

Immunohistochemical Association of HER-2 /Neuimmunoprotein with Histomorphological Variables in Patients in Gastric Carcinoma.

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Abstract: Gastric tumour is the fourth most common cancer and the second leading cause of death due to cancer worldwide. Gastric cancer is more common in male than in female in the ratio of 2:1. It is a disease of elderly. The histological and morphological types of gastric carcinomas are highly variable and may not correlate well with the prognosis of the patients. Molecular markers are vital in determining the disease progression and hence disease outcome, survival and prognosis. The objective of the study was to correlate the association of HER-2/Neu in Gastric adenocarcinoma with histomorphological variables. This was a retrospective study carried out in our institution on 100 cases. There was a significant association between HER-2 Neu overexpression and histological grading of adenocarcinoma.

Keywords: Gastric carcinoma, HER-2 Neu

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I. Introduction

An association between histomorphological features and molecular markers of gastric adeno carcinoma would give a clue toward the relationship between them and hence provide us an extra tool to combat the high mortality due to these carcinomas. HER-2/Neureceptor also known as c-Erb-2, encodes a transmembrane tyrosine kinase receptor is a growth factor receptor involved in growth and metastasis of malignant cells⁽¹⁰⁾. Overexpression of HER2 in gastric cancer is very much correlated with bad prognosis. It is also correlated with increased risk of local growth and distant metastasis. Over expression of HER-2/Neu is reported to have poorer prognosis, but some other studies showed no such association. The study herein describes the prevalence of HER-2/Neu expression in gastric adenocarcinoma and to correlate it with various histomorphological variables.

II. Material and Methods

This study was conducted in the department of pathology over a period of 3 years. Endoscopic biopsy from stomach as well as resected specimens (subtotal, total, radical and palliative gastrectomy) from the Department of Surgery, which were received in Department of Pathology, and reported as adenocarcinoma were included for the study.

Exclusion criteria: cases reported other than adenocarcinoma. All the specimens were fixed in 10% neutral formalin and were subjected to histopathological examination. sections of 4 micron thickness were made and routine staining with haematoxylin and eosin was done. histomorphological parameters evaluated include endoscopy, gross appearance and histological grade. Immunohistochemical expression of HER-2 Neuimmunoprotein was done on 100 cases of adenocarcinoma, based on peroxidase method with a standard HRP kit. The slides were analysed for the presence of reaction, cellular localisation, percentage of cells stained and intensity of staining and graded appropriately.

III. Results

Endoscopic appearance:

Out of 100 cases majority presented as ulcers (73%). Remaining presented as growth (27%). Table-1

Table -1: Distribution of Endoscopic appearance.

Endoscopic appearance	Frequency	Percent
Ulcer	73	73.0
Growth	27	27.0
Total	100	100.0

Gross appearance:

In my study population, the common gross pattern is proliferative (50%), the next being ulcerative (45%) and the least one is polypoidal (2%). Table-2 Fig.1

Table -2Distribution of gross appearance

Gross appearance	Frequency	Percent
Ulcerative	45	45.0
Proliferative	50	50.0
Polypoidal	2	2.0
Infiltrative	3	3.0
Total	100	100.0



Fig-1: Gastric Carcinoma (gross) – Ulcerative

Histologic grade:

In the study population, most of the cases are moderately differentiated (42%). Poorly differentiated tumours accounts for 41% and 17 % cases were well differentiated. Table-3. Fig 2,3&4

Table-3: Histological grade distribution

Histologic Grade	Frequency	Percent
Well differentiated	17	17.0
Moderately differentiated	42	42.0
Poorly differentiated	41	41.0
Total	100	100.0

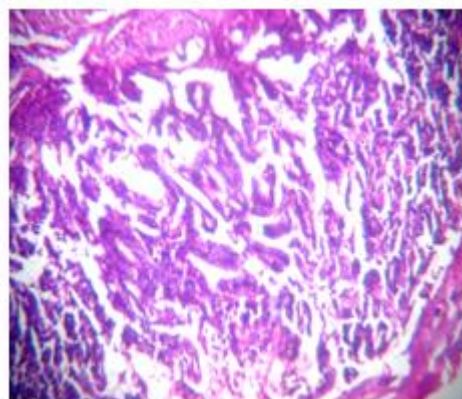
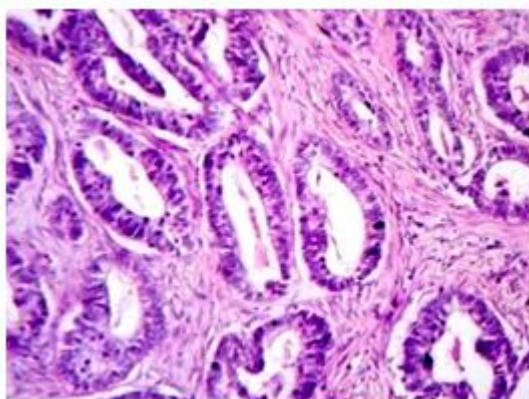


