Evaluation of Upper Gastrointestinal Endoscopic Biopsies

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Abstract: Introduction: The upper gastrointestinal flexible fibreoptic endoscope was a simple, safe and well tolerated procedure. The endoscopic biopsy not only permits exact diagnosis of a specific entity but also provides an opportunity to see H.pylori status and may detect gastric mucosal lesions at an early stage.

Aims & Objectives: To study the morphological spectrum of upper gastrointestinal lesions in endoscopic biopsies

Materials & Methods: A prospective study of 187 cases for a period of 2 yrs. The material was fixed in 10% formalin routinely processed and stained with H&E

Results: Out of 187 cases 34 were esophageal,135 from stomach and 9 each from esophagogastric junction and duodenum.

conclusion: squamous cell carcinoma was the commonest malignancy of the esophagus, seen in 6th and 7th decade, more frequent in males, had habitual association with betel nut chewing, more common in middle 1/3, presentation being as a stricture ,histologically most are moderately differentiated SCC. Adenocarcinoma was the commonest malignancy of stomach ,seen in 5th & 6th decade ,found to be predominant in males ,antrum was the commonest site, the commonest presentation was ulcerative growth , histologically most are intestinal type of adenocarcinomas, the common predisposing lesion was H.pylori infection. Cancers of the EGJ presented mostly as polypoid growths and histologically, they were tubular adenocarcinomas. The 2 cases of duodenal adenocarcinomas presented as fleshy and infiltrative growths. The other less common neoplasms of upper GIT include GIST, carcinoid tumor and lymphoma.

Keywords: upper gastrointestinal lesions, Risk factors, adenocarcinoma, Squamous cell carcinoma

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I. Introduction

The upper gastrointestinal flexible fibreoptic endoscope was first used in 1968 and proved to be a major breakthrough in the diagnosis of oesophago-gastro-duodenal lesions¹. The endoscopic biopsy not only permits exact diagnosis of a specific entity but also provides an opportunity to see H.pylori status and plans for specific medical or surgical therapy ^{2,3}]. Endoscopic screening may detect gastric mucosal lesions at an early stage especially atropy, intestinal metaplasia and dysplasia so as to prevent progress of these lesions to invasive cancer.^{4,5}.Diagnostic endoscopy is an invasive technique but has proved to be a simple, safe and well tolerated procedure ⁶. In routine clinical practice, histology is often considered as the "gold standard" against which other tests are compared.

II. Aims & objectives

1. To study the spectrum of Morphological lesions of the upper gastrointestinal tract by the examination of endoscopic biopsies.

2. To review the age and sex incidence of these lesions.

3. To correlate the occurrence of these lesions with certain personal habits.

4. To find the associated / predisposing lesions for neoplasms wherever possible, such as Human Papilloma Virus (HPV) related changes, Barrett's esophagus, Helicobacter pylori infection, intestinal metaplasia, and chronic atrophic gastritis.

Study Design:

III. Materials and Methods

Prospective study conducted in the department of pathology, Guntur Medical College Guntur, spanning over a period of two years starting from Aug-1st 2008 to July 31st, 2010. Eligibility criteria for patients:

All the patients both male and female with symptoms of heart burn, dyspesia, anaemia for evaluation, Gastric Outlet obstruction symptoms, unexplained weight loss. Upper abdominal pain, upper gastrointestinal bleeding are included in the study. Prior informed consent is taken .

IV. Results
Table 01: Distribution of Endoscopic biopsies

NUMBER(%)
34 (18.18%)
135 (72.19%)
9 (4.81%)
9 (4.81%)
187

Table 02 : Age Distribution of Non neoplastic lesions of Endoscopic Biopsies

	Age	Esophagus	Stomach	EGJ	Duodenum	Total
<20		0	1	0	1	2
21 - 30		2	7	0	0	9
31 - 40		1	11	1	2	15
41-50		2	19	2	4	27
51-60		1	14	1	0	16
61 - 70		3	18	0	0	21
71 - 80		1	1	0	0	2
>80		0	0	0	0	0
Total		10(8.8%)	71(77.17%)	4(4.34%)	7(7.6%)	92

