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ORIGINAL ARTICLE

KI-67 PROLIFERATION INDEX AND CLINICOPATHOLOGICAL PATTERNS IN UPPER GASTROINTESTINAL TRACT CARCINOMAS

A. Bhagyalakshmi[1], R. Vijaya Bhaskar[2], Shaik Ayesha Begum[3], B. V. S. Kartheek[4], A. Kasi Babu[5], P. Murali Krishna[6], N. Subba Rao[7], S. V. Kumar[8]

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ABSTRACT: BACKGROUND: Neoplasms of upper gastrointestinal tracts are common and one of the leading causes of death worldwide. In India esophageal and gastric cancers are the most common cancers found in men. Thus early detection and evaluation of prognosis by various methods plays an important role in management of patient. Proliferative activity of tumor assessed with respect to Ki-67 antigen expression is a useful prognostic parameter. This study aimed to correlate the various clinicopathological parameters of upper gastrointestinal tract carcinomas with Ki-67 tumor proliferative activity and to evaluate its prognostic significance. **METHODS:** This is a prospective study for a period of two years from August 2011 to July 2013 in the department of pathology, Andhra Medical College, Visakhapatnam. The various parameters like patient's age, sex, cancer site, histological type and differentiation of the tumor were studied. The above parameters were correlated with KI 67 proliferative indices of the respective cancers and were evaluated statistically. Chi-square tests were used for statistical correlation and p value of <0.05 was considered significant. **RESULTS:** Most common age group for occurrence of upper gastrointestinal carcinomas was from 4th to 6th with majority of patients being males (66%). The most common presenting complaints of esophagus and gastric carcinoma patients was dysphagia and dyspepsia respectively while most common presenting complaint of ampullary carcinoma was jaundice. 39% of the patients were alcoholics and 57% of the patients were smokers. Cellular proliferation as assessed by Ki-67 immunohistochemical staining in esophageal carcinoma showed no correlation with age, sex, site, histological type, and grade of the tumor. In carcinoma stomach, statistically significant correlation was seen between Ki-67 proliferation index (PI) and sex and histological type of tumor with males showing higher Ki-67 proliferation index than females, and intestinal type showing higher Ki-67 proliferation index than diffuse type but no correlation was seen between Ki-67 proliferation index and age, site, and grade of tumor. In ampullary carcinoma a correlation was seen between age of the patient and Ki-67 proliferation index with patients aged less than 55 years showing higher proliferation than patients aged more than 55 years but no correlation was seen between Ki-67 expression and sex and tumor differentiation. **CONCLUSION:** These results indicate that the determination of Ki-67 PI can be a reliable prognostic marker. However in view of the small sample size of the present study further studies are required with larger sample size.

KEYWORDS: Ki-67 Proliferation index, Upper gastrointestinal tract, Carcinoma.

BACKGROUND: Neoplasms of upper gastrointestinal tract (GIT) are common and one of the leading causes of death worldwide. These include tumors arising from esophagus, stomach and first part of duodenum up to opening of the bile duct in ampulla of vater. The prognosis of patients with cancer may be assessed by TNM staging system but it cannot predict perfectly the outcome for a particular

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individual. The final outcome of patients with cancer may be influenced by alterations in oncogenes or tumor suppressor genes that result in changes in cell proliferation kinetics hence proliferative activity of the tumor is a useful parameter in understanding tumor behavior. Attempts have been made to assess the proliferative activity of cancers by mitotic index or the S-phase fraction obtained by H-thymidine or bromodeoxiuridin.

The tumor proliferative activity can be assessed by Ki-67 immuno histochemical staining as this antigen is expressed exclusively in the nuclei of proliferating cells. In the present study an attempt has been made to evaluate the proliferative activity in upper gastrointestinal tract cancers as defined by Ki-67 expression in correlation with various clinicopathological and histopathological parameters.

AIM AND OBJECTIVES:

- To study the clinicopathological patterns of upper gastrointestinal tract carcinomas
- To study the tumor proliferative activity as defined by Ki-67 immunohistochemical staining in correlation with various clinicopathological parameters of upper gastrointestinal tract carcinomas.

MATERIALS AND METHODS: This is a prospective study for a period of two years from August 2011 to July 2013 in the department of pathology Andhra Medical College, Visakhapatnam. Total of 56 samples of various upper gastrointestinal carcinomas were included in study of which 17 were of esophagus, 28 samples were of carcinoma stomach and 11 were of ampullary carcinoma. 51 endoscopic biopsy samples were included and five excision specimens were included in this study, of which one was excision specimen of carcinoma of esophagus and two were total gastrectomy specimens and two excision specimens were of Whipple's resection done for periampullary carcinoma. Relevant clinical data and history was recorded from the patient. Tissue was formalin fixed and paraffin embedded, and were sectioned and stained with haematoxylin and eosin. The tumors were diagnosed and graded according to WHO classification and criteria. The paraffin blocks were subjected to Ki-67 immunostaining.

Specimens have been processed by the micropolymer method. Protein retrieval was done by microwave technique. The antibody clone used was Prediluted Rabbit Monoclonal Antibody Clone SP6 (Biocare medical).

