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A Correlation between Chronic gastritis, Helicobacter pylori, Intestinal metaplasia and Atrophic change with Advanced Gastric Adenocarcinoma : a study in 139 Gastrectomy

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Background : Atrophic gastritis with intestinal metaplasia is considered a precancerous lesion leading to intestinal type gastric adenocarcinoma. The current study aimed to describe the prevalence of gastric atrophy, intestinal metaplasia and H pylori infection in stomach with advanced gastric adenocarcinoma.

Methods : One hundred and thirty-nine specimens of gastrectomy with the diagnosis of advanced gastric adenocarcinoma were divided into three age groups (< 30 years old, 30-60 years old and > 60 years old). Macroscopic findings were reviewed for sites, location, size and macroscopic appearance of tumor. All sections were reviewed for cancer type, degree of differentiation, and features of angiolymphatic invasion, perineurial invasion, depth of tumor invasion and lymph node metastasis. Sections were scored on a visual analogue scale to evaluation of chronic gastritis status, atrophic change, and intestinal metaplasia with subtype. Helicobacter pylori in each location were identified.

Results : Tumor was found more often in male than female with the ratio of 3:2 and predominantly in the age group of >= 60 years old. No tumor was found in the age group of < 30 years. Most of the tumors were located in the posterior portion and lesser curvature of the antrum and the pylorus. Ulcerative type was found 65.9% followed by 15% of ulceroproliferative type, 15% of infiltrative type and 4% of fungating type. Adenocarcinoma was the common microscopic cell type (58.3%) followed by mixed adenocarcinoma and signet ring cell carcinoma 36.7% and pure signet ring cell carcinoma 5%. There was no statistically significant difference between cell types of tumor or cell differentiation with age group. More than 85% of tumor's size was larger than 2 cm in diameter. Lymph node metastasis, angiolymphatic invasion and perineurial invasion were significantly found in tumor with larger than 2 cm in diameter. Ulcerative, ulceroproliferative and infiltrative type had high incidences of angiolymphatic, perineurial invasion and lymph node metastasis comparing to fungating type. All microscopic cell types of tumor (adenocarcinoma, adenocarcinoma with signet ring cell and pure signet ring cell carcinoma) had also high incidences of angiolymphatic, perineurial invasion and lymph node metastasis. Chronic gastritis was found 91.2%

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associated with the tumor. Atrophic change with chronic gastritis was found in age group of > = 60 years. No significant statistical difference in comparing between macroscopic types and microscopic cell types of tumor with atrophic change. Intestinal metaplasia was found more common in male of age > = 60 years at both body and antrum with the most common of type I (intestinal type). No different incidence of Helicobacter pylori infection in male and female or age groups was found. Helicobacter pylori were found most commonly in both body and antrum with evidence of glanditis and lymphoid aggregation. No significant statistical difference in comparing between macroscopic types and microscopic cell types of tumor with incidence of intestinal metaplasia or Helicobacter pylori infection was found.

Conclusion : The pattern and distribution of the advanced gastric carcinoma in Thailand found to be the same as the national behavior of usual gastric carcinoma. The current hypothesis of gastric cancer *in this country is believed to follow by the high incidence of gastritis with* high *H. pylori* infection. Atrophic change and intestinal metaplasia may be blocked or prevented by dietary factors of excessive fresh fruits, vegetables and low salt intake. Thus, *H. pylori* is not insufficient to give rise to gastric carcinoma but many other cofactors or predisposing conditions must play a role in the etiology and pathogenesis of gastric carcinoma in Thailand.

เรื่องย่อ : **ความสัมพันธ์ของภาวะกระเพาะอาหารอักเสบเรื้อรัง, การติดเชื้อ** Helicobacter pylori, **ภาวะการฝ่อของเยื่อบุกระเพาะอาหาร และการแปรเปลี่ยนชนิดเซลล์เยื่อบุกระเพาะอาหารเป็นเซลล์บุลำไส้เล็ก กับลักษณะของมะเร็งกระเพาะอาหารในชิ้นเนื้อผ่าตัดกระเพาะอาหารจำนวน 139 รายที่เป็นมะเร็งกระเพาะอาหารชนิดลุกลาม**

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คณะผู้รายงานได้ทำการศึกษาลักษณะทางพยาธิวิทยาของมะเร็งกระเพาะอาหารชนิดลุกลามในชิ้นเนื้อผ่าตัดกระเพาะอาหารจำนวน 139 รายที่เป็นมะเร็งกระเพาะอาหารชนิดลุกลามและเปรียบเทียบลักษณะทางพยาธิวิทยาของมะเร็งกระเพาะอาหารกับภาวะกระเพาะอาหารอักเสบเรื้อรัง, การติดเชื้อ Helicobacter pylori, ภาวะการฝ่อของเยื่อบุกระเพาะอาหาร และการแปรเปลี่ยนชนิดเซลล์เยื่อบุกระเพาะอาหารเป็นเซลล์บุลำไส้เล็กที่พบในชิ้นเนื้อผ่าตัดกระเพาะอาหารที่ทำการศึกษา ผลการศึกษาพบว่าลักษณะของมะเร็งกระเพาะอาหารชนิดลุกลามในคนไทย ในมุมมองของการกระจายในกลุ่มอายุ, เพศ, ตำแหน่งของก้อนเนื้อร้าย, ลักษณะของก้อนเนื้อร้าย, ขนาด, ชนิดของเซลล์ และการแพร่กระจายของเซลล์มะเร็งในผนังกระเพาะอาหาร เส้นเลือด ระบบน้ำเหลืองและต่อมน้ำเหลือง ไม่แตกต่างจากการศึกษาที่ผ่านมาในข้อมูลการศึกษาลักษณะของมะเร็งกระเพาะอาหารชนิดลุกลามจากต่างประเทศ ส่วนการเปรียบเทียบกับภาวะกระเพาะอาหารอักเสบเรื้อรัง พบว่ามีภาวะกระเพาะอาหารอักเสบเรื้อรังในมะเร็งกระเพาะอาหารชนิดลุกลามถึง 91.4% แต่พบภาวะการฝ่อของเยื่อบุกระเพาะอาหารเพียง 26.8% อย่างไรก็ตามในภาวะกระเพาะอาหารอักเสบเรื้อรังร่วมกับภาวะการฝ่อของเยื่อบุกระเพาะพบการแปรเปลี่ยนชนิดเซลล์เยื่อบุกระเพาะอาหารเป็นเซลล์บุลำไส้เล็กมากถึง 89.4% ซึ่งส่วนใหญ่เป็นชนิดการแปรเปลี่ยนชนิดเซลล์เยื่อบุกระเพาะอาหารเป็นเซลล์บุลำไส้เล็กแบบสมบูรณ์ การติดเชื้อ Helicobacter pylori พบเพียง 36% ในชิ้นเนื้อผ่าตัดกระเพาะอาหารที่ทำการศึกษา

