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THE RELATIONSHIP OF HUMAN EPIDERMAL GROWTH FACTOR-2 RECEPTOR EXPRESSION IN GASTRIC CANCER WITH AGE, GENDER, STAGE AND DEGREE OF TUMOR DIFFERENTIATION

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АННОТАЦИЯ

Relevance: *Gastric cancer is a heterogeneous malignant disease. In carcinomas, HER2 functions as an oncogene, primarily due to high gene amplification, which leads to protein overexpression in the cell membrane, enhancing malignant cell properties. Identifying new and effective biomarkers is essential for improving gastric cancer diagnosis, refining prognostic accuracy, predicting disease progression, and developing more effective patient treatment strategies.*

The study aimed to *assess the correlation between HER2 expression in gastric cancer and key clinical factors, including age, gender, disease stage, and tumor differentiation degree.*

Methods: *This comparative descriptive study analyzed surgical specimens from 109 patients with gastric cancer (stages 0- IIIC) collected from the pathology department of Marat Ospanov West Kazakhstan Medical University (WKMU) Medical Center following gastric cancer surgeries performed between 2021 and 2022. Histological and immunohistochemical studies were conducted in the morphological laboratory of the WKMU Department of Histology. The collected data underwent statistical processing.*

Results: *In the present study, the rates of positive Her2/neu expression in GC statistically significantly differed depending on the age (p=0.026) and gender (p=0.023) of the patient but did not statistically significantly differ depending on the localization, histopathological differentiation of the tumor, and the stage of the disease.*

Conclusions: *Considering the tendency towards the significance of positive expression of Her2/neu in low-differentiated gastric cancer (50%) and stages II-III of the disease, the Her2/neu marker can be considered as a potential therapeutic target that requires preliminary testing when prescribing targeted therapy.*

Keywords: *gastric cancer, morphology, histology, immunohistochemistry, Her2/neu.*

Introduction: Gastric cancer (GC) is a heterogeneous malignant disease. In various forms of GC, such as carcinoma, several HER2 biomarkers act as an oncogenic factor based on high gene amplification with transition to a malignant cell. In 2022, Zh.E. Komekbay et al. noted that "overexpression of the protein occurs on the cell membrane surface when using the Her2/neu marker. Previously, we reviewed the literature on using and identifying new and effective biomarkers to improve the diagnosis of gastric cancer, more accurately determine the prognosis, predict pathogenesis, and establish a new and effective treatment option for patients with GC" [1].

Researcher N.D. Bakirov [2] noted that solving the problem "will improve the results of complex treatment of gastric cancer in both early and widespread, disseminated forms." Earlier in their work in 2015, L.A. Naumova and O.N. Osipova explained: "Understanding the biology of cancer is being formed today by integrating gene expression data with the network of molecular interactions" [3].

According to N.D. Bakirov, GC includes a complex of genetic disorders that determine the property of uncontrolled growth and the ability to metastasize [2], while L.A. Naumova and O.N. Osipova point to a heterogeneous disease with various molecular and histological subtypes [3]. Biomarker tests are also reliable methods for detecting precancerous lesions of the stomach. Endoscopic screening is still the gold standard for diagnosing GC [4]. The role of HER2 in developing many types of cancer in humans was noted by K. Mandleywala et al.: "Antibody-based imaging strategies specific for certain GCs overexpressing the antigen allow visualization of primary tumors and metastases with high contrast. In this context, PET antibodies and SPECT antibodies have the potential advantage of noninvasively detecting changes in antigen expression (e.g., HER2) and target interactions in both the primary tumor and metastases. The novel integration of fluorescence-labeled antibodies and confocal laser endoscopy for rapid visualization of dynamic molecular signatures also represents a promising avenue toward personalized therapy" [5].

An analysis of the available literature showed that overexpression of Her2/neu is associated with a poor prognosis in male patients with proximal GC localiza-

tion, intestinal type of tumor in the late stages of the disease, with metastasis to the lymph nodes, as well as with well-differentiated GC with distant metastases [2, 6].