KI-67 IMMUNOSTAINING PROCEDURE: Formalin fixed paraffin embedded tissue blocks were taken, 3-4μm thick sections were made and mounted on poly L-lysine coated slides. Sections were dried overnight at 70°C, then were deparafinized with xylene (3 changes) and rehydrated with graded alcohol (2 changes). The sections were put under running water and changed to distilled water for 5 minutes.

Endogenous peroxidase activity was blocked by incubating the slides in H2O2-methanol solution for 10 minutes. Antigen retrieval done by placing sections in citrate buffer (pH 6-6.2) for 2 cycles, 10 minutes each, at 105°C, then cooled for 30 minutes to reach room temperature. The sections were subjected to blocking of nonspecific antibody binding with bovine serum (Sniper protein block) for 15 minutes. The sections were incubated with primary antibody (clone SP6, Biocare 1:100 dilution) for 1 hour. The sections were incubated with secondary antibody (MACH4 Horseradish peroxidase polymer) for 15 minutes. Add 3'3 diamonobenzidine chromogen substrate addition for visualization for 5 minutes. The sections were rinsed with phosphate buffer saline (PBS)

following each of the above steps. Finally the slides were counterstained with Mayer's Haematoxylin and rinsed with distilled water. The sections were mounted with D.P.X. mountant.

INTERPRETATION OF KI-67 STAINING: Cells that displayed a dark brown nuclear stain were considered to be Ki-67 positive. The number of Ki-67 positive tumor cell nuclei and the total number of tumor cell nuclei were counted at 400x magnification. A minimum of 1000 nuclei per tumor was counted in the areas of the highest proliferative activity. The Ki-67 PI was defined as the number of tumor cells with positive nuclear immunostaining divided by the total number of tumor cells counted per section. Necrotic tissues, stromal cells, and lymphoid cells were not included in the recording. One case each of Burkitt lymphoma and high grade breast carcinoma which showed high degree of proliferative activity and hence high degree of immunostaining with Ki-67 were taken as positive controls.

Statistical Analysis: P value was calculated for individual variable using Chi-Square test and results were tabulated. The p value less than 0.05 was taken as significant.

RESULTS:

Distribution of Upper Gastrointestinal Tract Carcinomas: Of the 56 cases (Table-1) of upper gastrointestinal cancers, 17(30.4%) were of esophagus carcinoma (Figure 1), 28(50%) were stomach carcinoma and 11(19.6%) were ampullary carcinoma. (Figure 2)

Age Distribution in Various Upper Gastrointestinal Carcinomas: The age range of 56 cases were between 21 to 75 years. The peak age of occurrence of these carcinoma were from 4th to 6th decade (52%). The mean age of occurrence of esophagus, stomach and periampullary carcinoma was, 49, 53 and 55 years respectively. (Table-2)

Sex Distribution in Various Upper Gastrointestinal Tract Carcinomas: Male preponderance was seen for all sites at upper gastrointestinal tract cancers with 37/56 (66%) of the patients being males and 19/56 (34%) being females. 10/56 (18%) of patients were males in esophagus carcinoma and 24/56 (43%) & 3/56(5%) were males in stomach and periampullary carcinoma respectively. (Table-3)

Distribution of Site and Presenting Complaints of Patients: The most common presenting complaints of patients with esophagus carcinoma was dysphagia and vomiting whereas gastric carcinoma patients presented with dyspepsia, anorexia and weight loss while most common presenting complaint of ampullary carcinoma was jaundice. (Table-4)

Association of Alcoholism and Smoking with Site of Malignancy: Alcoholism is considered as risk factor for upper gastrointestinal carcinoma such as esophageal carcinoma but in the present study 22/56 (39%) were alcoholics in which 12/16 (66%) of stomach carcinoma patients were alcoholics. Male alcoholics were more in number 20/22 (91%) than female alcoholics who constituted only 2/22 (9%) of total alcoholic patients of upper gastrointestinal cancer. In our study 32/56 (57%) of patients were smokers of which 11/17 (64.7%) of patients of esophagus carcinoma were smokers. Male smokers were higher in number than female smokers in present study with 31/32(96%) of smokers being males with 1/32(4%) of smokers being females. (Table-5)

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Clinicopathological Parameters and their Relation to Ki-67 Proliferation Index (PI) in Esophageal Carcinoma (n=17): Ki 67–PI for 17 cases of esophageal carcinoma ranged from 4.3% to 90.4% and the mean, median, SD scores were 33.2, 28.8, and 24.48 respectively. In present study the mean Ki-67 PI was higher in females (40.14±18.64) than males (28.47±27.77) and patient <60 years had mean Ki-67 PI of (32.69±21.30) and for patients >60 years mean Ki-67 PI was (34.35±31.74). The mean Ki-67 PI for middle esophagus carcinoma was higher (45.92±33.1) compared to upper and lower esophagus which were 36.46±22.28 and 23.31±20.10 respectively, but there was no statistically significant correlation of Ki-67 expression to age, sex and site of tumor.

