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Gastric Cancer Incidence Estimation in a Resource-Limited Nation: Use of Endoscopy Registry Methodology

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Abstract

Purpose—Cancer epidemiology is challenging in developing nations, in the absence of reliable pathology-based cancer registries. Clinical experience suggests that the incidence of gastric cancer is high in Honduras, in contrast to the limited available national statistics at the time of study initiation (IARC GLOBOCAN 2002: males 15.2, females 10.8). We estimate the incidence of gastric cancer for Honduras using an endoscopy registry as a complimentary resource.

Methods—We conducted a retrospective analysis of incident noncardia gastric adenocarcinoma cases in Western Honduras for the period 2000–2009. This region is well circumscribed geopolitically with a single district hospital and established referral patterns, to provide a unique epidemiological niche to facilitate estimation of incidence rates. A prospective, comprehensive database of all endoscopy procedures from this hospital was utilized at the primary data source. The catchment area for gastroenterology services for the at-risk population was validated by calculating the overall endoscopy utilization rates for each municipality in western Honduras. Incident cases of gastric adenocarcinoma were determined by the endoscopic diagnosis. Pathology services are not financed by the Ministry of Health, and histology data was incorporated when available. Population statistics were obtained from the Honduras National Statistics Institute (INE). Age standardized incidence rates (ASIRs) were calculated using world standard population fractions.

Results—The catchment area for Western Honduras was validated with the municipality threshold of 30 endoscopies per 10⁶ person-years, with inclusion of a total of 40 municipalities. In the Western Honduras catchment area, there were 670 incident cases (439 M, 231 F) of noncardia gastric adenocarcinoma during the study decade 2000–2009. Notably, 67 (10.0%) and 165 (24.6%) of cases were under the ages of 45 and 55, respectively. The case-finding rate was 5.1 endoscopies performed for each new diagnosis of gastric cancer. The ASIRs for the decade were 30.8 for males and 13.9 for females. Clinically, 60.3% of gastric cancers were Borrmann type 3 (ulcerated mass), and evidence of advanced disease with pyloric obstruction was common

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(35.2%). Subtypes by the Lauren classification were distributed among diffuse (56%), intestinal (34%) and indeterminate (9.9%), in subjects with available pathology (526/670).

Conclusions—The endoscopy procedure registry may serve as a complimentary data resource for gastric cancer incidence estimation in resource-limited nation settings wherein pathology services and cancer registries are absent. The results remain an underestimation in this setting due to the challenges of access-to-care and related factors. The methodology helps to more fully characterize the high incidence of gastric cancer in western Honduras and this region of Central America, and demonstrate the need for additional epidemiology research and interventions focused on prevention and treatment.

Keywords

Gastric Cancer; Honduras; Cancer Epidemiology; Endoscopy; Incidence Rate; Central America

INTRODUCTION

Gastric adenocarcinoma is the second leading cause of global cancer mortality and the leading cause of infection-associated cancer mortality, with nearly one million incident cases annually [1–3]. It is projected to rise from fourteenth into the top ten in all-cause mortality in the near term, primarily due to growing and aging populations in the high incidence areas, including western Latin America and eastern Asia [2,4]. Gastric cancer demonstrates marked geographic variability, both regionally and within countries, which may relate to differences in host response and genotypes, *H. pylori* strain virulence, diet, and environmental factors [5–7]. The geographic variability affords the opportunity for focused scientific investigation and for targeted prevention programs.

In Latin America, at time of the initiation of the current study, the published International Agency for Research on Cancer (IARC, GLOBOCAN 2002) age-standardized incidence rates per 100,000 population (ASIRs) for gastric cancer ranged from 13 to 46 cases and 5 to 31 per 100,000 for males and females, respectively [8]. The highest rates were reported in Chile, Peru, Ecuador, Colombia and Costa Rica. It is worth noting that these nations represent middle income countries (MICs) in Latin America, suggesting that the lower incidence rates in low income countries (LICs) may suffer from the absence of data and under-reporting, rather than lack of cancer burden [9]. It is well known that cancer epidemiology is problematic in developing nations due to limited resources, infrastructure, and reliable national cancer registries [10]. In addition, the Ministries of Health (MOH) in resource-limited nations often prioritize metrics related to infectious diseases and maternal-child health, and also are unable to finance core services such as pathology, which are critical for cancer registries. Bray and colleagues, in their review of the global cancer burden, noted a lack of population-based cancer registries in 34 of 184 countries examined, of which, 32 were developing nations; vital statistics systems were also lacking in 88 countries (85 were developing nations) [11].

