Original Paper

Gastric Cancer in Gorj County - a Clinical-Statistical Study

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ABSTRACT: Gastric cancer (GC) is the fourth most common cause of cancer death worldwide, with about 769,000 deaths/year worldwide. Recent studies showed a continuous decrease in the incidence and mortality of gastric cancer mainly in developed countries, while the incidence remains increased in some countries in Eastern Asia and Eastern Europe. For the assessment of some parameters of gastric cancer in Gorj county, all the medical records of patients diagnosed with gastric cancer, found in the Archive of the County Emergency Hospital of Tg Jiu, were analyzed, namely the admission records within the Surgery and Oncology departments, the observation sheets of every individual patient, the biological test reports, the histopathological records of the patients with gastric cancer undergoing surgery, the histopathological records of gastric biopsies, the medical imaging records (ultrasound, x-ray, computer tomography and magnetic resonance). The analysis of the medical records showed that the disease mainly affects men, the ratio of men/women being 2/1-3/1. Most cases undergoing surgery within the County Hospital of Tg. Jiu were diagnosed in stages III or IV. The most numerous cases (over 85% of the total group of patients) were identified in people over 61 years old. The most common histopathological form of cancer was adenocarcinoma (95% of all gastric tumors).

KEYWORDS: Gastric cancer, incidence, adenocarcinomas, risk factors, Helicobacter pylori.

Introduction

Gastric cancer (GC) is the fourth most common cause of cancer death worldwide.

In 2020, more than one million cases of gastric cancer were diagnosed worldwide and more than 769,000 deaths of the same cause were recorded [1,2].

The prevalence of gastric cancer varies by geographic area and ethnicity, with a much higher prevalence in Eastern Asia and Eastern European countries.

In all populations and countries, gastric cancer is very rare in adults aged <50 years old.

Gastric cancer incidence rates increase with age and reach a plateau between the ages of 55 and 80 [3].

In recent years, the worldwide incidence rates of gastric cancer were approximately 15.7 in 100,000 men and 7.0 in 100,000 women [4].

Mortality rates in 2018 were 11.7 in 100,000 men and 5.2 in 100,000 women.

Globally, the lifetime risk of gastric cancer (0-74 years) is about 1 in 54 men and about 1 in 126 women [3].

Gastric cancer was the main cause of cancer death in the world until the 1980s, when it was exceeded by lung cancer.

This change was due to both the increasing incidence of lung cancer and the decreased gastric cancer incidence.

There was a steady decline in gastric cancer incidence and mortality rates since the mid 20th century in developed countries (North America, Northern Europe, Australia).

In recent years, downward trends were observed in areas with previous high gastric cancer incidence ratios (Japan, Korea).

However, gastric cancer maintains a high case fatality rate of 75% in most of the world and is a major contributor to the global financial burden on health systems [5].

Recent studies examining global trends in gastric cancer incidence and mortality confirmed a continuous decrease in this pathology worldwide [6,7].

10.12865/CHSJ.49.03.06

Geographically, over 60% of all gastric cancer cases in 2018 occurred in East and Southeast Asia.

In the present study, we aimed at assessing patients diagnosed with gastric cancer, found in the records of the Oncology Department within the County Hospital of Tg. Jiu and highlight their particularities regarding sex, age, risk factors, etc.

Material and Methods

In our study, we analyzed all the medical records of patients diagnosed with gastric cancer, found in the Archive of the County Emergency Hospital of Tg. Jiu, respectively the admission records within the Surgery and Oncology departments, the observation sheets of every individual patient, the biological test reports, the histopathological records of patients with gastric cancer undergoing surgery, the histopathological records of gastric biopsies, the medical imaging records (ultrasound, radiological, computer tomographic and magnetic resonance).

All selected data from medical records were inserted into Microsoft Excel tables for a more practical process of analysis.