คณะผู้รายงานได้ให้ความเห็นในสมมติฐานการเกิดมะเร็งกระเพาะอาหารชนิดลุกลามในคนไทย แม้จะมีอุบัติการณ์ในอัตราที่สูงในการเกิดภาวะกระเพาะอาหารอักเสบเรื้อรังร่วมกับการติดเชื้อ Helicobacter pylori แต่ภาวะกระเพาะอาหารอักเสบเรื้อรังร่วมกับภาวะการฝ่อของเยื่อบุกระเพาะและการแปรเปลี่ยนชนิดเซลล์เยื่อบุกระเพาะอาหารเป็นเซลล์บุลำไส้เล็กที่นำไปสู่การเกิดมะเร็งกระเพาะอาหารมีอัตราที่ต่ำ จึงเชื่อว่าสมมติฐานการเกิดมะเร็งกระเพาะอาหารชนิดลุกลามในคนไทย มีขบวนการยับยั้งในขั้นตอนของการเกิดภาวะการฝ่อของเยื่อบุกระเพาะและการแปรเปลี่ยนชนิดเซลล์เยื่อบุกระเพาะอาหารเป็นเซลล์บุลำไส้เล็ก ซึ่งขบวนการยับยั้งนี้อาจเป็นผลจากการที่คนไทยมีพฤติกรรมในการบริโภคอาหารที่เป็นผักสด, ผลไม้สดและอาหารรสไม่เค็ม

INTRODUCTION

The etiology of gastro-duodenal diseases was proposed to correlate with the patterns of gastritis. Gastric ulcers and gastric adenocarcinoma (intestinal type) were associated with pan-gastritis, extensive intestinal metaplasia with cellular dysplasia[1] while the duodenal ulcers were associated with minimal corpus gastritis. According to the low incidence of gastric adenocarcinoma in Thailand (< 5 cases per 100,000 people)[2,3] and the high incidence of Helicobacter pylori associated gastritis[4,5], the pathogenesis of gastric carcinoma in this country is the field of interest. We studied the topography and features of advanced gastric adenocarcinoma then evaluated the correlation between advanced gastric adenocarcinoma with gastritis status, atrophic change, intestinal metaplasia and H pylori infection in gastrectomy specimens.

MATERIALS AND METHODS

One hundred and seventy-six gastrectomy specimens of advanced gastric cancers in Siriraj Hospital, Bangkok, Thailand from the year 1995 to 2001 were screened for advanced gastric adenocarcinoma. Only one hundred and thirty-nine specimens were included in this study. Macroscopic findings were reviewed for sites, location, and size of tumor. Gross classification of tumors was done following the Borrmann's classification established in 1926.[6] All sections were reviewed for cancer type, degree of differentiation, and features of angiolymphatic invasion, perineurial invasion, depth of tumor invasion and lymph node metastasis. Sections were scored on a visual analogue scale to evaluation of chronic gastritis status, atrophic change, and intestinal metaplasia with subtype. Helicobacter pylori in each location were identified. The resected stomachs were opened along the greater curvature. The sections cut along the lesser and greater curvatures of the stomach in addition to the cancerous area. All sections were processed, embedded in paraffin wax, cut at 4 micron, and stained with a Hematoxylin and Eosin staining, Geimsa staining for *H. pylori*, Mucicarmine staining for mucous, and Alcian blue for highlighted areas of intestinal metaplasia. Tumors were microscopically classified in accordance with the system of Lauren as intestinal carcinoma and diffuse carcinoma[7]. The degree of differentiation of the intestinal type tumors were further subdivided, following the WHO classification[8], into three types (well, moderate and poorly differentiated adenocarcinoma) based on the degree of glandular formation. The extent of local growth and regional and distant spread was done following the UICC TNM Classification[9]. A visual analogue scale graded from 0(absent/normal) to three (mild, moderate and marked intensity) was used to score the presence of *H. pylori*, active inflammation, chronic inflammation and intestinal metaplasia[10]. All sections with intestinal metaplasia were stained with high iron diamine and sub-typed into Types I to III according to the system used by Jas[11,12]. Atrophy was defined as the loss of normal glands and included intestinal metaplasia and /or pseudo-pyloric metaplasia. Pseudo-pyloric metaplasia was identified by the presence of mucosa that was phenotypically antrum and was anatomically in a region where corpus would be expected.

Statistical Analysis

The main objective of the current study was to determine the prevalence of specific gastritis patterns in advanced cases of gastric carcinoma. To answer questions concerning probability and statistical significance, we examined the proportions of cases in each subset within a table were compared by the x^2 test. A p-value of < 0.05 was taken to be significant.