Honduras is representative of a developing nation in Latin America, wherein the gastric cancer burden is high based upon clinical experience, which stands in contrast with the limited available national statistics. Honduras, and neighbors Guatemala, El Salvador, and Nicaragua, are four of the six nations in Latin America with low global human development indices [11]. At the time of initiation of this study, in 2002, the IARC estimated gastric cancer ASIRs for Honduras of 15.2 and 10.8 per 100,000 person years for males and females, respectively [8]. These rates were primarily imputed in models based upon country registries in the region. In addition, the Honduras National Cancer Center (*Emma Romero de Callejas*) network of hospitals reported only 112 total gastric cancer cases in the 7-year

period from 1998–2004, the most recent national statistics at the time. We suggest that these previous estimates represent a significant underestimation [10].

The western region of Honduras provides a unique epidemiological niche to facilitate accurate estimation of the incidence of gastric cancer for Honduras, and its Central American neighbors. This rural region, with a population of over one half million people, is well-circumscribed by geopolitical boundaries. A single district hospital has provided the only endoscopy services in western Honduras, with a well-defined catchment area, and an established referral pattern. In sum, this hospital diagnoses and cares for the majority of gastric cancer cases that present for medical care. Our aim was to provide an estimation of the burden of gastric cancer in Honduras during the 10-year period from 2000–2009, by incorporating the detailed endoscopy registry as a complimentary resource.

METHODS

Study design and setting

We conducted a retrospective analysis of incident cases of noncardia gastric adenocarcinoma in western Honduras for the period from 2000–2009, using the existing data sources described herein. In brief, the principal sources included the endoscopy utilization database, the gastric cancer and pathology database from the Ministry of Health (regional hospital), and the national census statistics. The upper endoscopy utilization rates in the region were calculated to demarcate and validate the referral area. The incident case and population data were used to calculate the annual ASIRs for the western region and each of its political sub-divisions. The study was approved by the institutional review boards of the University of North Carolina, Chapel Hill, and the Western Regional Hospital.

The Western Regional Hospital (WRH) of the Ministry of Health, is located in Santa Rosa de Copán (2001 population, 39,000) in the state (*departamento*) of Copán, serving western Honduras. This triangular rural region is delineated by mountains to the east, and borders with Guatemala and El Salvador to the west and south, respectively. The WRH referral area includes the four states (Copán, and parts of Ocotepeque, Lempira, Santa Barbara); each state is comprised of municipalities (*municipios*), each with an average extent of approximately 400 km². The region has modest geographic isolation, wherein most health care is local, and with limited transit to the two metropolitan centers in Honduras, San Pedro Sula (northern industrial capital) and Tegucigalpa (central governmental capital).

National Census data

The official census and population data was obtained from the Honduras National Statistics Institute (*Instituto Nacional de Estadística* or INE). The most recent national census was in 2001. INE also provides precise estimates of annual population growth, specific for age, gender, and geopolitical divisions (e.g., village, municipality). We used the most recent projections for the non-census years of the current study, which were released in 2009.

Catchment area analysis

The catchment area for gastroenterology services for the Western Regional Hospital was delineated by calculation of upper endoscopy utilization rates during the study decade. The detailed WRH endoscopy database was used, which contained de-identified information on all patients undergoing for endoscopy in the Western Regional Hospital. This database included information on patient age, sex, and village and municipality of origin.

We calculated the crude upper endoscopy utilization rates (EUR), expressed per 100,000 person-years, for each municipality in western Honduras over the ten year period to validate

the catchment area for gastroenterology services of the WRH, and in turn the definitive at-risk population for the incident cases of gastric cancer within the catchment area. Endoscopy utilization rates were estimated for each municipality in the four western states of Honduras (Copán, Ocotopeque, Lempira, Santa Barbara). The 2001 census population of each municipality was used for calculation of the crude rates.

Using the state of Copán as a reference, we first identified the range of municipality-specific endoscopy utilization rates within the state of Copán in which the district hospital is located. We then verified whether these rates followed a normal distribution. An evident threshold of 30 endoscopies per 100,000 person-years was observed in Copán. This threshold was used to identify municipalities from the 3 neighboring states to include in the analysis and thus demarcate the WRH catchment area for endoscopy services. In general, the excluded municipalities (i.e., EUR <30 per 10⁶ person-years) pertained to neighboring regional health districts. This includes the municipalities located near the borders with El Salvador and Guatemala, whose residents may receive medical care in the neighboring countries. The Central America Integration System (*SICA*) for the four countries permits health care in the neighboring countries in the public and private sectors, regardless of nationality [personal communication, Dra. Maria Rodriguez, Minister of Health, El Salvador, May 31, 2012].

