ORIGINAL RESEARCH PAPER
Volume - 14 | Issue - 06 | June - 2025 | PRINT ISSN No. 2277 - 8179 | DOI : 10.36106/ijsr
INTERNATIONAL JOURNAL OF SCIENTIFIC RESEARCH

# RELEVANCE OF HER2 AS A BIOMARKER TODAY? ASSESSMENT OF THE TRUE INCIDENCE OF HER2 POSITIVITY: INSIGHTS FROM A TERTIARY CENTER IN SOUTHERN INDIA

Oncology

| | |
|---|---|
| **Dr. Rajeev L. K.** | Associate Professor, Department of Medical oncology, Kidwai Memorial Institute of Oncology. |
| **Dr. Kasturi Baruah*** | Senior Resident, Department of Medical oncology, Kidwai Memorial Institute of Oncology. *Corresponding Author |
| **Dr. M C Suresh Babu** | Professor and Head, Department of Medical oncology, Kidwai Memorial Institute of Oncology. |
| **Dr. Lokesh K. N.** | Associate Professor, Department of Medical oncology, Kidwai Memorial Institute of Oncology. |
| **Dr. Rudresha A. H.** | Associate Professor, Department of Medical oncology, Kidwai Memorial Institute of Oncology. |
| **Dr. Smitha C. Saldanha** | Associate Professor, Department of Medical oncology, Kidwai Memorial Institute of Oncology |

## ABSTRACT

**Introduction:** The expression of the human epidermal growth factor receptor 2 (HER2) protein in gastric and esophageal adenocarcinomas is related to worse prognosis, aggressive disease progression, and diminished chemotherapy efficacy. Patients with HER2-positive advanced gastric and gastroesophageal junction (GEJ) cancer are currently recommended to undergo trastuzumab, a monoclonal antibody that selectively targets HER2, in conjunction with chemotherapy as the revised standard of care. There are notable regional disparities in the reported prevalence of HER2 expression in gastric cancer. The objective of our research is to examine clinical features of HER2-positive gastroesophageal cancer. **Objective:** To determine the incidence of HER2 positivity among patients with newly diagnosed gastric/GEJ adenocarcinoma and evaluate the correlation between HER2 overexpression and demographic, clinicopathological, and disease parameters. **Materials And Methods:** From August 2022 to September 2024, 205 patients with gastric- esophageal cancer were prospectively assessed for the frequency of HER2 expression at a tertiary center in South India by employing Immunohistochemistry (IHC) and Fluorescence In Situ Hybridization (FISH). **Results:** Of 205 patients, 13 (6.34%) had verified HER2 overexpression. IHC results for three patients were inconclusive (2+); FISH analysis revealed a positive result for one patient. Regarding age, histological subtype, tumor site, tumor differentiation, serosal involvement, gender, and lymph node status, there were no variations in HER2 overexpression (positivity or negativity). **Conclusion:** HER2-Neu expression in gastric and GEJ adenocarcinomas has been associated to a lower survival rate and was found to be a sign of a bad prognosis, although being uncommon in our population.

## KEYWORDS

FISH, IHC–HER2 marker, HER2/neu protein, Gastric cancer, Gastric adenocarcinoma, Trastuzumab

## INTRODUCTION

Gastric cancer is ranked as the sixth most prevalent cancer globally. In 2022, it had been the fifth primary cause of death due to cancer. At that time, it ranked as sixth main reason of cancer-related deaths and seventh most prevalent cancer type in India (1). Multimodality therapy is most successful treatment for most localized gastroesophageal adenocarcinomas (GEAs) at stages II and III, with a 5-year survival rate of about 40%. Nevertheless, palliative care is the only available therapeutic option at advanced stages, which are characterized as unresectable, recurring, or metastatic illness, and the likelihood of a cure becomes very rare.The proto-oncogene HER2 is situated on chromosome 17. The activation of this receptor, part of EGFR family, activates signaling pathways that govern cell division, differentiation, proliferation, and anti-apoptotic mechanisms (2). Research indicates that HER2 overexpression or amplification is present in 7% to 34% of gastric tumors, demonstrating that HER2 is integral to the carcinogenesis of gastric cancer. Compared to gastric cancers, overexpression is more common in cancers at the gastroesophageal junction (GEJ) (3). It also varies by histological type, with intestinal cancers having higher rates than diffuse cancers, and by tumor differentiation, with well or moderately differentiated tumors having higher rates than poorly differentiated ones. (4). Compared to breast cancer, HER2 expression in GEA exhibits greater heterogeneity, and the immunostaining pattern is often basolateral rather than complete membrane staining (5). A 4-tiered HER2 scoring system, formed by Hoffman et al. and employed in ToGA trial, HER2 positive is defined as a minimum of five stained cells in biopsy samples or at least ten percent of marked tumor cells in resection specimens (6).