All investigations were performed with the approval of the management of the County Hospital of Tg. Jiu. 2 groups of gastric cancer patients were identified:

-group I-patients who were diagnosed with gastric cancer and were admitted within the Surgery Department of the Emergency County Hospital of Tg. Jiu, where they underwent surgery, hospitalized between
2017-2021;

-group II-patients with gastric cancer undergoing treatment within the Oncology Department in the County Emergency Hospital of Tg. Jiu.

Results

Study of the group of patients with gastric cancer admitted and treated within the Surgery Department of the Emergency County Hospital of Tg. Jiu

Between 2017-2021, within the Surgery Department of the County Emergency Hospital of Tg. Jiu, there were admitted and operated a number of 147 patients, with a number of 27-32 patients every year.

Of these, 109 (74.15%) were men, and 38 (25.85%) women, the ratio of men/women being 3/1.

Most cases were recorded in 2018 (32 cases), with the smallest number in 2020 (27 patients).

The ratio between men and women was maintained over the entire period of 5 years of the study, being about 3/1 (Figures 1 and 2).

Most cases admitted and operated within the County Emergency Hospital of Tg. Jiu represented medical emergencies, clinically manifested by upper digestive tract hemorrhages, respectively as hematemesis and melena.

Anamnesis revealed the fact that the majority of patients presented several digestive symptoms long before admission, but they were of low intensity and ignored by the patient.

The most common clinical signs were postprandial bloating, nausea, pyrosis, early satiety, increased weight loss, marked asthenia, hematemesis and melena.

The diagnosis of gastric cancer was established on the basis of the clinical, biological, imaging examination (gastric examination with contrast substance, lung x-rays, computer tomography) and gastroscopic examination.

Biological tests showed that almost all patients were infected with Helicobacter pilory bacteria.

In 56 patients (38%), the presence of anemia (mild, moderate or severe) was found with hemoglobin values below 12g/dl.

Because of this, several patients needed pre-and postoperative blood transfusion.

The relatively small number of patients with gastric cancer operated within the hospital of Tg. Jiu is due to the fact that some of them chose to go to other surgery clinics in the country (Craiova, Timișoara, Bucharest, Sibiu, Cluj-Napoca, etc).

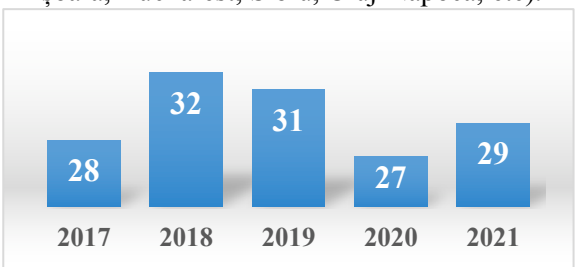

Figure 1. Gastric cancer cases admitted and operated within the County Hospital of Tg. Jiu between 2017-2021.

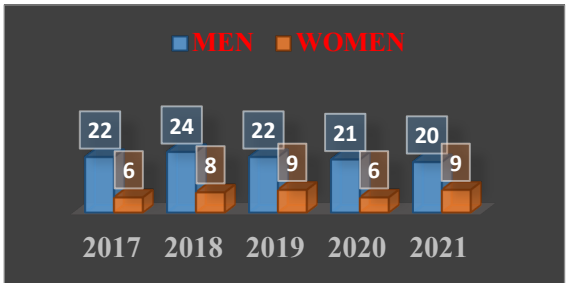

Figure 2. The distribution of new cases of gastric cancer admitted and operated within the Surgery Department in the County Hospital of Tg. Jiu by year and sex.

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Study of the group of patients with gastric cancer recorded within the Oncology Department of Tg. Jiu

In our study, we assessed the entire group of patients with gastric cancer, found in the records of the Oncology Department of the County Hospital of Tg. Jiu, at the end of 2021, to issue some results, as accurate as possible.

It is well known that gastric cancer is one of the most severe cancers of the digestive tract, and surgical resection is one of the best treatment methods, especially for cases that can be curatively resected.

