

Socio Demographic Profile and HER2 Status in Patients with Colorectal Carcinoma

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Abstract

Background : Colorectal carcinoma (CRC) is the most frequently observed malignancy worldwide. The incidence of CRC is 3.5% in Bangladesh. Conflicting data exist about the prevalence of HER-2/neu over expression in colorectal cancer ranging from 0 to 83%. The aim of this study was to evaluate the expression of Her-2/neu protein in colorectal cancers.

Materials and methods: This descriptive cross-sectional study was conducted in the Department of Pathology of Chittagong Medical College, Chittagong, Bangladesh from 1st January 2017 to 31st December 2017. A total of 52 cases with a histopathological diagnosis of colorectal cancers included in the study as sample size, HER2 status was evaluated by immunohistochemistry (IHC) in formalin fixed, paraffin embedded tissue. Positive expression was assigned a score from 0–3+. IHCs were analysed with grades of colon cancers.

Results: The mean age in this study was 47.62 years range from 12 to 85 years, 53.8% were female. Among 52 specimens 30 (57.7%) cases were from colon and all the cases were adenocarcinoma and rest of all (42.3%) were from rectum. 33 (63.5%) cases were Grade-I, 8 (15.4%) were Grade-II, and 11 (21.2%) were Grade-III. Only 8 (15.4%) of 52 cases showed HER2 positive, 4 (50.0%) cases were from grade-I and another 4 (50.0%) were grade-II tumours. HER2 overexpression were significantly associated with well differentiated CRC than poorly differentiated ($p=0.044$).

Conclusion: HER2/neu protein expression was observed in colorectal cancer but HER-2/neu protein is less likely to be expressed in colon cancer cell lines among our patients.

Key words: Colorectal cancer; Her2/neu; Immunohistochemistry.

INTRODUCTION

The prevalence and mortality of carcinoma is rapidly growing worldwide.¹ This reflects both aging and growth of the population as well as changes in the distribution of the risk factors for cancer, many of which are associated with socioeconomic development.^{2,3} Global observatory reports colorectal cancer ranks third according to cancer incidence, but second in terms of mortality.^{4,5} Socioeconomic status has a prominent effect on cancers.⁶ People living with low socioeconomic status, have less access to health care system, poor survival and more mortality, compared to high socioeconomic status.

The development of CRC is characterized by a complex interaction between various carcinogens, genetic variations, and the host immune system. Late diagnosis, relapse and metastasis are the main causes of death in CRC patients.^{8,9}

The HER2 protein is an 185-kDa transmembrane receptor tyrosine kinase. The tyrosine kinase activity of HER-2 intracellular domain which triggers signal transduction has important roles in cell proliferation, differentiation, and survival.

Aberrant expression of HER2 triggers the abnormal activation of multiple downstream signal transduction pathways; resulting in increased cell proliferation and differentiation, decreased apoptosis, and enhanced tumor cell motility and angiogenesis. HER-2 over expression is mainly achieved through gene amplification, resulting in increased transcription of the gene, increasing HER-2 receptors on the cell membrane, and consequently, increasing cell proliferation.¹⁰

The HER2/neu status is assessed immunohistochemically in combination with in situ hybridization using tumor tissue obtained through biopsy or resection.¹¹ It is a potential biomarker and therapeutic target in CRC.¹²

The aim of our study was to assess the influence of sociodemographic factors and Her-2 status in CRC in our population which might prove in future a useful prognostic factor with treatment and follow-up of colon cancer.

MATERIALS AND METHODS

This descriptive cross-sectional study was carried out in the Department of Pathology of Chittagong Medical College, Chattogram, Bangladesh over a period of one year from 1st January 2017 to 31st December 2017. A total of 52 patients who underwent colonoscopic biopsy or colectomy, fulfilling the predefined criteria were studied with detailed documentation of their clinical account and Institutional Ethical Approval.

