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An Investigation into the Recent Increase in Gastric Cancer in the USA

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Abstract

Background—The USA has among the lowest gastric cancer incidence rates worldwide.

Aim—To investigate whether increasing immigration from high cancer incidence countries has altered the GC incidence in a large US metropolitan area.

Methods—This was a retrospective cohort study among an underprivileged, multiethnic population in Texas. Gastric cancer cases diagnosed during 2005–2015 were identified using the cancer registry of the public medical care system for Harris County. All cases were histologically confirmed; demographic and clinical data were obtained from review of electronic medical records. Census data were used to determine the distribution of the adult county population by race/ethnicity and age. Two time periods (2005–2009 and 2010–2015) were studied to correspond with census reporting intervals.

Results—In total, 299 cases were included: average age 55 years, 59% males and 63% Hispanics (predominantly recent immigrants of Central-American origin). The gastric cancer incidence remained stable among non-Hispanic Whites and Blacks but increased significantly among Hispanics (from 10 to 17 cases/100,000 persons/year, RR = 2.0, 95% CI 1.4–2.5, $p = 0.001$). Among Hispanics, gastric cancer incidence rose significantly among persons aged 40–59 years and 60 years and was likely to be at advanced stage at the time of diagnosis even in the younger age population.

Conclusion—Gastric cancer incidence significantly increased among Hispanics residing in Houston resulting in changes in gastric cancer incidence becoming more unevenly experienced across the US population. Consideration should be given to gastric cancer preventive efforts, especially among immigrant populations from high gastric cancer risk countries.

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Author's contributions MB contributed to study conception, interpretation of results, manuscript writing and editing. RG contributed to data collection; AS contributed to data collection; DYG contributed to interpretation of results and manuscript editing; HM contributed to data analysis, interpretation, and manuscript editing. All authors approved the final draft submitted.

Compliance with ethical standards

Conflict of interest Dr. Graham is a consultant for RedHill Biopharma regarding novel *H. pylori* therapies and has received research support for culture of *Helicobacter pylori* and is the PI of an international study of the use of antimycobacterial therapy for Crohn's disease. He is also a consultant for BioGaia in relation to probiotic therapy for *H. pylori* infection and for Takeda in relation to *H. pylori* therapies. The other authors have nothing to disclose.

Keywords

Gastric cancer; Incidence rate; Race/ethnicity; Immigration; Hispanic; Cancer prevention

Introduction

Gastric cancer incidence has declined worldwide over the past century [1]. The pattern primarily reflects a reduction in the non-cardia subtype of gastric cancer and has been attributed mainly to the decreased prevalence of *Helicobacter pylori* (*H. pylori*) infection as well as technological advances in food storage and improved diets [2]. Nevertheless, gastric cancer remains a lethal disease and is the third leading cause of cancer-related death [3]. Within the USA, gastric cancer is associated with a dismal 26% 5-year survival rate, largely because it is typically detected when it is at an advanced stage [4].

The USA has among the lowest gastric cancer incidence rates worldwide (7.4/100,000 persons/year) while Eastern Asia, Eastern Europe, Central and South America have the highest (24.2, 13.5, and 10.3/100,000/year, respectively) [1]. Within the USA, however, there are substantial ethnic/racial disparities [5–7] as gastric cancer incidence is nearly double among Hispanics, Asians/Pacific Islanders, and Blacks (age standardized incidence rates [ASIR] 10.5, 10.6, 10.2 per 100,000/year, respectively, over 2000–2014) compared to non-Hispanic Whites (age standardized incidence rate [ASIR] 5.7/100,000/year) [8]. Studies that have examined gastric cancer by anatomic subtype have confirmed that it is specifically the non-cardia subtype that is disproportionately higher among non-White populations [6, 7].

Two separate analyses of gastric cancer cases identified in the Surveillance, Epidemiology, and End Results (SEER) registry between 1977 and 2006 uncovered an increase in non-cardia gastric cancer incidence among Whites aged 25–39 years and corpus cancers among Whites aged 40–59 years and Blacks in all age groups [9, 10]. While limitations in SEER data gathered over that time period prevented stratified analysis by ethnicity vis-a-vis Hispanic heritage in the overall study population, a more recent analysis of gastric cancer cases (that did not distinguish between cardia and non-cardia subtypes) identified in the SEER registry between 1992 and 2011, observed a significant rise in overall gastric cancer incidence specifically among Hispanic males aged 20–49 years [11]. If there is indeed an increase in gastric cancer concentrated mainly among persons of Hispanic ethnicity, it would exacerbate already existing racial/ethnic disparities.

