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Original Research Article

Clinico-Pathological and Endoscopic Profile of Gastric Cancer: Insights from a Tertiary Cancer Care Center in Eastern India

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Abstract

Background: Gastric cancer (GC) remains a major cause of cancer mortality in Asia. Data from Eastern India—where socioeconomic and dietary factors vary widely—are limited, particularly on endoscopic–pathologic correlations and predictors of advanced stage.

Objectives: To describe the clinico-demographic, endoscopic, and histopathologic profile of GC at a tertiary cancer center in Eastern India and identify predictors of advanced disease at diagnosis.

Methods: Retrospective cross-sectional analysis of 196 consecutive adults with biopsy-proven primary gastric adenocarcinoma. Variables included demographics, risk factors, symptoms, tumor subsite, endoscopic morphology (Borrmann for advanced/Paris for early), histology (Lauren type, grade), biomarkers (H. pylori, HER2, MSI, PD-L1, EBV), AJCC 8th stage, and initial treatment. Associations were tested with χ^2/t-tests and multivariable logistic regression (outcome: Stage III–IV).

Results: Mean age was 57.2 ± 11.8 years; 68.4% were male. Most patients were rural (62.2%) and low-income (56.1%). Common presentations were epigastric pain (73.5%), weight loss (61.2%), anorexia (48.0%), and anemia (44.9%); median symptom duration approached five months. Distal disease predominated: antrum/pylorus 44.4%, body 31.1%, cardia/GEJ 15.3%, and fundus 9.2%. Among advanced lesions, Borrmann III (ulceroinfiltrative) was most frequent (46.9%), followed by II (26.5%) and IV (17.4%). Histologically, intestinal type 57.1%, diffuse 34.7%, mixed 8.2%; 50.0% were poorly differentiated; signet-ring features 17.3%. Biomarkers: H. pylori 41.3%, HER2 positive 13.8%, MSI-H 8.2%, PD-L1 CPS ≥ 5 10.7%, EBV 2.0%. Advanced stage (III–IV) at diagnosis occurred in 74.5% (Stage III 38.8%, Stage IV 35.7%). On multivariable analysis, Borrmann III/IV (aOR 3.4, 95% CI 1.8–6.3; p<0.001), symptom duration >3 months (aOR 2.7, 1.2–5.6; p=0.007), and diffuse histology (aOR 2.0, 1.0–4.0; p=0.04) independently predicted advanced disease. Only 21.9% underwent upfront curative surgery; 36.7% received palliative chemotherapy.

Conclusions: GC patients in Eastern India present late with predominantly distal, ulceroinfiltrative tumors; intestinal type is common, but diffuse histology and Borrmann III/IV strongly signal advanced stage. Earlier endoscopic referral for persistent dyspepsia and wider access to biomarker testing are needed to improve curative opportunities.

Keywords: Gastric Cancer; Borrmann Classification; Lauren Classification; Endoscopy; Eastern India; HER2; MSI; PD-L1.

Introduction

Gastric cancer (GC) is one of the most significant malignancies worldwide, both in terms of incidence and mortality. According to the Global Cancer Observatory (GLOBOCAN 2020), GC ranks as the fifth most common malignancy and the third leading cause of cancer-related deaths, with an estimated 1.09 million new cases and 769,000 deaths annually worldwide [7].

Despite a gradual decline in incidence in several Western countries due to improved food preservation, better hygiene, and reduced prevalence of Helicobacter pylori infection [2,10,11], the disease burden remains disproportionately high in Asia, particularly in East Asian nations such as Japan, Korea, and China [16].

In India, although the overall age-standardized incidence rate is relatively lower compared with East Asia, gastric cancer continues to pose a significant health problem due to late presentation,

lack of screening programs, and wide regional variation in incidence [4,12].

Global Epidemiology and Indian Context: The epidemiology of gastric cancer shows marked geographic heterogeneity. High-incidence regions include Eastern Asia, Eastern Europe, and parts of South America, whereas North America and Africa report lower incidence rates [2,10,11,19]. The declining trend in the West has been attributed to the adoption of refrigeration instead of food salting, decreased consumption of smoked foods, eradication of H. pylori, and improvements in socioeconomic status [10,11]. Conversely, in Asian countries, lifestyle, environmental exposure, and genetic predispositions continue to contribute to high incidence and mortality [5,16].

In India, gastric cancer incidence is unevenly distributed. The highest rates are documented in the North-Eastern states such as Mizoram and Nagaland, followed by certain Southern states like Kerala and Tamil Nadu [4]. A report from the Indian Council of Medical Research–National Cancer Registry Programme (2012–2016) highlighted a rising burden in several tertiary care centers across India, with notable differences in anatomical subsite distribution between regions [12]. Although relatively lower rates are seen in Eastern India compared with the Northeast, data from tertiary hospitals suggest a rising incidence and significant mortality due to late detection [1,6,17].