Inclusion criteria

Histopathologically diagnosed cases of colorectal carcinoma. The presence of scattered Paneth cells, neuroendocrine cells or small foci of squamous cell differentiation is compatible with the diagnosis of adenocarcinoma.

Exclusion criteria

Patients with nonepithelial colorectal malignancy, with prior malignancies, those who had received chemotherapy or radiation therapy for colorectal cancer prior to surgery and patients refused participation. Biopsies or specimens of colon and rectum for Histopathological examination received at the Department of Pathology of Chittagong Medical College with a diagnosis of colorectal carcinoma. Representative tissue blocks were taken, paraffin blocks were prepared and processed for H&E staining.

After getting the histopathological result, eligible patients were invited for participation in the study. After taking informed consent a brief sociodemographic history was taken from each patient. History regarding high dietary fat and carbohydrate, low fiber, smoking and alcohol consumption was recorded. Family history of colon, breast, ovarian carcinoma was also recorded. Then immunohistochemistry was done.

The scoring method for HER2 expression is based on the cell membrane staining pattern and is as follows:

- i) 3+: Positive HER2 expression, uniform intense membrane staining of more than 30% of invasive tumor cells
- ii) 2+: Equivocal for HER2 protein expression, complete membrane staining that is either nonuniform or weak in intensity but has circumferential distribution in at least 10% of cells
- iii) 0 or 1+: Negative for HER2 protein expression.

Data was entered and analyzed using SPSS version 23. Finally, the influence of sociodemographic factors and Her-2 status in CRC was assessed by Chi-square test. A p-value of < 0.05 was considered as significant.

RESULTS

The socio demographic profile of the patients, clinical feature, histopathological findings and HER2 status displayed below :-

Table I Distribution of the patients by their age groups (n=52)

Age category	Frequency (n)	Percent (%)
<30 years	10	19.2
30-39 years	7	13.5
40-49 years	4	7.7
50-59 years	17	32.7
60-69 years	9	17.3
>=70 years	5	9.6
Total	52	100.0

Table I showed that, majority 17(32.7%) of the study samples of colorectal carcinoma were between 50 to 59 years of age. About 20% of patients were below 30 years.

Table II Sociodemographic profile of study population

Gender	Particulars	No. of Cases	%
	Male	24	53.80
	Female	28	46.20
Residence	Rural	32	61.5
	Urban	20	38.5
Monthly Income	High	4	7.69
	Average	30	57.69
	Below average	18	34.61
Religion	Islam	37	71.15
	Sanatan	15	28.85
Profession	Housewife	28	53.84
	Teacher	4	7.69
	Business	9	17.30
	Other Job	11	21.15

Table II shows that the frequencies were higher among female below 50 years of age than male groups. However, the differences were not statistically significant ($p > 0.05$). 38.5% patients were from urban area and 61.5% patients were from rural area. Most of them were housewife (53.84%) and from average (57.69%) socio-economic class.

Regarding dietary habit 67.3% patients reported taking of carbohydrate rich meal and rest of the patients reported intake of meat besides carbohydrate. Regarding clinical features of colorectal carcinoma 33(63.5%) patients had constipation and only 11(21.2%) patients reported per rectal bleeding during presentation. Out of 52 samples, 31 (59.62%) lesions were from colon and 21 (40.38%) were from rectum. All cases were diagnosed as adenocarcinoma by histopathological examination.

Table III Distribution of the patients by their lifestyle and dietary habits

Characteristics		Frequency (n)	Percentage (%)
Smoking habit	Yes	24	46.2
	No	28	53.8
Drinking alcohol	Yes	4	7.7
	No	48	92.3
Dietary habit	Rich in Carbohydrate	35	67.3
	Rich in protein and fat	17	32.7

Table III showed the distribution of the patients by their lifestyle and dietary habit. It showed that prevalence of smoking and alcohol intake was 24(46.2%) and 4(7.7%) respectively. Regarding dietary habit 35(67.3%) patients reported taking of carbohydrate rich meal and rest of the patients reported intake of meat besides carbohydrate.