Since not all investigations have shown inconsistent evidence of correlation between HER2 overexpression and poor outcomes (6), the prognostic importance of HER2 in GEA remains unclear(8).

Despite the high prevalence of HER2-positive GEA in India, there is a lack of comprehensive data on the clinicopathological, demographic, and clinical outcomes associated with HER2 expression. This study hopes to address and bridge the gaps that exist in the understanding of HER-2 positive gastroesophageal cancers and thus formulate effective treatment strategies.

## MATERIALS AND METHODS

### Study Design:

Prospective observational study conducted at a tertiary center in South India

### Sample Size:

Two hundred and five patients who consecutively reported to medical oncology OPD having adenocarcinoma of stomach and gastroesophageal region were included in the study.

### Patient Selection:

Patients with primary stomach or GEJ adenocarcinoma were enrolled in this observational prospective analysis, which was carried out at tertiary facility in South India between August 2022 and September 2024. Patient demographics, tumor location and stage, along with treatment details (that include adjuvant and neoadjuvant therapy) had been collected. The TNM 8th Edition criteria were followed in the staging of every case. Immunohistochemistry (IHC) was used to confirm HER2 positivity, and Fluorescence In Situ Hybridization (FISH) testing was used for instances that were unclear (2+). The research goal was to assess the clinical characteristics of newly diagnosed patients experiencing HER2-positive gastric cancer or GEA. The research aimed to ascertain the prevalence of HER2 positivity in patients with newly diagnosed gastric/GEA and to determine correlation among HER2 overexpression and clinical, clinicopathological, and demographic variables. Immunohistochemistry with a monoclonal primary antibody (“polyclonal rabbit anti-human cerbB-2 oncoprotein [DAKO], diluted

1:600") was employed to evaluate HER2 status. The Two-step Super Sensitive Polymer HRP IHC detection kit was utilized to perform IHC on 3-µm thick deparaffinized tumor sections, that include positive and negative controls in every experiment. HER2 expression was evaluated according to the CAP/ASCO consensus standards.

The IHC results were interpreted as follows:
0 or 1+: Negative, 3+: Positive, and 2+: Equivocal/borderline.
For a final classification, additional evaluation using FISH was necessary. (7)

Data from the cancer registry, telephone follow-ups, and hospital records have been utilized to gather information on overall survival and disease progression.

**Inclusion Criteria:**
1. Eligible patients of age 18 years or older
2. Patients with ECOG "Performance Status" (PS) of 0 to 3
3. Histologically or cytologically confirmed primary stomach and GEJ adenocarcinoma.
4. HER2 positivity by IHC and FISH in cases of IHC 2+

**Exclusion Criteria:**
1. Patients with non-adenocarcinoma or non-squamous histology.
2. Patients who did not give written informed consent.

**Primary Outcomes:** Determine the incidence of HER2 positivity among patients with newly diagnosed gastric/GEJ adenocarcinoma

**Secondary Outcome:** Evaluate the correlation between HER2 overexpression and demographic, clinicopathological, and disease parameters.

