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Expression of Cyclooxygenase 2 (COX-2) and Vascular Endothelial Growth Factor (VEGF) in Gastric Carcinoma and Relationship with Clinicopathological Parameters

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Abstract

Background: Gastric cancer remains one of the common and deadly cancers worldwide, especially among older males, identification of specific prognostic indicators might allow a better prognostic stratification and more effective therapy. The cyclooxygenase-2 (COX-2) protein has been detected insome tumors andits over expression is associated with there prognosis. The vascular endothelial growth factor (VEGF), as a cell regulatory factor that affects the blood vessel formation, growth and occurrence of tumors.

Aim of Study: To assess cyclooxygenase-2 (COX-2) and vascular endothelial growth factor (VEGF) immunohistochemical (IHC) expression in gastric carcinoma cases, whether these markers are useful in predicting Clinicopathological prognostic parameters and whether there is anassociation between the expression of cyclooxygenase-2 and vascular endothelial growth factor.

Material and Methods: A total of 50 archived, formalin fixed, paraffin embedded tissue blocks of 50 cases of gastric adenocarcinoma with different grades. The samples were immunohistochemically analysed for COX-2 & VEGF expressions using a streptavid in biotinperoxidase according to the manufacturers protocol. The relationships among COX-2 and VEGF expression and clinicopathological parameters were statistically analyzed.

Results: COX-2 and VEGF expressions were obviously higher in carcinoma tissues compared tonormal mucosae ($p<0.001$). Concerning COX-2 the expression rate was 62.%. COX-2 positive tumors were significantly correlated with Lauren classification, tumor grade ($p<0.006$, $p=0.041$). Concerning VEGF the expression rate was 66.%. VEGF was significantly associatedwith lymph node metastasis and tumor depth ($p<0.030$, $p<0.019$). There was significant associationbetween COX-2 and VEGF expression in gastric adenocarcinoma ($p=0.029$).

Conclusion: In gastric adenocarcinoma, COX-2 expression might serve as a powerful indicator forintestinal type carcinoma and tumor grade, while VEGF was relatedto loco-regional progression. COX-2 might be involved in the development of angiogenesis in gastric carcinoma through VEGF upregulation.

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Introduction

GASTRIC cancer is the 5th most common neoplasm and the 3rd most deadly cancer, with an estimated 783,000 deaths in 2019. Gastric cancer incidence and mortality are highly variable by region and highly dependent on diet and Helicobacter pylori infection [1]. In the latter half of the twentieth century, GC was the secondmost common cause of cancer-related deaths after lung carcinoma accounting to 11.3% of all cancer deaths [2]. The disease becomes symptomatic in an advanced stage. Five-year survival rate is relatively good only in Japan, where it reaches 90% [3]. In European countries, survival rates vary from ~10% to 30% [4]. High survival rate in Japan is probably achieved by early diagnosis by endoscopic examinations and consecutive early tumor resection [3]. In Egypt, gastric cancer is 12th in position regarding incidence and cancer-related deaths. About 65% of patients present with locally advanced or metastatic disease with 5-year survival rates of 30% and 5% respectively [4].

Nearly one third of the patients (29.9%) experienced recurrence after gastric surgery. One major difficulty in the therapy of GC is the presenceof only few prognostic indicators that can predict its clinical behavior. Therefore, identification of other specific prognostic markers might allow a better prognostic stratification and more effective therapy [2].

The cyclooxygenase (COX) isoenzymes, known as prostaglandin (PG) rate-limiting synthases, catalyze the metabolism of arachidonic acid (AA) to PGs. Finally, a series of biologically active prostaglandins and thromboxane are formed [5].

There are three isoforms of the enzyme that have been identified: COX-1, COX-2, and COX-3.COX-1 is constitutively expressed in human cells. COX-3, an alternate splice variant of COX-1, is most abundant in the canine cerebral cortex. COX-2 is an inducible enzyme and is associated with inflammatory diseases and carcinogenesis [5]. The COX-2 enzyme is encoded by the gene located on chromosome 1 at q31.1 [6]. COX-2 enzyme maystimulate cell proliferation, inhibit apoptosis, increase invasiveness and induce angiogenesis by elaborating some angiogenic factors such as vascular endothelial growth factor (VEGF) [7].