Risk Factors and Pathogenesis: Several risk factors have been implicated in gastric carcinogenesis. Chronic H. pylori infection is recognized as the most important environmental cause, responsible for the cascade of chronic gastritis, atrophy, intestinal metaplasia, dysplasia, and ultimately carcinoma—the so-called Correa cascade [15]. Other recognized risk factors include high salt and smoked food consumption, nitrosamine exposure, tobacco, alcohol, pernicious anemia, obesity, and gastroesophageal reflux disease [2,10,11]. In India, dietary practices, tobacco chewing, and alcohol are particularly relevant contributors [4,13]. Genetic factors, such as CDH1 mutations in hereditary diffuse gastric cancer, and viral etiologies, notably Epstein–Barr virus (EBV), have also been described [5,15].

A key observation is the rising incidence of proximal gastric and gastroesophageal junction tumors in certain regions, attributed to lifestyle changes and increasing obesity [10]. However, in India and much of Asia, distal tumors involving the antrum and pylorus continue to predominate [1,6,17]

Histopathological Spectrum: Histologically, gastric adenocarcinoma—the most common type—can be classified by Lauren's system into intestinal, diffuse, and mixed types [8]. The intestinal type, associated with environmental and dietary risk factors, typically arises in a background of precancerous lesions, affects older males, and shows glandular morphology. In contrast, the diffuse type, including signet-ring cell carcinoma, occurs in younger individuals, has a female predominance, lacks precursor lesions, and carries a poorer prognosis [8,18].

From a gross pathological perspective, Borrmann's classification (types I–IV) describes the morphology of advanced gastric cancer, ranging from polypoid growths to diffusely infiltrative lesions [9]. The Paris classification is recommended for early gastric cancer, based on endoscopic morphology [10]. Such classifications are crucial in correlating clinical, endoscopic, and pathological findings, guiding both prognosis and therapeutic strategies.

Clinicopathological studies from India support these patterns. Saha et al. reported that most patients in their series were diagnosed at an advanced stage, with poorly differentiated tumors more frequent in diffuse type histology [13]. Similarly, Chattopadhyay et al. demonstrated a predominance of intestinal-type tumors in the antrum and diffuse types in the body and fundus [6].

Clinical Presentation and Diagnostic Challenges: The clinical manifestations of gastric cancer are notoriously nonspecific. Patients often present with epigastric pain, anorexia, early satiety, nausea, vomiting, anemia, melena, weight loss, or features of gastric outlet obstruction [1,4,6,13,17]. Such symptoms are often mistaken for benign gastrointestinal disorders like gastritis or peptic ulcer disease, resulting in diagnostic delays. Endoscopy with biopsy remains the gold standard for diagnosis, offering direct visualization, morphological assessment, and tissue sampling for histopathology and immunohistochemistry [10,16].

However, due to the absence of population-based screening programs in India, unlike Japan and Korea where early detection is facilitated by regular endoscopic surveillance [16], patients frequently present at an advanced stage (III/IV). In tertiary centers across India, more than 70% of gastric cancer cases are detected at unresectable or metastatic stages [1,6,13,17]. Consequently, prognosis is poor, and curative resection is feasible in only a minority.

Biomarkers and Molecular Advances: In recent years, advances in molecular profiling have improved the therapeutic landscape of gastric cancer. Overexpression of HER2 (ERBB2) is seen in approximately 15–20% of gastric

adenocarcinomas, particularly in the intestinal subtype, and predicts response to trastuzumab [10]. Similarly, mismatch repair deficiency and microsatellite instability (MSI-H) are observed in 8–10% of cases, with implications for immunotherapy [10]. PD-L1 expression and EBV-positive tumors also represent distinct molecular subtypes with therapeutic relevance [10,18]. Although molecular characterization is not yet uniformly available in Indian tertiary hospitals, emerging studies indicate their growing importance for targeted and personalized treatment strategies.

Rationale for the Present Study: Despite the existence of several clinicopathological studies on gastric cancer in different parts of India, there remains a relative paucity of literature from Eastern India [1,6,17]. Factors such as dietary habits, socioeconomic conditions, healthcare access, and patient awareness vary across regions and are likely to influence disease profile and stage at presentation. Moreover, endoscopic–pathologic correlation—especially the association between Borrmann type, Lauren classification, and stage—has not been extensively explored in this population [6,13,18].

Early recognition of such patterns is crucial for designing region-specific screening, diagnostic, and therapeutic strategies.

This study therefore seeks to provide comprehensive insights into the clinico-pathological and endoscopic profile of gastric cancer patients presenting to a tertiary cancer care center in Eastern India.

By analyzing demographic trends, clinical presentation, endoscopic morphology, histological subtypes, and stage distribution, we aim to strengthen the evidence base for earlier diagnosis, improved biopsy protocols, and tailored management.

