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Expression of mucins in gastrectomy specimens for gastric adenocarcinoma and their relationship with pTNM staging in a quaternary care hospital in Bucaramanga, Colombia, 2020-2024

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Abstract

Introduction: Gastric cancer is the fifth most frequent neoplasm and the fourth leading cause of oncological mortality worldwide. Analyzing the immunohistochemical profiles of mucins in this neoplasm and its precursor lesions could be correlated with relevant histological variables and provide prognostic value within the clinicopathological context. **Objective:** To establish the relationship between the immunohistochemical profile of mucins and the pTNM severity in gastrectomy specimens for gastric adenocarcinoma received in the pathology laboratory of a quaternary care hospital in Bucaramanga, 2020-2024. **Methodology:** This was an analytical, observational, cross-sectional study of 41 samples. The expression of MUC1, MUC2, and MUC5AC was evaluated in tumor areas and tumor-adjacent mucosa showing intestinal metaplasia, and these findings were correlated with histological variables and pTNM staging parameters. **Results:** The mean age of the cases was 66.41 years, and 72.56% were male. Type III intestinal metaplasia occurred in 64.93% of cases (n = 27), and these cases more frequently exhibited variables related to poorer prognosis; likewise, in the tumor area, 53.1% of cases (n = 17) presented the gastric phenotype, which tended to show greater depth of invasion and distant metastasis, without a statistically significant association. **Conclusions:** Differential patterns of mucin expression were observed between metaplastic areas and the tumor. Type III intestinal metaplasia demonstrated a stronger association with aggressive histological features. No statistically significant correlation was found between mucin expression and pTNM parameters. These findings support the possible use of mucins as markers of differentiation and tumor progression in gastric cancer, although additional studies are required to confirm their clinical utility.

Keywords: Gastric Cancer; Mucins; Lymphatic Metastasis; Neoplasm Staging; Immunohistochemistry; Prognosis.

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Introduction

Gastric cancer (GC) is the fifth most common cancer and the fourth leading cause of cancer-related mortality worldwide[1]; in Colombia, in 2020, it was the leading cause of oncological mortality, accounting for 6,451 deaths[2]. The prognosis remains bleak in our setting due to late detection, as we lack systematic preventive guidelines.

Mucins are a family of high-molecular-weight glycoproteins that may be secreted (MUC2, MUC5, or MUC6) or bound to the gastric epithelial membrane as part of the glycocalyx (MUC1). Their function includes forming gels that protect the mucosa from external mechanical, chemical, or microbiological factors, as well as participating in cellular signaling pathways that regulate other molecules. Overexpression of certain mucins has been reported as occurring during carcinogenesis, employing mechanisms that previously served as defense mechanisms against tumor growth and dissemination[3].

In healthy gastric mucosa, neutral mucins such as MUC1, MUC5AC, and MUC6 are found, each with specific localization: MUC1 in the cell membrane of the foveolar epithelium and in mucous glands; MUC5AC in the corpus-antral foveolae; and MUC6 in the deep antral-pyloric glands and in the mucous neck cells of the gastric body[4]. Based on predisposing factors such as *Helicobacter pylori* (*Hp*) infection, a proinflammatory environment is favored, progressing through the sequence described by Pelayo Correa: intestinal metaplasia, followed by intestinal dysplasia, and finally GC[5]. This sequence alters the usual mucin expression, causing decreased MUC5AC, overexpression of MUC6, and de novo induction of MUC2, which is characteristic of intestinal metaplasia[6].

Intestinal metaplasia can be classified into three types according to the predominant mucin: type I, characterized by expression of MUC1 and/or MUC5AC; type II, with exclusive expression of MUC2; and type III or mixed, which coexpresses MUC2 along with MUC1 or MUC5AC. Likewise, gastric adenocarcinomas have been classified into four phenotypes: the gastric phenotype, which shows exclusive expression of MUC1, MUC5AC, and/or MUC6; the intestinal phenotype, which expresses MUC2, MUC3, MUC4, and/or MUC13; the mixed phenotype; and the null or unclassifiable phenotype, which does not express any of the aforementioned mucins[7] (**Table 1**). The frequency of these phenotypes varies across case series, and the data in the literature are inconsistent regarding which phenotype exhibits higher metastatic potential[8-11].

Table 1. Gastric adenocarcinoma phenotypes according to mucin expression

Phenotype	MUC5AC	MUC6	MUC2	MUC1	CD10	Description
Gastric	+ / ±	+ / ±	–	+ / ±	–	Expression of gastric mucins (MUC5AC, MUC6) with absence of intestinal markers (MUC2, CD10).
Intestinal	–	–	+	–	+	Expression of intestinal mucins (MUC2, CD10) with loss of gastric mucins.
Mixed	+ / ±	+ / ±	+	±	±	Coexpression of gastric and intestinal mucins (MUC5AC/MUC6 together with MUC2/CD10).
Null	–	–	–	–	–	Total absence of gastric and intestinal mucin expression.

