Research Article

Etiologies and Risk Factor Associated with Gastric Cancer - A Hospital Based Observational Study

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Abstract

Background: Worldwide approximately 9,90000 people are diagnosed with gastric cancer. It causes fourth most common cancer and second most common cause of cancer death worldwide. There is marked geographical variation reported about the incidence of gastric carcinoma. High Incidence were reported in China, Japan and eastern Europe while low incidence rate reported in India, Philippines, Australia and North America. Factors responsible for Stomach Cancer: Hereditary and genetic factor, Dietary Factor, Diet and Lifestyle, H-Pylori Infection.

Material and Method: We Included a study of 110 patients of primary gastric cancer diagnosed in department of Radiation Oncology at State Cancer Institute Patna from July 2021 to July 2022. All the patients were diagnosed on basis of clinical history, Endoscopy, Radiological examination. The diagnosis was confirmed by histological examination of endoscopic biopsy or by reselected specimen. All the histo-pathologically confirmed cases were included in the study.

Result: Most common age group in our study was 51-60 years 42.6% in Males and 20% in Females, Male: Female ratio was 1.7:1. Most common histopathology was adenocarcinoma 94% followed by squamous cell 6%. About 38% were poorly differentiated adenocarcinoma, 32% were well differentiated adenocarcinoma, 29% cancer were well differentiated adenocarcinoma. Most common symptom on presentation was pain in abdomen 87%, loss of appetite 72%, weight loss 55%, nausea 38%, vomiting 16%, dysphia in 11%. H-Pylori was tested in 110 patients among them 21 were positive and 89 were negative.

Practical Implication: Dietary modification diets with low consumption of red meat, High in fruits and vegetables may have some role in prevention of cancer. For H pylori, A vaccine would be cost effective to prevent gastric cancer and duodenal ulcers.

Keywords: Gastric Cancer; *H. pylori*; Adenocarcinoma

Background Information

Worldwide approximately 9,90000 people are diagnosed with gastric cancer [1]. It causes fourth most common cancer and second most common cause of cancer death worldwide [2]. There is marked geographical variation reported about the incidence of gastric carcinoma. High Incidence were reported in China, Japan and eastern Europe while low incidence rate reported in India, Philippines, Australia and North America [3]. Preventive measures can be possible if we know the etiology and risk factors responsible for gastric cancer. According to GLOBOCAN 2012 around one million new cases of gastric cancer diagnosed worldwide, ranked 5th most common cancer worldwide after lungs, breast, colorectal and prostate cancer [4]. In the USA incidence rate is decreasing annually by 1.7% in men and 0.8% in women reflex disease, obesity have been related with risk of gastric cancer [5]. From 1992 to 2010 with and overall decrease in cancer [5] incidence There is less decrease in incidence rate of gastric cancer in China as compared to other countries [6].

Risk Factor for gastric cancer

Gastric cancer is a multifacterial disease and both environmental and genetic factors are associated with gastric cancer. Many oth-

er risk factors like *H. Pylori* Infections dietary factors and lifestyle are also linked with gastric cancer etiology.

Hereditary and genetic factor

Hereditary diffuse gastric cancer is a autosomal dominant inherited, rare form of gastric cancer. It is highly imasive diffuse type with poor prognosis usually associated with late presentation [7]. Approximately 25% of families have inactive CDHI germline mutation with hereditary diffuse gastric cancer are also associated with other cancers like breast, pancreatic cancer and colorectal cancer [8]. A severe bacterial toxin (VaCA) includes multiples structural and functional alteration in gastric epithetical cells. These two cagA and VaCA are found to be associated with increased risk for developing intense tissue response in malignant and pre malignant lesion in distal stomach a functional cytotoxin which is secreted by *H. pylori* shows carrying CagAI VaCA [9,10].

Dietary factors

Some of the food carcinogens directly intended with gastric epithelial cells and can cause genetic mutation of epithelial cells [11,12]. Some of the studies on animal studies shown rich level of sodium chloride can cause damage to gastric mucosa leads to cell death and induce regenerative cell proliferation resulted into inflammation and injury [14,15]. Diet with high salt level has been found to be associated with colonization of *H. pylori*. Some studies done in Chinese, Korean and Japanese population showed relationship between single nucleotide polymorphism and gastric carcinoma like mucin, cell surface associated genes (MUC 1) [16]. Prostrate stem cell antigen gene (PSCA) and PLE 1. Two independent studies in Chinese reported additional loci such as multiple variant located in gene PLCE1 are associated with gastric cancer. Biological mechanism is not yet clear in these polymorphism [17,18].