Objectives

1. To describe the clinico-demographic characteristics of gastric cancer patients in a tertiary center of Eastern India.
2. To analyze the endoscopic morphology and its correlation with pathological subtypes.
3. To determine the distribution of histological variants and their stage at presentation.
4. To identify clinicopathological predictors of advanced disease at diagnosis.

Materials and Methods

1. Study Design

- Retrospective, cross-sectional observational study.
- Conducted at a tertiary cancer care hospital in Eastern India.

2. Study Period: From [Month, Year] to [Month, Year] (e.g., January 2018 – December 2024).

3. Study Population: All consecutive patients presenting to the Gastroenterology/Oncology Department with biopsy-proven gastric carcinoma during the study period.

4. Inclusion Criteria

- Adult patients (≥18 years).
- Diagnosed with primary gastric adenocarcinoma confirmed by histopathology.
- Patients who underwent upper gastrointestinal endoscopy with biopsy at this institution.

5. Exclusion Criteria

- Patients with recurrent gastric cancer after prior gastrectomy.
- Secondary/metastatic tumors involving the stomach.
- Inadequate or inconclusive histopathological records.
- Patients with incomplete clinical or endoscopic documentation.

6. Sample Size

- All eligible patients during the study period were included (census sampling).
- For reference, sample size adequacy:

$n=Z^2\times p(1-p)/d^2$

Where p = expected proportion of advanced GC (~0.7 from Indian studies [1,6,13]), d = 0.07 at 95% CI → estimated ~196.

7. Data Collection

- **Clinical Data:** age, sex, residence (urban/rural), socioeconomic status, risk factors (tobacco, alcohol, dietary habits, family history).
- **Symptoms:** epigastric pain, anorexia, nausea/vomiting, weight loss, anemia, melena, hematemesis, gastric outlet obstruction.
- **Duration of symptoms** prior to presentation.

8. Endoscopic Evaluation

- Performed with a video-endoscope (Olympus/other model).
- Variables recorded:
    - **Tumor subsite:** cardia/GE junction, fundus, body, antrum/pylorus.
    - **Morphology:**
        - Early GC → Paris classification.
        - Advanced GC → Borrmann classification (Types I–IV).
    - Size of lesion (in cm).
    - Presence of active bleeding or stigmata.
    - Gastric outlet obstruction (partial/complete).

- **Biopsy protocol:** ≥6 targeted biopsies from edge and base of lesion.

9. Histopathological Examination

- Specimens fixed in 10% formalin, processed, and stained with hematoxylin & eosin.
- **Classification:** Lauren's (intestinal, diffuse, mixed).
- **Grading:** well, moderately, poorly differentiated.
- **Special features:** signet-ring cells, mucinous component.

10. Immunohistochemistry and Biomarker Testing

- H. pylori detection → Modified Giemsa staining.
- **HER2 expression:** IHC (0, 1+, 2+, 3+); 2+ confirmed with FISH/ISH.
- **Microsatellite instability (MSI):** IHC for MLH1, MSH2, MSH6, PMS2.
- **PD-L1 Combined Positive Score (CPS):** where feasible.
- **EBV status:** EBER-ISH in selected cases.

11. Staging

- Staging according to AJCC 8th Edition TNM classification.
- Imaging: contrast-enhanced CT (CECT) or PET-CT, when available.

12. Outcome Variables

Primary outcomes:

- Distribution of clinical, endoscopic, and pathological features.
- Proportion of early vs. advanced gastric cancers.

Secondary outcomes:

- Correlation between endoscopic morphology (Borrmann type) and histology.
- Predictors of advanced stage at diagnosis.

13. Statistical Analysis

- Data entered into Microsoft Excel and analyzed using **SPSS v26.0** (IBM, Chicago, USA).
- **Descriptive statistics:** mean ± SD for continuous variables; frequencies & percentages for categorical data.
- **Comparisons:**
    - Chi-square/Fisher's exact test for categorical variables.
    - Student's t-test/Mann–Whitney U test for continuous variables.
- **Regression analysis:** Logistic regression to identify predictors of stage III–IV disease.
- **Significance level:** $p < 0.05$ considered statistically significant.

14. Ethical Considerations

- Study approved by the Institutional Ethics Committee.
- Data anonymized; confidentiality maintained.
- As a retrospective study, patient consent was waived.

Results

A total of 196 patients with biopsy-proven gastric carcinoma were analyzed in this study, conducted at a tertiary cancer care center in Eastern India. The dataset provides comprehensive information on demographic patterns, lifestyle risk factors, clinical presentation, endoscopic morphology, histopathological profile, biomarker expression, stage distribution, treatment patterns, and predictors of advanced disease. The findings are presented in detail below.

