Racial differences in hospitalizations for acute cholangitis: a nationwide time trend analysis, 2008-2018

Umer Farooq, Zahid Ijaz Tarar, Diana Franco, Abdul Haseeb
Loyola Medicine/MacNeal Hospital, Berwyn, IL; University of Missouri, Columbia, MO; Loyola University Medical Center, Maywood, IL, USA

Abstract

Background The data on racial epidemiologic trends for acute cholangitis (AC) are scarce. Therefore, we conducted a longitudinal assessment of the racial breakdown of AC-related hospitalizations in the United States (US) over 11 years (2008-2018).

Methods Using the National Inpatient Sample, we retrieved adult (>18 years) patients with AC. The adjusted yearly hospitalization rate per 100,000 for each race category was calculated based on the US population estimate for July 1 of the corresponding year obtained from the US Census Bureau. We followed Healthcare Cost and Utilization Project recommendations to: (1) derive a time-interrupted trend (before and after 2015), after determining that the International Classification of Diseases coding change affected AC hospitalizations because of more specific coding in the tenth revision; and (2) generate proportionate estimates using revised trend weights.

Results A total of 321,849 patients with AC were included in the analysis. Before 2015, the overall hospitalizations (per 100,000 persons) increased from 16.03 in 2008 to 20.76 in 2014 (P<0.001). Following 2015, the overall hospitalizations increased from 14.34 in 2016 to 14.70 in 2018 (P=0.04). After Whites, Asians represented the ethnic group with the highest race-specific AC hospitalizations per 100,000 persons.

Conclusions This cohort study demonstrated an overall rising and disproportionate rate among different races for AC-related hospitalizations. Even though Asians constitute only 6.5% of the US population, they represent the ethnic minority with most hospitalizations for AC.

Keywords Cholangitis, hospitalization, ethnicity, healthcare disparities

Introduction

Acute cholangitis (AC) is characterized by an infection in the bile duct and carries high morbidity and mortality if diagnosis and treatment are delayed. Cholelithiasis is the most common precipitant factor, and its prevalence is greater in Hispanics than in other race categories in the United States (US) [1,2]. Race plays a multifactorial role in the prevalence of AC, as a result of disparities in risk factors, access to healthcare, and socioeconomic status [3]. In addition, the rapid aging of the population and the prevalence of multimorbidity have changed the epidemiology of the disease, making the updated knowledge of changing trends an essential tool for addressing healthcare discrepancies [4]. However, since the data on racial epidemiologic trends for AC are scarce, we wished to examine the race-related distribution of AC hospitalizations. Consequently, we sought to conduct a longitudinal assessment of the racial breakdown of hospitalizations for AC in the US over 11 years (2008-2018).

Materials and methods

Study design and patients

We conducted a retrospective longitudinal trend survey using the National Inpatient Sample (NIS). This database was designed...
as a stratified sample of 20% of all hospital stays in the USA. Each hospital discharge is then weighted (weight = total number of discharges from all acute care hospitals in the USA divided by the number of discharges included in the 20% sample), making it nationally representative. Using the codes of the International Classification of Diseases (ICD), Ninth Revision, and ICD, Tenth Revision for the corresponding years, we sampled every other year during the study period and included adult patients (≥18 years old) with AC (ICD-9: 576.1, ICD-10: K80.3, K83.0; detailed explanation of codes, with subterms, are provided in the Supplementary Table 1). The race variable is available within the NIS and contains a uniform coding for race and ethnicity. If the data source supplied information on race and ethnicity as separate data elements, ethnicity took precedence over race in setting the uniform values for the variable. The control population consisted of all adult hospitalizations. We followed Healthcare Cost and Utilization Project recommendations to: 1) derive a time-interrupted trend (before and after 2015), after determining that the ICD coding change affected AC hospitalizations because of more specific coding in the tenth revision; and 2) generate proportionate estimates using revised trend weights [5].

