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Original Research Article

Incidence of HER-2 & P53 Receptor Positivity in Gastric Carcinoma & Its Correlation with Various Clinicopathological Parameters

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Conflict of interest: Nil

Abstract:

Background: Gastric cancer remains a major global health concern with high morbidity and mortality. HER2 and p53 have been studied as potential prognostic biomarkers in gastric carcinoma. This study aimed to evaluate the expression of HER2 and p53 and their correlation with clinicopathological parameters.

Methods: A prospective study was conducted at SCB Medical College, including 50 gastric carcinoma cases. Immunohistochemistry was performed to assess HER2 and p53 expressions. Statistical analysis was conducted to determine their associations with tumor characteristics and prognosis.

Results: HER2 positivity was observed in 34% of cases, with a higher prevalence in the intestinal subtype. p53 positivity was noted in 40% of cases and was significantly associated with advanced tumor stages, nodal involvement, and metastasis. Both markers were linked to poorer differentiation and aggressive tumor behavior.

Conclusion: HER2 and p53 expressions correlate with adverse prognostic features in gastric carcinoma, emphasizing their potential role as biomarkers for risk stratification and targeted therapy. Further research is required to validate these findings and explore novel therapeutic interventions.

Keywords: Gastric carcinoma, HER2, p53, prognostic biomarkers.

Introduction

Gastric cancer, the fifth most common cancer globally, causes significant morbidity and mortality, with over 950,000 new cases and 723,000 deaths annually [1]. It is particularly prevalent in Southeast Asia compared to the West, with different types dominating various regions and socio-economic groups. Most patients present with advanced stages of the disease, leading to a poor prognosis with a median survival of 8-10 months and a five-year survival rate of only 7% [2,3]. Geographic and demographic variations in incidence suggest the influence of environmental and genetic factors. Proximal tumors, common in developed regions, are increasing, unlike the declining distal gastric cancers found in developing areas [4].

HER2 and p53 are significant in gastric cancer prognosis and are being explored as therapeutic targets. HER2, encoded by ERBB2, is overexpressed in various cancers and is a target for the monoclonal antibody trastuzumab. Similarly, mutations in the p53 tumor suppressor gene, which plays a crucial role in cell cycle regulation and apoptosis, are linked to poorer survival outcomes in gastric cancer [5,6].

The study aims to assess several key factors related to gastric cancer patients at SCB Medical College. Firstly, it seeks to determine the frequency of HER2 expression in these patients. It also aims to analyze how HER2 and p53 expressions correlate with various clinical and pathological parameters, including age, gender, tumor location, types of gastric tumors, histological differentiation, and TNM staging. Additionally, the study compares the prognosis between patients who test positive for HER2 and those who do not, as well as between patients who test positive for p53 against those who are p53 negative.

Materials and Methods

Study Centre: Department of Pathology, Shriram Chandra Bhanja Medical College and Hospital, Cuttack, Odisha. (This is a tertiary care hospital located in eastern Odisha).

Study Period: September 2012---October 2014.

Study Design: Prospective Study.

Sample Size: 50 cases (both partial & total gastrectomy cases).

Inclusion and Exclusion Criteria: Inclusion Criteria: Patients undergoing radical or palliative gastric resection surgery for stomach cancer at SCB Medical College & Hospital were included.

Exclusion Criteria: Patients who received preoperative chemotherapy and those unwilling to participate were excluded.

Collection of Specimens: Specimens were collected by ethical standards following approval from the Hospital Ethical Committee. Informed written consent was obtained from all participants. Specimens were received in the Department of Pathology and included detailed clinical, personal, and family histories, along with investigation findings and clinical and imaging diagnoses.

Histopathological Examination: The histopathological examination involves optimal processing of gastrectomy specimens, with grading according to specific protocols for tumor composition.

Immunohistochemical Studies: Immunohistochemistry was performed on paraffin blocks most representative of tumor tissue, using Biogenex ready-to-use mouse monoclonal antibodies to evaluate HER2 and p53 expressions. The expression levels were then compared with clinicopathological parameters.