Gastric cancer case ascertainment

We utilized the comprehensive endoscopy database of all noncardia gastric adenocarcinoma cases presenting to the Western Regional Hospital (WRH) for identification of incident cases 2000–2009. All patients who presented were symptomatic, with indications for endoscopy. A unique identification code prevented duplicate case entry.

Historically, the Honduras Ministry of Health has been unable to finance pathology services in the majority of public hospitals in Honduras, including the Western Regional Hospital. Patients are asked to pay out-of-pocket if they are able, and the majority of patients are unable to do so, leaving most without a final diagnosis anchored with pathology. An ongoing prospective gastric cancer case-control study based at the WRH (NIH CA1255884, DRM), has had the secondary clinical benefit of providing pathology results for many subjects in recent years during the 2000–2009 period. When pathology results were available, these were included in the overall database, and were used to confirm case identification. In cases where biopsy was not performed or pathology was non-diagnostic (e.g. necrotic material from a mass lesion), the endoscopic diagnosis was considered final. The database also provided clinical data such as the endoscopy appearance (e.g., Borrmann classification). Similarly, cross-sectional imaging is generally unavailable; pyloric obstruction was used as a surrogate for advanced disease.

Age standardized incidence rate calculations

Crude incidence rates were calculated for males and females by both age group and by municipality. Age standardized incidence rates (ASIRs) were calculated using the world standard population fractions for the five age groups: 0–14, 15–44, 45–54, 55–64, and over 65 [12]. The ASIRs were calculated for each year, as well as for the decade. As noted, the validated catchment area population defined as the population at-risk for the ASIR calculations.

RESULTS

Catchment area

The crude upper endoscopy utilization rate (EUR) with the utilization threshold of 30 per 100,000 person-years was used to delineate the at-risk base population served by the

Western Regional Hospital. Of the 95 municipalities in the 4 states of western Honduras, 40 municipalities had an EUR greater than 30 for validation of the catchment area. Nearly all municipalities within the state of Copán were included (22/23), with the exception of one municipality on the border with Guatemala. In the other 3 states, 18 municipalities met the threshold criteria for inclusion: Lempira (5/28), Ocotepeque (8/16), and Santa Barbara (5/28); in Santa Barbara, located in the north, 18 of the 23 excluded municipalities did not have endoscopy referrals during the study decade. In parallel, WRH physician expert opinion, blinded to the analysis, generated an independent list of municipalities of the WRH referral area; near-complete agreement was noted, as the EUR analysis included two additional municipalities, and excluded only one from the physician generated list.

In the study decade, a total of 3936 endoscopies were performed at the Western Regional Hospital, of which 3431 (87%) pertained to municipalities in the validated catchment area. Of the 3431 total endoscopies in the referral area, a reasonable balance of endoscopy volume was observed among the municipalities in the states neighboring Copán (69%): Lempira (11.0%), Ocotepeque (9.0%), and Santa Barbara (11.0%). In the catchment area over the decade, the mean crude EUR was 63.5 and 131.6 per 10⁶ person-years, for all residents and for all adults age 20 or older, respectively.

Age standardized incidence rates

In Western Honduras catchment area, during the decade 2000–2009, a total of 670 incident cases of incident gastric adenocarcinoma cases were diagnosed, of whom 439 were male (65.5%) and 231 were female (34.5%). An estimated 5.1 endoscopies were performed for each new diagnosis of gastric cancer. We observed 67 (10.0%) and 165 (24.6%) of cases under the ages of 45 and 55, respectively. The crude gender-specific rates were 28.1 per 10⁶ person-years for males and 14.0 per 10⁶ person-years for females. (Table 1). When stratified by age, the highest crude incidence was in persons 65 years and older: 233.4 and 93.9 per 10⁶ person-years for males and females, respectively. In the 10 year period of this analysis, the annual standardized incidence rates per 10⁶ population (ASIRs) were 30.8 for males and 13.9 for females. (Table 2). The ASIRs of gastric cancer were fairly stable during the study decade, with modest annual variability (range for males, 25.2–39.8, and for females, 9.4–22.5). Stratification by municipality identified eight municipalities with higher male gastric cancer incidence rates, thereby highlighting areas for prevention programs and/or epidemiology investigation.