Fig-2 Well differentiated H&E (40x)**Fig-3** Moderately differentiated H&E(40 X)

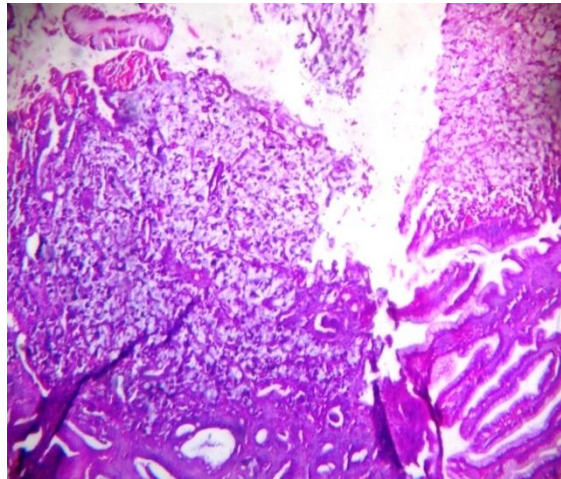


Fig -4: Poorly differentiated H&E(40X)

Her -2 / Neu receptor expression:

25% of cases were positive for Her-2/Neu receptor. Moderately differentiated (52%) and well differentiated (28%) tumours shows more positivity than poorly differentiated tumours(20%). Table-4

Table-4Expression of Her -2/Neu receptor in study population

Her - 2 Status	Frequency	Percent
Positive	25	25.0
Negative	75	75.0
Total	100	100.0

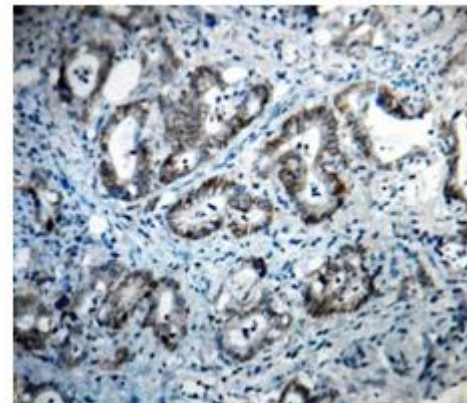
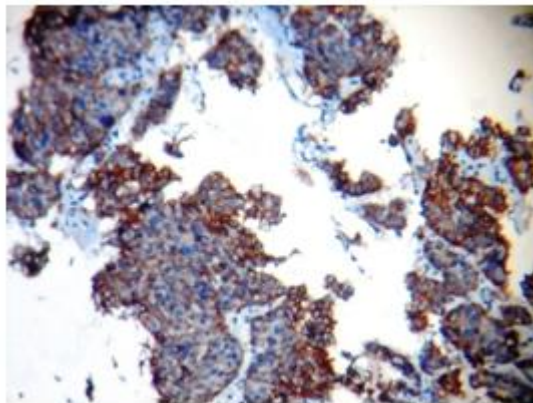


Fig-5HER-2/ Neu score 3+**Fig -6**HER-2/Neu score2+

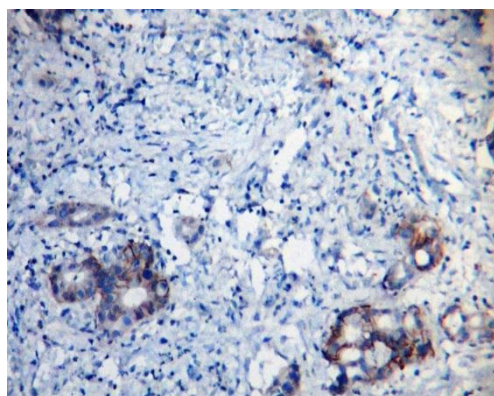


Fig -7HER-2/Neu score1+

Correlation of HER -2 with Varioushistomorphological Factors:

Table -5: Association of Endoscopic Appearance with HER-2/Neu Expression

			HER - 2		Total
			Positive	Negative	
ENDOSCOPY	Ulcer	No of cases	20	53	73
		% with HER - 2	80.0%	70.7%	73.0%
	Growth	No of cases	5	22	27
		% with HER - 2	20.0%	29.3%	27.0%
Total		No of cases	25	75	100
		% with HER - 2	100.0%	100.0%	100.0%

P Value: 0.363

Among HER-2/Neu positive cases,ulcer accounts for 80% and growth accounts 20%. No statistical significance was found between two groups.