Diet and lifestyle

WCRF and AICR reported in 2007, non steroid vegetables including specific allium and fluids(Rich source in Anti-Oxidants) have some protective effect on stomach cancer. 50gm fruits per day can decrease the risk up to 23% [19,20], A meta analysis population attributed risk for smokers in male varies 1.53 fold in males and 28.6% and among females between 11% and 14% from the US and Europe.

H. pylori infection

A gram negative bacteria estimated to cause 65% to 80% of all gastric cancer [21,22]. It has been characterized by WHO since 1944 as a class I carcinogen of gastric cancer [23]. Two major mechanisms are involved in oncogenic effects of *H. pylori* infections direct action of bacteria on gastric Epithelial cells other is Indirect action caused by inflammatory response some of the *H. pylori* strain could also directly modulate epithelial cells function by bacterial agents such as CagA [24]. Cytoterin associated gene. FAP caused by germline mutation in APC gene is the most common form of familial intestinal gastric cancer. It is an autosomal dormant [25] inherited predispastian to adenomatous polyps [9]. PJS is characterised by haematomalous gastro intestinal polypasis. It is rare autosomal dormant inherited condition [26]. IL 17 and IL 10 has been associated an elevated risk of gastric carcinoma commonly found in Asian population [9,27]. Some of the studies done in Chinese, Korean and Japanese population single nucleotide polymorphism and gastric carcinoma like mucin 1, cell surface associated gene (MUC I) Prostrate stem cell antigen gene (PSCA) and PLE 1 [16-18]. Non steroidal Anti Inflammatory drugs and stale intake have inverse relation with gastric cancer risk [28,29]. Several Malignancies including naso pharynged carcinoma, Hodgkin's Lymphoma, Burkitts Lymphoma and Immuno suppressant related Lymphoma [30]. EBV is a ubiglutious infectious agent prevalent in 90% of adult population. Around 5-10% of gastric cancer have been associated with EBV, gastric cancer is two times more common in Male as compared to Females. It is more common in gastric cardia or post surgical gastric stump area [25]. Some of the recent studies suggested that EBV and coinfection with *H. Pylori* increases the incidence of gastric carcinoma [26]. However etiological role of EBV is still unclear in gastric carcinogenesis [27]. Other risk factors including age, sex, lack of physical activity, low socio economical status, family history, blood group, radiation have been associated with cardia and non cardia gastric cancers. Whereas gastro esophagal reflex have been related with increased risk of cardia stomach cancer [5]. Risk of gastric cancer may increase with salt intake by direct damage of gastric mucosa, causing gastritis or other mechanism [15].

Material and Method

We Included a study of 110 patients of primary gastric cancer diagnosed in department of Radiation Oncology at State Cancer Institute Patna from July 2021 to July 2022. All the patients were diagnosed on basis of clinical history, Endoscopy, Radiological examina-

tion. The diagnosis was confirmed by histological examination of endoscopic biopsy or by reselected specimen. All the histo-pathologically confirmed cases were included in the study. Complete history was taken and staging done on the basis of available clinical and Endoscopic and radiological finding history regarding dietary habits, family history, intake of spices, smoking habits, drinking habits, drinking water resources. Consumption of alcohol, history of intake of fruits and vegetables, histological grades, TNM staying and metastatine involvement, Helicobacter pylori testing is done by rapid urease test by using kit.

Results

We Included 110 patients of Gastric Carcinoma in our study. All the observations are based upon the study done on these 110 patients in department of Radiation Oncology at State Cancer Institute Patna from July 2021 to July 2022.

Table 1: Incidence of symptoms in Carcinoma Stomach.

