Artificial Intelligence formulated this projection for compatibility purposes from the original article published at Global Journals. However, this technology is currently in beta. *Therefore, kindly ignore odd layouts, missed formulae, text, tables, or figures.*

Her2/Neu Overexpression in Gastric Cancer and its Correlation with Histopathological Grade and Subtype

³ Dr. Kuldeep Kaur¹, Dr. Molly Joseph², Dr. Jagriti Yadav³, Dr. Hema Goyal⁴ and Dr. Richa Jindal⁵

¹ St. Stephen?s Hospital, Delhi

Received: 6 December 2019 Accepted: 31 December 2019 Published: 15 January 2020

8 Abstract

Gastric cancer is one of the leading causes of cancer mortality in the world. At advanced stage
majority of cases are diagnosed. The survival rate of patients with advanced unresectable

¹¹ gastric cancers remains poor despite new treatment strategies, such as perioperative

¹² chemotherapy or adjuvant chemoradiation [1]. In certain gastric tumors added therapy gives

¹³ superior survival benefits. One such targeted protein of interest is HER2 /neu. We have

 $_{\rm 14}$ $\,$ undertaken this study to evaluate the overexpression of HER-2/Neu gene in gastric cancer and

¹⁵ its correlation with several pathological features.

16

5

6

Index terms — gastric adenocarcinoma, grade a n d subtype, her2/neu overexpression, immunohistochemistry,
her 2 scoring in gastric cancer, trastuzumab.

¹⁹ 1 Her2/Neu Overexpression in Gastric Cancer and its Correla ²⁰ tion with Histopathological Grade and Subtype

Keywords: gastric adenocarcinoma, grade and subtype, her2/neu overexpression, immunohistochemistry, her 2
scoring in gastric cancer, trastuzumab.

HER2/neu gene. Amplification of HER2/neu gene is seen at different sites like breast, stomach, colon, etc.
and its overexpression is associated with poor prognosis.

Recently published data, from the randomised, prospective phase III clinical trial TOGA provided first documentation of the clinical benefit of Trastuzumab, anti-HER2/neu an antibody, when used in combination with chemotherapy in the setting of advanced gastric carcinoma ??4]. The Stage is the most important prognostic

factor for gastric carcinoma followed by the histological subtype and since there is limited data available on HER2/neu overexpression in gastric cancer and its correlation to histopathological stage, grade and subtype, we

³⁰ propose to conduct this study to evaluate the same since an accurate assessment of HER2/neu overexpression in

31 gastric cancer patients is of great utility in the optimal selection of patients for Trastuzumab therapy.

32 **2** II.

33 Material and Methods III.

³⁴ **3** Statistical Analysis

35 Qualitative variables are expressed as frequencies/percentages and compared between groups using Chi-square

Test. Quantitative variables are expressed as mean \pm sd and compared across groups using ANOVA and unpaired t-test. A p-value < 0.05 is considered statistically significant. The data is analysed using Statistical Package for

38 Social Sciences (SPSS) version 16.0 software.

³⁹ 4 Study Design: Cross-sectional study

40 5 Sample size determination:

41 The formula used for sample size estimation is:n = $z^2 P(1 - P)/d^2$

Introduction astric cancer is one of the leading causes of cancer mortality in the world, with the majority of cases presenting at an advanced stage. Gastric cancer is the fifth most common cancer overall and it is the third most common cause tumor-related deaths globally **??**1]. The incidence of gastric cancer in India is 10.6 per 100000 population **??**2].

Human epidermal growth factor receptor 2 (HER2/neu) protein is a cellular target for the added therapy. It is a growth factor of EGFR family with intrinsic protein tyrosine kinase activity and is associated with tumor proliferation, migration and differentiation. The production of HER2/neu protein, is regulated by the G The mainstay of treatment is surgical resection and can cure patients with early-stage cancer. The survival rate of patients with advanced resectable gastric or gastroesophageal junction (GEJ) tumors, however, remains poor despite new treatment strategies, such as perioperative chemotherapy or adjuvant chemoradiation ??3].

Improvements in the treatment modality of gastric cancer, including combination chemotherapy, have resulted in improved overall survival. In certain gastric tumors added therapy gives superior survival benefits.

A total of 49 patients, with gastric carcinoma, were included in this study period of seven years (Jan 2011 to May 2018) in the Department of Pathology, St.

Stephen's Hospital, New Delhi, India. The detailed clinical history and results of relevant investigations were
obtained from the patient's case files. The method of study was immunohistochemistry, using the HER-2/Neu
antibody.

59 IV.

60 6 Result and discussion

⁶¹ 7 a) Demographic data in our study

62 Our study included 50 cases. The age of the patients varied from 24 years to 85 years, with a mean age of 57.69 63 years. In our study, the incidence of gastric carcinoma in males and females were 77.1% and 22.9% respectively 64 (male: female ratio =3:1)

⁶⁵ 8 b) Clinical manifestations

In our study, chief complaints of patients were dysphagia (43.7%) followed by loss of appetite (35.4%), pain abdomen (33.3%), vomiting (29.2%), weight loss (22.9%), hematemesis (6.2%) and melena (4.2%). Gastric carcinoma often produces no specific symptoms when it is superficial and can be removed surgically, although up to 50% of patients may have nonspecific gastrointestinal complaints such as dysphagia, anorexia, nausea, vomiting, weight loss as well as abdominal pain that is vague and insidious.