MUC5AC: High–molecular-weight glycoprotein MUC5AC; **MUC6:** High–molecular-weight glycoprotein MUC6; **MUC2:** High–molecular-weight glycoprotein MUC2; **MUC1:** High–molecular-weight glycoprotein MUC1; **CD10:** Membrane-bound glycoprotein.

Given the broad available evidence and the additional need to generate population-specific knowledge, the present study was proposed to be conducted in the metropolitan area of Bucaramanga, using gastrectomy specimens submitted to the pathology laboratory of the Hospital Universitario de Santander (H.U.S) to establish the relationship between the immunohistochemical profile of mucins and pTNM severity in gastrectomies for adenocarcinoma between 2020 and 2024. The characterization of mucins represents a simple and cost-effective tool for identifying histological patterns associated with poorer prognosis[12].

Methodology

Study type, population, and sample

This was an analytical, observational, cross-sectional study using non-probabilistic sampling to determine the association between mucin expression and selected histopathological variables. Patients aged over 18 years who underwent total or subtotal gastrectomy and had their specimens submitted for histopathological analysis to the pathology laboratory of the H.U.S. between 2020 and 2024 were selected. Patients with a history of unknown primary tumor, a history of another gastrointestinal tract neoplasm other than gastric, a history of prior treatment for oncological disease, and tumors of histologic type other than adenocarcinoma were excluded.

For the sample size calculation, the findings of Wang et al.[13] were taken into account. They evaluated in 76 patients the association between MUC5AC and the presence of lymph node metastasis, an outcome related to poorer prognosis, determining a calculated Odds Ratio (OR) of 0.08 and a 90% event rate among unexposed subjects, yielding a minimum sample size of 36 specimens with an additional 10% (4 specimens) included to account for losses, for a total of 40 gastrectomy specimens.

Procedure

Immunohistochemical staining and evaluation of MUC expression

Three types of mucins were used, acquired from the commercial supplier ZETA Corporation in the form of primary murine monoclonal antibodies: MUC-1 (ZM32) (concentrated format, 0.5 ml), MUC-2 (Ccp58) (concentrated format, 0.5 ml), and MUC-5AC (ZM148) (concentrated format 0.5 ml); each antibody was supplied as buffer with protein carrier, and preservative. These antibodies were stored at 2 to 8°C and show cytoplasmic expression for MUC1 and membrane expression for MUC2 and MUC5AC. Quality control for these antibodies was performed using positive control tissues: breast carcinoma for MUC1, colon carcinoma for MUC2, and gastric carcinoma for MUC5, provided by the histotechnologist.

Data collection

Histopathological reports of 41 patients stored in the Pathology Department archives and meeting the established inclusion criteria were reviewed; of these, 40 also had available sociodemographic data. Each case was assigned a consecutive number, which was used to record data in an Excel database without including names, identification documents, or other personal data. Subsequently, the corresponding paraffin blocks were retrieved to obtain six slides per patient: three with mucin immunohistochemistry in the tumor-adjacent area and three in the tumor area. The histological evaluation was performed using the OLGA System for grading atrophy, the OLGIM System for intestinal metaplasia, and the Vienna Classification for assessing epithelial dysplasia. The histological subtype of adenocarcinoma was established according to the WHO Histological Classification (2019), complemented by the determination of each mucin's expression pattern. The histological review and immunohistochemical interpretation were performed by a second-year resident, in collaboration with a pathologist with more than 35 years of experience in interpreting gastric biopsies. In cases with discrepancies in staining patterns, the slide was reviewed by a third evaluator with expertise in the subject. No interobserver variability study was performed. The data derived from the analysis were recorded in an Excel database specifically designed for this study.

Statistical analysis

Univariate analysis

The analysis was performed based on variables collected from the H.U.S. admission clinical record, as well as from the histological evaluation and the operation report recorded in the Pathology Department. The variables were analyzed according to their level of measurement: means or medians were calculated for continuous variables, and proportions for categorical or nominal variables, each accompanied by corresponding 95% confidence intervals. Group comparisons were performed after verifying data normality, using the Mann-Whitney test or

the t-test for quantitative variables, and the chi-square (χ^2) test or Fisher's exact test for qualitative variables. Differences with a p-value <0.05 were considered statistically significant.