Table-6: Association of Gross Appearance with HER-2/Neu

			HER - 2		Total
			Positive	Negative	
GROSS	Ulcerative	Count	12	33	45
		% within HER - 2	48.0%	44.0%	45.0%
	Proliferative	Count	13	37	50
		% within HER - 2	52.0%	49.3%	50.0%
	Polypoidal	Count	0	2	2
		% within HER - 2	0.0%	2.7%	2.0%
	Infiltrative	Count	0	3	3
		% within HER - 2	0.0%	4.0%	3.0%
Total		Count	25	75	100
		% within HER - 2	100.0%	100.0%	100.0%

P value: 0.624 (>0.05%)

Among the cases showing HER-2/Neu over expression, 48% were ulcerative type, 52% were proliferative type and none were polypoidal and infiltrative type. No statistically significant association was found between gross appearance and HER-2/Neu over expression. Table7

Table-7: Association of Tumour Grade with HER-2/Neu expression

			HER - 2		Total
			Positive	Negative	
HPE	Well differentiated	Count	7	10	17
		% within HER - 2	28.0%	13.3%	17.0%
	Moderately differentiated	Count	13	29	42
		% within HER - 2	52.0%	38.7%	42.0%
	Poorly differentiated	Count	5	36	41
		% within HER - 2	20.0%	48.0%	41.0%
Total		Count	25	75	100
		% within HER - 2	100.0%	100.0%	100.0%

P value: 0.034 (<0.05)

Positivity for HER-2/Neu was seen more with moderately differentiated cases (52%) than well differentiated (28%) or poorly differentiated (20%) cases and the association was statistically significant. (P value < 0.05) .Table 7

IV. Discussion

In this study, immunohistochemical evaluation was done in 100 gastric carcinoma cases; attempt was made to correlate the expressionof HER-2/Neu with various histomorphologicalfactors .

The most common gross appearance seen in our study population is proliferative pattern (50%) and least one is polypoidal with incidence of 2%.[1,2,3]

In this study moderately differentiated tumours were more common than other grades accounting for 42% of cases, which is correlated with Fondevila et al study and Hamilton (49%)[4]

Her -2 Overexpression is seen in 25% of cases correlated with Tanner et al got 36.6% results and in Yano et al study 27 % of cases were positive for Her -2 receptor.[5,6]

Variables like gross and endoscopic appearance were found to be statistically not significant.

Zhiyong Liam et al (2008) studied 100 cases and found no significant association of over expression of HER-2/Neu with any clinicopathological factors.

Similarly ,S. D. Xie et al (2009)⁽⁶⁰⁾ and Xie Li Zhang et al (2009) were not able to demonstrate association with any other known clinicopathological and prognostic factors.[7,8]

In this study, a statistically significant association was obtained between histological grade and HER-2/Neu overexpression.

Positivity for HER-2/Neu was seem to be more with moderately differentiated cases (52%) than well differentiated (28%) or poorly differentiated (20%) cases with P value < 0.05. This is correlated with Razeet al , who found that Her -2 over expression in noted in Moderately differentiated (67%) and well differentiated tumours (20%).[9-13]

V. Conclusion

In this retrospective study of 100 cases of gastric adenocarcinoma that were evaluated showed that there was no significant association between gross and endoscopic appearance with HER-2/Neu expression.

The most common histologic grade is moderate differentiation. 25% of gastric adenocarcinoma cases showed HER-2/Neu receptor over expression. Statistical significance was found out between HER-2/Neu-2 receptor over expression and histological grade.

Delays in diagnosis and limitation of therapeutic options contribute to poor prognosis of gastric adenocarcinoma. Hence, the contribution of these genetic markers like HER-2 /Neu receptor towards prediction of progression and prognosis along with newer therapeutic modalities like targetted therapy could be of immense benefit in gastric cancer patients.

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