DEPARTMENT OF CURCEDVA COMERNIA



# **Original Research Paper**

# Surgery

# " A STUDY ON ASSOCIATION OF HELICOBACTER PYLORI IN GASTRIC DISORDERS

DR SELVAM KAVERI	DHARMAPURI MEDICAL COLLEGE AND HOSPITAL, DHARMAPURI, TAMILNADU,INDIA
DR ARAVIND MANNARGOUNDER PACHIAPPAN	ASSISTANT PROFESSOR , DEPARTMENT OF SURGERY, GOVERNMENT DHARMAPURI MEDICAL COLLEGE AND HOSPITAL, DHARMAPURI, TAMILNADU, INDIA
DRSELVAMUTHUKU MARANGUNASEKAR AN	SENIOR ASSISTANT PROFESSOR , DEPARTMENT OF SURGERY, GOVERNMENT DHARMAPURI MEDICAL COLLEGE AND HOSPITAL, DHARMAPURI, TAMILNADU,INDIA

-----

# ABSTRACT Background

Gastric disorders ( benign and malignant ) remains a major public health problem in several developed and developing countries, especially in Asia. In the past 2 decades the association between Helicobacter pylori infection and gastric disorders has been firmly established. Indeed, the International Agency for Research on Cancer categorized H. pylori as a Group I carcinogen for gastric cancer

# METHODOLOGY

This study was done from Jan 2014 till Aug 2015, 62 patients were included. All patients were admitted and routinely investigated. The following parameters were observed age of presentation, risk factors associated, clinical features, investigations like blood routine, ultrasound, upper gastrointestinal endoscope, rapid urease test, histopathology.

Rapid urease test is the endoscopic investigation of choice as it is simple, easy to read, has high sensitivity and specificity for detection of H. pylori than any other tests and hence it is used in this study.

## RESULTS

After analyzing all the data using SPSS, Syntax software version 16.0, Chi square analysis the following are observed.

Age incidence for malignancy is more in 5th and 6th decade. 78% were males and 22% were females. The mean age group was 60 years.

Histopathology showed well differentiated adenocarcinoma (27.7%), moderately differentiated adenocarcinoma (5.5%), poorly differentiated adenocarcinoma (66.67%). Rapid urease test was positive in 20% of patients in malignancy group.

Age incidence for benign gastric diseases is in 4th decade. Gastritis is the most common than gastric ulcers and others in that HPE finding of chronic gastritis is the most common. Rapid urease test was positive in 25.71% of the patients in the benign group.

# CONCLUSION

We conclude that there is association between H pylori infection and gastric disorders (both benign and malignant) but it is less (<30%), which is in contrast to the literature which show high association (>50%) and this may be due to improved hygiene, empirical antibiotic usage for H.Pylori, other common causes like smoking, alcohol, genetic factors and also may be due to population studied.

# KEYWORDS : H.Pylori, Rapid Urease Test, Benign and Malignant Gastric disorders.

# INTRODUCTION

Helicobacter pylori is a ubiquitous organism that can be seen in 50% of general population. It's association with various gastric disorders are well established in numerous studies after its discovery in 1983.Peptic ulcer disease is the most studied disease related to *H pylori* infection. H. pylori is seen in 90% of duodenal ulcer and 75% of gastric ulcer Patients. This bacterium is also involved in the pathogenesis of several extragastric diseases, such as mucosa-associated lymphoid tissue lymphomas (MALTomas) gastroes phageal reflux disease (GERD) and gastric carcinomas. In some population H. pylori is labeled as a definite carcinogen in 1994 by the international agency for cancer research. It is associated with gastric adenocarcinoma, gastric lymphoma and MALTomas.

# OBJECTIVES

- 1. To study the association of H pylori in benign and malignant disorders of stomach.
- To study presence of H pylori in association with different histological types of carcinoma Stomach and benign gastric diseases (such as gastritis, gastric ulcers, erosions and polyps).