We undertook this study to evaluate racial/ethnic trends in non-cardia cancer incidence between 2005 and 2015 in the Harris Health System (Harris County, Texas). The Harris Health System is the second largest county-funded medical system in the USA and provides medical care to a large economically disadvantaged and ethnically diverse urban population. The current study aimed to examine how noncardia gastric cancer incidence has changed over a 10-year period by race/ethnicity and age.

Methods

Data Sources

This was a retrospective cohort study conducted from January 1, 2005, to March 31, 2015, among adults 18 years and older newly diagnosed with non-cardia gastric adenocarcinoma within the Harris Health System (HHS). The HHS is a county-based public medical care system that serves the indigent residents of Harris County, TX, irrespective of immigration status and includes two county hospitals—Ben Taub General Hospital and Lyndon B. Johnson Hospital— and twenty-four county-funded outpatient centers. Data were obtained from the internal cancer registry, established in 1997, that includes cancer cases diagnosed across HHS. The Institutional Review Board of Baylor College of Medicine approved current study.

Patients are automatically entered into the Harris Health internal cancer registry upon diagnosis or initial treatment of a newly found incident cancer. Data from the registry were used for subsequent submission of reportable cancers to the Surveillance, Epidemiology, and End Results (SEER) database.

Study Cases

Primary gastric adenocarcinoma cases were identified using ICD-O-3 codes and SEER Site Recodes (81403, 84903, 81453, 81443, 82113, 82102, 84803, 80103, 85603). All gastric adenocarcinoma cases were confirmed by manual review of histology, endoscopic, and surgical reports. Cardia cancer cases were excluded; only non-cardia cancers were included in our patient cohort. Cardia cancer was defined as adenocarcinoma arising from the gastroesophageal junction based on Siewert's classification [12]. Based on this classification, cancers extending up to 5 cm into the stomach from the gastroesophageal (GE) junction are considered cardia/GE junction gastric cancers. Non-cardia gastric cancer was defined as an adenocarcinoma arising from the gastric fundus, body, antrum, pylorus, lesser curve, or greater curve. In cases of "overlapping lesion" and "stomach NOS," a manual review of endoscopy and/or surgical report was performed. Those with involvement of the cardia were classified as cardia gastric cancer, and those cases were excluded from our patient cohort.

Study Variables

Demographic data and cancer-related information were obtained from the cancer registry and confirmed by manual review of the medical records. Tumor location, grade, and stage were collected for each case. Race/ethnicity was classified as non-Hispanic White, non-Hispanic Black, Hispanic, and other (e.g., American Indian/Aleutian, Eskimo; Chinese; Filipino; Korean; Vietnamese; South Asian [Indian/Pakistani]; other Asian including Asian/Oriental/NOS; Pacific Islander NOS). Place of birth was derived using demographic data from electronic medical records and was classified as born within or outside the USA.

Statistical Analysis

We classified the study periods into two time periods: the first from January 1, 2005, to December 31, 2009, and the second from January 1, 2010, to March 31, 2015. We used

county-level census data for each study period to identify the distribution of the adult population based on race/ethnicity and age. We calculated age-adjusted and age-specific incidence rates of gastric cancer stratified by race/ethnicity for each study period. Rate ratios were used to compare the incidence rates between study periods. All statistical testing was at the level of significance $P < 0.05$. SAS program version 9.3 (SAS Institute Inc., Cary, NC, USA) was used for statistical analyses.

In the current study, we classified race/ethnicity into 3 categories—White, Black, and Hispanic. We excluded other races/ethnic groups because the small sample sizes could potentially alter the accuracy of the incidence calculations. The population of Harris County derived from census data served as the denominator. The incidence rate was calculated as per 100,000 persons/year.

All co-authors had access to the study data, reviewed, and approved the final manuscript.