There were an additional 139 incident cases of gastric cancer diagnosed by endoscopy at the Western Regional Hospital in the period 2000–2009, for patients residing in municipalities outside of the validated catchment area, ie, from municipalities pertaining to other health districts for gastroenterology services. These comprised 17.2% (139/809) of the total number of gastric cancer cases, which was similar to the percent of endoscopy volume 12.8% (505/3936) from these areas. The demographic and clinical characteristics of patients from municipalities outside of the catchment area were similar (data not shown); one difference was noted: males ages 55–64 formed a higher percentage of total cases (35.2%, versus 26.2% in the catchment area).

Clinical characteristics of gastric cancer cases

The clinical characteristics of the incident gastric adenocarcinoma cases underscore the reality of advanced disease at the time of diagnosis for the majority of patients in the region. All patients were symptomatic at the time of presentation and endoscopy. As noted, the case-finding rate was 5.1 upper endoscopies per new diagnosis. The most frequent gross endoscopic appearance of gastric cancers was Borrmann type 3 (ulcerated mass), which represented 60.3% of cases. (Table 3). Pyloric obstruction was a common presentation,

35.2% (236/670) overall, of whom 16.6% and 18.7% were completely and incompletely obstructed, respectively.

Definitive pathology was available for 526 of the 670 subjects. The histology by the Lauren classification was distributed among the diffuse (56%), intestinal (34%) and indeterminate (9.9%). The age and sex distribution of the incident gastric cancer cases by histologic subtype was not statistically different from the overall distribution in Table 1. In the 144 subjects without definitive pathology, 14.1% (95/670) did not have biopsies performed, including 24 patients proceeded directly to surgery. 7.3% (49/670) of patients had inconclusive histology, the majority of whom had histology demonstrating ulceration or necrotic material associated with a mass lesion (e.g., Borrmann type 1, 2, 3), wherein the specificity of endoscopic features approaches 100%. Cases with the following features at endoscopy were conservatively excluded from the analysis: early gastric cancers, flat lesions (e.g., Borrmann IV), and benign-appearing gastric ulcers. As indicated, pathology services are not financed through the government, and the majority of the financing has been facilitated by an ongoing gastric cancer initiative at the locale (NIH CA1255884, DRM). In summary, these clinical findings echo the IARC data which show nearly equal incidence and mortality rates, suggesting that patients present relatively late and have limited therapeutic options in this resource limited setting of Central America.

DISCUSSION

A high incidence of gastric cancer is observed in western Honduras, facilitated by methodology using a detailed endoscopy database to compliment regional cancer and pathology data, and thereby serve as a cancer registry surrogate in the absence of a national cancer registry. The incidence rates we have calculated for this region rival other known high incidence countries in Latin America such as Costa Rica and Chile. The incidence rates for the past decade in Western Honduras (ASIRs of 30.8 and 13.9 per 10⁶ person-years for males and females, respectively) are substantially higher than the IARC (GLOBOCAN 2002: ASIRs of 15.2 and 10.8 per 10⁶ person-years for males and females, respectively) estimates for Honduras which were available at the time of study initiation. The gastric cancer incidence estimates herein have been presented in preliminary form for earlier periods (e.g., 1996–2000) [7], which has served to provide input for the more recent IARC estimates (GLOBOCAN 2008: ASIRs of 31.4 and 25.9 for males and females, respectively) [2].

Unbiased estimates of incidence rates require accuracy of both numerator (case ascertainment) and denominator (corresponding at-risk population) data. In resource-limited settings where pathology services and cancer registry data are often unavailable, accurate incidence data are difficult to capture. In addition, in many low income countries, large capital cities suffer from significant immigration from the rural areas, and often do not have the infrastructure to document incident cases in the urban public and private health care sectors. This study took advantage of a unique geopolitical and logistical model to improve upon previous approximations imputed from Central American as a whole.

The study of endoscopy utilization is useful for trend and resource allocation analyses in high income countries [13,14]. In resource-limited nations, the use of a comprehensive endoscopy registry may serve as a complimentary methodology for gastrointestinal cancer registries. We used the endoscopy database both to validate the at-risk population by calculation of endoscopy utilization (endoscopy “incidence”) in the area, and for gastric adenocarcinoma case ascertainment. This may be a useful tool in similar developing nation environments, in order to streamline public health and prevention programs, given the predicted growth in the global cancer burden. In addition, the estimation of incidence rates

at the level of each municipality, albeit subject to imprecision due to the smaller number of cases, could help focus prevention programs to specific municipalities or states within a given country.

