

## Audit of advanced gastric cancer at Ibn Sina Hospital, Khartoum, Sudan Khalid Alsir *FSMSB*<sup>1</sup>, A magid M Masaad, *FRCSP*<sup>2</sup>. MAM Ibnouf, *FRCSEd*<sup>3</sup>, Mohd Abdelhameid, *MD*<sup>4</sup>

**Background:** Worldwide, gastric cancer is the second most common cancer (second to lung cancer). In Sudan incidence and prevalence are not clear because of absence of National Cancer Registry.

**Aim:** To find out the frequency of the gastric mesenchymal tumours, whether gender and age influences the clinico-pathological features of gastric cancer and to audit the outcome of management of advanced gastric cancer at Ibn Sina Hospital.

**Methods:** This is a retrospective study in 139 gastric cancer patients admitted from May 1997 through November 2004. Demographic data, details of the clinical, endoscopic features of gastric cancer, as well as the operative details, and histopathology, the post-operative complication, and hospital mortality were analysed. Available data on family history of cancer; smoking and alcohol consumption was also collected.

**Results:** Mesenchymal tumours account for 15(10.9%) of all gastric cancer. Lymphoma alone constituted 5.8% while leiomyosarcoma constituted 4.4%. Hospital mortality rate was zero%, 2.8%, and 3.6% in distal subtotal, proximal subtotal and total gastrectomy respectively. Hospital mortality was 18 (12.9%) patients.

Age and sex have no significance on the clinicopathological features of advanced gastric cancer.

There is no perfect National Cancer Registry in Sudan. Environmental factors, dietary change, increased awareness and improvement in roads might have increased the influx of cancer patients for treatment.

Radioactive material whether buried or originally present in soil with spread of this radiation through the deep waters or by direct pollution of the environment, and canned food aid, during the long years of drought and civil war, potassium bromide, dioxin, and some organophosphorous compounds used in agriculture as fertilizers, insecticides and pesticides may have increased the magnitude of cancer. Extensive epidemiological studies are urgently needed to find out the effect of high salt consumption in salted fish (Fasikh and Malouha, and Kagiak) and starchy (rice), pickled, and smoked foods (Probably Salat and Shia); and low caloric, low fresh fruits and fresh vegetables intake, drinking of contaminated water and pollution of water by tar on the surface of the skin containers in villages (Girba).

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Environmental factors are of greater importance in triggering the disease in patients with genetic predisposition. Unfortunately almost all gastric cancer patients referred to Ibn Sina Hospital have advanced disease. This is either due to the late presentation of patients to the medical facilities available, and/or in part some delay may occur when gastric ulcers are treated as if it is only a benign condition. However, patients seem to be forced to come to the surgeons when the manifestations of late cancer as anaemia, loss of weight, recurrent vomiting and pain exist.

### **Aim:**

To find out the frequency of the gastric mesenchymal tumours in patients seen at the specialized gastro-intestinal unit based at Ibn Sina Hospital. Also to see gender and age influences on clinico-pathological features of gastric carcinoma as a base line for future immunohistochemical and genetic studies in Sudanese patients with gastric cancer in and to audit the outcome of management of advanced gastric cancer.

### **Patients and methods:**

**Definition:** The advanced gastric carcinoma is defined as gastric tumours that invade the muscularis propria and/or associated with metastases to regional lymph nodes or invade adjacent or distant structure.

Hospital mortality is defined as death within 30 days after surgery.

**Methods:**

Retrospective study of 139 patients admitted to the surgical unit at Ibn Sina Hospital with a diagnosis of carcinoma of the stomach from May 1997 through November 2004.

**Selection criteria:**

Files of all patients admitted to the surgical unit at Ibn Sina Hospital with the diagnosis of gastric cancer which fulfilled the criteria for the definition of advanced gastric cancer stated above were included in this study.

Demographic data as well as the clinical features such as epigastric pain, vomiting, loss of weight and all information obtained by clinical examination as pallor, cachexia, epigastric mass, enlarged left supraclavicular lymph node and by investigations like the haemoglobin concentration, endoscopic features, site of gastric cancer, and the operative findings such as site, size of the tumour, enlarged lymph nodes, fixity of the tumour, its invasion to adjacent structures, liver metastasis and peritoneal seedlings were retrieved from the files. Details of histology reports on involvement of lymph nodes were also included. Types of gastric resection was noted and complications as well as hospital mortality in one month was registered. Available data on family history of cancer, smoking snuff and alcohol consumption was collected. The patients were then categorised into three limbs according to their age <40, 40-60 and > 60 years. The disease characteristics was worked up in each age group in an attempt to find out whether there is specific clinicopathological pattern of gastric cancer related to age or sex.