Furthermore, Her2/neu expression results were quantitatively higher in Asian studies compared to European ones. Y. Y. Lei et al. (2017) showed that the level of HER2 expression in Asians may be higher than in Europeans and proposed a convenient way to select patients for appropriate HER2 detection and subsequent treatment [6].

Later, in 2019, M Smolińska et al. found that HER2 and SATB1 are overexpressed in gastric cancer tumor tissues compared to normal gastric mucosa. The expression of the former protein was observed to differ depending on some clinicopathological features but without statistical significance, while the expression of the latter protein was not significantly associated with any of them [7].

As noted by several researchers, the overall reliability of immunohistochemical (IHC) assessment of HER2 may be affected by various preanalytical, analytical, and postanalytical variations, as discussed earlier. Thus, GC requires a standardized, unified system for assessing the IHC expression of HER2 and an expert interpretation of these data [8].

Other authors note that "the compatibility rate of IHC and fluorescence in situ hybridization (FISH) results was more than 90%. However, according to the literature, the false-negative rate in mucosal biopsy was low. IHC should be applied to the entire tumor area to exclude false-negative results due to tumor heterogeneity. HER-2/neu gene amplification correlated with the histological type of the tumor. Six of 21 cases in which FISH analysis was performed were of the diffuse type, and all of them were FISH-negative. Nine (60%) of 15 cases with the intestinal type were FISH+ (p=0.019)" [9].

HB Wang et al. showed that according to the ToGA study, HER2 positivity was either IHC3 (+) or IHC2 (+) with DISH (+). There was no relationship between HER2 positivity and the depth of tumor invasion and venous and lymphatic invasion (p>0.05). However, in men with intestinal-type cancer and moderately/well-differentiated GC, the frequency of HER2-positivity was higher than in women with diffuse/mixed type and poorly differentiated cancer [10].

The DI Park et al. study showed that the frequency of HER-2/neu amplification in intestinal-type cancer was higher than in diffuse-type cancer (P < 0.05). Tumors with HER-2/neu amplification were associated with low median survival (922 versus 3243 days) and 5-year survival (21.4% versus 63.0%; P < 0.05). According to the authors, using multivariate analysis, it was found that age, TNM stage, and HER-2/neu amplification were independently associated with survival. HER-2/neu amplification may be an independent prognostic factor in patients with GC, and patients with HER-2/neu amplification may be potential candidates for new adjuvant therapy, including humanized monoclonal antibodies [11].

Y. Li et al. proposed a prognostic model for HER2 status in resectable GC using contrast-enhanced multiphase CT images and serum tumor markers. "We found that arterial phase enhancement ratio, intratumoral necrosis, tumor margin, and CA125 level were independent risk factors for positive HER2 expression in GC" [12].

As early as 2022, D Bao et al. stated that "the prediction model built based on preoperative tumor invasion and serum markers CA125 and CA72-4 demonstrates high specificity and accuracy concerning the incidence of peritoneal dissemination. We expect that the results of our study can provide clinical value for preoperative assessment of patients with GC and selection of individual treatment for patients" [13].

Iranian scientists A. Feizy et al. noted a significant relationship in positive HER2/neu gene expression between men and women (46.2% in men versus none in women) (p<0.05) [14]. This study showed no statistical differences between the two groups of patients with and without HER2 overexpression in variables such as survival, histopathological type of cancer (according to Lauren classification), and primary anatomical site of the tumor. It was also noted that the results revealed a very close (p=0.051) association between HER2 expression and tumor grade. This association may be statistically insignificant but appears to be clinically important. Moreover, the results of the current study differed from those of other studies, especially in non-Iranian patients. The authors strongly recommend that future studies focus on the race of patients with a more accurate assessment of HER2 expression status and its polymorphisms. The authors argue that due to the genetic diversity of patients, it is better to conduct a meta-analysis within the same race or at least with geographic restrictions [14].

