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PREVALENCE, MACROSCOPIC AND MICROSCOPIC FEATURES IN GASTRIC CANCER- A RETROSPECTIVE STUDY

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SUMMARY:
This study wanted to assess the prevalence of gastric cancer (GC) among the patients who underwent upper digestive endoscopy (UDE) in a four years period, as well as some features regarding this disease. ***Material and methods****: We examined 14,348 pts, from which 404 were diagnosed with GC. In all cases we performed biopsies. Results: Sex ratio M:F was 3:1. 56% were living in the countryside. The prevalence was higher between the ages of 60-70 years. In½ of the cases the tumors were localized in the antrum. 61% were tubular adenocarcinomas, mostly weakly differentiated. 27% were signet cell carcinomas with minimal endoscopic changes. Conclusion: The importance of UDE in the diagnose of GC, the need of more modern techniques that makes the diagnose of early forms easier, implementation of screening strategies, the need of change in dietary habits.*

Key Words: *Gastric cancer, endoscopy, histology, diet*

PREVALENTA, TRĂSĂTURILE MACROSCOPICE ŞI MICROSCOPICE ÎN CANCERUL GASTRIC - STUDIU RETROSPECTIV

Rezumat*:*
Acest studiul stabileşte prevalenţa cancerului gastric (GC) printre pacenţii care au fost supuşi endoscopiei digestive superioare într-o perioada de 4 ani şi deasemenea câteva caracteristici ale acestei boli. ***Material şi metode****: Am examinat 14 348 de pacenţi dintre care 404 au fost diagnosticaţi cu cancer gastric. În toate cazurile s-au efectuat biopsii.* ***Rezultate:*** *Raportul bărbţi femie a fost 3:1; 56% dintre pacenţi proveneau din mediul rural; prevalenţa a fost mai ridicată în decada de vârstă 60-70 ani. În jumatate dintre cazuri tumorile au fost localizate în antrul gastric, 61% au fost adenocarcinoame tubulare majoritatea slab diferenţiate, 27% au fost carcinoame cu celule în pecete, cu modificări minime vizibile endoscopic.* ***Concluzii:*** *În urma acestui studiu s-au ajuns la următoarele concluzii: importanţa endoscopiei digestive superioare în diagnosticul cancerului gastric; nevoia unor tehnici tot mai moderne care faciliteaza un diagnostic mai uşor în formele incipiente ale tumorii; implementarea unor strategii de screening; nevoia de a schimba unele obiceiuri alimentare.*

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According to the National Cancer Institute (NCI), approximately 760,000 cases of stomach cancer are diagnosed worldwide and more than 24,000 cases are diagnosed in the United States each year. Incidence is highest in Japan, South America, Eastern Europe, and parts of the Middle East. Worldwide, stomach cancer is the second leading cause of cancer-related deaths.[15, 19]

Stomach cancer occurs twice as often in men and is more common in people over the age of 55. In the United States, incidence is higher in African Americans than in Caucasians.

Changes in diet and food preparation have led to a recent decrease in the incidence of cancer of the lower stomach (distal gastric cancer). However, incidence of cancer of the upper stomach (proximal gastric cancer) has increased, primarily as a result of the prevalence of obesity and gastroesophageal reflux disease (GERD).[20]

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Several factors are implicated in the development of gastric cancer, including diet, Helicobacter pylori infection, previous gastric surgery, pernicious anemia, adenomatous polyps, chronic atrophic gastritis, prior radiation exposure or inherited syndromes. Gastric cancer may often be multifactorial involving both inherited predisposition and environmental factors.· (5)