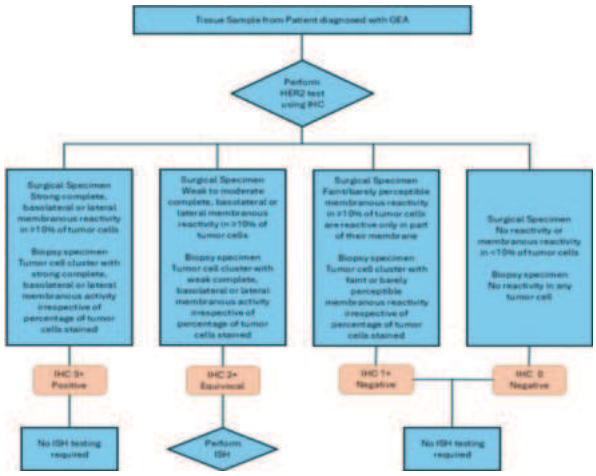
**Ethics:**
Ethical committee approval had been obtained before the study, Vide Letter Number KMIO/MEC/2022/07/PG/MO/14.

**Statistical Analysis:**
IBM SPSS software was utilized to analyze the data used in our investigation. The correlation among HER2 expression and clinical, pathological, and tumor differentiation features was analyzed utilizing "Pearson's chi-square test". Overall survival (OS) and Disease-Free Survival (DFS) had been determined by employing Kaplan–Meier analysis, with comparisons conducted using log-rank testing. Statistical significance had been established as a p-value below 0.05.

**Table 1: Guidelines For IHC Interpretation**

| SCORING GUIDELINES FOR IHC INTERPRETATION | | | |
|---|---|---|---|
| Surgical Specimen-Staining Pattern | Biopsy Specimen-Staining Pattern | Score | HER2 Expression Assessment |
| Less than 10% of tumor cells had neither observable reactivity nor membranous reactivity. | No tumor cells have any observable reactivity or membrane reactivity. | 0 | Negative |
| 10% or more of tumor cells have faint or scarcely perceptible membrane reactivity; these cells only show reactivity in certain areas of their membrane. | Regardless of the proportion of tumor cells stained, tumor cell clusters* exhibit weak or hardly perceptible membrane reactivity. | 1+ | Negative |
| 10% or more of tumor cells have full, basolateral, or adjacent membrane reactivity that is insufficient to moderate. | Despite of the percentage of stained tumor cells, a tumor cell cluster has inadequate moderate complete, basolateral, or lateral membranous reactivity. | 2+ | Equivocal |
| Strong lateral, basolateral, or complete membrane sensitivity in at least 10% of tumor cells. | Irrespective of the percentage of stained tumor cells, a tumor cell cluster has a notably strong basolateral or lateral membranous reactivity. | 3+ | Positive |

*Tumor cell cluster (≥ 5 neoplastic cells)




**Flowchart 1:** Algorithm For Her 2 Evaluation

**RESULTS**

The 205 patients with gastric or GEA that had been histologically verified with IHC and FISH. The study population's median age was 56 years (age range: 23–88).There were 140 men (68.29%) and 65 women (31.70%) in the group, yielding a male-to-female ratio of 2.15:1. Approximately 65% of the patients were over the age of 50. The predominant tumor site were distal stomach, particularly antrum, and pylorus, followed by the gastric body. Poor histological differentiation (grade 3) was observed in 56% of cases. A majority (95.6%) of patients presented with advanced T-stage disease, and 86.34% showed locoregional nodal involvement at diagnosis. Additionally, a significant proportion had metastatic disease at presentation (40.48%).

**Table 2: Patient Demographics And Clinical Characteristics**

| Characteristics | Frequency (n) | Percentage (%) |
|---|---|---|
| Age: 56 years (23-88) | | |
| Gender: Male: Female: 140: 65 | | |
| Site: | | |
| Gastroesophageal | 46 | 22.43% |
| Gastric cardia | 19 | 09.26% |
| Gastric body | 52 | 25.36% |
| Distal gastric (antrum/pylorus) | 88 | 42.92% |
| Tumor differentiation: | | |
| Grade I | 16 | 07.80% |
| Grade II | 71 | 34.63% |
| Grade III | 118 | 56.56% |
| T Staging: | | |
| T1 and T2 | 9 | 04.39% |
| T3 and T4 | 196 | 95.60% |
| N Staging: | | |
| N Negative | 28 | 13.65% |
| N positive | 177 | 86.34% |
| M Staging: | | |
| M0 | 122 | 59.51% |
| M1 | 83 | 40.48% |

**Table 3: Expression Profile Of Her 2 NEU In Study Cohort**

| IHC scoring | Frequency | Interpretation |
|---|---|---|
| 0/1+ | 192 | Negative |
| 2+ FISH positive | 3 | Positive |
| 3+ | 10 | Positive |

**Association And Correlation Of Her 2 Status With Clinicopathological Features**

**HER2 Positivity Rate And Gastric Cancer Site:**
Among the 13 HER2-positive patients, the most frequently affected site was the distal stomach (antrum/pylorus) with 7(53.84%) cases, followed by the gastroesophageal junction with 5 (24.39%) cases, and the gastric body with 1(7.69%) case.