#### **METHODOLOGY:**

A prospective clinical study was undertaken at Government

Dharmapuri medical college hospital, Dharmapuri to know the various upper gastro-intestinal endoscopic findings in patients presenting with dyspepsia The study was conducted from Jan 2014 to August 2015. The patient selection was by convenience sampling.

A detailed clinically history was elucidated, followed by careful clinical examination, which were recorded as per the proforma. All the patients included in the study underwent upper gastrointestinal endoscopy and the findings were noted.

# The inclusion and exclusion criterias were as follows: INCLUSION CRITERIA:

1. Patients above 13 years of age.

2. Patients showing symptoms of gastric disorders (abdominal pain , vomiting, hemetemesis , malena, dyspepsia , loss of apetite, loss of weight, etc.)

# EXCLUSION CRITERIA:

- 1. Patients below 12 years of age.
- 2.Pregnant and lactating women.
- 3. Patients who has taken Anti H. pylori drugs in the past 6 months
- ${\tt 4. Patients \, on \, NSAID's \, for \, more \, than \, one \, month \, duration.}$
- 5. Unwilling or unfit patients for endoscopy.

#### PROCEDURE:

All the patients in this study group, on inpatient basis underwent upper gastro-intestinal endoscopy under topical anesthesia. The patients were asked to fast for 12 hours prior to the procedure. Only a few patients were given 5-10mg diazepam intravenously for sedation.

Lignocaine viscous or oral lignocaine sprays were given to the patient 5-10 minutes before the procedure for the local anaesthetic effect. The upper gastro-intestinal endoscopy was conducted with olympus, flexible, fibreoptic endoscope with patients in left lateral positions.

The instrument is advanced under direct vision, with the tip of the endoscope in central lumen. Using the optimal insufflations to keep the lumen of the esophagus well distended. Esophagus was looked for any inflammatory changes, growth. The gastro-esophageal mucosal junction was identified at 38-40cms from the incisors. (This junction is usually serrated and readily identified by the color difference between the esophageal and gastric mucosa, called as Z line).

The position of the esophageal hiatus in the diaphragm is identified by asking the patient to inhale deeply, the diaphragmatic hiatus during inspiration creates an imprint on the esophageal and gastric wall. The position of both the hiatus and the mucosal junction are recorded in order to document the possibility of a hernia or of a columnar lined esophagus. Gastro-esophageal junction should be observed for closed or widely patulous. On entering the stomach, endoscope slightly down and towards the left, a view of greater curvature and of the posterior wall is obtained. Aspiration of all retained liquid is done to reduce the risk of aspiration and to allow proper examination of the stomach. A rotation movement of the tip of the instrument allows examination of the anterior and posterior walls of the body of the stomach. The lesser curvature down to the angulus and the greater curvature are viewed by the same position motion. The most proximal part of both the curvatures are better examined when using the J manoeuvre. Stomach was looked for inflammatory changes, ulcer, growth, erosions, polyps.

By rotating and angulating the tip endoscope is advanced to assess the antrum. Prepyloric and pyloric ring observed directly, the passage through the pylorus being done under direct vision. When the pylorus yields, complete assessment of the duodenum is done upto second part.

Endoscopic biopsies were taken from the antrum, growth and the edge of the ulcer crater depending on the findings.

Antral biopsy is used for rapid urease test in which the RUT card is used. Here the biopsied tissue is placed over the card which contains a yellow coloured medium. Then a drop of distilled water is placed over it and the results are studied after 15 mins, 30 mins and at 24 hrs . If the tissue contains urease enzyme which is produced exclusively by H . pylori , the yellow coloured medium changes to pink or red colour then the test is considered positive . If colour change doesn't occur then the test is considered negative and the results are noted.

Biopsy specimens were also sent in formalin solution for histopathology . Each of the biopsy specimens were fixed in 10% buffered formalin, routinely processed to paraffin and 3  $\mu$ m sections cut.

