

# Gastrointestinal, Hepatic, and Pancreatobiliary Malignancies; A Histopathological, and Cytopathological Study from a Specialized Center in Iraq.

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## ABSTRACT:

**BACKGROUND:** A review of histopathology and cytopathology cases of one year work, with an emphasis on the malignant cases that have been diagnosed in the gastroenterology and hepatology teaching hospital/ Baghdad was done.

**PATEINTS AND METHODS:** We did a review of 2796 cases that were diagnosed in our lab during the time period from Aug. 7th. 2003 to Aug. 7th. 2004. These cases were divided as: (1) 2279 patients were diagnosed by histopathological examination of their endoscopic or surgical tissue specimens. (2) 277 patients were diagnosed by cytopathological examination of ascitic fluid. (3) 142 patients were diagnosed by cytopathological examination of fine needle aspiration (FNA) cytological smears (most of them taken under ultrasound guidance). (4) 98 patients were diagnosed by cytopathological examination of FNA cytological smears as well as histopathological examination of FNA needle biopsies (most of them taken under ultrasound guidance).

**RESULTS:** Our results showed that out of 2279 biopsies that were reviewed 177 (7.77%) cases were positive for malignancy. The age range was 15-90 years with a mean 52.7 and male to female (M: F) ratio 1.5:1. There were 20.9% of patients below 40 years age. Regarding esophageal malignancy, squamous cell carcinoma was the predominant type. In gastric malignancy, 51/59 (86.4%) patients had carcinomas while 8/59 (13.6%) had lymphomas. Forty nine (96.08%) patients with gastric carcinoma were above forty years age (68.62% were 40-70 years) while only two patients were below this age. Diffuse type adenocarcinoma was more prevalent compared to the intestinal type. We had 62 patients with colorectal carcinoma, Twenty (32.25%) patients were under 40 years while 42 (67.75%) were above this age, 26/62 (41.9%) of cases were in rectosigmoid area while 36/62 (58.1%) of the other parts of the colon; young patients had a statistically significant more advanced tumor stage. By ascitic fluid cytological examination we were able to diagnose 21/277 (7.58%) cases of malignancy, 19 cases (90.48%) with metastatic adenocarcinoma, and 2 cases (9.52%) were diagnosed as NHL. We reviewed 142 fine needle aspiration (FNA) cytological smear specimens & we found that 119 (83.80%) of them were diagnosed as malignant. We examined 98 cases of various sites FNA cytology accompanied by FNA needle biopsy and we detected carcinoma in 41 (41.87%) of cases.

**CONCLUSION:** We concluded from this study that gastrointestinal malignancies are common. In Iraq histological typing of malignant neoplasms of the stomach showed that diffuse type adenocarcinoma was commoner than intestinal type. There is an increase in the incidence of occurrence of colorectal carcinoma particularly in young male individuals with a relative decrease in rectosigmoid carcinoma due to a shift in location towards the proximal colon, and finally FNA cytology is a valuable method in diagnosis of malignancy especially if combined with FNA needle biopsy.

Key word: Gastrointestinal malignancy, histopathological and cytopathological study.

## INTRODUCTION:

The gastroenterology and hepatology teaching hospital has been established as a separate hospital and as part of the medical city teaching hospital campus in Sep. 22nd. 2002. The hospital constitutes departments, surgical theaters, and endoscopy department in which upper (OGD) and lower (colonoscopy) endoscopies are done. There are also an endoscopic retrograde

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equipped radiological unit.

The lab department was established in Aug. 7th.2003, with biochemistry, hematology, in addition to histopathology & cytopathology divisions. Now after one year, we reviewed our histopathology and cytopathology cases of one year work, with an emphasis on the malignant cases that have been diagnosed.

### PATIENTS AND METHODS:

A retrospective analysis of data collected from the lab record was used to review the incidence of malignancy during the time period from Aug. 7th.2003 to Aug.7th.2004; these data were analyzed according to site, age, sex, and relative frequency. A total of 2796 cases were sub grouped as:

" 2279 patients were diagnosed by histopathological examination of their endoscopic or surgical tissue specimens.

" 277 patients were diagnosed by cytopathological examination of ascitic fluid.

" 142 patients were diagnosed by cytopathological examination of fine needle aspiration (FNA) cytological smears (most of them taken under ultrasound guide).

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" 98 patients were diagnosed by cytopathological examination of FNA cytological smears as well as histopathological examination of FNA needle biopsies (most of them taken under ultrasound guidance).

