BRIEF REPORT

Impact of COVID-19 pandemic on pharmacist-led allergy assessments and penicillin skin testing

Justin Spivey, PharmD¹, Connor R. Deri, PharmD^{1,*}, Rebekah H. Wrenn, PharmD¹, Nicholas A. Turner, MD, MSHc²

1 Department of Pharmacy, Duke University Hospital, Durham, USA

2 Division of Infectious Diseases, Department of Medicine, Duke University School of Medicine, Durham, USA

Abstract

Allergy assessments and penicillin skin testing are associated with reductions in high-*Clostridioides difficile* infection (CDI)-risk antibiotic use and lower hospital-acquired CDI rates; however, these activities require substantial personnel and resource allocation. Recently, many antimicrobial stewardship programs' (ASPs) focus shifted towards supporting the COVID-19 pandemic response. We evaluated the impact of the COVID-19 pandemic on a pharmacist-led allergy assessment and penicillin skin testing program. Patients undergoing allergy assessment and/or penicillin skin testing (PST) from 1 January 2017 through 30 April 2021 were included for review. Monthly PST and allergy assessment rates were calculated and defined as the number of PSTs or allergy assessments per 1000 unique patient encounters for each month, respectively. The study used interrupted time series regression to assess potential level and slope changes in allergy assessments and PSTs during the pandemic. 200 058 total inpatient encounters by 188 867 unique patients occurred during the study period. ASP performed 918 allergy assessments and 204 PSTs. The local onset of the SARS-CoV-2 pandemic during March 2020 was associated with significant level reductions in allergy assessments and PSTs. Additional responsibilities added to the ASP team during the COVID-19 pandemic limited the ability to perform core antimicrobial stewardship activities with proven patient care benefits.

Keywords: COVID-19, penicillin skin testing, antimicrobial stewardship.

INTRODUCTION

The COVID-19 pandemic has challenged healthcare personnel and antimicrobial stewardship programs (ASPs) across the globe. The current SARS-CoV-2 outbreak has highlighted numerous opportunities for ASPs to support the pandemic response including COVID-19 treatment guideline development and inpatient vaccination support, among others.¹ However, a shift in ASP focus and resource utilisation is not without consequence. Shifting ASP focus may directly affect routine stewardship activities, such as audit with feedback, handshake stewardship rounds, and conducting antimicrobial allergy assessments with penicillin skin testing (PST). Additionally, the need to reduce SARS-CoV-2 transmission and conserve personal protective equipment creates

E-mail: connor.deri@duke.edu

additional difficulty in performing such interventions (*e.g.* PSTs).

The Infectious Diseases Society of America (IDSA) suggests ASP promotion of antimicrobial allergy assessments and PST to enhance the use of first-line agents (i.e. beta-lactam antimicrobials).² Nearly 10% of inpatients report beta-lactam allergies, which often limits optimal antimicrobial selection.^{3,4} Allergy assessments and PSTs have been largely unstudied as primary ASP interventions to improve clinical outcomes associated with reported penicillin allergies. Our group recently published the impact of our Duke University Medical Center (DUMC) pharmacist-led penicillin allergy assessment program and allergy delabeling.⁵ We found temporal associations with decreased use of non-penicillin alternative antibiotics as well as high-CDI-risk antibiotics in patients with allergy assessment alone and lower hospital-acquired CDI rates in PST patients.⁵

Thus, we aimed to investigate the impact of COVID-19 on the incidence of PST and allergy assessments performed in follow-up to the previously published longitudinal analysis of a pharmacist-led allergy assessment program.

^{*}Address for correspondence: Connor R. Deri, Department of Pharmacy, Duke University Hospital, 2301 Erwin Road, Durham, NC 27710, USA.

Justin Spivey and Connor Deri contributed equally and should be considered first authors

MATERIALS AND METHODS

Data Collection and Analysis

The Antimicrobial Stewardship Evaluation Team (ASET) identifies DUMC patients for penicillin allergy assessment and PST via chart review and/or consult placed by the inpatient provider. Penicillin allergic patients populate into a shared Epic list for allergy assessment review. Clinical pharmacy interns and ASET members perform patient interviews from this list to determine eligibility and feasibility for PST. Additionally, a PST consult order was developed enabling primary providers to consult ASET team members for targeted review of patients thought to be candidates for inpatient PST. Completed allergy assessments are documented in an iVent, an Epic documentation tool, along with progress notes; PSTs are documented in a secure REDCap database in addition to the aforementioned locations. All patient encounters at DUMC from 1 January 2017 to 30 April 2021 were included for analysis. Monthly PST and allergy assessment rates were calculated during the study period. Rates were defined as the number of PSTs or allergy assessments per 1000 unique patient encounters for each month, respectively.