According to oncological protocols, at present, most patients can obtain a good prognosis through a complex treatment on surgery, radiotherapy, chemotherapy and adjuvant immunotherapy.

However, dispensary and careful follow-up of patients with gastric cancer, through the oncology network and through the GP, is necessary, because due to tumor heterogeneity, some patients are prone to relapses or metastases after surgery.

As we can see in Table 1, a number of 403 patients with gastric cancer, operated and treated with chemotherapy, were registered in the records of the Oncology Department.

Of these, 260 patients, representing 65%, were male, and 143, representing 35%, were female.

From the analysis of the medical records related to risk factors, we observed that most patients had previously been infected with Helicobacter pylori, and 38 (9.43%) stated that they were alcohol and tobacco users.

Comparing the two sexes, it was observed that men were mainly heavy drinkers and chronic smokers.

Table 1. Total number of gastric cancer cases recorded within the Oncology Department of Tg. Jiu at the end of 2021.

TOTAL of PATIENTS	MEN	WOMEN
403 (100%)	260 (65%)	143 (35%)

The gastric tumors, as found during the intraoperative macroscopic evaluation, had a different localization.

Thus, the most frequent localization was at the level of the gastric body (162 cases) and at the level of the upper pole of the stomach, namely at the level of the fornix (160 cases).

The 2 localizations had a total number of 322 cases, i.e. 79.51% of the entire group of.

Cancer with cardial localization was highlighted only in 60 cases, i.e. about 15% of the total group, while the antral cancer had a total number of only 11 cases, i.e. less than 3% of the entire group.

Gastric cancer with multiple localizations (synchronous cancer) had a total number of only 10 cases, i.e. about 2.5% of our entire group (Figure 3).

The localization of gastric cancer also provides information on the pathophysiological mechanisms that occur during tumorigenesis.

It seems that the main risk factors (Helicobacter pylori, smoking, alcohol, smoked foods, etc.) act predominantly on the gastric mucosa at the level of the gastric body and fornix, generating atrophic gastritis, hypochlorhydria, chronic inflammation and finally dysplasia and neoplasia.

Gastric cancer at onset is characterized by the progressive reduction of hydrochloric acid producing oxyntic cells; subsequently, the whole mucosa is invaded by neoplastic cells with the formation of a totally different tumor micro environment from the normal gastric mucosa.

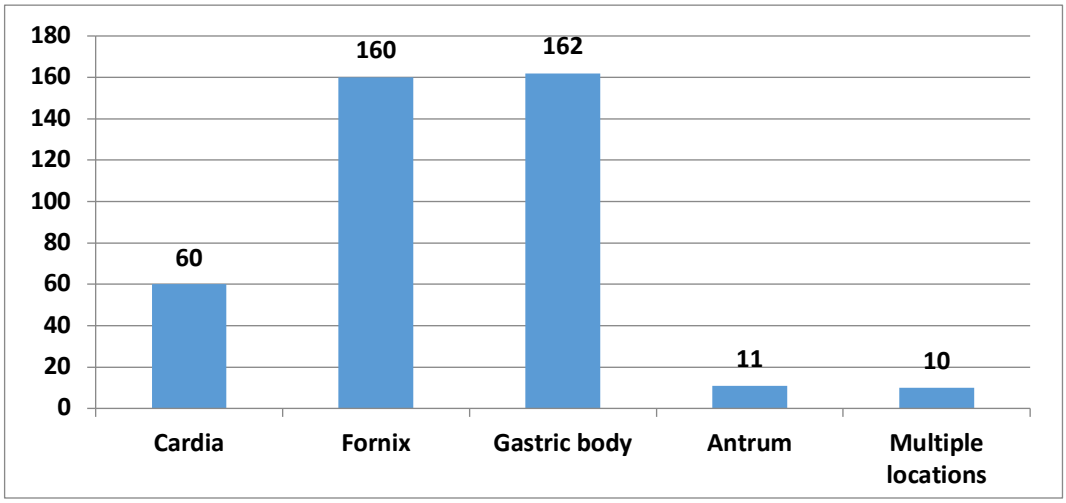

Figure 3. Anatomical localization of gastric cancer in patients from the records of the Oncology Department of Tg. Jiu.

