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Original article

Clinical, histological, and endoscopic characterization of gastric cancer at the Hospital de Especialidades Dr. Abel Gilbert Pontón, Ecuador

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Abstract

Introduction: Gastric cancer is one of the most common causes of death worldwide, with a varying incidence. In Ecuador, it is the second leading cause of death in men and the fourth in women. **Objectives:** To establish the socio-demographic, clinical, histological, and endoscopic characteristics of patients with gastric cancer and to determine the correlation between location and histology in this population treated at the Hospital de Especialidades Guayaquil Dr. Abel Gilbert Pontón. **Materials and methods:** Analytical and prospective prevalence study. Outpatient and emergency upper gastrointestinal endoscopies with signs of suspected gastric cancer performed at the Hospital de Especialidades Guayaquil Dr. Abel Gilbert Pontón - Ecuador between January 2018 through December 2019 were included. **Results:** The study included 62 patients diagnosed with gastric adenocarcinoma. 72.6% were male and 27.4% were female; the age range was between 27 and 95 years, with an average of 60.96 ± 15.1 years, the age of onset being between 60 and 70 years. Pain was the most frequent symptom in 98.4% of cases, followed by weight loss in 64.5%. The antrum was the most common site of cancer (50.0%), and Borrmann type III was the most common morphology. Intestinal cancer was found in 64.5% of cases, while diffuse gastric cancer was found in 29.0%. Intestinal cancer was more common in older ages (60-69%) and the most frequent site of presentation was the body of the stomach (71.4%) with a proximal location. In contrast, diffuse gastric cancer was more frequent in younger patients aged between 27-39 years, more often in the antrum (32.3%) at a more distal location. **Conclusions:** Gastric cancer is more often found in men and is usually diagnosed in advanced stages. Intestinal gastric cancer was most commonly seen at advanced ages in our hospital, most frequently at the proximal site and in the Borrmann type III according to the classification of advanced gastric cancer, affecting its treatment and prognosis. The results obtained support the implementation of programs to diagnose and treat this severe disease in a timely manner.

Keywords

Gastric cancer; Gastric tumor; Gastric neoplasms; Gastric adenocarcinoma; Gastric histology.

INTRODUCTION

The International Agency for Research on Cancer (IARC), through GLOBOCAN, reported the estimated number of new cancer cases in 2018 worldwide, revealing that gastric cancer ranked fifth with 1 033 701 cases (5.7 %) [1,2]. According to the report, countries in East Asia, Eastern Europe and South America had the highest gastric cancer incidence rates, while North America and parts of Africa had the lowest rates, showing that they vary among geographic regions, with more than 70% occurring in developing countries [3].

In Latin America and the Caribbean, gastric cancer accounts for 11 % of new cancer cases and 18 % of cancer

mortality, while in North America, it accounts for 3 % of cancer cases and 4 % of cancer mortality. In South America, the countries with the highest incidence of this type of cancer are Chile, Costa Rica, and Colombia. Estimated age-standardized mortality rates for men per 100 000 people are high in Honduras (22.3), Costa Rica (16.8), Peru (18.2), Chile (15.0) and Ecuador (20.7), compared with lower rates in some regions of Latin America, such as Argentina [5,6] and Mexico (6.7) [4]. Latin America has a high prevalence of *Helicobacter pylori* infection, and some of the highest gastric cancer incidence rates in the world [5].

In GLOBOCAN 2018, Ecuador ranked third, with 2589 cases (9.2 %) across the country; in terms of sex, gastric cancer is the second most common type of cancer in males, with 1364 cases (10.7 %), and the fourth in females, with 1225 cases (8 %). Gastric cancer is the third leading cause of mortality worldwide, with 782 685 cases (8.2%) [1,2]. The Sociedad de Lucha Contra el Cáncer del Ecuador (Ecuador Institute for Cancer Control - SOLCA) and the Instituto Ecuatoriano de Estadísticas y Censos (Ecuadorian Institute of Statistics and Census - INEC) reported that gastric cancer is the leading cause of death for all types of cancers (11.58%). Of the 3291 cancer cases reported that year, 234 died, in other words, 7.11 %. The province with the largest number of cases was Pichincha, with 944 (28.68 %); followed by Guayas, with 428 cases (13.01 %); Manabí, with 329 (10 %); Azuay, with 322 cases (9.78%); and Loja, with 275 cases (8.36 %) [6-8].

