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Medicine

RETROSPECTIVE ANALYSIS OF OESOPHAGEAL CANCER

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ABSTRACT

INTRODUCTION Esophageal cancer is the 5th and 7th most common cancer in males and females, respectively.. Only two histopathological variants are commonly seen, namely squamous cell carcinoma and adenocarcinoma. Squamous cell carcinoma is more common than adenocarcinoma until recently.Now, the incidence of adenocarcinoma arising from Barrett's esophagus is increasing, and the incidence of squamous cell carcinoma of the esophagus is decreasing. This study is a retrospective one which includes 150 oesophageal biopsies and specimens sent from the medical, surgical and surgical gastroenterology departments

MATERIALS AND METHODS This study is undertakeni during the period from August 2013 to August 2015. During this study period, both the surgical specimens and biopsy material were processed and histopathological diagnosis was made in the department of pathology.. All the resected specimens were fixed in 10% formalin for 24-48 hours.

The biopsies were submitted in toto for histopathological examination. From the specimens, detailed gross examination was done, including tumor size, type of growth, depth of invasion, margin status and presence and number of lymph nodes. Bits were taken according to the recommendations The tissue slice was processed in various grades of alcohol and xylol and embedded in the paraffin wax. Paraffin sections of 4um thickness were subjected to routine Haematoxylin and Eosin (H&E) staining.

OBSERVATION AND RESULTS This study is a retrospective one which includes 150 oesophageal biopsies and specimens during the period of August 2013 to August 2015.

Out of the 150 samples, 113 were biopsies and 37 were surgical specimens. Of that10 were negative for malignancy on histopathological examination. The rest of 140 samples were taken for study.

Incidence of esophageal carcinoma was 6.16%. Out of 140 materials including in the biopsies and specimen taken for the study excluding the 10 which were negative for malignancy,131 were diagnosed as carcinoma, and 9 were squamous intraepithelial neoplasm(both high grade and low grade.

More number of cases in the middle 1/3 , 2nd most common site is OG junction and least common site is upper1/3.. Among squamous cell carcinomas were common in the middle1/3 of esophagus (51/92 cases of squamous cell carcinomas).

For Adenocarcinoma,common site was OG junction-21 cases were reported out of 32 cases of Adenocarcinomas. Basaloid variant of squamous cell carcinoma was 1 in number, located in the lower 1/3.Spindle cell variant of squamous cell carcinoma was one in number, located in middle 1/3. High Grade squamous intraepithelial lesion were 4 in number(2-upper,1-middle,1-lower)

CONCLUSIONS

In this study, of the total 150 esophageal biopsies and specimens received 131 are carcinomas and 9 are squamous intraepithelial lesions.Esophageal carcinomas incidence is 6.16% of all cancers in the study period from August 2013 to August 2015.The age incidence ranges from 26 to 83 years with median of 54.5 years. Male to Female ratio was 3:2.The maximum number of lesions occurred in the middle one third of esophagus (41.43%) followed by oesophago gastric junction (26.43), lower one third 17.14% and least number of lesions were seen in the upper one third (15%) of esophagus. Adenocarcinoma is restricted to the lower one third and gastro esophageal junction, while squamous cell carcinomas was found in all the portion of esophagus and the commonest site is in the middle third.

KEYWORDS : ESOPHAGUS, BIOPSY, SQUMOUS CELL CARCINOMA, ADENO CARCINOMA

INTRODUCTION

Esophageal cancer is the 5th and 7th most common cancer in males and females, respectively, and is one of the most aggressive tumors. Male: Female incidence ratio is 3:4. According to world cancer statistics, the incidence of oesophageal carcinomas was 481 per lakh population and death occurred in 406 per lakh of affected patients. [1,2] It has a poor prognosis despite ongoing advances in treatment. Only two histopathological variants are commonly seen, namely squamous cell carcinoma and adenocarcinoma. Squamous cell carcinoma is more common than adenocarcinoma until recently. Now, the incidence of adenocarcinoma arising from Barrett's esophagus is increasing, and the incidence of squamous cell carcinoma of the esophagus is decreasing.[3,4]

Tobacco and alcohol are two major two risk factors in 90% of squamous cell carcinomas. Other risk factors include hot beverages, increased exposure of carcinogens (N-nitrosamines), radiation, premalignant lesions like achalasia and Plummer Vinson syndrome.

MATERIALS AND METHODS

This study is undertaken in the department of pathology, Madurai Medical College, Madurai during the period from August 2013 to August 2015. During this study period, both the surgical specimens and biopsy material were processed and histopathological diagnosis was made in the department of pathology, Madurai Medical College, Madurai. All the resected specimens were fixed in 10% formalin for 24-48 hours. We have received a total of 37 esophagectomy specimens and 113 esophageal biopsies. Out of 37 resected esophageal specimens, 24 are squamous cell carcinomas and 13 are adenocarcinomas. Out of 113 esophageal biopsies received, 94 were diagnosed as neoplastic. Details of age, sex, clinical symptoms and site of involvement were recorded .