- Diet (2, 4)
  - A diet rich in pickled vegetables, salted fish, excessive dietary salt, and smoked meats correlates with an increased incidence of gastric cancer.
  - A diet that includes fruits and vegetables rich in vitamin C may have a protective effect.
- Smoking (10)
  - Smoking is associated with an increased incidence of stomach cancer in a dose-dependent manner, both for number of cigarettes and duration of smoking.
  - Smoking increases the risk of cardiac and noncardiac forms of stomach cancer. Cessation of smoking reduces the risk.
  - A meta-analysis of 40 studies estimated that the risk was increased by approximately 1.5- to 1.6-fold and was higher in men.[**5**]
- Helicobacter pylori infection (6)
  - Chronic bacterial infection with H pylori is the strongest risk factor for stomach cancer.
  - *H pylori* may infect 50% of the world's population, but much less than 5% of infected individuals develop cancer. It may be that only a particular strain of H pylori, one of which is capable of producing the greatest amount of inflammation, is especially associated with the risk of malignancy. The full malignant transformation of affected parts of the stomach may require that the human host have a particular genotype of interleukin-Ibeta to cause the increased inflammation and an increased suppression of gastric acid secretion.
  - H pylori infection is associated with chronic atrophic gastritis, and patients with a history of prolonged gastritis have a 6-fold increase in their risk of developing gastric cancer. Interestingly, this association is particularly strong for tumors located in the antrum, body, and fundus of the stomach but does not seem to hold for tumors originating in the cardia.[**6**]
- Previous gastric surgery
  - Previous surgery is implicated as a risk factor. The rationale is that surgery alters the normal pH of the stomach, which may in turn lead to metaplastic and dysplastic changes in luminal cells.[**7**]
  - Retrospective studies demonstrate that a small percentage of patients who undergo gastric polyp removal have evidence of invasive carcinoma within the polyp. This discovery has led some researchers to conclude that polyps might represent premalignant conditions.
- Genetic factors (1, 13)
  - Some 10% of stomach cancer cases are familial in origin.
  - Genetic factors involved in gastric cancer remain poorly understood, though specific mutations have been identified in a subset of gastric cancer patients. For example, germ-line truncating mutations of the E-cadherin gene are detected in 50% of diffuse-type gastric cancers and families that harbor these mutations have an autosomal dominant pattern of inheritance with a very high penetrance.[**8**]
  - Other hereditary syndromes with a predisposition for stomach cancer include hereditary nonpolyposis colorectal cancer, Li-Fraumeni syndrome, familial adenomatous polyposis, and Peutz-Jeghers syndrome.
  - Ebstein-Barr virus: The Epstein-Barr virus may be associated with an unusual form of stomach cancer (<1%), lymphoepitheliomalike carcinoma.
  - Pernicious anemia: Pernicious anemia associated with advanced atrophic gastritis and intrinsic factor deficiency is a risk factor for gastric carcinoma.
- Gastric ulcers
  - Gastric cancer may develop in the remaining portion of the stomach following a partial gastrectomy for gastric ulcer.
  - Benign gastric ulcers may themselves develop into malignancy.
- Obesity: Obesity increases the risk of gastric cardiac cancer.
- Radiation exposure: Atomic bomb survivors exposed to radiation have had an increased risk of stomach cancer. Other populations exposed to radiation may also have an increased risk of stomach cancer.