Table 03: Age distribution of Neoplastic lesions of Endoscopic biopsies

Age	Oesophagus	Stomach	EGJ	Deudenum	Total
<30	3(12.5%)	4(6.25%)	1	0	8
31-40	3(12.5%)	8(12.5%)	0	1	12
41-50	5(20.83%)	18(28.12%)	2(40%)	1	23
51-60	6(25%)	15(23.43%)	0	0	24
61-70	5(20.83%)	10(15.62)	1	0	16
71-80	2(8.33%)	8(12.5%)	0	0	10
>80	0	1(1.56%)	1	0	2
Total	24	64	5	2	95

Table 04:Sex Distribution of Endoscopic Biopsies

Site	Female	Male	Total
Esophagus	10 (29.41)	24(70.58)	34(18.18)
Stomach	41(30.37)	94(69.62)	135(72.19)
EGJ	3(33.33)	6(66.66)	9(41.81)
Duodenum	1(11.11)	8(88.88)	9(4.81)
Total	55(29.41)	132(70.58)	187(100)

Table 05 : Sex distribution of neoplastic lesions of the upper GI tract

Site	Female	Male	Total
Esophagus	7	17	24
Stomach	22	42	64
EGJ	1	4	5
Duodenum	0	2	2
Total	30 (31.57%)	65 (68.42%)	95 (100%)

Table06: Presenting complaints of Upper Gastrointestinal lesions

Properting Complaints	Site				Total
Fresenting Complaints	Esophagus	Stomach	EGJ	Duodenum	Total
Dysphagia	10	0	0	0	10
Dyspepsia	4	57	4	2	49
Dysphagia & weight loss	15	1	4	0	20
Dysphagia, Dyspepsia & weight Loss	1	1	0	0	2
Dyspepsia & weight loss	1	2	0	0	3
Anorexia & Weight loss	2	40	1	0	43
Anaemia & weight loss	0	5	0	0	5
Abdominal distention, Vomiting & weight loss	0	14	0	0	32
Abdominal pain & vomiting	0	15	0	7	22
Stridor	1	0	0	0	1
Upper GI Bleed	0	0	0	0	0
Total	34	135	9	9	187

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	Betel Nut		Smoking		Alcohol	
	Male	Female	Male	Female	Male	Female
Esophagus	11	7	15	0	12	0
Stomach	9	2	34	0	30	0
EGJ	0	0	2	0	3	0
Duodenum	0	0	0	0	1	0
Total	20	9	51	0	46	0

Table07: Relationship of habits with gastroesophageal neoplasms

Table 08: Morphological spectrum of lesions from biopsies of esophagus

Type of lesion	Number (%)
Non neoplastic	10 (29.41%)
Neoplastic	24 (70.58%)
Total	34 (100%)

Table09 : Subsite presentation and histopathological diagnosis of esophageal lesions

Subsite	Malignant lesions		IEN / Dyanlasia	Barret's	Inconclusive	Total
Subsite	Subsite SCC Adeno IEN / Dysplasia		esophagus	mconclusive	10181	
Upper 1/3	2	0	1	0	1	4
Middle 1/3	16	0	3	0	2	21
Lower 1/3	3	3	0	2	1	9
Total	21	3	4	2	4	34

SCC: Squamous cell Carcinoma, Adeno: Adeno Carcinoma, IEN: Intra epithelial neoplasia

Table10 : Subsite presentation and histopathological diagnosis of esophageal lesions

	Malignant tumors					
Subsite	SCC			Adeno Carcinoma Total		
	WD SCC	MD SCC	PD SCC			
Upper 1/3	0	2	0	0	2(8.33%)	
Middle 1/3	5	11	0	0	16 (66.66%)	
Lower 1/3	0	1	2	3	6(25%)	
Total	5	14	2	3	24(100%)	

Table11: Endoscopic presentation and histopathological diagnosis of esophageal biopsies

	· ·					
Endoscopic	Malignant tumors		IEN/Dyenlasia	Inconclusive	BE	Total
presentation	SCC	Adeno	iEiv/Dyspiasia	Inconclusive	DL	Total
Constricting growth as	15	1	0	0	0	16
stricture	15	1	0	0	0	10
Ulcerative	3	0	2	0	0	5
Infiltrative	2	0	0	0	0	2
Nodular	1	0	0	0	0	1
Irregular mucosa	0	0	0	2	2	4
Polypoidal	0	2	2	0	2	6
Total	21	3	4	2	4	34

SCC: Squamous cell Carcinoma, Adeno: Adeno Carcinoma, IEN: Intra epithelial neopla.

