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The histopathological characteristics of gastric carcinoma in Bhutanese population: a Retrospective study

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ABSTRACT

Introduction: Gastric cancer is not only the most common cancer, but also the cancer with the highest mortality in Bhutan. The baseline data on the histological phenotype of gastric cancer in Bhutan is not established. Different histological phenotypes have distinct etiology, clinical features, and prognosis. We aimed to assess the histological phenotypes of gastric carcinoma, evaluate the grading, staging, and the association of depth of invasion with the clinicopathological findings. **Methods:** We conducted a retrospective study, involving 494 cases diagnosed with gastric carcinoma from January 2018 to June 2021. The histopathological characteristics of the patients were presented in frequency, percentage, and mean ± standard deviation. **Results:** Gastric carcinoma was most prevalent in males (60.7%) and predominantly diagnosed in patients more than 60 years of age (67.6%). Antrum (76.5%) was the most common location for gastric carcinoma, and tubular adenocarcinoma (81.6%) was the most common histological phenotype in this study followed by poorly cohesive carcinoma, signet-ring-cell type (12.8%). Most of the patients were at an advanced stage (pT4) at the time of diagnosis (32.7%). **Conclusions:** The histopathological characteristics of gastric carcinoma in the Bhutanese population were similar to regions with high gastric cancer incidence with the preponderance of distal location of the tumor and tubular adenocarcinoma being the most common subtype. As established in other regions, gastric carcinomas were more prevalent among males and patients over 60 years in Bhutan.

Keywords: Gastric carcinoma; Histological phenotypes; Histopathology.

INTRODUCTION

Gastric cancer is the leading cancer in Bhutan, both in terms of incidence and mortality. It was reported to be the most common malignancy of the gastrointestinal tract in Bhutan, with an incidence rate of approximately 0.9/10000 per year[1]. The incidence of gastric cancer in Bhutan [17.7 ASR (Age Standardized Rates) per 100,000 in 2020] was much higher than the incidence rate of its neighboring country India (4.5 ASR per 100,000) but not as high as its other neighboring country China (20.6 ASR per 100,000)[2].

Gastric cancer is multifactorial in etiology, majority occurs sporadically and only 10% of the cases develop in the familial setting[3]. Some of the environmental risk factors include Helicobacter pylori (H. pylori) infection, tobacco smoking, alcohol, obesity, and low socioeconomic status[4,5]. The presence of H. pylori infection is known to increase the risk of developing gastric cancer by twofold[6-8].

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Adenocarcinoma is the commonest histological type, with tubular adenocarcinoma being the most frequent subtype[3]. H. pylori infection is thought to be responsible for the development of adenocarcinoma and type-I enterochromafin-like cell neuroendocrine tumors, while etiology for squamous cell carcinoma, adenosquamous carcinoma, undifferentiated carcinoma, and gastroblastoma are not known[3]. Patients with poorly cohesive carcinoma with abundant fibrous stroma have the worst prognosis with a 5-year survival rate of < 15%[3].

Although gastric cancer is one of the commonest cancers in Bhutan, there is no baseline data regarding its histological phenotypes. Since different histological phenotypes of cancer have distinct etiology, clinical features, treatment response and prognosis, we aimed to assess the histological characteristics of gastric carcinoma in Bhutanese patients. We also aimed to evaluate the grading, staging, and the association of depth of invasion to tumor (pT) with the clinicopathological findings.

METHODS

After obtaining ethical clearance from Research Ethics Board of Health (REBH), Ministry of Health, (REBH/Approval/2021/110), we conducted a retrospective study of histologically confirmed gastric carcinoma cases between January 2018 to June 2021,

diagnosed at the Department of Pathology and Laboratory Medicine, Jigme Dorji Wangchuck National Referral Hospital (JDWNRH). We included all cases of malignant epithelial tumors (carcinoma). In situations where both a gastric biopsy and a gastrectomy had been performed, we included gastrectomy to minimize patient duplication. Non-epithelial gastric malignancies (neuroendocrine tumor, lymphoma, mesenchymal tumor) were excluded.

Clinical information regarding age, sex, procedure, H. pylori status, and location of tumor were obtained from the histopathology register and verified via laboratory information system (LIS).