## Results of the study are listed below:

#### AGE DISTRIBUTION



Age range	Benign	Malignant
Upto 25yrs	8	0
26-35 yrs	7	1
36-45 yrs	12	2
46-55 yrs	7	1
56-65 yrs	8	9
Above 65 yrs	2	5
Total	44	18

#### SEX DISTRIBUTION



	BENIGN	MALIGNANT	TOTAL
MALE	29	14	43
FEMALE	15	4	19
TOTAL	44	18	62



#### ENDOSCOPIC FINDINGS:

During endoscopy the following findings were noted, 36 patients had gastritis and among these 36 pts , 5 persons had co existing Duodenal Ulcer.

Ulceroproliferative growth were second common findings which was seen in 18 patients

FINDINGS	MALE	FEMALE
GASTRITIS	23	13
GROWTH/MALIGNANCY	14	4
POLYP	2	2
EROSIONS	5	3
GASTRIC ULCER	3	0

#### HISTOPATHOLOGICAL EXAMINATION:

HPE of the biopsied tissue shows the following: Among the benign group 30 patients had chronic gastritis, 10 patients had acute gastritis, 4 patients had hyperplastic polyp.

#### RESULTS

Among the malignancy group , 12 patients had poorly

differentiated adeno carcinoma, 5 patients had well differentiated adenocarcinoma and one patient had moderately differentiated carcinoma.



SYMPTOM ANALYSIS:





In most of the patients in the malignancy group , common complaint was abdominal pain (94.44%) followed by vomiting (77.8%) , loss of apetite (61.11%) , weight loss (55.6%) ,dyspepsia (44.44%) , hemetemesis (11.11%), malena (5.5%).

In patients with benign gastric diseases most common symptom is abdominal pain (95.5%), followed by vomiting (38.6%), dyspepsia (11.4%), hemetemesis (9.1%), and loss of apetite, loss of weight and malena (4.5% each)

## **RAPID UREASE TEST RESULTS**

All patients underwent endoscopy and biopsy were taken from the antrum and body. Rapid urease test using RUT DRY TEST kit was done for all patients. The results are as follows:



Of the 35 patients in benign group five patients had co existing duodenal ulcer and out of these 5 patients four had positivity for Rapid urease test.





Volume-6, Issue-4, April - 2017 • ISSN No 2277 - 8160

#### Volume-6, Issue-4, April - 2017 • ISSN No 2277 - 8160

			BM		Total
			Malignant	Benign	
RUT	-	Count	15	35	50
		% within BM	83.3%	79.5%	80.6%
	+	Count	3	9	12
		% within BM	16.7%	20.5%	19.4%
Total	Count	18	44	62	
	% within BM	100.0%	100.0%	100.0%	

The collected data was analysed with SPSS 16.0 version. To describe about the data descriptive statistics frequency analysis, percentage analysis, cross tabulation and the mean and S.D were used. To find the significance difference between the bivariate samples in Independent groups (Malignant & Benign) Independent t test was used. To find the significance in categorical data Chi-Square test was used. In all the above statistical tools the probability value .05 is considered as significant level. **PVALUEIS 0.732.** 

#### DISCUSSION

A prospective study entitled "A study on Association of Helicobacter pylori in Gastric disorders" was undertaken in Government Dharmapuri medical college hospital to study the presence of H. pylori in various gastric disorders.

Eslick GD et al did a meta analysis of observational epidemiological studies. A total of 42 studies met the selection criteria and were categorized by the type of study design: eight cohort and 34 case-control studies. They concluded that H. pylori infection is associated with a 2-fold increased risk of developing gastric adenocarcinoma Xue FB et al also did a meta analysis observational epidemiological studies. Twenty-one papers of case-control studies were selected, including 11 on gastric cancer, 7 on precancerous lesion of stomach and 3 on lymphoma of stomach and the results of Meta analysis present a strong evidence to support the conclusion that H. pylori infection is a risk factor for gastric carcinoma.

Kang JK et al studied the association of helicobacter pylori in gastritis and peptic ulcer disease. H. pylori were present in 96.6% of patients with active chronic gastritis, 100% of patients with duodenal ulcer and 76.9% of patients with gastric ulcer, while present in only 6.3% of individuals with histologically normal gastric mucosa. The bacteria colonized the antral mucosa more frequently than the body or than the duodenal cap mucosa.