Earlier, in our work (Zh.E. Komekbay, G.A. Temirova), GC revealed a close relationship between the expression of Ki-67 and the degree of histopathological differentiation of the tumor (P=0.039). However, it was not possible to establish a statistically significant difference with age (p=0.664), patient gender (P=0.928), tumor localization (p=0.860), and disease stage (p=0.894). Thus, the appropriateness of targeted therapy in GC is based on the results of histological and IHC studies of the contents of the tumor material [15].

Tumor marker levels vary with different diseases; the result may be false negative or false positive.

The study aimed to assess the correlation between HER2 expression in gastric cancer and key clinical factors, including age, gender, disease stage, and tumor differentiation degree.

Materials and methods: The study was conducted on a cohort of patients with gastric cancer previously selected to analyze the expression of the Ki-67 marker [15].

Study design: This comparative descriptive study was conducted following the biostatistics and clinical epidemiology sector protocol of West Kazakhstan Marat Ospanov Medical University (WKMU). The WKMU Local Bioethics Commission has approved the choice of material and research methods (Protocol No. 8, dated October 15, 2021).

General population: Continuous sample. Surgical material was collected from 109 patients with various forms of stage 0-IIIC gastric cancer after surgeries for this disease from the WKMU Pathology Department in 2021-2022. *Inclusion criteria:* Patients of all ages operated on for stage 0-IIIC gastric cancer. *Exclusion criteria:* stage IV gastric cancer, as well as the presence of any other malignant neoplasms [15].

Research methods: Histological and IHC studies were performed in the morphological laboratory of the WKMU Department of Histology. The study followed the SOP "I ZKMU 65-03" of 01/10/2020. When determining the area of the anatomical location of the tumor (cardiac section, body, fundus, antral or pyloric section), we were guided by the WHO recommendations and the clinical protocol for RZh No. 174 dated 11/21/2022 of the Joint Commission on the Quality of Medical Services of the Ministry of Health of the Republic of Kazakhstan [15].

The work presents a comparative analysis of gastric cancer cases according to the histopathological classification of gastric tumors: G1 (highly differentiated), G2 (moderately differentiated), G3 (poorly differentiated), and G4 (undifferentiated) [15].

The surgical material was fixed in 10% buffered formalin. A sled microtome was used to prepare histological sections. After the paraffinization stage, histological sections of the stomach with a thickness of 4-5 μm were prepared from paraffin blocks [16]. The micro preparations were stained with hematoxylin and eosin to confirm that the cuttings were gastric tissue. The material was evaluated using an AxioLab A1 laboratory medical video microscope (Carl Zeiss Microscopy GmbH, Germany) at different magnifications (×50, ×100, ×400, ×1000) [15].

To study the proliferative activity, monoclonal rabbit antibodies RMab (clone: RBT-Her2) to Her2 and the Mouse/ Rabbit PolyDetector Plus DAB HRP Brown Detection System (Immuno DNA Washer 20x, Tinto Deparaffinator EDTA 20x (Bio SB, Santa Barbara, CA, USA) were used. All reagents were stored at 4°C before use. IHC analysis was performed using the detection system according to the manual IHC staining protocol. Stained sections were assessed at a high magnification of 400x, and 100 cells were counted in each field. In this case, 5 fields for each section were randomly selected and examined, and the number and intensity of positively stained cells were recorded and averaged [15].

The level of Her2neu expression positivity was defined according to the National Comprehensive Cancer Network (NCCN) guidelines [17]. HER2 expression was graded as 3+ with intense continuous membranous staining in more than 10% of tumor cells, 2+ corresponded to moderate continuous membranous staining in more than 10% of cells or intense continuous membranous staining in less than 10% of cells [15]. Grade 1+ was assigned to weak discontinuous membranous staining in more than 10% of cells. Grade 0 corresponded to observations where weak membranous staining was less than 10% of cells or absent. Grades 2+ and 3+ were classified as HER2 overexpression. Microscopic slides with a known, verified result of HER2 overexpression served as external controls [18, 19].