RESULTS

Assessment of location, size, macroscopic type, microscopic cell type and invasive behavior of tumor

Gastric resections were obtained from one hundred and thirty-nine patients with gastric adenocarcinoma. Tumor was found more often in male than female with the ratio of 3:2 and predominantly in the age group of > = 60 years old. (Figure 1) Sites of tumor were localized as esophagogastric junction, cardia, body, antrum and pylorus. Most of the tumors were located in the antrum or the pylorus and on the posterior portion of the lesser curvature in both genders without statistically significant difference. (Figure 2) The macroscopic type of tumor by Borrmann's classification shows 65.9% of ulcerative type, followed by 15% of ulceroproliferative type, 15% of infiltrating type and 4% of fungating type. (Figure 3) The histological pattern of adenocarcinoma was common in the intestinal type (pure adenocarcinoma) by 58.3% and followed by36.7% of the mixed intestinal-diffuse type (adenocarcinoma with signet ring cell transformation). The pure diffuse type or signet ring cell carcinoma was found only 5%. (Figure 4) There was no statistically significant difference between histological pattern, tumor cell differentiation and age-group. In this study, more than 85% of the advanced gastric carcinoma had the tumor size of greater than 2 cm in diameter. According to the size of tumor as less than 2 cm and larger than 2 cm, the angiolymphatic invasion, perineurial invasion and lymph node metastasis were correlated. Lymph node metastasis, angiolymphatic invasion and perineurial invasion were significantly found in the tumor with the size larger than 2 cm in diameter. (Figure 5) In table 1, the invasion of tumor in different macroscopic types was shown. The ulcerative type, ulceroproliferative type and infiltrative type had high incidences approximately over 80% of angiolymphatic invasion, perineurial invasion and lymph node metastasis comparing to fungating type of 60%. (Due to the small number of cases in fungating type, statistical analysis can not be assessed). In all studied cases, the depth of invasion was predominantly found in the subserosal layer and only approximately 20% with omental involvement. In table 2, the invasive behavior of microscopic cell types of tumor show that all the three microscopic cell types had also high incidence of angiolymphatic invasion, perineurial invasion and lymph node metastasis except for the diffuse type that had lower incidence of 42.9% for angiolymphatic invasion. The depth of invasion of tumor assessed by microscopic cell types also show the predominantly invasion into subserosal layer with the average of omental involvement in 25%.

Assessment of chronic gastritis status, Helicobacter pylori infection, atrophic change and intestinal metaplasia.

Chronic gastritis of the non-tumor gastric tissue was found in 91.4% of the cases. Only 26.8% show atrophic change while 73.2% of the tissue was non-atrophic gastritis. (Figure 6) Atrophic change with chronic gastritis was predominantly found in the age-group of > = 60 years old compared to other two age-groups of < 30 years old and 30-60 years old ($p < 0.05$). (Table 3) There was no significant statistically difference in the comparing between macroscopic type of tumor with the atrophic or non-atrophic status of gastritis (Table 4) or microscopic cell type of tumor with the atrophic or non-atrophic status of gastritis. (Table 5) The comparisons also show predominantly chronic non-atrophic gastritis in both macroscopic type of tumor and microscopic cell type of tumor.

Helicobacter pylori infection was found in 36% of the cases without difference in the gender and the age-groups. The most common site of gastric infection by H. pylori was mixed body and antrum (pangastritis). Evidence of focal active glanditis and lymphoid aggregation were common findings. (Table 6) No significant statistically difference in comparing

between microscopic cell types of tumor with *H. pylori* infection was found. (Figure 7)

Intestinal metaplasia was found in 59% of the studied cases. Even though, the low incidence of atrophic gastritis found in this study, intestinal metaplasia was seen in 89.4% accompany with atrophic change comparing to 51.6% in the non-atrophic gastritis. Male was common than female and high incidence in the age-group of > = 60 years old. The site was common in the pan-involvement of antrum and body or the pure antrum site but rare in the pure body site. Complete type (intestinal type or type I) was the most common type by 89.9% and low incidence of incomplete type (type IIa and type IIb) by 6.7% and 3.4% respecitively. (Figure 8)

Table 1. Macroscopic types of tumor with invasive behavior

	Ulcerative type (n = 87)		Fungating type (n = 5)		Ulceroproliferative type (n = 20)		Infiltrating type (n = 20)	
	+	-	+	-	+	-	+	-
Angiolymphatic invasion	82.8%	17.2%	60%	40%	85%	15%	80%	20%
Perineural invasion	82.6%	17.4%	40%	60%	85%	15%	100%	0%
Lymph node involvement	78.1%	21.9%	40%	60%	95%	5%	80%	20%
Depth of invasion								
- mucosa	0%		20%		0%		0%	
- submucosa	2.4%		0%		0%		0%	
- muscular	7.2%		0%		0%		15.8%	
- subserosa	70.2%		60%		72.2%		57.9%	
- omentum	20.2%		20%		27.8%		26.3%	

Table 2. Microscopic cell type of tumor with invasive behavior

	Intestinal type (Adenocarcinoma) (n = 84)		Mixed intestinal and diffuse type (Adenocarcinoma with signet ring cell transformation) (n = 51)		Diffuse type (Signet ring cell carcinoma) (n = 7)	
	+	-	+	-	+	-
Angiolymphatic invasion	87.7%	12.3%	78.4%	21.6%	42.9%	57.1%
Perineural invasion	80.0%	20.0%	92.2%	7.8%	71.4%	28.6%
Lymph node involvement	76.9%	23.1%	85.7%	14.3%	71.4%	28.6%
Depth of invasion						
- mucosa	1.3%		0%		0%	
- submucosa	1.3%		0%		16.7%	
- muscular	7.9%		6%		0%	
- subserosa	65.8%		78%		50.0%	
- omentum	23.7%		16%		33.3%	

Table 3. Chronic gastritis with atrophic change compared with age group

	Chronic gastritis	Chronic gastritis without atrophic change	Chronic gastritis with atrophic change
< 30 years	0%	0%	0%
30 - 60 years	47.2%	52.7%	34%
> = 60 years	52.8%	47.3%	66%