The biopsies were submitted in toto for histopathological examination. From the specimens, detailed gross examination was done, including tumor size, type of growth, depth of invasion, margin status and presence and number of lymph nodes. Bits were taken according to the recommendations as follows.

Tumor proper
Tumor interface
Proximal resected surgical margins
Distal resected surgical margins
Lymph nodes

The tissue slice was processed in various grades of alcohol and xylol and embedded in the paraffin wax. Paraffin sections of 4um thickness were subjected to routine Haematoxylin and Eosin (H&E) staining.

OBSERVATION AND RESULTS

This study is a retrospective one which includes 150 oesophageal biopsies and specimens sent from the medical, surgical and surgical

gastroenterology departments at Madurai medical college, to the Department of Pathology, during the period of August 2013 to August 2015.

Out of the 150 samples, 113 were biopsies and 37 were surgical specimens. Of that10 were negative for malignancy on histopathological examination. The rest of 140 samples were taken for study.

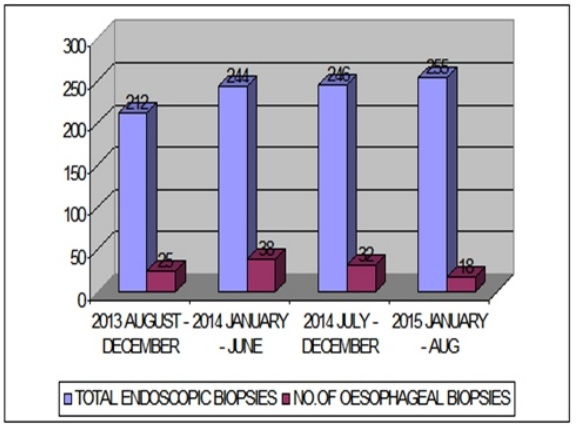
I. FRACTIONS OF OESOPHAGEAL BIOPSIES OF ALL ENDOSCOPIC BIOPSIES

The total number of endoscopic biopsies received from the Gastroenterology Department was 977, which included biopsies from the hypopharynx, pharynx, oesophagus, stomach, intestines, rectum, of which biopsies from the oesophagus was 977, which is about 11.56 % (Table 1, chart 1)

TABLE 1: FRACTION OF OESOPHAGEAL BIOPSIES OF ALL ENDOSCOPIC BIOPSIES

S.NO	PERIOD	TOTAL ENDOSCOPIC BIOPSIES	NO.OF OESOPHAGEAL BIOPSIES
1	2013 AUGUST – DECEMBER	212	25
2	2014 JANUARY – JUNE	244	38
3	2014 JULY – DECEMBER	246	32
4	2015 JANUARY – AUG	255	18
TOTAL		977	113
PERCENTAGE OF ESOPHAGEAL NEOPLASM:11.56%			

CHART 1: FRACTION OF OESOPHAGEAL BIOPSIES OF ALL ENDOSCOPIC BIOPSIES



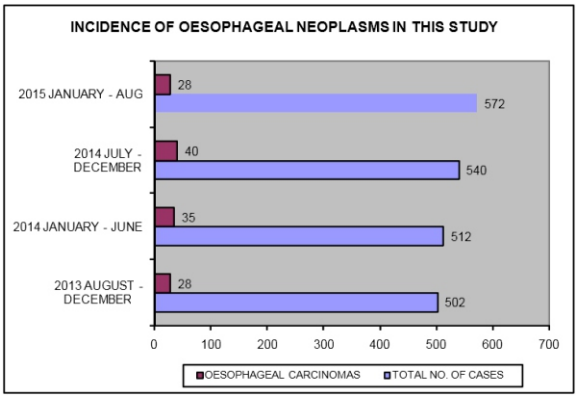
During the period of August 2013 to August 2015, total number of carcinomas reported in the Department of Pathology, Madurai Medical College was 2126 of which esophageal carcinomas were 131 in number accounting to 6.16% all carcinomas. (Table 2, Chart2).