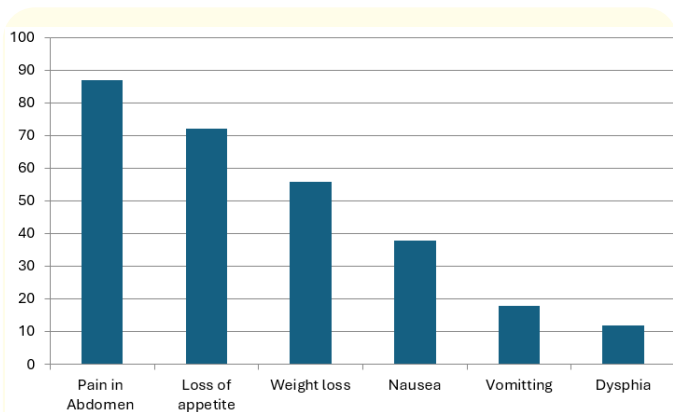| Symptoms	M	No of Patient	P Value
Pain in abdomen	87.2%	96	0.241
Loss of appetite	72.7%	80	0.104
Weight Loss	55.4%	61	0.013
Nausea	38.18%	42.1	0.051
Vomiting	16.3%	20.1	0.006
Dysphia	11.8%	13	0.031

Figure 1: Incidence of symptoms in Carcinoma Stomach.

Most common symptom on presentation was pain in abdomen 87%, loss of appetite 72%, weight loss 55%, nausea 38%, vomiting 16%, dysphia in 11%. About 75% patients present with abdominal lump on Radiological examination.

Table 2: Dietary History distribution gender wise.

	Male (75)	Female (35)
Smoking	5(6.6%)	2(5.7%)
Alcohol	38(50.6%)	0
Smoking+ Alcohol	21(28%)	-
Non-Veg Diet	52(69%)	28(80%)
Fruit Diet	11(14.6%)	9(25.7%)
History of Empty Stomach	37(49.3%)	23(65%)
Spicy food	68(90.6%)	32(91.4%)

Out of 110 patients no patient had a family history. History of taking spicy food were present in 90% of Males and 91 % in Females, Only 18% of patients were having history of taking fruits. About 70% of patients had poor drinking habits (unfiltered water). Nearly 47% of Males and 2% of females had smoking history. Combined smoking and alcohol intake was present in 28% of Males.

Table 3: Age Incidence distribution gender wise.

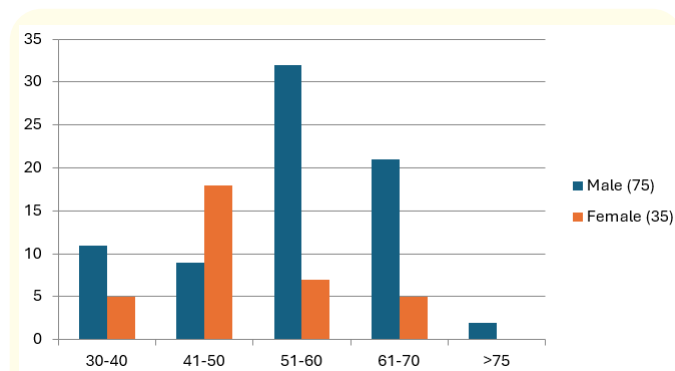| Age	Male (75)	Female (35)	Total
30-40	11(14.6%)	5(14.2%)	16
41-50	9(12%)	18(51.4%)	27
51-60	32(42.6%)	7(20%)	39
61-70	21(28%)	5(14.2%)	26
>75	2(2.6%)	0	2
Total	75	35	110

Figure 2: Age Incidence distribution gender wise.

Most common age group in our study was 51-60 years 42.6% In Males and 20% in Females, Male: Female ratio was 1.7:1. Second most common age group was 61-70 years in Males 21(28%) and 51-60 years 7 (20%) were Females. Male: Female ratio was 3:1. Distribution age varied from 30 year to 75 years majority of men were between 55 year to 60 years, followed by 61 - 70 years old category, followed by 30-40 years age group.

Table 4: Tumor Site distribution.

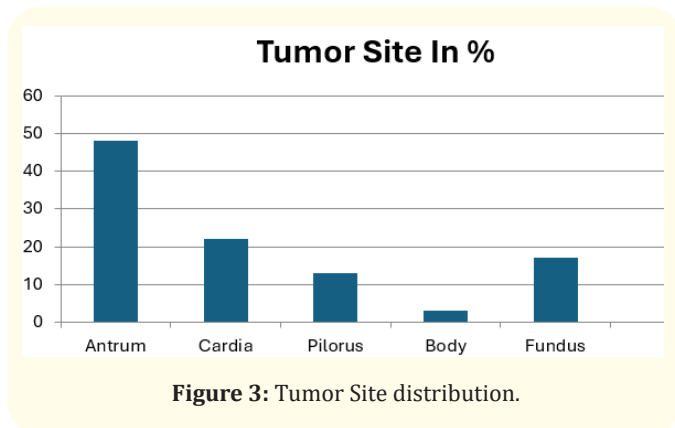| Antrum	48.18%(53)
Cardia	21.8%(24)
Pilorus	12.7%(14)
Body	2.7%(4)
Fundus	13.6%(15)

Figure 3: Tumor Site distribution.

