

Trends of gastric malignancies: Case study of Ibn Sina Hospital 2010-2011.

Alagib Abdulatif Ibrahim¹, Mutaz Salah Eldeen², El sagad Eltayeb³, Tarig M Hussien², Mohamed OM Sulaiman², MAM Ibnouf², Abdulmagid M Masaad².

Abstract

Back ground: Gastric malignancies carry poor prognosis, because they commonly present at an advanced stage.

Objective: to find out mode of presentation and its impact on the outcome and management of gastric cancer and to find if there are changes in trends of gastric malignancies over the last decade.

Patients and methods: A review of 53 patients with gastric malignancies, treated at Ibn Sina Hospital from August 2010 through August 2011. Their demographic data, pattern of clinical presentation, histopathology grading and staging, type of management and hospital mortality were studied.

Statistical analysis: Data was fed to Statistical Package for Social Sciences. Means and correlations were computed where appropriate. One sample *t*-test was performed. Statistical significance was taken at $P = 0.05$.

Results: Out of 53 patients males comprise 30(56.6%) males. The peak frequency was at the age group 55-70 years. Patients from the Northern Region of Sudan constituted 34%. Adenocarcinoma comprised 43(81.3%), GIST 8(15%), lymphoma 1(1.9%) and carcinoid 1(1.9%). Epigastric pain was the commonest symptom in 47(88.7%) patients. Smoking and snuff (Tombak) and high salt diet were found in 7.5% and 5.7% and 3.8% patients respectively. Blood group A and O was found in 22.6% and 60.4% respectively. Family cancer syndrome was found in 11.3% patients. Malignancies of the antrum constitute 27(65.85%), cardia 4(9.8%), body 7(17.1%), and whole stomach 3(7.3%) patients. There were only 6.25% clinically early cases. Potentially curative resection was attempted in 31.7%. The mean hospital stay was 12 days.

Conclusion: Patients presented at stage III and IV comprise 30 (93.75%) out of 32 carcinoma patients. The hospital morbidity was 13(24.6%) patients and mortality 4(7.5%) patients. When compared with results from same hospital there is improvement in outcome over a decade.

Keywords: Adenocarcinoma, lymphoma, carcinoid, dysphagia.

Gastric cancer is the fourth most common cancer worldwide (after lung, breast and colorectal cancer)¹ It is the second common cause of cancer death worldwide². The risk of developing gastric cancer was relatively lower in the Middle East and North Africa compared with those of western countries³.

In 1976 Malik MO et al reported gastric cancer as the third GIT cancer in Sudan.

He found the male to female ratio to be 2:1 with peak frequency rate at the age group 50-70 years⁴.

This study intended to find if there are changes in trends of gastric malignancies. Ibn Sina specialized Hospital was selected to be the site for our study because it has a specialized centre for gastrointestinal and liver diseases.

Objectives:

to find out mode of presentation and its impact on the outcome and management of gastric cancer and to find if there are changes in trends of gastric malignancies over the last decade.

1.Surgical registrar.

2.Consultant surgeons.

3.Assistant professor Alneelain university.

*Correspondence to Alagib Abdulatif Ibrahim

Tel: 00249912583797

Patients and methods:

This is a hospital based, non-randomized, prospective case series study for gastric malignancies.

Set up: Ibn Sina Specialized Hospital was established as a donation from the Japan International Corporation Agency (JICA) in 1983. The hospital has a specialized centre for gastrointestinal and liver diseases.

Period of study: From August 2010 through August 2011.

Methods: Patients were interviewed, examined; details of the results of investigations and operative data as well as the hospital mortality rate were collected. Results were then correlated with results of data published from the same hospital a decade ago.

Inclusion Criteria: All patients who proved to have gastric malignancy during the study period were included in the study.

Exclusion Criteria: Cases with missed histopathological confirmation.

Variables in the study: Demographic data, diet; social habits such as smoking, snuffing and alcohol consumption were obtained. Associated co-morbidities were included. Family history of gastric cancer and other familial cancer syndromes were also noted. Clinical examination was performed and notes were taken on cachexia, pallor, weight, presence of palpable abdominal mass and signs of metastasis such as Sister Mary Joseph nodule, Plummer shelf and/or Virchow’s lymph node. Results of CBC, urinalysis, blood group, LFT, RFT, ECG, CXR and the endoscopic findings of the site and naked eye appearance.