Results

Description of the Study Cases

We identified 397 cases of newly diagnosed primary gastric adenocarcinoma in the HHS Cancer Registry during the study period 2005–2015. After excluding 98 cases of cardia cancer, a total of 299 cases of non-cardia gastric cancer diagnosed between 2005 and 2015 were included in the final analysis.

Patient demographic and disease characteristics are summarized in Table 1. The overall average age of studied patients was 55 years, 59% were male, and 63% were Hispanic. The distribution of age and sex were not different between time periods. There was a significantly lower proportion of Blacks ($p = 0.002$) and significantly higher proportion of Hispanics ($p = 0.02$) diagnosed with gastric cancer in 2010–2015 than in 2005–2009. The proportion of patients who were born outside of the USA was 18% in 2005–2009 and 59% in 2010–2015 ($p < 0.05$).

Most patients had advanced disease at presentation (stage III, 13%; stage IV, 61%). The tumors were most commonly located in the antrum (24%) or corpus (19%) and were poorly differentiated (69%). Tumor histology was 50% diffuse and 43% intestinal. Cancer stage, grade, histology, and anatomic location did not change significantly over the two time periods.

Effect of Race/Ethnicity and Age on the Changing Pattern of the Incidence of Gastric Cancer Over Time

In 2005–2009, the highest gastric cancer incidence rate was observed among Blacks (18/100,000 persons/year) followed by Hispanics (10/100,000 persons/year). In 2010–2015, gastric cancer incidence was highest among Hispanics (17/100,000 persons/year) followed by Blacks (13 per 100,000 persons/year).

Age-adjusted incidence rates stratified by race/ethnicity were compared between the two time periods using rate ratios (Fig. 1). Gastric cancer incidence increased significantly

among Hispanics (from 10 to 17 per 100,000 persons/ year, $RR = 2.0$, 95% CI 1.4–2.5, $p = 0.001$) from 2005–2009 to 2010–2015. Gastric cancer incidence declined among Blacks and slightly increased among Whites; however, neither trend reached statistical significance (Fig. 1).

Changes in gastric cancer incidence stratified by age from 2005–2009 to 2010–2015 are shown in Table 2. Among Hispanics, gastric cancer incidence increased significantly among persons aged 40–59 years and ≥ 60 years (16.2 to 22.8 per 100,000 persons/year and 17.1–28.0 per 100,000 persons/year, respectively) (Table 2). Gastric cancer incidence also increased significantly among non-Hispanic Whites ≥ 60 years from 2.8 to 6.5 per 100,000 persons/year.

Discussion

Racial disparities in gastric cancer are well documented in the USA [13, 14]. The overall incidence of non-cardia gastric cancer within the USA has dropped over time [15]. However, recent data suggest a possible reversal of this trend over the past few years [16] and also raise the question as to whether any increase has disproportionately affected specific racial subgroups [11].

Based on local observations, we hypothesized that gastric cancer incidence has risen mainly due to an increase in the immigrant Hispanic population originating in high gastric cancer incidence countries. We found that non-cardia gastric cancer incidence significantly increased nearly doubling among Hispanics (from 10 to 17 cases/100,000/year) between 2005 and 2015. Most affected were Hispanics aged 40 years and over who were predominantly immigrants. During this same period, gastric cancer incidence remained stable overall among non-Hispanic Whites and Blacks.

Our findings add to the accumulating and troubling evidence pointing to an increasing incidence of non-cardia gastric cancer among Hispanics in the USA, potentially driving even greater gastric cancer disparities. Two separate SEER analyses have detected increases in non-cardia gastric cancer among pockets of the US population [9, 10]. Anderson et al. observed a doubling of non-cardia gastric cancer incidence among Whites aged 25–39 years (from 0.27 to 0.45/100,000 persons/year) from 1977 to 2006 [9]. In an analysis of gastric cancer incidence by anatomic subsite, Carmargo et al. also observed that corpus cancer incidence rose among Whites aged 40–59 years and Blacks of all age groups [10]. Neither analysis was able to pinpoint whether the increases were attributable to persons of Hispanic heritage. However, Merchant et al. in a later analysis of SEER data from 1992 to 2011—which included greater ethnic specificity with regard to Hispanic heritage—observed a significant increase in gastric adenocarcinoma incidence among Hispanic males aged 20–49 (EAPC 1.55%) with an increasing incidence of stage IV disease (EAPC 4.34%) in this subgroup [11]. That study, however, was limited by a grouping of gastric adenocarcinoma in the analysis without distinguishing between the cardia and non-cardia subtypes which are biologically and epidemiologically distinct entities. Our study, which examined racial/ethnic trends of exclusively non-cardia gastric cancer incidence, takes the findings of previous studies a step further by demonstrating that specifically non-cardia gastric cancer appeared

