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Original Research Paper

Characterization of Gastric Malignancies and the Trend of Gastric Carcinoma. A Study of (155) Cases between 2008-2013 in Duhok City-Iraq.

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Background and Objectives: *Gastric cancer is one of the common human malignancies particularly gastric adenocarcinoma. The stomach also represents the commonest gastrointestinal site for extra-nodal non-Hodgkin's lymphoma. This study aims to find out the major types of gastric malignancies in Duhok city, their age and gender distribution and the trend of the types of gastric adenocarcinoma over a six year period from January 2008 till December 2013.*

Methods: *This study included nearly all cases of gastric malignancies diagnosed in Duhok City and enrolled 155 cases. The type of malignancy was diagnosed by histopathological examination and supported in some cases by immunohistochemical staining procedures and investigations. The trend of the two major types of gastric carcinoma was determined over this six year period.*

Results: *The results of this study showed that the carcinoma constitutes the largest proportion of gastric malignancies (87.7%), followed by lymphoma (6.5%) and then Gastrointestinal stromal tumor (GIST) (4.2%) and lastly neuroendocrine tumors (1.3%). The mean age of the intestinal type (62.1 years) was higher than that of the diffuse type (50.15 years) and the difference was statistically significant ($P < 0.05$). Similarly the diffuse type was more common in women than men and also the difference was statistically significant ($P < 0.05$). The results of this study show that the trend of intestinal type over a six year period is on the rise side while the trend of the diffuse type is more or less the same.*

Conclusions: *Gastric carcinoma is the most common gastric malignancy in the Duhok City with a male predominance and most patients had some bad prognostic factors and there is no decline in the prevalence of the intestinal type.*

Keywords: Gastric, Carcinoma, Lymphoma, Gastrointestinal stromal tumor, Malignancy

INTRODUCTION

Although the incidence of gastric cancer in the United States has been decreasing, gastric cancer is still the fourth most common malignancy and the second leading cause of cancer-related death worldwide. Most patients with gastric cancer present with advanced stage disease with an overall survival of approximately 20%. Despite the improvements of treatment modalities in recent years, the 5-year survival is still dismal which remains less than 30% [1].

Gastric cancer incidence has markedly decreased in some countries, such as United States but it remains high in others such as Japan and Iran. It is the first leading cause of cancer-related deaths in men, and the second one among women in Iran [2]. Gastric cancer is rare before the age of 40, but its incidence steadily climbs thereafter and peaks in the seventh decade of life [3]. Gastric carcinoma in the young when compared with older patients was found to be different in the

high proportion of females, the frequency of the diffuse, signet ring, and infiltrating histological types, and the infrequency of associated gastritis and intestinal metaplasia [4].

Adenocarcinoma is the most common malignancy of the stomach, comprising over 90-95% of all gastric cancers. Early symptoms resemble those of chronic gastritis, including dyspepsia, dysphagia, and nausea. As a result, these tumors are often discovered in advanced stages, when symptoms such as weight loss, anorexia, altered bowel habits, anemia, and hemorrhage trigger further diagnostic evaluation [5,6].

There are several histological classification systems, but the most frequently used worldwide is the Laurén classification. Other widely used systems include that of the World Health Organization (WHO) and the classification of the Japanese Gastric Cancer Association. The Laurén classification recognizes two main histological types: intestinal and diffuse, which present differences in clinical and epidemiological characteristics. A small percentage of adenocarcinomas is mixed, presenting features of both types [6]. The 2010 WHO classification recognizes four major histologic patterns of gastric cancers: tubular, papillary, mucinous and poorly cohesive (including signet ring cell carcinoma), plus uncommon histologic variants [7].

Primary gastric lymphomas are defined as lymphomas originating from the stomach and contiguous lymph nodes. Lymphomas at this site are considered primary if the main bulk of disease is located in the stomach. The majority of gastric lymphomas is high-grade B-cell lymphomas, some of which have developed through a progression from low-grade lymphomas of mucosa associated lymphoid tissue (MALT) [8].

Approximately 40% of all non-Hodgkin lymphomas arise at extranodal sites, with the gastrointestinal tract, as the commonest extranodal site, accounting for about 4-18% of all non-Hodgkin lymphomas in Western countries and up to 25% of cases in the Middle East. Within the gastrointestinal tract, the stomach is the most frequent site of involvement in Western countries, while the small intestine is most frequently affected in Middle Eastern countries [8].

This study aims to:

1. Find out the histopathological types of malignant gastric tumors.
2. Find the age and gender distribution of these tumors.
3. Study the trend of gastric carcinoma in the period between 2008-2013.