Bivariate analysis

The association between the tumor phenotype and each independent variable of the tumor, lymph node, metastasis (pTNM) staging system was explored. Simple logistic regression models were used, with Odds Ratio (OR) as a measure of effect. Variables that showed a stronger effect estimate, identified by a p-value <0.20, were selected and, when required, subsequently dichotomized according to values described in the literature. The data were exported and analyzed using Stata 12.0. All tests were two-tailed, and p-values <0.05 were considered statistically significant.

Ethical considerations

The study was approved by the Technical Scientific Research Committee of the H.U.S. (Minutes No. 02 of February 28, 2024) and the Scientific Research Ethics Committee (CEINCI) of the Universidad Industrial de Santander (Minutes No. 06 of April 12, 2024), regarding the study design and methodology.

Results

A total of 40 patients with their respective gastrectomy specimens were included in the sociodemographic analysis, and an additional gastrectomy specimen without clinical data was added. Of these, 72.5% (n = 29) were male; more than half reported a history of smoking, one-third reported chronic alcohol consumption, and 10.2% (n = 4) had a family history of GC (**Table 2**).

Table 2. Descriptive analysis of clinical data

Variable	% (n) (40)
Mean age ± SD	66.41 ± 12.60
Sex	
Female	27.52 (11)
Male	72.56 (29)
Toxicological history	
Alcoholism	26.84 (11)
Smoking	51.23 (21)
Family history of GC	10.26 (4)

SD: Standard deviation

The presence of *Hp* in the specimens was minimal, with only one positive case (2.43%, n = 1), and in very low quantity. In the histological findings related to preneoplastic pathology in tumor-adjacent areas, moderate intestinal metaplasia and low-grade dysplasia were the two most common, identified in 56.13% (n = 23) and 39.02% (n = 16), respectively. The mean largest tumor diameter was 5.33 cm; the most common histological subtype was tubular (53.65%, n = 22), followed by mixed (24.42%, n = 10), with histological grades 2 and 3 occurring in similar proportions. The mean number of lymph nodes involved by tumor was 6.22 (**Table 3**).

Table 3. Descriptive analysis of histopathological data

Variable	% (n)
Presence of *H. pylori*	
+/++++	2.43 (1)
++/++++	0
+++/++++	0
++++/++++	0
Atrophy	
Mild	7.32 (1)
Moderate	9.76 (4)
Severe	2.44 (1)
Intestinal metaplasia	
Mild	29.27 (12)
Moderate	56.13 (23)
Severe	14.63 (6)
Not assessable	4.88 (2)
Dysplasia	
Low grade	39.02 (16)
High grade	36.59 (15)
Histological subtype of adenocarcinoma	
Tubular	53.66 (22)
Mixed	24.39 (10)
Mucinous	9.76 (4)
Poorly cohesive	12.2 (5)
Tumor differentiation grade	
Well differentiated	0
Moderately differentiated	53.66 (22)
Poorly differentiated	46.39 (19)
Mean largest tumor diameter ± SD	5.33 ± 2.64
Mean number of positive lymph nodes ± SD	6.22 ± 8.76

SD: Standard deviation

Descriptive analysis of variables according to mucin expression in the metaplastic area

Type III intestinal metaplasia was the most prevalent, present in 64.93% (n = 27) of cases. It was related to tubular and mixed histological subtypes and showed a higher frequency of variables associated with poorer clinical courses, such as depth of invasion up to the serosa (61.94%, n = 25), lymphovascular invasion (61.23%, n = 19), perineural invasion (68.75%, n = 11), tumor necrosis (73.94%, n = 17), lymph node metastases (68.93%, n = 20), and distant metastases (60%, n = 3) (Table 4). The predominant immunohistochemical pattern was intense positivity for MUC1 and MUC2, along with the absence of MUC5AC. Type I metaplasia, in turn, occurred in the same adenocarcinoma subtypes, although with a higher mean number of lymph nodes involved and a greater mean diameter of metastatic deposit (1.14 cm).

Table 4. Variables according to mucin expression in the metaplastic area

Type of intestinal metaplasia	Lymphovascular invasion	Perineural invasion	Tumor necrosis	Lymph node metastasis	Mean number of positive lymph nodes	Distant metastasis
	% (n)	% (n)	% (n)	% (n)	Mean ± SD	% (n)
Type I	25.81 (8)	18.84 (3)	17.42 (4)	24.11 (7)	7.78 ± 14.72	40 (2)
Type II	12.92 (4)	12.51 (2)	8.73 (2)	6.92 (2)	6.75 ± 8.30	0
Type III	61.23 (19)	68.75 (11)	73.94 (17)	68.93 (20)	5.96 ± 6.64	60 (3)