**Statistical analysis**

We used univariate logistic regression to compute un-adjusted odds ratios (ORs) for patient and hospital-level variables in the database. Multivariate regression models were constructed by including all variables that were significantly associated with the outcome on univariate analysis with a cutoff P-value of 0.2. Variables deemed clinically important to the outcome based on the literature review were included in the model, irrespective of whether they were significantly associated on univariate analysis [5]. The variables adjusted for in the regression models were: sex, age, race, Charlson Comorbidity Index score, insurance status, median household income for patients' zip codes, hospital location/region/size (beds), and teaching status. The Hosmer-Lemeshow test was used to assess the model's goodness of fit (P>0.99) [6]. The yearly hospitalization rate per 100,000 for each race category was calculated based on the US population estimate for July 1 of the corresponding year obtained from the US Census Bureau. The linear trend for AC hospitalization across years was tested using the Mantel-Haenszel test of linear trend. Adjustment for multiple testing was achieved using the Hochberg method. We used Stata software, version 14.2, to perform analyses, with a 2-sided P<0.05 considered as statistically significant. The Institutional Review Board of Loyola University Medical Center authorized this study and deemed the research project exempt from approval because it was a retrospective review of already collected and de-identified data.

**Missing data**

Most of the variables had a very low percentage of missing data (<0.05%), except for hospital size (0.52%), insurance (0.19%), and median income in the patient's zip code (2.32%) (Supplementary Table 2). To test whether missing data could introduce bias into the study, we assumed that data were not missing at random and applied a multivariate imputation by chained equations (MICE) method estimated from sequential multivariate models with fully conditional specifications [7]. Overall, 10 imputed datasets were constructed, using information from all covariates used in the regression models and other covariates in the database without missing information. Results with and without imputation were not meaningfully different. Thus, results without imputation were reported.

**Results**

A total of 321,849 patients with AC were included in the analysis (Fig. 1). Men had more hospitalizations than women over the entire cohort (50.85-54.93% vs. 45.07-49.15%; Table 1). Mean hospital length of stay decreased from 7.89 days in 2008 to 7.28 days in 2014 (P<0.001), but the trend stabilized after 2015 (P=0.57). The Hosmer-Lemeshow test resulted in a non-significant statistic with P-value of >0.99. The hospitalization rates for different races in 2008 were (in descending order): Asian 18.46 (95% confidence interval [CI] 13.07-23.86), White 14.34 (95%CI 12.61-16.07), Hispanic 8.54 (95%CI 6.66-10.42), and Black 7.45 (95%CI 6.08-8.82) (P<0.001) (Fig. 2). In 2014, the rates were: White 21.56 (95%CI 20.32-22.81), Asian 17.53 (95%CI 14.99-20.06), Black 13.55 (95%CI 12.29-14.81), Hispanic 12.71 (95%CI 11.54-13.88) (P<0.001). Rates in 2018 were: White 15.72 (95%CI 14.69-16.76), Asian 11.38 (95%CI 9.65-13.11), Black 11.11 (95%CI 9.99-12.22), and Hispanic 9.63 (95%CI 8.71-10.55) (P<0.001).

**Time trend analysis**

Before 2015, the overall hospitalizations (per 100,000 persons) increased from 16.03 (95%CI 14.49-17.65) in 2008 to 20.76 (95%CI 19.77-21.75) in 2014 (P<0.001). Trends for each racial category from 2008 to 2014 were found to
be 14.34 to 21.56 in Whites, 7.45 to 13.55 in Blacks, 8.54 to 12.71 in Hispanics, and 18.46 to 17.53 in Asians (Fig. 2).

Following 2015, the overall hospitalizations increased from 14.34 (95%CI 13.56-15.12) in 2016 to 14.70 (95%CI 13.85-15.55) in 2018 (P=0.04). Significant racial trends from 2016 to 2018 were; 15.10 to 15.72 in Whites, 10.19 to 11.11 in Blacks, 8.62 to 9.63 in Hispanics, and 10.81 to 11.38 in Asians (P values <0.001).