Corral *et al.* published a study on gastric cancer conducted in Quito in 2018 describing a decrease in incidence, going from 28.5% in men and 21.7% in women in the period 1985-1988, to 20.3 % in men and women of 14.5 % in 2009-2013, with a 95 % confidence interval (CI): -2.7 to -0.5. They also reported a decrease in mortality, which went from 16.7 % in men and 13.8 % in women in 1985-1988 to 15.2 % in men and 10.0 % in women in 2009-2013, with a 95 %CI of: -1.7 to -0.1 The decline in both incidence and mortality is probably related to better socioeconomic conditions and the improvement of the quality of food and its preservation, rather than to the intervention of health services in early diagnosis. Nevertheless, it can be concluded that the decrease was significant from 1998 to 2013 (adjusted R2: -2.4; 95% CI: 3.8-1.1) in both men and women [9].

Gastric cancer is a heterogeneous disease that affects older people between the sixth and seventh decades of life (80 % of cases are diagnosed in people older than 65 years), with predominance in men and low-socioeconomic status [10]. Risk factors for gastric cancer are consistent with multifactorial pathogenesis such as smoking, alcohol consumption, high consumption of red or processed meats, and excessive salt consumption, which are associated with a moderate increase in the risk of developing gastric cancer. In contrast, high levels of education, fruit consumption and total vegetable consumption were associated with a moderately reduced risk for gastric cancer [11]. In a study published by Sierra *et al.* in 2016, it was reported that the prevalence of *H. pylori* infection and other risk factors may impact the incidence rate of gastric cancer, since its age-standardized incidence and mortality rates may be 3 times higher in men from countries such as Chile, Costa Rica, Colombia, Ecuador, Brazil, and Peru than in women [12].

Worldwide, *H. pylori* infection is recognized as the primary cause of gastric cancer, but several risk factors have also been identified, including socioeconomic status, diet high in salt and low in antioxidants, and alcohol and tobacco use. In Ecuador, multiple geographic, physical, and biological variables converge, but also social, economic, and cultural variables that could be related to the occurrence and course of the disease. This is explained by the fact that the association of risk factors for gastric cancer in Latin America is based on comparisons of cases and controls that have uncertain reliability, particularly with respect to diet [11,13].

According to Lauren, its histology is divided into intestinal and diffuse types, which could have epidemiological, pathophysiological, and prognostic differences that may condition the diagnostic and therapeutic approach; in addition, in 10 % to 20 % of cases, there may be an undifferentiated or unclassifiable form. Anatomically speaking, 2 regions are distinguished, which could be classified into proximal stomach (proximal fundus and body) and distal stomach (distal body, antrum, and pylorus). The development of gastric cancer is a multifactorial, complex, and long-evolving process [10].

Therefore, the objectives of this study are to establish sociodemographic, clinical, histological, and endoscopic characteristics and to determine the most frequent sites according to histology in a population of patients with gastric cancer treated at the Hospital de Guayaquil.

MATERIALS AND METHODS

Analytical prevalence, correlational cross-sectional, prospective study. It was carried out between January 2018 and December 2019, with patients hospitalized in the gastroenterology unit of the Hospital de Especialidades de Guayaquil - Dr. Abel Gilbert Pontón, Ecuador, which is a tertiary care center attached to the postgraduate degree in Gastroenterology of the Universidad de Guayaquil.

The main objective of the study was to establish the sociodemographic, clinical, histological, and endoscopic characteristics of gastric cancer in patients undergoing upper gastrointestinal endoscopy with signs of suspected cancer in the outpatient and emergency departments. The

study population included adult patients who underwent upper gastrointestinal endoscopy and had a neoplastic lesion according to the Borrmann classification, with a histopathological result according to the Lauren classification, and who also agreed to participate in the study.

Patients with a previous diagnosis of gastric cancer, a history of gastric cancer surgery, no histopathological or lost results, or neoplasms other than adenocarcinoma (such as neuroendocrine, lymphoma, gastrointestinal stromal tumors, among others), localized cancer in the gastroesophageal junction and those who refused to participate in the study were excluded.