SD: Standard deviation

Descriptive analysis of variables according to mucin expression in the tumor area

In the phenotypic classification of tumors according to mucin expression, the gastric phenotype was the most frequent (52.52%, n = 22), followed by the mixed phenotype (42.51%, n = 17). The former exhibited a greater mean tumor diameter (5.98 cm) and a predominance of tubular and poorly cohesive subtypes. It also showed higher frequencies of lymphovascular invasion (53.11%, n = 17), tumor necrosis (58.33%, n = 14), lymph node metastases (53.32%, n = 16), distant metastases (66.74%, n = 4), and poorer tumor differentiation (**Table 5**). In the comparative analysis of tumor phenotypes and histological subtypes of adenocarcinoma, the gastric phenotype was predominant among tubular (n = 15) and poorly cohesive (n = 4) tumors, whereas the mixed phenotype was most commonly associated with tubular (n = 5) and mixed adenocarcinomas (n = 7).

Table 5. Variables according to mucin expression in the tumor area

Phenotype	Lymphovascular invasion	Perineural invasion	Tumor necrosis	Lymph node metastasis	Mean number of involved lymph nodes	Distant metastasis
	% (n)	% (n)	% (n)	% (n)	Mean ± SD	% (n)
Gastric	53.11 (17)	38.94 (7)	58.33 (14)	53.32 (16)	6.76 ± 10.60	66.74 (4)
Intestinal	0	0	0	0	0	0
Mixed	40.62 (13)	55.51 (10)	37.54 (9)	40 (12)	5.35 ± 6.92	33.31 (2)
Null	6.23 (2)	5.62 (1)	4.21 (1)	6.73 (2)	8 ± 5.66	0

SD: Standard deviation

The mixed phenotype showed greater perineural invasion (55.51%, n = 10) and involvement up to the serosa (29%, n = 12); however, it was the gastric phenotype that invaded adjacent organs in 76.94% (n = 10) of cases. Only two cases showed the null phenotype; nonetheless, this group had the highest mean number of lymph nodes involved (8 ± 5.66) and the largest diameter of lymph node metastasis at 2.65 cm. When considering expression type and degree of differentiation, MUC2 was the most frequently expressed mucin in moderately differentiated tumors (63.61%, n = 26) and poorly differentiated tumors (68.42%, n = 28).

Bivariate analysis between mucin expression variables and pTNM variables

For the bivariate analysis, the mucins most frequently expressed in the tumor area or by tumor phenotype, along with the three pTNM variables, were considered. No statistically significant association was found, as all p-values were >0.05 and the confidence intervals included 1 **(Tables 6 and 7)**. Likewise, when comparing tumor size among the three groups of intestinal metaplasia and among the different tumor phenotypes, no significant differences were observed.

Table 6. Bivariate analysis using simple logistic regression models between mucins expressed in the tumor area and the pTNM variables

Expression in tumor area	Depth of invasion		Distant metastasis	
	OR (95% CI)	P*	OR (95% CI)	P*
MUC1	1.10 (0.38 – 3.19)	0.853	1.04 (0.22 – 4.98)	0.953
MUC2	0.66 (0.16 – 2.71)	0.565	0.83 (0.07 – 8.70)	0.879
MUC5AC	0.62 (0.22 – 1.75)	0.372	—	—

OR: Odds Ratio; 95% CI: 95% confidence interval; P*: Wald test of the simple logistic regression model; MUC1: High-molecular-weight glycoprotein MUC1; MUC2: High-molecular-weight glycoprotein MUC2; MUC5AC: High-molecular-weight glycoprotein MUC5AC.

Table 7. Bivariate analysis using simple logistic regression models between tumor phenotype and the pTNM variables

Phenotype	Depth of invasion		Lymph node metastasis		Distant metastasis	
	OR (95% CI)	P*	OR (95% CI)	P*	OR (95% CI)	P*
Gastric	2.08 (0.74–5.83)	0.161	1.06 (0.25–4.43)	0.929	2.11 (0.34–13.09)	0.420
Mixed	0.55 (0.19–1.52)	0.253	0.63 (0.15–2.65)	0.530	0.66 (0.10–4.13)	0.663
Null	0.60 (0.06–5.60)	0.657	—	—	—	—

OR: Odds Ratio; 95% CI: 95% confidence interval; P*: Wald test of the simple logistic regression model.

Discussion

We found a clear predominance of male patients, with histories of smoking and alcohol consumption, and a low presence of *Hp* infection. Based on mucin classification, type III intestinal metaplasia and the gastric tumor phenotype were the most common subtypes and were, in a greater number of cases, associated with deep tumor invasion, lymphovascular involvement, tumor necrosis, lymph node metastases, and distant metastases. These lesions mostly showed an intense MUC1 immunohistochemical expression pattern, variable MUC2 expression, and absence of MUC5AC.