The histopathological examinations on the surgical pieces showed that, out of the 403 cases of gastric tumors, the vast majority were represented by gastric adenocarcinomas, more or less differentiated (Figures 4 and 5); among men, there were recorded 246 adenocarcinomas, while only 136 adenocarcinomas were recorded in women. In total, in the records of the Oncology Department of Tg. Jiu, during the study, there were recorded, under treatment and monitoring, a number of 382 patients with gastric adenocarcinomas, which represents almost 95% of all patients.

Gastric lymphoma, known as the second most common gastric malignant tumor, in our study, was found only in 9 patients (6 men and 3 women), which represents about 2.2% of the total group.

Also, the ratio 2/1 between men and women was preserved.

Other types of gastric tumors with a low incidence, recorded in our group, were gastric stromal tumors (GIST), adenoacanthomas and squamous cell carcinomas.

All these histopathological types summed up only 12 cases, which represents below 3% of the total studied group (Table 2, Figure 6).

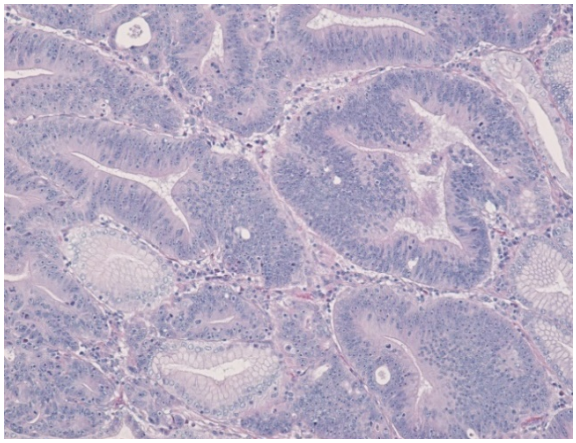

Figure 4. Well-differentiated gastric adenocarcinoma. HE staining x 100.

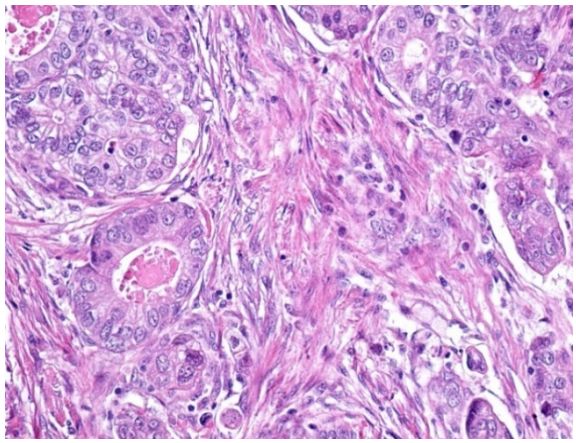

Figure 5. Moderately differentiated gastric adenocarcinoma. HE staining x 200.

Table 2. Histopathological types of tumors in patients recorded with in the Oncology Department of the County Hospital of Tg. Jiu.

	Adenocarcinoma	Lymphoma	Stromal tumor GIST	Adenoacanthoma	Squamous cell carcinoma
Men	246	6	4	2	2
Women	136	3	3	1	0
Total	**382**	**9**	**7**	**3**	**2**

