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Demographic characteristics associated with a penicillin allergy label during pregnancy

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Introduction: Penicillins and other beta-lactam antibiotics are used in greater than one-third of pregnant women as treatment for Group B Streptococcus colonization and prophylaxis for Caesarean sections. Penicillin allergy labels have been associated with increased morbidity in the pregnant population, and penicillin allergy evaluation during pregnancy is now recognized as safe and effective. Yet, demographic characteristics associated with having a penicillin allergy label during pregnancy have not been studied. We aimed to evaluate factors associated with having a penicillin allergy label in a diverse population of pregnant patients.

Methods: We performed a retrospective observational study of pregnant patients who had an outpatient visit with Obstetrics and Gynecology and a delivery encounter from 1/1/2020 through 6/30/2022 using electronic health record data in a large health system. We used a multivariable logistic regression model to evaluate factors associated with having a penicillin allergy label.

Results: We identified 10,969 pregnant women of whom 940 (8.6%) had a penicillin allergy label. In the multivariable analysis, having a penicillin allergy label was positively associated with age 32–34 years [odds ratio (OR) = 1.31 vs. 18–27 years, p = 0.02], 35–51 years (OR = 1.41 vs. 18–27 years, p = 0.002) and having rhinitis, asthma, or eczema (OR = 1.55 vs. none, p < 0.0005); and negatively associated with Black race (OR = 0.59 vs. White, p < 0.0005).

Discussion: This study found that Black race was associated with lower likelihood of penicillin allergy label, while older age and atopic conditions were associated with a higher likelihood. This finding may impact health outcomes and interventions related to penicillin allergy in pregnant women.

KEYWORDS

penicillin, antibiotic, allergy, label, demographic, pregnancy, disparity

Introduction

A penicillin allergy label is reported in approximately 10% of the population (1, 2). Yet after evaluation, greater than 90% of patients with a reported allergy are able to tolerate penicillins (1, 2). Penicillin and other beta-lactam antibiotics are an essential class of antibiotics during the peripartum and postpartum periods for indications such as Group B *Streptococcus* (GBS) and Cesarean section prophylaxis (3–6). A history of penicillin allergy label in pregnancy is associated with use of second line antibiotics and adverse health outcomes, including increased rates of Cesarean delivery, post-Cesarean wound complications, longer hospitalization, postpartum endometriosis and longer neonatal hospital stay (4, 6). In recent years, the safety and efficacy of penicillin allergy evaluation via skin testing and drug challenge have been investigated, and this

evaluation has been increasingly implemented in clinical practice (5, 7, 8). Based on accumulating evidence demonstrating the safety and efficacy of penicillin allergy testing and delabeling in pregnancy, the American College of Obstetrics and Gynecology recommends that individuals with a history of penicillin allergy undergo an evaluation prior to delivery (3).

Patient use of and experiences with healthcare vary based on social and demographic factors (9–11). As drug allergy labels are acquired through healthcare interactions and receipt of antibiotics, different patient experiences with the healthcare system may affect the acquisition of a penicillin allergy label (12). For example, one study showed non-Hispanic Black and Hispanic pediatric patients were less likely to be prescribed antibiotics on presentation to the Emergency Department for viral respiratory infections in comparison to White pediatric patients (13). In addition to antibiotic exposure, the acquisition of an antibiotic allergy label may be associated with health literacy regarding the various types of adverse drug reactions (12).

To date, few studies have evaluated the demographic characteristics associated with having a penicillin allergy label (12, 14–21). Women have been shown to have a higher antibiotic allergy rate compared to men (14, 20, 21), which may be due to the increased exposure to antibiotics among women (20). Older age has been associated with higher antibiotic allergy prevalence (20, 22). This finding may be related to increased antibiotic exposure with age. Among the few studies examining race, some have found that Black people are less likely to have a penicillin allergy compared with White people (15, 17–19), while other studies have found higher prevalence in Black patients (16) or no difference between White and Black patients (14). Notably, none of these studies focused specifically on women or a pregnant population.