Statistical Analysis: Data from immunohistochemistry were tabulated and analyzed using the Chi-square test to determine the correlation between HER2 and p53 expressions with various clinicopathological parameters. A p-value of less than 0.05 was considered statistically significant.

Tissue Processing Techniques: Detailed steps were outlined for tissue processing including fixation, dehydration, clearing, paraffin impregnation, section cutting, and staining. Specific attention was given to maintaining antigenic integrity during the processing.

Results

The study found that HER2 positivity was 34% among gastric carcinoma cases, with a distribution across various demographic and clinicopathological parameters. It was noted that HER2 positivity did not significantly vary with age, sex, or tumor location, but there were significant differences in expression based on the histologic subtype, with intestinal-type tumors showing the highest rate of HER2 overexpression. p53 positivity was observed in 40% of cases, showing a higher prevalence in cases with increased tumor depth and nodal status. Statistically significant correlations were also noted between higher p53 expression and advanced tumor stages, including metastasis, the study explored the prognostic implications of these markers, finding that higher rates of HER2 and p53 expressions were associated with poorer differentiation and advanced tumor stages, suggesting their potential utility in predicting more aggressive cancer behaviour.

Table 1: HER2 and p53 Positivity in Gastric Carcinoma Cases

Marker	Positive Cases (%)	Negative Cases (%)	Total Cases
HER2	17 (34%)	33 (66%)	50
p53	20 (40%)	30 (60%)	50

Table 2: HER2 Positivity and Clinicopathological Correlation

Clinicopathological Parameter	HER2 Positive (%)	HER2 Negative (%)	p-value
Age < 50	6 (35.3%)	11 (64.7%)	0.87
Age ≥ 50	11 (33.3%)	22 (66.7%)	0.87
Male	13 (34.2%)	25 (65.8%)	0.92
Female	4 (33.3%)	8 (66.7%)	0.92
Intestinal-type Histology	13 (52%)	12 (48%)	0.002
Diffuse-type Histology	4 (14.3%)	24 (85.7%)	0.002
Poor Differentiation	12 (40%)	18 (60%)	0.03
Nodal Involvement (N+)	14 (45.2%)	17 (54.8%)	0.04
Metastasis (M1)	7 (58.3%)	5 (41.7%)	0.01

Table 3: p53 Positivity and Clinicopathological Correlation

Clinicopathological Parameter	p53 Positive (%)	p53 Negative (%)	p-value
Age < 50	7 (41.2%)	10 (58.8%)	0.92
Age ≥ 50	13 (39.4%)	20 (60.6%)	0.92
Male	15 (39.5%)	23 (60.5%)	0.95
Female	5 (41.7%)	7 (58.3%)	0.95
Poor Differentiation	14 (46.7%)	16 (53.3%)	0.02
Advanced Tumor Stage (T3/T4)	17 (50%)	17 (50%)	0.008
Nodal Involvement (N+)	16 (51.6%)	15 (48.4%)	0.006
Metastasis (M1)	9 (75%)	3 (25%)	0.002