71 9 Site

72 The most common site of gastric carcinoma in our study was the antral region.

Table 1: Comparison of Location of Gastric Carcinoma: c) Histopathological subtype

In our study, poorly cohesive carcinoma (66%) was the most common subtype followed by tubular carcinoma 75 (26%). However, intestinal-type was the most common subtype (Lauren's classification) according to studies done 76 by Raziee et al. (??) and ToGA trial (4). This difference could be explained by the low sample size in our study 77 and heterogeneity of pathological classifications. The increase in the proportion of poorly cohesive carcinoma 78 can be explained by changes in the pathological classification systems used to characterise these cancers. Since 79 the publication of the WHO classification of gastric cancers in 1990, signet ring cell adenocarcinoma constitutes 80 one specific histotype and therefore can be better identified among gastric cancers. WHO 2010 further classified 81 Signet ring cell and diffuse variety into a single group of poorly cohesive carcinoma. Previously, signet-ring cell 82 adenocarcinoma was classified as "diffuse-type" according to Lauren's classification ??8] and "infiltrative type" 83 by Ming[9]. During January 2011 to May 2018, a total of 50 samples (from 49 patients) reported as gastric 84 adenocarcinoma on histopathological examination at St.Stephen's hospital, Delhi were included in the study. 85

⁸⁶ 11 d) Histopathological grade

Among 49 patients, gastric carcinoma had a peak incidence in the age group of 50 to 60 years. The oldest age of presentation was 85 years and the youngest was 24 years.

In our study, poorly differentiated grade tumors were more common than other grades accounting for 54% of

so cases, which is similar to observations made by Lazar et al. (64%) and Fondevila et al. (49%) in their studies.

⁹¹ 12 Depth of Infiltration

⁹² In our study, a higher proportion of tumours belonged to T4 subtype 63.6% which is similar to the observation

⁹³ made by Lazar et al ??8] (approximately 50%). This is explained by later presentation of gastric carcinoma due

⁹⁴ to nonspecific symptoms and hence delayed diagnosis.

95 13 HER2 Overexpression

96 In our study, HER2 overexpression is noted in 20% of cases, which is similar to observations made worldwide by ??arx et al.(19%)



Figure 1:

 $\mathbf{2}$

Year 2020 16

Figure 2: Table 2 :

97

3

Her2/Neu Overexpression in Gastric Cancer and its Correlation with Histopathological Grade and Subtype Authors Raziee et al. [5] Hofmann et Year Population studied No of patients 2007 Iranians 100 2007 al. [11]

Marx et al. [12]2009GermansXie et al. [13] Lee et al. [14] Sekaran2009 2010 Australians Chinese 2011 Indians 2014 Indians 2014 Japanet al. [2] Lakshmi V et al. [15]Yoshida et al. [16] Our study

In our study, there is no correlation between HER-2/neu overexpression and various

clinicopathological factors such as age, gender, complaints, site or gross appearance in gastrectomy specimer

[Note: [MODERATELY DIFFERENTIATED][POORLY DIFFERENTIATED ADENOCARCINOMA]]

Figure 3: Table 3 :

Her2/Neu Overexpression in Gastric Cancer and its Correlation with Histopathological Grade and Subtype

independent predictors of tumour recurrence and

survival following curative resection of gastric cancer. Br J Cancer. 2004; 90(1): 206-215.

7. Czyzewska J, Guzi?ska-Ustymowicz K, Lebelt A,

Zalewski B, Kemona A. Evaluation of proliferating

markers Ki-67, PCNA in gastric cancers. Roczniki

Akademii Medycznej wBiałymstoku (1995). 2004;

49: 64-6.

8. Lauren P. The two histological main types of gastric

carcinoma: diffuse and so-called intestinal-type

Yearcarcinoma: an attempt at a histo-clinical clas-

2020sification. Acta Pathologica Microbiologica Scandinavica. 1965; 64(1):31-49. 9. Ming SC. Gastric carcinoma: a pathobiological

20 classification. Cancer. 1977 Jun; 39(6): 2475-85.

Volúmė0. 10.Lazar D, Taban S, Sporea I, Dema XX A, Cornianu M, Lazar E, et al. The immuno-Is- histochemical expression of the p53-protein in sue gastric carcinomas. Correlation with clinico-II pathological factors and survival of patients. Ver-Rom J Morphol Embryol. 2010; 51(2): 249sion 57. 11. Hofmann M,

(D

D

D

- D
-) C

Glob**XI**. 1. Larger sample size and follow up Jourmight shed more Recommendation Increasing nal the sample size in future studies, and designing prospective studies with close observation of of Medsurvival, the utility of HER2/neu overexpression as an important prognostic marker can be ical enhanced. 2. Geographical differences, tumor Re- heterogeneity, molecular target therapy. tusearch or progression besides avoiding the failure of assessment of its role in gastric carcinogenesis and staining and scoring methods for accurate proteins. It is mandatory to standardize Her2/neu the current therapeutic approaches targeting those and progression need to be

detected to modulate 3. The precise role of

Her2/neu in cancer development 2/neu posi-

References Références Referencias 1. Macdonald JS, Smalley SR, Benedetti J, Hundahl SA, Estes NC, Stemmermann GN, et al. Chemoradiotherapy after surgery compared with surgery alone for adenocarcinoma of the stomach A

or gastroesophageal junction. N Engl J of Med. 2001; 345(10):725-30.

Basic Med Sci. 2007; 10(2):139-145.histolopathologic subtype grade and stage. Iran J resectablegastric cancer and its relationship with T, Ghavamnasiri MR. HER-2/neu expression in 5. Raziee HR, Kermani TA, Ghaffarzadegan Κ, Shakeri controlled trial. Lancet. 2010; 8; 376(9742):687-97. cancer (ToGA): a phase 3, openlabel, randomised advanced gastric or gastro-oesophageal junction chemotherapy alone for treatment of HER2positive combination with