**Statistical analysis:**

The data was fed into a Statistical Package of Social Sciences (SPSS 11.5 Chicago-Illinois). Analysis was done using cross tabulation,  $\chi^2$  where appropriate considering the significant level at  $P = 0.05$ .

**Results:**

Data of 139 patients with proven diagnosis of advanced gastric cancer showed that they were 93 (66.9%) males and 46 (33.1%) females. The mean age ( $\pm$ SD) was 53.17 ( $\pm$ 15.36) range (15-90) years. The peak frequency of the disease was at the age group 50-65 years comprising 64(46%) of the total population. However, 29 (20.9%) patients were younger than 40 years (figure 1). The gender distribution according to age is depicted in Fig 2 which shows similar frequency in both sexes below the age of 40 years but the frequency tends to increase with age.

Fig 1: Age distribution of patients with carcinoma of the stomach

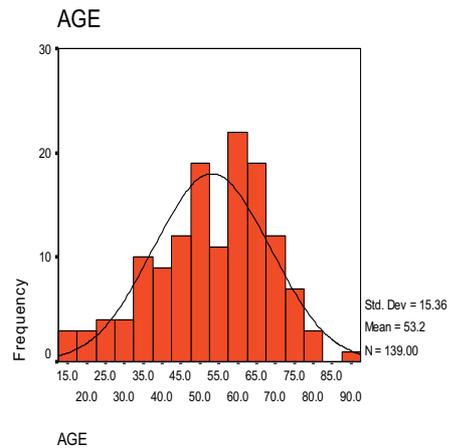
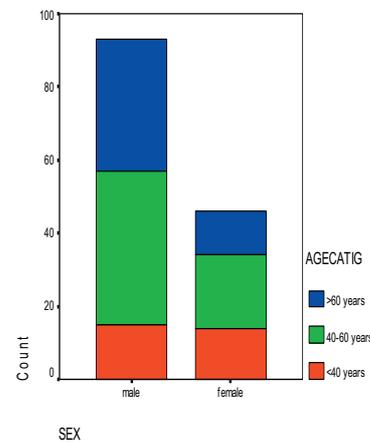


Fig 2: Male predominance in gastric cancer

**Dysphagia:**

23 (16.5%) of the study population suffered from dysphagia. The frequency of dysphagia seems to be in direct proportion with advancing age i.e. carcinoma of the cardia increases with age with 14 out of 23 patients in the age group >60 years ( $P = 0.012$ ). Also, dysphagia seems to be higher in males compared to females i.e. 16(69.6%) males compared to 7(30.4%) females due to the sex composition of the cohort.

**Pain:**

Epigastric pain is a predominant feature of advanced gastric cancer in all age groups ( $P = 0.009$ ). Like dysphagia the number of male patients who admitted to have epigastric pain 85(66.9%) is double that of 42(33.1%) females who complain of pain. Yet, this difference in gender has no significant statistical difference ( $P = 0.985$ ).

**Vomiting:**

A large number of patients with advanced gastric cancer suffer from vomiting but there is no statistical significant difference in the frequency of vomiting in both males and females (P 0.465). Likewise there is no significant statistical difference in frequency of vomiting in the different age categories (P 0.12)

**Weight loss:**

81 male and 39 females complained of loss of weight. However, there is no significant impact of gender on weight loss (P 0.709)

**Haemoglobin concentration:**

In this study anaemia is found to be very common in advanced gastric cancer in all age groups. Haemoglobin is categorized into 2 categories namely below 10 gm/dl and equal to or more than 10 gm/dl. Just more than half of the patients in each age category suffered from haemoglobin level below 10gm/dl. 88 (63.3%) have Hb less than 10gm/dl. 33(37.5%) females out of the 88 patients presented with Hb less than 10gm/dl but these 33 females comprise 71.7% of the total female population and the 55 males comprise 59.1% of the total male population in the study.

