

Prognostic Importance of HER2 Expression in Gastric Carcinoma

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Abstract

Introduction: Carcinoma of the stomach accounts for majority of deaths in the world. Targeted therapy with anti-HER2/neu therapies in in-vitro and in-vivo models of gastric carcinoma are under clinical trails as per the pre-clinical data.

Materials & Methods: A prospective study was done from 2017 to 2020 for a period of 3 years from Narayana Medical College & Hospital, Nellore. Cases diagnosed as Gastric carcinoma during the study period were included and HER2/neu immunohistochemistry was done.

Results: We received a total of 250 gastric biopsies, out of which 83 were gastric adenocarcinoma accounting for 33.2% with a peak incidence of 61 to 80 years old and male predominance. the most common type was Ulceroproliferative type, with tubular adenocarcinoma being the most common histologic type. As per the grading, moderately differentiated grade was predominant. HER2/neu over expression was noted in 16.95% of all the cases. Association was between HER2/neu over expression and grade of the tumour was significant. There was no association between HER2/neu expression and age of the person, morphological features, lymphovascular invasion or perineural invasion.

Conclusion: HER2/neu expression in gastric carcinoma can be of great use in therapeutic modalities for gastric carcinoma.

Keywords: Carcinoma; Targeted; A prospective; received; HER2/neu.

Introduction:

Manuscript:

Gastric carcinoma accounts for morbidity and mortality world wide, 3rd most common cause of death after lung carcinoma.¹ It is multifactorial with H.pylori being a preventive etiological factor.

NSAIDS, tobacco, alcohol, gastric hyperacidity and duoneno-gastric reflux account other causes of gastric carcinoma. Majority of the gastric carcinomas are sporadic, while only a few are familial. Imbalance between defence and damaging forces is the main pathogenic mechanism accounting for gastric carcinoma. Prognostic factors are age, sex, immune

How to cite this article:

Bhavana Grandhi, Nandam Mohan Rao, Syamasundara Rao, et al, Prognostic Importance of HER2 Expression in Gastric Carcinoma/Indian J Pathol Res Pract. 2021;10(4):169-172.

status, stage of the tumor, its location, histological type and grade.² Human epidermal growth factor receptor² (Her2/neu) which is also called as Erb-2, a proto-oncogene encodes a transmembrane tyrosine kinase receptor protein, involved in the growth and progression of tumors.^{3,4} Various malignancies have Her2/neu overexpression and targeted therapy against Her2/neu is the new field of interest in research lately.³ We have tried to study the expression of Her2/neu expression in gastric adenocarcinoma with emphasis on its prognostic significance.

Materials & Methods:

A prospective study was done from 2017 to 2020 for a period of 3 years in the Department of Pathology, Narayana Medical College & Hospital, Nellore. A total of 250 gastric biopsies were received from department of General Surgery and Gastroenterology departments, out of which 83 were gastric adenocarcinoma. They were processed and Histopathological examination with Immunohistochemical staining was done. All the slides were thoroughly examined and scoring of the immunohistochemical staining was also done.

Results:

We received a total of 250 gastric biopsies, out of which 83 were gastric adenocarcinoma accounting for 33.2% with a peak incidence of 61 to 80 years old and male predominance.

Table 1: Sex distribution of the lesions.

Sex	No. of cases	%
Males	59	71.08
Females	24	28.92
Total	100	100

Table 2: Age distribution of the lesions.

Age group	No. of cases	%
0-20	3	3.61
20-40	22	26.50
40-60	39	46.98
60-80	19	22.89

Table 1 & 2 Among the 83 cases, (59.32%) were males, and 24 cases (40.68%) were females. According to the morphological features, Ulcer proliferative type (37.29%) was the most common, (Figure 1) followed by ulcerative type (30.51%), nodular type (20.34%), proliferative type (6.78%) and diffuse type (5.08%)



Fig. 1: Ulceroproliferative lesion seen in the stomach

Table 3: Gross appearance of the lesions.

Type	No. of cases	%
Nodular	17	20.34
Ulcerative	25	30.51
Proliferative	06	6.78
Ulceroproliferative	31	37.29
Diffuse	04	5.08
Total	83	100

(Table 3) Histological examination reveals tubular adenocarcinoma (Figure 2) as the most common histologic type.



Fig. 2: Diffuse thickening of the wall of the stomach

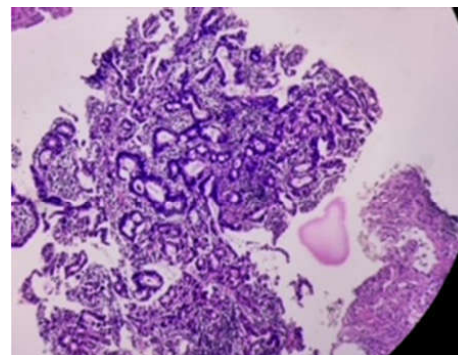


Fig. 3: Tumor composed of glands arranged in small glands/intestinal type (H&E 40x)