Table IV HER2 status of colorectal adenocarcinoma in study patients (n=52)

HER 2 Status	HER 2 Score	Frequency (n)	Percentage (%)
Negative	0	37	71.2
	1+	4	7.7
Borderline	2+	3	5.8
Positive	3+	8	15.4
	Total	52	100.0

Immunohistochemical staining for HER2/neu was performed in all the 52 cases of CRC. Most of them 41 (78.8%) were HER-2 negative and in 8 (15.4%) cases, HER-2 positive immunostaining were detected. Rest of the 3 (5.8%) were borderline positive (Table IV).

Table V Association between HER2 status and family history of the patients(n=52)

Family history	HER2 status			Total	
	Negative	Borderline	Positive		
Absent	n	33	1	8	42
	%	78.6%	2.4%	19.0%	80.8%
Present	n	8	2	0	10
	%	80.0%	20.0%	0.0%	19.2%

$$\chi^2 = 6.25, df = 2, p = 0.047$$

Table V showed out of total 10, 8 with positive family history showed HER-2 negative status. The difference was statistically significant (p<0.05).

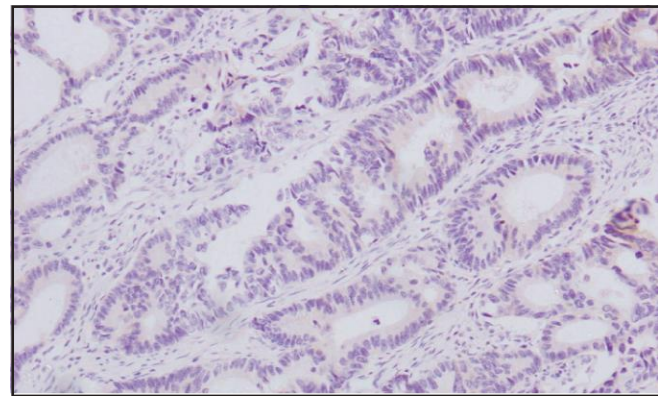


Figure 1 Well Differentiated adenocarcinoma Grade-I x 400 (HER2 score 2+)

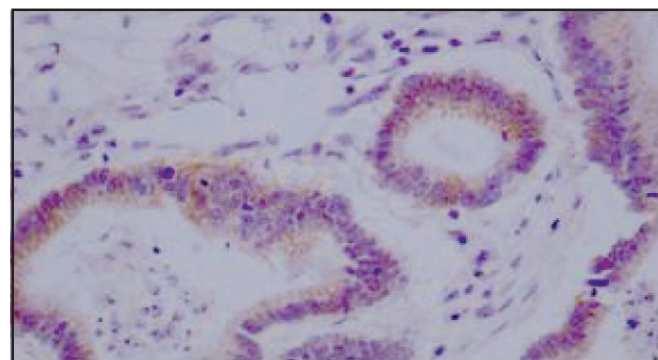


Figure 2 Well Differentiated adenocarcinoma Grade-I x 200 (HER2 score 1+)

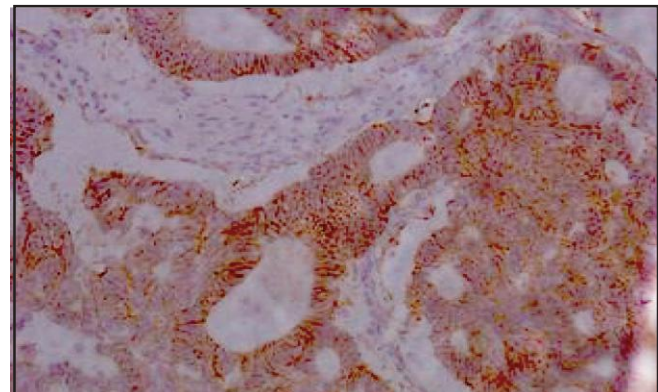


Figure 3 Moderately Differentiated adenocarcinoma Grade-II x 200 (HER2 score 3+)