Patient with tumour in Antrum 48%, Cardiac 21%,Fundus 13%,Pilorous 12% and body 2%.

Table 5: Tumor grade distribution according to total number.

Tumor Grade	Well differentiated adenocarcinoma	36(32%)
	Moderately differentiated adenocarcinoma	32(29%)
	Poorly differentiated adenocarcinoma	42(38%)
	Total	110

Most common histopathology was adenocarcinoma 94% followed by squamous cell 6%. About 38% were poorly differentiated adenocarcinoma, 32% were well differentiated adenocarcinoma, 29% cancer were well differentiated adenocarcinoma.

Out of 110 patients which were Included in our study, when we classified our patients on the basis of Educational qualification most of them were Illiterate, around 28% in males and 85.7% in Females. In our study around 33% completed their Secondary Education.
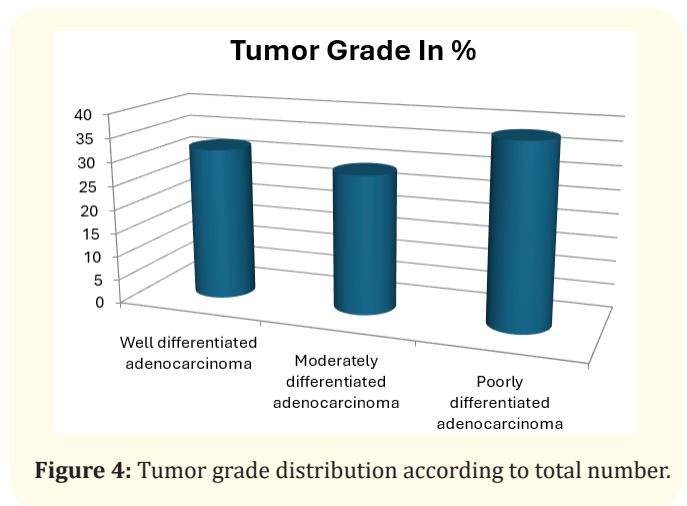

Figure 4: Tumor grade distribution according to total number.

Table 6: Distribution Gender wise according to Educational Qualifications.

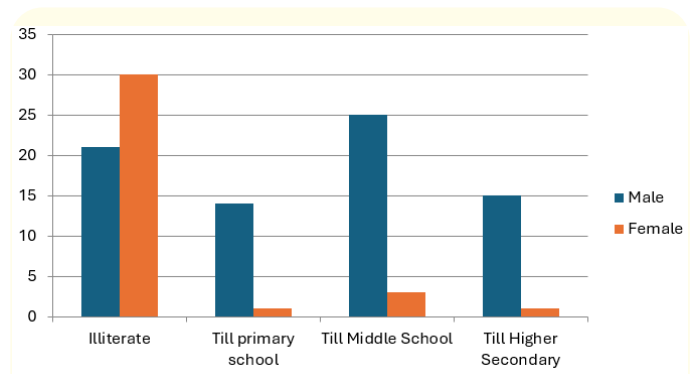|	Male (75)	Female (35)
Illiterate	21(28%)	30(85.7%)
Till Primary School	14(18.6%)	1(2.55%)
Till Middle School	25(33%)	3(8.5%)
Till Higher Secondary	15(20%)	1(2.85%)

Figure 5: Distribution Gender wise according to Educational Qualifications.

Regarding occupation most of the patients around 44% in Males and around 42% in Females were from agricultural background, belonging to poor socioeconomic class. These may be the reason that the patients were presented in advanced stage and at the same time they are very much reluctant for treatment or not able to afford treatment due to their economical condition.

Table 7: Distribution Gender wise according to Occupation.

Occupation	Male (75)	Female (35)
Farmer and Agricultural	33(44%)	15(42.85%)
Labour	24(32%)	17(48.57%)
Shopkeeper	18(24%)	3(8.5%)

Figure 6: Distribution Gender wise according to Occupation.

Table 8: Type of distribution.

