy data of the patients in the SZ cohort during the same period. All statistics were analyzed using IBM SPSS Statistics 27.0 (IBM Corp.). This study was approved by the institutional review board of the University of Hong Kong/Hospital Authority Hong Kong West Cluster (UW20-631) and HKU-SZH (ChiCTR2400088781). Informed consent was not required.

Over the 4-year period, there were 7 474 838 and 1 857 980 individuals in the HK and SZ cohorts, respectively. A total of 638 183 drug allergy labels were recorded (HK, 7.40% [552 897/7 474 838]; SZ, 4.59% [85 286/1 857 980]) (Supplementary Table 1). The female-to-male ratio was 1.72 (HK, 1.68; SZ, 1.93). Age distributions are shown in Supplementary Figure 1. Anti-infective agents were the most frequently labeled drug class, with ß-lactams accounting for 26.0% of all allergy labels in Hong Kong and 63.3% in Shenzhen (OR, 4.91; 95%CI, 4.84-4.99). Penicillin labels alone were significantly more common in Shenzhen (47.1% vs 21.6% [OR, 3.24; 95%CI, 3.19-3.29]; $P<.01$) (Supplementary Tables 1 and 2).

Subgroup analysis of ß-lactam labels across different age groups demonstrated a gradual decrease in the proportion of labels as age increased in the SZ cohort (74.1% among patients aged 0-9 years, decreasing to 50.0% among those aged ≥90 years) (Figure). In comparison, a bimodal distribution was observed for the HK cohort (33.4% among patients aged 0-9 years, increasing to 50.6% among those aged ≥90 years). Overall, the SZ cohort had a significantly larger proportion of ß-lactam allergy labels (OR, 5.71 [95%CI, 5.05-6.46]; $P<.01$). However, this discrepancy waned with age, resulting in no significant differences among those aged ≥90 years (OR, 0.98 [95%CI, 0.819-1.16; $P=.79$).

Given the similar ethnic composition and proximity of the 2 cohorts, our unique comparative study highlights the significance of evidence-based drug allergy practices. In the SZ cohort, the prevalence of ß-lactam labels was more than double that of the HK cohort, constituting half of all allergy labels. Interestingly, disparities in labeling between the 2 cohorts appeared to diminish among individuals aged ≥90 years. One possible explanation could be that some of

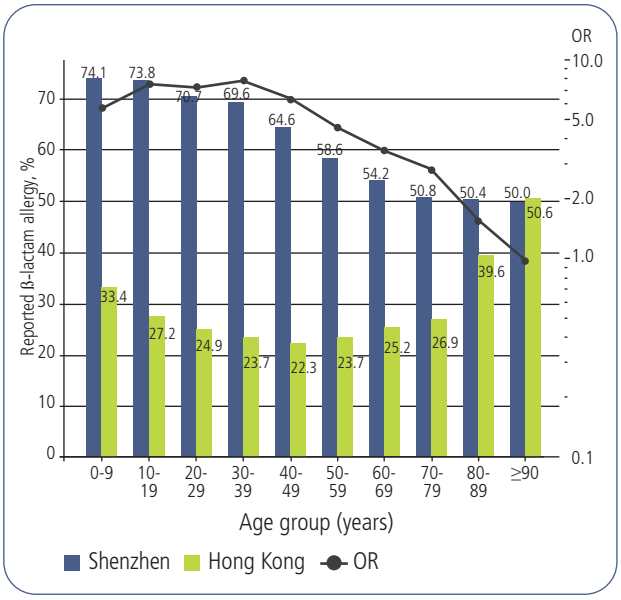

Figure. Comparison between age groups and proportion of ß-lactam allergy labels (among all drug allergies) in the Hong Kong and Shenzhen cohorts.

these individuals may have undergone penicillin allergy testing in Mainland China before relocating to Hong Kong, potentially influencing labeling practices. Alternatively, historical factors such as shared cultural perceptions of penicillin allergy or limited access to accurate diagnostic tools in earlier decades may contribute to this observed similarity. Although mainly focusing on ß-lactams, we also observed variations in labeling for other drug classes, such as nonsteroidal anti-inflammatory drugs (NSAIDs). The higher prevalence of NSAID labeling in Hong Kong could suggest variations in prescription practices, patient demographics, health care–seeking behaviors, or exposures within specific patient populations, as recently documented among individuals with a history of stroke [11]. Further dedicated studies could reveal the underlying reasons for these discrepancies between such closely related and neighboring populations.

Being the second most populated country in the world, China is likely the world's largest contributor to mislabeled penicillin allergies, thus highlighting the need for immediate intervention [6]. Implementing strategies that leverage Hong Kong's experience in evidence-based drug allergy education, multidisciplinary delabeling initiatives, and referral pathways may prove beneficial [12-15]. However, the absence of guidelines for drug allergy delabeling in Mainland China raises uncertainties about potential obstacles such as lack of expertise or systemic barriers (eg, inability to perform direct provocation testing due to compulsory PST) that might hinder implementation. This also emphasizes the importance of establishing standardized delabeling protocols worldwide.

The limitations of this study included its observational design, lack of detailed multivariate analysis, and limited data from the SZ cohort, which were obtained from a single large institution in Guangdong and may not accurately represent the entirety of China. More specific clinical information, such as ethnicity (eg, non-Han Chinese vs Han Chinese), labeling location, the duration of the allergy label, the severity or type of reported allergic reactions (eg, immediate versus nonimmediate), or any medical comorbidities, was not available to calculate adjusted ORs. Despite our subgroup analysis of different age groups, we were unable to perform individual age- or sex-matching.

In conclusion, we highlight the impact of inappropriate allergy practices on drug (mis)labelling. With globalization, labels are likely to proliferate not only within China but also beyond its borders. We advocate for international collaboration to address this ongoing threat to global antimicrobial stewardship.

Funding

The authors declare that no funding was received for the present study.

Conflicts of Interest

The authors declare that they have no conflicts of interest.

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Manuscript received February 4, 2025; accepted for publication February 16, 2025.

Philip H Li
Department of Medicine
The University of Hong Kong, China
4/F, Professorial Block, Queen Mary Hospital
102 Pokfulam Road
Hong Kong SAR, China
E-mail: liphilip@hku.hk