Squamous cell carcinomas showed higher mean Ki-67 PI of (37.36±24.60) than adenocarcinomas (20±21.61) and poorly differentiated squamous cell carcinomas (Figure:3a & 3b) had higher mean Ki-67 (80.3±14.28) compared to well (Figure:4a & 4b) (11.26±3.5) and moderately (Figure:5a & 5b) (36.41±13.6) differentiated squamous cell carcinomas. But no statistically significant correlation was seen between Ki-67 PI histological type and grade of tumor. (Table-6)

Clinicopathological parameters and their relation to Ki-67 PI in carcinoma stomach (n=28): Ki-67 PI for 28 cases of stomach carcinoma ranged from 5.6% to 73.3% with mean, median and standard deviation of 36%, 40.4%, and 17.5% respectively. A significant correlation was seen with sex of patients and Ki-67 PI (P=0.007) with male patients showing higher Ki-67 PI of (38.4±17.67) than females (21.6±6.36). Ki-67 PI also correlated with histological type of the tumor with intestinal type 25/28(89%) showed higher mean Ki-67 PI (38.96±15.94) than diffuse type (11.26±7.67). Moderately differentiated adenocarcinoma (Figure: 6a & 6b) 14/28(50%) had higher Ki-67 PI of (42.93±15.33) than well differentiated adenocarcinoma(Figure: 7a & 7b) 11/28(39%) which showed Ki-67 PI of (36.51±16.76) but this association was statistically insignificant. 3 cases of diffuse infiltrating adenocarcinoma(Figure:8a & 8b) showed a mean Ki-67 PI of (7.2±1.44). No correlation was found between age, and site of tumor and Ki-67 PI. (Table-7)

Clinicopathological Parameters and their Relation to Ki-67 Proliferation Index in Ampullary Carcinoma(n=11): The Ki-67 P.I in 11 cases of ampullary carcinoma ranged from 20% to 35.6% with mean, median and standard deviation of 42.2%, 37.6% and 21.3% respectively. A significant correlation was seen between Ki-67 PI and age of patient (P=0.04) with higher mean Ki-67 PI of (56.8±26.4) was seen in < 55years patients than >55 years (33.8±13.57). Males showed mean Ki-67 PI of 52.5±24.55 which was higher than females with Ki-67 PI of 38.33±20.37. But no statistically significant correlation was found between sex of patient and Ki-67 PI.

All the tumors in ampulla were adenocarcinomas in our study with 6/11(54%) being well differentiated adenocarcinoma and 3/11(27%), and 2/11(19%) being moderately and poorly differentiated adenocarcinoma respectively. Mean Ki-67 PI for well, moderate and poorly differentiated adenocarcinoma (Figure: 9a & 9b) was 51.6±23.9, 35.5±6.22 and 24±16.4 respectively. Well differentiated adenocarcinoma showed higher Ki-67 PI than moderately and poorly differentiated adenocarcinoma but this association was statistically insignificant. (Table-8).

DISCUSSION: In the present study the age range of patients was from 21 to 75 years with peak incidence of occurrence of carcinoma was at 41 to 60 years of age. Nafees A Oureshi et al[1] from Birmingham UK studied 74 cases in age group of 17-92 years. Vidyavathi K et al[2] studied 58 cases in age group of 25-80 years with peak incidence occurring in age group of 51-60 years.

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In our study the upper gastrointestinal cancers were more common in males (66%) than females (34%) with male to female ratio of 1.9:1. In a study by Vidyavathi K et al [2] males were 37/58 (64%) more in number than females 21/58 (36%) with male to female ratio of 1.7:1. In a study by Kuylenstierna R et al[3] 122/163 (75%) were males and 41/163 (25%) were females with male to female ratio of 2.9:1.

Clinicopathological Parameters of Esophageal Carcinomas in Comparison to other Studies: In our study 17 cases of esophageal carcinoma were analyzed. Patient's age ranged from 21 to 74 years. 35% of the cases tumor occurred in upper third of esophagus 24% in middle third, and 41% occurred in the lower third of esophagus.

Yazdanbod A et al[4] studied 50 cases with age range from 37 to 71 years. In his study 6(12%) cases occurred in upper third, 21(42%) in middle third and 23(46%) in lower third of esophagus respectively. Wakshi J et al [5] studied 80 cases, age ranging from 38 to 78 years with 17/80 (21.2%) in upper third, 31/80(38%) middle third, and 32/80 (40%) in lower third of esophagus respectively. In our study majority of cases were squamous cell carcinoma 13/17(76%) and 4/17(24%) of cases were adenocarcinoma. In the study by Jaskiewicz K et al[6] and Kuylenstierna R et al[3] the incidence of squamous cell carcinoma of esophagus was 294/413(71.4%) and 155/163 (95%) respectively and incidence of adenocarcinoma was 60/413 (28.6%) and 6/163 (4%) respectively.

Clinicopathological Parameters and their Relation to ki-67 PI in Esophageal Carcinoma: In the present study the Ki-67 PI had no significant correlation with age, sex and site of the tumor which is consistent with study by King Yin Lam et al[7] and Yousef et al.[8] Y.Okuno et al[9] also found no statistically significant correlation between age and sex of patient but found significant correlation between site of tumor and Ki-67 proliferation index with tumors in thoracic esophagus showing higher proliferation index than tumors in cervical esophagus.