Table 4. Macroscopic type of tumor with atrophic change in chronic gastritis

	Ulcerative type (n = 87)	Fungating type (n = 5)	Ulceroproliferative type (n = 20)	Infiltrating type (n = 20)
Non atrophic chronic gastritis	70.1%	60%	75%	55%
Atrophic chronic gastritis	35.6%	40%	25%	35%

Table 5. Microscopic type of tumor with atrophic change in chronic gastritis

	Intestinal type (Adenocarcinoma) (n = 84)	Mixed intestinal and diffuse type (Adenocarcinoma with signet ring cell transformation) (n = 51)	Diffuse type (Signet ring cell carcinoma) (n = 7)
Non atrophic chronic gastritis	66.7%	64.7%	57.1%
Atrophic chronic gastritis	33.3%	33.3%	28.6%

Table 6. Helicobacter pylori, sex, age group, location and active glanditis and lymphoid aggregation

Helicobacter pylori 36%							
Sex		**Age-group**		**Location**		**Active glanditis and lymphoid aggregation**	
Male	54%	< 30 years	0%	Body	18%	No glanditis	18%
Female	46%	30-60 years	52%	Antrum	12%	With glanditis	82%
		> = 60 years	48%	Body and antrum	70%	With lymphoid	94%

Table 7. Intestinal metaplasia, sex, age group, location and subtype

Intestinal metaplasia 59%							
Sex		**Age-group**		**Location**		**Subtype**	
Male	61%	< 30 years	0%	Body	6.1%	Type I	89.9%
Female	39%	30 - 60 years	32.9%	Antrum	42.7%	Type IIa	6.7%
		> = 60 years	67.1%	Body and antrum	51.2%	Type IIb	3.4%

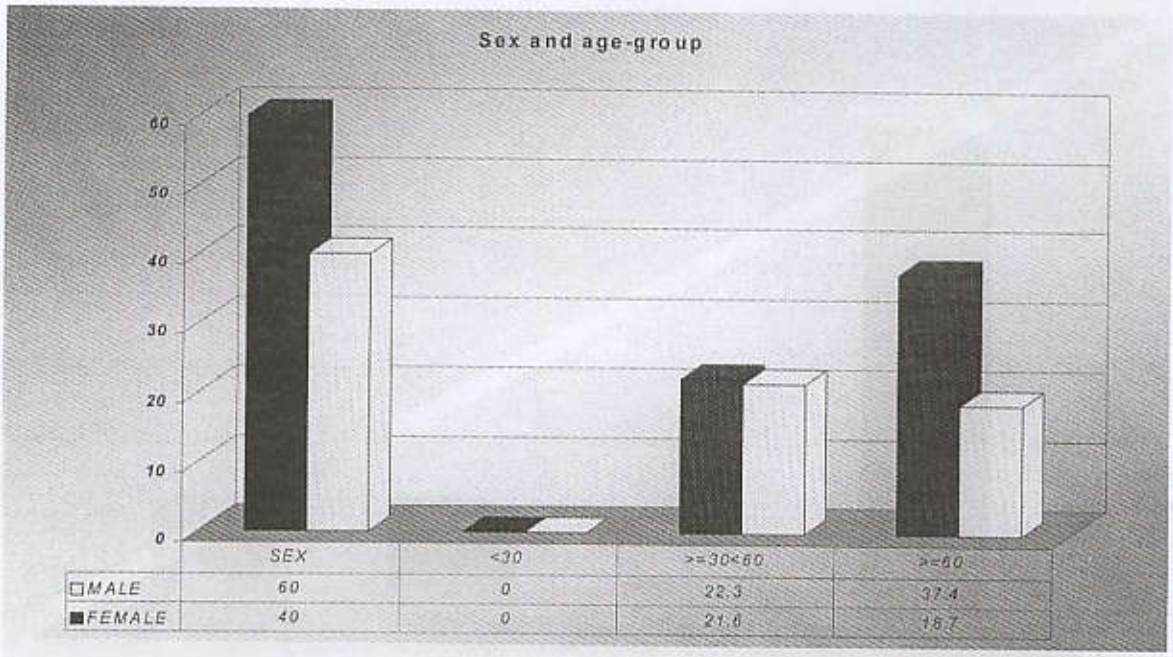

Figure 1. Distribution of sex and age-group.