Statistical analysis was done by use of SPSS version 7.5 computer software (statistical package for social science) in association with Excel version 5. P value less than 0.05 was considered to be significant.

### RESULTS:

#### Histopathological Examination Results:

Our results showed that out of 2279 biopsies that were reviewed 177 (7.77%) cases were positive for malignancy, Table (1). The age range was 15-90 years with a mean of 52.7 and male to female (M: F) ratio of 1.5:1. There were 20.9% of patients below 40 years age. Carcinoma of the colorectum was the most common gastrointestinal tumor followed by stomach and esophagus.

Organ	Cases		Age		Sex	
	No.	%	Range	Mean	Male	Female
esophagus	11	6.21	28-83	55.82	8	3
Stomach	59	33.33	22-90	58.19	40	19
Duodenum	6	3.39	25-80	57.33	3	3
Ampulla	8	4.52	44-70	58.8	4	4
Colon	62	35.03	15-90	47.31	41	21
Anus	4	2.26	50-63	56.25	3	1
Liver	8	4.52	25-70	48	4	4
Spleen	2	1.14	29-38	33.50	1	1
Pancreas	1	0.56	60	60	0	1
Abdominal Mass	13	7.34	25-56	41.15	3	10
Lymph Node	2	1.14	38-63	50.5	0	2
Skin	1	0.56	66	66	0	1
Total	177	100	15-90	52.7	107	170

**Table (1):** Organ involvement by various types of malignancy diagnosed by histopathological examination



Out of the sixty one esophageal biopsies that we had received, 11 (18.03%) cases had malignancy. Squamous cell carcinoma was the predominant type as it was detected in 9 (81.8%) patients, the majority of cases (66.7%) were of moderately differentiated grade, while adenocarcinoma was detected in two cases (18.2%), one with well and the other with moderately differentiated grade, table (2).

Organ	Well Diff.		Mod. Diff.		Poorly diff.		Total	
	No.	%	No.	%	No.	%	No.	%
esophagus	3	27.27	7	63.63	1	9.1	11	100
Stomach	5	9.8	15	29.4	31	60.8	51	100
Duodenum	1	16.7	2	33.3	3	50	6	100
Ampulla	3	37.5	3	37.5	2	25	8	100
Colon	7	11.3	49	79.03	6	9.67	62	100
Anus	0	0	4	100	0	0	4	100

**Table (2):** Grades of carcinoma involving various gastrointestinal tract organs.

We had received 598 gastric biopsies, malignancy was found in 59(9.86%) of them. 51/59 (86.4%) patients had carcinomas while 8/59 (13.6%) had lymphomas. Forty nine (96.08%) patients with gastric carcinoma were above forty years age (68.62% were 40-70 years) while only two patients were below this age. Gastric carcinoma exhibited histological features of diffuse type (most of those had signet ring cell component) in 60.8% of patients with a mean age of 56.54 years (age range: 30-82 years), while only 39.2% of patients were found to have intestinal type adenocarcinoma with a mean age of 62.95 years (age range: 42-90 years). Correlation has not been observed between the age of the patients and the type of carcinoma ( $P=0.145$ ). Fifty percent of the diffuse type patients were females versus 25% in the intestinal type. The carcinomas in all gastrectomy surgical specimens were invading the wall and were associated with regional lymph nodes involvement (T3N1 pathological stage). All the cases of gastric lymphoma were of non-Hodgkin (NHL) mucosa associated lymphoid tissue (MALT) type. Histologically, four of our patients (50%) had low grade lymphoma (2 cases were associated with duodenal involvement) and 4 patients (50%) had intermediate grade NHL. We had received 682 duodenal biopsies most of them were submitted to assess villous length; carcinoma was diagnosed in 6 (0.87%) patients (one with gastric involvement), table (2). All the ampulla of Vater malignancies were adenocarcinomas (8 cases), 25% were poorly

differentiated (one with signet ring cell component), table (2). Out of 852 colonic biopsies we had 62(7.27%) colorectal carcinomas. The age range of our patients was wide (15-90 years) with a mean of 47 years and the male: female (M: F) ratio was 2:1.

Regarding the tumor site, 26/62 (41.9%) of cases were in the rectosigmoid while 36/62(58.1%) the carcinoma involved other parts of the colon.