**Site of gastric tumour:**

The commonest site of carcinoma of the stomach is the antrum 55 (39.6%) followed by the cardia 34(24.5%) which seems to increase with age (P 0.208). Comparable pattern of distribution is found in both males and females with no significant statistical difference (P 0.713)

**Naked eye appearance:**

Endoscopic reports and operative findings showed that the ulcerative type of gastric cancer is the commonest type followed by the fungating tumours. When the naked eye appearance of advanced gastric cancer is plotted against age the ulcerative type is the most frequently seen type in all age groups (P 0.089) and in both sexes (P 0.223).

**Histopathological types of gastric cancer:**

The commonest type of gastric cancer encountered is adenocarcinoma comprising 118 (84.8%) but only 8 (5.8%) patients had lymphoma, 6(4.4%) had leiomyosarcoma and one patient had carcinoid tumour. The age distribution of the histological types of cancer shows predominance of adenocarcinoma at all age

groups but lymphoma is more at the younger age groups while leiomyosarcoma is common at the age group 40-60 years with similar predominance of adenocarcinoma in both sexes. All cases of lymphoma were encountered in the males while 3 cases of leiomyosarcoma were encountered in each sex group (P 0.05).

**The predisposing factors:**

Only 5 patients were recorded to have positive family history of cancer while 12 patients had positive history of alcohol consumption and 14 patients had history of cigarette smoking.

**Types of surgery:**

The commonest type of surgery was distal subtotal gastrectomy in 42 patients. It is followed by total gastrectomy in 25 patients, proximal subtotal gastrectomy in 15 patients and wedge resection in 5 patients. The tumour was irresectable in 52 patients. Patients who have irresectable tumours had only palliative type of management in the form of gastrojejunostomy in 16 patients, gastrostomy feeding tube in 12 patients and jejunostomy feeding tube in 21 patients while in 3 patients biopsies were taken only.

**Outcome:**

18(12.9%) patients died within one month of surgery with the least mortality in younger than 40 years of age comprising 3 out of 26 young adults. The mortality among males was 11 comprising 61.1% of the total mortality rate. The commonest cause of death was advanced disease in 14 patients followed by pulmonary embolism in three patients and myocardial infarction in one patient. 13(9.3%) patients developed complications.

**Discussion**

Worldwide, gastric adenocarcinoma is the second most common cancer (second to lung cancer). The mesenchymal gastric cancer is rare world wide<sup>1-6</sup>.

The global incidence of gastric cancer differs in different geographical areas. The highest incidence i.e. >30 cases per 100,000 population is in Japan, Russia, China, South America, and Eastern Europe. The lowest incidence i.e. <3.7 cases per 100,000 population is in North America, Western Europe, Australia, and New Zealand<sup>7-10</sup>. A marked reduction has been observed in the incidence of gastric carcinoma in North America and Western Europe in the last 50 years.

However, the 5-year survival rate is less than 20%, as most patients present late and are unsuitable for curative, radical surgery<sup>9,10</sup>. In comparison because there is no National Cancer Registry in Sudan, we do not know the accurate incidence or prevalence of any sort of this disease.

In this study, there is statistically significant male predominance ( $P = 0.04$ ). The male predominance seen is consistent with the fact that gastric cancer is more common in males as reported in literature<sup>11-14</sup>.

Also we found that the male to female ratio in patients less than 39 years of age to be 1:1.1 which is very much comparable to the finding of Shun LO et al<sup>11</sup>. The reason for this equity is not clear and the reason why after the age of 40 males are more prone to develop carcinoma of the stomach than females needs further investigations. The peak frequency of gastric cancer was at the age group 50-65 years comprising 64(46%) of the total population in the study. However 29 (20.9%) patients were under the age of 40 years and this is much higher than the 3.7 % reported by Shun LO et al<sup>11</sup>. The high prevalence of gastric cancer among patients younger than 39 years of age in our study needs explanation by further studies to find out the impact of environmental and genetic factors on the prevalence of gastric cancer in this relatively young age group in Sudan.

Epigastric pain, which is a feature of advanced gastric cancer, is a predominant feature in all age groups; however, it is significantly less in patients older than 60 years of age ( $P = 0.009$ ). This may be explained by the fact that older people are probably more tolerant than young people. On the other hand, gender has no specific effect on frequency of pain ( $P = 0.985$ ).

23 (16.5%) of the study population suffer from dysphagia. The frequency of dysphagia seems to be in a direct proportion with advancing age ( $P = 0.012$ ). However, dysphagia seems to have no predilection for any particular sex ( $P = 0.769$ ).