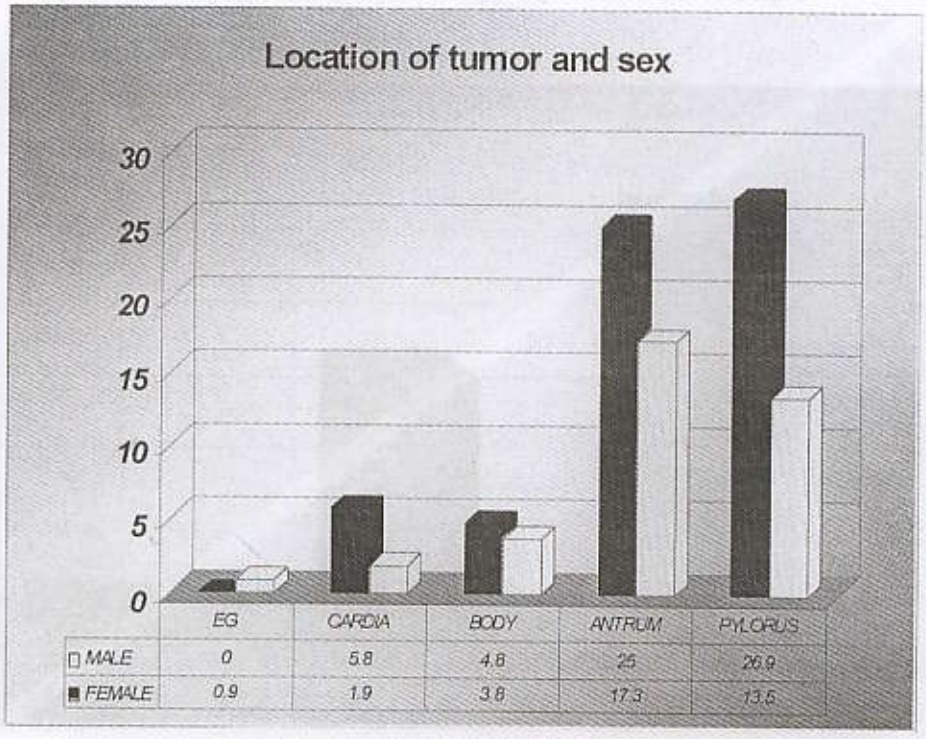

Figure 2. Location of tumor and sex.

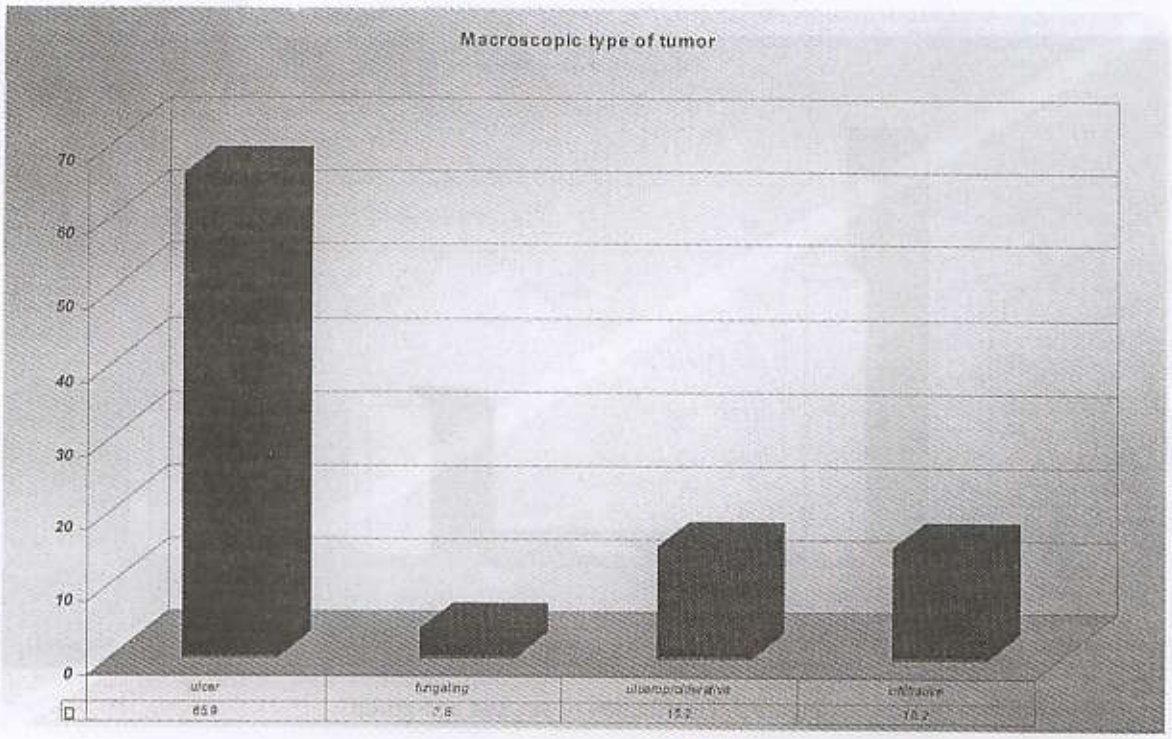

Figure 3. The macroscopic type of tumor by Borrmann's classification.

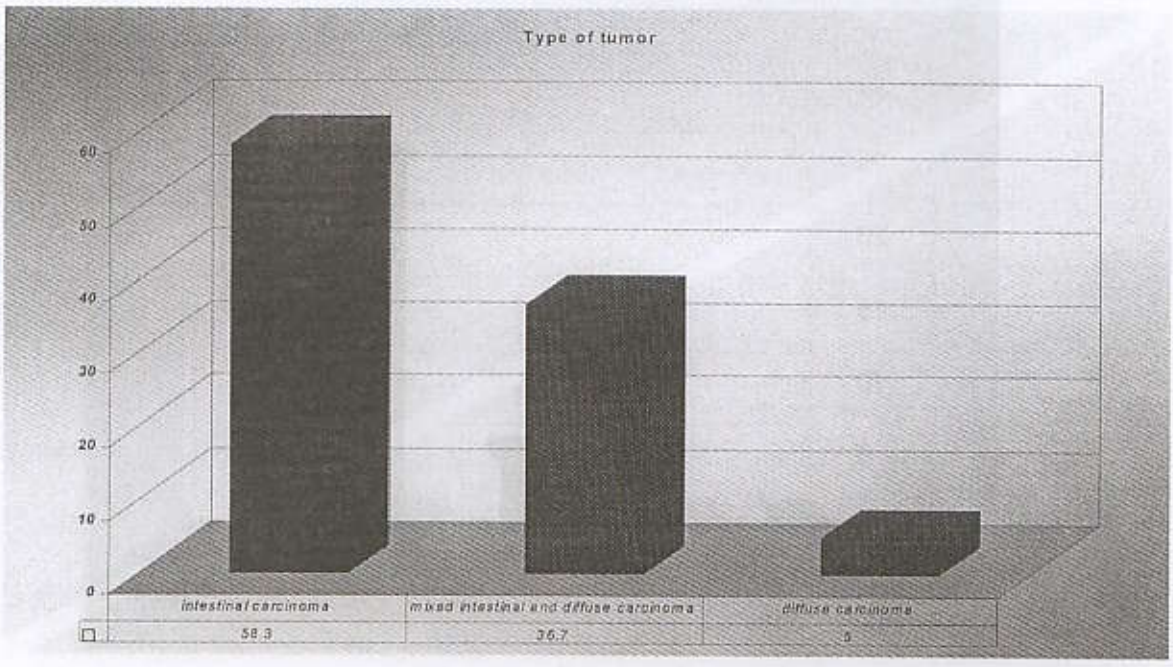

Figure 4. The histological pattern of gastric adenocarcinoma.