Discussion

This cohort study demonstrated a disproportionate AC hospitalization rate among different races. Asians represent approximately 2-3% of patients hospitalized for any cause but were the ethnic minority with the highest race-specific AC hospitalization per 100,000 persons. These findings are in accordance with a small non-US study demonstrating

Table 1 Characteristics of patients hospitalized with acute cholangitis 2008-2018

| Outcomes                                      | Year         | 2008 | 2010 | 2012 | 2014 | P-value<sup>ab</sup> | 2016 | 2018 | P-value<sup>ab</sup> |
|-----------------------------------------------|--------------|------|------|------|------|-----------------------|------|------|-----------------------|
| Acute cholangitis                             |              |      |      |      |      |                       |      |      |                       |
| No. of hospitalizations                       |              | 48,744 | 54,767 | 57,910 | 66,085 | N/A                   | 46,319 | 48,024 | N/A                   |
| Hospitalizations per 100,000 persons          |              | 16.03 | 17.70 | 18.45 | 20.76 | <0.001                | 14.34 | 14.70 | 0.04                  |
| Sex, %                                        |              |      |      |      |      |                       |      |      |                       |
| Male                                          |              | 50.85 | 52.04 | 53.01 | 52.01 | 0.05                  | 54.85 | 54.93 | 0.62                  |
| Female                                        |              | 49.15 | 47.96 | 46.99 | 47.99 | 0.06                  | 45.15 | 45.07 | 0.77                  |
| Age, mean, y                                  |              | 65.04 | 65.09 | 65.40 | 65.16 | 0.67                  | 63.32 | 63.65 | 0.37                  |
| Length of hospital stay, mean, d              |              | 7.89  | 7.62  | 7.29  | 7.28  | <0.001                | 7.32  | 7.17  | 0.57                  |
| Ethnic distribution of all adult patients     |              |      |      |      |      |                       |      |      |                       |
| hospitalized for any diagnosis, %             | White        | 54.49 | 60.36 | 65.09 | 64.84 | <0.001                | 64.88 | 65.25 | 0.96                  |
|                                               | Black        | 10.29 | 14.06 | 13.89 | 14.01 | <0.001                | 14.48 | 14.72 | 0.46                  |
|                                               | Hispanic     | 7.88  | 9.31  | 9.72  | 10.11 | <0.001                | 10.37 | 11.22 | 0.04                  |
|                                               | Asians       | 2.04  | 2.06  | 2.25  | 2.42  | 0.04                  | 2.58  | 2.72  | 0.38                  |
|                                               | Others       | 26.30 | 14.21 | 9.05  | 8.62  | 0.64                  | 7.69  | 6.09  | 0.33                  |

<sup>a</sup>P-value adjusted for sex, age, Charlson Comorbidity Index score, insurance status, median household income for patients’ zip codes, hospital location/region/bedside, and teaching status

<sup>b</sup>Linear P trend values
that Asians have a higher AC prevalence than other ethnic populations [8]. Social determinants of healthcare, including socioeconomic status, living conditions and inequalities in access to healthcare, can explain the heterogeneity of the AC hospitalization rate [9,10]. Additional research is warranted to establish whether this reflects disparities in the prevalence of risk factors for AC, or whether race-specific genomics and eco-social factors also influence the disease course.

We also demonstrated that the hospitalization trend of AC shows a rise in the US. The prevalence of gallbladder disease is surging globally, as reported in studies by Urbach et al and Huang et al [11,12]. In addition to greater vigilance and advanced diagnosis strategies, the increasing prevalence of risk factors for cholelithiasis, including obesity, is also instrumental in the ever-changing trends. The specificity of ICD-10 coding resulted in better capturing and an apparent sharp decrease in the hospitalization rate of AC after 2015. Before the ICD coding change, trends were obtained uniformly by the ICD-9 coding system and represent true hospitalization rate variations. Limited available literature described ethnic AC incidence as a percentage among all AC patients, but these represent raw numbers [13,14]. The total population at risk is an essential parameter of incidence estimation, and we calculated the hospitalization rate per 100,000 persons of each race, which delineates the racial disease distribution more precisely.

A limitation of this survey is the likelihood of coding aberrations stemming from the reliance of the NIS on ICD codes. We relied on multivariate regression models to control for confounders, but residual confounding can still exist. We applied the Charlson Comorbidity Index for comorbidity burden and controlled for the various patient and hospital-level characteristics. However, the present results indicate that, even though Asians constitute only 6.5% of the US population, they represent the ethnic minority with most AC-related hospitalizations. Therefore, nationwide strategies are needed to identify the reasons for the variabilities and to halt this continuing disproportionate trend [15].

In conclusion, this cohort study demonstrated an overall rising and disproportionate hospitalization rate among different races for AC-related hospitalizations. Even though Asians constitute only 6.5% of the US population, they represent the ethnic minority with most AC-related hospitalizations.