Sung-Hsin Kuo and Ann-Lii Cheng studied association of h. pylori in MALTomas. Low-grade mucosa-associated lymphoid tissue (MALT) lymphoma of the stomach, gastric MALT lymphoma, is associated with Helicobacter pylori infection. The eradication of H pylori using antibiotics is successful in 60% to 80% of affected patients.

The association between H. pylori and gastric cancer was proven by numerous case control studies nested in large cohorts which could prospectively examine the H. pylori status of gastric cancer patients. This association was considered sufficient by the Working Group of the International Agency for Research on Cancer / World Health Organization to recognize H. pylori as a Group I carcinogen for humans in 1994.

After informed consent 62 cases of various gastric disorders were included in the study and were studied clinically as per the proforma from Jan 2014 to August 2015 In this study males have a preponderance to have both benign and malignant disorders. In benign group 66% were males and 34% were females.In the malignancy group 78% were males and 22% were females. Of the benign group gastritis is most common.In malignant group poorly differentiated carcinomas are more common.

Mean age for benign diseases is 42 years and for malignancy mean age is 60 years . It is common in 5th and 6th decade of life which is comparable with other literature .

In most of the patients in the malignancy group , common complaint was abdominal pain (94.44%) followed by vomiting (77.8%) , loss of apetite (61.11%) and weight (55.6%) ,dyspepsia (44.44%) , hemetemesis (11.11%), malena (5.5%).

In patients with benign gastric diseases most common symptom is abdominal pain (95.5%), followed by vomiting (38.6%), dyspepsia (11.4%), hemetemesis (9.1%) ,and loss of apetite , loss of weight and malena (4.5% each)

HPE of the biopsied tissue shows the following :

Among the benign group 30 patients had chronic gastritis, 10 patients had acute gastritis, 4 patients had hyperplastic polyp.

Among the malignancy group , 12 patients had poorly differentiated adeno carcinoma, 5 patients had well differentiated adenocarcinoma and one patient had moderately differentiated carcinoma.

 ${\rm In}\,{\rm my}\,{\rm study}\,{\rm there}\,{\rm were}\,{\rm no}\,{\rm cases}\,{\rm of}\,{\rm gastric}\,{\rm lymphoma}\,{\rm or}\,{\rm MALToma}.$ 

# COMPARISON TABLE: MALIGNANCY GROUP

S NO.	VARIABLES		M.A. Majid Et	OUR STUDY
			AI(N = 140)	(11-10)
1.	SEX	М	75%	78%
		F	25%	22%
2.	AGE	MEAN	51.48	60
3.	INVESTIGATION	RUT	24.28%	20%

Rapid urease test was done to find the presence of Helicobacter pylori in these patients . Since Rapid urease test has high sensitivity and specificity which is about 95% , this test is used for this study. The test was positive in 20% of patients in malignancy group and 25.71% of patients in benign group.

In the benign group with RUT positivity 88.9%% of patients had chronic gastritis, 11.1% had acute gastritis in HPE.

In malignancy group with RUT positivity 66.7% had poorly differentiated carcinoma, and 33.3% had well differentiated carcinoma in HPE.

# CONCLUSION

On analyzing the data, we found that Rapid urease test is positive in 20% of patients with malignancy and 25.71% of patients with benign gastric disorders . This shows that H. pylori is one of the causes for benign diseases (gastritis) and also a risk factor for malignant transformation of gastric mucosa.

- Histopathology showed well differentiated carcinoma (27.7%), moderately differentiated carcinoma (5.5%) and poorly differentiated carcinoma (66.6%).
- 80% of Duodenal ulcer patients had positivity for H. pylori which is significant.
- Thus we conclude that there is association between H pylori infection and gastric disorders(both benign and malignant) but it is less (<30%), which is in contrast to the literature which show high association (>50%) and this may be due to improved hygiene, empirical antibiotic usage for H.Pylori, other common causes like smoking, alcohol, genetic factors and also may be due to population studied.