In this study a large number of patients with advanced gastric cancer suffer from vomiting. There is no statistically significant difference in the frequency of vomiting in the different age categories and in males and females. This could be explained by the fact that the ulcerative type of gastric cancer is the commonest type encountered in our study comprising 62(44.6%).

Advanced gastric cancer invades the gastric mucosa, ulcerates and leads to unnoticeable blood loss in the lumen of the gastrointestinal tract. In this study anaemia is found to be very common in

advanced gastric cancer in all age groups and in both sexes which explains the low concentration of haemoglobin.

About 60-65% in all age groups has haemoglobin level less than 10gm/dl. Although 33(71.7%) females have haemoglobin level less than 10 gm/dl compared to 55(59.1%) this does not have any statistically significant difference ( $P = 0.147$ ). Our finding of large percentage of patients with advanced gastric cancer suffering from low haemoglobin level is very much consistent with the finding of Nakata Y et al<sup>15</sup>.

Although the gastric antrum is the commonest site affected by cancer at all age groups, the frequency of affliction of the gastric antrum cancer has no statistically significant difference over involvement of other sites of the stomach in all age categories ( $P = 0.208$ ) nor in males and females ( $P = 0.713$ ). The intestinal type of gastric cancer, is more likely to involve the distal stomach and to occur in patients with atrophic gastritis. This type has a strong environmental association. The diffuse type with poorly cohesive cells tends to infiltrate the gastric wall.

Tumours of this type may involve any part of the stomach, especially the cardia, and have a worse prognosis. Unlike type 1 gastric cancers, type 2 cancers have a similar frequency in all geographic areas.

Before 1950, most gastric tumours were located in the antrum. Since then, the location has gradually shifted from the antrum to the body and fundus because of the rapidly increasing incidence of carcinoma in the gastric cardia and lower oesophagus. As a consequence, 30% of the lesions are found in the antrum, 30% are in the body, and 40% are in the fundus and cardia. The declining incidence of gastric cancer in the USA and Western Europe largely reflects a decline in distal lesions. In contrast, there has been a steady rise in the incidence of adenocarcinoma of the proximal stomach and the gastroesophageal junction in the USA and Europe<sup>16, 17, 18</sup>. However, more recent data from Sweden indicate an overall decline in incidence of cancers distal to the cardia by 9% [6-12%] per year, but did not confirm a rise of cardia cancer which has remained stable<sup>19</sup>. Gastric carcinoma is twice more common in men than in women.

Table: The morbidity of advanced gastric cancer.

	Complication	
	Count	%
No complications	126	90.6%
*biliary fistula	2	1.4%
oesophageal stricture	2	1.4%
Afferent loop obstruction	1	.7%
Faecal fistula	1	.7%
*slipped feeding tube	1	.7%
*hemiplegia	1	.7%
Bleeding	1	.7%
Infected wound	3	2.2%
Dehiscence	1	.7%

Moreover, carcinoma of the cardia of the stomach is up to 7 times as common in men as in women<sup>15</sup>.

When the naked eye appearance of advanced gastric cancer is plotted against age the ulcerative type is the most frequently seen type. However, gastric cancer seems to have the same pattern of naked eye appearance in all age groups and both sexes.

Adenocarcinoma is the commonest type of gastric cancer in all age groups and in both sexes. When the histopathology results were plotted against gender in this study it showed statistically significant difference ( $P$  0.05) which could be explained by the fact that gastric lymphoma and signet ring were found predominantly in males. However, this may need further verification by studying larger number of patients. In this study mesenchymal tumours such as lymphoma, leiomyosarcoma and carcinoids tumours constituted 15(10.9%) of all gastric cancer. Lymphoma alone comprise 5.8% while leiomyosarcoma constitute 4.4% of all gastric carcinoma, but gastric carcinoids tumour is extremely rare and was encountered in only one case of all gastric carcinoma. The frequency of mesenchymal gastric cancers as seen in this study is in keeping with the rarity of this type of cancer world wide as published in literature<sup>1-6</sup>.

In this study 18 out of 61 patients were previously diagnosed to be suffering benign ulcer and were given treatment for not less than 3 months. It appears that awareness of young

doctors need to be raised to consider malignancy when treating gastric ulcer.

Alcohol consumption was found in 12 (8.6%) patients. All patients who had admitted to take regularly alcohol were above 40 years of age. Likewise regular cigarette smoking was found in 14(10.8%) patients all of whom were above 40 years of age and were predominantly males. Nonetheless, studying of predisposing factors for cancer needs multidisciplinary research and rather big financial budgets.