**HER2 Positivity Rate And Tumor Grade/differentiation:**
Of the 13 patients, 11(84.61%) had tumors with grade 1 or 2 (well or moderately differentiated), while 2(15.38%) had grade 3 (poorly differentiated) tumors.

**HER2 positivity rate and TNM staging:**
A major number of HER2-positive patients (11 out of 13) presented with T4 disease, 12 patients had nodal involvement, and 11 patients had metastatic disease at diagnosis.

**Table 4: Association Between HER 2 And Clinical Parameters**

| | | | HER IHC | | Total | p-value |
|---|---|---|---|---|---|---|
| | | | Negative | Positive | | |
| AGE GROUP | <=5 | Count | 68 | 3 | 71 | 0.28 |
| | | % | 95.8% | 4.2% | 100.0% | |
| | >50 | Count | 124 | 10 | 134 | |
| | | % | 92.5% | 7.5% | 100.0% | |
| SEX | FEMALE | Count | 62 | 3 | 65 | 0.36 |
| | | % | 95.4% | 4.6% | 100.0% | |
| | MALE | Count | 130 | 10 | 140 | |
| | | % | 92.9% | 7.1% | 100.0% | |
| PRIMARY | ESOPHAGUS | Count | 51 | 4 | 55 | 0.001 |
| | | % | 94.4% | 5.6% | 100.0% | |
| | STOMACH | Count | 141 | 9 | 150 | |
| | | % | 94.0% | 6.0% | 100.0% | |
| SUBSITE | BODY | Count | 51 | 1 | 52 | 0.318 |
| | | % | 98.1% | 1.9% | 100.0% | |
| | DISTAL | Count | 81 | 7 | 88 | |
| | | % | 92.0% | 8.0% | 100.0% | |
| | PROXIMAL | Count | 60 | 5 | 65 | |
| | | % | 92.3% | 7.7% | 100.0% | |
| cT | 2.00 | Count | 8 | 1 | 9 | 0.212 |
| | | % | 88.9% | 11.1% | 100.0% | |
| | 3.00 | Count | 51 | 1 | 52 | |
| | | % | 98.1% | 1.9% | 100.0% | |
| | 4.00 | Count | 133 | 11 | 144 | |
| | | % | 92.4% | 7.6% | 100.0% | |
| cN | .00 | Count | 27 | 1 | 28 | 0.845 |
| | | % | 96.4% | 3.6% | 100.0% | |
| | 1.00 | Count | 160 | 12 | 172 | |
| | | % | 93.0% | 7.0% | 100.0% | |
| | 2.00 | Count | 3 | 0 | 3 | |
| | | % | 100.0% | 0.0% | 100.0% | |
| | 3.00 | Count | 2 | 0 | 2 | |
| | | % | 100.0% | 0.0% | 100.0% | |
| **cM** | .00 | Count | 120 | 2 | 122 | **0.001** |
| | | % | 98.4% | 1.6% | 100.0% | |
| | 1.00 | Count | 72 | 11 | 83 | |
| | | % | 86.7% | 13.3% | 100.0% | |
| **STAGE** | STAGE 2 | Count | 14 | 1 | 15 | **0.016** |
| | | % | 93.3% | 6.7% | 100.0% | |
| | STAGE 3 | Count | 91 | 1 | 92 | |
| | | % | 98.9% | 1.1% | 100.0% | |
| | STAGE 4 | Count | 87 | 11 | 98 | |
| | | % | 88.8% | 11.2% | 100.0% | |
| **HISTOLOGY** | ADENO | Count | 192 | 13 | 205 | |
| | | % | 93.7% | 6.3% | 100.0% | |
| **DIFFERENTIATION** | G I | Count | 15 | 1 | 16 | **0.003** |
| | | % | 93.8% | 6.3% | 100.0% | |
| | G II | Count | 61 | 10 | 71 | |
| | | % | 85.9% | 14.1% | 100.0% | |
| | G III | Count | 116 | 2 | 118 | |
| | | % | 98.3% | 1.7% | 100.0% | |
| Total | | Count | 192 | 13 | 205 | |
| | | % | 93.7% | 6.3% | 100.0% | |