Testing for H.pylori through “CLO” test was also and CT-scan findings were gathered.

Detailed intra – operative findings were obtained The tumour size was categorized into less than 5cm, 5 – 10 cm and more than 10 centimetres. Type of performed surgery was noted, aim of surgery whether curative or palliative was also registered and so did the type of reconstruction after surgery. Post operative follow up of patients up to 30 days following surgery.

Statistical analysis:

Data was fed into Statistical Package of Social Sciences(SPSS). Means, correlations and One sample *t*-test were computed and statistical significance was taken at *P* = 0.05.

Results:

A total of 53 patients proved to have gastric cancer were studied. The males constituted 30(56.6%).

with a male to female ratio of 1.3:1. Mean age at presentation was 61.46 years for males and 51.43 years for females. Young patients “≤40 years” were 9(17%) patients figure (1). The origin for 18(34%) patients was the Northern Region.

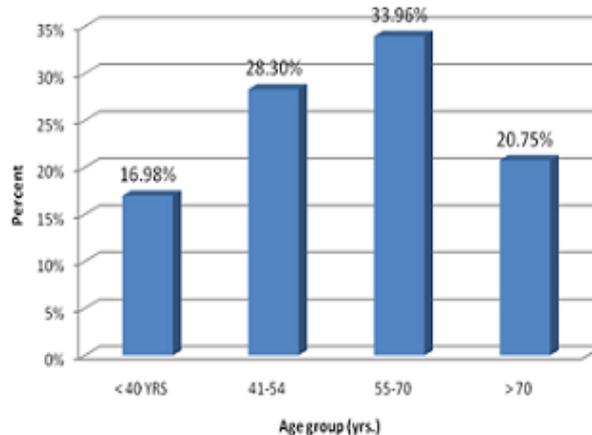


Fig (1): Distribution of the study population according to age group

Epigastric pain was the commonest presenting symptom seen in 47(88.7%) patients, followed by vomiting in 29(54.7%) patients as shown in table (1). Minimal duration of symptoms was one month in 3(5.7%) patients, and the maximum was 24 months in 1(1.9%) patient. However, the mean duration of symptoms in patients was 5.2 months.

Salted diet as a risk factor was obtained in only 2(3.8%) patients. However, 6(11.3%) patients used to take alcohol, 4(7.5%) patients were smokers and (5.6%) were snuffer, while 3(5.6%) patients were both smoker and alcoholic.

Family history of gastric cancer was obtained from one patient (1.9%). However, 23(43.4%) patients have associated co-morbidities such

as diabetes mellitus, hypertension, IHD, CRF...etc”. Past history of anaemia and blood transfusion was found in 34(64.15%) patients. The commonest type of blood was blood group O in 32(60.37%) patients.

Table 1: Distribution of gastric malignancy patients according to symptoms

Symptom	Frequency	%
Abdominal pain	47	88.7%
Dyspepsia	15	28.3%
Anorexia	9	17
Loss of weight	26	49.1%
Heart Burn	6	11.3%
Dysphagia	5	9.4%
Regurgitation	2	3.8%
Vomiting	29	54.7%
Haematemesis	11	20.8%
Malaena	16	30.2%
Back Pain	5	9.4%
Symptoms of anaemia	15	28.3%
Small bowel obstruction	1	1.9%

The mean weight of patients at presentation was 57.3kg, 28(52.8%) patients were cachectic, 37(69.8%) patients were pale and 23(43.4%) patients were dehydrated. Abdominal mass was found in 20(37.7%) patients and ascites was demonstrated in 4(7.5%) patients.

Investigations proved that 22(41.5%) patients had haemoglobin <10gm/dl, 24(45.3%) patients had hypokalaemia, and 5(9.4%) patients had impaired renal function. Albumin was low in 13(24.5%) patients. Chest x-Ray revealed consolidation and pleural effusion in 5(9.4%) patients, and ECG ischaemic changes in 4(7.5%) patients.