TABLE 2: INCIDENCE OF OESOPHAGEAL CARCINOMAS AMONG OTHER CARCINOMAS

S.NO	PERIOD	TOTAL NO OF CARCINOMAS	NO. OF OESOPHAGEAL CARCINOMAS
1	2013 AUGUST – DECEMBER	502	28
2	2014 JANUARY – JUNE	512	35
3	2014 JULY – DECEMBER	540	40
4	2015 JANUARY – AUG	572	28
	TOTAL	2126	131

Incidence of esophageal carcinoma-6.16%

CHART2: INCIDENCE OF OESOPHAGEAL NEOPLASMS IN THIS STUDY



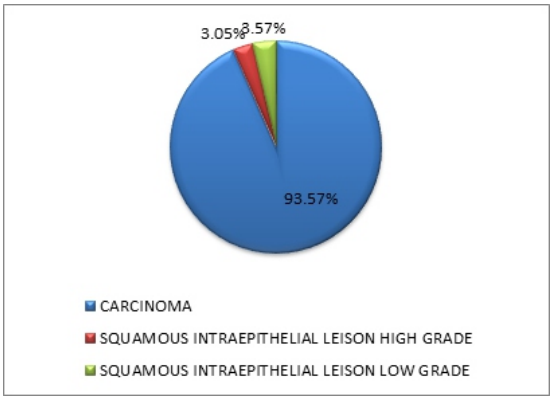
II.FREQUENCIES OF THE LEISONS IN THE STUDY

Out of 140 materials including in the biopsies and specimen taken for the study excluding the 10 which were negative for malignancy,131 were diagnosed as carcinoma, and 9 were squamous intraepithelial neoplasm(both high grade and low grade) (Table 3,Chart 3)

TABLE 3. FREQUENCIES OF THE LEISONS IN THE STUDY

S.NO	LESIONS DIAGNOSED		NUMBER	PERCEMT
1	CARCINOMA		131	93.57
2	SQUAMOUS INTRAEPITHELIAL LESION	HIGH GRADE	4	3.05
		LOW GRADE	5	3.57
	TOTAL		140	100

CHART 3. FREQUENCIES OF THE LEISONS IN THE STUDY



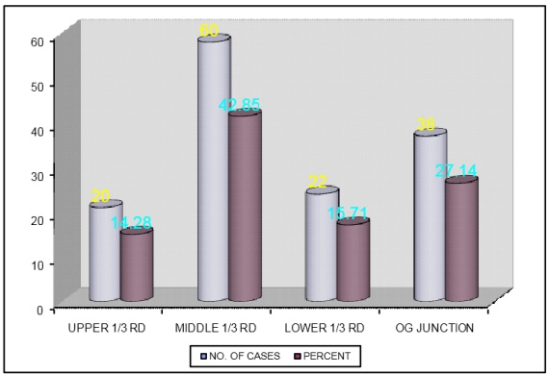
IV.FREQUENCIES OF SITE INVOLVEMENT

Out of 150 cases, excluding 10 cases that were negative for malignancy, 20/140(14.28%) cases were located in the upper 1/3rd, 60/140 cases were located in middle 1/3 (42.85%), for lower-22/140 cases(15.71%) and OG jun-38/140cases(27.14%).(Table 4, Chart 4)

TABLE 4. FREQUENCIES OF SITE INVOLVEMENT

SITE	NO. OF CASES	PERCENT
UPPER 1/3 RD	20	14.28
MIDDLE 1/3 RD	60	42.85
LOWER 1/3 RD	22	15.71
OG JUNCTION	38	27.14
TOTAL	140	100

CHART 4. FREQUENCIES OF SITE INVOLVEMENT



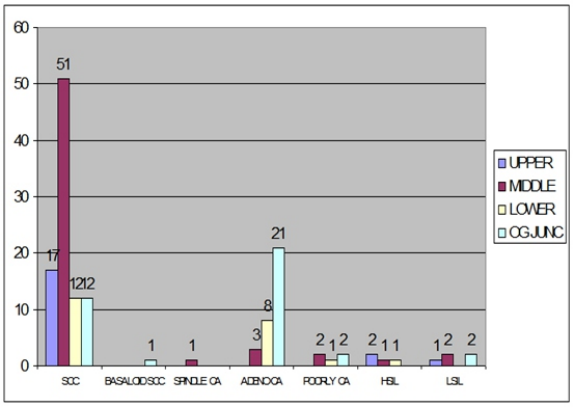
V.SITE OF INCIDENCE OF VARIOUS ESOPHAGEAL LEISONS IN THE STUDY

Out of 150 cases , excluding 10 cases that were negative for malignancy, 20 cases were located in the upper 1/3rd,60 cases were located in middle 1/3,lower-22 and OG Junction-38cases.More number of cases in the middle 1/3 , 2nd most common site is OG junction and least common site is upper1/3.Among squamous cell carcinomas were common in the middle1/3 of esophagus(51/92 cases of squamous cell carcinomas).For Adenocarcinoma,common site was OG junction-21 cases were reported out of 32 cases of Adenoc arcinomas. Basaloid variant of squamous cell carcinoma was 1 in number, located in the lower 1/3.Spindle cell variant of squamous cell carcinoma was one in number, located in middle 1/3. High Grade squamous intraepithelial lesion were 4 in number(2-upper,1-middle,1-lower) (Table 5, Chart 5).