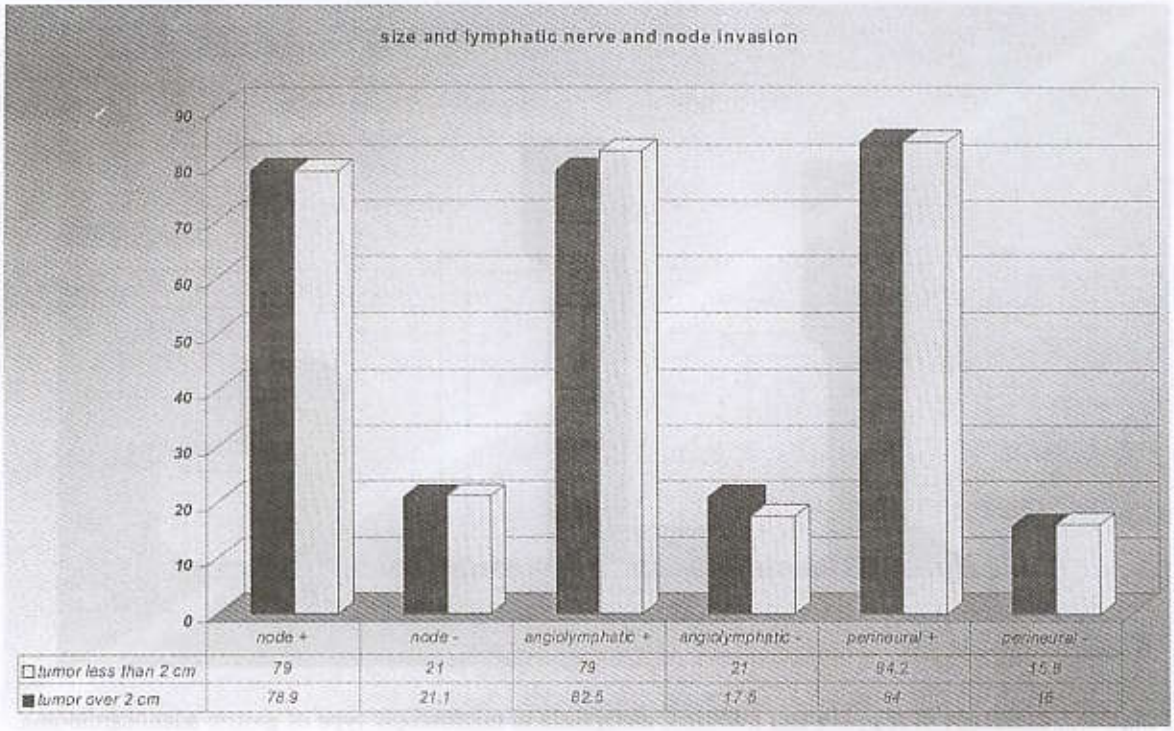

Figure 5. Invasive behavior of gastric adenocarcinoma and size of tumor.

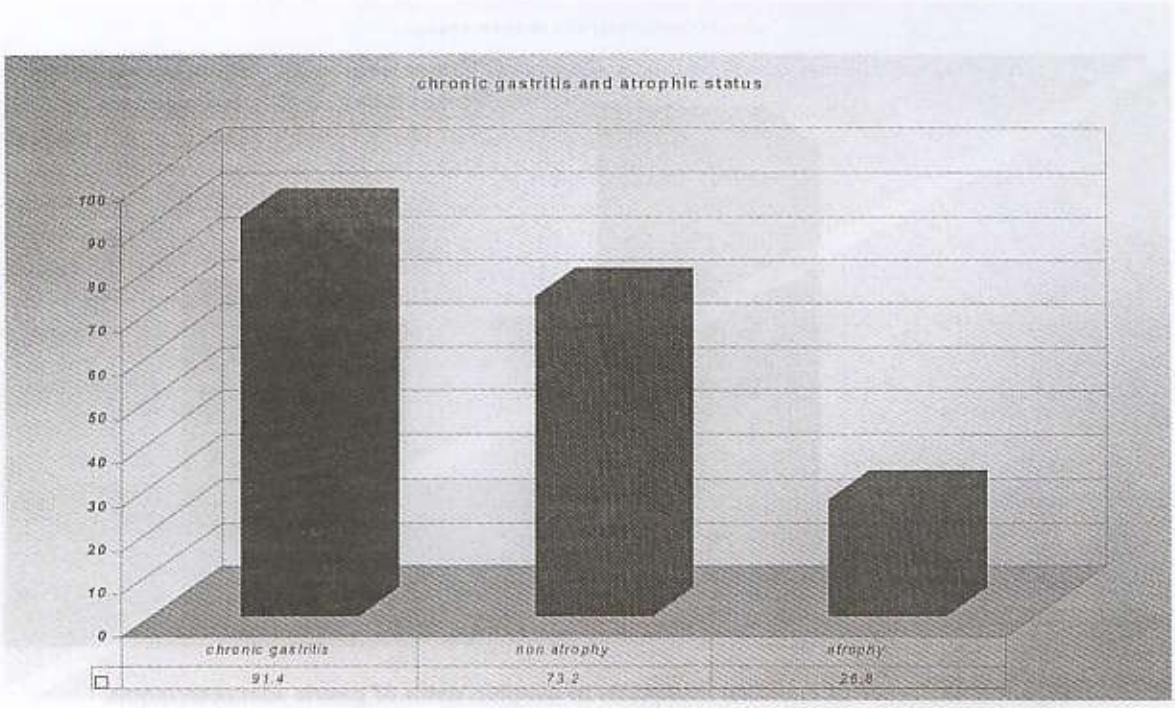

Figure 6. The incidence of chronic gastritis in gastric adenocarcinoma and status of atrophic change.