During endoscopy 33(62.3%) patients had antral lesions, 12(22.6%) had tumours in the cardia, and in 3(5.7%) patients the tumour was infiltrating whole stomach. The naked eye appearance was a cauliflower in 37(69.8%), ulcer in 7(13.2%) and 6(11.3%) patients had gastric polyps.

The histo-pathological examinations reported adenocarcinoma in 45(84.9%). Helicobacter

testing through CLO “Cod liver oil” was positive in 33(97%) out of the 34 patients).

However, 47(88.7%) patients were preoperatively transfused with blood, and the mean volume of blood received was 4.9 units per patient. Total number of patients who were fit for surgery was 41(77.4%) patients. They were 32(78%) patients with carcinoma, 8(19.5%) patients had GIST and 1(2.41%) patient had carcinoid tumour.

During the intra-operative assessment the tumour was infiltrating the pyloric antrum in 27(65.85%) patients, while in 4(9.8%) patient the tumour was in the cardia. The body of the stomach was involved in 7(17.1%) patients and whole organ (pan-gastric) infiltration was seen in only 3(7.3%) patients. The operative staging is shown in Fig(2) . The size of the tumour was 5-10 cm in 27(65.9%) patients. Pancreatic invasion occurred in 16(39%) patients.

Operative staging showed that 30(93.75%) out of 32 carcinoma patients were found to have advanced gastric cancer i.e. stage III –IV as depicted in fig (2).

Therefore, palliative resection was performed in 28(68.3%) out of 41 patients operated, The palliative resection was in the form of partial gastrectomy in 12(29.26%) patients, palliative total gastrectomy in 3(7.3%) patients, but, bypass “gastro-jejunostomy” was performed in 10(24.4%) patients and jejunostomy or gastrostomy feeding tube was inserted in another 3(7.3%) patients. However, extended gastrectomy was performed in only two cases. Curative surgery was contemplated in 13(31.7%) patients. Curative total gastrectomy was done in 1(2.43%) patient, while curative partial resection was completed in 10(24.4%) patients. On the other side, extended gastrectomy with curative intention was carried out in 2(4.87%).

The total number of patient who underwent partial gastrectomy for both curative and palliative purpose was 21(51.2%). Of them 12(29.26%) patients had distal gastrectomy, 5(12.19%) patients wide wedge resection and 4(9.75%) patients proximal gastrectomy. Billroth II gastrectomy was the commonest reconstruction in 8(38.09%) patients. The

spleen was resected en-block with the tumour in 3(7.3%) patients, and the tail of the pancreas was resected in 1(2.43%) patient.

Bilious vomiting occurred in 8(19.5%) patients. The frequency of postoperative complications are shown in table (2).

The mean hospital stay for those who were operated was 12 days, and on discharge the symptomatic relief was satisfactory in 28(80%) out of 41. The hospital mortality was 4(7.5%) patients.

Table 2: Frequency of the post operative complication

Post-operative complications	Frequency	%
Biliary vomiting	8	19.5%
Fistula	2	4.9%
Afferent loop syndrome	2	4.9%
Wound infection	1	2.4%
No complications	28	68.3%

Discussion:

In this study we studied prospectively the data of 53 patients with gastric malignancies. These are consecutive patients who attended Ibn Sina Hospital for treatment in the period from August 2010 through August 2011. We noticed that carcinoma of the stomach has 1.3:1. This is in keeping with the international literature².

One decade before our study Khalid Al sir et al⁵ conducted a retrospective study of 139 patients admitted to the surgical unit at Ibn Sina Hospital with a diagnosis of gastric malignancies. In his study the male to female ratio was 2:1 compared to 1.3:1 in ours. However the male to female ratios in both studies is in keeping with the international literature. There was no change in the pattern of clinical presentation and tumour site. Also, the distal gastric tumours outnumber the proximal ones, and the palliative surgery is the commonest surgery for the majority of patients. The hospital mortality past these years had declined from 12.5% in Khalid study to 7.5% in our study. This is possibly due to the improvement in managing critical cases that took place during the last years in

Ibn Sina Hospital .See table (3). The highest frequency at the age group 55-70 years which is consistent with the published international reports⁶. However, in our study those who were younger than 40 years constituted 16.98%. This is rather higher than the