PATIENTS AND METHODS

This study included nearly all gastric cancer patients in Duhok city from January 2008 till December 2013. Gastric cancer cases were collected from the Central laboratory and the main private laboratories in the city. It was put into consideration that a minority of patients may be missed because the attend clinics and hospitals outside Duhok City and a similar minority was patients who were residents in other cities but they consulted doctors in Duhok city. However, both minorities seemed not to influence the results significantly.

Both gastric endoscopic biopsies and gastrectomy specimens were studied and patients were classified according to their gender and age. The gross appearance of the tumor was noted in addition to its location within the stomach.

Histological types of cancer were determined by histopathological examination of tissue sections and undifferentiated malignancies were further investigated by immunohistochemical markers. Immunohistological markers

used included carcinoma markers, lymphoma markers, GIST markers and markers for neuroendocrine tumors (Pankeratin, Carcinoembryonic antigen, CD 117, CD 34, Actin, S-100 protein, CD 45, CD 20, CD 30, CD 3, Cycline D1, CD56 and chromogranin). Of course, the use of immunohistochemical markers was individualized according to the case. Special stains like PAS and PASD were also used for a limited number of cases.

For gastrectomy cases, the surgical margins, the lymphovascular structures and the lymph nodes were sought and carefully examined for the presence of tumor cells. The peritoneum, liver, spleen and ovaries were also searched for metastases when these organs or part of them were included in the surgical specimens.

The trend of the major histopathological types of gastric carcinoma was determined over the years 2008 till 2013.

RESULTS

The present study included (91) gastric endoscopic biopsies and (64) gastrectomy specimens (Total of 155 cases). The youngest patient was (21) years age and the oldest was (93) years age. The mean age was (60.27) years. Fourteen patients (9%) were below 40 years age, (10) of them had diffuse type gastric carcinoma, two with mixed type and another two with intestinal type. Figure (1) shows the age distribution of the enrolled patients. Out of the (155) patients; (90) were males and (65) were females with a male to female ratio of (1.38: 1) and figure (2) shows the gender distribution.

Carcinomas constitute the largest category (136) cases (87.7%) followed by lymphomas (10) cases (6.5%), GIST (7) cases (4.5%) and neuroendocrine tumors (2) cases (1.3%). Table (1) shows the final diagnoses of all the included patients. The carcinoma group includes intestinal type (84) cases, diffuse type (40) cases, mixed type (7) cases, mucinous carcinoma (3) cases, tubular carcinoma (1) case and one case was an early gastric carcinoma in adenomatous polyp. Table (2) shows the number of cases of each type by the year from 2008 till 2013 and figure (3) shows the trend of the intestinal type and the diffuse type over those years. Comparing the mean age for the intestinal type (62.1 years) and that of diffuse signet ring type (50.15 years), the difference was statistically significant (p value: < 0.05). Similarly, when the gender is considered the signet ring carcinoma was found to be more common in females (p value: < 0.05).

Regarding the location of carcinoma with the stomach, (9.6%) (13) cases are in the cardia, (3.7%) (5) cases in the fundus, (26.5%) (36) cases in the body, (45.6%) (62) cases in the pylorus and antrum and the rest (14.7%) (20) cases involved wide area of the stomach extensively (Figure 4). Considering the grade of carcinoma, only two cases were well differentiated intestinal type, (40) cases were moderately differentiated intestinal type and (42) cases were poorly differentiated intestinal type.

There were (64) gastrectomy specimens. Lymph node metastases were detected in (30) cases, the surgical margin was involved in (9) cases, evidences of lymphovascular invasion and perineural invasion were detected in (20) and (2) cases respectively.

Regarding GIST patients, (5) were males and two were females with a mean age of (67.14) years. The lymphoma patients were (10), nine of them had diffuse large B- cell lymphoma and one had MALToma. Regarding their gender, (4) were males and (6) were females. The mean age for lymphoma cases was (60.9) years.