Table12: Subsite distribution of gastric biopsies

Site	No. of Cases
Fundus	16 (11.85%)
Body	41 (30.37%)
Antrum & pre pylorus	75 (55.55%)
GJ Stoma	3 (2.22%)
Total	135(100%)

Table13:Morphological spectrum of gastric lesions in endoscopic biopsies

Type of lesion	No. of Cases
Non Neoplastic	71(52.59%)
Neoplastic	64(47.40%)
Total	135 (100%)

Table14: Subsite distribution of neoplastic lesions of stomach

Site	No. of Cases
Fundus	8 (12.50%)
Body	15 (23.43%)
Antrum & pre pylorus	39 (60.93%)

GJ Stoma	2 (3.12%)
Total	64(100%)

Table15: Endoscopic presentation of neoplastic le	esions of stomach
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Endoscopic presentation	Total No %
Ulcerative	28 (43.75%)
Infiltrative	19(29.68%)
Polypoidal	10(15.62%)
Linitis plastic	7(10.93%)
Total	64(100%)

Table 16: Morplological spectrum of neoplastic lesions of stomach

Epithelial neoplasms		Others		Non epithelial	
According to Laurens	No.		No.		No.
classification					
1.Intestinal type of	44				
adenocarcinoma					
2.Diffusely infiltrating	15	SCC	2	CIST	1
adenocarcinoma		sec	2	0151	1
According to WHO					
classification					
Tubular carcinoma	38				
Papillary Adenocarcinoma	3				
Mucinous carcinoma	2	Carcinoid	1	Lymphoma	1
mucin secreting	1				
adenocarcinoma					
Signet ring carcinoma	15				

SCC: Squamous cell Carcinoma, GIST:Gastrointestinal Stromal Tumor

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Table17: Histopathological types according to Tubular differentiation

Type of differentiation	No. of cases
Well differentiated	8(21.05%)
Moderately differentiated	23(60.52%)
poorly differentiated	7(18.42%)
Total	38



Fig 1: Stricture esophagus



Fig 2: Carcinoma in stomach



Fig 3 : Benign ulcer in stomach



Fig 5 : Well differentiated SCC



Fig 4: Malignant ulcer in stomach



Fig 6: Moderately differentiated SCC



Fig7 : Poorly differentiaed SCC



Fig 8 : Well differentiated adenocarcinoma



Fig 09: Moderately Differentiated Adenocarcinoma Fig 10: poorlydifferentiated Adenocarcinoma



Fig 11: Intestinal type Adenocarcinoma



Fig 12 : Diffusely infiltrating Adenocarcinoma



Fig 13: Sinnet ring cell carcinoma



Fig 14 : Papillary Adenocarcinoma



Fig 15: Mucinous carcinoma



Fig 17 : Gastric carcinoid tumor



Fig 16 : Spindle cell variant of SCC



Fig 18 : Gastric lymphoma



Fig 19 : Gastric GIST



Fig 20: Adenosquamous carcinoma

V. Discussion

Endoscopy with endoscopic biopsy is currently the major method of diagnosis of gastrointestinal (GI) lesions. A total of 3970 specimens were received in the laboratory from August 1^{st} 2008 to July 31^{st} 2010 among which 187 (4.71%) were endoscopic biopsies from the upper Gastrointestinal tract.

The biopsies that were included in the study comprised 34 (18.18%) esophageal biopsies and 135 (72.19%) gastric biopsies. The remaining accounted for 9 cases each (4.81%) from the esophagogastric junction and duodenum. (Table 1).

1. AGE AND SEX INCIDENCE:

AGE INCIDENCE:

Patients with upper gastrointestinal lesions presented between ages ranging from 2nd decade to 8th decade. The mean age of patient was 52.5 years old. The peak incidence was seen in the 4th to 7th decade (Table02&03).