So in cases of benign gastric disorders endoscopic biopsy with rapid

urease test followed by anti H.pylori therapy will decrease the future development of carcinoma.

#### REFERENCES

- T.W.Sadler: Digestive system. In, Susan katz (eds): Langman's medicalembryology, 8th Edn. Lippincott, William and wilkin's 2000; 270-76.
- Lawrence H, Bannister, Martin M, Berry: Gastrointestinal system in Gray'sAnatomy 39th Edn. Churchill livingstone 2008.1140-1150.
- Mercer DW, Liu TH, Castaneda A: Anatomy and physiology of the stomach, in Zuidema GD, Yeo CJ (eds): Shackelford's Surgery of the Alimentary Tract, 5th ed., Vol. II. Philadelphia: Saunders, 2002, p 3. Copyright Elsevier.
- David W. Mercer M.D.Emily K. Robinson M.D: Stomach in SabistonTextbook of Surgery, 17th Edn. Saunders company 2004.1265-1312.
- Moody F, McGreevy J, Miller T: Stomach. In Schwartz SI, Shires GT [eds]: Principles of Surgery, 5th ed. New York, McGraw-Hill, 1989.
- Hermanek P, et al (eds): TNM Atlas: Illustrated Guide to the TNM/pTNMClassification of Malignant Tumours, 4th ed. Berlin: Springer-Verlag, 1997, p82–83.
- Moody F, McGreevy J, Miller T: Stomach. In Schwartz SI, Shires GT [eds]: Principles of Surgery, 5th ed. New York, McGraw-Hill, 1989. 892-894.
- Mercer D, Liu T: Open truncal vagotomy. In Operative Techniques in General Surgery 5:8–85, 2003.
- 9. The esophagus and stomach, in Fawcett DW: Bloom and Fawcett's Textbook of Histology, 11th ed. Philadelphia: Saunders, 1986, p 625.
- Mercer DW, Liu TH, Castaneda A: Anatomy and physiology of the stomach, in Zuidema GD, Yeo CJ (eds): Shackelford's Surgery of the Alimentary Tract, 5th ed, Vol. II. Philadelphia: Saunders, 2002, p 3.
- Antonioli DA, Madara JL: Functional anatomy of the gastrointestinal tract, in Ming S-C, Goldman H (eds): Pathology of the Gastrointestinal Tract, 2nd ed.Baltimore: Williams & Wilkins, 1998, p 13.
- 12. Bloom W, Fawcett DW: A Textbook of Histology. Philadelphia: Saunders, 1975, p 639.
- Bell GH, Davidson N, Scarborough G: Textbook of Physiology and Biochemistry, 6th ed. Livingstone, 1965.
- 14. Charles J. yeo, Dana K. Andersen: Stomach in Schwartz's Principles ofSurgery, 9th Edn. McGraw-Hill Companies 2010 p 894-896.
- 15. Charles J. yeo, Dana K. Andersen: Stomach in Schwartz's Principles ofSurgery, 9th Edn. McGraw-Hill Companies 2010 p 896-898.
- Cadle RM, Mansouri MD, Logan N, et al: Association of proton-pumpinhibitors with outcomes in Clostridium difficile colitis. Am J Health SystPharm 64:2359, 2007.
- Williams C, McColl KEL: Proton pump inhibitors and bacterial overgrowth. Aliment Pharmacol Ther 23:3, 2006.
- Mössner J, Caca K: Developments in the inhibition of gastric acid secretion. EurJ Clin Invest 35:469, 2005.
- Wolfe MM, Soll AH: The physiology of gastric acid secretion. N Engl J Med 319:707, 1988.
- Zuidema G: Shackelford's Surgery of the Alimentary Tract, 4th ed.Philadelphia, WB Saunders, 1995.
- Lloyd KCK, Debas HT: Hormonal and neural regulation of gastric acidsecretion, in Johnson LR (ed): Physiology of the Gastrointestinal Tract, 3rd ed.New York: Raven, 1993.
- Del Valle J, Todisco A: Gastric secretion, in Yamada T, et al (eds): Textbook of Gastroenterology, 4th ed. Philadelphia: Lippincott, Williams & Wilkins, 2003, p 266.
- William F. Ganong. Stomach in Gastrointestinal function in Review of Medical Physiology, 22nd Edn. McGraw-Hill Companies 2005.
- 24. Wallace JL: Gastric resistance to acid: Is the "mucus-bicarbonate barrier" functionally redundant? Am J Physiol 256:31, 1989.
- Allen A, Flemstrom G, et al: Gastroduodenal mucosal protection. Physiol Rev 73:823, 1993.
- Fauci A, Braunwald E: Infectious diseases in Harrison's Principles of Internal Medicine, 17th Edn. McGraw-Hill Companies 2008 p 886.
- Leung WK, Ng EKW, Sung JJY: Tumors of the stomach, in Yamada T, et al (eds): Textbook of Gastroenterology, 4th ed. Philadelphia: Lippincott, Williams & Wilkins, 2003, p 1416.
- Naomi U, Shiro O, Soichiro Y, Nobutoshi M: helicobacter pylori infection and the development of gastric cancer, N Engl J Med, vol. 345, no. 11.september 13, 2001.
- Parsonet J, FriedmanGD: Helicobacter pylori infection and the risk of gastric carcinoma, NEngl J Med 1991;325:1127-31.
- Forman D, Newell GD: Association between infection with Helicobacterpylori and risk of gastric cancer: evidence from a prospective investigation, BMJ 1991;302:1302-5
- J Parsonnet, G D Friedman, N Orentreich, H Vogelman: Risk for gastriccancer in people with CagA positive or CagA negative Helicobacter pyloriinfection Gut 1997; 40: 297-301.
- Sergio A Con, Ana L Valerín: Helicobacter pylori CagA status associated with gastric cancer incidence rate variability in Costa Rican regions, Int JCancer. 1998 Oct 5;78(2):135-9.
- Blaser, M.J., Perez-Perez, G.I., Kleanthous, H., Cover, T.L., Peek, R.M., Chyou, P.H., Stemmermann, G.N. and Nomura, A., Infection withHelicobacter pylori strains possessing cagA is associated with an increasedrisk of developing adenocarcinoma of the stomach. Cancer Res., 55, 2111–2115 (1995).
- Dulciene MM. Queiroz1, Edilberto NM: CagA-positive helicobacter pyloriand risk for developing gastric carcinoma in brazil, int. J. Cancer: 78, 135–139(1998).
- Parsonnet J: Clinician-discoverers—Marshall, Warren, and H. pylori. N Engl J Med 353:2421, 2005. Photomicrographs courtesy of Dr. Manuel Amieva, Stanford University.
- Parsonnet J: Clinician-discoverers—Marshall, Warren, and H. pylori. N Engl J Med 353:2421,2005.
- 37. Blaser MJ, Atherton JC: Helicobacter pylori persistence: Biology and disease. J Clin