The incidence of GC is approximately twice as high in men as in women, a pattern that is particularly evident in Asian countries such as Mongolia, Japan, and South Korea[14,15]. In Colombia, a retrospective study conducted at Clínica Las Américas in Medellín evaluated 130 gastrectomy cases, showing a predominance of male patients, a mean age of 62.2 years, 20% with a family history of GC, and 30% with *Hp* infection[16].

The presence of *Hp* in our population was strikingly low. In contrast, Gómez et al., in 2012, reported *Hp* infection in 50% of patients younger than 40 years and in 75.2% of those older than 40 years with a diagnosis of gastric adenocarcinoma[17]. Although its role in gastric carcinogenesis is well established, several factors could explain its low detection in our study: first, prior antibiotic use that was not assessed in the medical records; second, postoperative ischemia time; third, inadequate fixation of surgical specimens; or fourth, observer-related errors in the histological assessment of the tumor-adjacent area. In tumor areas, the microenvironment may become hostile to the survival of bacilli due to parietal cell dysfunction (with consequent changes in pH), loss of epithelial niches resulting from intestinal metaplasia or neoplasia, accelerated and disorganized tumor growth, hypoxia, and immunological changes, including infiltration by tumor-associated macrophages, dendritic cells, and regulatory T lymphocytes[18,19]. Other microorganisms of the gastric microbiota may play a role in oncogenesis, such as *Fusobacterium nucleatum*, which has been associated with poorer prognosis in GC even after *Hp* eradication[20]. Moreover, *Hp* becomes secondary in studies such as that of Oosterlinck et al.[7], in which microorganisms such as *Neisseria*, *Prevotella*, and *Veillonella*, commonly found in the oral flora, are increased and modify the microbiota in

tumors expressing MUC13, a marker of the intestinal phenotype associated with a poorer prognosis. Conversely, adenocarcinomas with high MUC2 levels and intermediate MUC4 levels show decreased *Streptococcus* and abundance of *Lactobacillus*, improving survival[7].

The global prevalence of preneoplastic lesions such as atrophic gastritis, intestinal metaplasia, and dysplasia has been estimated at 25.4%, 16.2%, and 2%, respectively; these lesions are more frequent in countries with intermediate-to-high GC incidence ($p < 0.01$) and in *Hp*-infected patients ($p < 0.01$)[21-23]. In Colombia, Carlosama et al. applied the OLGA system as a risk marker for GC in a case-control study conducted with a population from the southwest region of the country. They found intestinal metaplasia in 59% of cases, chronic atrophic gastritis in 23%, dysplasia in 10%, and gastric adenocarcinoma in 8%, with no significant difference in *Hp* infection between cases and controls[24].

Our findings, characterized by diffuse MUC1 expression, variable MUC2 expression, and absence of MUC5, are consistent with the phenotypic shift toward intestinal phenotypes described by Correa, in which there is a progressive decrease in gastric mucins and an increase in intestinal mucins (sialomucins and sulfomucins)[6]; however, they contrast with the findings of similar studies conducted in our continent, such as that by Peraza et al., in which MUC5 and MUC2 were among the main mucins expressed[25]. In our work, type III or incomplete intestinal metaplasia (IIM) was the most frequent, a finding associated with a fivefold increased risk of progression to gastric cancer or dysplasia compared with the complete form. When compared with other metaplasia subtypes in Western populations, type III shows a significantly higher risk of these outcomes than types II and I (RR: 4.65; 95% CI: 2.30–9.42)[23].

Regarding tumor stage stratification, Mantziari in 2023 demonstrated the excellent discriminatory capacity of the eighth edition of the pTNM classification, showing decreased survival as tumor stage increases. This classification has been validated in America, Europe, and Asia according to multiple databases[15]. On our continent, several investigations have been conducted to evaluate each component of the classification: tumor size, lymph node metastases, and distant metastases. Universities in Bogotá, in collaboration with the National Cancer Institute, analyzed a cohort of 332 patients who underwent gastrectomy for GC, reporting a mean tumor size of 5 cm[26]. Tapia et al. in Chile found a mean tumor size of 65.4 mm, results comparable to ours[27]. Finally, a retrospective South Korean cohort study including 655 patients who underwent total gastrectomy for adenocarcinoma of the proximal third of the stomach found that tumors measuring 4.1 cm or larger were associated with a higher incidence of lymph node metastases (40.0%) compared with smaller tumors (20.4%)[16].