The variables included in the study were age, sex of the patient, histological type according to Lauren classification (diffuse and intestinal), and histologic grade (differentiated, moderately differentiated and undifferentiated). Based on endoscopic characteristics, location was determined considering the highest point of tumor involvement (fundus, body, and antrum) and morphology according to the Borrmann classification (I, II, III and IV).

Data collection was carried out using the instrument developed based on the study variables. Data were digitized using Excel 8.0 and analyzed using IBM SPSS Statistics 22. Continuous variables were expressed as mean ± standard deviation (SD), while discrete variables were expressed in frequency and proportions. A bivariate analysis of some variables of interest was also performed using the chi-square test (χ^2).

The study did not pose any risk to the patients, as it was done using routine information from the gastroenterology service after obtaining informed consent and keeping the data confidential.

RESULTS

During the study period, from January 2018 to December 2019, 68 patients with gastric tumor were found, of which 6 did not meet the inclusion criteria and were excluded: 4 gastric lymphomas, a gastrointestinal stromal tumor, and a neuroendocrine tumor. The study was carried out with 62 patients diagnosed with gastric adenocarcinoma; the male sex represented 72.6 % of the sample with 45 cases and the female sex, 27.4 % with 17 cases, for a male-to-female ratio of 2.64:1.00. The age range of the patients was between 27 and 95 years, the mean age being 60.96 ± 15.1 years, and the majority were distributed between 60-79 and 40-59 years of age, with 53.2 % (33 cases) and 27.4 % (17 cases), respectively (**Table 1**). Regarding habits, alcohol was associated with gastric cancer in 43.5 % of the sample, with 27 cases, and cigarette smoking in 30.6 %, with 19 cases. Concerning family history of cancer, only 5 % reported a history of gastric cancer in a first-degree relative (1 case) and two second-degree of relatives (2 cases). The most frequent symptoms were pain (98.4 %), weight loss (64.5 %), vomiting (40.3 %), melena (38.7 %), and hematemesis (16.1 %) (**Table 1**).

Table 1. Sociodemographic and clinical characteristics

Variables	Frequency	Percentage
Sex		
- Female	17	27.4
- Male	45	72.6
Age		
- Mean ± SD	60.96 ± 15.1	
- Range	27-95	
- ≤ 39	6	9.7
- 40-59	17	27.4
- 60-79	33	53.2
- > 80	6	9.7
Habits		
- Cigarette consumption	19	30.6
- Alcohol consumption	27	43.5
Clinical features		
- Pain	61	98.4
- Weight loss	40	64.5
- Vomiting	25	40.3
- Melena	24	38.7
- Hematemesis	10	16.1

As for the location of cancer, 50 % were located in the antrum; 45.2 % in the body and 4.8 % in the fundus. With respect to morphology, according to the Borrmann classification, 6.5 % were type I; 19.4 % were type II; 62.9 % were type III; and 11.3 % were type IV. Concerning histological type according to Lauren classification, 40 (64.5%) patients presented with intestinal gastric cancer, 19 (29.0 %) with diffuse gastric cancer, and 4 (6.5 %) with mixed tumors.

When correlating histology according to the Lauren classification and tumor location, it was found that the intestinal type is more frequently located in the body (20 cases, 71.4 %), whereas the diffuse type is located in the antrum (10 cases, 32.3 %). The correlation of histology with Borrmann classification revealed that type III is more frequent in patients with gastric intestinal cancer (24 cases,

61.5 %) than in diffuse gastric cancer (13 cases, 33.3 %). A bivariate analysis was performed using the histologic grade and Borrmann morphology variables, with an interval correlation (r = 0.312), finding that the histologic type correlates with histologic grade in an interval correlation (r = 0.453). Finally, a significant Pearson correlation was found at levels of 0.05 and 0.01 (**Table 2**).