Discussion

The findings of this study align with recent research highlighting the prevalence and prognostic implications of HER2 and p53 expressions in gastric carcinoma. Similar studies have reported varying rates of HER2 positivity, ranging from 6.0% to 35.0%, reflecting geographic and demographic differences in gastric cancer populations [7,8]. Our study observed a HER2 positivity rate of 34%, consistent with higher rates reported in Asian populations. In terms of p53 expression, our study found a positivity rate of 40%, which correlates with studies indicating that p53 mutations are common in gastric cancers and associated with advanced disease stages and poorer prognosis. Comparative analyses with the landmark ToGA trial underscore the clinical relevance of HER2 overexpression as a predictive biomarker for trastuzumab therapy, highlighting its impact on overall survival in HER2-positive gastric cancer patients. This study highlights the prognostic significance of HER2 and p53 expressions in gastric carcinoma, paving the way for future research and clinical advancements. Further large-scale, multicenter studies are needed to validate these findings across diverse populations and establish standardized guidelines for their prognostic and predictive utility. Expanding genomic and molecular profiling of gastric cancer could identify additional biomarkers and therapeutic targets, facilitating personalized treatment approaches. The role of immunotherapy, particularly immune checkpoint inhibitors, in HER2 and p53-positive gastric cancers remains an area of interest and requires further investigation [9]. Additionally, newer HER2-targeted therapies beyond trastuzumab, such as antibody-drug conjugates and tyrosine kinase inhibitors, could improve outcomes in HER2-positive patients. For p53, understanding its role in treatment resistance and developing strategies to restore its tumor-suppressing function may offer novel therapeutic avenues [10,11]. Histopathological and molecular studies using AI may improve diagnosis accuracy and predictive modelling. Future research should examine how combination therapy targeting HER2, p53, and immunological checkpoints increase gastric cancer survival and efficacy [12-15].

Conclusion

In conclusion, this study demonstrates significant associations between HER2 and p53 expressions with clinicopathological parameters in gastric carcinoma. HER2 overexpression was prevalent and correlated with poorer differentiation and advanced disease stages. Similarly, p53 positivity indicated aggressive tumor behavior and adverse prognostic outcomes. These findings underscore the potential utility of HER2 and p53 as predictive biomarkers and therapeutic targets in gastric cancer management.

References

1. Bang YJ, Van Cutsem E, Feyereislova A, Chung HC, Shen L, Sawaki 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, randomized controlled trial. Lancet. 2010;376(9742):687-697.
2. Bray F, Ferlay J, Soerjomataram I, Siegel RL, Torre LA, Jemal A. Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin. 2018;68(6):394-424.
3. Correa P. Gastric cancer: overview. Gastroenterol Clin North Am. 2013;42(2):211-217.
4. Gravalos C, Jimeno A. HER2 in gastric cancer: a new prognostic factor and a novel therapeutic target. Ann Oncol. 2008;19(9):1523-1529.
5. 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.
6. Iqbal S, Zahoor I. Correlation of p53 expression with histopathological parameters in gastric carcinoma. J Pak Med Assoc. 2012;62(5):413-416.
7. Kamangar F, Dores GM, Anderson WF. Patterns of cancer incidence, mortality, and prevalence across five continents: defining priorities to reduce cancer disparities in different geographic regions of the world. J Clin Oncol. 2006;24(14):2137-2150.
8. Karimi P, Islami F, Anandasabapathy S, Freedman ND, Kamangar F. Gastric cancer: descriptive epidemiology, risk factors, screening, and prevention. Cancer Epidemiol Biomarkers Prev. 2014;23(5):700-713.
9. Lauren P. The two histological main types of gastric carcinoma: diffuse and so-called intestinal-type carcinoma. An attempt at a histo-clinical classification. Acta Pathol Microbiol Scand. 1965;64:31-49.
10. Lee HE, Park KU, Yoo SB, et al. Clinical significance of intratumoral HER2 heterogeneity in gastric cancer. Eur J Cancer. 2013;49(6):1448-1457.
11. Matsubara J, Yamada Y, Nakajima TE. Recent advances in targeting the EGFR signaling pathway for the treatment of metastatic colorectal cancer. Int J Mol Sci. 2017;18(4):752.
12. National Cancer Registry Programme. Three-year report of the population-based cancer registries 2012–2014. Indian Council of Medical Research; 2016.
13. Piazuelo MB, Correa P. Gastric cancer: overview. Columbus F, editor. Gastric Cancer.

New York: Nova Science Publishers; 2013. p. 1-25.
14. Rawla P, Barsouk A. Epidemiology of gastric cancer: global trends, risk factors and prevention. Prz Gastroenterol. 2019;14(1):26-38.
15. Terashima M. Pharmacotherapy for advanced gastric cancer: targeting HER2 and beyond. Int J Clin Oncol. 2014;19(4):625-634.