Ethnic Disparities in Early-Onset Gastric Cancer Persist across Rural–Urban Geographies

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ABSTRACT

Background: The incidence of noncardia gastric cancer is increasing in adults ages less than 50 years old. Early-onset gastric cancer (EOGC) is characterized by ethnic disparities occurring more in Hispanic persons than non-Hispanic persons. It is unknown whether rural–urban disparities exist in EOGC and if this intersects with ethnic disparities.

Methods: We utilized the Surveillance Epidemiology and End Results 17 Census Tract-level Socioeconomic Status and Rurality Database from 2006 to 2018 to calculate incidence rates and incidence rate ratios of EOGC among Hispanic and non-Hispanic persons by census tract rural–urban location, age, gender, persistent poverty, and stage of disease. We used the Tiwari Method to estimate incidence rate ratios with 95% confidence intervals (CI).

Results: Hispanic persons had higher incidence rates of EOGC compared with non-Hispanic persons in both rural [incident rate ratios (IRR), 2.12; 95% confidence interval (CI), 1.64–2.73] and urban census tracts (IRR, 2.03; 95% CI, 1.91–2.16). Similar findings were seen when comparing Hispanic to non-Hispanic persons in rural and urban census tracts by age, stage of disease, and persistent poverty.

Conclusions: Higher incidence rates of EOGC among Hispanic persons persist across rural–urban locations. Further research is needed to understand the etiology of this elevated risk in young Hispanics and interventions that may help to modify their outcome.

Impact: While other cancers have ethnic disparities which may differ by rural–urban location, the ethnic disparity in EOGC among Hispanic and non-Hispanic persons does not differ by rural–urban residence.

Introduction

Despite an overall decline in incidence and mortality rates of gastric cancer in the United States, recent studies report increases of non-cardia gastric cancer among younger adults (age <50 years, hereafter early-onset gastric cancer; EOGC; ref. 1). Subsite-specific trends have been reported in the United States with an increase in incidence rates of EOGC among younger persons (2). This rise in EOGC has been noted among both Hispanic and non-Hispanic White persons, notably in areas with less than 20% prevalence of poverty (2).

In recent years, ethnic disparities among persons with EOGC have been noted (3). Compared with non-Hispanic persons, Hispanic persons have higher incidence rates of EOGC, are more likely to be diagnosed with EOGC at a younger age, and have more aggressive grade tumors (3). The reasons for these disparities are unclear. First, socioeconomic status (SES) may influence EOGC incidence because persons with lower SES often have higher incidence rates of non-cardia gastric cancer (4). Second, ethnic disparities in EOGC may also be partially attributed to the higher prevalence of *Helicobacter pylori* (*H. pylori*) among Hispanic persons (2, 5–7). Third, among other cancer types, such as lung, cervical, and colorectal cancers, disparities in incidence rates have also been due to differences in rural and urban living (8, 9). For example, non-Hispanic white women in rural settings had higher incidence rates for all stages of cervical cancer compared with those in urban settings (10). While there are known ethnic disparities in EOGC, it is unknown whether rural–urban disparities exist in EOGC and if this intersects with racial and ethnic disparities given the majority of Hispanic persons reside in urban areas.

To address these gaps, we aimed to estimate the incidence rates of EOGC among Hispanic and non-Hispanics living in rural versus urban census tracts by gender, age, poverty level, and stage of disease. We used population-based data from Surveillance, Epidemiology, and End Results (SEER) database to estimate incidence rates of EOGC among Hispanics and non-Hispanics living in rural versus urban census tracts. We hypothesized that the incidence rates of EOGC are higher among Hispanics living in urban settings given the majority of Hispanic persons reside in urban areas.