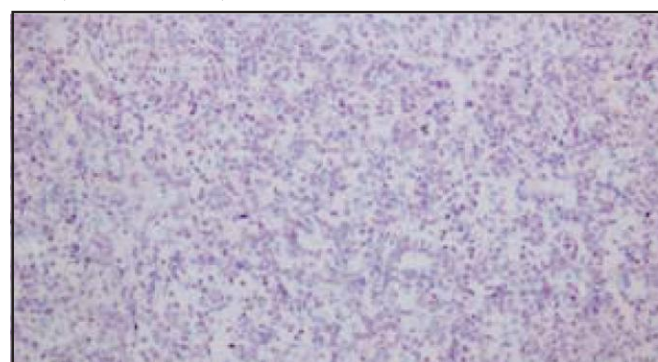


Figure 4 Poorly Differentiated adenocarcinoma Grade-III x 200 (HER2 score 0)

DISCUSSION

In this study, 28(53.8%) of the cases were female and 24(46.2%) were male. The results are similar with the findings of Cressey et al but differ from the findings of Raza et al. who has reported slightly male predominance of CRC.^{13,14} Peak incidence of colorectal cancer in this study was 50-59 years which is lower than that of western and other countries. 24 (46.2%) were smoker and 4(7.7%) were habituated to alcohol consumption. Courtney et al. showed 12% cases of colorectal cancer are related to smoking.¹⁵

In this study most of the cases 30(57.69%) cases were from average socioeconomic condition, 18(34.61%) were poor and only 4(7.69%) from high socioeconomic status according to the patient statement. In Gopakumar et al showed that out of 100 cases 54% cases belonged to middle income range which is similar to this study.¹⁶ This may be due to fact that patients attended at a government hospital and most of the people of average and poor socio economic conditions usually come here to get treatment.

Regarding personal habit of the patients out of 52 patients 24 (46.2%) were smoker and 4(7.7%) was habituated to alcohol consumption. Courtney et al showed 12% cases of colorectal cancer are related to smoking. The present study also showed tobacco smoking may be associated with CRC.¹⁷

In this study the positivity rate of HER2/neu in membranes was 15.4%. This findings are completely agreement with the findings of Elwy et al. (2012) where out of 50 specimens, 7 (14%) were strongly positive (Score 3+).¹⁸ A retrospective study was done by Suma et al where among 50 cases 24% cases were strongly positive. But according to Nathanson et al among 139 cases HER-2/neu overexpression was seen in 5 cases (3.6%).^{19,20} A large cohort of CRC, the expression of HER-2/neu was reported in 81.8% patients.²¹ These variations

can be attributed to multiple factors like, technical variability in the IHC performance (Differences in tissue fixation, processing, epitope retrieval, primary antibody, interpretation and reporting of pathologist, ununified and widely acceptable scoring systems for evaluation of HER2/neu expression) sample size, heterogeneity of study population, racial differences and varied experimental designs.

In this study out of 52 patient 10 (19.23%) had family history of colorectal carcinoma in first degree relatives. Neagoe et al showed 27.6% had family history which showed similarities with the present study. Out of total 10, 2 (20%) cases had HER-2 positive. The difference was statistically significant ($p < 0.05$).²²

We have now come across that HER-2/neu protein is less likely to expressed in colon cancer cell lines in our patients and the positive HER2 exhibits relatively distinct localization patterns in these tumors especially where the histological grade is low or moderate. Overexpression was found in some patients and this could be a guideline to new adjuvant therapy for these patients. More prospective analyses should be followed in our population, relating to its prognostic implication, where the serum and tissue levels of HER 2/neuinsociodemographically high risk and colorectal cancer patients might suggest an assessment of tumor burden in advanced disease.

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DISCLOSURE

All the authors declared no competing interest.

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