Table 2. Endoscopic and histological characteristics according to the histological types of gastric cancer of patients treated at the Hospital de Especialidades Dr. Abel Gilbert Pontón

	Histopathology, n (%)			Total
	Diffuse	Intestinal	Mixed	
Localization				
- Antrum	10 (32.3)	18 (58.1)	3 (9.7)	31 (50.0)
- Body	7 (25.0)	20 (71.4)	1 (3.6)	28 (45.2)
- Fundus	1 (33.3)	2 (66.7)	0 (0.0)	3 (4.8)
Morphology				
- Borrmann I	1 (25.0)	3 (75.0)	0 (0.0)	4 (6.5)
- Borrmann II	1 (8.3)	9 (72.0)	2 (16.7)	12 (19.4)
- Borrmann III	13 (33.3)	24 (61.5)	2 (5.1)	39 (62.9)
- Borrmann IV	3 (42.9)	4 (57.1)	0 (0.0)	7 (11.3)
Histological grade				
- Differentiated	0 (0.0)	6 (75.0)	2 (25.0)	8 (12.9)
- Moderately differentiated	6 (20.0)	22 (73.3)	2 (6.7)	30 (48.4)
- Undifferentiated	12 (50.0)	12 (50.0)	0 (0.0)	24 (38.7)

As for the degree of differentiation, it was differentiated in 8 cases (12.9 %), moderately differentiated in 30 (48.4 %), and undifferentiated in 24 (38.7 %). Also, it was found that 75 % of the differentiated and 73.3 % of the moderately differentiated were patients with intestinal gastric cancer, and there was no difference in undifferentiated patients with 50 % for intestinal and diffuse types, as shown in **Table 2**.

Figures 1 and **2** show the distribution of histology type according to Lauren by age group and sex. The intestinal type was observed in 31 (77.5 %) males, and, in females, the diffuse type was observed in 8 (44.4 %) and the intestinal type in 9 (22.5 %). The male:female ratio for the intestinal type was 3.44:1.00 (31/9) and for the diffuse type was 1.25:1.00 (10/8). In men, an increase in intestinal adenocarcinoma was observed after the age of 50, with a peak at 60-69 years old, whereas the diffuse type remains the same (**Figure 1**). In women, it was observed that the diffuse type of increase in early ages (27 to 39 years of age) but remains the same as age increases, unlike the intestinal type, in which an increase is observed between 60 and 69 years of age, period in which a peak was presented (**Figure 2**).

DISCUSSION

An epidemiological analysis made at the Hospital Carlos Andrade Marín in Quito, Ecuador, showed that the prevalence of gastric cancer is 61 % in men and 39 % in women, with an average age of 68 years for both sexes. The associated factors are *H. pylori* (46 %), alcohol consumption (36 %), and tobacco consumption (35 %) [14]. In Mexico, it is among the main causes of hospital morbidity in men, and the highest rate is in the 75-79 age group (47 out of 100 000 men), followed by the 64-74-age group (38 out of 100 000). It is well known that one of the most common types of malignant tumors that kill Mexican patients is gastric cancer, which is the third leading cause of death in both the female (7 %) and the male population (8.6 %) [10]. Novo *et al.* reported that 75 % of gastric cancer cases occur in men and 25 % in women, mainly between the ages of 70 and 80 years (50 %) and between 60 and 70 years (34 %), respectively [15]. This is in line with our study, in which males are the most affected, with 72.6 % of the cases, as opposed to females, with 27.4 % of the cases, with a male:female ratio of 2.64: 1.00, as in the aforementioned studies.

Common symptoms and signs include early satiety, weight and appetite loss, epigastric pain, and vomiting; advanced ulcerated adenocarcinomas may manifest with hematemesis or melena, and if it affects the pyloric antrum, it may cause a gastric outlet obstruction in the duodenum and cause a pyloric syndrome [16]. Our study showed that the most frequent symptom was pain (98.4 %), followed by weight loss (64.5 %), vomiting and melena (less than 40 %), which coincides with studies such as Sánchez *et al.*, who reported that the symptoms of gastric cancer are not specific and may mimic other gastroduodenal diseases, usually pain (70 %), anorexia, nausea and weight loss (50 %), dysphagia (20 %), and gastrointestinal bleeding (5 %) [17].