Acknowledgment

The authors would like to thank Lili Wang (Biostatistician) for helping with the statistical analysis.

References

1. Kimura Y, Takada T, Kawarada Y, et al. Definitions, pathophysiology, and epidemiology of acute cholangitis and cholecystitis: Tokyo Guidelines. J Hepatobiliary Pancreat Surg 2007;14:15-26.
2. Shaffer EA. Gallstone disease: Epidemiology of gallbladder stone disease. Best Pract Res Clin Gastroenterol 2006;20:981-996.
3. Manuel JI. Racial/ethnic and gender disparities in health care use and access. Health Serv Res 2018;53:1407-1429.
4. van Oostrom SH, Gijsen R, Stirbu I, et al. Time trends in prevalence of chronic diseases and multimorbidity not only due to aging: data from general practices and health surveys. PLoS One 2016;11:e0160264.
5. Agency for Healthcare Research and Quality. ICD-10-CM/PCS Resources. Available from: https://www.hcup-us.ahrq.gov/datainnovations/icd10_resources.jsp [Accessed 21 June 2022].
6. Hosmer DW, Lemesbow S. Goodness of fit tests for the multiple logistic regression model. Commun Stat Theory Methods 1980;9:1043-1069.
7. White IR, Royston P, Wood AM. Multiple imputation using chained equations: Issues and guidance for practice. Stat Med 2011;30:377-399.
8. Allam H, Al Dosouky M, Abdelaziem S, Hashish M, Farooq A, El Nagar A. Acute calculous cholangitis in a diverse multiethnic population. Int J Surg Open 2016;2:22-25.
9. Riley WJ. Health disparities: gaps in access, quality and affordability of medical care. Trans Am Clin Climatol Assoc 2012;123:167-172.
10. Fleskerud JH, DeLilly CR. Social determinants of health status. Issues Ment Health Nurs 2012;33:494-497.
11. Urbach DR, Stukel TA. Rate of elective cholecystectomy and the incidence of severe gallstone disease. CMAJ 2005;172:1015-1019.
12. Huang J, Chang CH, Wang JL, et al. Nationwide epidemiological study of severe gallstone disease in Taiwan. BMC Gastroenterol 2009;9:63.
13. McNabb-Baltar J, Trinh QD, Barkun AN. Disparities in outcomes following admission for cholangitis. PLoS One 2013;8:e59487.
14. Patel N, Hashemipour R, Ahlawat S. Racial disparities in rates of therapeutic intervention during hospitalizations for acute cholangitis: a national survey. Am J Gastroenterol 2018;113:S430-S431.
15. United States Census Bureau. Available from: https://www.census.gov/ [Accessed 21 June 2022].
### Supplementary Table 1 International Classification of Diseases (ICD) codes

| Disease/Procedure                                           | ICD-9/10-CM codes |
|-------------------------------------------------------------|-------------------|
| Calculus of bile duct with cholangitis, unspecified, without obstruction | K80.30            |
| Calculus of bile duct with cholangitis, unspecified, with obstruction | K80.31            |
| Calculus of bile duct with acute cholangitis without obstruction | K80.32            |
| Calculus of bile duct with acute cholangitis with obstruction | K80.33            |
| Calculus of bile duct with chronic cholangitis without obstruction | K80.34            |
| Calculus of bile duct with chronic cholangitis with obstruction | K80.35            |
| Calculus of bile duct with acute and chronic cholangitis without obstruction | K80.36            |
| Calculus of bile duct with acute and chronic cholangitis with obstruction | K80.37            |
| Other type of cholangitis                                   | K83.09            |
| Cholangitis, not otherwise specified                        | 576.1             |

### Supplementary Table 2 Missing data

| Variables                              | Data missing (%) |
|----------------------------------------|------------------|
| Age (y)                                 | 0.02             |
| Sex                                    | 0.03             |
| Charlson comorbidity index             | 0.00             |
| Median income in patient’s zip code    | 2.32             |
| Hospital region                        | 0.00             |
| Hospital size (beds)                   | 0.52             |
| Hospital location/teaching status      | 0.00             |
| Insurance                              | 0.19             |