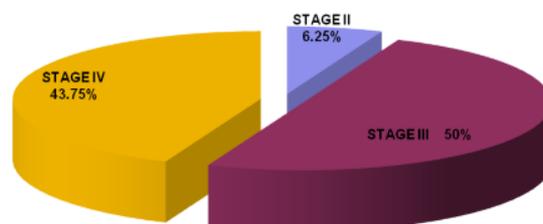


Fig (2): The frequency of the different stages of gastric cancer

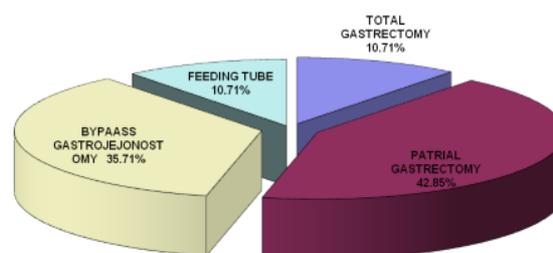


Fig (3): the frequency of the different modalities of the performed palliative surgery (n = 28)

international reported percentage for this age group which is less than 5%⁶. We do not have specific explanation for this, therefore, genetic background and environmental factors need further studies in this aspect. First degree relatives of gastric cancer have 2-3 folds, increase risk of developing gastric cancer^{7,8}. Also, we found that family history of other malignancies like kidney, gynaecological, pancreas and biliary cancer in 6(11.3%) patients. Here, we need future studies particularly concerned with genetics among Sudanese patients to define or validate our findings. Yet, Helicobacter pylori infection was present in 33 out of 34 patients tested. This is most likely a chronic disease in our patients and had probably existed since childhood. Salted diet and partially cooked fish (Maloha) is common among patients of

northern origin. This could also be in agreement with the fact that salt is linked to H.pylori⁹.

Table (3): Comparison of the current study variables with 139 case study* of gastric malignancies conducted in Ibn Sina Hospital, 1997-2004.

	Current study	Ibn Study in (1997-2004)
Male: female ratio	1.3:1	2:1
Age at peak frequency	55-70 yrs.	50-65 yrs.
Carcinoma	81.3%	84.8%
GIST *	15%	4.4%
Lymphoma	1.9%	5.8%
Carcinoid	1.9%	0.7%
Epigastric pain	88.7%	91.36%
Cardia malignancies	9.75%	24.5%
Antral malignancies	65.85%	39.6%
Resectability	44.18%	62.6%
Hospital mortality	7.5%	12.9%

* Khalid Al sir, et al (-1997-2004).

On the other hand, 32(60.4%) patients had the blood group O. This seems to be inconsistent with the reported predominance of the disease in patients with group A. But, recently it had been proved that individuals with the blood group O were at risk of developing duodenal ulcers, gastric ulcer, and gastric malignancies¹⁰. Nonetheless, we found it interesting that one of our patients had carcinoma of the stump of the stomach following distal gastrectomy about 40 years before presentation. This could be explained by the effect of chronic bile reflux into the stump of the stomach¹¹.

A total of 23(43.4%) of our patients have co-morbid diseases and a total of 64.15% patients have anaemia that necessitated blood transfusion before and after surgery. All this

could explain the rate of morbidity and mortality we had during the management of the population in this study.

The majority of our patients i.e. 47(88.7%) presented with epigastric pain. This indicates that they presented at advanced stage.

Vomiting was noted in 29(54.7%) patients.