Materials and Methods

Study population

For this study we used population-based data from SEER 17 census tract-level SES and rurality database from 2006 to 2018. This specialized SEER database has five census tract-level attributes: two SES, two rurality variables, and persistent poverty (SEER Datasets and Software, RRID:SCR_003293). The registry collects data on patient demographics and clinical information of cancers diagnosed from 2006 to 2018 among the 17 SEER registry sites. SEER 17 registries cover approximately 27% of the U.S. population and include Atlanta, Greater California, Connecticut, rural Georgia, greater Georgia, Hawaii, Iowa, Kentucky, Los Angeles, Louisiana, New Jersey, New Mexico, San Francisco-Oakland, San Jose-Monterey, Seattle-Puget Sound, and Utah (SEER Datasets and Software, RRID:SCR_003293). Persons were included if they were diagnosed with incident noncardia gastric cancer and an International Classification of Diseases for Oncology, third edition (ICD-O–3) histology code for adenocarcinoma, linitis, intestinal, diffuse, signet, as well as those missing histology information. Our study was limited to persons ages 20 to 49 years who identified as

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Hispanic or non-Hispanic based on the North American Association of Central Cancer Registries Gold Certification standards (NAACR) Hispanic Identification Algorithm (NHIA). Persons with unknown race were excluded.

Covariates

The following covariates were included in analysis: age, stage of EOGC at diagnosis, persistent poverty, gender, and census-tract level rurality variable. Age groups were divided into 20 to 39 and 40 to 49 to ensure adequate counts to maintain confidentiality. Stage at diagnosis was based on the NCI's SEER summary stage, defined as in situ/local/regional and distant. *In situ*, local, and regional disease were combined to maintain confidentiality due to lower case counts. The persistent poverty variable identifies census tracts as being persistently poor if 20% or more of the population has lived below the poverty level for a period spanning about 30 years based on 1990, 2000 decennial censuses, and 2007 to 2011 and 2015 to 2019 American Community Survey 5-year estimates (SEER, RRID:SCR_006902). This variable was created by the NCI in collaboration with the United States Department of Agriculture, Economic Research Service. Census-level rurality variable was based on the U.S. Department of Agriculture Rural Urban Commuting Areas (RUCA) with two categories: Urban area commuting focused (codes 1.0, 1.1, 2.0, 2.1, 3.0, 4.1, 5.1, 7.1, 8.1, and 10.1) and not urban area commuting focused (all other codes) (11).

Incidence rates and rate ratios

We estimated age-adjusted (to the 2000 U.S. standard population) incidence rates (IR) per 100,000 persons for Hispanic and non-Hispanic persons in both rural and urban census tracts using SEER*-Stat version 8.4.0 (SEER Datasets and Software, RRID:SCR_003293). Incidence rate ratios (IRRs) comparing incidence rates in Hispanic to non-Hispanic persons with 95% confidence intervals (CI) were calculated using the Tiwari method which uses gamma approximations to compare age-adjusted rates (12). Separately for urban and rural census tracts, IRs and IRRs for Hispanic and non-Hispanic persons were calculated overall and by age group (20–39, 40–49), sex, persistent poverty, and stage of disease (*in situ*/local/regional, distant, unknown). This study was considered exempt by the Institutional Review Board at the University of Texas Southwestern Medical Center (Dallas, TX).

Data availability

The data analyzed in this study are available from the SEER 17 census tract-level socioeconomic status and rurality database, which is available from the NCI (https://seer.cancer.gov/data/access.html; SEER, RRID:SCR_006902).

Results

There were 43,953 persons diagnosed with noncardia gastric cancer from 2006 to 2018. Of these, 4,690 (10.7%) were at ages 20 to 49 with 4,356 (92.9%) in urban census tracts and 334 (7.1%) in rural census tracts. In rural census tracts, almost 75% of persons are non-Hispanic; however, this distribution changes in urban census tracts, where almost 40% of persons are Hispanic (**Table 1**). Furthermore, the majority of cases in both rural and urban census tracts occur in persons ages 40 to 49. Demographic characteristics are further described in **Table 1**.