Patients with esophageal cancer presented with ages ranging from 3^{rd} to 8^{th} decade. Mean age of the patients was 50.5 years with peak between the 5^{th} to 7^{th} decade. Patients with gastric cancer presented with ages ranging from $4^{th} - 8^{th}$ decade. The mean age of patients was 56.5 years with a peak incidence (26.76%) in the 5^{th} and 6^{th} decade. The observations were similar with study done by Gauri – Bazaz-Malik, shows a peak between the 5^{th} to 7^{th} decade. Cancer of Esophagogastric junction presented with ages ranging from the 2^{nd} to 8^{th} decade. The youngest patient was 20yrs and the oldest was 81yrs. The mean age of the patient was50.5 yrs with a peak(40%) in the 5^{th} decade. The earlier age at presentation of patients could be attributed to the role of dietary, environmental and genetic factors and the occurrence among patients in 8^{th} decade could be attributed to improved medical care. Patients with duodenal neoplasms presented with mean age of 45yrs and were seen to be distributed equally (50% each) in 4^{th} and 5^{th} decade.

SEX INCIDENCE:

Upper gastro intestinal lesions were more common in males 132 (70.58%) than female 55 (29.41%). The male, female ratio was 2.4:1 (Tableo4). Esophageal cancers showed a slight male preponderance with 17 (70.83%) male and 7 (29.16%) female patients. Similar observation are noted in other studies⁸.

Gastric cancer was more common in males 42 (65.62%) as compared to females 22(34.37%). The male: female ratio was 1.9:1 (42 male and 22 females). Other studies on gastric cancer observed that, it had a male female ratio of 2.1:1. The slight difference in the incidence could be attributed to differences in habits, dietary factors and role of genetic factors or presence of a low socioeconomic status^{8,9}. (Table-5)

Patients with EGJ cancers and duodenal neoplasms also showed a male preponderance with 80% male patients and 20% female patients.

ASSOCIATION OF HABITS WITH GASTROINTESTINAL NEOPLASMS:-

In the present study of all the patients presenting with esophageal cancer 75% were beter nut/ leaf chewers; 62.5% were smokers and 50% consumed alcohol. The most common habit was chewing of betelnut. Other studies on esophageal cancer claimed that more than 80 percent of cases of esophageal cancer in industrialized countries can be attributed to exposure of tobacco and alcohol either singly or joint1¹⁰ and that the risk of developing esophageal carcinoma increased by 3.16 times with the daily habit of chewing betel leaf and tobacco¹¹ (Table07)

When gastric cancer was considered, 34(53.12%) were smokers and 30 (47.88%) consumed alcohol. The relationship between smoking and gastric carcinoma is still unclear with some studies showing a weak to moderate association while some have found none, while others have found a relative risk of less than two fold⁸. There was little evidence to support any association between alcohol and gastric cancer (Table07).

It was seen that habitual associations were more common among male patients when compared to female patients (Table07). This probably accounts for the slightly higher incidence of esophago gastric cancers in males.

I. SPECTRUM OF LESIONS

Among 34 esophageal biopsies studied 10 were non neoplastic and 24 were neoplastic lesions (Table-9).

ESOPHAGEAL NEOPLASTIC LESIONS:

Of the 34 Esophageal biopsies studed 24 (70.58%) were malignant neoplasms. SCC was the most common malignancy in the esophagus 21 (87.5%) cases. The other malignant neoplasms were adenocarcinomas 3 (12.5%). SCCs and adenocarcinomas formed 99% of the total esophageal cancers (table - 10) other studies showed similar finding where more than 90% of esophageal cancers were squomous cell carcinomas and adenocarcinomas¹²

Among the patients presenting with SCC esophagus, 66.66% presented with a growth in the middle third of esophagus, with 25% present in the lower third, and 8.33% present in the upper third. The most common type of presentation was a constricting growth as a stricture 16 (71.42%) followed by ulcerative growth in 3 (14.28%) and infiltrative growth 2(9.52%) (Table 12). Other studies noted that esophageal SCC is commonly seen in the middle and lower third^{88,77}, with most of them presenting as circumferential, often ulcerated lesions¹³.

In the present study moderately differentiated SCC accounted for 14 cases (66.66%) while well differentiated SCC accounted for 5 cases (23.80%) and poorly differentiated 2cases (9.52%) (Table 10).