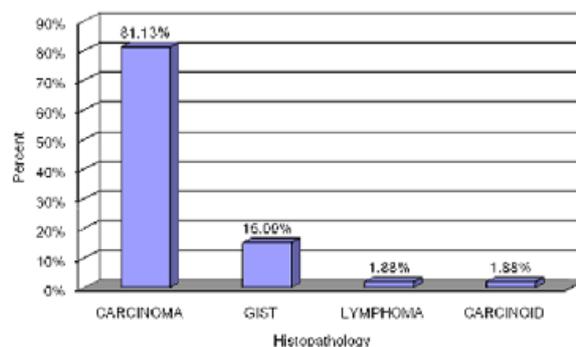


Fig (4): Results of histopathology

This reflects the frequency of advanced disease causing obstruction. We found that there is significant statistical difference in the symptoms as related to the site of the tumour (P = 0.0020). Also cancer at the body of the stomach leads to significant blood loss (P = 0.0090). Similarly carcinoma of the cardia leads to dysphagia (P = 0.0001). Sudan is one of the developing countries, where the intestinal distal gastric malignancy is still dominant over the proximal one, this could be linked to H. pylori infections¹². In this link we have supporting evidence that H. pylori is a strong causative agent because 62.26% of our patients had H. pylori and that carcinoma of the antrum, body of stomach and diffuse gastric cancer was encountered in 65.85% 17.07%, 7.31% respectively, making a total of 90.23%. However the remaining cases i.e. 9.75% who had carcinoma of the cardia of the stomach, may be due to the hypothesis that patients with H.pylori at a decrease risk of developing adenocarcinoma of the cardia, as H.pylori induce corpus gastritis, which decrease the acid secretion and creating a less damaging reflux and thus reduce the risk of Barrett's oesophagus, the precursor lesion of the tumour¹³.

Interestingly, one of our patients had one of the para-neoplastic features, acanthosis nigricans (dark pigmented lesion involving the skin and axilla) for which she sought medical advice and the endoscopy revealed the gastric cancer.

Endoscopy was conclusive in 43(95.5%) patients, as there were two patients discovered to have GIST and carcinoid tumour after post operative histopathological examination.

The eight patients (GIST) comprised 15% from the total number (n=53). This is higher than the reported the prevalence of gastric GIST. However, this is consistent with the previous report that GIST in Sudan is more common than Jordan¹⁴.

The operated patients were 41(77.4%). These were, 32(60.37%) patients with carcinoma, 8(15.09%) GIST and 1(1.9%) was carcinoid. The resectability rate was 100% for GIST, 44.18% for adenocarcinoma, and 100% for carcinoid. However, 28(68.3%) had palliative resection. This makes the potentially curative resection to be 13(31.7%). Limited lymphadenectomy, few dissected nodes and serosal involvement should be considered to be risk factors of postoperative recurrence of lymph node-negative gastric cancer patients¹⁵. Literature proves that the 5-year survival rate is influenced by the tumour size, gross type, serosal invasion, extragastric lymph node metastasis, liver metastasis, peritoneal dissemination, stage of disease (III and IV), involved resection margin, and operative curability (R0). Of these, independent prognostic factors were proven by literature are three tumour findings: serosal invasion, extragastric lymph node metastasis, and liver metastasis. However, the same literature reported that the survival was not significantly associated with any of the patient factors or type of operation and the extent of lymph node dissection¹⁶. Palliative chemotherapy was attempted in 8 patients (18.6%).

All GIST patients and the single patient who had carcinoid tumour underwent curative resection. One lymphoma patient was referred to chemotherapy.

The morbidity rate among this small series of patients is 13(24.6%). This morbidity rate is fairly comparable with that reported from Japan in a small number of patients comparable to the population size of our study. The Japanese researchers reported that "The study patients comprised 53 men (74.6%) and 18 women (25.4%) aged 39-89 years (mean, 68.9 years). Nineteen patients (26.8%) had postoperative morbidity: pancreatic fistula developed in 6 patients (8.5%) and was the most frequent complication, followed by anastomosis stricture in 5 patients (7.0%). During the follow-up period, 28 patients (39.4%) died because of gastric cancer recurrence, and 3 (4.2%) died because of another disease or accident.

Hospital mortality (4 patients) (7.5%), they were all carcinoma with advanced disease.

Our results are in keeping with a study performed in Korea. The Korean study reported that "Patients with T4 gastric carcinoma might be benefited from curative resection. The results also emphasize the improved survivorship of T4 gastric carcinoma patients with resection compared with those who did not undergo resection. Although curative resection cannot be undertaken in patients with T4 gastric carcinoma, we recommend performing resection in patients with locally advanced gastric carcinoma, regardless of curability¹⁷.

The prognosis for gastric carcinoma patients with peritoneal dissemination is very poor. Yet they seem to benefit from resection followed by chemotherapy¹⁸.