TABLE 5 SITE OF INCIDENCE OF VARIOUS ESOPHAGEAL LEISONS IN THE STUDY

LESIONS	UPPER	MIDDLE	LOWER	OG JUNC	TOTAL
SQUAMOUS CEEL CARCINOMA	17	51	12	12	92
BASALOID VARIANT	-	-	-	1	1
SPINDLE CELL VARIANT	-	1	-	-	1
ADENOCARCINOMA	-	3	8	21	32
POORLY DIFFENENTIATED CARCINOMA	-	2	1	2	5
HSIL	2	1	1	-	4
LSIL	1	2	-	2	5
TOTAL	20	60	22	38	140

.CHART 5 -SITE OF INCIDENCE OF VARIOUS ESOPHAGEAL LEISONS IN THE STUDY



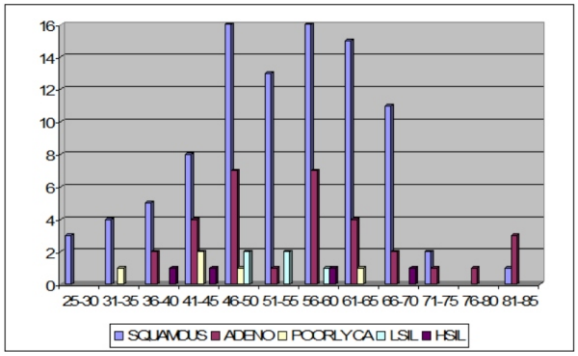
VI. AGE WISE DISTRIBUTION OF THE OESOPHAGEAL LEISONS IN THE STUDY

All the esophageal lesions included in the study were analysed and age wise incidence of each type of lesions was categorized and tabulated. Squamous cell carcinomas show peak age incidence between 46-50 years(16/92cases) and 56-60 years(16/92cases). Adenocarciomas show peak age incidence between 46-50 years(7/32cases). For poorly differentiated carcinomas, out of total 5 cases, 2 cases were between 41-45years. (Table 6, Chart 6).

TABLE 6: AGE WISE DISTRIBUTION OF THE OESOPHAGEAL LEISONS IN THE STUDY

AGE	SCC	ADENO CA	POORLY CA	LSIL	HSIL	TOTAL
25-30	3					3
31-35	4		1			5
36-40	5	2			1	8
41-45	8	4	2		1	15
46-50	16	7	1	2		26
51-55	13	1		2		16
56-60	16	7		1	1	25
61-65	15	4	1			20
66-70	11	2			1	14
71-75	2	1				3
76-80		1				1
81-85	1	3				4
TOTAL	94	32	5	5	4	140

CHART6: AGE WISE DISTRIBUTION OF THE OESOPHAGEAL LEISONS IN THE STUDY



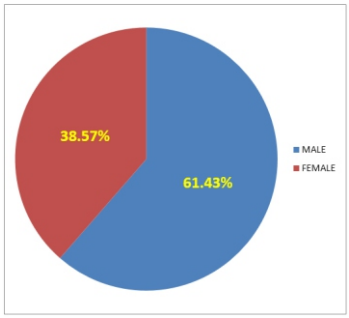
VII. SEX RATIO OF OESOPHAGEAL CARCINOMA IN THE STUDY

Out of the total biopsies received, including precursor lesions, frank malignancies 86 cases were obtained from male and 54 cases were from female patients.86/140-Male accounts for 61.43% of the study and 54/140 females represent 38.57% of the study. Males had more incidence rates with compared to females. The male: female ratio of this study is 1.6:1. (Table 6, Chart 6)

TABLE 7: SEX RATIO OF OESOPHAGEAL CARCINOMA IN THE STUDY

SEX	NO. OF CASES	PERCENT
MALE	86	61.43%
FEMALE	54	38.57%
TOTAL	140	100.00

CHART 7: SEX RATIO OF OESOPHAGEAL LESIONS IN THE STUDY



VIII. SEX WISE DISTRIBUTION IN VARIOUS OESOPHAGEAL LEISONS IN THE STUDY

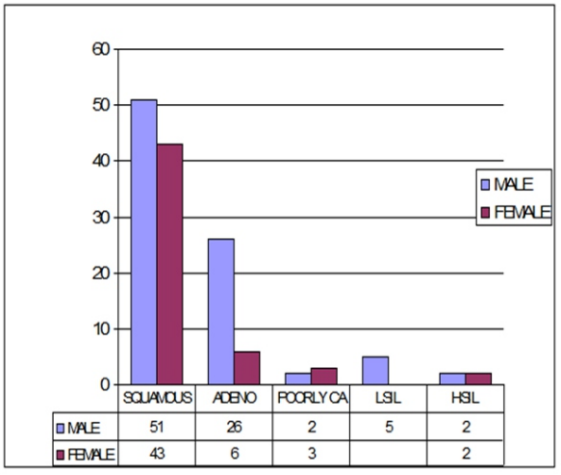
Out of total 140 cases, including carcinomas and precursor lesions, the