Statistical processing of the obtained results was performed using the Statistica 10 computer software system (StatSoft Inc., USA) and SPSS 25 with a 95% confidence interval (CI). The studied nonparametric groups were analyzed using the Mann-Whitney, Student's t-test, and Pearson's chi-square tests. StatTech v.3.0.9 (StatTech LLC, Russia) was used for statistical analysis. Quantitative indicators with normal distribution are described using arithmetic means (M) and standard deviations (SD), 95% CI. Quantitative data were calculated without normal distribution using the median (Me), lower, and upper quartiles (Q1-Q3). A comparison of percentages in the analysis of multifield contingency tables was performed using the Pearson chi-square test [15].

Results: A total of 109 cases of GC were included in the study, including 77 men (70.6%) and 32 women (29.4%). The age of patients at diagnosis ranged from 27 to 81 years (median: 63 years) (Table 1).

Table 1 – Age of patients (descriptive statistics of quantitative variables)

Indicator	Median, Me	Quartile, Q_1-Q_3	Sample size, n	Minimum range, min	Maximum range, max
Age	63	59-70	109	27	81

Tumors were predominantly found in the body of the stomach (47.7%) and less often in the cardiac (38.5%) and antral (13.8%) sections. According to the histopathological classification of gastric cancer, the following types of tumors were identified: highly differentiated – 4 (3.7%), moderately differentiated – 27 (24.8%), poorly differentiated – 46 (42.2%), and undifferentiated – 32 (29.4%).

In this study, cases of gastric cancer were distributed according to the TNM classification as follows: stage I – 6 (5.5%), stage II – 45 (41.3%), and stage III – 58 (53.2%) [15].

The level of Her2/neu expression showed "no membrane reactivity" in 57 (52.3%) cases, "+" weak or barely noticeable membrane reactivity – in 19 (17.4%), "++" "moderate or lateral membrane" reaction – in 21 (19.3%) and "+++," which means "complete basolateral" expression – only in 12 (11.0%) cases (Table 2).

As shown in Table 3 and Figure 1, statistically significant differences in Her2 expression levels were found depending on age (p=0.026) (method used: Mann-Whitney U test) [15].

Table 2 – Clinicopathological data and HER2 marker expression (descriptive statistics of categorical variables)

Indicator	Category	Abs.	Percent (%)	Confidence interval (95% CI)
Gender (F, M)	wives	32	29.4	21.0-38.8
	husband	77	70.6	61.2-79.0
Tumor localization	cardiac section	42	38.5	29.4-48.3
	body of the stomach	52	47.7	38.1-57.5
	antral and pyloric sections	15	13.8	7.9-21.7
Histopathological differentiation (high G1, medium G2, low G3, non-differentiable G4)	G1	4	3.7	1.0-9.1
	G2	27	24.8	17.0-34.0
	G3	46	42.2	32.8-52.0
	G4	32	29.4	21.0-38.8
pTNM stage (I, II, III)	I	6	5.5	2.0-11.6
	II	45	41.3	31.9-51.1
	III	58	53.2	43.4-62.8
Her2 expression	negative (-; +)	76	69.7	59.2-77.3
	positive (++; +++)	33	30.3	22.7-40.8

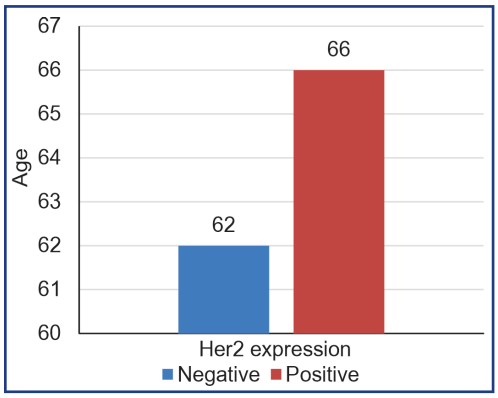

Figure 1 – The ratio of the parameters "Age" and "Her2 expression (negative, positive)" in gastric cancer

Table 3 – Her2 expression (negative, positive) depending on the patient's age

Indicator	Categories	Age			Significance level, p
		Median, Me	Quartile, Q_1-Q_3	Sample size, n	
Her2 expression	negative	62	54-69	75	0.026*
	positive	66	62-72	34	

*Note: * – differences in indicators are statistically significant (p<0.05)*

As shown in Table 4 and Figure 2, statistically significant differences in Her2 expression levels were found depending on gender (p=0.023) (method used: Pearson Chi-square) [15].