Considering the carcinoma grade, 50/62(80.6%) were moderately differentiated, 7/62(11.3%) were well differentiated, while 5/62(8.06%) cases of mucinous carcinoma with signet ring cell component and one case (1.6%) of small cell carcinoma. Mucin production showed a statistically significant correlation with the tumor grade ( $P=0.001$ ), but not with tumor stage ( $p=0.720$ ) nor tumor site ( $p=0.319$ ). Colectomy surgical specimens showed that 61.54% of patients were modified Dukes pathological stage B, 23.08% stage C & 15.38% stage D. Colorectal carcinoma patients were divided into two groups: (A) patients under 40 years & (B) patients above 40 years age. Twenty (32.25%) patients were under 40 years while 42 (67.75%) were above this age. Comparison between the two groups showed that in group A; Females formed 30% of patients versus 35.7% ( $P=0.753$ ). Thirty percent of carcinomas were involving the rectum versus 47.65% ( $P=0.117$ ). Poorly differentiated grade was found in 10% versus 9.5% of patients

( $P=0.903$ ). Eighty percent of patients had advanced tumor stage (modified Dukes C&D) versus 12.5 % ( $P=0.001$  highly significant). Mucinous and signet



ring components were found in 5% versus 9.5% of carcinomas ( $P=0.574$ ). We had four patients with anal canal malignancy, three adenocarcinomas & one squamous cell carcinoma table (2). However we were not able to be definitely sure whether these adenocarcinomas were of a primary anal origin or a directly extending rectal adenocarcinoma. Since our hospital is a specialized center for liver diseases, we received liver biopsies of patients who are newly diagnosed to have liver function disorders, patients with chronic liver disease (to assess activity grade & stage of fibrosis) and patients with single or multiple focal liver lesions. We received ninety five liver biopsies, eight (8.42%) were diagnosed as malignant; one was hepatocellular carcinoma with pseudoglandular differentiation while the other biopsies were diagnosed as metastatic adenocarcinoma. The age range was 25-70 years and (M: F) ratio was 1:1. With splenectomy two cases of lymphoma were diagnosed, one was a female with high grade immunoblastic NHL & the other was a male with Hodgkin's disease (HD) nodular sclerosis, type A. Two cervical lymph node biopsies diagnosed

as involved by metastatic malignancy, one by NHL intermediate grade (63 years old female) & one by metastatic adenocarcinoma (38 years old female). Thirteen biopsies from other abdominal sites were diagnosed as malignant, table (3).

Site	No.	Age Range	Sex		Diagnosis
			Male	Female	
Omentum	4	25-40	2	2	Met.Adeno.Ca
Portahepatis	2	35-48	0	2	Cholangio.Ca
Peripancreatic	1	40	0	1	Met.Adeno.Ca
Peritoneum	2	30-56	0	2	Met.Adeno.Ca
Retrperitonium	1	34	0	1	Chondrosarcoma
Rt.Hypochondrium	1	45	0	1	Sarcomatoid Ca
Other	2	39-50	1	1	Met.Adeno.Ca

**Table (3):** Other sites malignant abdominal masses diagnosed by histopathological examination.

### Ascitic Fluid Cytological Examination Results:

By ascitic fluid cytological examination we were able to diagnose 21/277(7.58%) cases of malignancy, the patients were five males and sixteen females with an age range of 17-70 years (mean 52 years). 19 cases (90.48%) were metastatic adenocarcinoma; the patients had an age range of 35-70 years & M: F ratio 4:1, while 2 cases (9.52%) were diagnosed as NHL, intermediate grade (17 years old male & 35 years old female).



**FNA Cytological Examination Results:** We had reviewed hundred forty two fine needle aspiration (FNA) cytological smear specimens. We diagnosed 119 (83.80%) of them as malignant, table (4).

Cytology	Cases		Age		Sex	
	No.	%	Range	Mean	Male	Female
Liver	97	81.51	3-85	58.14	68	29
Pancreas	9	7.57	21-74	53.11	7	2
Abdominal Mass	10	8.40	35-70	51.3	6	4
Others	3	2.52	16-70	44	1	2
Total	119	100	3-85	51.07	82	37

**Table (4):** Malignancy diagnosed by examining FNA cytological smear.

With liver mass FNA cytological examination, we diagnosed malignancy in 97/173 (56.06%) cases, table (5).