incidence rate is higher in male than in females when stratified against both squamous cell carcinomas and adenocarcinomas. Out of 94 squamous cell carcinoma cases, 51 are male and 43 are female. Out of 32 adenocarcinoma cases, 26 cases are male and 6 cases are female. Low grade squamous intraepithelial lesions are found only in males. High grade squamous intraepithelial lesions (4 cases) are equally distributed in males and females. (TABLE 8, CHART 8).

TABLE: VIII SEX WISE DISTRIBUTION IN VARIOUS OESOPHAGEAL LEISONS IN THE STUDY

LEISONS	MALE	FEMALE
SQUAMOUS CA	51	43
ADENO CA	26	6
POORLY CA	2	3
LSIL	5	0
HSIL	2	2
TOTAL	86	54

CHART: VIII SEX WISE DISTRIBUTION IN VARIOUS OESOPHAGEAL LEISONS IN THE STUDY



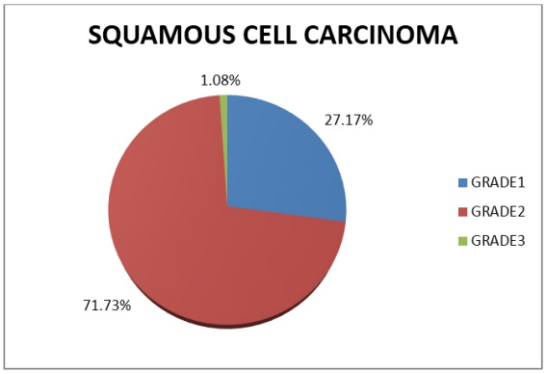
IX. HISTOLOGICAL GRADES OF OESOPHAGEAL SQUAMOUS CELL CARCINOMAS

The total number of squamous cell carcinomas in this study was 92. 25/92 are G1(well differentiated)that accounts 27.17% of all squamous cell carcinomas. 66/92 i.e., the maximum proportion are G2(moderately differentiated) that is about 71.73% and only 1/92 which is 1.08% of the total squamous cell carcinomas are G3(Poorly differentiated). (Table 9, Chart 9)

TABLE IX. INCIDENCE OF GRADES OF ESOPHAGEAL SQUAMOUS CELL CARCINOMA

GRADES	G1(WELL)	G2(MODERATE)	G3(POOR)
SQUAMOUS CELL CARCINOMA	25	66	1
PERCENT	27.17	71.73	1.08

CHART: 9 INCIDENCE OF GRADES OF ESOPHAGEAL SQUAMOUS CELL CARCINOMA



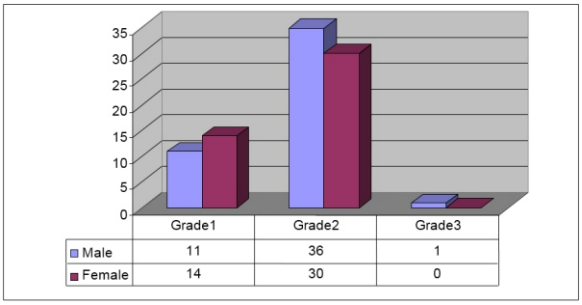
X. HISTOLOGICAL GRADES OF ESOPHAGEAL SQUAMOUS CELL CARCINOMAS WITH SEX CORRE LATION

Out of 25 Grade 1 squamous cell carcinomas 11 are male and 14 are female in number. Out of 66 Grade 2 cases 36 are male and 30 are female. Grade 3 lesion is seen in a male. (Table 10, Chart 10)

TABLE: 10 HISTOLOGICAL GRADES OF ESOPHAGEAL SQUAMOUS CELL CARCINOMAS WITH SEX CORR ELATION

	GRADE I	GRADE II	GRADE III
Male	11	36	1
Female	14	30	0

CHART10.HISTOLOGICAL GRADES OF ESOPHAGEAL SQUAMOUS CELL CARCINOMAS WITH SEX CORR ELATION



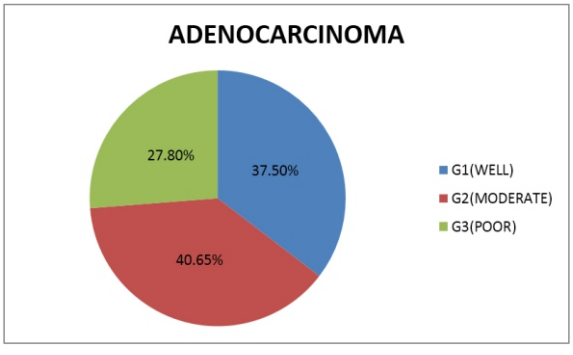
XI .HISTOLOGICAL GRADES OF ESOPHAGEAL ADENOCARCINOMAS

Out of total 32 cases of adenocarcinomas, 12 have grade1[G1], 13 have grade2 [G2] and 7 have grade 3 [G3] lesions. (Table 11, Chart 11)