Comparison of tumor localization and Her2 expression levels (negative, positive) using the Pearson Chi-square method did not show statistically significant differences (p=0.148) (Table 5, Figure 3) [15].

Comparison of histopathological differentiation indices and Her2 expression (negative, positive) using the Pearson Chi-square method did not show statistically significant differences (p=0.441) (Table 6, Figure 4).

Comparison of tumor staging and Her2 expression (negative, positive) did not show significant differences (p=0.683) (Table 7, Figure 5).

Table 4 – Her2 expression level (negative, positive) in gastric cancer depending on the patient's gender

Indicator	Categories	Her2 expression		Significance level, p
		negative	positive	
Floor (F, M)	wives	17 (22.7)	15 (44.1)	0.023*
	husband	58 (77.3)	19 (55.9)	

*Note: * – differences in indicators are statistically significant (p<0.05)*

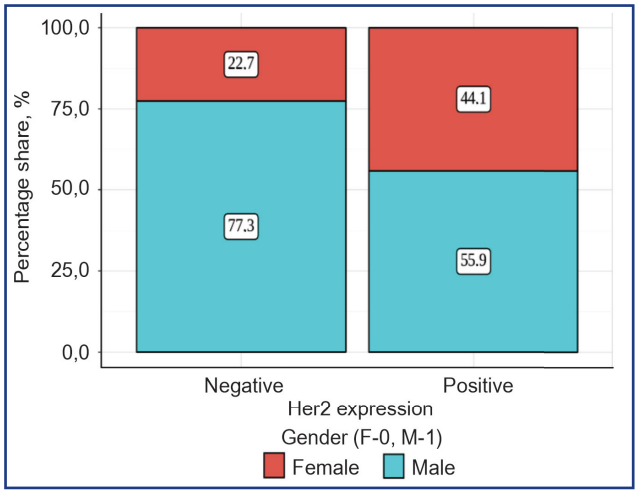

Figure 2 – Ratio of Her2 expression rates (negative, positive) depending on the patient's gender in gastric cancer

Table 5 – Her2 expression level (negative, positive) in gastric cancer depending on tumor location

Indicator	Categories	Her2 expression		Significance level, p
		negative	positive	
Tumor localization	cardiac section	33 (44.0)	9 (26.5)	0.148
	body of the stomach	34 (45.3)	18 (52.9)	
	pyloric and antral sections	8 (10.7)	7 (20.6)	

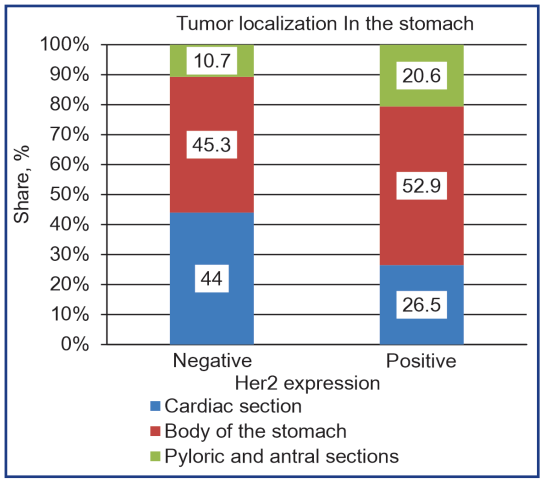

Figure 3 – The ratio of the indicators "Tumor localization" and "Her2 expression (negative, positive)" in gastric cancer

Table 6 – Her2 expression level (negative, positive) in gastric cancer depending on the histopathological differentiation of the tumor

Indicator	Categories	Her2 expression		Significance level, p
		negative	positive	
Histopathological differentiation of the tumor (high – G1, medium – G2, low – G3, undifferentiated – G4)	G1	2 (2.7)	2 (5.9)	0.441
	G2	19 (25.3)	8 (23.5)	
	G3	29 (38.7)	17 (50.0)	
	G4	25 (33.3)	7 (20.6)	