In present study no correlation was seen between Ki-67 PI and histological type and differentiation of tumor. This is consistent with study by Y. Okuno et al[9] and Yousef et al.[8] Though King Yin Lam et al[7] found no significant correlation between histological type of tumor and Ki-67 proliferation index they found a significant correlation between tumor differentiation of squamous cell carcinoma and Ki-67 proliferation index with poorly differentiated squamous cell carcinoma showing higher proliferative index than moderately and well differentiated squamous cell carcinoma.

Clinicopathological Parameters in Comparison with other Studies in Carcinoma Stomach: Total of 28 cases of carcinoma stomach were analyzed with mean age of patients being 53 years with age ranging from 35 to 75 years. 85% patients were males and 15% were females. Study by Giovanni de Manzon P et al[10] done on 56 patients of gastric carcinoma had 39(70%) males and 17 (30%) females with average age of patients being 65.9 years. This is similar to study by Misra V et al[11] and Khan MI et al[12] who studied 54 and 56 cases of carcinoma stomach respectively. In study by Misra V et al[11] mean age of gastric carcinoma patients was 52 years with 36(67%) of patients being males and 18 (33%) of patients being females. And in study by Khan MI et al[12] mean age of patients was 53.85 years with 42(82%) of patients being males and 14(18%) of patients being females.

Histologically in our study 25/28 (89%) of cases were intestinal type and 3/28(11%) were of diffuse type of adenocarcinoma whereas in study by Misra V et. al[11] 25/54(46%) of cases were intestinal type and 29(54%) of cases were diffuse type of adenocarcinoma. (Table-9)

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Clinicopathological Parameters and their Relation to ki-67 PI in Carcinoma Stomach: In present study a statistically significant correlation was seen in Ki-67 PI and sex of the patients with mean Ki-67 PI for males being 38.4±17.67 higher than that for females 21.6±6.36. In present study there was no correlation between Ki-67 PI and age of the patient which is consistent with studies by Elpek GO et al,[13] Giovanni de Manzon P et al[10] and Lazar D et al[14] who also found no significant correlation between age of patient and Ki-67 proliferation index.

In present study a significant correlation was seen between Ki-67 PI and histological type (Lauren's classification) of the tumor where intestinal type showed higher mean Ki-67 PI of 38.96±15.94 than diffuse type with mean Ki-67 PI of (11.26±7.67). In study by Czyewska J et al[15] showed significant positive association between expression of Ki-67 PI and tumor type but elpek GO et al, [13] Giovanni de Manzon P et. al[10] and Lazar D et al[14] found no correlation between cell proliferation and histological type by Laurens classification. There was no statistically significant correlation between Ki-67 PI and site of tumor in present study which is consistent with study by Czyzewska J et al.[15]

In our study no significant correlation was seen between Ki-67 PI and differentiation of the tumor which is consistent with study by Yukuta Yonemora et al[16] whereas in study by Czyzewka J et al[15] and Lazar D et al[14] a close correlation was seen between the degree of tumor differentiation and the Ki-67 PI ($P<0.001$).

Clinico Pathological Parameters and their Relation to ki-67 PI in Periampullary Carcinoma: In our study 11 cases of periampullary carcinoma were analyzed. The mean age of the patients were 55 years. 4/11(36%) were males and 7/11(64%) of patients were females in our study. In the Study by James R. et al[17] among 123 patients mean age of patients was 65.6 years respectively and 77/123 (54.5%) were men and 56/123 (45.5%) were females.

In present study all the tumors in ampulla were adenocarcinomas with 6/11(54%) being well differentiated, 3/11(27%) and 2/11(19%) being moderate and poorly differentiated adenocarcinoma respectively. No significant correlation was seen between Ki-67 PI and sex of the patients but mean Ki-67 PI for males (52.5±24.55) was slightly higher than females (38.33±20.37).

A significant correlation was seen between Ki-67 PI and age of patient with <55 years patient having higher Ki-67 PI of 56.8.±26.48 than > 55 years patients with mean ±SD of 33.8±13.57. There was no significant correlation between Ki-67 PI and tumor differentiation in present study with mean Ki- 67 PI for well, moderate and poorly differentiated carcinoma being 51.6±23.9, 35.5±6.22, 24±16.40 respectively. In study by Aliysius M Met al[18] patients with > 70 years with periampullary carcinoma had higher Ki-67 PI compared with patients <70 years and he found a correlation between Ki-67 PI and tumor differentiation.

CONCLUSION: Most common age group for occurrence of upper gastrointestinal carcinomas were from 4th to 6th with majority of patients being males (66%). In carcinoma stomach, statistically significant correlation was seen between Ki-67 PI, sex and histological type of tumor with males showing higher Ki-67 PI than females, and intestinal type showing higher Ki-67 PI than diffuse type.

In ampullary carcinoma a correlation was seen between age of the patient and Ki-67 PI with patients aged less than 55 years showing higher proliferation than patients aged more than 55 years.

These results indicate that the determination of Ki-67 PI can be a reliable prognostic marker.

However in view of the small sample size of the present study further studies are required with larger sample size.