Liver Malignancy		Cases		Age		Sex	
		No.	%	Range	Mean	Male	female
HCC		7	7.22	48-71	61.43	5	2
Poorly diff. Ca		11	11.34	30-85	61.91	10	1
Metastatic Ca	Adeno Ca.	52	53.61	20-82	57.75	35	17
	Small Cell Ca.	9	9.28	60-85	69	8	1
	Sarcoma	5	5.15	17-77	55.8	4	1
	Lymphoma	2	2.06	3-55	29	0	2
	Poorly diff.Ca	11	11.34	21-70	50.9	6	5
Total		97	100	3-85	55.11	68	29

**Table (5):** Types of malignancy involving the liver diagnosed by FNA cytological examination.

Pancreatic mass FNA cytological examination revealed 9/17(52.9%) cases of malignancy. six cases, with an age range 37-70 years and M: F ratio of 5:1, were diagnosed as adenocarcinoma, two males (35&42 years old) had poorly differentiated carcinoma and a female, 21 years old, had a papillary solid and cystic epithelial neoplasm of pancreas. Abdominal mass FNA cytological examination (seventeen cases) showed 10 (58.82%) malignancies; four metastatic adenocarcinoma with age range 48-70 and M:F ratio of 3:1, three spindle cell tumors mostly gastrointestinal stromal tumor (2 males & one female) with age range 35-66 years, one 40 years old female with poorly differentiated malignancy (carcinoma versus lymphoma), one 39 years old male of poorly differentiated carcinoma (carcinoma versus mesothelioma), in which we were not be able to give a definitive diagnosis because of the unavailability of immunocytochemical stains, and one 70 years old female with NHL. Adenocarcinoma was also diagnosed in 2 females one 47 years with axillary tail mass and the other 60 years with pleural fluid aspiration and a male 70 years with gallbladder mass.

#### FNA Cytological Examination Accompanied By Needle Biopsy Histopathological Examination Results:

We examined ninety eight cases of FNA cytology accompanied by FNA needle biopsy and we detected carcinoma in 41(41.84%) of cases. The age range was 5-78 years and the M: F ratio was 3:1. Thirty two (78.05%) of cases had liver masses and were diagnosed by ultrasound guided FNA and biopsy. Hepatocellular carcinoma was detected in 8 cases (with age range 47-72 years and M: F ratio 7:1), metastatic adenocarcinoma was detected in 18 patients (with age range 30-78 years and M: F ratio 5: 1), three cases were diagnosed as poorly differentiated malignancy (2 males, 24 & 30 years old, and a female 55 years old), a 40 years old male with metastatic sarcoma, a 5 years old female with hepatoblastoma, and one 70 years old female with metastatic small cell carcinoma. Of six patients with pancreatic masses, 4 had adenocarcinoma (with age range 38-71years and M: F ratio 3:1), one had endocrine cell tumor (a female 21 years old), and one patient had sarcomatoid carcinoma (a male 45 years old).



We had also a 70 years old male patient with gallbladder adenocarcinoma, a 70 years old male with billiary squamous cell carcinoma, and a 60 years old male with adenocarcinoma of the duodenum.

### DISCUSSION:

In our study, the most common GIT malignancies were the colorectal followed by the gastric and the esophageal cancers. Similar study was done in Saudi Arabia by Assem O. Al-Radi et al. colorectal carcinoma was the commonest cause of gastrointestinal malignancy followed by hepatocellular carcinoma, gastric, and esophageal carcinoma. Furthermore this study showed results that were relatively similar to that obtained in ours regarding the mean age of the patients (58 years), M: F ratio (1.6:1), and the percentage of patients who were below 40 years (20%) (1). Regarding esophageal malignancy, our results were relatively similar to Naji F. and Hamudi S. study that was done in Iraq (2) and indicates that adenocarcinoma is still of low frequency in our region compared to other studies which showed that adenocarcinoma is being recognized at higher percentage (3). Our results regarding gastric carcinoma were relatively similar to that demonstrated in a study done by Kassir Z. and Kassir A. in which the Patients age ranged from 21-85 years, however, 75% of patients were between 40-70 years & 3.4% were below 30 years age. In the present study, a variation in prevalence of different histological types of gastric adenocarcinoma was observed supports the hypothesis that these two types differ not only structurally and epidemiologically but also etiologically. Similarly, in Kassir Z. and Kassir A. study the carcinoma was well advanced in all the patients (418 cases), therefore the curative measures were not feasible and therapeutic measures were palliative (4).