Tumor angiogenesis, (the growth of new capillary blood vessels), is a hallmark of cancer and is essential for tumor growth and progression [8,9]. Vascular endothelial growth factor (VEGF) is a critical factor for tumor angiogenesis in numerous solid malignancies, and tumor cells overexpress and secrete VEGF. Paracrine VEGF acts on vascular endothelial cells and induces their proliferation, differentiation and migration, resulting in angiogenesis and providing oxygen and nutrients to the tumor [8,9].

The importance of VEGF-induced angiogenesis in tumor growth is strongly supported by studies showing that blockade of VEGF and its receptors results in decreased angiogenesis and subsequent abrogation of cancer growth [8,9,10].

Some substances such as, EGF, COX-2 induces VEGF production in cancer cells, and the paracrine VEGF activates vascular endothelial cells to promote tumor angiogenesis and thus supports tumor cell growth in an angiogenesis-dependent manner [11].

Material and Methods

The current work is a retrospective study that consisted of fifity cases of gastric carcinoma (25 cases of low grade & 25 cases of high grade) and one case of colonic cancer (as a positive control for COX-2). Eighteen cases out of fivity cases contain peri-tumoral normal mucosa which serve as internal control for expression of COX-2 and VEGF.

Paraffin blocks were obtained from the archives of the Pathology Department of Al-Azhar University Hospitals during the period from July 2016 to July 2020. Clinicpathological data including age, sex, location, histological type, grade, depth of invasion, nodal status and Helicobacter pylori (H. pylori) infection in the non neoplasticadjacent mucosa were determined from the pathology reports. The histological typing of gastric adenocarcinoma was made according to Lauren classification and (WHO) classification system, 2018 (Not applicaple).

Processing:

Sections of 4-µm thickness were cut by microtome from the formalin fixed, paraffin embedded tumor blocks. Three sections were prepared from each tumor tissue paraffin block:

- One slide for Hematoxylin and Eosin (H&E) staining for histopathological reassessment.
- Two positively charged slides for immunohistochemical staining by COX-2 & VEGF monoclonal antibodies.
- All slides were examined under light microscope.

Immunohistochemical methods:

The slides were subjected to IHC staining using a streptavidin-biotin-peroxidase according to the manufacturers protocol using BenchMark XT automated slide stainer (a product of Ventana Medical Systems). All sections were deparaffinized by xylene, rehydrated by a graded series of ethanol, and treated with 0.3% H_2O_2 for 5min at room temperature to block endogenous peroxidase activity. Heat-based antigen retrieval was performed to obtain optimal results. Sections were treated with 5% bovine serum albumin to block non-specific staining. The slides were incubated with the primary antibody, anti-COX-2 antibody (monoclonal rabbit anti-human, clone SP2, in a dilution of 1:100, Thermo Scientific, USA) and antihuman VEGF antibody (monoclonal mouse, clone VG 1, M7273, Dako Cytomation, Denmark, at a 1:50 dilution). Diaminobenzidine was used as a chromogen and hematoxylinas a counterstain.

Positive and negative controls:

- Negative controls were prepared by replacing the primary antibody with Phosphate Buffered Saline (PBS).
- Positive staining controls for COX-2 included sections of colonic carcinoma, and Positive staining controls for VEGF was then eigh bouring blood vessels.

Interpretation of immunostaining:

- The expression of COX-2 and VEGF were assessed independently by two pathologists.
- COX-2 and VEGF immunoreactivity was detected in the cytoplasm of the cells.
- The IHC score was calculated by adding the percentage of positively stained cells to the staining intensity. The percentage of positive

cells ranged between 0 and 3, i.e. 0, if less than 10% of tumor cells were stained; 1, if 10-25% of tumor cells were stained; 2, if 25-50% were positive; and 3, if >50% were positive. The staining intensity was scored as: 0, negative immuno reaction; 1, weak intensity; 2, moderate intensity; and 3, strong intensity.