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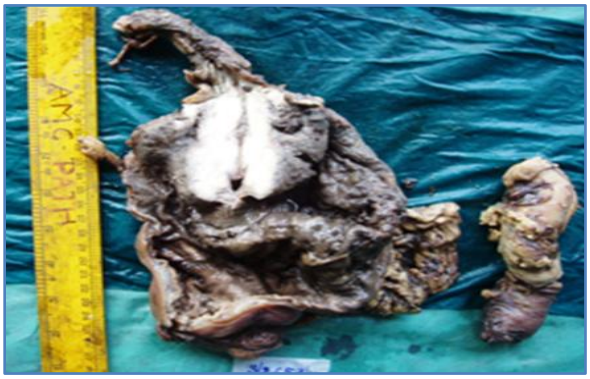

Figure 1

Fig. 1: Gross photograph showing lower end of esophagus with stomach showing irregular grey white growth in lower end of esophagus.

Figure 2

Fig. 2: Gross photograph of Whipple's resection specimen showing irregular grey white growth in ampullary region.

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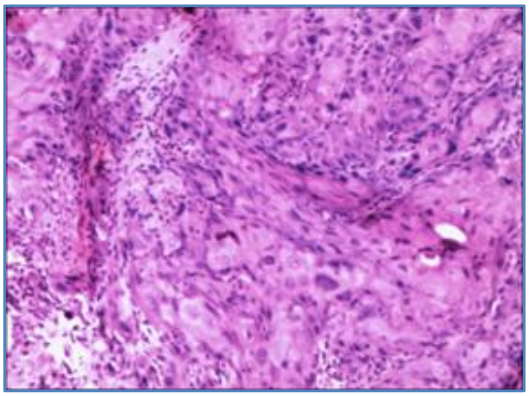

Figure 3a

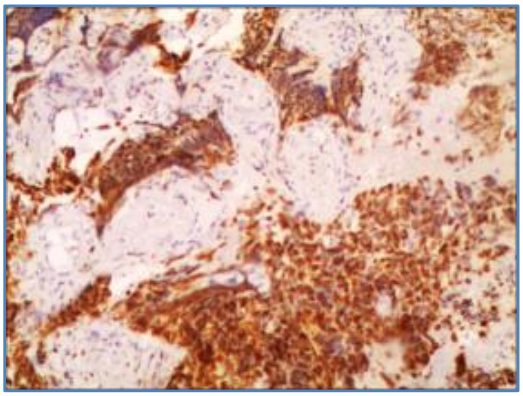

Figure 3b

Fig. 3: POORLY DIFFERENTITED SQUAMOUS CELL CARCINOMA: a) microphotograph showing malignant squamous cells with pleomorphic hyperchromatic nuclei. (H&E;100X);
b) microphotograph showing intense nuclear positivity for Ki-67(IHC; 100X).

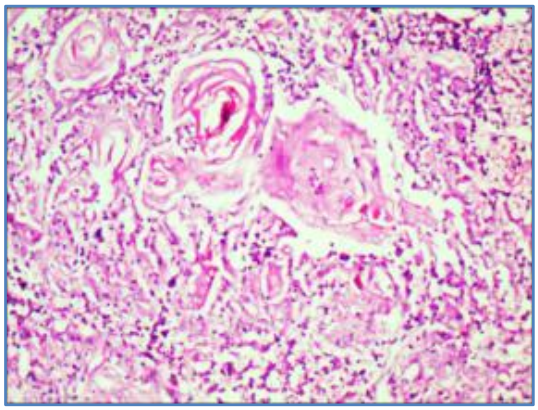

Figure 4a

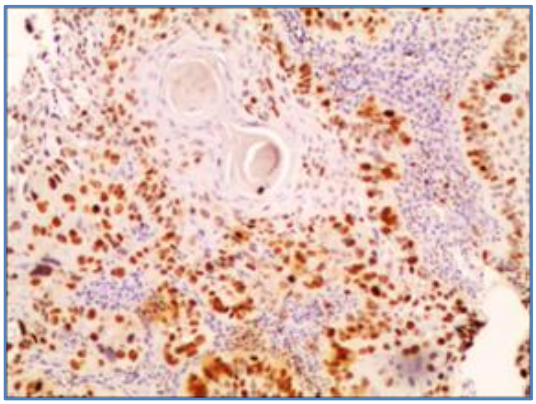

Figure 4b

Fig. 4: WELL DIFFERENTIATED SQUAMOUS CELL CARCINOMA: a) microphotograph showing areas of keratinization and squamous pearl formation (H&E;100X);
b) microphotograph showing Ki-67 nuclear positivity of tumor cells (H & E;100X)