The location of gastric cancer in the pyloric antrum in between 40 % and 60 % of the cases, the body in 20 % -25 %, and the fundus in 15 % -20 %. The histological intestinal type is the most frequent [16], which coincides with our study, in which the body and antrum showed equal percentages, but there was a slight difference in the percentage of the fundus (4.8 %) that may explained by the sample size. Regarding histology, clinical differences have been observed between cancer types, either diffuse or intesti-

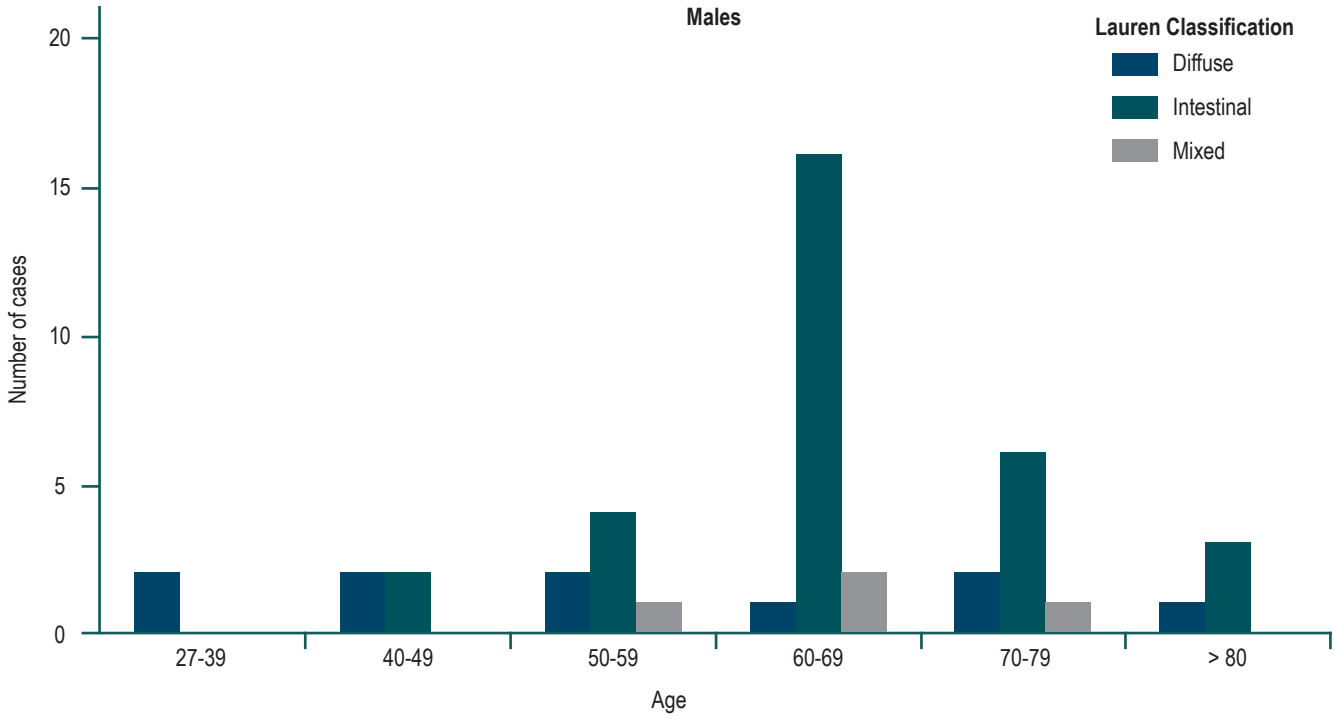

Figure 1. Distribution of histological types by age groups in men.