The sum of the two parameters varied between 0 and 6. In our study, we considered: A negative immunoreaction, for scores between 0 and 2; a weakly positive immunoreaction (+), for scores 3 and 4; a strongly positive immunoreaction (++), for scores 5 and 6. Cases with scores equal to or higher than 3, were considered as positive **[7,12]**.

Statistical methods:

Data were fed to the computer and analyzed using IBM SPSS software package version 20.0. (Armonk, NY: IBM Corp) Qualitative data were described using number and percent. The Kolmogorov-Smirnov test was used to verify the normality of distribution Quantitative data were described using range (minimum and maximum), mean, standard deviation, median and interquartile range (IQR). p-value less than or equal 0.05 was considered statistically significant.

The used tests were:

1- *Chi-square test:* For categorical variables, to compare between different groups.

2- *Fisher's Exact or Monte Carlo correction:* Correction for chi-square when more than 20% of the cells have expected count less than 5.

3- *Student t-test:* For normally distributed quantitative variables, to compare between two studied groups.

Results

Clinicopathological characteristics of the studied cases and their correlation with COX-2 expression are summarised in (Table 1).

COX-2 protein expression:

COX-2 immunostaining was identified in (31/50) (62%) of the studied cases, while (19/50) (38%) of the studied cases showed negative COX-2 expression.

Among 18 cases with peri-tumoral normal mucosa, 13 cases of GC positive for COX-2, and 5 cases were negative for COX-2. While one case of peri-tumoral normal mucosa was positive for COX-2, and 17 cases were negative for COX-2. COX-2 expression was significantly higher in gastric cancer tissuesvs. Peri-tumoral normal mucosae (p<0.001).

Fifteen cases (30%) of gastric carcinoma were associatedwith intestinal metaplasia in neighboring mucosae. In two cases, epithelial cells in the adjacent intestinal metaplastic region showed moderate COX-2 staining (score++), and two cases showed weak COX-2 staining (score+), while 11 cases showed -ve staining, and also, out of 6 cases (12%) of gastric carcinoma associated with dysplasia, one case, showed moderate COX-2 staining (score++), while 5 cases showed weak COX-2 staining (score+).

COX-2 positive tumors were noted in 22 (59.1%) GC cases of the intestinal-type and in 9 (40.9%) of the diffuse type, the expression was significantly higher inthe intestinal than in the diffuse carcinomas (p<0.006). (Table 1).

COX-2 positive tumors were noted in 19 (76%) GC cases of the low grade type and in 12 (48%) of the high grade type, the expression was significantly higher in the low grade type than in the high grade type carcinomas (p<0.041). (Table 1).

COX-2 expression was lower in signet-ring cell carcinoma and undifferentiated carcinoma than other subtypes; however the statistics were not valid as the numbers of some histological subtypes were very low.

There were no significant relationships between the levels of COX-2 expression and each of age, sex, location, lymph node status, depth of invasion, H. pylori (p>0.05).

Clinicopathological characteristics of the studied cases and their correlation with VEGF expression are summarised in (Table 2).

VEGF protein expression:

VEGF immunostaining was identified in (33/50) (66%) of the studied cases, while (17/50) (34%) of the studied cases showed negative VEGF expression.

Among 18 cases with peri-tumoral normal mucosa, 13 cases of GC positive for VEGF, and 5 cases were negative for VEGF. while one case of peri-tumoral normal mucosa showed weak expression for VEGF, and 17 cases were negative for VEGF. VEGF expression was significantly higher in gastric cancer tissuesvs. peri-tumoral normal mucosae (p<0.001).

Fifteen cases (30%) of gastric carcinoma were associated with intestinal metaplasia in neighboring

mucosae. In 4 cases, epithelial cells in the adjacent intestinal metaplastic region showed weak VEGF staining (score+), while 11 cases showed negative VEGF staining, and also, out of 6 cases (12%) of gastric carcinoma associated with dysplasia, two cases, showed weak VEGF staining (score+), while 4 cases showed negative VEGF staining.