The hematoxylin and eosin slides of all cases were retrieved from the histopathology unit archive and reviewed under light microscopy (ZEISS primotech) by two pathologists to confirm the diagnosis and classify as per the terminology and diagnostic criteria of the World Health Organization (WHO) classification of tumors of digestive system, 5th edition[3].

The Cancer staging/depth of tumor invasion pT (for operated cases) was done as per the American Joint Committee on Cancer (AJCC) staging system, 8th Edition. Histopathological information (gross finding, status of lymphovascular, perineural, margin and lymph node) for gastrectomy specimens were obtained from original pathological report archived in LIS. The histological grading was used in accordance with the criteria, such as: tumors composed of more than 95% glands were classified as well-differentiated (Grade 1), those containing 50%-95% of glands as moderately differentiated (Grade 2), and cases with <50% of glands as poorly-differentiated (Grade 3). Poorly cohesive carcinoma and mixed carcinoma with poorly cohesive components were classified as Grade 3.

Descriptive statistical analysis was performed by using SPSS 25.0 software (IBM, Armonk, NY, USA). Data was reported as mean± SD or number (%). The T-test (parametric) was used to compare means and the Mann-Whitney U-test (non-parametric test) was used to compare median of continuous variables. The Chi-squared test or Fisher's exact test was used to assess the differences between categorical variables as appropriate. A *p*-value of <0.05 was considered statistically significant.

RESULTS

The histopathological characteristics of gastric carcinoma in Bhutanese population

Five hundred and forty-eight patients were diagnosed with gastric malignancy during the study period. We excluded 6 cases of gastrointestinal stromal tumor (GIST), 4 cases of lymphoma (MALToma), and 44 cases with repeated procedures. The total number of cases enrolled for this study was 494. The age of the patients enrolled in this study ranged from 21-91 years. Gastric carcinoma was seen in 60.7% males and 39.3% females.

67.6% of the patients were over 60 years old while patients under the age of 40 accounted for 4.9%. Antrum (76.5%) was the most frequent location for gastric carcinoma. Tubular adenocarcinoma (81.6%) was the most common histological phenotype of gastric carcinoma, followed by poorly cohesive carcinoma (PCC), signet ring cell type (12.8%). Majority of the cases were poorly differentiated (44.1%) at the time of diagnosis. Of 494 cases, 82 cases (16.6%) had associated H. pylori infection which was detected with Giemsa stain. The age, sex and pathological characteristics of gastric carcinoma in Bhutanese population are summarized in Table 1.

Table 1. Demographic and histopathological characteristics of patients with gastric carcinoma at JDWNRH‡, Bhutan, from January 2018 - June 2021(*n*=494)

Variable	Frequency (%)
1. Sex	
Male	300 (60.7 %)
Female	194 (39.3 %)
2. Age in years (mean± SD)	(65.09±13.19)
≤ 40	24 (4.9 %)
41-60	136 (27.5 %)
> 60	334 (67.6 %)
3. Procedure	
Endoscopic biopsy	396 (80.2 %)
Surgical resection	98 (19.8 %)
4. Tumour site	
Antrum	378 (76.5 %)
Body	33 (6.7 %)
Pylorus	23 (4.7 %)
Cardia	13 (2.6 %)
Not specified	47 (9.5 %)
5. Histological Diagnosis	
Tubular adenocarcinoma	403 (81.6%)
PCC* - Signet-ring-cell type	63 (12.8%)
PCC*-NOS†	18 (3.6%)
Mucinous adenocarcinoma	3 (0.6%)
Mixed tubular and PCC*	5 (1.0%)
Papillary adenocarcinoma	1 (0.2%)
Hepatoid adenocarcinoma	1 (0.2%)
6. Histological grading	
Grade 1	120 (24.3%)
Grade 2	156 (31.6%)
Grade 3	218 (44.1)
7. Helicobacter pylori	
Present	82 (16.6%)
Absent	349 (70.6%)
Not known	63 (12.8%)

**poorly cohesive carcinoma; †non-signet-ring cell type*
‡Jigme Dorji Wangchuck National Referral Hospital

This study showed significant association of H. pylori infection with tumor site (p value: <0.0001). However, other variables showed no significant association. The clinicopathological profile and association of H. pylori infection in patients with gastric carcinoma is summarized in Table 2.