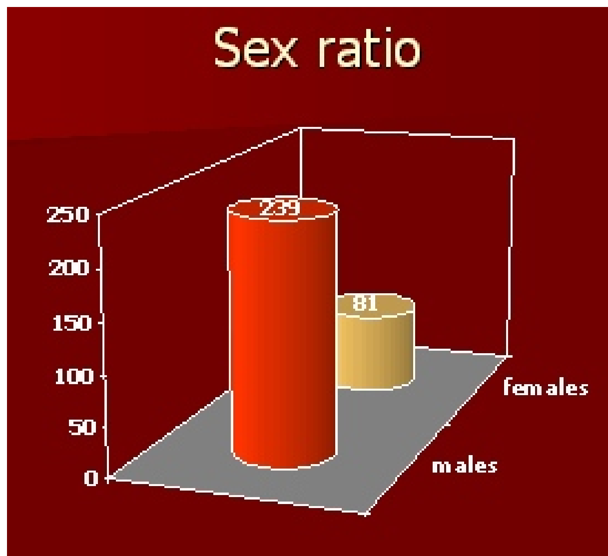

Fig. 1

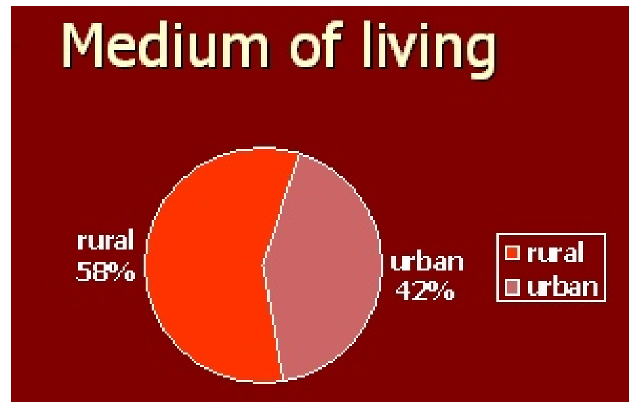

Fig. 2

AIM OF STUDY

In this study we wanted to assess the prevalence of gastric cancer (GC), upon patients who underwent upper digestive endoscopy (UDE), in a period of five years – January 2003- December 2007- in the digestive endoscopy laboratory of the Mures County Universitary Hospital , Romania. We also analyzed the macroscopic and microscopic features, sex ratio, age, medium of life for all these patients (pts).

MATERIAL AND METHODS

In the above mentioned period, 14,348 pts were referred for UDE. Among these we diagnosed 404 with gastric cancer. In all cases we performed biopsies, analyzed in the pathology laboratory. In our endoscopy unit pts from central part of Romania are routinely referred.

RESULTS

The prevalence of males was 73.26% which leads to a sex ratio M: F of 3:1 compared to most of the studies in which the ratio is 2:1. (fig. 1) [16]

56% of the pts were living at countryside while the rest of 42% were of urban provenience (fig.2)

Most of the cases of GC are discovered between the ages of 60 and 70. In our study, age ranges between 20 to 87 are covered with a high prevalence in the 7th decade, and 1 case below 19 years old. (fig.3)

Regarding the location of the lesions usually ½ are localized in the antrum, ¼ in fundical region while the other ¼ invades both these regions. In our study, the location of the lesions was as in figure 4. [17]