Similarly, Song et al. identified a higher frequency of intestinal and mixed phenotypes. In the former, 20% of tumors were poorly differentiated, whereas the latter showed greater depth of invasion; these authors theorized that the progressive loss of glandular architecture facilitates invasion into the submucosa and is associated with a higher risk of lymph node metastases—an observation reflected in our series, which showed a higher mean number of positive lymph nodes in that subgroup[8]. We also observed a trend indicating that adenocarcinomas with the mixed phenotype had the smallest mean tumor size (4.07 cm), and tumors below this size threshold had a 5.5-fold higher probability of exhibiting this phenotype ($p = 0.014$; 95% CI: 1.41–21.37).

Regarding the mucins studied in this work, Wang et al. note that MUC2 expression is significantly associated with tumors of higher histological grade but with a lower incidence of lymphovascular invasion; in contrast, when expressed, MUC5AC shows a lower frequency of lymph node metastases, yet is associated with greater depth of tumor invasion and a high histological grade. MUC1 expression was significantly associated with vascular and lymphatic invasion, lymph node metastases, diffuse histological subtype, advanced disease, and the presence of distant metastases, when compared with negative cases[28].

Most studies on mucin-targeted therapeutic strategies have been conducted using murine or in vitro models, mainly with pancreatic adenocarcinoma, where MUC1 plays a fundamental role. Over the past five years, this molecule has been established as the most promising therapeutic target due to its overexpression and aberrant glycosylation[29], which has driven the development of radiopharmaceuticals, nanomedicines, therapeutic vaccines, and cell-based immunotherapies such as CAR-T and CAR-M; among these, the TAB004 antibody is emerging as

the most promising[30]. Mucins are not yet used routinely in therapeutic decision-making, and a targeted therapy with demonstrated clinical efficacy is not yet available.

One of the main strengths of this study lies in its regional focus, as it was conducted in an area with a high GC prevalence. Additionally, despite the limited sample size (n = 41), the results obtained regarding the immunohistochemical profile of MUC1, MUC2, and MUC5AC are consistent with those reported in international meta-analyses and systematic reviews, thereby supporting their external validity. The costs of immunohistochemistry and the small sample size precluded multivariate analyses to establish associations. Possible biases include selection bias, as we considered only a single referral center rather than a population-based registry. Likewise, measurement bias cannot be ruled out, since immunohistochemical interpretation is subject to interobserver variability.

GC remains a highly prevalent disease worldwide and in our population, and is strongly associated with risk factors such as smoking and alcohol consumption. In this context, mucins enable the identification of patterns linked to more aggressive biological behavior. The study of mucins not only provides complementary diagnostic value but also contributes to a better understanding of tumor differentiation processes and to potential prognostic stratification in gastric adenocarcinomas.

Although no association was found between mucin expression and histopathological variables, the findings provide a basis for formulating relevant hypotheses regarding the possible role of these markers in GC progression. These findings reinforce the need to continue this line of research through multicenter studies with greater statistical power and multivariate analyses, which allow confirmation of these observations and a deeper exploration of their prognostic utility.

Conclusions

A common immunohistochemical pattern was identified in both intestinal metaplasia and tumor areas, characterized by diffuse MUC1 expression, variable MUC2 expression, and absence of MUC5AC, a profile consistent with type III intestinal metaplasia and a mixed tumor phenotype. These variants, widely associated in the literature with poorer prognosis, were related in our study to unfavorable morphological characteristics, deep invasion, necrosis, lymphovascular involvement, and lymph node involvement, although statistical significance was not achieved due to sample size.

Author contributions

NE and DA designed and developed the study, and prepared the report and manuscript. JC provided thematic guidance. LA and TM advised on the statistical and methodological analyses. All authors read, edited, and approved the manuscript.

Ethical considerations

The management of information in this study was conducted in accordance with international guidelines for the protection of human rights, guided by the principles of the Belmont Report and the Council for International Organizations of Medical Sciences (CIOMS). This study is classified as "minimal risk" research according to item "A" of Article 11 of Resolution 008430 of 1993 of the Ministry of Health of Colombia and the Declaration of Helsinki.

Conflict of interest

The authors declare no conflicts of interest.

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The authors report that they did not use Artificial Intelligence, language models, machine learning, or similar technologies to create or assist with the creation or editing of any of the content in this manuscript.