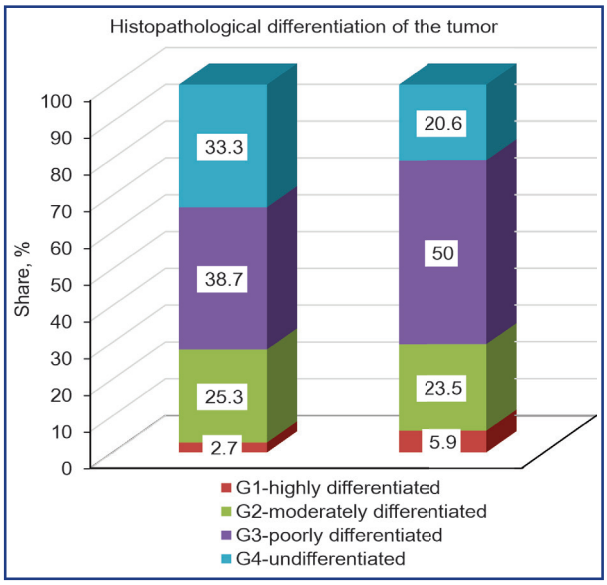

Figure 4 – Histopathological differentiation of gastric cancer depending on the indicator "Her2 expression (negative, positive)"

Table 7 – Expression level of the Her2 marker in gastric cancer

Indicator	Categories	Her2 expression		Significance level, p
		negative	positive	
pTNM stages	I	4 (5.3)	2 (5.9)	0.683
	II	29 (38.7)	16 (47.1)	
	III	42 (56.0)	16 (47.1)	

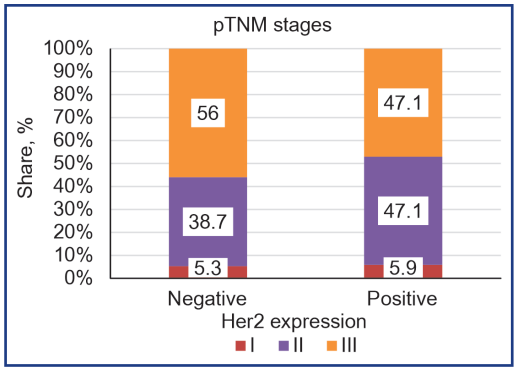

Figure 5 – The proportion of cases of gastric cancer by stage of the disease depending on the indicator "Her2 expression (negative, positive)"

Discussion: Z. Wei et al. noted that "in non-metastatic gastric adenocarcinoma, Her2 expression and the combined expression of Her2 and Ki-67 were associated with several clinicopathological factors including tumor differentiation and stage, and only +++ Her2 expression was associated with worse prognosis in multivariate analysis with marginal significance in their study, whereas Ki-67 alone had limited clinicopathological and prognostic value" [20]. HER2 overexpression results in the receptors transmitting excessive signals for cell proliferation to the nucleus. It has been suggested that HER2-positive cells directly contribute to tumors' pathogenesis and clinical aggressiveness. In 2020, researchers from the University of South China (Ye D.M., Xu G., Ma W., Li Y., Luo W., Xiao Y., Liu Y., and Zhang Z.) noted that "identification of new and effective biomarkers is necessary to improve the diagnosis of gastric cancer in order to increase the accuracy of gastric cancer diagnosis, determine prognosis and predict pathogenesis…" [21].

HER2 overexpression in gastric cancer is associated with poor prognosis. Thus, according to M. Razmi et al., the detection of tumor cell markers is mainly associated with worse treatment outcomes in patients with gastric cancer, both overall and individually. Detection of a combined marker panel may be useful as a prognostic marker for determining tumor aggressiveness and poor prognosis in patients with gastric cancer, which will likely identify new potential targets for therapeutic approaches [22].