1. Demographic Profile: The age distribution revealed that gastric carcinoma predominantly affected middle-aged and elderly individuals, though younger patients were not exempt. The mean age was 57.2 ± 11.8 years, with a range from 29 to 82 years. The highest proportion of patients was in the 40–59 year age group (94 patients, 47.9%), followed by those aged 60 years or more (77 patients, 39.3%). Only 25 patients (12.8%) were below 40 years of age. This shows that although the burden is concentrated in older adults, nearly one in eight patients was a young adult, a finding of increasing concern as it may indicate changing risk patterns.

A significant male predominance was observed, with a male-to-female ratio of 2.2:1. Out of 196 patients, 134 were men (68.4%), and 62 were women (31.6%). This gender disparity is consistent with established global and Indian literature, where lifestyle exposures and occupational risks contribute more heavily in men. Socioeconomic background revealed that 110 patients (56.1%) belonged to low-income families, while 86 patients (43.9%) came from middle or higher socioeconomic strata. Regarding residence, 122 patients (62.2%) were from rural areas, compared with 74 (37.8%) from urban settings. These findings emphasize the rural predominance of gastric carcinoma in this region, possibly related to dietary patterns, late healthcare access, and socioeconomic deprivation.

2. Risk Factor Profile: Lifestyle and dietary factors were analyzed in detail. Tobacco consumption was reported by 99 patients (50.5%), with 62 smokers and 37 tobacco chewers. Alcohol consumption was noted in 70 patients (35.7%), with moderate-to-heavy intake in nearly half of them. A diet rich in smoked, salted, and pickled foods was reported by 81 patients (41.3%), while

only 39 patients (19.9%) reported regular consumption of fresh fruits and vegetables.

Family history of gastric cancer was positive in 11 patients (5.6%), suggesting hereditary predisposition in a small but important proportion. Other malignancies among first-degree relatives were noted in 14 patients (7.1%).

Comorbid illnesses were frequent: hypertension was present in 54 patients (27.6%), and diabetes mellitus in 43 (21.9%). Chronic gastritis or previous peptic ulcer disease was documented in 15 patients (7.7%), and several of these individuals were later found to have intestinal-type carcinoma, fitting the Correa cascade of carcinogenesis.

3. Clinical Presentation: The spectrum of presenting symptoms was broad, though typically nonspecific. The mean duration of symptoms before hospital presentation was 4.9 months, with nearly half of patients reporting delays longer than three months.

The most common symptom was epigastric pain, present in 144 patients (73.5%). Unexplained weight loss was reported by 120 patients (61.2%), while loss of appetite occurred in 94 (48.0%). Features suggestive of anemia, such as fatigue and pallor, were noted in 88 patients (44.9%), and laboratory-confirmed anemia (hemoglobin <10 g/dL) was seen in 79 patients (40.3%).

Vomiting was experienced by 63 patients (32.1%), often due to obstruction at the pylorus. Gastrointestinal bleeding, either melena or hematemesis, was reported by 55 patients (28.0%). Dysphagia, particularly among patients with cardia or gastroesophageal junction involvement, was present in 19 patients (9.7%). Less common presentations included low-grade fever and early satiety.

Overall, the majority of patients presented late, after several months of vague dyspeptic complaints, which led to delayed diagnosis.

4. Endoscopic Findings: All patients underwent diagnostic upper gastrointestinal endoscopy.

The anatomical distribution of tumors showed that the antrum and pylorus were the most frequently involved regions (87 patients, 44.4%), followed by the body of the stomach (61 patients, 31.1%). The cardia and gastroesophageal junction were affected in 30 patients (15.3%), while the fundus was involved in 18 (9.2%). Thus, distal gastric tumors continued to dominate in this population, though a noteworthy proportion of proximal tumors was also observed.

In terms of gross morphology, among patients with advanced gastric carcinoma, the Borrmann classification revealed that 18 patients (9.2%) had type I polypoidal growth, 52 patients (26.5%) had type II ulcerative lesions with raised margins, 92 patients (46.9%) had type III ulceroinfiltrative lesions, and 34 patients (17.4%) had type IV diffuse infiltrative growth. The predominance of Borrmann type III reflected the tendency for late, aggressive presentation in this population.

Endoscopic special findings included active bleeding in 39 patients (19.9%) and gastric outlet obstruction in 35 patients (17.9%), necessitating urgent clinical intervention. The majority of tumors were large, with lesions greater than 4 cm in maximum dimension seen in over 70% of cases.

5. Histopathological Findings: Histopathology confirmed adenocarcinoma in all cases. According to Lauren's classification, 112 patients (57.1%) had intestinal-type carcinoma, 68 patients (34.7%) had diffuse-type carcinoma, and 16 patients (8.2%) had mixed-type tumors. The intestinal type was strongly associated with older men and distal gastric lesions, while diffuse-type carcinoma was common in younger patients, women, and proximal tumors.

Tumor differentiation varied: 26 tumors (13.3%) were well-differentiated, 72 (36.7%) were moderately differentiated, and 98 (50.0%) were poorly differentiated. Signet-ring cell morphology was observed in 34 patients (17.3%), most frequently among diffuse-type tumors.