We used interrupted time series regression to assess potential level and slope changes in allergy assessments and PSTs during the pandemic. Separate count models were fitted for allergy assessments and penicillin skin tests, each using number of hospital encounters as an offset term to adjust for fluctuations in hospital census. Inspection of quantile-quantile plots suggested a negative binomial distribution was a reasonable assumption. Each model included terms for time, an indicator of local onset of the SARS-CoV-2 pandemic, and time since pandemic onset as suggested by Wagner et al.⁶ The pandemic onset term was used to assess level change, while the time since onset of pandemic was used to assess slope change. The model was assessed for autocorrelation by Breusch-Godfrey test. Without standardized methods for power analysis of interrupted time series regression, no formal power calculations were conducted. p < 0.05 was considered statistically significant; all tests were 2-sided.

RESULTS

From 1 January 2017 to 30 April 2021, there were 200 058 inpatient encounters by 188 867 unique patients at DUMC. During these encounters, 918 penicillin allergy assessments and 204 PSTs were performed. We did observe a modest reduction in PST volume over

time pre-COVID which approached significance but was not statistically significant (rate ratio 0.99, 95% CI 0.97-1.00, p = 0.05). The local onset of the SARS-CoV-2 pandemic in March 2020 temporally correlated with significant level reductions in both allergy assessments (rate ratio: 0.46, 95% CI: 0.29-0.73, p < 0.01) and penicillin skin tests (rate ratio: 0.37, 95% CI 0.19–0.72, p < 0.01; Figure 1). The level change associated with COVID remained significant even when accounting for the baseline trend towards fewer tests over time. However, there was no significant slope change among antibiotic allergy assessments or PSTs during the study period (p = 0.5and p = 0.56, respectively). The rate of antibiotic allergy assessments and PSTs continued below pre-pandemic levels through the remainder of the study period (March 2020 through April 2021).

DISCUSSION

A previously published analysis of pharmacist-led allergy assessment and allergy de-labelling conducted at DUMC from 2014-2020 reported a temporal association of PST with lower rates of CDI. Additionally, patients with an allergy assessment were less likely to be discharged on a high-CDI-risk antibiotic⁵ The current analysis was conducted to evaluate the impact of the SARS-CoV-2 pandemic on an active pharmacist-led allergy delabelling program. A statistically significant reduction in the rate of completed antibiotic allergy assessments and PSTs was temporally associated with the start of the SARS-CoV-2 pandemic. Although there was significant variation from month to month in procedure rate, a properly specified count model accounts for this when calculating the 95% confidence intervals and p-values. We did observe a modest reduction in PST volume over time pre-COVID. It is possible the modest trend in PST reduction over time relates to clearance of allergies among frequently admitted subjects, or to the increasing effect of outpatient PSTs. Additionally, the number of trained and available ASET personnel to perform PSTs varied throughout the study period with an ID pharmacist job vacancy from December 2019 to July 2020. Notably, the level change associated with COVID remained significant even when accounting for the baseline trend towards fewer tests over time.

Our team has been critical in supporting the generation of COVID-19 therapeutic guidelines and operational aspects of treatment across our health system. Thus, ASET pharmacist job priorities have shifted to support the creation and rapid modification of COVID-19 therapeutic guidelines, operationalisation of COVID-19 therapeutics, COVID-19 restricted