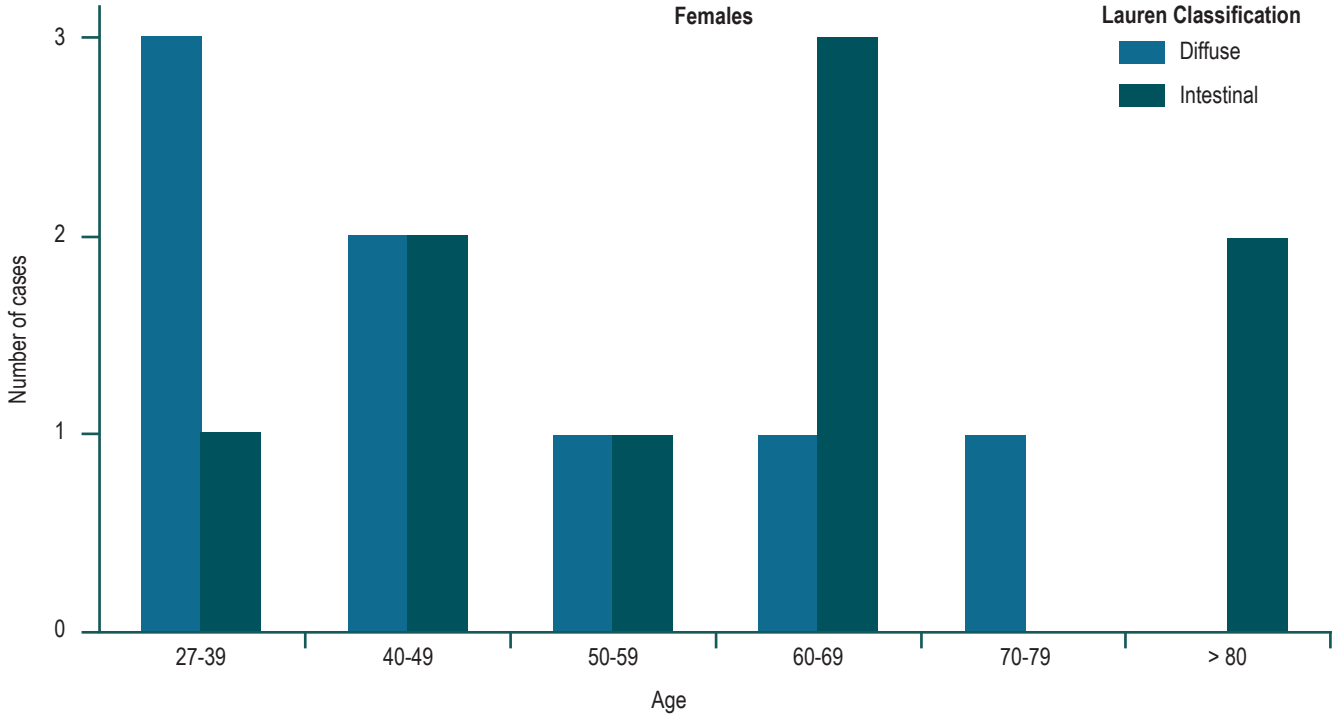

Figure 2. Distribution of histological types by age groups in women.

nal (according to Lauren classification). The diffuse type is found in all age groups with a similar distribution with respect to sex, unlike the intestinal type, which predominates in men and the elderly. It is also found in the body of the stomach, while the intestinal type predominates more in the antrum and incisura. Furthermore, the diffuse type tends to invade the gastric wall and produce metastases, in addition to having a more rapid progression and a poorer prognosis [18].

Regarding histology, according to the Lauren classification and tumor location, our study found that intestinal type predominates in men, with 31 cases (77.5 %), and was located in the body in 20 cases (71.4 %), while the diffuse type was predominant in women, with 8 cases (44.4 %) and located mostly in the antrum, with 10 cases (32.3 %). In this regard, there were differences with the studies already mentioned above, which could be related to the sample size and duration of our study.

In Ecuador, Andrade *et al.* demonstrated that the most frequent gastric cancer types, according to the Lauren classification, were diffuse adenocarcinoma (60 %) and intestinal adenocarcinoma (40 %) [14]. Borch *et al.* reported that the intestinal type accounted for 52.7 % of the cases, followed by diffuse, with 33.4 %, and mixed, with 13.9 % [19]. In turn, in 2015, Martínez-Galindo *et al.* published in Mexico a study with 415 cases of gastric adenocarcinoma in which 230 cases (55.2 %) presented with the diffuse type, the mean age was 54.02 years, 51.3 % of the sample were men, 118 cases (28.2 %) presented with the intestinal type, and the mean age of presentation was 63.43 years [10]. There are great differences both in regions and in countries with respect to the most frequent histological type, which was the intestinal type in our study (64.5 %), followed by the diffuse type (29 %), as demonstrated in studies already published such as that of Borch *et al.* [19] and Marín *et al.* [20]. However, recent studies, such as that of Martínez-Galindo *et al.* [10], and Quiñones *et al.* [21], report that the most common is the diffuse type. In Ecuador, Andrade *et al.* demonstrated that the diffuse type is the most frequent due to the decrease in the incidence of intestinal cancers or to the change of provinces, but this latter aspect should be studied in another research considering the few works on this issue in the country.