**Table 5: Comparison Between HER2 Incidence Of Different Indian Regions**

| | East India 2019 | South India 2015 | South India 2012 | North India 2015 | West India 2013 | Current study 2024 |
|---|---|---|---|---|---|---|
| Sample size | 68 | 60 | 52 | 70 | 43 | 205 |
| Incidence | 56% | 26.7% | 44.2% | 21.4% | 7% | 6.34% |

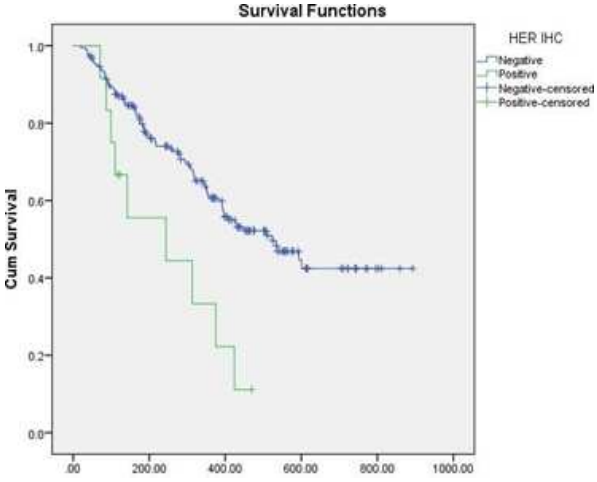



**Figure 1:** Kaplan–Meyer curve showing overall survival comparison between Her 2 negative and positive cohort

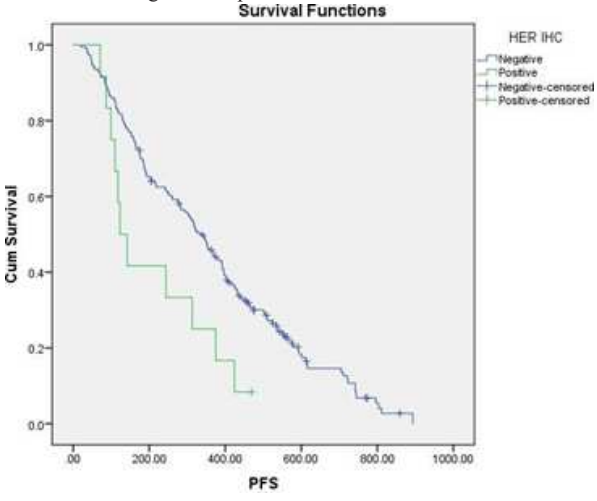



**Figure 2:** Kaplan–Meyer curve illustrating progression free survival comparison between Her 2 negative and positive cohort

**Survival:**
Median OS for HER2-negative disease was 17.46 months (range: 12.4–22.5 months). The median OS for HER2-positive disease 8.13 months (range: 1–17.53 months). Progression-free survival for HER2-negative disease was 11.2 months (ranging from 9.7 to 12.6 months), while for HER2-positive disease, it was 4.1 months (ranging from 1 to 5.43 months).

## DISCUSSION

India has a relatively low incidence of stomach cancer when compared to other nations. Regional differences are noticeable, too, with Southern and Eastern India reporting the greatest rates. Across the Indian subcontinent, the incidence of HER2 positivity varies widely, ranging from as high as 56% in Eastern India (10) to as low as 7% in Western India(11). It is quite a paradox that despite a high prevalence of HER2 positive diseases in our country, the robust establishment of associated clinicopathological, demographic and clinical outcome data is lacking.