HER2 expression in gastric cancer has been known for many years. In addition to its involvement in cancer pathogenesis, HER2 has also been evaluated in targeted therapy. HER-2 is currently considered a potential therapeutic target requiring preliminary testing for HER2 status. In 2018, Malaysian researchers P. Rajadurai et al. indicated that HER2 overexpression was significantly more common (p<0.001) in diffuse-type tumors (39.8%) than in intestinal-type tumors (14.9%) [23]. Egyptian researchers R.A. Abdel-Salam et al. noted a high frequency of HER2/neu-positivity in resectable gastric carcinomas (about 54%). The only statistically significant association was found between positive Her2/neu expression and the intestinal Lauren type [24]. In our study, the overall HER2 positivity rate was 30.3%. At the same time, in the work of A. Shabbir et al . HER2 was significantly expressed in poorly differentiated GC, mainly observed in women aged >60 years and stage IIIC tumors [25], whereas according to Y. Lei et al. HER2 overexpression correlated with various clinicopathological parameters in patients with GC: male gender, proximally located tumor, and poorly differentiated tumor [6]. In our study, there was a statistically significant association between HER2 positive expression and the age of patients, who were predominantly observed at the age <66 (p=0.026), and statistically significant differences (p=0.023) were also established when assessing the "sex of patients" parameter. However, we did not find any significant correlation between HER2 overexpression and tumor localization, histopathological differentiation of the tumor, and the stage of the disease according to TNM. There is a tendency towards the significance of HER2, positive expression in poorly differentiated GC (50%) and stage II-III of the disease. Many authors did not report any significant association between tumor localization and HER2 positivity, and conflicting results were reported regarding tumor localization and HER2 expression. In our study, tumors located in the body of the stomach account for 52.9% of cases, which may be the reason for a higher rate of HER2 positivity (p=0.148), although this indicator is statistically insignificant.

Conclusion: In this study, the dependence of HER2 marker expression on age, gender, disease stage, and differentiation degree was determined in 109 patients operated on for stage 0-IIIC gastric cancer. Thus, positive HER2/neu expression in gastric cancer depends on the age (p=0.026) and gender (p=0.023) of the patient but does not depend on the localization and histopathological differentiation of the tumor and the stage of the disease. Considering the positive expression of HER2/neu in poorly differentiated gastric cancer (50%) and stages II-III of the disease, this marker can be considered as a potential therapeutic target that requires preliminary testing when prescribing targeted therapy.

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АҢДАТПА

АСҚАЗАННЫҢ ҚАТЕРЛІ ІСІГІНДЕ АДАМНЫҢ ЭПИДЕРМАЛЫҚ ӨСУ ФАКТОР-2 РЕЦЕПТОР ЭКСПРЕССИЯСЫНЫҢ АУРУДЫҢ ЖАСЫМЕН, ЖЫНЫСЫМЕН, ІСІКТІҢ ДИФФЕРЕНЦИАЦИЯЛЫҚ САТЫСЫ ЖӘНЕ ДӘРЕЖЕСІМЕН БАЙЛАНЫСЫ

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Өзектілігі: *Асқазанның қатерлі ісігі (АҚІ) – гетерогенді қатерлі ауру. Карциномаларда HER2 онкоген ретінде әрекет етеді, себебі геннің жоғары күшейтілуі жасуша мембранасындағы ақуыздың шамадан тыс экспрессиясын және кейіннен қатерлі жасуша үшін пайдалы қасиеттерді алуды тудырады. Жаңа және тиімді биомаркерлерді анықтау асқазан обырының диагностикасын жақсарту, асқазан обыры диагностикасының дәлдігін жақсарту, болжамды анықтау және патогенезді болжау, асқазан обыры бар науқастарды емдеудің жаңа және тиімді нұсқасын құру үшін қажет.*

Зерттеудің мақсаты: *асқазан обырындағы HER2 маркерінің экспрессиясын аурудың жасы, жынысы, ісік дифференциациясының сатысы және дәрежесі арасындағы байланысты бағалау.*