VEGF positive tumors were noted in 21 (75%) GC cases of the intestinal-type and in 12 (54.5%) of the diffuse type. The relation between VEGF and Lauren classification was a statistically insignificant (p-value=.130). (Table 2).

The relation between VEGF immunohistochemical score and depth of invasion in the studied GC cases was statistically significant (p-value=.019), where VEGF positive tumors were noted in T3 (66.7%) and T4 (85.7%) higher than T1 (40%) and T2 (33.3%) of GC cases.

VEGF immunohistochemical score was statistically significant with lymph node status (p-value=.030), where VEGF positive tumors were noted in 29 (74%) GC cases with lymph node positive, while only 4 (36%) GC cases with lymph node negative showed VEGF expression.

There were no significant relationships between the levels of VEGF expression and each of age, sex, location, grade, H. pylori (p>0.05).

Relation between immunohistochemical score of COX-2 and VEGF:

In order to explain the relation between the IHC expression of COX-2 and tumor angiogenesis, we have evaluated the association between VEGF and COX-2 expression (Table 3).VEGF was higher in patients with COX-2 expression than inthose without which was statistically significant (p-value=.029).

Table (1): Relation between Result of Immuno COX-2 and clinicopathological data.

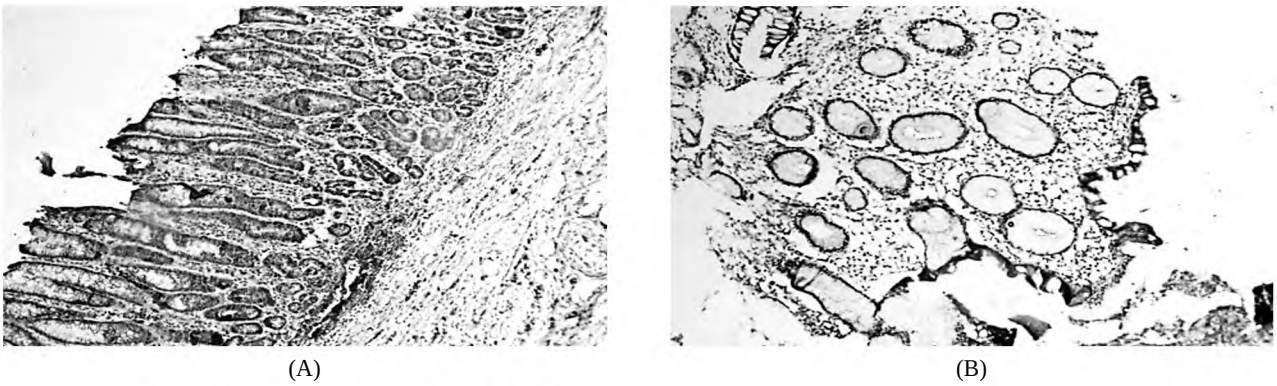
Clinicopathological data	N	Result of immuno COX-2				Test of Sig.	p
		Negative (n=19)		Positive (n=31)			
		No.	%	No.	%		
Age (years):							
<60	35	12	34.3	23	65.7	χ^2=0.683	0.409
60	15	7	46.7	8	53.3		
Min. - Max.		35.0-79.0		29.0-87.0		t=0.299	0.766
Mean ± SD.		54.32±11.79		53.16±14.05			
Median		56.0		52.0			
Sex:							
Male	32	10	31.3	22	68.8	χ^2=1.719	0.190
Female	18	9	50.0	9	50.0		
Location:							
Antram	25	10	400	15	60.0	χ^2=0.127	0.938
Fundus	9	3	33.3	6	66.7		
Body	16	6	37.5	10	62.5		
Lauren classification:							
Diffuse type	22	13	59.1	9	40.9	7.417	0.006
Intestinal type	28	6	21.4	22	78.6		
Grade:							
Low	25	6	24.0	19	76.0	4.160	0.041
High	25	13	52.0	12	48.0		
L. node:							
Negative	11	2	18.2	9	81.8	χ^2=2.351	FEp=0.170
Positive	39	17	43.6	22	56.4		
Depth of invasion:							
T1	5	2	40.0	3	60.0	χ^2=3.609	MCp=0.337
T2	9	4	44.4	5	55.6		
T3	15	8	53.3	7	46.7		
T4	21	5	23.8	16	76.2		
H. pylori infect:							
Negative	19	9	47.4	10	52.6	χ^2=1.142	0.285
Positive	31	10	32.3	21	67.7		

Table (2): Clinicopathological characteristics of the studied cases and their correlation with VEGF expression.