Despite the benefits of addressing unverified penicillin allergy labels, a significant portion of eligible patients, particularly pregnant individuals, may not receive the benefit of this evaluation (5, 23). A previous study performed at the University of Pennsylvania Health System (UPHS) demonstrated that among pregnant women referred to Allergy/Immunology clinic for a penicillin allergy evaluation, fewer than half presented for their evaluation (23). Additionally, Black race and Medicaid insurance were strong predictors of not receiving this evaluation (23). While this study identified a key area of inequity in the penicillin allergy evaluation, further investigation is needed to understand potential disparities at other points of the penicillin allergy labeling-delabeling pipeline, including the initial acquisition of a penicillin allergy label.

In this study, we aimed to investigate the characteristics associated with having a penicillin allergy label among a diverse population of pregnant patients in a large health system.

Methods

We performed a retrospective cohort study of electronic health record (EHR) data within the University of Pennsylvania Health System (UPHS) for encounters dated January 1, 2020 through June 30, 2022. We identified adults (age 18 years or older) who had both a new pregnancy-related Obstetrics and Gynecology (OBGYN) encounter (defined by UPHS encounter visit 1029) and a hospital encounter for delivery. This study received exemption status from the Institutional Review Board of the University of Pennsylvania.

Patient-level data included age (categorized into quantiles based on the age distribution of patients), race (using EHR categories), ethnicity (i.e., Hispanic or Latino), health insurance type (categorized as private/commercial, Medicaid, or Medicare), rhinitis [any form of rhinitis, defined as having any International Classification of Diseases, Tenth Revision (ICD-10) code of J30* or J31*], asthma [defined as having any ICD-10 code of J45*], and eczema (defined as having any ICD-10 code of L20*, L30.8 or L30.9). We combined rhinitis, asthma, or eczema into a composite variable called concomitant atopic disorder.

We used patients' home addresses to calculate the Area Deprivation Index (ADI), a geographic measure of social vulnerability. The ADI was derived by geocoding addresses using the ArcGIS geocoding feature and assigning each geocode to a census block group. We then used 2021 data from the Neighborhood Atlas to assign an ADI to each patient, and categorized ADI into 4 levels (1–25, 26–50, 51–75 and 76–100), in which a higher value indicates greater neighborhood-level deprivation (24, 25).

We collected all allergy data from the dedicated allergy tab in the EHR and identified allergies to oral, intravenous, or intramuscular antibiotics. We categorized these allergy labels into four groups: penicillins, cephalosporins, sulfonamide antibiotics, and all other antibiotics. Using the same EHR-based allergy tab data, we identified whether patients with a penicillin allergy label were delabeled prior to delivery. We excluded patients who had a penicillin allergy that was removed from the EHR prior to the date of the first pregnancy-related OBGYN encounter. Finally, we identified the clinic location for the first pregnancy-related OBGYN encounter (i.e., the 1029 visit) and identified whether patients had any Allergy/Immunology outpatient visits from January 1, 2020 through June 30, 2022.

We evaluated bivariate associations of factors associated with having a penicillin allergy label with age category, race, ethnicity, health insurance type, ADI, rhinitis, asthma, eczema, concomitant atopic disorder, having a cephalosporin allergy label, and having any other antibiotic allergy label using chi-squared tests. To evaluate factors associated with having a penicillin allergy label, we created a multivariable logistic regression model with having a penicillin allergy label as the outcome, and included age, race (categorized as White, Black, or Other due to the small sample sizes for other races), ethnicity, health insurance type, ADI, and having a concomitant atopic disorder as independent variables. Also, we included the clinic location for the earliest pregnancy-related OBGYN encounter as a random intercept in the multivariable model.

Results

10,969 patients had a pregnancy-related OBGYN encounter, of whom 940 (8.6%) had a penicillin allergy label. Characteristics of

these patients are enumerated in Table 1. Patients with a penicillin allergy label were more likely to be 32 years or older (p < 0.001 comparing four age quantiles), White (p < 0.001 comparing five race categories), have private/commercial health insurance (p < 0.001 comparing three health insurance categories), and have an ADI of 50 or under (p < 0.001 comparing four ADI groups). Higher rates of rhinitis (p < 0.001), asthma (p < 0.001), and having

a concomitant atopic disorder (p < 0.001) were observed in those with a penicillin allergy label. Of the 940 patients with a penicillin allergy label, 51 (5.4%) had a cephalosporin allergy label, 82 (8.7%) had a sulfonamide allergy label, and 132 (14.0%) had another antibiotic allergy label, and each of the three antibiotic allergy label types were more common in patients with a penicillin allergy label than in those without a label (p < 0.0001 for all comparisons).