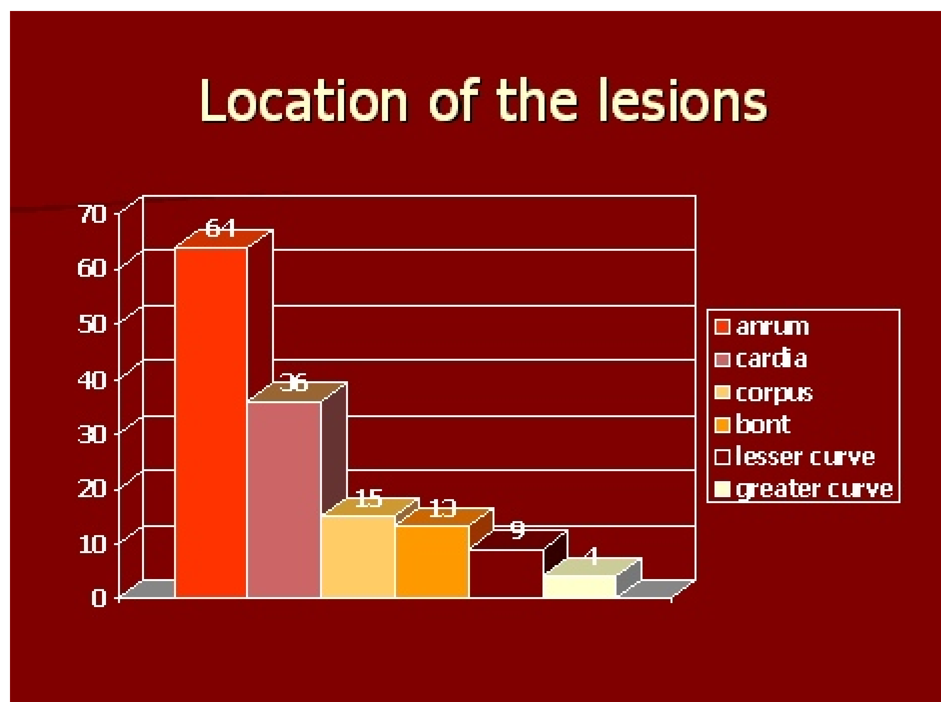

Fig. 3

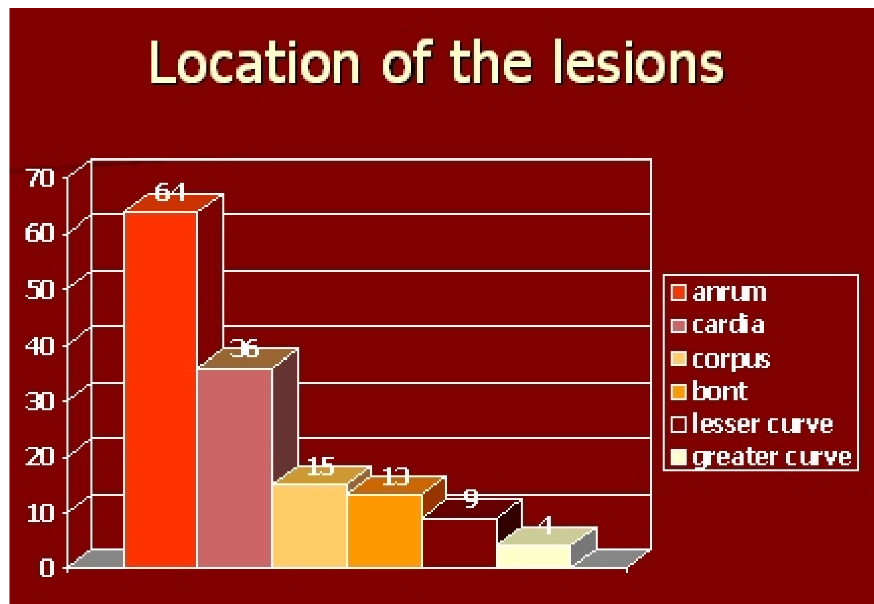

Fig. 4

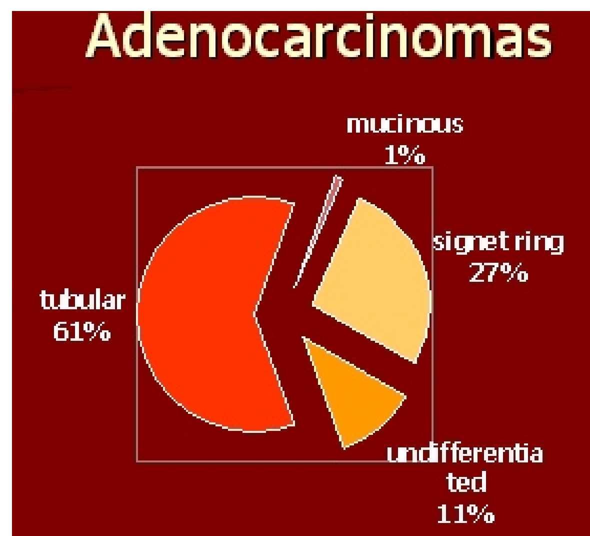

Fig.5

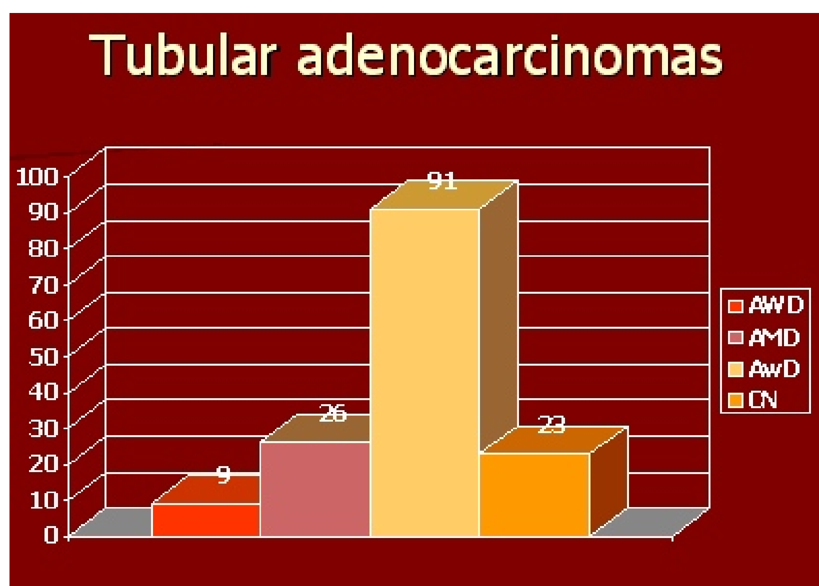

Fig. 6 AWD-well differentiated, AMD- medium, AwD- weakly, CN- undifferentiated

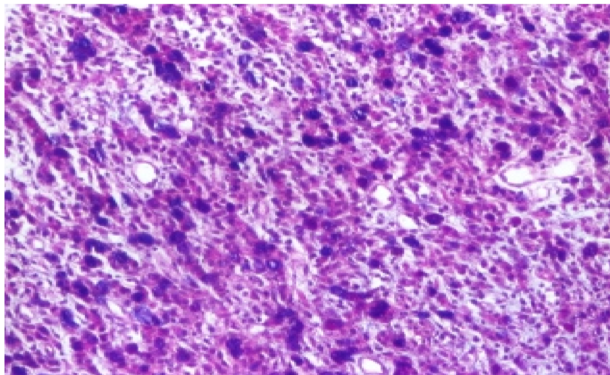

Fig. 7. Signet cell carcinoma

Histological aspects in our study showed the predominance of tubular adenocarcinomas. (fig 5)

Among tubular adenocarcinomas, the weakly differentiated were predominant.

A particular attention should be given to the cases of signet-cell carcinoma in our study. From all the cases, 55, (27%) of patients were diagnosed with this aggressive type. All of them were under 55 years and what was more interesting and also very important in not skipping the diagnose was the fact that the endoscopic features were equivocal, with minimal lesions, small and superficial ulcerations or small areas of hyperemia, suggesting benign lesions. [8, 14]

DISCUSSION

Adenocarcinoma of the stomach is subclassified according to histologic description as follows: tubular, papillary, mucinous, or signet-ring cells, and undifferentiated lesions. [11, 9]

Pathology specimens are also classified by gross appearance. In general, researchers consider gastric cancers ulcerative, polypoid, scirrhous (ie, diffuse linitis plastica), superficial spreading, multicentric, or Barrett ectopic adenocarcinoma..

Researchers also employ a variety of other classification schemes. The Lauren system classifies gastric cancer pathology as either Type I (intestinal) or Type II (diffuse). An appealing feature of classifying patients according to the Lauren system is that the descriptive pathologic entities have clinically relevant differences.

Intestinal, expansive, epidemic-type gastric cancer is associated with chronic atrophic gastritis, retained glandular structure, little invasiveness, and a sharp margin. The pathologic presentation classified as epidemic by the Lauren system is associated with most environmental risk factors, carries a better prognosis, and shows no familial history.