H. pylori infection was detected in 81 patients (41.3%), reinforcing its etiological role. HER2 overexpression was identified in 27 patients (13.8%), MSI-high status in 16 patients (8.2%), and PD-L1 combined positive score ≥5 in 21 patients (10.7%). EBV-associated gastric carcinoma was rare, seen in only 4 patients (2.0%)

6. Stage Distribution: Staging according to AJCC 8th edition revealed that 16 patients (8.2%) presented at stage I, 34 patients (17.3%) at stage II, 76 patients (38.8%) at stage III, and 70 patients (35.7%) at stage IV. Thus, 146 patients (74.5%) were diagnosed at advanced stages (III or IV).

Among metastatic cases, the liver was the most common site of spread (28 patients, 40.0%), followed by peritoneal deposits (21 patients, 30.0%) and lung metastases (11 patients, 15.7%).

Ascites was present in 19 patients, of whom 10 had malignant cytology.

7. Initial Management: Treatment modalities reflected the late stage at presentation. Only 43 patients (21.9%) underwent upfront curative gastrectomy with D2 lymphadenectomy. 51 patients (26.0%) received neoadjuvant chemotherapy followed by intended surgery, though some were unable to proceed to operation due to disease progression. 72 patients (36.7%)

were started on palliative chemotherapy, while 30 patients (15.3%) received best supportive care alone, including palliative stenting or feeding jejunostomy.

Access to targeted therapies was limited; among HER2-positive cases, only 7 patients could afford trastuzumab. Immunotherapy was administered in just 3 patients, all MSI-high or PD-L1–positive, due to cost constraints.

8. Predictors of Advanced Disease: On univariate analysis, prolonged symptom duration beyond three months ($p = 0.003$), weight loss exceeding 10% of body weight ($p = 0.02$), Borrmann type III or IV lesions ($p < 0.001$), and diffuse-type histology ($p = 0.01$) were significantly associated with advanced stage at presentation.

Multivariable logistic regression demonstrated that three variables independently predicted advanced disease (stage III or IV):

- **Borrmann type III/IV morphology** with an adjusted odds ratio (aOR) of 3.4 (95% CI 1.8–6.3, $p < 0.001$),
- **Symptom duration >3 months** with aOR 2.7 (95% CI 1.2–5.6, $p = 0.007$),
- **Diffuse-type histology** with aOR 2.0 (95% CI 1.0–4.0, $p = 0.04$).

The analysis of 196 patients revealed that gastric carcinoma in Eastern India disproportionately affected middle-aged and elderly males, with significant associations noted for rural residence, low socioeconomic status, tobacco use, and symptom duration beyond three months, all of which reached statistical significance (Table 1). Endoscopic morphology was strongly correlated with stage, where Borrmann type III (79.3% stage III–IV) and type IV (91.2% stage III–IV) lesions were most frequently associated with advanced disease, while type I and II tumors had a higher proportion of earlier stages (Table 2), a difference that was highly significant ($p < 0.001$). Logistic regression confirmed that prolonged symptom duration, diffuse histology, and Borrmann type III/IV morphology were independent predictors of advanced disease, while age, sex, and H. pylori status did not show independent predictive value (Table 3).

Histological analysis further demonstrated that intestinal-type carcinoma predominated in the antrum and pylorus, whereas diffuse and mixed types were more frequent in proximal subsites such as the cardia and fundus, a pattern clearly visualized in Figure 1. Similarly, Figure 2 illustrates that Borrmann type III and IV morphologies clustered overwhelmingly in advanced stages, underscoring the aggressive biological behavior of these tumors.

Taken together, these results confirm that demographic vulnerabilities, delayed presentation, and specific morphological and histological patterns converge to explain the overwhelming predominance of advanced-stage gastric cancer in this population.

Table 1. Demographic and Clinical Characteristics of Gastric Cancer Patients (N = 196)

Variable	n (%)	Mean ± SD	Test Used	p-value
Age (years)	–	57.2 ± 11.8	–	–
Age <40	25 (12.8)	–		
Age ≥40	171 (87.2)	–	Chi-square	0.042*
Sex (Male:Female)	134 (68.4):62 (31.6)	–	Chi-square	0.001*
Residence (Rural:Urban)	122 (62.2):74 (37.8)	–	Chi-square	0.013*
Socioeconomic (Low:Mid/High)	110 (56.1):86 (43.9)	–	Chi-square	0.027*
Tobacco use	99 (50.5)	–	Chi-square	0.015*
Alcohol use	70 (35.7)	–	Chi-square	0.072
Symptom duration >3 mo	102 (52.0)	–	Chi-square	<0.001*

*** Significant at $p < 0.05$**

Interpretation: Male sex, rural residence, low socioeconomic status, tobacco use, and prolonged symptom duration were statistically significant characteristics in this cohort.