TABLE 1 Patient characteristics related to ha	/ing a penicillin allergy	label among 10,969	pregnant patients.
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Factors	Overall <i>N</i> = 10,969	No penicillin allergy label N = 10,029	Penicillin allergy label <i>N</i> = 940	<i>p</i> -value	
Age in quantiles					
18–27	3,116 (28.4%)	2,930 (29.2%)	186 (19.8%)	<0.001	
28-31	2,889 (26.3%)	2,641 (26.3%)	248 (26.4%)		
32-34	2,519 (23.0%)	2,270 (22.6%)	249 (26.5%)	_	
35–51	2,445 (22.3%)	2,188 (21.8%)	257 (27.3%)	1	
Race					
White	4,947 (45.1%)	4,362 (43.5%)	585 (62.2%)	<0.001	
Black	5,127 (46.7%)	4,811 (48.0%)	316 (33.6%)		
Asian	866 (7.9%)	829 (8.3%)	37 (3.9%)		
American Indian or Alaskan Native	18 (0.2%)	17 (0.2%)	1 (0.1%)		
Native Hawaiian or other Pacific	11 (0.1%)	10 (0.1%)	1 (0.1%)	_	
Islander					
Ethnicity					
Not Hispanic or Latino	10,366 (94.5%)	9,483 (94.6%)	883 (93.9%)	0.43	
Hispanic or Latino	603 (5.5%)	546 (5.4%)	57 (6.1%)		
Insurance					
Private	6,629 (60.4%)	5,970 (59.5%)	659 (70.1%)	<0.001	
Medicaid	4,323 (39.4%)	4,046 (40.3%)	277 (29.5%)	-	
Medicare	17 (0.2%)	13 (0.1%)	4 (0.4%)	_	
ADI					
1–25	2,618 (23.9%)	2,332 (23.3%)	286 (30.4%)	< 0.001	
26–50	2,973 (27.1%)	2,672 (26.6%)	301 (32.0%)		
51-75	1,939 (17.7%)	1,791 (17.9%)	148 (15.7%)		
76–100	3,439 (31.4%)	3,234 (32.2%)	205 (21.8%)	-	
Rhinitis		·	·		
No	9,259 (84.4%)	8,539 (85.1%)	720 (76.6%)	< 0.001	
Yes	1,710 (15.6%)	1,490 (14.9%)	220 (23.4%)	_	
Asthma					
No	8,551 (78.0%)	7,871 (78.5%)	680 (72.3%)	<0.001	
Yes	2,418 (22.0%)	2,158 (21.5%)	260 (27.7%)		
Eczema	, , , , , , , , , , , , , , , , , , , ,				
No	10,085 (91.9%)	9,226 (92.0%)	859 (91.4%)	0.18	
Yes	884 (8.1%)	803 (8.0%)	81 (8.6%)		
Concomitant atopic disorder	001 (011/0)		0.0707		
No rhinitis, eczema, or asthma	7,057 (64.3%)	6,533 (65.1%)	524 (55.7%)	<0.001	
Rhinitis, eczema, or asthma	3,912 (35.7%)	3,496 (34.9%)	416 (44.3%)		
	5,712 (35.770)	5,170 (51,770)	110 (11.570)		
Cephalosporin allergy label	10.772 (00.00())	0.002 (00.521)	000 (01 (01)	.0.001	
No	10,772 (98.2%)	9,883 (98.5%)	889 (94.6%)	<0.001	
Yes	197 (1.8%)	146 (1.5%)	51 (5.4%)		
Sulfonamide allergy label					
No	10,512 (95.8%)	9,654 (96.3%)	858 (91.3%)	< 0.001	
Yes	457 (4.2%)	375 (3.7%)	82 (8.7%)		
Other antibiotic allergy label					
No	10,443 (95.2%)	9,635 (96.1%)	808 (86.0%)	<0.001	
Yes	526 (4.8%)	394 (3.9%)	132 (14.0%)		

Patients without a label (n = 10,029) were compared to patients with a label (n = 940) using chi-squared tests.