As compared with non-Hispanic persons, Hispanic persons had an increased risk of EOGC but the rates were similar in both rural (IRR, 2.12; 95% CI, 1.64–2.73) and urban census tracts (IRR, 2.03; 95% CI, 1.91–2.16). Similar findings were seen when comparing Hispanic to non-Hispanic persons in rural and urban census tracts by age, sex, stage of disease, and persistent poverty (**Table 2**; **Fig. 1**). For example, Hispanic persons in both rural and urban census tracts had an increased risk for distant stage of disease at the time of diagnosis as compared with non-Hispanic persons (rural IRR, 3.02; 95% CI, 1.93–4.61; urban IRR, 2.55; 95% CI, 2.30–2.83). Hispanic persons ages 20 to 49 with persistent poverty had an increased risk of EOGC in urban census tracts (IRR, 1.34; 95% CI, 1.14–1.59); while this similar trend was seen in rural census tracts, this did not reach statistical significance (IRR, 1.12; 95% CI, 0.60–1.94; **Table 2**).

Discussion

In this population-based study, we found higher IRRs of EOGC when comparing Hispanic persons with non-Hispanic persons overall, by age, gender, persistent poverty, and stage in both rural and urban census tracts. Persistent poverty appeared to be the only equalizer as there was a minimal difference in incidence rates of EOGC among 20

Table 1. Demographic characteristics of Hispanics and non-Hispanics in rural and urban census tracts[a] with EOGC from 2006 to 2018 based on SEER17 data.

	Rural		Urban	
	Hispanic ***N*** **= 85 (25.4%)**	**Non-Hispanic** ***N*** **= 249 (74.6%)**	**Hispanic** ***N*** **= 1,698 (39%)**	**Non-Hispanic** ***N*** **= 2,658 (61%)**
Gender				
Female	35 (41.2%)	126 (50.6%)	838 (49.4%)	1,392 (52.4%)
Male	50 (58.8%)	123 (49.4%)	860 (50.6%)	1,266 (47.6%)
Age				
20–39	30 (35.3%)	65 (26.1%)	633 (37.3%)	763 (28.7%)
40–49	55 (64.7%)	184 (73.9%)	1,065 (62.7%)	1,895 (71.3%)
Persistent poverty				
Ages 20–39	+	23 (9.2%)	110 (6.5%)	95 (3.6%)
Ages 40–49	+	47 (18.9%)	190 (11.2%)	190 (7.1%)
Stage				
In situ/localized/regional	45 (52.9%)	152 (61.0%)	817 (48.1%)	1,527 (57.4%)
Distant	34 (40%)	69 (27.7%)	662 (39.0%)	812 (30.5%)
Unknown	+	28 (11.2%)	219 (12.9%)	319 (12.0%)

[a]Unknown census tract: 42 Hispanics, 127 Non-Hispanics; + cell counts suppressed per SEER reporting guidelines for counts <11.

Table 2. Age-adjusted IRs and IRR of EOGC among Hispanics and non-Hispanics in rural and urban census tracts by gender, age, persistent poverty, and stage of disease from 2006 to 2018 based on SEER17 data.

	Rural			Urban		
	Hispanic IR	Non-Hispanic IR	IRR[a]	Hispanic IR	Non-Hispanic IR	IRR[a]
All IRs	1.44 (1.15–1.78)	0.68 (0.6–0.77)	2.12 (1.64–2.73)	1.75 (1.66–1.83)	0.86 (0.83–0.89)	2.03 (1.91–2.16)
Gender						
Male	1.50 (1.10–2.00)	0.70 (0.50–0.80)	2.35 (1.65–3.29)	1.70 (1.60–1.90)	0.80 (0.80–0.90)	2.11 (1.94–2.31)
Female	1.30 (0.90–1.80)	0.70 (0.60–0.80)	1.88 (1.25–2.75)	1.70 (1.60–1.90)	0.90 (0.80–0.90)	1.96 (1.80–2.14)
Age						
20–39	0.68 (0.46–0.97)	0.30(0.23–0.38)	2.28 (1.43–3.57)	0.87 (0.81–0.95)	0.40 (0.37–0.43)	2.44 (1.97–2.44)
40–49	2.84 (2.14–3.69)	1.38 (1.18–1.59)	2.06 (1.50–2.80)	3.35 (3.15–3.55)	1.70 (1.63–1.78)	1.97 (1.82–2.12)
Persistent poverty						
Ages 20–49	1.1 (0.63–1.78)	0.99 (0.77–1.25)	1.12 (0.60–1.94)	2.08 (1.85–2.33)	1.55 (1.37–1.74)	1.34 (1.14–1.59)
Ages 20–39	0.54 (0.20–1.16)	0.54 (0.34–0.80)	1.00 (0.33–2.50)	0.94 (0.77–1.14)	0.75 (0.60–0.92)	1.26 (0.94–1.68)
Ages 40–49	2.14 (1.02–3.93)	1.81 (1.33–2.41)	1.18 (0.53–2.37)	4.16 (3.59–4.79)	3.01 (2.59–3.47)	1.38 (1.12–1.70)
Stage						
In situ/Localized/Regional	0.77 (0.56–1.03)	0.41 (0.35–0.49)	1.86 (1.30–2.60)	0.85 (0.79–0.91)	0.49 (0.47–0.52)	1.73 (1.59–1.89)
Distant	0.57 (0.39–0.79)	0.19 (0.15–0.24)	3.02 (1.93–4.61)	0.67 (0.62–0.72)	0.26 (0.25–0.28)	2.55 (2.30–2.83)