Positive family history of cancer was found in only 5(3.6%) patients.

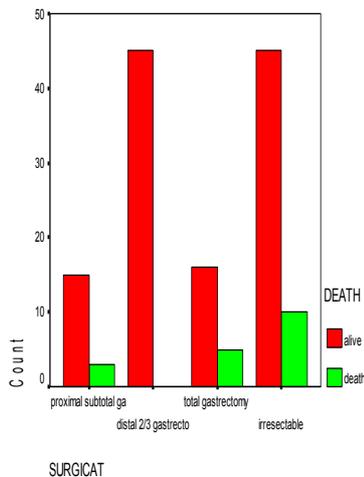
The hospital mortality was 18 (12.9%). There is no significant statistical difference in the hospital mortality rate in the different age groups and gender ( $P$  0.853 and  $P$  0.575 respectively). Lymph node metastases occurred in approximately 80% of patients with gastric cancer. The frequency is related to the size and depth of the tumour. The local perigastric nodes are involved first, followed by the regional (celiac, hepatic, left gastric, splenic) and distant (left supraclavicular and axillary) nodes. The local nodes (N1) are located in the prepyloric region and in the gastrocolic and gastrohepatic ligaments. These nodes are removed by performing the standard gastrectomy procedure. The regional nodes (N2) are not removed by the gastrectomy procedure; thus, their detection is more important. The N2 nodes are in the porta-hepatis, hepatoduodenal ligament, and peripancreatic region. In the TNM classification, nodal staging is related to the number of regional nodes involved in the perigastric group and around the celiac axis. Enlarged nodes elsewhere (e.g. in the retroperitoneum and mesentery) are classified as distant metastases.

Several reports used the WHO-classification, while others used the histologic classification according to the Lauren. Thus, there is confusion among physicians. It is therefore useful and of practical value to see whether these two classification systems can easily and simply be combined. Indeed, well and moderately differentiated cancer of WHO correspond to intestinal type according to Lauren, whereas poor differentiated or undifferentiated or signet ring cell -carcinoma to the diffuse type carcinoma respectively. The decline in overall incidence of gastric carcinoma during this century appears to be largely attributable to a decrease of the intestinal-type lesions, while the occurrence of diffuse type is thought to have remained more stable<sup>20-22</sup>. Most recent epidemiological data from

North Europe (Sweden) however, indicate that both types decline markedly, at similar rapidity, and with no significant trend differences between the intestinal and diffuse types<sup>23</sup>

In this study the hospital mortality is related to the late presentation of advanced disease because 14 patients died with inoperable tumours. The mortality rate was zero%, 2.8%, and 3.6% in distal subtotal, proximal subtotal and total gastrectomy respectively (Fig 3).

Fig 3: Outcome of gastric surgery



The relationship between prognosis and age distribution of patients with gastric cancer has been controversial. Many series<sup>24, 25</sup> showed a poorer prognosis in young patients, but some series<sup>26, 27</sup> demonstrated that the difference of prognosis between young and old patients can be attributable to the difference in tumour stages. In this study lymph node metastasis did not show any statistically significant difference ( $P$  0.380).

In conclusion gastric carcinoma in this study was found to be more common in males. It has a similar clinicopathological pattern in all age groups and in both sexes. Mesenchymal tumours occurred in 15(10.9%) of all gastric cancer. The hospital mortality rate was zero%, 2.8%, and 3.6% in distal subtotal, proximal subtotal and total gastrectomy respectively. We feel strongly that good budget should be located for further environmental and immunohistochemical studies to find out the influence of genetic predisposition and the effect of salted fish Like Fasiekh, Malouha and Kagiiek as well as the levels of toxic penetration of tar painted local leather water coolers in pollution of drinking water.