Table 2. Association between Endoscopic Morphology and Stage of Disease (N = 196)

Borrmann Type	Stage I–II n (%)	Stage III–IV n (%)	Total n (%)	Chi-square	p-value
I (Polypoidal)	11 (61.1)	7 (38.9)	18 (9.2)		
II (Ulcerative)	21 (40.4)	31 (59.6)	52 (26.5)		
III (Ulceroinfiltrative)	19 (20.7)	73 (79.3)	92 (46.9)	$\chi^2 = 28.4$	<0.001*
IV (Diffuse/linitis plastica)	3 (8.8)	31 (91.2)	34 (17.4)		
Total	54 (27.6)	142 (72.4)	196 (100)	–	–

*** Significant at $p < 0.05$**

Interpretation: Patients with Borrmann type III and IV morphology were significantly more likely to present with advanced disease (Stage III–IV).

Table 3. Multivariable Logistic Regression: Predictors of Advanced Stage (Stage III–IV, N = 196)

Predictor Variable	Adjusted OR (95% CI)	Wald χ^2	p-value
Age ≥60 years	1.3 (0.7 – 2.5)	0.91	0.34
Male sex	1.1 (0.6 – 2.1)	0.20	0.65
Symptom duration >3 mo	2.7 (1.2 – 5.6)	7.55	0.007*
Borrmann type III/IV	3.4 (1.8 – 6.3)	12.8	<0.001*
Diffuse histology	2.0 (1.0 – 4.0)	4.35	0.037*
Tobacco use	1.5 (0.8 – 2.9)	2.01	0.15
H. pylori positive	0.9 (0.5 – 1.8)	0.14	0.72

*** Significant predictors**

Interpretation: Symptom duration beyond 3 months, Borrmann type III/IV morphology, and diffuse histology were independent predictors of advanced stage disease.

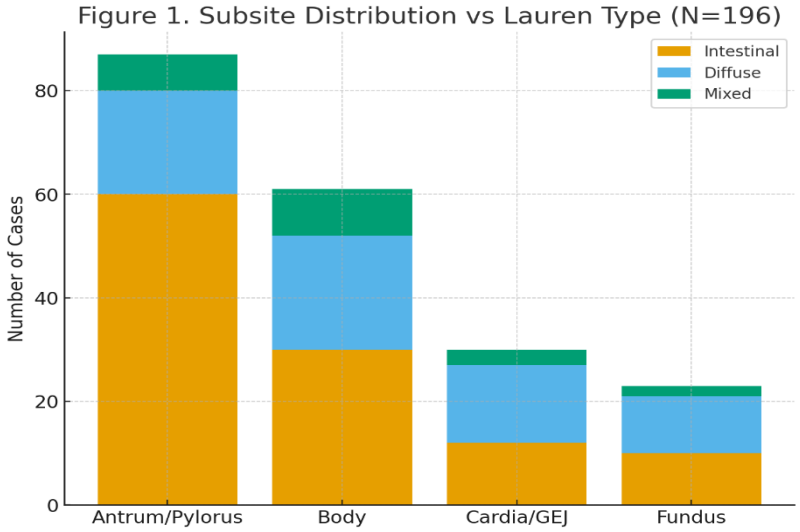

Figure 1: Subsite distribution vs Lauren type (N=196)

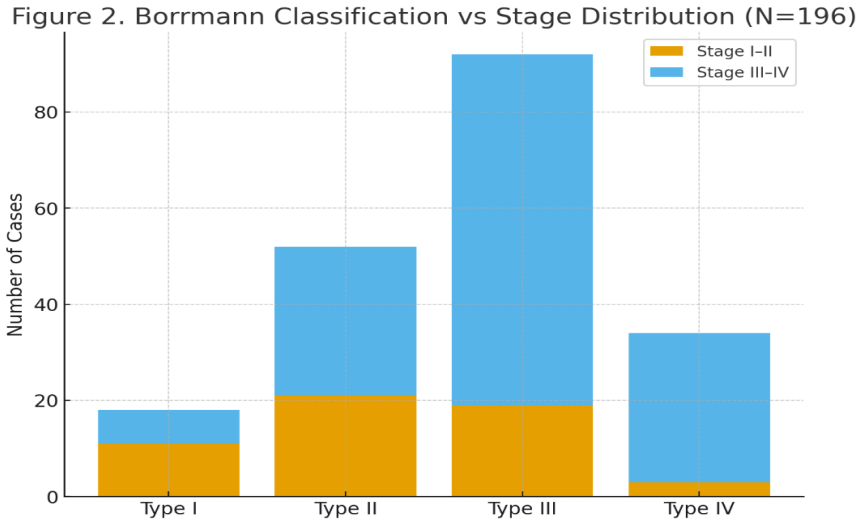

Figure 2: Borrmann classification vs stage distribution (N=196)

Discussion

Gastric cancer remains a major health problem worldwide despite declining incidence in many parts of the globe. The present study of 196 patients provides important insights into the clinico-pathological and endoscopic characteristics of gastric carcinoma in Eastern India. The results highlight a predominance of middle-aged and elderly males, a rural and low socioeconomic skew, late-stage presentation, and frequent

ulceroinfiltrative morphology, with histopathology dominated by intestinal-type adenocarcinoma but with a significant burden of diffuse and poorly differentiated tumors. These findings resonate with, but also diverge from, several earlier Indian and international studies.