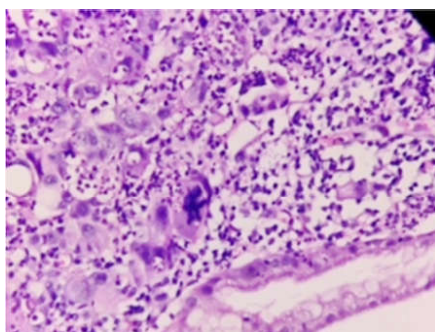


Fig. 4: Tumor composed of tumor cells arranged individually with few signet ring cells/diffuse type(H&E 40x)

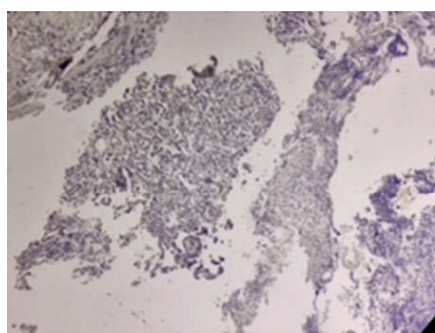


Fig. 5: IHC: tumor cells show 2+ positivity in moderately differentiated adenocarcinoma

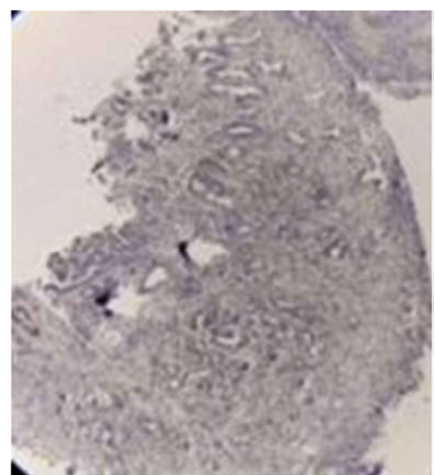


Fig. 6: IHC: Tumor cells show 1+ Positivity in well Differentiated Adenocarcinoma

Table 4: Histological type of the lesions.

Lauren Type	No. of cases	%
Intestinal	49	59.03
Diffuse	34	40.97
Intermediate	-	-
Total	83	100

Table 4. Moderately differentiated was the predominant grade among all of our cases in our study.

Table 5: Grading of the lesions

Differentiation	No. of cases	%
Well	18	22.03
Moderate	34	40.68
Poor	31	37.29
Total	83	100

Table 5. HER2/neu overexpression was noted in 16.95% of all the cases.

Table 6: HER2 neu expression in relation with the differentiation of tumors

HER2neu	Well(18)	Moderate(34)	Poor(31)
Negative	13	0	21
0	1	1	2
1+	1	1	3
2+	1	28	3
3+	2	2	2

Table 6 Association was between HER2/neu overexpression and grade of the tumour was significant. Among the 83 gastric biopsies, 8 were resected specimens. All of these cases 100%(8) showed lymphatic invasion, vascular invasion was seen in 62.5%(5) with perineural invasion seen only in 37.5%(3) of cases. 87.5% (7) of cases showed lymphocytic response. HER2/neu expression. Thus in our study, association was seen between tumour grade with HER2/neu expression but no association was found between HER2/neu expression and age of the person, morphological features, lymphovascular invasion or perineural invasion.

Discussion:

A number of biological markers are being evaluated across the globe to identify their potential role in gastric carcinoma and their outcome. Prognostic value has been proposed for immunohistochemical staining for cell adhesion molecule E cadherin, cell cycle regulator p53 and growth factor receptors Her-2/Neu and EGFR.⁵

Gastric carcinoma has a higher incidence in males when compared to females 59.32% and 40.68% respectively in our study, similar to the study by Nobuyuki Igarashi et al⁶ who observed an incidence of 74.1% in males and 25.9% in females.

In relation to the histological types, tubular

carcinoma was the most common type accounting for 67.8% of cases in this study, which is in concurrence to that observed by Daniel et al⁷ and Kakeji et al⁸ in their studies.

In the current study, moderately differentiated tumors were more common than well differentiated and poorly differentiated grades accounting for 40.68% of cases, which did not correlate with the observations made by Daniel et al⁷ and Razei et al⁹

H R Raziee et al⁹ in their study found a significant association of HER2/neu overexpression with Lauren's intestinal type of tumor and well-differentiated grade but no association between age, gender, tumour location, and depth of tumor infiltration. Xie Li Zhang et al¹⁰ studied 102 cases of gastric cancer in Korea and found a significant association between HER-2/Neu over expression and Lauren's type and depth of infiltration with no association with the grade, histological type or survival. Zhiyong Liam et al¹¹ in their study found no significant association of overexpression of HER-2/Neu with any clinicopathological factors. S. D. Xie et al studied 218 were able to demonstrate a statistically significant association of HER-2/Neu overexpression with the patient's survival, though they were unable to demonstrate an association with any other known clinico pathological and prognostic factors.

In our study, a statistically significant association was obtained between tumor grade and HER2/neu overexpression. Increased frequency of Her2/neu overexpressed cases were of Lauren's intestinal type, well differentiated grade, showing T3 level of infiltration. Still, the statistically significant association could not be ascertained. No association was found between HER2/neu overexpression and histological subtype, lympho vascular invasion and perineural invasion.

Conclusion:

In this age of advances in science, evaluation of HER2/neu expression in gastric carcinoma can be of great use in therapeutic modalities. Targeted therapy is the treatment of choice and thus our study has been done to work upon insights of this marker.

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