References

1. Etemadi A, Safiri S, Sepanlou SG, Ikuta K, Bisignano C, Shakeri R, et al. The global, regional, and national burden of stomach cancer in 195 countries, 1990–2017: a systematic analysis for the Global Burden of Disease study 2017. Lancet Gastroenterol Hepatol. 2020; 5(1): 42–54. doi: https://doi.org/10.1016/S2468-1253(19)30328-0

2. Barreto CP, Limas LM, Porras A, Rico Mendoza A. Carga de enfermedad de cáncer gástrico desde 2010 hasta 2019 en Tunja, Boyacá, Colombia. Rev Colomb Gastroenterol. 2023; 38(1): 12–8. doi: https://doi.org/10.22516/25007440.916

3. Bhatia R, Gautam SK, Cannon A, Thompson C, Hall BR, Aithal A, et al. Cancer-associated mucins: role in immune modulation and metastasis. Cancer Metastasis Rev. 2019; 38(1-2): 223-236. doi: https://doi.org/10.1007/s10555-018-09775-0

4. Battista S, Ambrosio MR, Limarzi F, Gallo G, Saragoni L. Molecular Alterations in Gastric Preneoplastic Lesions and Early Gastric Cancer. Int J Mol Sci. 2021; 22(13): 6652. doi: https://doi.org/10.3390/ijms22136652

5. Correa P, Piazuelo MB. Cáncer gástrico: el enigma colombiano. Rev Col Gastroenterol. 2010; 25(4): 334-337. http://www.scielo.org.co/scielo.php?script=sci_arttext&pid=S0120-99572010000400001&lng=en

6. Correa P, Piazuelo MB, Wilson KT. Pathology of gastric intestinal metaplasia: clinical implications. Am J Gastroenterol. 2010; 105(3): 493-8. doi: https://doi.org/10.1038/ajg.2009.728

7. Oosterlinck B, Ceuleers H, Arras W, De Man JG, Geboes K, De Schepper H, et al. Mucin- microbiome signatures shape the tumor microenvironment in gastric cancer. Microbiome. 2023; 11(1) :86. doi: https://doi.org/10.1186/s40168-023-01534-w

8. Song K, Yang Q, Yan Y, Yu X, Xu K, Xu J. Gastric mucin phenotype indicates aggressive biological behaviour in early differentiated gastric adenocarcinomas following endoscopic treatment. Diagn Pathol. 2021; 16(1): 62. doi: https://doi.org/10.1186/s13000-021-01122-2

9. Hu L, Su W, Guo X, Xu T, Wang H, Yu M. Prognostic role of MUC-2 expression in patients with gastric carcinoma: a systematic review and meta-analysis. Eur Rev Med Pharmacol Sci. 2021; 25(10): 3700-3708. doi: https://doi.org/10.26355/eurrev_202105_25936

10. Kim YI, Pecha RL, Keihanian T, Mercado M, Peña SV, Lang K, et al. MUC1 Expressions and Its Prognostic Values in US Gastric Cancer Patients. Cancers. 2023; 15(4): 998. doi: https://doi.org/10.3390/cancers15040998

11. Kim DH, Shin N, Kim GH, Song GA, Jeon TY, Kim DH, et al. Mucin expression in gastric cancer: reappraisal of its clinicopathologic and prognostic significance. Arch Pathol Lab Med. 2013; 137(8): 1047–53. doi: https://doi.org/10.5858/arpa.2012-0193-OA

12. Lewis D, Jimenez L, Mansour MH, Horton S, Wong WWL. A Systematic Review of Cost-Effectiveness Studies on Gastric Cancer Screening. Cancers (Basel). 2024; 16(13): 2353. doi: https://doi.org/10.3390/cancers16132353

13. Wang RQ, Fang DC. Alterations of MUC1 and MUC3 expression in gastric carcinoma: relevance to patient clinicopathological features. J Clin Pathol. 2003; 56(5): 378–84. doi: https://doi.org/10.1136/jcp.56.5.378

14. Morgan E, Arnold M, Camargo MC, Gini A, Kunzmann AT, Matsuda T, et al. The current and future incidence and mortality of gastric cancer in 185 countries, 2020–40: A population-based modelling study. EClinicalMedicine. 2022; 47: 101404. doi: https://doi.org/10.1016/j.eclinm.2022.101404

15. Mantziari S, St Amour P, Abboretti F, Teixeira-Farinha H, Gaspar Figueiredo S, Gronnier C, et al. A Comprehensive Review of Prognostic Factors in Patients with Gastric Adenocarcinoma. Cancers (Basel). 2023; 15(5): 1628. doi: https://doi.org/10.3390/cancers15051628

16. Montoya M, Gómez R, Ahumada F, Martelo A, Toro J, Pérez E, et al. Caracterización de 130 pacientes sometidos a gastrectomía por cáncer gástrico en el Instituto de Cancerología–Clínica Las Américas de Medellín. Revista Colombiana de Cancerología. 2016; 20(2): 73–8. doi: https://doi.org/10.1016/j.rccan.2016.01.002