TABLE11: HISTOLOGICAL GRADES OF ESOPHAGEAL ADENOCARCINOMAS

GRADES	GI(WELL)	G2(MODERATE)	G3(POOR)
ADENOCARCINOMA	12	13	7
PERCENT	37.5%	40.65%	21.87%

CHART 11: HISTOLOGICAL GRADES OF ESOPHAGEAL ADENOCARCINOMAS



DISCUSSION

INCIDENCE

Esophageal carcinoma affects more than 4.5 lakhs people worldwide. Esophageal cancer is the eighth most common cancer worldwide, responsible for 316,000 new cases in 1990 (3.9% of the total), and the sixth most common cause of death from cancer, with 286,000 deaths (5.5% of the total). In 2012, it downgraded to eighth-most common cancer with 456,000 new cases during that year.Cancer of the esophagus is the 4th site having a very poor survival rate other than liver, pancreas, and lung. 10% patients survive at least 5 years in the United States 8 and 5% in Europe.5,6 The worldwide incidence rate of esophageal squamous cell carcinoma in 2012 was 5.2 new cases per 100,000 person-years, with a male predominance (7.7 per 100,000 in

men vs. 2.8 in women).Adenocarcinoma and squamous cell carcinoma differ in rate of incidence and pathogenesis. Katrina F. Trivers et al have reported a decrease in esophageal squamous cell carcinoma by 3.6%/year and a simultaneous increase in esophageal adenocarcinoma by 2.1%/year.[7,8,9]

The incidence of esophageal carcinoma in this study is 6.16% as depicted in table1.Esophageal cancer constitutes 1% all new cancer cases.

AGE INCIDENCE

Since 1988, incidence rates in males have risen significantly by about 1% per year and in females have risen significantly by about 2% per year. The rate of esophageal cancer is currently three times higher among males than females. Most recently, the age-adjusted incidence rate of esophageal cancer was 8.5 new cases per 100,000 males and 2.7 new cases per 100,000 females. The male predominance peaks around 50–54 years then decreases. The rate of esophageal cancer increases with age for both sexes.10,11 Furthermore, the esophageal adenocarcinoma age-adjusted incidence rate in females aged 80 and above increases with age unlike their male counterparts.

Study on esophageal carcinoma by N.A khan et al in Kashmir showed the mean age of occurrence as 54.3years. In Kolkata,a studywas conducted by Urmi sen et al in 1998-12 1999 on 11,700 cases. In that study, incidence rate of esophageal carcinoma among male was nil between the ages 0 to 25 years, 0.2% between the ages 25-34years, 1.6% between the ages35-44years,5.9% between the ages 45-54years,18% between the ages 55-64years, 29.3% between the ages 65-74years and 36.9% when the age was more than 75 years. In Female up to 35years the incidence was nil,0.7% between the ages 35-44years,3.7% between the ages 45-54years,9.5% between the ages 55-64years,28.3% between the ages65-74years and when the age was more than 75 years, the incidence was 42.7%.

In the present study, incidence among female is more in squamous cell carcinoma cases up to 45 years of age, and between 46-65years, male cases are more in number(2:1ratio). And after 70 years, male cases are few in number and no one is female (male,3-squamous cell carcinoma,5-adenocarcinoma).Adenocarcinoma is more common in male [26 in number](evenly distributed) than in female [6 in number] in this study(table7,8 and chart 7,8)

TABLE: 15

S.NO	STUDY	AGE RANGE	MEAN
1	Yokie sato Kuwabara et al[35]	37-80	57
2	K.Mimura et al	45-81	65.3
3	Yosuf Bafandehi et al[57]	16-83	61
4	Present study	26-83	56.5

SEX INCIDENCE

Studies indicate that among males, the overall age-adjusted incidence rate of esophageal cancer rose after 1935 and peaked between 1955 and 1959. Since then, incidence rates have been relatively stable. Among females, the overall esophageal cancer rate has not changed markedly since 1935. The incidence of squamous cell carcinoma has reduced, but adenocarcinoma showed a continuous increase. A fivefold increase in adenocarcinoma of the esophagus were observed in males and a threefold increase were observed among females between 1970 and 1989.The observed increasing trend for adenocarcinoma of the esophagus is mainly from cancers arising in the lower third of the esophagus and primarily among Whites, especially White males.[13,14]

In 2011, there were 8,332 new cases of esophageal cancer in the UK. Among them 5,582 (67%) were men and 2,750 (33%) w women with male: female ratio of around 2:1. For every 100,000 males, 18 new cases are identified in the UK, and 9 for every 100,000 females. In the present study, out of 91 cases reported as squamous cell carcinomas, 48 were male and 43 were female. Out of 32 cases reported as adenocarcinomas, 26 cases were male and 6 were female.