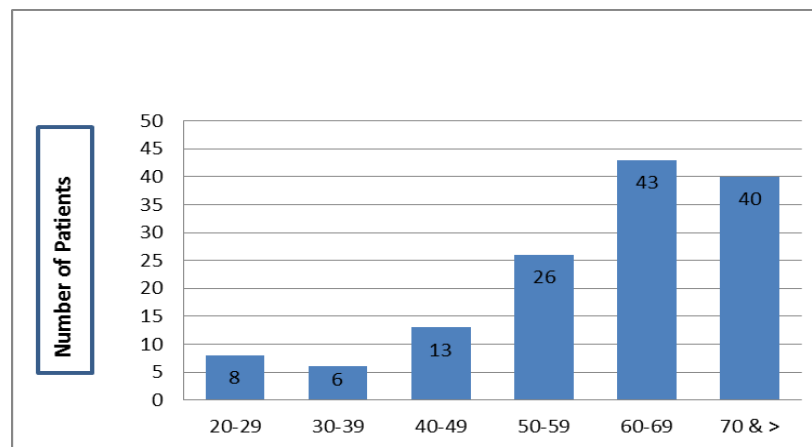


Figure 1: The age group of the included (155) patients

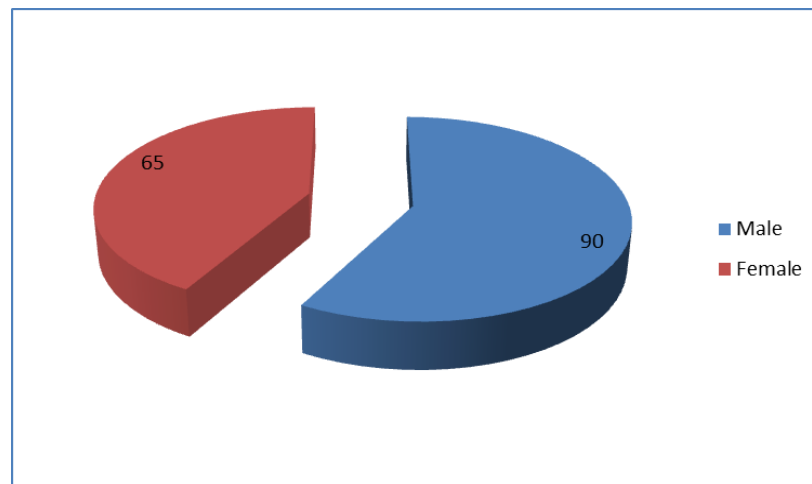


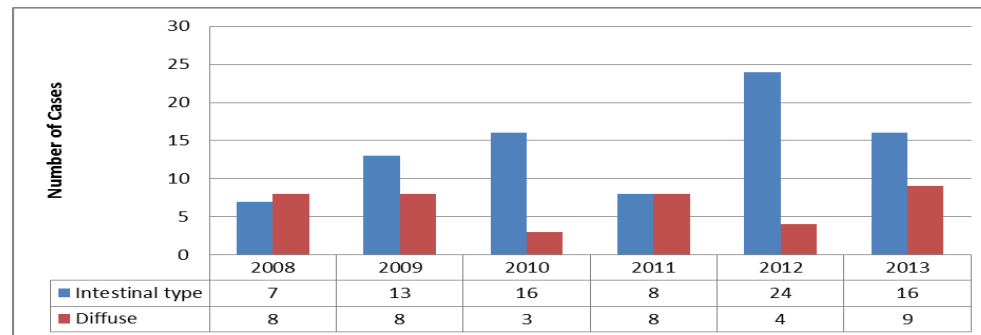
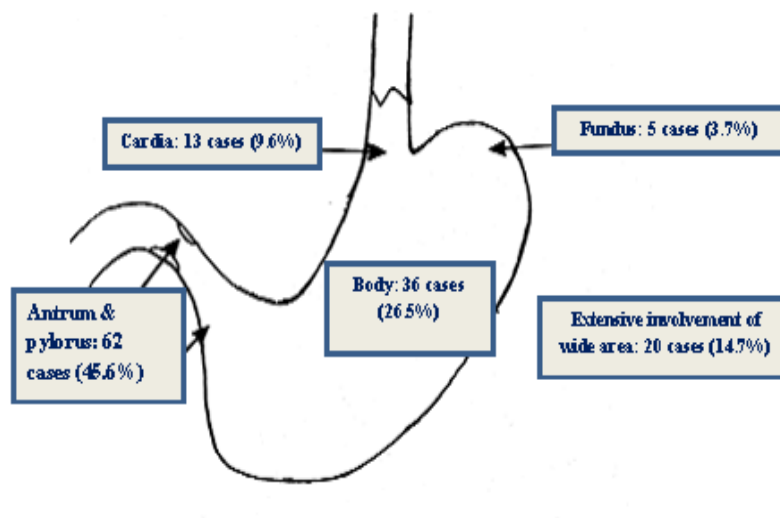
Figure 2: The gender of the included patients

Table 1: The final diagnoses of all included patients.

Category	Subcategory	Number	Percentage
Carcinoma	Intestinal type	84	54.2
	Diffuse	40	25.8
	Mixed	7	4.51
	Mucinous	3	1.94
	Tubular	1	0.65
	Early gastric carcinoma in adenomatous polyp	1	0.65
Lymphoma	Diffuse large B-Cell lymphoma	9	5.8
	MALT	1	0.65
GIST		7	4.5
Neuroendocrine tumor	Low grade	1	0.65
	High grade	1	0.65
Total		155	100%

Table 2: The types of carcinoma over the period from 2008-2013.