Our study, consistent with previous research, found that HER2 positivity is prevalent in men. In Eastern and Southern India, the antrum is frequently the primary site for HER2-positive tumors (12)(13). However, some studies from Southern India have noted a shift toward cancers occurring in the cardia or proximal stomach (14). Changes in Helicobacter pylori colonization, atrophic gastritis, obesity, dietary patterns, lifestyle, along with gastroesophageal reflux may all be contributing reasons to this trend (15). In accordance with the research performed by Gupta et al. and Panda et al. (16)(17), we identified a substantial correlation between HER2 expression and well or moderately differentiated (grades 1 and 2) adenocarcinomas.

This study is especially useful because there is a dearth of information

on survival outcomes for Indian patients experiencing HER2-positive gastric cancer. In our sample, patients experiencing HER2-positive malignancies showed lower overall and in remission survival rates than those with HER2-negative tumors. However, a significant weakness of this study is the limited usage of trastuzumab because of financial limitations.

The ToGA trial highlighted variability in HER2 staining between biopsy and surgical specimens. In the trial, 68% of tumor samples were obtained through biopsy, while 32% came from surgical specimens, with differences in staining intensities across tissue sections (3).

One of the strengths of our study is that all HER2 evaluations were performed exclusively on biopsy specimens, avoiding the variability seen in surgical samples. HER2 positivity was significantly higher in biopsy specimens (31.2%) compared to gastrectomy specimens (8.8%) (P = 0.0003) (18). Heterogeneous HER2 expression in surgical samples contributed to false- negative results. However, the concordance rate among biopsy and surgical specimens was 74.1%. The potential limitation of our study is lacking data on intestinal versus diffuse type tumor phenotype which is an essential prognostic marker.

## CONCLUSION:

HER2-Neu expression in stomach and GEJ adenocarcinomas, albeit infrequent in our population, correlates with reduced survival rates and is acknowledged as an indicator of adverse prognosis.

## Conflict Of Interest

None declared.

## Source Of Funding

Nil

## Acknowledgment

The authors thank the Medical Oncology Department, Kidwai Memorial Institute of Oncology, Bengaluru, Karnataka.