The well differentiated tumors histologically bear a striking similarity to the cells of normal squamous epithelium. The cells are generally large with hyperchromatic nuclei and bright abundant eosinophilic cytoplasm. Intercellular bridging is usually easily discernible. Individual cell keratinisation and keratin pearl formation is also seen (fig.5)

Moderately differentiated tumors are histologically characterized by individual cell keratinisation but no pearl formation. Loss of attachment of cells are more prominent (fig.6)

Poorly differentiated tumors are histologically characterized by markedly increased nuclear cytoplasmic ratio and pleomorphism. There is a little evidence that the tumor is of squamous origin. Individual cell keratinisation is lacking (fig.7)

Esophageal SCC are most often moderately differentiated SCC^{13} accounts for 66.66% of all cases of SCC,¹⁴ most commonly seen in the middle $1/3^{rd}$ of the esophagus presenting as constricting growth or as a stricture.

There were 3 cases of adenocarcinoma of the esophagus, all arising from the lower third and presenting as predominantly as a polypoidal growth followed by constricting growth as a stricture (Table 11). Adenocarcinoma usually arises from the lower 1/3 of the esophagus⁷⁸ commonly.

Histologically all the 3 cases were well differentiated tubular adenocarcinomas and were characterized by the presence of irregular tubules lined by pleomorphic cells with hyperchromatic nuclei (fig. 8).

2. SPECTRUM OF GASTRIC LESIONS:

The present study included 135 gastric biopsies of which 71 (52.59%) were non neoplastic and 64 (47.40%) were neoplastic (Table.13). The Predominant site of presentation was from antrum and prepylorus (Table 12&14). All the neoplasms were malignant.

NEOPLASTIC LESIONS

The 64 neoplasms comprised of 44 (68.75%) cases of Intestinal type of adenocarcinomas, 15 (23.43%) cases of signet ring carcinoma, and a single case each of carcinoid tumor, malignant lymphoma and GIST (1.56%). The other 2 tumors were SCCs. All the neoplasms were malignant (Table 16).

The commonest site of presentation of gastric adenocarcinoma was the antrum and prepylorus 39 (60.93%) followed by body 15 cases (23.43%) and fundus 8 (12.5%). There were 2 cases of recurrence, where involvement of gastro jejunostomy stoma was seen. The most common type of growth encountered was ulcerative growth in 28 cases (43.75%), infiltrative 19 (29.68%) and polypoidal growth in 10 (15.62%).

Similar findings were noted in other studies with the commonest site being the antrum and the commonest presentation being the ulcerative type of growth. Various studies have noted that adenocarcinomas account for 90-95% of gastric cancers^{8,9,15}. This correlated with the present study where adenocarcinomas constituted 91.66% of all gastric cancers.

When the histopathological types of gastric adenocarcinomas were considered 44 were intestinal type of adenocarcanoms, 15 were diffusely infiltrating adenocarcinomas. (According to Laurens classification) (Table 16).

The intestinal type of adenocarcinomas were seen most commonly in the antrum and prepylorus. Histologically characterized predominantly by cohesive mucin secreting cells that form tubules, gland like structures mimicking carcinoma of the colon (Fig11.)

The diffusely infiltrating adenocarcinomas were most commonly evenly distributed in all parts of the stomach with slight predominance in the antrum and prepylorus (Fig. 12).

According to W.H.O. classification Tubular carcinoma, Papillary adenocarcinoma, Mucinous carcinoma and Mucin secreating adenocarcinoma come under the category of intestinal type of adenocarcinoma in Laurence classification. Signet ring carcinoma come under the category of diffusely infiltrating adenocarcinoma in Laurence classification (fig 13,14,15).

2 cases of squamous cell carcinomas were reported one was a moderately differentiated squamous cell carcinoma seen in 48 yr old female in the antral region which presented endoscopically as a infiltrative growth pattern and the other case was a spindle cell variant of squamous cell carcinoma which presented in a 60yr old male in body of the stomach, and endoscopically presented as a infiltrative growth pattern(fig 16).

In the present study, we encountered one case (1.56%) of gastric carcinoid in a 35 year old male patient who presented with a small polypoid growth in the body (Table16),(fig 17).

The case of GIST (1.56%) in our study was seen in a 65 year old lady who presented with a submucosal polypoidal growth in the body (Table 16).(fig 19).

We encountered a single (1.56%) case of high grade gastric lymphoma in a 65 year male, who had an ulcerated growth in the antrum (Table 16),(fig:18).