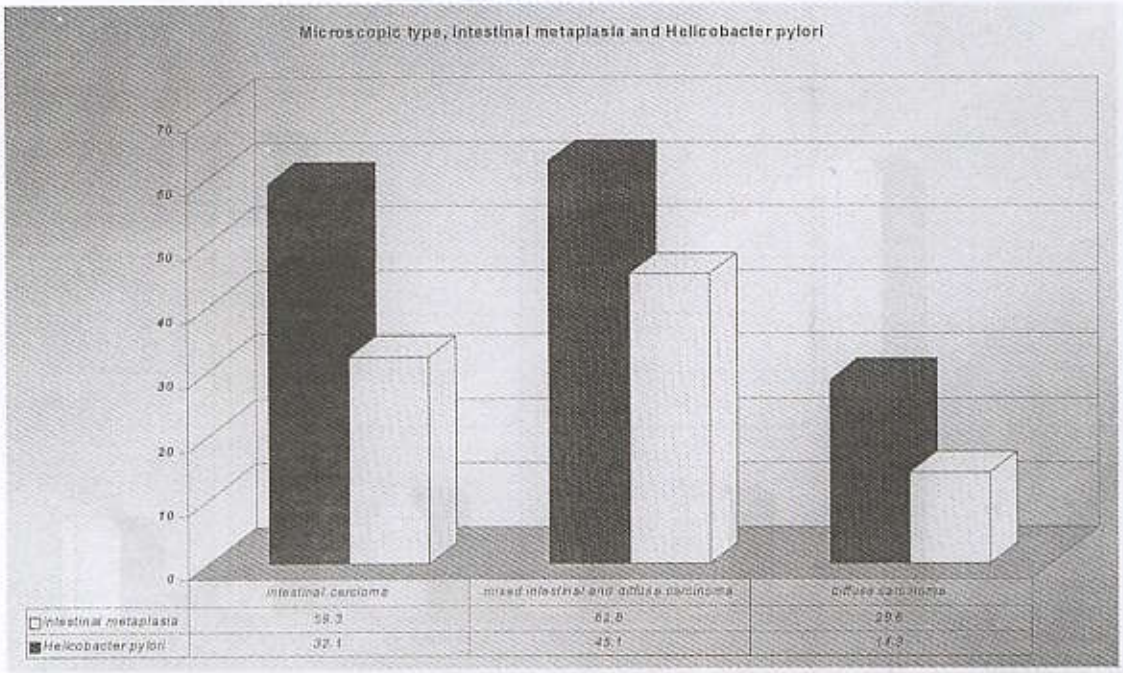

Figure 7. Incidence of *H.pylori* and intestinal metaplasia in microscopic type of gastric adenocarcinoma.

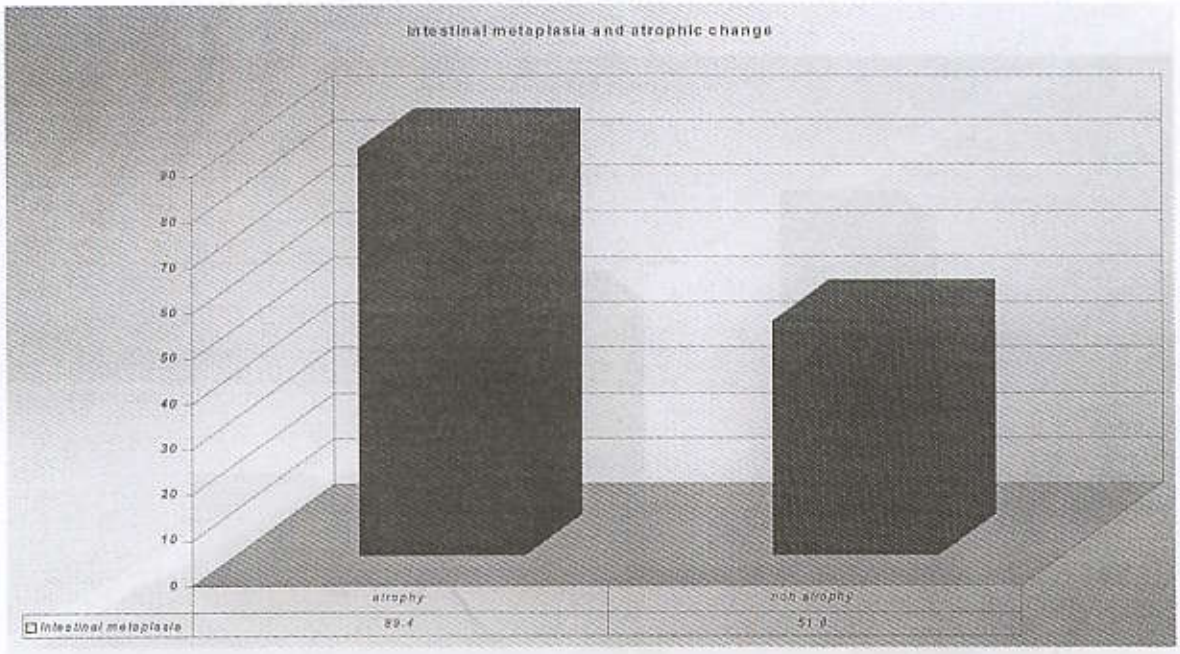

Figure 8. Incidence of intestinal metaplasia in atrophic status of gastric adenocarcinoma.