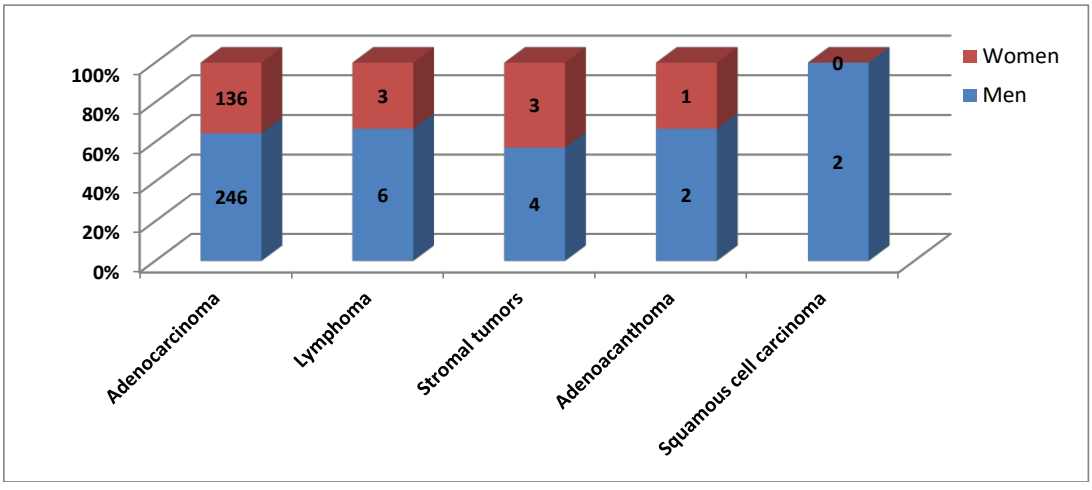

Figure 6. Graphic representation of histopathological types of gastric cancer in the studied group.

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Knowing that one of the risk factors in cancer is age, we performed an analysis of the age of gastric cancer patients from the Oncology Department within the County Hospital of Tg. Jiu.

As it can be seen from Figure 7, the incidence of gastric cancer increased with age; if, before the age of 40, few cases of gastric cancer were recorded (only 24), after the age of 60 the incidence of gastric cancer increased 6-7 times.

In our study, we found that the number of patients with gastric neoplasia after the age of 61 represents over 85% of the entire group of patients (Figure 7).

That is why we believe that people over 60 years old require a special medical program for early detection and treatment of gastric cancer.

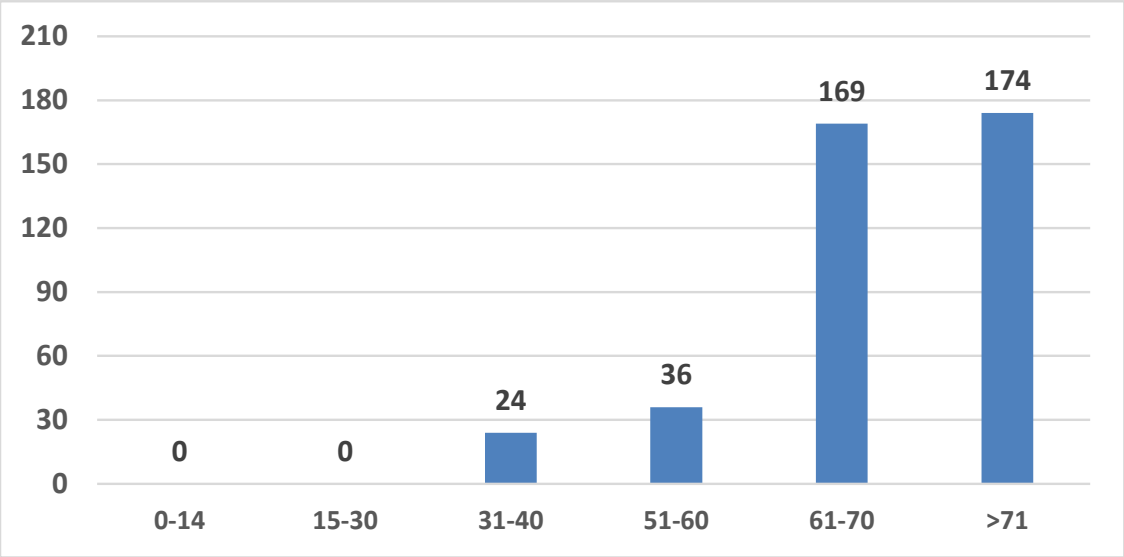

Figure 7. Age group distribution of gastric cancer patients.