The second type, diffuse, infiltrative, endemic cancer, consists of scattered cell clusters with poor differentiation and dangerously deceptive margins. Margins that appear clear to the operating surgeon and examining pathologist often are determined retrospectively to be involved. The endemic-type tumor invades large areas of the stomach. This type of tumor is also not recognizably influenced by environment or diet, is more virulent in women, and occurs more often in relatively young patients. This pathologic entity is associated with genetic factors (such as E-cadherin), blood groups, and a family history of gastric cancer. [12]

CONCLUSIONS

Diagnosing forms of early gastric cancer remains a goal to achieve, which implies a better medical education among pts and physicians and nevertheless the use of modern endoscopic techniques such as magnification, chromoendoscopy, narrow band imaging and probably conphocal microscopy.

We consider that the great number of advanced gastric cancer in our study is the result of still poor/ medium social-economic conditions and medical education in our geographic region.

A special attention is to be accorded to signet cell carcinomas, that occur at young age and have equivocal endoscopic features, often suggesting a benign disease.

The fact that most of our cases had an antral location, make these cases easier to diagnose and with a better outcome. The prevalence of antral located tumors can probably be explained by the dietary habits in this part of the country, with salted and smoked meat products. Cigarette smoking was also frequent among the pts. [3, 10, 17]

Nevertheless we want to emphasize the importance of upper digestive endoscopy in the diagnosis of gastric cancer.

The necessity of implementing strategies for the diagnose of high grade dysplasias and early gastric cancers.

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