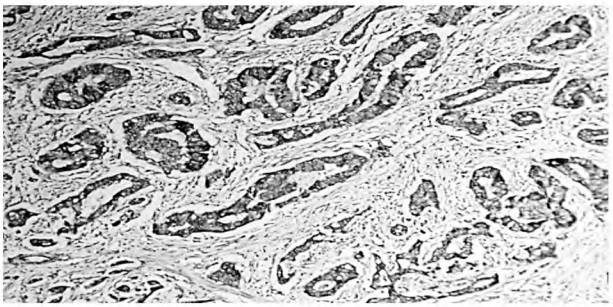
Clinicopathological data	N	Result of immuno VEGF				Test of Sig.	*p*
		Negative (n=17)		Positive (n=33)			
		No.	%	No.	%		
Age (years):							
<60	35	10	28.6	25	71.4	ξ^2=1.532	0.216
60	15	7	46.7	8	53.3		
Min. - Max.		35.0-87.0		29.0-79.0		*t*=1.565	0.124
Mean ± SD.		57.59±14.79		51.55±11.91			
Median		56.0		52.0			
Sex:							
Male	32	8	25.0	24	75.0	ξ^2=3.209	0.073
Female	18	9	50.0	9	50.0		
Lauren classifica.:							
Diffuse type	22	10	45.5	12	54.5	2.297	0.130
Intestinal type	28	7	25.0	21	75.0		
Depth of invasion:							
T1	5	3	60.0	2	40.0	9.291*	0.019
T2	9	6	66.7	3	33.3		
T3	15	5	33.3	10	66.7		
T4	21	3	14.3	18	85.7		
L. node:							
Negative	11	7	63.6	4	36.4	5.520	0.030
Positive	39	10	25.6	29	74.4		
Location:							
Antram	25	8	32.0	17	68.0	ξ^2=0.536	0.765
Fundus	9	4	44.4	5	55.6		
Body	16	5	31.3	11	68.8		
Grade:							
Low	25	9	36.0	16	64.0	ξ^2=30.089	0.765
High	25	8	32.0	17	68.0		
H. pylori infect:							
Negative	19	8	42.1	11	57.9	ξ^2=0.897	0.344
Positive	31	9	29.0	22	71.0		

Table (3): Relation between Result of Immuno. of COX-2 and VEGF.

Result of Immuno VEGF	N	Result of immuno COX-2				ξ^2	*p*
		Negative (n=19)		Positive (n=31)			
		No.	%	No.	%		
Negative	17	10	58.8	7	41.2	4.741	0.029
Positive	33	9	27.3	24	72.7		

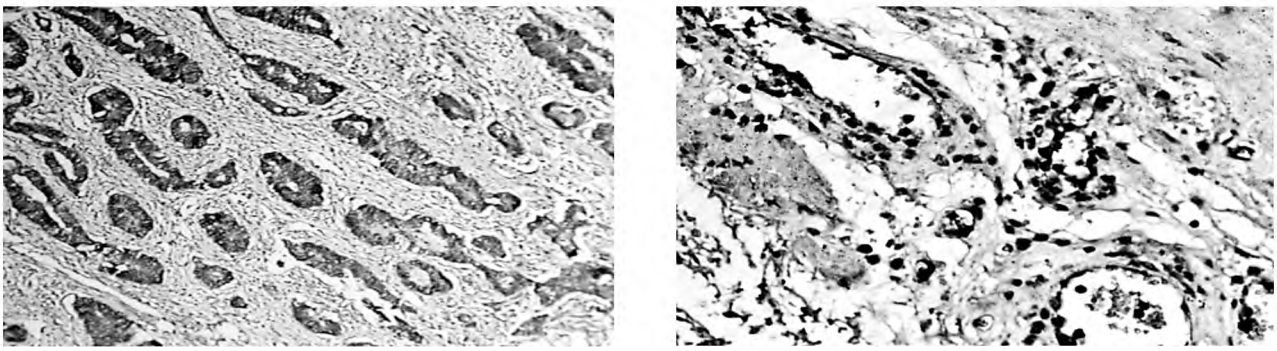


(A) (B)