In western countries primary gastric lymphoma is less frequent compared to our region (5). On the other hand, In Naji F. and Hamudi S. study, 57.1% of gastric non Hodgkin's lymphomas were of high grade while 42.9% were of low grade (2). Neoplastic processes of small intestine, especially non Hodgkin's lymphoma, were not diagnosed in our lab, not because. Moreover a significant proportion of the critical cases were referred to private specialized laboratories. Colorectal carcinoma is a common malignancy in our country, there is a slight but steady rise in frequency in both sexes as it constitutes 4% of cancers with a crude incidence rate of about 1.823/100000/year and annual incidence rate of 333 patients (6) compared to the nearby countries as the United Arab Emirates & Qatar in which the mean annual incidence was 12 and 24 patients / year respectively. This low incidence is attributable to certain factors such as young population, high intake of fruits & vegetables, and the life style of the people

in these countries (7) (8). The age range of our patients was wide (15-90 years) with a mean of 47 years, which is less than the mean age of incidence that was reported in the west (62 years) (9).

We found that the male: female (M: F) ratio was 2:1 in contrast to western reports of equal sex affection (9). In Iraq, a ten years period study (1981-1990) was done by Al-Saleem T. and colleagues. showed that the commonest site of colorectal carcinoma was in the rectosigmoid area 65.5%, while 24% were in the other parts of the colon and the site was not specified in 10.5% (10). Western studies showed that approximately 50% of all colonic carcinoma occur in the rectosigmoid area, although their relative incidence seems to be decreasing in the sense that a shift in location toward the proximal colon during the last few decades has been noted (11).

The majority of our patients presented with a tumor stage B. Mohammed I. Ayyub et al. study was done in Saudi Arabia showed that the patients relatively presented in late stage (38.8% stage B, 38.1% stage C, & 23.1% stage D) (12).

Our results showed that there was a correlation between the patients' age below 40 years and the tumor stage, and tumor mucin secretion, although the correlation in the latter was not significant. Al-Khatt M. et al. study was done in the north of Iraq showed that 41.5% of patients with colorectal carcinoma were 40 years age and below with high incidence of mucinous variety and advanced tumor stage (13). In Jordan Tareq M. Al-Jaberi et al. found that 20.2% of the patients with colorectal carcinoma were less than 40 years age and young patients had a statistically significant more advanced stage and more mucin secreting tumor (14).

Malignant ascites accounted for 32% of the ascitis cases, the sensitivity and specificity of the cytology in diagnosing malignancy in malignant ascites were 74% and 100% respectively (15). Different types of metastatic tumors may involve the peritoneal cavity. Many studies showed that the most common sites of primary tumors are female genital tract (particularly ovary) followed by large bowel and pancreas (9). However, in Saleh S., Al-Hashimi A. & Al-Alwan N. study adenocarcinoma of stomach accounted for the highest incidence of malignant ascites (20.5%), followed by adenocarcinoma of the colon (18%), and adenocarcinoma of the ovary (15.4%) (15). Our hospital is a referral center for patients with chronic liver disease, therefore the majority of ascites were inflammatory and non neoplastic belonging mainly to those patients and this explains the low incidence of malignant ascites (7.58%). Single or multiple focal abnormalities in the liver demonstrated by palpation, and/or ultrasounography constitute the main indication for FNA cytology of the liver.

Metastatic tumor deposits are by far the commonest cause of such focal abnormalities. Other causes include primary tumors, congenital and acquired



cysts, and abscesses. Abdul Ghany M. and Alash N. study showed that the sensitivity & specificity of ultrasound guided FNA cytology in malignancy was 87.5% and 100% respectively (16). In this regard, relatively similar to our results were reported by Abdul Ghany M. and Alash N. where metastatic tumors were detected in 60.4% of patients with focal liver lesion and the secondary to primary liver tumor ratio was 4.6:1. Among these, metastatic adenocarcinoma was the commonest (81.3%) followed by poorly differentiated carcinoma (15.6%), and sarcoma (1.3%) (16). Generally speaking, the high sensitivity of ultrasound guided FNA cytology in detecting malignancy in focal liver lesions and the simplicity of the procedure makes it a valuable tool for diagnosing malignancy in such a lesions.

### CONCLUSION:

We concluded from this study that gastrointestinal malignancies are common. Histological typing of malignant neoplasms of the stomach showed that diffuse type of adenocarcinoma was commoner than intestinal type that might be attributable to different etiological factors; on the other hand gastric lymphoma was more frequent in our patients compared to that reported in western countries. There is an increase in the incidence of occurrence of colorectal carcinoma particularly in young male individuals with a relative decrease in rectosigmoid carcinoma due to a shift in location towards the proximal colon and patients under forty years age had a statistically significant more advanced tumor stage than patients above this age. Finally FNA cytology is a valuable method in diagnosis of malignancy especially if combined with FNA needle biopsy since it will increase the sensitivity of the cytological examination.

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