This shows high incidence of male cases in esophageal neoplasm. This result was observed in patients with both SCC and ADC, without a difference.

TABLE:16

GROUPS	MALE	FEMALE	TOTAL
SQUAMOUS(GROUP1)	48	43	91
ADENO CA(GROUP2)	26	6	32

TABLE:17 COMPARISON OF THE SEX INCIDENCE OF THIS STUDY WITH OTHERS

	D.Max parkin et al		Malcolm A Moore et al		PRESENT STUDY	
	MALE	FEMALE	MALE	FEMALE	MALE	FEMALE
INCIDENCE	5%	2.7%	6.7%	3.4%	3.9%	2.95%

The present study is in agreement with the studies of D.Max parkin et al and Malcolm A[15,16]

Moore et al as shown in the above table.

SITE INCIDENCE

The majority of esophageal cancers are located in middle and lower third of esophagus (cutler and young 1975, waterhouse1974, Martinez 1969).[17,18] 5.9-17.3% of esophageal cancers are located in the upper third..Adenocarcinomas mostly occur in the lower thirds and esophago- gastric junction. Adenocarcinoma has overtaken SCC as the predominant histological type in most western countries. As a result, most cancers in the west occur in the lower esophagus or at the esophago-gastric junction.,

TABLE:18

STUDY	UPPER	MIDDLE	LOWER	OG JN
Toshiyuki Kabuto et al	8	14	9	-
Yousef Bafandehl et al	43(12.2%)	119(34%)	120(34.2%)	68(19.4%)
Present study	17(12.9%)	56(42.47%)	20(15.26%)	32(24.42%)

In the present study, most common site for esophageal carcinoma is in the middle third of esophagus (42.47%) and second most common site is OG junction (24.42%). This is in agreement with the studies of Toshiyuki Kabuto et al and Yousef Bafandehl et al19 ,20as shown in the table.

INCIDENCE OF VARIOUS GRADES IN DIFFERENT STUDIES

Histologically, SCCs show varying grades of differentiation ranging from a well-differentiated to undifferentiated tumors. Well-differentiated keratinizing carcinomas have a high proportion of large differentiated squamous cells and a low proportion of small basal-type cells, which are typically located at the periphery of the tumor cell nests. Less well-differentiated tumors consist of round, polygonal, fusiform, or rarely, small nonkeratinizing cells. Most tumors are well- to moderately differentiated lesions. Cytokeratin 14 immunostains may help to identify squamous cell in origin in poorly differentiated carcinoma.[21,22,23]

TABLE:19

STUDY	G1[Grade 1]	G2[Grade 2]	G3[Grade 3]	G4[Grade 4]
Yukie Sato Kuwabara et al	62(31.2%)	92(46.7%)	42(21.1%)	2(1%)
Emile M. Youssef et al	17(24%)	34(47%)	21(29%)	-
Present Study	34(27%)	75(60%)	15(13%)	-

In the present study, more cases were in grade2 category (60%) and grade 1 differentiation was seen in 27% of the tumors and very few cases showed (13%) grade3 differentiation.

SUMMARY AND CONCLUSIONS

- Of the total 150 esophageal biopsies and specimens received 131 are carcinomas and 9 are squamous intraepithelial lesions.
- Esophageal carcinomas incidence is 6.16% of all cancers in the study period from August 2013 to August 2015.
- The age incidence ranges from 26 to 83 years with median of 54.5 years. Male to Female ratio was 3:2.

- The maximum number of lesions occurred in the middle one third of esophagus (41.43%) followed by oesophago gastric junction (26.43), lower one third 17.14% and least number of lesions were seen in the upper one third (15%) of esophagus. Adenocarcinoma is restricted to the lower one third and gastro esophageal junction, while squamous cell carcinomas was found in all the portion of esophagus and the commonest site is in the middle third.