17. Gómez M, Otero W, Caminos JE. Cáncer gástrico en pacientes jóvenes en Colombia. Rev Colomb Gastroenterol. 2012; 27(3): 166–72. http://www.scielo.org.co/scielo.php?script=sci_arttext&pid=S0120-99572012000300004&lng=en

18. Shah SAR, Mumtaz M, Sharif S, Mustafa I, Nayila I. Helicobacter pylori and gastric cancer: current insights and nanoparticle-based interventions. RSC Adv. 2025; 15(7): 5558–70. doi: https://doi.org/10.1039/d4ra07886a

19. Li Z, Zhang W, Bai J, Li J, Li H. Emerging Role of Helicobacter pylori in the Immune Evasion Mechanism of Gastric Cancer: An Insight Into Tumor Microenvironment-Pathogen Interaction. Front Oncol. 2022; 12: 862462. doi: https://doi.org/10.3389/fonc.2022.862462

20. Liu Z, Zhang D, Chen S. Unveiling the gastric microbiota: implications for gastric carcinogenesis, immune responses, and clinical prospects. Journal of Experimental & Clinical Cancer Research. 2024; 43(1): 118. doi: https://doi.org/10.1186/s13046-024-03034-7

21. Olmez S, Aslan M, Erten R, Sayar S, Bayram I. The Prevalence of Gastric Intestinal Metaplasia and Distribution of Helicobacter pylori Infection, Atrophy, Dysplasia, and Cancer in Its Subtypes. Gastroenterol Res Pract. 2015; 2015: 434039. doi: https://doi.org/10.1155/2015/434039

22. Wei N, Zhou M, Lei S, Zhong Z, Shi R. A meta-analysis and systematic review on subtypes of gastric intestinal metaplasia and neoplasia risk. Cancer Cell Int. 2021; 21(1): 173. doi: https://doi.org/10.1186/s12935-021-01869-0

23. Mülder DT, Hahn AI, Huang RJ, Zhou MJ, Blake B, Omofuma O, et al. Prevalence of Gastric Precursor Lesions in Countries With Differential Gastric Cancer Burden: A Systematic Review and Meta-analysis. Clinical Gastroenterology and Hepatology. 2024; 22(8): 1605-1617.e46. doi: https://doi.org/10.1016/j.cgh.2024.02.023

24. Carlosama YH, Acosta CP, Sierra CH, Rosero CY, Bolaños HJ. The Operative Link on Gastritis Assessment (OLGA) system as a marker for gastric cancer and dysplasia in a Colombian population at risk: A multicenter study. Biomedica. 2023; 43: 30–40. doi: https://doi.org/10.7705/biomedica.6995

25. Peraza S, Gutiérrez Y, Castillo A, Márquez R, Shimizu A, López G, et al . Expresión de mucinas: MUC1, MUC2, MUC5AC, MUC6, HGM y CD10 en carcinomas gástricos y lesiones pre-neoplasicas adyacentes. Gen. 2015; 69(3): 64-70. http://ve.scielo.org/scielo.php?script=sci_arttext&pid=S0016-35032015000300003&lng=es

26. Oliveros R, Pinilla RE, Sánchez R, Facundo H, Sánchez EF, Buitrago DA. Morbilidad y mortalidad en pacientes llevados a gastrectomía por cáncer gástrico. Revista Colombiana de Cirugía. 2023; 38(3): 459-467. doi: https://doi.org/10.30944/20117582.2272

27. Tapia Ó, Roa JC, Manterola C, Puga V, Villaseca M, Araya JC. Factores asociados al pronóstico de pacientes operados por cáncer gástrico avanzado. Revista chilena de cirugía. 2011; 63(2): 154–61. doi: https://doi.org/10.4067/S0718-40262011000200005

28. Wang S, Mu Y, Zhang J, Wang C. Prognostic and clinicopathological significance of mucin family members expression in gastric cancer: a meta-analysis. Front Oncol. 2025; 14: 1512971. doi: https://doi.org/10.3389/fonc.2024.1512971

29. Sun L, Zhang Y, Li W, Zhang J, Zhang Y. Mucin Glycans: A Target for Cancer Therapy. Molecules. 2023; 28(20): 7033. doi: https://doi.org/10.3390/molecules28207033

30. Bose M, Sanders A, De C, Zhou R, Lala P, Shwartz S, et al. Targeting tumor-associated MUC1 overcomes anoikis-resistance in pancreatic cancer. Transl Res. 2023; 253: 41-56. doi: https://doi.org/10.1016/j.trsl.2022.08.010