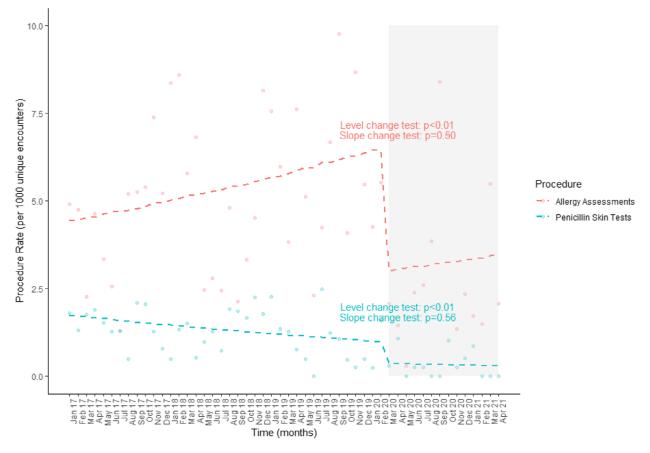


Figure 1 Poisson model of rate of allergy assessment and penicillin skin test.

antimicrobial review (e.g. remdesivir), COVID-19 vaccination campaign, establishment of a PGY2 ID pharmacy residency program, and hospital-onset CDI review in addition to routine job duties which may explain the continued below pre-pandemic rate of PSTs. As the pandemic continues, ASET job priorities include COVID-related updates and changes for the health system, which may explain why the rate of allergy assessments and PSTs has continued below pre-pandemic levels. With antimicrobial stewardship teams often being under resourced, additional responsibilities limit the ability to perform core antimicrobial stewardship activities that have proven benefit in improving patient safety.^{7,8} Although DUMC saw a reduction in the daily census during this time period (data not shown), this is unlikely to have impacted these findings through the use of the rate of change of antibiotic allergy assessments and PST per 1000 patient encounters. The patient and health system benefits of antibiotic allergy de-labelling and antimicrobial stewardship are paramount to improving patient care. Healthcare facilities should be aware of the impact of the pandemic on core functions of stewardship

programs, such as allergy assessments and PSTs, which optimize patient care and their outcomes.

ACKNOWLEDGEMENTS

No financial support provided relevant to this article.

CONFLICTS OF INTEREST STATEMENT

The authors declare that they have no conflicts of interest.

AUTHORSHIP STATEMENT

All listed authors comply with the *Journal's* authorship policy.

ETHICS STATEMENT

This study was approved by the institutional review board at DUMC with waiver of informed consent for collection of data. The waiver was granted because the study was observational, and all data could be gathered in a secure, retrospective manner without requiring any interventions on participants for study purposes.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

Supporting information

Additional supporting information may be found in the online version of this article:

Figure S1. Trend in admissions with a reported penicillin allergy from January 2017 to April 2021. Monthly admission counts are shown in blue dots.

REFERENCES

 Stevens MP, Patel PK, Nori P. Involving antimicrobial stewardship programs in COVID-19 response efforts: all hands on deck. *Infect Control Hosp Epidemiol* 2020; **41**: 744–5.

- 2 Barlam TF, Cosgrove SE, Abbo LM, MacDougall LM, Schuetz LM, Septimus LM, et al. Implementing an antibiotic stewardship program: Guidelines by the Infectious Diseases Society of America and the Society for Healthcare Epidemiology of America. *Clin Infect Dis* 2016; **62**: e51–77.
- 3 Macy E, Contreras R. Health care use and serious infection prevalence associated with penicillin "allergy" in hospitalized patients: a cohort study. J Allergy Clin Immunol 2014; 133: 790–6.
- 4 Solensky R. Hypersensitivity reactions to beta-lactam antibiotics. *Clin Rev Allergy Immunol* 2003; 24: 201–20.
- 5 Turner NA, Wrenn R, Saribbi C, Kleris R, Lugar PL, Radojicic C, et al. Evaluation of a pharmacist-led penicillin allergy assessment program and allergy Delabeling in a tertiary care hospital. *JAMA Netw Open* 2021; 3;4: e219820.
- 6 Wagner AK, Soumerai SB, Zhang F, Ross-Degnan D. Segmented regression analysis of interrupted time series studies in medication use research. J Clin Pharm Ther 2002; 27: 299–309.
- 7 Doernberg SB, Abbo LM, Burdette SD, Goodman SD, Kravitz SD, Fishman NO, et al. Essential resources and strategies for antibiotic stewardship programs in the acute care setting. *Clin Infect Dis* 2018; 67: 1168–74.
- 8 Greene MH, Nesbitt WJ, Nelson GE. Antimicrobial stewardship staffing: How much is enough? *Infect Control Hosp Epidemiol* 2020; 41: 102–12.

Received: 19 October 2021 Revised version received: 08 March 2022 Accepted: 19 March 2022