to be rapidly rising among Hispanics while remaining stable among non-Hispanic Whites and Blacks.

A rise in GC incidence among Hispanics has serious public health implications. Hispanics represent a large and increasing demographic within the USA. Within Harris County, TX, the Hispanic population grew 66% from 2000 to 2014 (from 1,119,751 to 1,855,540) [17] primarily reflecting immigration. Currently, the Hispanic population represents 42% of the overall population [18]. Thus, even a small rise in gastric cancer incidence can translate into a large number of persons affected by this lethal disease, suggesting that greater attention be paid to developing primary prevention and/or screening strategies in these higher-risk groups.

The observed increase in non-cardia cancer among Hispanics appears to be primarily related to immigration of individuals whose cancer risk was acquired in their home countries and persists despite moving to the USA. In our study, 78% of Hispanics were immigrants from Central America where gastric cancer incidence is estimated at 9.3/100,000 persons/year [1, 19]. Using California cancer registry data, Chang et al. also found that foreign-born Hispanics had a higher non-cardia cancer incidence rate than US born Hispanics [20]. Other studies have similarly noted that gastric cancer rates among Latin American, Korean, and Japanese immigrants are higher than their US native counterparts and closer to, though quite reaching, the rates of their native countries [5, 21, 22].

H. pylori infection is generally considered a necessary prerequisite for non-cardia gastric cancer [23]. The infection is usually acquired in childhood and, if untreated, may progress to gastric atrophy that can culminate in gastric adenocarcinoma. Most of the developed world has experienced a “birth cohort effect” where *H. pylori* prevalence has declined significantly with successive generations. This is the purported reason for the decline in gastric cancer worldwide [23]. In Latin American countries, however, *H. pylori* prevalence persists at an estimated 70–80% [24, 25]. Within the USA itself, the prevalence of *H. pylori* is also significantly higher among resident Hispanics [26]. For example, age-adjusted *H. pylori* seroprevalence was three times greater in Mexican-Americans compared to Whites (64% vs. 21.2%) in an NHANES based analysis of data from 1999 to 2000 [27]. This same analysis further found that *H. pylori* seroprevalence had declined when compared to rates over 1988–1991 among Whites but was unchanged among Mexican-Americans.

Other explanations for the observed increased in gastric cancer incidence among Hispanics include socioeconomic disparities, dietary exposures, and genetic or biologic susceptibility to gastric cancer. Low socioeconomic position itself is associated with increased incidence of gastric cancer [28] likely through greater *H. pylori* acquisition risk and potentially reduced access to fruits and vegetables. A recent large study performed within a single health system in Southern California found that Hispanic ethnicity was associated with higher risk of gastric cancer compared to non-Hispanic Whites (OR 1.4, 95% CI 1.22–1.57) and also found low socioeconomic status was associated with increased risk of gastric cancer [5]. Given that nearly our entire study population was indigent, socioeconomic factors are less likely to explain the divergent trends by race/ethnicity. Finally, it is possible that Hispanics may carry a yet uncharacterized genetic susceptibility to gastric cancer. This

has not been extensively studied in Hispanics and unique markers conferring higher risk in this population have not yet been found.