(C)

Fig. (1): COX-2 expression: (A) Normal gastric mucosa showing positive cytoplasmic COX-2 expression, (IHC x 100). (B) Intestinal metaplasia showing positive cytoplasmic COX-2 expression, (IHC x100). (C) Moderatly differentiated adenocarcinoma (grade II) showing positive cytoplasmic COX-2 expression, (IHC x100).



(A) (B)

Fig. (2): VEGF expression: (A) Moderatly differentiated adenocarcinoma (grade II) showing positive cytoplasmic VEGF expression, (IHC x 100). (B) Blood vessels showing positiveVEGF expression (IHC x 100).

Discussion

Previous studies have concluded that COX-2 and VEGF expressions played important roles in the growth and metastasisof many human tumors including gastrointestinal cancers. Because of their high expression in tumors, they constitutepotential targets in cancer prevention and treatment **[13]**. These studies prompted us to evaluate COX-2 and VEGF expression at protein levels in tissues with GC and assess the relationship with clinicopathological data.

Our result showed that COX-2 and VEGF expression is elevated in gastric carcinoma when compared with peritumoral normal mucosae, which was statistically significant (p<0.001). These findings were in concordance with those of Jianli et al., **[13]**, Nesreen et al., **[14]** and Liu et al., **[15]** who reported that the expressions of COX-2 and VEGF in gastric cancer tissues were significantly increased compared with those in normal tumor-adjacent tissues, confirming that COX-2 protein plays an important role in gastric carcinogenesis.

The current study showed that COX-2 protein expression was detected in 62% of the studied GC cases while 38% of cases were negative. This finding was similar to the results of Lazar et al., 2008, **[16]** who reported that positive expression of COX-2 in 57.2% of cases. Higher results reported by Jianli et al., **[14]** and Sun et al., **[17]** who found that COX-2 expression was 76% & 80% respectively, in the tumor.

An explanation of these results was suggested by Wang et al., [18], and Sierra et al., [19] who reported that H. pylori infection causes up-regulation of COX-2 mRNA expression in GC cases. Since it is proven that H. pylori infection varies from area to area in the world, the expression of COX-2 protein also varies. In an agreement with these conclusions, 67% of our H. pylori infected cases were positive to COX-2 protein.

In the current study, some cases of intestinal metaplasia and dysplasia in neighboring mucosae, showed moderate and weak expression for COX-2. These findings confirmed previous observations of Nesreen et al., [13], Zhang et al., [20], Lazar et al., [16] that indicated that COX-2 might be involved in the early stages of gastric cancer development. Wang et al., [18] found that COX-2 expression in the metaplasia or dysplasia tissues was related to H. pylori infection. This was in close with our rsults which showed that the most cases of the study were infected with H. pylori.

In the current study, COX-2 was expressed predominantly by the intestinal type GC, in contrast to carcinoma of diffuse type, which was a statistically significant (p<0.006). This finding was concordant with Lazar et al., [13] and Nesreen et al., [16] who reported that positive expression of COX-2 in intestinal type (73% & 69% respectively) of GC higher than diffuse type (29% & 31% respectively). These findings were not matching with results reported by Ugras et al., [2] and Chen et al., [21], who documented insignificant relation of COX-2 expression between intestinal and diffuse type of GC cases. The explanation of these results was related to the fact that H. pylori infection has been identified in almost 90% of intestinal type carcinoma which induced COX-2 expression in GC cells [18]. Therefor, COX-2 can be used as agood indicator for intestinal type of GC.