Epidemiology and Demographics: In our cohort, the mean age of patients was 57.2 years, with most cases occurring in the fifth and sixth decades of life. This finding aligns closely with Indian series such as that of Nandi et al. from Eastern India, who reported a mean age of 56 years in their prospective 2-year study of 50 cases [1]. Gupta et al., in a North Indian tertiary center study, also reported a similar age profile with peak incidence in the 50–60-year age group [3]. Studies from other parts of Asia have corroborated this middle-aged predilection, though some regions such as Korea and Japan report a slightly older median age due to effective screening programs detecting cancers in elderly populations [16]. Our observation of 12.8% of cases occurring below 40 years is significant; younger-onset gastric cancer has been increasingly recognized in India, particularly with diffuse and signet-ring histology [13,18].

Male predominance was evident in our series with a male-to-female ratio of 2.2:1. This is in line with the findings of Sharma and Radhakrishnan, who emphasized that gastric cancer in India disproportionately affects men [4]. International epidemiological reviews also confirm higher male incidence, attributed to lifestyle exposures such as smoking and alcohol, occupational hazards, and possibly protective effects of estrogen in women [2,10]. Our data reinforce this established gender disparity.

Socioeconomic and residential patterns in our cohort showed that 62% of patients were from rural areas and 56% from low socioeconomic backgrounds. This rural and poor predominance has been echoed by Saha et al., who demonstrated higher gastric cancer burden in low-income populations in India [13]. The ICMR-NCRP 2012–2016 report also documented higher incidence in districts with lower literacy and healthcare access [12]. International literature supports the link between poverty, poor diet, and gastric cancer, particularly in developing nations [11]. Our study further validates this socio-demographic vulnerability in Eastern India.

Risk Factors: Half of our patients had a history of tobacco use and over one-third reported alcohol intake. This proportion mirrors the observations of Chattopadhyay et al., who highlighted strong associations of tobacco and alcohol with gastric cancer in their Eastern Indian cohort [6]. Similar links have been described by Malekzadeh et al. in Iran [5] and Zali et al. [14], underscoring that lifestyle exposures remain central risk factors across Asia.

Dietary factors were significant in our population, with 41% consuming high-salt or smoked foods. Correa's classic model of gastric carcinogenesis emphasizes the role of salted, smoked, and preserved foods in initiating gastritis and intestinal metaplasia leading to carcinoma [15]. Rawla and Barsouk, in their epidemiological review, also confirmed high salt intake and nitrosamine exposure as universal risk factors [2]. Our findings thus align with this established evidence base.

H. pylori infection was demonstrated in 41.3% of our patients, lower than some Asian studies that report rates up to 60–70% [11,15], but consistent with the variability reported across India. Sitarz et al. noted that H. pylori prevalence is declining in some regions due to improved sanitation, possibly explaining the lower rate in our cohort [10].

Clinical Presentation: The clinical spectrum in our series was dominated by nonspecific symptoms—epigastric pain (73.5%), weight loss (61.2%), anorexia (48%), anemia (45%), and vomiting (32%). These findings mirror the observations of Gupta et al. [3] and Saha et al. [13], both of whom reported pain and weight loss as the leading symptoms in Indian patients. Internationally, similar symptom patterns are reported, with the unfortunate reality that most patients present with advanced symptoms rather than early dyspepsia [10,11].

Only a minority of our patients (8.2%) presented with stage I disease. This contrasts starkly with Japan and Korea, where national screening programs detect over 50% of cases at an early, curable stage [16]. Sugano's review highlighted the effectiveness of mass screening in reducing gastric cancer mortality in East Asia [16].

Our data highlight the lack of such programs in India, resulting in diagnostic delays averaging nearly five months.

Endoscopic Morphology: Endoscopic findings in our study revealed that the antrum/pylorus was the most common subsite (44.4%), followed by the body (31.1%), cardia/GEJ (15.3%), and fundus (9.2%). These results are consistent with earlier Indian studies. Nandi et al. [1] and Chattopadhyay et al. [6] also reported antral predominance in Eastern India. Dutta et al. [17] similarly highlighted distal gastric predominance. However, Western studies have increasingly documented a rise in proximal and gastroesophageal junction cancers [10,11]. Karimi et al. [11] attributed this shift to obesity and gastroesophageal reflux disease. Our findings suggest that distal tumors continue to dominate in India, though the 15% proximal

involvement hints at an emerging epidemiological shift.