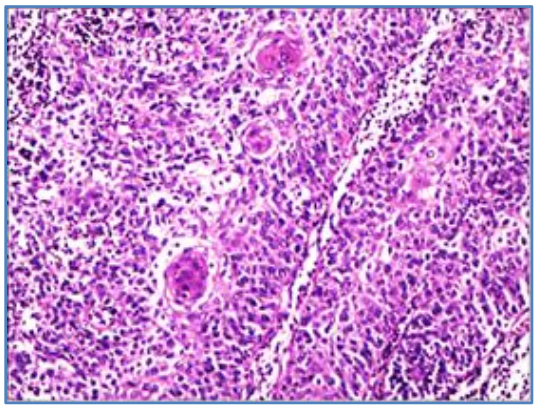

Figure 5a

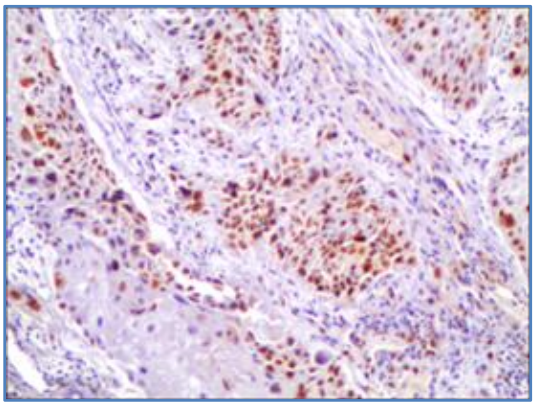

Figure 5b

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Fig. 5: MODERATELY DIFFERENTIATED SQUAMOUS CELL CARCINOMA: a) microphotograph showing sheets of basaloid cells with focal keratin pearl formation (H&E 100X);
b) microphotograph showing strong nuclear positivity of tumor cells for Ki-67 (IHC-100X)

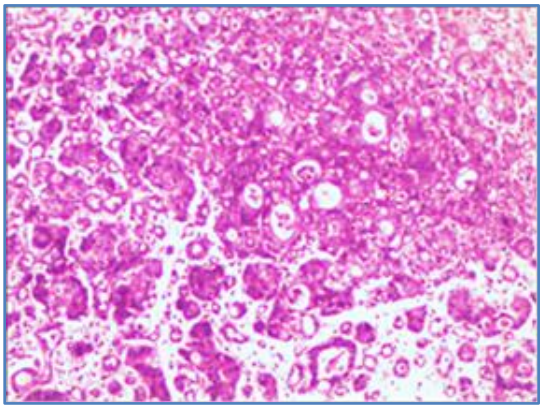

Figure 6a

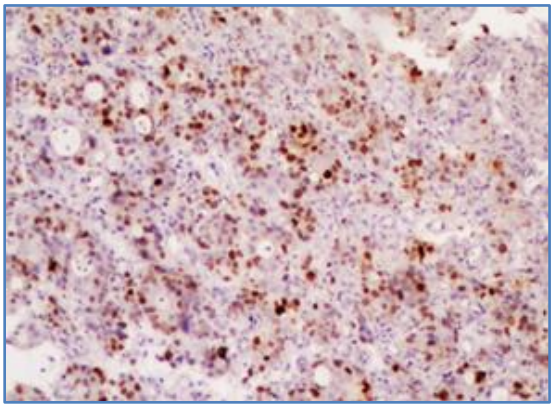

Figure 6b

Fig. 6: MODERATELY DIFFERENTIATED ADENOCARCINOMA: a) microphotograph showing tumor cells arranged in solid sheets with focal well-formed glands (H&E;100X);
b) microphotograph showing tumor cells of showing intense nuclear positivity for Ki-67 (IHC; 100X)

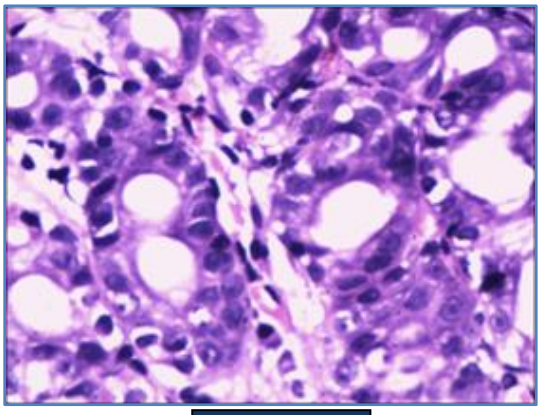

Figure 7a

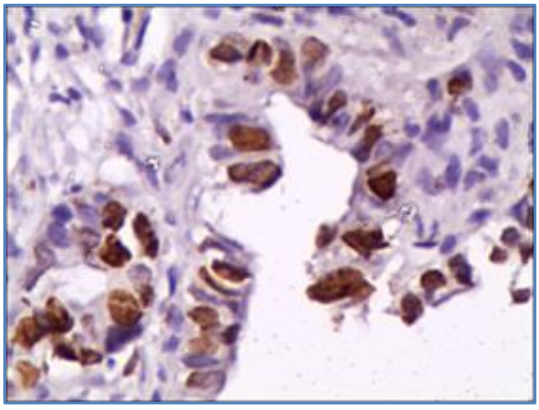

Figure 7b

Fig. 7: WELL DIFFERENTIATED ADENOCARCINOMA: a) microphotograph showing well-formed glands lined by dysplastic cells (H&E 100X);
b) microphotograph showing well-formed glands showing nuclear positivity for Ki-67 in tumor cells (IHC;100X)