As regards, COX-2 expression and tumor grade, in our study, COX-2 expression was detected most frequently in low grade than high grade tumor which were inverse significant statistically (p-value=0.04). This was in agreement with the review of Lazar et al., [16], and Zhao et al., [22] who reported significant statistical relation of COX-2 expression with tumor grade and found that the expression of the COX-2 protein was significantly higher in well differentiated adenocarcinoma than in poorly differentiated one, suggesting main role of the COX-2 in GC sequence. These results were not in concert with the results of Gou et al., [23] and Nesreen et al., [13] who reported non significant relation between COX-2 expression and tumor grade.

In agreement with Ugras et al., [2] and Nesreen et al., [13] no significant association was found between COX-2 expression and age, sex, tumor location, depth of invasion, H.pylori and lymph node status. These results were not in concert with the results of Lazar et al., [16] who revealed that COX-2 expression was significantly associated with tumor differentiation and lymph node status. Mao et al., [24] demonstrated that the expression was related to lymph nodes metastasis. Thiel et al., [25] concluded that the COX-2 expression is more frequent in proximal than in distal gastric location.

In the current study, some cases of intestinal metaplasia and dysplasia in neighboring mucosae, showed weak expression for VEGF. These findings confirmed previous observations of Nesreen et al., [13] and Liu et al., [15] and they reported that it is the expression of an early tumor angiogenesis during the natural evolution from the normal mucosa to carcinoma.

According to the current study, our data revealed that VEGF was expressed in 75% of the intestinal type GC, in contrast to (54.5%) of carcinoma of diffuse type, which indicate higher expression in intestinal type GC than diffuse type, which may be due to higher expression of COX-2 in intestinal type GC which induces more VEGF production in intestinal type of GC [11], but this relation was statistically insignificant (p-value=0.765). This finding was concordant with Nesreen et al., [13] and Guo et al., [23] and Shi et al., [26] who detected insignificant relation between VEGF expression and the Lauren histopathological types of cases. In contrast to these results, Zhao et al., [27] and Yu et al., 2014 [28] reported significant relation between VEGF expression and Lauren histopathological types.

In the current study,the positive immunostaining rates of VEGF correlate with lymph node metastasis, depth of invasion, (p-value=0.03 & p-value= 0.01). This was matching with results obtained by Nesreen et al., [13] & Zhao et al., [27] & Kolev et al., [29] and Shi et al., [26] who reported that the VEGF expression was positively related with advanced stage and lymph node metastasis, suggested that VEGF might be useful as a biomarker of tumor aggressiveness. In contrast, Guo et al., [29] detected no association between VEGF expression and tumor stage & lymph node metastasis.

In agreement with Gou et al., [23] and Nesreen et al., [13] no significant association was found between COX-2 expression and age, sex, tumor location, grade and H.pylori. Previous studies have demonstrated a positive association with tumor location [28,30] as well as histological type and grade [27,28] [13,25] . Others reported a positive relation between VEGF expression in and H. pylori gastric cancer cells [15,29].

In the current study, the relation between COX-2 immunohistochemical (IHC) score and VEGF immunohistochemical staining in the studied GC cases was statistically significant (p-value=0.03). Our results were in agreement with Nesreen et al., [13], Zhang et al., [20], Lazar et al., [16], Kolev et al., [29] and Zhao et al., [22] who reported that the COX-2 expression was significantly associated with VEGF suggested that COX-2 was involved in the development of angiogenesis in gastric carcinoma cases through VEGF upregulation. In contrast, Gou et al., [23] reported non significant relation between the COX-2 expression and VEGF.

In conclusion, a significant relation between the expressions of COX-2 and VEGF in gastric carcinomas, suggesting the involvement of COX-2 in tumor angiogenesis. COX-2 and VEGF are important tumor markers which are involved in GC tumourigenesis and also involved in GC prognosis. COX-2 expression is significantly related to intestinal type carcinoma which can be used as agood indicator for it. VEGF expression is significantly associated with loco-regional progression, suggesting poor prognosis and high risk of metastasis in patients with GC. Blocking of the COX-2-VEGF-dependent pathway may play useful therapeutic role against malignant solid tumors.