[a]Comparing Hispanic IR with non-Hispanic IR.

to 39 years old Hispanic and non-Hispanic persons in rural census tracts. However, these rates then increased as both ethnic groups continued to age which may signal a component of cumulative risk over time in persistent poverty census tracts. Although Hispanic persons account for a small percentage of the population in rural census tracts, our study found that there were marked disparities in incidence rates of EOGC among Hispanics and non-Hispanics, but these disparities did not differ by rural–urban locations.

Studies of other cancer types, such as lung and colorectal cancer, have reported higher incidence rates across gender and ethnic groups in rural settings related in part to higher prevalence of poverty and modifiable risk factors such as smoking (8, 13). However, our study found that disparities in EOGC did not differ by rural–urban locations, even after evaluating for persistent poverty among rural–urban locations. This increased risk of EOGC among Hispanic persons may be due to both modifiable (obesity, *H.pylori)* and non-modifiable risk factors (genetic risk, socioeconomic status).

First, the prevalence of obesity among Hispanic persons is higher than non-Hispanic and obesity is a risk factor for the development of noncardia gastric cancer (14, 15). While studies have found that many Hispanic persons often immigrate to the United States at a healthy weight, the change in their lifestyle and access to both healthy foods and safe physical activities puts them at risk for the development of obesity in the United States. Furthermore, Hispanic Americans are 1.2 times more likely to be