Conclusion:

Adenocarcinoma is the commonest histopathological type (81.13%) of gastric malignancies, followed by mesenchymal tumours (GIST) (15%) and the least common is carcinoid and gastric lymphoma. Gastric antrum is the commonest site (65.85%) for this disease. H. pylori may play strong role in carcinoma of the stomach in our study. Indigestion, belching, and feeling of weakness and unexplained loss of weight are alarming signs. These symptoms are enough

to request gastroscopy if early gastric cancer is to be diagnosed. Surgeons and gastroenterologists should have high index of suspicion for GIST tumours. There's a significant group of patients less than 40 years of age. In these cases genetic counselling is better to be advised and palliative surgery should not be denied to patients with advanced disease. Hospital mortality is (7.5%) related to the late presentation.

References

1. Parkin DM, Bray, Fernley. J; Pisani P. "Global cancer statistics 2002" CA: Cancer Journal for Clinician 2005;55:74 -108.
2. Altekruse SF, Kosary M, Krapcho M et al (eds): SEER cancer statistics Review ,1975-2007,Nationalcancer Institute Bethesda MD.
3. Parkin DM, Stjernsward J and Muir CS. Estimate of the world wide frequency of twelve major cancer .Bull world health organ, 1984; 62(2):P.163-82.
4. Malik MO; Zaki El Din Z; El Masri SH. Cancer of the Alimentary tract in Sudan: a study of 546 cases, Cancer . 1976 May; 37 (5): 2533 – 42.
5. Khalid Elsir, Abdelmagid M Masaad. M A Ibnouf. Audit of advanced gastric cancer at Ibn Sina Hospital, Sudan. SudJMS 2006; 1(1): 52-57.
6. Parkin DM, Pisani P, and Ferlay J. Estimates of the worldwide incidence of 25 major cancers in 1990 Int J Cancer, 1999. 80(6): p. 827-41.
7. Dhillon PK, Farrow TC; Vaughan TL et al: Family history of cancer and risk of oesophageal and gastric cancer in United States Int. J. cancer 2001; 93: 146 -52.
8. Wai K leung, Fuders KW Ng, Wing Y chan et al: Risk factors associated with the development of Intestinal Metaplasia in the first degree relatives of gastric cancer patients. Cancer epidemiology Bio Markers Prev. 2005, 14 (12): 2982 – 2986.
9. Tsugane S: Salt and salted food intake and risk of gastric cancer epidemiological evidence, cancer sci 2005; 96 (1): 1-6.
10. Doll R, Drane H, Newell AC. Secretion of blood substances in Du, Gu, gastric carcinoma and DM. International Journal of gastroenterology and hepatology. Gut. 1961 December; 2 (4) : 352 – 359.
11. Schaefer N, Sinning C, standop J et al: treatment and prognosis of gastric stump carcinoma in comparison with primary proximal gastric cancer; Ann. J. Surg 194: 63, 2007.
12. Sitas F, Yarnell J, Forman D. Helicobacter pylori infection rates in relation to ages and social class in apopulation of Wales men. Gut 1992, 33:1583.
13. Mc Coll KE; Watabe H; Derakhshan MH : Role of gastric atrophy in mediating negative association between Helicobaeter Pylori infection and reflux oesophagitis; Barret's oesophagus, and oesophageal Adeno Carcinoma. Gut 57: 721, 2008. Freedman LS, Edwards BK, Ries LAG et al. Eds 2006. Cancer incidence in four members Countries Cyprus, Egypt, Israel and Jordan of Middle East – Cancer consortium (MECC) compared with US. SEER: Bethesda National Cancer Institute (NCI) pp 14.
14. Deng J, Liang H, Sun D, et al. prognosis of gastric cancer patients with node negative metastasis following curative resection outcome of survival and recurrence. Can j gastroenterol 2008; 22(10):835-839.
15. Shiraishi N, Sato K, Yasuda K, et al. Multivariate prognostic study on large gastric cancer. J Surg Oncol. 2007 Jul 1;96 (1):14-8.
16. Fukuda N, Sugiyama Y, Wada J. Prognostic factors of T4 gastric cancer patients undergoing potentially curative resection. World J Gastroenterol. 2011 Mar 7; 17(9): 1180-4.
17. Kim DY, Joo JK, Seo KW, et al. T4 Gastric carcinoma: the benefit of non-curative resection. ANZ J Surg. 2006.