DISCUSSION

The clinical presentation of gastric cancers in this study was all in the advanced gastric cancer. The age and gender distribution, the site of tumor was corresponding well with the previous study that found mainly in males with increased age, located mostly in the antrum or pylorus and on the posterior portion of lesser curvature[13]. Ulcerative and ulceroproliferative types were the most common macroscopic type of Borrmann's classification was the same finding as in many literatures. The histologic types of gastric adenocarcinoma in this study was commonly with intestinal carcinoma by Lauren's classification or tubular adenocarcinoma by WHO classification and the diffuse carcinoma or signet ring cell carcinoma or poorly differentiated carcinoma was found only 5%. Mixed intestinal and diffuse carcinoma was found 36.7% with predominantly poorly differentiated. The high prevalence of intestinal carcinoma and mixed intestinal carcinoma with signet ring cell transformation was correlated well with the hypothesis of chronic gastritis induced intestinal metaplasia and finally changed into gastric adenocarcinoma. At the time of this study, the tumor-size was over 2 cm in 85.1% of the cases and the majority is in 6-10 cm. We found that the cutting point of tumor-size at 2 cm had no statistically significant difference in the invasive behavior of tumor. The entire tumor with diameter less than 2 cm or over 2 cm in size had the high incidence of the perineural invasion, angiolymphatic invasion and lymph node metastasis. This is contrast to the previous study of Yamao that shows lymph node metastasis depending on the size, the depth of invasion, degree of histological differentiation and lymphatic invasion[14]. In Johansen study, the tumor less than 1 cm in diameter only had a 4 percent likelihood of lymph node metastasis versus 18 percent for tumors larger than 4 cm[15]. The macroscopic types and microscopic types of tumor were also correlated and evaluated with the invasive behavior. Ulcerative, ulceroproliferative and infiltrating types had high incidence of angiolymphatic invasion, perineural invasion and lymph node metastasis and corresponded to the previous study of Hirota that found the frequency of lymph node metastasis increasing in the tumor of ulcerative type[16]. The fungating type had better invasive behavior. Invasive behavior of gastric carcinoma appeared to be related to tumor cell type. We found that the intestinal carcinoma show frequently vascular, lymphatic invasion, perineural invasion and lymph node metastasis. In contrast, the diffuse carcinoma was less common in angiolymphatic invasion. Both intestinal and diffuse carcinoma had high lymph node metastasis. The diffuse carcinoma also had a higher percentage to spread through the wall by direct extension. Most of the tumor invaded into subserosal layer and there was no significant difference in the depth of invasion of tumor comparing with macroscopic types or microscopic cell types.

Pathogenic mechanisms of gastric adenocarcinoma in Thailand have come to be challenge topics due to the country with low incidence of gastric adenocarcinoma (< 5 cases per 100,000 people)[2,3] but high incidence of *H. pylori* associated gastritis.[4,5]

In this country, dietary factors may not be the risk factors due to low salt consumption and high intake of fresh fruits, vegetables comparing with high concentration of salt in dietary soy bean paste and salted fish in Japan.[17] Also herbs, garlic and onions that contain allyl sulfides are main components in most of Thai-foods and have also been documented to inhibit cell proliferation and tumor growth with increased protective effects in gastric cancer.[18] Also adequate intake of fresh fruits and vegetables can lower the risk of gastric carcinoma by increasing antioxidant effects[19]. Salt intake in Thai population is not the traditional culture and may be one factor that lowers the incidence in this country[20]. In the study of Atisook et al[4], a nationwide study of 3,776 dyspeptic patients in Thailand, the infection with *H. pylori* was found 48.2% and appeared to play an important role of gastritis with 98.2% of *H. pylori* associated gastritis.

It seems to be that the hypothesis of gastric cancer in Thailand must have the high incidence and follows the sequential steps of developing gastric carcinoma but it is not. Conversely, the low incidence of gastric atrophy 11.6% and intestinal metaplasia 8.2% were found. We have previously shown in this study that chronic gastritis was found 91.4% accompany with the gastric adenocarcinoma and

only 26.8% show atrophic change. The incidence of atrophic change and intestinal metaplasia increased number with increasing age. The incidence of intestinal metaplasia found in the cases with atrophic change was high as 89.4% but the subtype of intestinal metaplasia was predominantly the complete type (type I or mature type) of intestinal type that was known to have low risk of malignant change.[21] Why was the atrophic change not common finding in this study? Is there anything that block or prevent the process of atrophic change? Does the high intake of fresh fruits and vegetables really decrease the process of atrophic change?

Macroscopic types of tumor of tumor were not changed the incidence of atrophic or non-atrophic gastritis and there was no statistically significant difference in this study. Also in the correlation between microscopic types of tumor with atrophic change, there was no significant difference. All had high incidence with non-atrophic gastritis but not atrophic gastritis.

Even the role of Helicobacter pylori and the pathogenesis of gastritis are clearly understood but for the gastric carcinoma, it is not a causal relationship. In many previous studies of epidemiologic association between *H. pylori* and gastric cancer, they found a number of contradictory findings which complicate the role of *H.pylori* in the etiology of gastric carcinoma and these are the same findings in our study[22,23,24]. In our study, gastric carcinoma found in a small number of cases infected with *H.pylori* (36%) with low incidence of atrophic change and intestinal metaplasia.

In conclusion, the pattern and distribution of the advanced gastric carcinoma in Thailand found to be the same as the national behavior of usual gastric carcinoma. The current hypothesis of gastric cancer in this country is believed to follow by the high incidence of gastritis with high *H. pylori* infection. Atrophic change and intestinal metaplasia may be blocked or prevented by dietary factors of excessive fresh fruits, vegetables and low salt intake. Thus, *H. pylori* is not insufficient to give rise to gastric carcinoma but many other cofactors or predisposing conditions must play a role in the etiology and pathogenesis of gastric carcinoma in Thailand.

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