- Invest 113:321, 2004.
- 38. Fox JG, Wang TC: Inflammation, atrophy, and gastric cancer. J Clin Invest117:60, 2007.
- 39. Suerbaum S, Michetti P: Helicobacter pylori infection. N Engl J Med 347:1175, 2002.
- Peek RM Jr., Blaser MJ: Pathophysiology of Helicobacter pylori-inducedgastritis and peptic ulcer disease. Am J Med 102:200, 1997.
- 41. Fauci AS, kasper DL, Braunwald E , Hauser SL , Longo DL, Janson JL,Loscalzal ; Principles of Internal Medicine, 17th Edn.
- Fauci A, Braunwald E: Infectious diseases in Harrison's Principles of Internal Medicine, 16th Edn. McGraw-Hill Companies 2008 p 887-888.
- Moody F, McGreevy J, Miller T: Stomach. In Schwartz SI, Shires GT [eds]: Principles of Surgery, 5th ed. New York, McGraw-Hill, 1989 p 926-928.
- Charles J. yeo, Dana K. Andersen: Stomach in Schwartz's Principles ofSurgery, 9th Edn. McGraw-Hill Companies 2010, p926.
- Ming S-C (ed): Tumors of the Esophagus and Stomach, AFIP Atlas of TumorPathology, Second Series, Fascicle 7. Washington DC: American Registry of Pathology, 1973, p 82, Table VI.
- Jemal A, Siegel R, Ward E, Hao Y, Xu J, Murray T, et al. Cancer statistics, 2008. CA Cancer J Clin. 2008;58:71-96.
- Lambert R, Guilloux A, Oshima A, Pompe-Kirn V, Bray F, Parkin M, et al.Incidence and mortality from stomach cancer in Japan, Slovenia and the USA.Int J Cancer. 2002;97:811-8.
- Hermanek P, et al (eds): TNM Atlas: Illustrated Guide to the TNM/pTNMClassification of Malignant Tumours, 4th ed. Berlin: Springer-Verlag, 1997, p82–83.
- Shikata K, Kiyohara Y, Kubo M, Yonemoto K, Ninomiya T, Shirota T, et al. A prospective study of dietary salt intake and gastric cancer incidence in adefined Japanese population: the Hisayama study. Int J Cancer. 2006;119:196-201
- Sung NY, Choi KS, Park EC, Park K, Lee SY, Lee AK, et al. Smoking, alcohol and gastric cancer risk in Korean men: the National Health InsuranceCorporation Study. Br J Cancer. 2007;97:700-4.
- Chao A, Thun MJ, Henley SJ, Jacobs EJ, McCullough ML, Calle EE Cigarette smoking, use of other tobacco products and stomach cancer mortality in US adults: The Cancer Prevention Study II. Int J Cancer. 2002;101:380-9.
- Helicobacter and Cancer Collaborative Group. Gastric cancer and Helicobacter pylori: a combined analysis of 12 case control studies nested within prospective cohorts. Gut. 2001;49:347-53.
- International Agency for Research on Cancer. Schistosomes, Liver Flukes and Helicobacter pylori. Lyon: International Agency for Research on Cancer;
- Charles J. yeo, Dana K. Andersen: Stomach in Schwartz's Principles of Surgery, 9th Edn. McGraw-Hill Companies 2010, p927, table 26-14.
- Aird I, Bentall H. A relationship between cancer of the stomach and the ABO blood group. BMJ 1953:799.
- Charles J. yeo, Dana K. Andersen: Stomach in Schwartz's Principles ofSurgery, 9th Edn. McGraw-Hill Companies 2010, p927.
- Moody F, McGreevy J, Miller T: Stomach. In Schwartz SI, Shires GT [eds]: Principles of Surgery, 5th ed. New York, McGraw-Hill, 1989 p 928-929.