## REFERENCES

1. Sung H, Ferlay J, Siegel RL, et al. Global Cancer Statistics 2020: GLOBOCAN Estimates of Incidence and Mortality Worldwide for 36 Cancers in 185 Countries. CA Cancer J Clin. 2021;71(3):209-249. https://doi:10.3322/caac.21660
2. Akiyama T, Sudo C, Ogawara H, Toyoshima K, Yamamoto T. The product of the human c-erbB-2 gene: a 185-kilodalton glycoprotein with tyrosine kinase activity. Science. 1986;232(4758):1644-1646. https://doi:10.1126/science.3012781
3. Bang YJ, Van Cutsem E, Feyereislova A, et al. Trastuzumab in combination with chemotherapy versus chemotherapy alone for treatment of HER2-positive advanced gastric or gastro-oesophageal junction cancer (ToGA): a phase 3, open-label, randomised controlled trial [published correction appears in Lancet. 2010 Oct 16;376(9749):1302]. Lancet. 2010;376(9742):687-697. https://doi:10.1016/S0140-6736(10)61121-X
4. Ajani JA, D'Amico TA, Almhanna K, et al. Gastric Cancer, Version 3.2016, NCCN Clinical Practice Guidelines in Oncology. J Natl Compr Canc Netw. 2016;14(10):1286-1312. https://doi:10.6004/jnccn.2016.0137
5. Pirrelli M, Caruso ML, Di Maggio M, Armentano R, Valentini AM. Are biopsy specimens predictive of HER2 status in gastric cancer patients?. Dig Dis Sci. 2013;58(2):397-404. https://doi:10.1007/s10620-012-2357-3
6. Hofmann M, Stoss O, Shi D, et al. Assessment of a HER2 scoring system for gastric cancer: results from a validation study. Histopathology. 2008;52(7):797-805. https://doi:10.1111/j.1365-2559.2008.03028.x
7. Bartley AN, Washington MK, Colasacco C, et al. HER2 Testing and Clinical Decision Making in Gastroesophageal Adenocarcinoma: Guideline From the College of American Pathologists, American Society for Clinical Pathology, and the American Society of Clinical Oncology. J Clin Oncol. 2017;35(4):446-464. https://doi:10.1200/JCO.2016.69.4836
8. Tanner M, Hollmén M, Junttila TT, et al. Amplification of HER-2 in gastric carcinoma: association with Topoisomerase IIalpha gene amplification, intestinal type, poor prognosis and sensitivity to trastuzumab. Ann Oncol. 2005;16(2):273-278. https://doi:10.1093/annonc/mdi064
9. Van Cutsem E, Bang YJ, Feng-Yi F, et al. HER2 screening data from ToGA: targeting HER2 in gastric and gastroesophageal junction cancer. Gastric Cancer. 2015;18(3):476-484. https://doi:10.1007/s10120-014-0402-y
10. Roy PS, Nyodu T, Hazarika M, et al. Prevalence of HER2 Expression and Its Correlation with Clinicopathological Parameters in Gastric or Gastroesophageal Junction Adenocarcinoma in North-East Indian Population. Asian Pac J Cancer Prev. 2019;20(4):1139-1145.Published2019Apr29. https://doi:10.31557/APJCP.2019.20.4.1139
11. Patil PS, Mehta SA, Mohandas KM. Over-expression of HER2 in Indian patients with gastric cancer. Indian J Gastroenterol. 2013;32(5):350. https://doi:10.1007/s12664-012-0279-9
12. Sekaran A, Kandagaddala RS, Darisetty S, et al. HER2 expression in gastric cancer in Indian population--an immunohistochemistry and fluorescence in situ hybridization study. Indian J Gastroenterol. 2012;31(3):106-110. https://doi:10.1007/s12664-012-0214-0
13. Rajagopal I, Niveditha SR, Sahadev R, Nagappa PK, Rajendra SG. HER 2 Expression in Gastric and Gastro-esophageal Junction (GEJ) Adenocarcinomas. J Clin Diagn Res. 2015;9(3):EC06-EC10. https://doi:10.7860/JCDR/2015/12581.5630
14. Harikumar R, Chettupuzha AP, Harish K, Kumar KS, Thomas V. Sub-site specific time trends of carcinoma stomach in North Kerala--a retrospective analysis. Trop Gastroenterol. 2005;26(2):76-79.
15. Mukaisho K, Nakayama T, Hagiwara T, Hattori T, Sugihara H. Two distinct etiologies of gastric cardia adenocarcinoma: interactions among pH, Helicobacter pylori, and bile acids. Front Microbiol. 2015; 6:412. Published 2015 May 11. https://doi:10.3389/fmicb.2015.00412
16. Gupta P, Rao S, Bhalla S. Human epidermal growth factor receptor 2 expression in gastric carcinoma and its association with histopathological parameters in Indian population. Indian J Cancer. 2016;53(4):505-511. https://doi:10.4103/ijc.IJC_513_16
17. Panda, S. K., Panda, A., Jn, M., & Bhuyan, P. (2015). A study of the incidence and prognostic value of HER-2 overexpression in patients with gastric adenocarcinoma in Odisha. Global Surgery, 1(1). https://doi.org/10.15761/gos.1000103
18. Pirrelli M, Caruso ML, Di Maggio M, Armentano R, Valentini AM. Are biopsy specimens predictive of HER2 status in gastric cancer patients?. Dig Dis Sci. 2013;58(2):397-404. https://doi:10.1007/s10620-012-2357-3
19. Tewari M, Kumar A, Mishra RR, Kumar M, Shukla HS. HER2 Expression in Gastric and Gastroesophageal Cancer: Report from a Tertiary Care Hospital in North India. Indian J Surg. 2015;77(Suppl 2):447-451. https://doi:10.1007/s12262-013-0871-y
20. Bartley AN, Washington MK, Ventura CB, et al. HER2 Testing and Clinical Decision Making in Gastroesophageal Adenocarcinoma: Guideline From the College of American Pathologists, American Society for Clinical Pathology, and American Society of Clinical Oncology. Arch Pathol Lab Med. 2016;140(12):1345-1363. https://doi:10.5858/arpa.2016-0331-CP