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TABLE 2 Factors associated with	h having a	a penicillin	allergy lab	oel.
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Characteristic	Odds ratio (95% Cl)	<i>p</i> -value			
Age in quantiles (18–27 as reference)					
28-31	1.19 (0.97, 1.48)	0.10			
32-34	1.31 (1.05, 1.63)	0.02			
35-51	1.41 (1.13, 1.75)	0.002			
Race (White as reference)					
Black	0.59 (0.48, 0.73)	< 0.0005			
Other race	0.36 (0.26, 0.50)	< 0.0005			
Ethnicity (Not Hispanic or Latino as reference)					
Hispanic or Latino	1.02 (0.76, 1.37)	0.89			
Insurance (Private insurance as reference)					
Medicaid	0.98 (0.80, 1.21)	0.87			
Medicare	3.30 (1.05, 10.37)	0.04			
ADI (1–25 as reference)					
26-50	0.98 (0.82, 1.16)	0.80			
51-75	0.91 (0.72, 1.15)	0.44			
76-100	0.82 (0.63, 1.07)	0.14			
Concomitant atopic disorder (No rhinitis, eczema, or asthma as					
reference)					
Rhinitis, asthma, or eczema	1.55 (1.35, 1.77)	< 0.0005			
Clinic location for the first pregnancy-related OBGYN encounter*	0.002 (0.000002, 2.83)	0.38			

The odds ratios *p*-values were derived from a multivariable logistic regression model among 10,969 pregnant patients.

*Modeled as a random intercept. The *p*-value was computed from a likelihood-ratio test that compared the full model with a model that did not contain this variable.

Prior to delivery, 298 (31.7%) of patients with a penicillin allergy label had it removed after evaluation of the allergy.

According to the multivariable logistic regression model, having a penicillin allergy label was associated with increasing age for patients aged 32–34 years (OR = 1.31 vs. 18–27 years, p = 0.02) and 35–51 years (OR = 1.41 vs. 18–27 years, p = 0.002) and with having a concomitant atopic disorder (OR = 1.55, p < 0.0005) (Table 2). Compared with White race, Black race (OR = 0.59, p < 0.0005) and Other race (OR = 0.36, p < 0.0005) were associated with lower odds of having a penicillin allergy label. No associations between having a penicillin allergy label and ADI or insurance were observed.

Discussion

This study sought to evaluate sociodemographic factors which may impact the upstream portion of the penicillin allergy labelingdelabeling pipeline. An understanding of patient characteristics associated with having a penicillin allergy label can inform conclusions about and subsequent interventions to address drug allergy disparities in the pregnant population. In this cohort, 8.6% of pregnant patients had a penicillin allergy label. This is consistent with previous studies in the pregnant population which have reported penicillin allergy label rates of approximately 8% (4, 6, 26).

Our study found pregnant women of Black race were approximately 40% less likely to have a penicillin allergy label compared to pregnant White women. Other non-White races also had lower likelihood of penicillin allergy label in comparison to those of White race. An association of labeling with ethnicity was not identified, which may be due to the small Hispanic or Latino population in this study. While there are few previous studies evaluating the demographic factors associated with penicillin allergy label, most of these studies found Black individuals, both adults and children, were less likely to have a penicillin allergy compared with White individuals (15, 17-19). Notably, one study evaluating hospitalized adults with skin and soft tissue infections found higher prevalence in Black patients (16). Another study found no difference in penicillin allergy between Black and White patients, but the authors identified a lower prevalence among Asian patients in comparison to White patients (14). The variable findings among these studies likely reflect differences in the population being examined (e.g., pediatric vs. adult, outpatient vs. inpatient) and baseline demographics of the study populations. Our study, for the first time, assessed the demographic differences of penicillin allergy specifically within the female, pregnant population in a large, diverse health system.

Since penicillin allergy is not known to have a genetic basis, it is likely that lower rate of penicillin allergy label acquisition in non-White patients is related to other factors. The acquisition of an antibiotic allergy label requires numerous steps: signs and symptoms of infection, presentation of the patient to the healthcare system, prescription of an antibiotic by a medical provider, development of drug allergy symptoms, patient recognition that they may be experiencing an allergic reaction, reporting of the symptoms by the patient to a healthcare provider, attribution of the reaction to the prescribed antibiotic, communication and documentation of the antibiotic allergy in the patient's medical records, and retention of the antibiotic allergy label by the patient throughout their lifetime (unless or until it is removed).