Stage	T1	5(4.54%)
	T2	16(14.54%)
	T3	79(71.8%)
	T4	10(9.09%)
N	N0	7(6.3%)
	N1	25(22.72%)
	N2	40(36.36%)
	N3	38(34.54%)
M0	M0	87(79.09%)
	M1	23(21%)

Majority of patients were of T3(71%) category followed by T2 and T4. In nodal presentation N0- 6%, N1-23%, N2-36%, N3-35%.

Table 9: Distribution according to Type of Lesion.

Type of Lesion	110
Ulcerative	52(47.2%)
Ulceroproliferative	36(32.7%)
Polypoidal	22(20%)

Regarding Distribution according to type of Lesion Ulcerative type was found in around 47% of the patient, Ulceroproliferative was found among 32% as well as polypoidal was found in around 20% of the Patient.
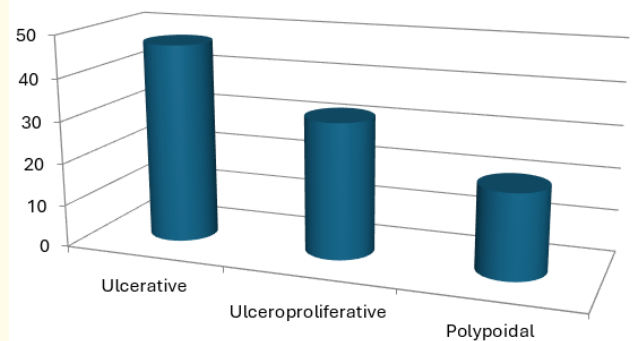

Figure 7

Table 10: Subtype of Gastric Cancer.

Intestinal Type	46	41.81%
Diffuse Type	30	27.27%
Intermediate Type	34	30.90%

Regarding Subtype of gastric cancer the most prominent was Intestinal type that was found in around 41% of the patient, Intermediate type was in around 30% of the patient and Diffuse type was found in around 27% of the patient.
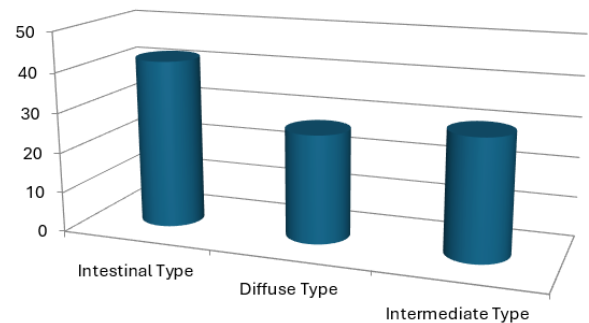

Figure 8: Distribution according to Type of Lesion.

H-Pylori was tested in 110 patients among them 35 were tested positive and 75 were negative.

Discussion

Incidence of carcinoma stomach varies in different part of the world. South Asian countries, Japan, China and South Korea noted high incidence of gastric cancer [31,32]. In western countries like USA the median age of occurrence was 71 which was low in Asian

countries like Japan it was 6, in Saudi Arabia it was 47, In Pakistan it was 48 ± 4.47 years [38]. In our country the incidence varies in different parts. The overall incidence of carcinoma stomach is less as compared to different parts of world [33-35] certain region of India. The study done at south India shown median age was 54.13 ± 12.53 years and in another study shown common age was 58 years in Male and 57 years in females, In an study we found common age.

Male: Female ratio in an study is 2:1 which was comparable to other studies conducted in North Eastern India, Mizoram 2.3:1, Pakistan 1.5:1, South India 2.7:1, Kashmir 3.3:1 [36-38]. In our study the most common age group was 41-50 years in females and 57-60 years in males. Which is comparable to other studies conducted in North Eastern India, Kashmir [39,40]. Most common symptoms in our study was pain in abdomen in 87.2%, Loss of appetite in 72.7%, Weight loss in 56.4%. Sometimes patients may not have pain in abdomen but presented with nausea and vomiting, dysphasia 16.3%,38.18% and 11.8% respectively. These symptoms may be due to growth at another study conducted by Kabir., *et al*. [41] shown Abdominal Pain (100%), most common symptoms vomiting in 78% patients, dysphasia 24% and weight loss 62% were most common symptoms in gastric cancer. A review study by American College of surgeons, In 18365 patient shown weight loss (66.6%), Abdominal Pain 51.6%, Nausea Vomiting in 34%, Anorexia 32% and Maleva in 20% cases. Our study shown Antrum was commonest site of involvement followed by cardia and body, Japanese and Korean population has predominant incidence of noncardia cancer, Non cardia cancer in Iranian study. Recent study from Kerala, India showed antrum mucosa was predominant site with a trend toward proximal shift. Reported [16] Afridi., *et al*. growth at antrum in 40% cardia and 32% and in pylorus in 6.7% of patients [38]. Macroscopically most common presentation with ulcerative lesion (47.2%) ulceroproliferative (32.7%), polypoidal lesion in 22%, which is comparable to study done by Kabir., *et al*. shown ulcerative lesion 50% ulceroproliferative lesion 10%, polypoidal 34% [41] while Qurieshi., *et al*. shown ulceroproliferative in 35.5%, proliferative 26%, ulcerative 31% and 7.4 % infiltrated lesion during endoscopic examination in Kashmiri Patients [13].