## References

1. Nishida T, Hirota S: Biological and clinical review of stromal tumours in the gastrointestinal tract. *Histology and Histopathology Journal* 2000; 15(4): 1293-30.
2. Miettinen M, Lasota J: Gastrointestinal stromal tumours--definition, clinical, histological, immunohistochemical, and molecular genetic features and differential diagnosis. *Virchows Archives* 2001; 438(1): 1-12.
3. Berman J, O'Leary TJ: Gastrointestinal stromal tumour workshop. *Human Pathology Journal* 2001; 32(6): 578-82.
4. Pierie JP, Choudry U, Muzikansky A: The effect of surgery and grade on outcome of gastrointestinal stromal tumours. *Archives of Surgery* 2001; 136(4): 383-9.
5. Pidhorecky I, Cheney RT, Kraybill WG, et al: Gastrointestinal stromal tumours: current diagnosis, biologic behavior, and management. *Annals of Surgery and Oncology* 2000; 7(9): 705-12.
6. Antoniole DA, Goldman H. Changes in the location and type of gastric adenocarcinoma. *Cancer* 1982; 775-81.
7. Haggitt RC. Premalignant lesions of the gastrointestinal tract. *View Dig Dis* 1985; 1-4.
8. Nagayot. Histopathology of gastric Dysplasia. In: Filipe MI, Jass JR. First edition. *Gastric carcinoma*. Edinbrugh: Churchill Livingstone. 1981; 16-31.
9. Silverberg E, Boring CC, Squares TS. *Cancer statistics*. *Canadian Cancer Journal Clinics* 1990; 9-26.
10. Aoki K, Tominaga S, Kuroishi T. Age adjusted death rates for cancer by site in 50 countries in 1975. *Japan Journal of Cancer Research* 1981; 2251-74.
11. Su-Shun Lo, Hsu-Sung Kuo, Chew-Wun Wu, et al. Poorer prognosis in young patients with gastric cancer. *Hepato-gastroenterology* 1999; 46: 2690-93.
12. Isozaki H, Fujii K, Nomura E, et al. Prognostic factors of advanced gastric carcinoma

without serosal invasion (pT2 gastric carcinoma). *Hepato-gastroenterology* 1999; 46: 2669-72.

13. Wansik Yu, Kim HS, Choi GS, et al. Perigastric lymph nodes with metastasis in gastric cancer. *Hepato-gastroenterology* 1999; 46: 2658-61.

14. Piso P, Meyer HJ, Edris C, et al. Surgical therapy of gastric stump carcinoma- a retrospective analysis of 109 patients. *Hepato-gastroenterology* 1999; 46: 2643- 47.

15. Nakata Y, Kimura K, Tomioka N, et al. Gastric exclusion for unresectable gastric cancer. *Hepato-gastroenterology* 1999; 46: 2654-57.

16. Fuchs CS, Mayer RJ. Gastric carcinoma. *New Engl J Med* 1995; 333: 32-41.

17. Craanen ME, Dekker W, Blok P, et al. Time trends in gastric carcinoma: changing pattern type and location. *Am J Gastroenterol* 1992; 87: 572-9.

18. Blot WJ, Devesa SS, Kneller RW, et al. Rising incidence of adenocarcinoma of the esophagus and gastric cardia. *JAMA* 1991; 265: 1287-9.

19. Ekstrom AM, Serafini M, Nyren O, et al. Dietary antioxidant intake and the risk of cardia cancer and nocardia cancer of the intestinal and diffuse types: a population-based case-control study in Sweden. *Int J Cancer* 2000; 87(1): 133-40.

20. Roukos DH. Current status and future perspectives in gastric cancer management. *Cancer Treat Rev.* 2000 ;26(4):243-55.

21. Lauren PA, Nevalainen JT. Epidemiology of intestinal and diffuse types of gastric carcinoma: a new-trend study in Finland with comparison between studies from high- and low-risk areas. *Cancer* 1993; 71: 2926-33

22. Munoz N, Connelly R. Time trends of intestinal and diffuse types of gastric cancer in the United States. *Int J Cancer* 1971; 8: 158-64.

23. Ekstrom AM, Hansson LE, Signorello LB, et al. Decreasing incidence of both major histologic subtypes of gastric adenocarcinoma--a population-based study in Sweden. *Br J Cancer* 2000 Aug; 83(3): 391-6.

24. Bloss RS, Miller TA, Copeland E. Carcinoma of the stomach in the young adults. *Surg Gyne Obstet* 1980; 150: 883- 886.

25. Tamura PY, Curtiss C. Carcinoma of the stomach in the young adults. *Cancer* 1960; 13: 379- 385.

26. Mately PJ, Dent DM, Madden MV, et al. Gastric carcinoma in young adults. *Ann Surg* 1988; 208: 593-596.

27. Grabiec J, Owen DA. Carcinoma of the stomach in young persons. *Cancer* 1985; 56: 388-396.