In the current study, there was an recommendation that needs to be addressed. The sample size was relatively small. Therefore, Further works with larger samplesize are required to evaluate the negative relationships. Also further studies are needed to address the role of blocking of the COX-2-VEGF-dependent pathway on the therapeutic tools against gastric carcinoma.

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التعبير المناعى الهستوكيميائى لكل من (سيكلو أوكسجينيز ٢) و (فإيجيإف) فى سرطان المعدة

\المقدمة: إن سرطان المعدة هو من أكثر أنواع السرطان شيوعاً والسبب الثانى الأكثر شيوعاً للوفيات المتعلقة بالسرطان فى العالم وخصوصاً بين المرضى الذكور. وعلى الرغم من تشخيص وعلاج سرطان المعدة فإن التنبؤ بمصير هذا المرض مازال غير معروف بشكل كافى، فثلث مرضى سرطان المعدة يعانون من رجوعه مرة أخرى بعد استئصاله جراحياً، ولذلك من المهم إكتشاف مواد تنبئية وتكهنية والتى قد تساعد على دراسة سلوك هذا السرطان والتنبؤ بمستقبلية خطورته وانتشاره ومدى تأثير العلاجات الخاصة به .

\الأهداف: الهدف من العمل الحالى هو دراسة الأنماط الهستوباثولوجية المختلفة للحالات المتوفرة من سرطان المعدة، ودراسة التعبير الهستوكيميائى المناعى للكوكس ٢ وفى إى جى إف فى حالات سرطان المعدة ومقارنة التعبير الهستوكيميائى المناعى لكل من الكو كس ٢ وفى إى جى إف بنوع الورم ودرجته لتقييم أهميتها فى التنبؤ بالسلوك البيولوجى للورم.

\الطرق: تم تنفيذ العمل الحالى على ٥٠ حالة من حالات سرطان المعدة والتى تم تجميعها بأثر رجعى من أرشيفات قسم الباثولوجى بطب أزهر القاهرة خلال الفترة من يوليو ٢٠١٦ إلى يوليو ٢٠٢٠.

\النتائج: أظهرت النتائج الهستوكيميائية المناعية أن التعبير الكيميائى لكل من الكوكس ٢ وفى إى جى إف فى الخلايا السرطانية أعلى من الخلايا الطبيعية المجاورة لها والتى كانت ذات دلالة إحصائية. وأن ٦٢٪ من حالات سرطان المعدة كانت إيجابية التعبير للكوكس ٢ بينما ٣٨٪ من الحالات كانت سلبية، وأظهرت النتائج أن التعبير الهستوكيميائى المناعى للكوكس ٢ ذات دلالة إحصائية مع تقسيم لورين ودرجة التمايز وكذلك أن ٦٦٪ من حالات سرطان المعدة كانت إيجابية التعبير لـ فى إى جى إف بينما ٣٤٪ من الحالات كانت سلبية، وأظهرت النتائج أن التعبير الهستو كيميائى المناعى لـ فى إى جى إف ذات دلالة إحصائية مع درجة اختراق الورم ونقائل الغدد الليمفاوية وأن هناك دلالة إحصائية بين الناتج الهستوكيميائى المناعى للكوكس ٢ وفى إى جى إف فى الحالات المدروسة من سرطان المعدة.

\الخلاصة: خلصنا إلى أن الكوكس ٢ وفى إى جى إف من الدلالات الورمية المهمة فى سرطان المعدة والتيى لها دور مهم فى تولد الأوعية الدموية والتنبؤ بمآل الورم وسرعة انتشاره وأن تعبير الكوكس ٢ له علاقة تربطه بحدوث النوع المعوى من سرطان المعدة ولذلك يمكن الاستدلال به عليها وكذلك دور بروتين ال فى إى جى إف فى عملية تولد الأوعية الدموية والتى هى عامل مهم فى زيادة الانتشار الموضعى والمحلى لسرطان المعدة.