Discussion

Although the incidence and mortality of gastric cancer highly decreased in the last 70 years, especially in Western countries, it still remains an important health problem worldwide; in 2000, about 880,000 people were diagnosed with gastric cancer and about 650 000 died due to the disease [8].

Gastric cancer is a multifactorial disease. Most frequently, gastric cancers are sporadic and their occurrence is believed to be due to the progressive accumulation of genotypic and phenotypic changes in the mucosa stem cells, most often triggered by chronic gastritis caused by infection with *Helicobacter pylori* (HP) [9,10].

In our study, we observed that the majority of patients with gastric cancer declared that they were infected with *H. pylori* but, from the medical records attached to their oncological monitoring and follow-up record, this was not specified.

It is possible that some medical documents were not attached to the oncological monitoring records.

We make these clarifications because a previous study, carried out in the same geographical area on a number of 1525 of patients with gastric pathology, showed that 63.67% of them were infected with HP [11].

In 1994, the International Agency for Cancer Research (IARC) acknowledged that *H. Pylori* infection is a type I carcinogenic risk factor.

It is thought that *H. Pylori* infection is responsible for more than 75 % of all antral gastric cancers, and furthermore, it is associated with both intestinal and diffuse histopathologies; the association of HP infection with proximal carcinomas could not be fully demonstrated.

HP infection is thought to induce carcinogenesis in the antral area or at the level of the gastric angle, from where it progresses to the gastric body, and in advanced forms, may progress to the level of the fornix [13].

H. pylori is a spiral, Gram-negative bacterium endowed with a variety of pathophysiological mechanisms that allow the germ to colonize the gastric mucosa and also to alter the immune response of the host [14].

The infection is usually acquired in childhood and can persist for decades unless treated and the bacteria eradicated.

The exact mechanisms behind the transmission of the bacteria are still unknown, but it is believed to be passed from one person to another through saliva.

HP infection is also thought to be the most commonly found chronic bacterial infection through the world [8].

Countries with high incidence of gastric cancer have also a high prevalence of H pylori infection, and the decline of *H pylori* prevalence in developed countries is linked to a decline in gastric cancer incidence.

H pylori infection is usually acquired during early childhood, most probably through oral ingestion, and the infection persists throughout the life of the patient.

Prevalence is tightly bound to socio-economic key factors such as low income, poor education, poor hygienic conditions, as well as overcrowding [15,16].

A close association between chronic *H pylori* infection and the development of gastric cancer is now a well proved fact.

In Correa's model of gastric carcinogenesis, *H pylori* infection is thought to trigger the progressive sequence of gastric lesions from chronic gastritis, gastric atrophy, intestinal metaplasia, dysplasia, and, in the end, gastric adenocarcinoma.

Relevant case-control studies showed significant associations between *H pylori* serological positivity and the risk of developing gastric cancer, with an approximately 2.1-to 16.7-fold increased risk compared with non-infected cases [17,18].

Prospective studies also support the idea of a strong association between *H pylori* infection and the risk of gastric cancer.

The most convincing proof of the tight connection between *H pylori* and gastric cancer originates with a prospective study on 1.526 Japanese participants, where it was found that gastric cancer developed in 2.9% of infected persons, but in none of the uninfected individuals [19].

Interestingly, gastric carcinomas were detected in 4.7% of *H pylori*-infected individuals with non-ulcer dyspepsia.

The risk of developing gastric cancer is amplified if the infection harbors a more virulent *H Pylori* strain that bears the gene Associated Cytotoxin (*cagA*) [20].

Compared to the *cagA*-strain, infection with *H Pylori cagA*+strain was associated with an increased risk for aggressive atrophic gastritis and distal gastric cancer [21].

It is essential to mention that, in Western countries, about 60% of *H pylori* isolated strains are *cagA*+, while in Japan, almost 100% of the strains possess the cytotoxin *cagA*+ [22].