In spite of our detailed methodology, the study likely underestimates the incidence of gastric cancer in Western Honduras for several reasons. First, in the absence of a formal screening program for gastric cancer, only symptomatic cases are evident, and all asymptomatic cases will remain undiagnosed and unreported. Second, in the impoverished rural areas, symptomatic patients may not present to medical facilities and expire at home; this may be due to transportation difficulties (e.g., rainy season), or cultural issues (e.g., suspicion of hospitals) [15]. This phenomenon would be expected to affect rates among older subjects in particular. A verbal autopsy program conducted by social promoters could help in this regard. [16,17] Third, in this rural area, there is modest flux of patients to medical facilities outside of the catchment area for specialty services. A percentage of patients residing in the western, southern and northeastern municipalities of the catchment areas, may seek care in the urban centers in neighboring Guatemala, El Salvador, and northern Honduras (San Pedro Sula), respectively. Importantly, there is no appreciable flow of into the public district hospital of Western Honduras from these urban areas. Thus, the incidence estimates herein are conservative. Lastly, natural disasters and political events may affect regional health. During the political turmoil in Honduras in the latter half of 2009, strict curfews and highway closures were commonplace, which affected access to health care. For example, a 50% decrease in endoscopy volume was observed in 2009 for patients from the state of Santa Barbara, which may in part explain the lower ASIR for males in 2009.

In conclusion, an endoscopy database may serve as a complimentary data resource and methodology for gastric cancer incidence estimations in resource-limited nation settings wherein cancer registries are nonexistent or unreliable. The gastric cancer incidence rates for western Honduras are substantially higher than the international estimates at the time of study initiation, and helped provide data for the more accurate recent estimates, in spite of conservative methods and probable underestimation. These results help more fully characterize the high incidence of gastric cancer in western Honduras and this region of Central America, and demonstrate the need for additional epidemiologic research and interventions focused on prevention and treatment.

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Table 1

Incident Gastric Adenocarcinoma in Western Honduras, 2000–2009.

Age	Gastric cancer cases ^a		Total person-years ^b		Crude Gastric Cancer Incidence Rates		World standardized rates	
	Male n (%)	Female n (%)	Male	Female	Male	Female	Male	Female
15–44	41	26	1,197,121	1,237,382	3.4	2.1	1.5	0.9
45–54	61	37	164,489	187,384	37.1	19.7	4.1	2.2
55–64	115	62	102,953	117,564	111.7	52.7	8.9	4.2
65	222	106	95,117	112,925	233.4	93.9	16.3	6.6
Total	439	231	1,559,680	1,655,255	28.1	14.0	30.8	13.9

The age standardized incidence rates are expressed per 100,000 person-years. Age standardization performed using world standard population proportions for the listed age strata [12].

^aTwo patients with missing data on sex were excluded from this analysis.

^bPerson-years calculated for each year from 2000–2009, from population data and projections from the Honduras National Statistics [Census] Institute (INE).

Table 2

Gastric Cancer Annual Standardized Incidence Rates, Western Honduras, 2000–2009.

	2000–2009	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009
Males	30.8	39.8	29.9	29.1	28.5	35.4	26.3	39.8	25.2	35.6	21.0
Females	13.9	20.2	22.5	14.0	15.3	13.5	11.9	15.1	9.6	9.4	11.1

The age standardized incidence rates are expressed per 100,000 person-years. Age standardization performed using world standard population proportions for the listed age strata [12].

Table 3

Clinical characteristics of gastric cancer, Western Honduras, 2000–2009

Endoscopy summary	N/n
Endoscopies performed	5.1
per incident gastric cancer	(3431/670)
Borrmann classification (N= 670)	n (%)
Type 1 (polypoid)	6 (0.9%)
Type 2 (fungating mass)	64 (9.6%)
Type 3 (ulcerated mass)	404 (60.3%)
Type 4 (diffuse infiltrative)	48 (7.2%)
Type 5 (unclassified, not 1–4)	101 (15.1%)
Unknown	47 (7.0)
Pyloric obstruction (N= 670)	n (%)
Total (incomplete or complete)	236 (35.2%)
Incomplete	125 (18.7%)
Complete	111 (16.6%)
None	434 (64.8%)
Pathology, Lauren classification (N= 526) ^a	n (%)
Diffuse	296 (56.3%)
Intestinal	178 (33.8%)
Indeterminant	52 (9.9%)

^aThe Honduras Ministry of Health does not finance pathology services for the regional hospitals; available pathology has been financed by external sources.