- Shimoyama S, Aoki F, Kawahara M, et al: Early gastric cancer developmentin a familial adenomatous polyposis patient. Dig Dis Sci 49:260, 2004.
- Correa P, Houghton J: Carcinogenesis of Helicobacter pylori.Gastroenterology 133:659, 2007.
- Ting Kin Cheung, Harry H.X. Xia, and Benjamin C.Y. Wong Helicobacterpylori eradication for gastric cancer prevention.J Gastroenterol 2007;42.
- Schaefer N, Sinning C, Standop J, et al: Treatment and prognosis of gastricstump carcinoma in comparison with primary proximal gastric cancer. Am JSurg 194:63, 2007.
- 62. Norton JA, Ham CM, Dam JV, et al: CDH1 truncating mutations in the Ecadherin gene: An indication for total gastrectomy to treat hereditary diffusegastric cancer. Ann Surg 245:873, 2007.
- Leung WK, Ng EKW, Sung JJY: Tumors of the stomach, in Yamada T et al(eds): Textbook of Gastroenterology, 4th ed. Philadelphia: Lippincott, Williams & Wilkins, 2003, p 1416.
- Moody F, McGreevy J, Miller T: Stomach. In Schwartz SI, Shires GT [eds]: Principles of Surgery, 5th ed. New York, McGraw-Hill, 1989 p 931
- Fenoglio-Preiser CM et al: Pathologic and phenotypic features of gastriccancer. Semin Oncol 23(3):292, 1996.
- Ming S-C, Hirota T: Malignant epithelial tumors of the stomach, in Ming S-C Goldman H (eds): Pathology of the Gastrointestinal Tract, 2nd ed. Baltimore: Williams & Wilkins, 1998.
- American Joint Committee on Cancer (AJCC), Chicago, Illinois. The original source for this material is the AJCC Cancer Staging Manual, Sixth Edition(2002) published by Springer Science and Business Media LLC.
- Chen J, Cheong JH, Yun MJ, et al: Improvement in preoperative staging ofgastric adenocarcinoma with positron emission tomography. Cancer 103:2383,
- Sarela AI, Lefkowitz R, Brennan MF, et al: Selection of patients with gastric adenocarcinoma for laparoscopic staging. Am J Surg 191:134, 2006.
- Dicken BJ, Bigam DL, Cass C, et al: Gastric adenocarcinoma: Review and consid erations for future directions. Ann Surg 241:27, 2005.
- Cho CS, Brennan MF: Gastric adenocarcinoma, in Cameron JL (ed): Current Surgical Therapy, 9th ed. Philadelphia: Mosby, 2008.
- Daly JM, Cady B, Low DW (eds): Atlas of Surgical Oncology. St. Louis: Mosby-Year Book, 1993, p 231.
- 73. Zinner MJ (ed): Atlas of Gastric Surgery. New York: Churchill Livingstone, 1992, p 167.
- 74. Cho CS, Brennan MF: Gastric adenocarcinoma, in Cameron JL (ed): Current Surgical Therapy, 9th ed. Philadelphia:Mosby, 2008.
- 75. Karpeh MS, Leon L, Klimstra D, et al: Lymph node staging in gastric cancer: Is location moreimportant than number? An analysis of 1,038 patients. Ann Surg 232:362, 2000.
- Sasako M, Sano T, Yamamoto S, et al: D2 lymphadenectomy alone or withpara-aortic nodal dissection for gastric cancer. NEngl J Med 359:453, 2008.
- Yoon SS, Coit DG, Portlock CS, et al: The diminishing role of surgery in thetreatment of gastric lymphoma. Ann Surg 240:28, 2004.