REFERENCES

1. Montgomery, EA; et al. (2014). "Oesophageal Cancer". In Stewart, BW; Wild, CP. World Cancer Report 2014. World Health Organization. pp. 528–543.
2. Ferri, FF, ed. (2012). "Esophageal Tumors". Ferri's clinical advisor 2013. Philadelphia, PA: Mosby (Elsevier)
3. Whittemore, edited by David Schottenfeld, Joseph F. Fraumeni Jr.; associate editors, Graham A. Colditz, Jonathan M. Samet, Alice S. (2006). Cancer epidemiology and prevention (3rd ed.). Oxford: Oxford University Press. p. 697.
4. Zhang, HZ; Jin, GF; Shen, HB (Jun 2012). "Epidemiologic differences in esophageal cancer between Asian and Western populations.". Chinese journal of cancer. 31 (6): 281–6. .
5. Akhtar, S (February 2013). "Areca nut chewing and esophageal squamous-cell carcinoma risk in Asians: a meta-analysis of case-control studies". Cancer Causes & Control. 24 (2): 257–65.
6. Stahl, M; Mariette, C; Haustermans, K; Cervantes, A; Arnold, D; ESMO Guidelines Working, Group (Oct 2013). "Oesophageal cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up.". Annals of Oncology. 24 Suppl 6: vi51–6. doi:10.1093/annonc/mdt342. PMID 24078662.
7. Lozano, R; Naghavi, M; Foreman, K; Lim, S; Shibuya, K; Aboyans, V; Abraham, J; Adair, T; et al. (Dec 15, 2012). "Global and regional mortality from 235 causes of death for 20 age groups in 1990 and 2010: a systematic analysis for the Global Burden of Disease Study 2010". Lancet. 380 (9859): 2095–128. doi:10.1016/S0140-6736(12)61728-0.
8. Enzinger PC, Mayer RJ (2003). "Esophageal cancer" (PDF). N. Engl. J. Med. 349 (23): 2241–52.
9. "SEER Stat Fact Sheets: Esophageal Cancer". National Cancer Institute. Retrieved 18 June 2014.
10. Mayer RJ (2008). "Gastrointestinal Tract Cancer". In Longo DL, Fauci AS, Kasper DL, Hauser SL, Jameson JL, Loscalzo J. Harrison's principles of internal medicine. 1 (18th ed.). New York: McGraw-Hill Medical Publishing Division. pp. 764–5.
11. Cheifetz, Adam S; Brown, Alphonso; Curry, Michael; Moss, Alan C (2011). Oxford American Handbook of Gastroenterology and Hepatology. Oxford University Press. p. 106. .
12. Pennathur A, Gibson MK, Jobe BA, Luketich JD (February 2013). "Oesophageal carcinoma". Lancet. 381 (9864): 400–12.
13. Yamada, Tadataka (2011). Textbook of Gastroenterology. John Wiley & Sons. pp. 1590–1.
14. Gerdes, Hans; Ferguson, Mark K (2002). "Palliation of Esophageal Cancer". In Posner, Mitchell C; Vokes, Everett E; Weichselbaum, Ralph R. Cancer of the Upper Gastrointestinal Tract. PMPH-USA. p. 184.
15. Lao-Sirieix, P; Caldas, C; Fitzgerald, RC (June 2010). "Genetic predisposition to gastro-oesophageal cancer". Current Opinion in Genetics & Development. 20 (3): 210–7.
16. Tobias JS, Hochhauser D (2013). Cancer and its management (6th ed.). p. 254
17. Prabhu, A; Obi, KO; Rubenstein, JH (June 2014). "The synergistic effects of alcohol and tobacco consumption on the risk of esophageal squamous cell carcinoma: a meta-analysis". The American Journal of Gastroenterology. 109 (6): 822–7.
18. Loomis, D; Guyton, KZ; Grosse, Y; et al. (July 2016). "Carcinogenicity of drinking coffee, mate, and very hot beverages." (PDF). The Lancet. Oncology. 17 (7): 877–8
19. Hunter, edited by Blair A. Jobe, Charles R. Thomas Jr., John G. (2009). Esophageal cancer principles and practice. New York: Demos Medical. p. 93.
20. Rutegård M, Lagergren P, Nordenstedt H, Lagergren J (July 2011). "Oesophageal adenocarcinoma: the new epidemic in men?". Maturitas. 69 (3): 244–8.
21. Turati F, Tramacere I, La Vecchia C, Negri E (March 2013). "A meta-analysis of body mass index and esophageal and gastric cardia adenocarcinoma". Annals of Oncology. 24 (3): 609–17.
22. Lagergren J (June 2011). "Influence of obesity on the risk of esophageal disorders". Nature Reviews. Gastroenterology & Hepatology. 8 (6): 340–7.
23. Lagergren, J; Lagergren, P (2013). "Recent developments in esophageal adenocarcinoma". CA: A Cancer Journal for Clinicians. 63 (4): 232–48. .