Our study has some limitations. The study population, having been derived from a county-funded medical system, was uniformly of low socioeconomic status. This was both a weakness and strength insofar as we could not assess the impact of socioeconomic status on gastric cancer incidence, but, on the other hand, socioeconomic status likely did not confound our findings. Because of a paucity of patients of other races/ethnicities, we had to limit our analysis to White, Black, and Hispanic persons. Therefore, we could not assess incidence rates among other ethnic subgroups such as Asians or indigenous groups. Finally, although our findings are derived from a single, albeit large and ethnically diverse, county health care system within Texas, the time period was only 10 years and was subdivided into two 5-year intervals to correspond with census reporting intervals. Finally, use of a population derived from a county medical system may have introduced selection bias due to over-representation of Hispanic and Black persons and underrepresentation of Whites among the included study population. The very small number of gastric cancer cases observed among Whites limited our ability to detect changes in incidence rates over time. Nonetheless, these findings are useful and relevant for understanding gastric cancer trends within Harris County and future epidemiological studies are needed to evaluate whether similar trends are observed regionally and nationally.

In summary, we found that non-cardia gastric cancer is increasing significantly among persons of Hispanic ethnicity over the age of 40 years. These findings suggest that progress in gastric cancer has been unevenly experienced across the US population. Greater consideration should be given to preventive efforts among higher-risk subpopulations such as Hispanics and among other immigrants from high cancer risk regions.

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Fig. 1.
Non-cardiac gastric cancer incidence by race and ethnicity

Table 1

Demographic and clinicopathologic characteristics

	2005–2009		2010–2015		Overall	
	No.	%	No.	%	No.	%
Harris county population	2,842,392		3,201,260		–	
Total cancers	111		188		299	
<hr/>						
<i>Sex</i>						
Male	71	64	106	56	177	59
Female	40	36	82	44	122	41
<i>Age</i>						
20–39	13	12	26	14	39	13
40–59	58	52	98	52	156	52
60–69	26	23	43	23	69	23
70	14	13	21	11	35	12
<i>Race/ethnicity</i>						
White	6	5	17	9	23	8
Black	45	41	44	23	89	30
Hispanic	60	54	127	68	187	62
<i>Nativity</i>						
Born in USA	52	47	76	40	128	43
Born outside of USA	20	18	110	59	130	43
Unknown	39	35	2	1	41	14
<i>Stage</i>						
1	10	9	12	6	22	7
2	10	9	22	12	32	11
3	8	7	30	16	38	13
4	75	68	108	57	183	61
Unknown	8	7	16	9	24	8
<i>Anatomic location</i>						
Fundus	3	3	9	5	12	4

	2005–2009		2010–2015		Overall
Harris county population	2,842,392		3,201,260		–
Total cancers	111		188		299
	No.	%	No.	%	No. %
Corpus	27	24	30	16	57 19
Antrum	29	26	44	23	73 24
Pylorus	4	4	6	3	10 3
Lesser curvature	9	8	31	16	40 13
Greater curvature	4	4	11	6	15 5
Overlapping lesion	22	20	42	22	64 21
Undetermined location	13	12	15	8	28 9
<i>Tumor grade</i>					
Well differentiated	1	1	6	3	7 2
Moderate differentiated	18	16	31	16	49 16
Poorly differentiated	61	55	146	78	207 69
Unknown	31	28	5	3	36 12
<i>Histology</i>					
Diffuse	57	51	92	49	149 50
Intestinal	39	35	91	48	130 43
Other	0	0	5	3	5 2
Unknown	15	14	0	–	15 5

Table 2

Incidence of non-cardia gastric cancer among racial/ethnic groups by age group (incidence rate/100,000/persons/year)

Age group	2005–2009	2010–2015	Rate ratio (95% CI)	P value
<i>Non-Hispanic White</i>				
20–39y	0.0	1.0	–	–
40–59y	3.9	5.0	1.4 (1.7–2.8)	0.31
60y	2.8	6.5	2.1 (1.4–2.9)	0.02 *
<i>Hispanic</i>				
20–39y	5.7	6.8	1.4 (1.6–2.9)	0.34
40–59y	16.2	22.8	1.6 (1.1–2.5)	0.02 *
60y	17.1	28.0	2.1 (1.3–3.5)	0.009 *
<i>Non-Hispanic Black</i>				
20–39y	1.7	1.4	0.8 (0.9–1.5)	0.20
40–59y	23	20	0.8 (0.9–2.8)	0.28
60y	41.1	30.0	0.7 (1.0–2.8)	0.30

* Significant at p value < 0.05