3.ESOPHAGOGASTIC JUNCTION (EGJ) LESIONS:

The present study includes 9 EGJ lesions out of which 4 were non neoplastic 5 were neoplastic. The present study had 5 cases of neoplastic lesions of the esophagogastric junction, out of which 4 (80%) cases had a polypoid growth with 1 case (20%) having an infiltrative growth. The histology of the biopsies showed features of well differentiated tubular adenocarcinomas in 3 cases (60%), one case being moderately differentiated squamous cell carcinoma, and another one adenosquamous carcinoma.

The present study had one case of adeno squamous carcinoma, presenting at the EGJ. Endoscopically it presented as a polypoidal growth and was characterized histologically by the presence of both invasive adenocarcinoma and squamous cell carcinoma(fig.20).

4.DUODENAL LESIONS

The present study had 9 duodenal biopsies of which 7 (77.77%) were non neoplastic and 2 (22.22%)were neoplastic. Of these 7 non neoplastic lesions all were duodenal perforations. Among neoplastic lesions, one was poorly differentiated adenocarcinoma infiltrating from the stomach and the other was periampullary carcinoma.

VI. Summary & Conclusion

- The present study included 187 cases of which 34 (18.18%)were esophageal, 135(72.19%) were from stomach, 9 (4.81%) were from esophagogastric junction and 9 (4.81%) were from duodenum.
- The most common neoplasm's of upper gastrointestinal tact were from stomach(72.19%) followed by esophagus (18.18%), EGJ (4.81%) and duodenum (4.81%).
- Most of the neoplasms encountered in the study were malignant.
- The first common neoplasm in the upper GIT was adenocarcinoma (37.43%). It was seen predominantly in the stomach (92.18%) followed by EGJ (60%), lower esophagus (12.5%). Both cases of esophageal adenocarcinoma were seen commonly in the lower third of the esophagus as polypoidal growth.
- SCC was the commonest (87.5%)malignancy of the the esophagus. These neoplasms were commonly seen in the 6th and 7th decade and were more frequent in males. Patients with SCC of the esophagus had a strong habitual association with betel nut chewing, smoking and consumption of alcohol. The middle third of the esophagus was the commonest site for SCC (66.66%), with the most common presentation being a constricting growth as a stricture (66.66%). Histologically, most of the SCCs were moderately differentiated carcinomas (58.33%).
- ★ Adenocarcinoma was the commonest malignancy of stomach. Gastric adenocarcinomas were seen commonly in the 5th and 6th decade and found to be predominant in males. The antrum was the commonest site for gastric adenocarcinomas (60.93%) and the commonest type of presentation was an ulcerative growth (43.75%). Histologically, they presented as intestinal type , diffuse, tubular, papillary adenocarcinomas, mucinous carcinoma and signet ring cancers.
- Cancers of the EGJ presented mostly as polypoid growths and histologically, they were tubular adenocarcinomas. The 2 cases of duodenal adenocarcinomas presented as fleshy and infiltrative growths.
- The other less common neoplasms of upper GIT include GIST, carcinoid tumor and lymphoma.
- Number of associated/predisposing lesions encountered in esophagogastric cancers was lesser as compared to other studies. This could be attributed to the lack of adequate biopsy material from the surroundings sites.
- Some of the endoscopic biopsies contain mucosa only with scanty/no submucosal tissue. This accounted for some inconclusive reports as well as the false negative recording of no evidence of malignancy even though there was a strong clinical suspicion of malignancy
- growths. Histologically, most of the adenocarcinomas were intestinal type, tubular (68.75%) followed by diffuse (23.43%). The common associated /predisposing lesions were H.pylori infection (19.6%) and chronic atrophic gastritis (13.72%). The other less common gastric neoplasms encountered in the study were squamous cell carcinoma,GIST, carcinoid tumor and lymphoma.
- Patients with EGJ lesions were evenly distributed from the 5th to 8th decade with a male: female ratio of 2:1. Among 9 cases, 4 were non specific inflammations and the other 5 were neoplastic. These cancers presented mainly as polypoid growths (80%) and were histologically seen to be well differentiated adenocarcinomas, one squamous cell carcinoma and the other adenosquamous carcinoma.

The duodenal lesions encountered in the study were seen in the 2nd to 6th decade with a male: female ratio of 2:1. They included 7 cases of duodenal perforation and 2 cases of adenocarcinoma.

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