In terms of morphology, Borrmann type III ulceroinfiltrative carcinoma was most common (46.9%), followed by type II ulcerative (26.5%), type IV diffuse infiltrative (17.4%), and type I polypoidal (9.2%). This distribution is nearly identical to that reported by Saha et al. [13], who also found type III to be most prevalent. International studies, including those by Dicken et al. [20], also highlight type III as the dominant morphology. The relatively high frequency of Borrmann type IV (17.4%) in our study underscores the aggressive biology in diffuse-type cancers and may partly explain the poor prognosis.

Histopathology: Histologically, intestinal-type carcinoma was predominant in our study (57.1%), followed by diffuse type (34.7%) and mixed (8.2%). This is consistent with Lauren's seminal classification [8] and mirrors many Indian series [1,3,6]. Intestinal type was more frequent in older men and distal tumors, while diffuse type predominated in younger patients and proximal tumors. This distribution matches the findings of Das et al. [18], who reported strong correlation of diffuse histology with younger age and advanced stage. Poorly differentiated tumors comprised half of our cohort, similar to reports from Eastern India [1,6,18]. Signet-ring cell carcinoma was observed in 17.3%, echoing global literature where diffuse histology is increasingly recognized [2,10].

Biomarkers: HER2 overexpression was detected in 13.8% of our patients, close to the 15–20% range reported internationally [10,20]. MSI-high status was present in 8.2%, consistent with Karimi et al. [11] and Sitarz et al. [10], who reported MSI-H in 8–10% of gastric cancers. PD-L1 expression was seen in 10.7%, again mirroring global data [10]. EBV positivity was rare (2.0%), similar to other Indian studies [18]. These findings underscore that although biomarker-defined subgroups exist, only a minority of Indian patients are eligible for targeted or immunotherapy approaches, and cost remains a major barrier.

Stage at Presentation: Alarmingly, 74.5% of our patients presented with stage III or IV disease. This is consistent with Nandi et al. [1] and Chattopadhyay et al. [6], who reported over two-thirds of Indian patients presenting at advanced stages. By contrast, Japanese and Korean cohorts report early-stage detection rates exceeding 50% due to screening [16]. This discrepancy underscores systemic differences in healthcare infrastructure. Metastatic spread in our study was most commonly to the liver, followed by peritoneum and lung. These findings align with global patterns reported by Dicken et al. [20].

Treatment Patterns: Only 21.9% of our patients underwent upfront curative gastrectomy, while the majority received neoadjuvant or palliative chemotherapy. This is comparable to Saha et al. [13], who also noted that only a minority of Indian patients are surgical candidates at diagnosis. Limited access to targeted therapy was evident in our study, as only 7 HER2-positive patients received trastuzumab. This reflects economic constraints and highlights the inequity in cancer care access in resource-limited settings.

Predictors of Advanced Disease: Our regression analysis identified prolonged symptom duration, diffuse histology, and Borrmann type III/IV morphology as independent predictors of advanced stage. These findings are supported by Das et al. [18], who also reported diffuse histology as a predictor of late-stage disease. International reviews confirm that symptom duration beyond three months significantly increases the likelihood of advanced disease [2,10]. Our findings reinforce the critical importance of early endoscopic evaluation of persistent dyspeptic symptoms.

Strengths, Limitations, and Recommendations (≈300 words)

Strengths: This study adds to the limited literature on gastric cancer from Eastern India, providing a reasonably large cohort of 196 patients with comprehensive clinico-pathological and endoscopic analysis.

It incorporates biomarker evaluation (HER2, MSI, PD-L1, EBV), which has rarely been reported in Indian series. The inclusion of logistic regression analysis adds robustness by identifying independent predictors of advanced disease.

Limitations: The retrospective design may have introduced documentation bias. Some biomarker testing was incomplete due to cost constraints, limiting generalizability of molecular findings. Being a single-center hospital-based study, referral bias is possible as the center may disproportionately attract advanced cases. Survival outcomes were not analyzed due to limited follow-up, precluding prognostic assessment.

Recommendations:

1. **Early Detection:** Routine endoscopic evaluation of persistent dyspeptic symptoms in individuals over 40 years should be encouraged.
2. **Awareness Programs:** Community-level campaigns in rural and semi-urban areas should focus on modifiable risk factors (tobacco, alcohol, diet).
3. **Screening Initiatives:** Pilot screening programs in high-incidence districts may help

detect cases earlier, modeled on East Asian successes.

4. **Access to Biomarkers:** Wider availability of HER2, MSI, and PD-L1 testing is needed to guide therapy.
5. **Financial Support:** Government and NGO schemes should subsidize targeted and immunotherapy drugs for eligible patients.
6. **Multicenter Collaboration:** Larger prospective studies across different regions of India would improve generalizability and allow survival analysis.

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