Host-related factors associated with an increased risk of gastric cancer include also carrier genetic polymorphisms that lead to a higher expression of proinflammatory cytokines [23].

In our study, we noticed that in some medical records (clinical observation sheets, referral letters, hospital discharge letter) there were also data on the consumption of toxic substances (alcohol, tobacco).

Unfortunately, the number of patients with gastric cancer and the consumption of toxic substances could not be accurately determined.

Only 38 patients (9.43% of the whole group) declared that they were consumers of toxic substances (alcohol and tobacco).

Commonly, patients avoid taking responsibility for the consumption of toxic substances.

We brought up the consumption of toxic substances because some of them are incriminated as risk factors in the etiopathogenesis of gastric cancer.

Tobacco smoking is considered a risk factor for gastritis, ulcers, but also for gastric cancers. Some studies showed that tobacco is incriminated in up to 18% of cancer cases and there is evidence that there is an intense interaction between tobacco smoking, *H. Pylori* and gastric cancer [24].

A major role in cancer is also played by food.

Among the diet-related factors, it was found out that a high salt intake is associated with a higher risk of gastric cancer, mainly in combination with *H. Pylori* infection.

Many case-control studies found a clear-cut positive association between intake of salted fish, salted meat, salted vegetables, and the development of gastric cancer, and this association was more recently confirmed by a systematic review of the available epidemiological literature data [25,26].

Diets rich in meat have also been thought as a risk factor for the Europe population.

More studies showed that there is a clear-cut correlation between meat intake and the development of distal gastric cancer; this

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association was discovered higher for subjects infected with *H. Pylori* [27].

Foods preserved with salt and dietary nitrites, sometimes found in abundance in canned meat, are potentially carcinogenic.

Salt-induced mucosa lesions may increase the possibility of persistent *H pylori* infection [28], and N-nitroso compounds formed in the human stomach from dietary nitrites are shown to be carcinogenic in animal experiments [29].

In the etiopathogenesis of gastric cancer there are also factors related to the individual (host).

Thus, the risk of gastric cancer was associated with numerous genetic polymorphisms, mainly with the one that leads to genes related to inflammation (for example, IL1B, IL1RN, IL10 and TNF).

The risk of developing gastric cancer is 2-10 folds higher for subjects with a family history of gastric cancer [27].

Gastric cancer also develops as part of familial cancer syndromes, such as hereditary diffuse gastric cancer syndrome, familial adenomatous polyposis, Lynch syndrome, Peutz-Jeghers syndrome, and Li-Fraumeni syndrome [30,31].

Another risk factor identified by us, involved in gastric cancer, was age.

Of the 403 patients with gastric cancer, from the records of the Oncology Department of the County Hospital of Tg. Jiu, 343 patients (85%) were over 60 years old.

Our data confirm other studies showing that, overall, the incidence of cancer increases with age [32].

Regarding the gender of gastric cancer patients, in our study we found that 65% of patients were male and 35% female.

In general, the prevalence of gastric cancer is twice as high in men compared to women and varies geographically, with a much higher prevalence found in some Eastern Asian and Eastern European countries [1,2].

We, like other authors, found that most cases of gastric cancer were diagnosed late, in stages III and IV, when clinical signs of cancer complications occured.

According to some studies, diagnosing the disease in advanced stages will have a weak therapeutic result [33,34].

We believe that the early diagnosis of gastric cancer is the gold standard for the management of all types of cancer.

In this sense, we mention that "Japanese guidelines for gastric cancer screening" recommended routine endoscopic screening every 2 years, for people over 50 years old.

Conclusions

Gastric cancer represents a public health problem for healthcare services in Gorj County, due to the large number of cases on record and treatment.

The disease predominantly affects men, with a male/female ratio of 2/1-3/1.

The most numerous cases (over 85% of the entire group of patients) were identified in people over 61 years old.

The most common histopathological form of cancer was adenocarcinoma (95% of all gastric tumors).

Conflict of interests

None to declare.

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10.12865/CHSJ.49.03.06