Studies from South India (Gajalakshmi and Shanta 1996) [43] and studies from North East States (Phukan., *et al*. 2005) [40] showing cigarette smoking in a significant risk factor. Another meta analysis Tredaniel., *et al*. 1975 [44] have shown smokers have 1.5 times risk for smokers to develop gastric cancer. In our study 44.3% cases have history of smoking, 50.6 % having history of Alcohol and 28% have having history of both. Dietary habits like history of spicy food in both cases in 90.6% cases in males and

91.4% in females. Another factor history of nonveg diet, low intake of fresh fruits, history of empty stomach that decrease consumption of fresh fruit and smoked meat can increases the risk of cancer also shown in our Study. Study done by Trichopoulos., *et al*. [45,46] 1985, and Huge., *et al*. 1988, shown that spicy foods, salted pickles which are used by a large population have been identified as high risk for gastric carcinomas, study done by Barad., *et al*. [47] in North Eastern Region shown history of consumption of smoked meat, consumption of dried, fermented fish. Dried fish consumption has high risk to increase gastric cancer [47]. In our study majority of tumors were adeno carcinoma subtype. Shown poorly different carcinoma in 32.7% and Qurieshi., *et al*. showed 38.2% poorly differentiated adeno carcinoma and 60% of moderately differentiated adeno carcinoma [39]. In our study Intestinal type and Intermediate type were more common than diffuse type 42%, 31% respectively. This results were comparable to study done by Kabir., *et al*. in which Intestinal, diffuse and intermediate type were 52%, 28%, 20% respectively [41]. Several studies shown significant association with Helicobacter Pylori and risk function of Adenocarcinoma. It has been shown the risk is 2:1 to 1.67 fold higher than negative patients [5,30]. Study done by Kabir., *et al*. [41] also showed prevalence of *H. pylori* shown 71.8% of gastric cancer. Among the patient of gastric cancer with Intestinal type histology *H. pylori* was present in 86.96%, 50% diffuse type and poorly differentiated type of gastric cancer which Qurieshi., *et al*. and Satti., *et al*. [37] showed that 39% and 37% of Patients of intestinal type were present [13]. Patient with diffuse signet ring type 29% were *H. pylori* positive [10]. Some other Indian studies did not shown any association with *H. pylori* and gastric carcinoma [34-37]. In an study 38.6% gastric cancer patient shown positively, in which 32.6% of intestinal type and 2% in diffuse type.

Conclusion

To Summarize, this study Male :Female ratio was 2:1. Median age of stomach in our study was 51-60 years. Abdominal Pain and lump in abdomen was the most common symptoms. In presentation the most common site was present in both sexes. Histologically poorly differentiated Adenocarcinoma was most common and Intestinal type was the most common subtype. Macroscopically ulcerative type was the most common. *H Pylori* infection positivity rate shown in our patients. Some of the preventive programme like screening programme, tobacco and alcohol prevention, Dietary modification diets with low consumption of red meat, High in fruits and vegetables may have some role in prevention of cancer. For *H pylori*, A vaccine would be cost effective to prevent gastric cancer and duodenal ulcers [9]. Some of the preventive tools like mass screening programme, tobacco and alcohol prevention, Dietary modifications, Diet with low consumption of red meat, high fruits

and vegetable intake may have some role in prevention of gastric cancer. For *H Pylori* a prophylactic vaccine would be cost effective to prevent gastric cancer and duodenal ulcers [9].

Declaration of Conflict of Interest

No conflict of Interest among the authors declared.

Disclosures

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