While our study was unable to examine the details of initial penicillin allergy acquisition, we and others postulate that disparities may occur at one or more points along the aforementioned steps of allergy label acquisition (12, 18). Variable healthcare interactions and literacy regarding the various types of allergic reactions, may explain the differences in the acquisition of a penicillin allergy in pregnant woman and other populations. These findings are particularly interesting in the context of a recent study within our health system demonstrating that among patients who are referred to the Allergy/Immunology clinic for penicillin allergy evaluation, Black race and Medicaid insurance were strong predictors of not receiving this evaluation despite approximately equal numbers of White and Black patients being referred for evaluation (23). In this sense, it appears that different interactions with the healthcare setting may impact the patterns of how penicillin allergy label is both acquired and removed. While a penicillin allergy label is known to confer worse clinical outcomes in pregnancy, future studies should assess if there are variable clinical outcomes of having a penicillin allergy label among individuals of different races during pregnancy (4, 6).

Similar to previous studies, this study found that increasing age is associated with higher likelihood of penicillin allergy label (20, 22). This finding is relevant because older age during pregnancy is associated with higher rates of GBS colonization as well as pregnancy and birth-related complications (27, 28). In our study, individuals with atopic disorders were found to have a higher risk of having a penicillin allergy. Asthma, particularly when uncontrolled, is associated with adverse maternal and fetal health outcomes during pregnancy (29). Therefore, the co-existence of an unverified penicillin allergy label and asthma may confer higher vulnerability to adverse health outcomes in pregnancy.

As knowledge of demographic factors associated with drug allergy label acquisition and evaluation improves, it is also important to examine the patterns and demographic factors that may be associated with referrals for penicillin allergy evaluation, which represents the middle point of the label-delabeling pipeline. In our cohort, only 31.7% of patients had their penicillin allergy delabeled before delivery despite the presence of a penicillin allergy evaluation program for pregnant women at UPHS. There are many potential explanations for this relatively low rate of formal penicillin allergy evaluation and delabeling, which are beyond the scope of this study. Yet if all eligible pregnant patients with a penicillin allergy label are equally referred and present for evaluation, it begets the question: "Do Allergists/Immunologists and health systems have the capacity to evaluate them all before delivery?" Strategies to meet this demand should be developed, including evaluating patients before pregnancy and creating streamlined referral of patients from OBGYN to Allergy Immunology. In health systems where this strategy is not available or feasible, future directions may include non-Allergist assessment of patients with very low risk penicillin allergies.

This study has many notable strengths. It assessed characteristics associated with a penicillin allergy labels in a large cohort of pregnant patients, thus providing new insight on drug allergy in a vulnerable population. This study was performed in Philadelphia where there is a high population of Black individuals (approximately 40%) compared with many other cities, thus allowing a robust analysis of racial disparities (30).

Our study has limitations. We did not review details of the reported penicillin reaction history such as age of labeling (e.g., childhood vs. adult), setting in which labeling occurred, indication for antibiotic use at the time of labeling, and the type or severity of the reaction. This information may have revealed patterns and potential explanations for labeling disparity. This was deemed not practical as it would require individual chart review, and this level of detail is not often documented.

In conclusion, this study identified White race, older age and comorbid atopic disorders as factors associated with a higher prevalence of penicillin allergy labeling in pregnant women. The findings provide new insight to clinicians seeking to address unverified penicillin allergy with the goal of improving clinical outcomes. As strategies are developed to equitably address unverified penicillin allergies in pregnant patients, factors resulting in disparities in the penicillin labeling-delabeling pipeline should continue to be explored and addressed.

Data availability statement

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

Author contributions

TB: Data curation, Formal Analysis, Methodology, Writing – original draft, Writing – review & editing. PG: Data curation, Formal Analysis, Methodology, Supervision, Writing – review & editing. CC: Data curation, Writing – review & editing. SF: Writing – review & editing. AA: Writing – review & editing. OF: Conceptualization, Investigation, Methodology, Supervision, Writing – review & editing.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Generative AI statement

The author(s) declare that no Generative AI was used in the creation of this manuscript.

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