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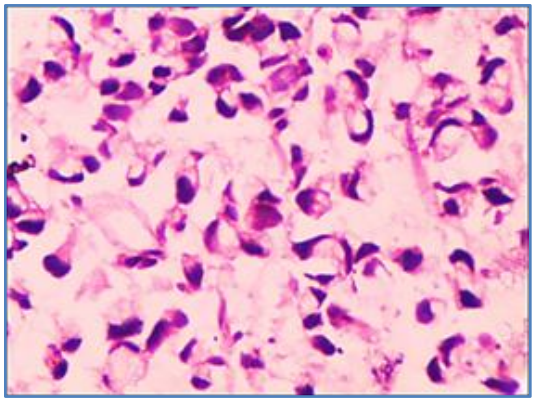

Figure 8a

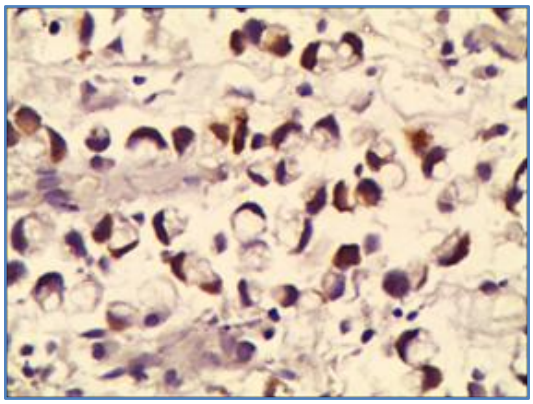

Figure 8b

Fig. 8: SIGNET RING CELL CARCINOMA: a) microphotograph showing sheets of signet cell with eccentric nuclei and central globoid droplet of cytoplasmic mucin. (H&E; 400X);
b) microphotograph showing tumor cells showing nuclear staining for Ki-67 in signet cells (IHC;400X).

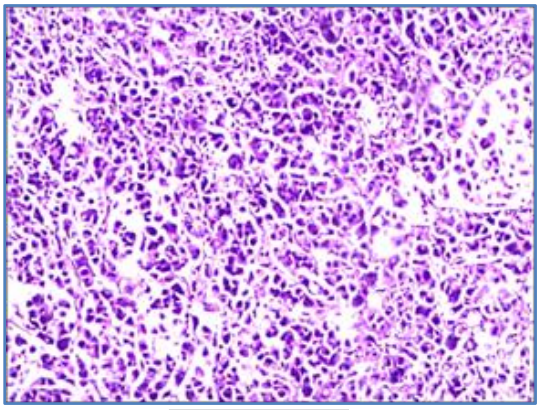

Figure 9a

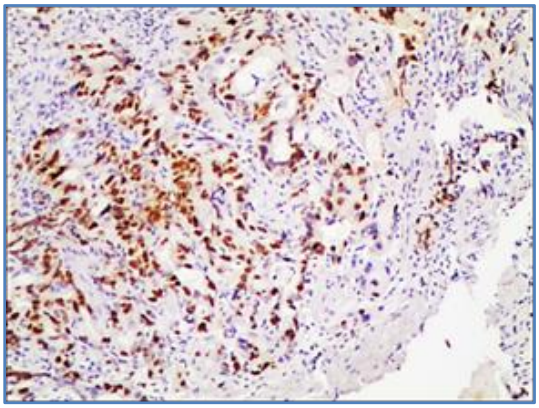

Figure 9b

Fig. 9: POORLY DIFFERENTIATED ADENOCARCINOMA: a) microphotograph showing sheets of pleomorphic tumor cells (H&E; 100X)
b) microphotograph showing tumor cells with intense nuclear positivity for Ki-67 (IHC; 100X)

Site	Number of Cases	Percentage
Esophagus	17	30.4 %
Stomach	28	50%
Ampulla	11	19.6%
Total	**56**	**100%**

Table 1: Distribution of Upper Gastrointestinal Tract Carcinomas

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Age (in years)	Esophagus		Stomach		Ampulla		Total (%)
	Number	%	Number	%	Number	%	
20-40	5	9%	5	9%	2	3%	12(21%)
41-60	7	13%	16	28%	6	11%	29(52%)
61-80	5	9%	7	13%	3	5%	15(27%)
TOTAL	**17**	**31%**	**28**	**50%**	**11**	**19%**	**56(100%)**

Table 2: Age Distribution In Various Upper Gastrointestinal Carcinomas

Site	Male		Female		Total (%)
	No of cases	percentage	Number of cases	percentage	
Esophagus	10	18%	7	13%	17(31%)
Stomach	24	43%	4	7%	28(50%)
Ampulla	3	5%	8	14%	11(19%)
Total	**37**	**66%**	**19**	**34%**	**56(100%)**

Table 3: Sex distribution in various upper gastrointestinal tract carcinomas

Presenting complaints	Site distribution of lesions		
	Esophagus	Stomach	Ampulla
Anorexia	0	12	2
Dyspepsia	5	18	0
Weight loss	4	13	5
Dysphagia	11	0	0
Upper GI bleed	2	0	0
Vomiting	7	2	0
Jaundice	0	0	9
Abdominal pain	0	0	4

Table 4: Distribution of site and presenting complaints of patients

Site	Alcoholism		Smoking	
	Male	Female	Male	Female
Esophagus	6	1	10	1
Stomach	11	1	16	0
Ampulla	3	0	6	0
Total	**20(91%)**	**2(9%)**	**31(96%)**	**1(4%)**