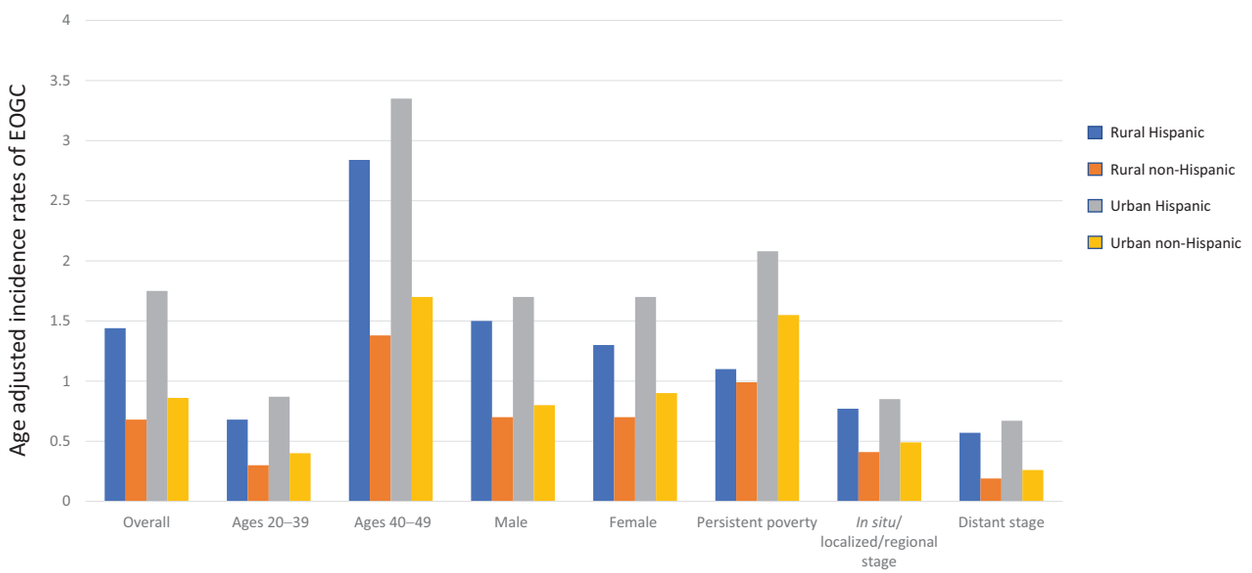

Figure 1.
Early-onset gastric cancer incidence rates, 2006 to 2018, 17 SEER registry sites.

obese than non-Hispanics and this rate was even higher among Hispanic American children (16). While the pathway linking obesity to noncardia gastric cancer has not been completely elucidated, early adulthood obesity has been linked to an increased risk of gastric cancer and may partially explain the elevated risk among young Hispanics in our study (17).

Second, both lower socioeconomic status and *H. pylori* may also contribute to the increased risk of EOGC among Hispanics. Prior studies have found higher overall incidence rates among Hispanic persons who have lower socioeconomic status and reside in ethnic enclaves (4, 18). These higher incidence rates have also been partially attributed to the higher prevalence of *H. pylori* infection, which increases the risk of developing noncardia gastric cancer (19, 20). Common features among Hispanic enclaves in the United States, such as higher household crowding, lower education level, and lower socioeconomic status are also risk factors associated with *H. pylori* infection (21, 22). Despite the overall incidence of *H. pylori* declining in the United States, disparities persist with higher rates of *H. pylori* in Hispanics (23). Specifically, the strain CagA-positive *H. pylori*, which has a higher risk of gastric cancer, has been noted to have a higher prevalence among Hispanics compared with whites (23, 24). This strain specific characteristic may contribute to the ethnic disparities noted in our study.

Although EOGC is a multifactorial disease with environmental and hereditary risk factors, studies suggest that genetics may play a larger role in pathogenesis than environmental exposures, which may help explain the persistence of higher incidence rates among Hispanics across location (25). When compared with persons diagnosed with noncardia gastric cancer at older ages, EOGC is known to have differences at a molecular genetic level, such as germline *CDH1* mutations. *CDH1* mutations are a cause of hereditary diffuse gastric cancer syndrome but were also found in Hispanic/Latinos with gastric cancer in the absence of family history (25). It is unclear what the exact mechanism of carcinogenesis is among Hispanics with EOGC but future studies should explore whether a distinct molecular profile is found in EOGC.

We acknowledge limitations to our study. First, census tracts are derived from address at diagnosis and may not be indicative of prior residence. Second, SEER does not have individual data on environmental exposures such as *H. pylori* or tobacco use. Third, there is the possibility of misclassification of ethnicity. Despite limitations, this is the first study to use census level rural–urban data to understand disparities in the incidence of EOGC among Hispanic and non-Hispanic persons.

In conclusion, the higher incidence rates of EOGC among Hispanic persons persist across rural–urban locations. Further studies are needed to determine factors contributing to disparities among Hispanic and non-Hispanic persons with EOGC and interventions that may mitigate these risks.

Authors' Disclosures

S.L. Pruitt reports personal fees from Pfizer outside the submitted work. C.C. Murphy reports personal fees from Freenome outside the submitted work. No disclosures were reported by the other authors.

Authors' Contributions

M. Narasimman: Data curation, investigation, methodology, writing–original draft, writing–review and editing. **S.L. Pruitt:** Writing–review and editing. **C.C. Murphy:** Writing–review and editing. **A.G. Singal:** Writing–review and editing. **A. Tavakkoli:** Conceptualization, resources, data curation, supervision, investigation, methodology, writing–review and editing.

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