#### Volume-6, Issue-4, April - 2017 • ISSN No 2277 - 8160

- Yoon SS, Coit DG, Portlock CS, et al: The diminishing role of surgery in the treatment of 78. Gold JS, DeMatteo RP: Combined surgical and molecular therapy: The
- 79. gastrointestinal stromal tumor model. Ann Surg 244:176, 2006.
- Rubin BP, Heinrich MC, Corless CL: Gastrointestinal stromal tumour. Lancet 369:1731, 80. 2007.
- 81. Stelow EB, Murad FM, Debol SM, et al: A limited immunocytochemicalpanel for the distinction of subepithelial gastrointestinal mesenchymalneoplasms sampled by endoscopic ultrasound-guided fine-needle aspiration.Am J Clin Pathol 129:219, 2008.
- 82. Gold JS, DeMatteo RP: Combined surgical and molecular therapy: Thegastro intestinal stromal tumor model. Ann Surg 244:176, 2006
- 83. Raut CP, Kulke MH, Glickman JN, et al: Carcinoid tumors. Curr Probl Surg43:383, 2006.
- 84. Modlin IM, Kidd M, Latich I, et al: Current status of gastrointestin alcarcinoids. Gastroenterology 128:1717, 2005.
- 85. Mulkeen A, Cha C: Gastric carcinoid. Curr Opin Oncol 17:1, 2005.
- 86. Majid MA,et al: Association of Helicobacter pylori infection with gastric carcinoma. Bangladesh Med Res Counc Bull 2009; 35: 7-10.