Table 5: Association of alcoholism and smoking with site of malignancy

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VARIABLES	CARCINOMA OF OESOPHAGUS				
SEX	**Number of cases**	**Mean**	**±SD**	**Median**	**P value**
Male	10(59%)	28.47	27.77	17.95	0.092
Female	7(41%)	40.14	18.64	40	NS
AGE					
<60	11(65%)	32.69	21.30	39.6	0.402
>60	6(35%)	34.35	31.74	22.15	NS
Site					
Upper	6(35%)	36.46	22.28	34.4	0.327
Middle	4(24%)	45.92	33.1	41.45	NS
Lower	7(41%)	23.31	20.10	15.5	
Histological type					
Sq.cell.ca	13(76%)	37.36	24.60	39.6	0.312
Adeno.ca	4(24%)	20	21.61	12.6	NS
Grade					
Squamous cell carcinoma					
WDS	3(18%)	11.26	3.5	10.4	
MDS	8((47%)	36.41	13.6	39.8	NS
PDS	2(11%)	80.3	14.28	80.3	
Adenocarcinoma					
WDA	3(18%)	19.33	5	26.47	
MDA	1(6%)	20.2	0	0	
PDA	0	0	0	0	

Table 6: Clinicopathological parameters and their relation to Ki-67 proliferation index (PI) in esophageal carcinoma (n=17)

VARIABLES	CARCINOMA OF STOMACH				
Sex	**Number of cases (%)**	**Mean**	**±SD**	**Median**	**P value**
Male	24(85%)	38.4	17.67	41.1	0.007
Female	4(15%)	21.6	6.36	20.1	
Age					
<50	11(39%)	36.51	16.76	40.4	0.246
>50	17(61%)	35.56	18.69	40.4	NS
Site					
Fundus	2(7%)	25.65	7	25.65	0.143
Body	9(32%)	35.25	17.7	40.4	NS
Pylorus & antrum	17(61%)	37.60	18.46	40.8	
Histological type (Lauren's)					
Intestinal type	25(89%)	38.96	15.94	40.8	0.023
Diffuse type	3(11%)	11.26	7.67	8.2	

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Grade					
WDA	11(39%)	36.51	16.76	40.4	0.201 NS
MDA	14(50%)	42.93	15.33	42.85	
PDA	0(0%)	0	0	0	
DIA	3(11%)	7.2	1.44	8	

Table 7: Clinicopathological parameters and their relation to Ki-67 PI in carcinoma stomach (n=28)

VARIABLES	CARCINOMA OF AMPULLA				
Sex	**Number of cases (%)**	**Mean**	**±SD**	**Median**	**P- value**
Male	3(27%)	52.5	24.55	56.2	0.20 NS
Female	8(73%)	38.33	20.37	36.6	
age					
<55	4(36%)	56.8	26.48	65	0.04
>55	7(64%)	33.8	13.57	35.6	
Grade					
WDA	6(54%)	51.6	23.9	55.6	0.07 NS
MDA	3(27%)	35.5	6.22	37.6	
PDA	2(19%)	24	16.40	24	

Table 8: Clinicopathological parameters and their relation to Ki-67 proliferation index in ampullary carcinoma(n=11)

Studies	No. of Cases	Mean Age	Sex		Histological Type	
			Male	Female	Intestinal	Diffuse
Present study	28	53	24(85%)	4(15%)	25(89%)	3(11%)
Giovanni de Manzon P et.al[4]	56	65.9	39(70%)	17(30%)	-	-
Misra Vet. al. [11]	54	52	36(67%)	18(33%)	25(46%)	29(54%)
Khan MI et. Al[7]	56	53.85	42(82%)	14(18%)	-	-

Table 9: Clinicopathological parameters in comparison with other studies in carcinoma stomach

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AUTHORS:

1. A. Bhagyalakshmi
2. R. Vijaya Bhaskar
3. Shaik Ayesha Begum
4. B. V. S. Kartheek
5. A. Kasi Babu
6. P. Murali Krishna
7. N. Subba Rao
8. S. V. Kumar

PARTICULARS OF CONTRIBUTORS:

1. Professor and HOD, Department of Pathology, Andhra Medical College, Visakhapatnam.
2. Associate Professor, Department of Pathology, Andhra Medical College, Visakhapatnam.
3. Post Graduate, Department of Pathology, Andhra Medical College, Visakhapatnam.
4. Senior Resident, Department of Pathology, Andhra Medical College, Visakhapatnam.
5. Professor, Department of Biochemistry, Andhra Medical College, Visakhapatnam.
6. Professor and HOD, Department of Gastroenterology, Andhra Medical College, Visakhapatnam.
7. Professor and HOD, Department of Surgery, Andhra Medical College, Visakhapatnam.
8. Professor of Surgery & Principal, Andhra Medical College, Visakhapatnam.

NAME ADDRESS EMAIL ID OF THE CORRESPONDING AUTHOR:

Dr. A. Bhagyalakshmi,
Professor and HOD,
Department of Pathology,
Andhra Medical College, Vishakhapatnam.
E-mail: dr.a.bhagyalakshmi@gmail.com

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