	2008	2009	2010	2011	2012	2013	Total
Intestinal type	7	13	16	8	24	16	84
Mixed	1	1	2	1	0	2	7
Diffuse	8	8	3	8	4	9	40
Mucinous	1		1	1			3
Tubular				1			1
Early gastric carcinoma in adenomatous poly					1		1
Total	17	22	22	19	29	27	136

**Figure 3:** The trend of diffuse and intestinal types of gastric carcinomas from 2008-2013**Figure 4:** The distribution of carcinoma cases within the stomach.

DISCUSSION

Gastric cancer incidence and mortality has fallen dramatically over the last 50 years in many regions, but remains the second most common cancer worldwide [9]. In Duhok City- according to the statistics of directory of health (DOH) - gastric cancer ranks 7th among other malignancies in 2013. This statistical finding was obtained from the oncology department in Azady Teaching Hospital, which enrolled only those patients who required post-operative chemotherapy and represents a clear underestimate of the true rates of gastric cancer.

This study is the largest one conducted in Duhok City concerning this issue. It included nearly all patients with gastric malignancies over a six year period. The results of this study are not different from what was reported worldwide in that gastric carcinoma is the commonest type of gastric malignancies [10, 11] and in the present work it represents (87.7%) of all gastric malignancies. The male predominance is also reported by others [11, 12, 13, 14] and in this study; there is a male to female ratio of (1.38:1). This ratio reflects the results of high exposure to carcinogens in male including smoking, dietary habits and probably higher incidence of *H. pylori*. Concerning the age factor, the mean age for the diffuse type was (50.15 years) significantly lower than the mean age of the intestinal type (62.1 years) and also the diffuse type was more common in women, in addition, for the age group below (40 years), there was a more diffuse type (6 cases) than the intestinal type (2) cases. These differences in the age and gender distribution was noted by Luren himself and documented by others [4, 15]. The explanation for these differences is that these two types of cancer develop through different mechanisms, while the intestinal type is more related to environmental factors like dietary factors, lifestyle and *H. pylori* infection; the diffuse type is more linked to genetic factors.

The results of this study show that the trend of intestinal type over a six year period is on the rise side – or at least there is no decline - while trend of the diffuse type is more or less the same. This is different from what was reported by Hamilton and Aaltonen, who mentioned that there is a steady decline in the incidence and mortality rates of gastric carcinoma worldwide over the past several decades and that analysis of time trends by histological types indicates that the incidence decline results from a decline in the intestinal type of carcinoma [8]. Probably, the rise – or non-decline -of intestinal type in Duhok region is the result of dietary habits, high prevalence of *H. pylori* and high rate of smokers among our population.

Many of the included patients had some factors that influence the prognosis adversely (20 cases with extensive involvement of the stomach, 40 cases of the diffuse type, 42 cases of poorly differentiated intestinal type, 30 cases with lymph node metastases and 20 cases with lymphovascular invasion). This finding can be easily explained by the fact that most gastric cancers are discovered late, in addition to the absence of screening or preventive strategies in our locality. The lack of early symptoms often delays the diagnosis of gastric cancer. Consequently, 80- 90% of Western patients with gastric cancers present to the physician with advanced tumors that have poor rates of curability. In Japan, where gastric cancer is common, the government has encouraged mass screening of the adult population for this tumor. Approximately 80% of gastric malignancies detected by such screening programs are early gastric cancers. However, many individuals do not choose to participate in these screening

programs, and consequently only approximately 50% of all gastric cancers in Japan are diagnosed at an early stage [8]. The results of this study clearly highlight our deficiencies in the preventive and diagnostic strategies of early gastric cancer in the sense that all the included patients -but one- had advanced or invasive gastric carcinoma, while early gastric cancer represents approximately 20% of all newly diagnosed cancers in the United States and up to 60% in Japan and South Korea [16].

Location wise, the results of the present work demonstrated that more than two thirds of cases involved the body and the distal part of the stomach and this is in great consistence with what was reported from Japan [17, 18] and India [19].

CONCLUSION

1. Gastric carcinoma is the most common gastric malignancy in Duhok City.
2. Males are affected more than females.
3. The majority of patients have bad prognostic factors.
4. There is no decline in the prevalence of the intestinal type.

RECOMMENDATIONS

1. A preventative strategy needs to be setup to reduce the incidence of gastric cancer by searching for risk factors like *H. pylori* and mass education to change the dietary and lifestyle habits.
2. Early diagnostic procedures, including screening endoscopy should be considered especially for high risk groups.

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