Әдістері мен материалдары: *Зерттеу дизайны салыстырмалы сипаттамалық зерттеу болып табылады. Зерттеуге 2021-2022 жылдар аралығында Марат Оспанов атындағы Батыс Қазақстан медицина университетінің медициналық орталығының патологоанатомиялық бөлімшесінен асқазан обырына операция жасау кезінде алынған асқазан обырының 0-IIIC сатысы бар 109 науқастың хирургиялық материалы қолданылды. Гистологиялық және иммуногистохимиялық зерттеулер Марат Оспанов атындағы БҚМУ гистология кафедрасының морфологиялық зертханасында жүргізілді. Алынған мәліметтер статистикалық өңдеуден өтті.*

Нәтижелері: *Осы зерттеуде GC-де оң Her2/neu экспрессиясының көрсеткіштері науқастың жасына (p=0,026) және жынысына (p=0,023) байланысты статистикалық түрде айтарлықтай ерекшеленді, бірақ локализацияға, ісіктің гистологиялық дифференциациясына және аурудың сатысына байланысты статистикалық айтарлықтай ерекшеленбеді.*

Қорытынды: *Төмен дифференцирленген асқазан обырында (50%) және аурудың II-III сатыларында Her2/neu оң экспрессиясының маңыздылығына тенденцияны ескере отырып, Her2/neu маркері мақсатты терапияны тағайындау кезінде алдын ала тестілеуді қажет ететін әлеуетті терапевтік мақсат ретінде қарастырылуы мүмкін.*

Түйінді сөздер: *асқазанның қатерлі ісігі, морфология, гистология, иммуногистохимия, Her2/neu.*

АННОТАЦИЯ

СВЯЗЬ ЭКСПРЕССИИ РЕЦЕПТОРА ЧЕЛОВЕЧЕСКОГО ЭПИДЕРМАЛЬНОГО ФАКТОРА РОСТА-2 ПРИ РАКЕ ЖЕЛУДКА С ВОЗРАСТОМ И ПОЛОМ ПАЦИЕНТА, СТАДИЕЙ И СТЕПЕНЬЮ ДИФФЕРЕНЦИРОВКИ ОПУХОЛИ

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Актуальность: *Рак желудка (РЖ) представляет собой гетерогенное злокачественное заболевание. При различных формах РЖ, например, карциноме, биомаркеры рецепторов эпидермального фактора роста человека Her2/neu выполняют роль онкогенного фактора, в основе которого лежит процесс высокой амплификации гена с переходом в злокачественную клетку. Сверхэкспрессия белка происходит на поверхности клеточной мембраны. В связи с этим необходимо расставить приоритеты по прогнозу, патогенезу и представить наиболее оптимальный по эффективности вариант лечения для пациентов с РЖ.*

Цель исследования *– оценить уровень экспрессии Her2/neu при раке желудка с учётом пола и возраста пациента, стадии заболевания и степени дифференцировки опухоли.*

Методы: *Нами было проведено сравнительное описательное исследование операционного материала, полученного от 109 пациентов с раком желудка со стадиями 0-IIIC после операций по поводу данного заболевания из патологоанатомического отделения НАО МЦ «ЗКМУ имени Марата Оспанова» в 2021-2022 гг. Различные гистологические и иммуногистохимические исследования проводили на кафедре гистологии морфологической лаборатории ЗКМУ им. Марата Оспанова. Полученные результаты обработаны различными методами статистической обработки.*

Результаты: *Настоящее исследование показало, что показатели положительной экспрессии Her2/neu при РЖ статистически значимо различаются в зависимости от возраста (p=0,026) и пола (p=0,023) пациента, но статистически не значимо различаются в зависимости от локализации, гистопатологической дифференцировки опухоли и стадии заболевания.*

Заключение: *Учитывая тенденцию к значимости положительной экспрессии Her2/neu при низкодифференцированном РЖ (50%) и II-III стадиях заболевания, маркер Her2/neu можно рассматривать как потенциальную терапевтическую мишень, требующую предварительного тестирования при назначении таргетной терапии.*

Ключевые слова: *рак желудка (РЖ), морфология, гистология, иммуногистохимия, Her2/neu.*

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