The study conducted by Quiñones *et al.*, published in 2011, showed that in Peru the diffuse type was more frequent (51.5 %), followed by the intestinal type (33.9 %), and an association was found between the intestinal type and the distal location (58.3% vs. 44.1 %, $p = 0.004$), and between the diffuse type and the proximal location (19.3 % vs. 12.4 %; $p = 0.049$) [21]. Marín *et al.* published about the types of proximal neoplasms; the intestinal (51 %) and diffuse (49 %) types are observed almost in the same proportion, whereas the prevalence is intestinal in 64 %, as opposed to diffuse, with 36 %, for distal locations [20]. These findings coincide with our study, in which the intestinal type was more proximal (71.4 %) and was more common in men, whereas the diffuse type was more distal (32.4 %) in women, unlike the study of Quiñones *et al.* [21]

Regarding staging, Andrade *et al.*, in a study conducted at the at the Hospital de Especialidades Carlos Andrade Marín in Quito, Ecuador, showed that 84 % of the sample were treated in an advanced stage, in which Borrmann type III or infiltrative ulceration was found to be the most frequent with 42 %. This type of tumor was located mainly in the antrum (39 %), followed by the body (22.7 %), with a distal location in the stomach (61 %).[14] Andrade *et al.* conducted a study in Cauca, Colombia, between 2003 and 2006, with 225 cases of gastric cancer, of which 66 % were in men, 84 % in elderly patients, with distal location in 68 % of the cases, an advanced stage in 92 %, and with macroscopic Borrmann classification type III in 58 % and Borrmann IV in 23 %; histology showed that 79 % of the tumors were intestinal type and 21 % diffuse type[22]. The results of the previous study coincide with ours in that the Borrmann III type is the most frequent (62.9 %) and, regarding the histological type, the intestinal type was the most frequent (61.5 %).

In an epidemiological analysis performed in Ecuador, according to histological grade, differentiated gastric cancer was observed in 15 % of the cases, moderately differentiated in 25 %, poorly differentiated in 45 %, and undifferentiated in 15 % [14]. Finally, Nakamura *et al.* [23] stated that differential gastric cancer is more likely to be of the intestinal type and that undifferentiated or poorly undifferentiated gastric cancer is more diffuse [24].

However, prospective, long-term studies with larger sample sizes, as well as multicenter studies should be conducted to confirm the findings of our study. Our hospital is a referral center in the province of Guayas, so the present findings may not be generalized to the entire Ecuadorian population; however, they could be taken into account to provide a closer look at the characteristics of patients with gastric cancer in the province, because this is a referral hospital of the Ministry of Health in that region. The limitation of this study is the lack of specialized pathologists in our unit to report results in cases whose histopathological reports had a delay time of more than 15 to 30 days.

CONCLUSIONS

Gastric cancer is diagnosed in advanced stages, is more common in men than women, and its most common age

of presentation is between 60 and 70 years old. There was a relationship with alcohol and tobacco use as a risk factor, and the most predominant symptoms were pain and weight loss. Its most frequent location was the antrum, and the most frequent type of gastric cancer was the intestinal type, followed by the diffuse type. The intestinal type occurred at a more advanced age and is more frequent in the body at a proximal location; on the other hand, the diffuse type was more common at early ages and was more frequently observed in the antrum and at a distal location. It could be said that, in our hospital, intestinal gastric cancer occurred in advanced ages, more frequently at the proximal level, and in the classification of advanced gastric cancer according to Borrmann type III, which could have an impact on treatment and prognosis. The results obtained herein justify the implementation of programs for the timely detection and treatment of this serious disease.

Data confidentiality

The authors state that they have followed the protocols in force at their work centers on the disclosure of patient data.

Right to privacy and informed consent

The authors obtained informed consent from the patients or subjects referred to in the article. This document is held in the possession of the corresponding author.

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Conflicts of interest

None declared by the authors.

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