Table 2. Correlation of Helicobacter pylori infection with demographic-pathological characteristics of patients with gastric carcinoma at JDWNRH[‡], Bhutan, from January 2018 - June 2021(*n*=494)

Variables	Total carcinoma	H. pylori + *n* (%)	H. pylori- *n* (%)	*p* value
	494 (100%)	**82 (16.6%)**	**349 (70.6%)**	
1.Age in years (mean± SD)	(65.09±13.19)			0.317
≤ 40	24 (4.9 %)	6 (25.0%)	17 (70.8%)	
41-60	136 (27.5 %)	25 (18.4%)	90 (66.2%)	
> 60	334 (67.6 %)	51 (15.3%)	242 (72.5%)	
2.Gender				0.540
Male	300 (60.7 %)	53 (17.7%)	212 (70.0%)	
Female	194 (39.3 %)	29 (14.9%)	137 (70.6%)	
3. Tumour site				<0.0001
Antrum	378 (76.5 %)	69 (18.3%)	289 (73.5%)	
Body	33 (6.7 %)	5 (15.2%)	22 (66.7%)	
Pylorus	23 (4.7 %)	4 (17.4%)	17 (73.9%)	
Cardia	13 (2.6 %)	1 (7.7%)	10 (76.9%)	
4.Histological phenotypes				0.941
1. Tubular adenocarcinoma	403 (81.6%)	66 (16.4%)	284 (70.5%)	
2. PCC*- Signet-ring-cell type	63 (12.8%)	12 (19.0%)	44 (69.8%)	
3. PCC*, NOS†	18 (3.6%)	3 (16.7%)	14 (77.8 %)	
4. Mucinous adenocarcinoma	3 (0.6%)	0 (0.0%)	2 (66.7%)	
5. Mixed tubular and PCC*	5 (1.0%)	1 (20.0%)	3 (60.0 %)	
6. Papillary adenocarcinoma	1 (0.2%)	0 (0.0%)	1 (100%)	
7. Hepatoid adenocarcinoma	1 (0.2%)	0 (0.0%)	1 (100%)	
5.Histological grading				0.622
Grade 1	120 (24.3%)	21 (17.5%)	83 (69.2%)	
Grade 2	156 (31.6%)	30 (19.2%)	106 (67.9%)	
Grade 3	218 (44.1)	31 (14.2%)	160 (73.4%)	

**poorly cohesive carcinoma, †non-signet -ring cell type*
‡Jigme Dorji Wangchuck National Referral Hospital

Table 3. Gender and age distribution of histological phenotypes characteristics of patients with gastric carcinoma at JDWNRH[‡], Bhutan, from January 2018 - June 2021 (*n*=494)

Histological-variants	Gender		Age (in years)		
	Male n (%)	Female n (%)	≤ 40 n (%)	41-60 n (%)	>60 n (%)
i. Tubular adenocarcinoma	244 (60.5%)	159 (39.5%)	13 (3.2%)	111(27.5%)	279 (69.2%)
ii. PCC*, Signet ring cell type	36 (57.1%)	27 (42.9%)	5 (7.9%)	19 (30.2%)	39 (61.9%)
iii. PCC*-NOS†	14 (77.8%)	4 (22.2%)	5 (27.8%)	5 (27.8%)	8(44.4%)
iv. Mucinous carcinoma	1 (33.3%)	2 (66.7%)	0 (0.0%)	1(33.3%)	2(66.7%)
v. Mixed tubular and PCC*	5 (100%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	5 (100%)
vi. Papillary adenocarcinoma	0 (0.0%)	1 (100%)	0 (0.0%)	0 (0.0%)	1 (100%)
vii. Hepatoid adenocarcinoma	0 (0.0%)	1 (100%)	1 (100%)	0 (0.0%)	0 (0.0%)

**poorly cohesive carcinoma; †non-signet -ring cell type, ‡Jigme Dorji Wangchuck National Referral Hospital*

Table 4. Correlation of tumor extent with age, gender and pathological findings in gastrectomy specimens of patients with gastric carcinoma at JDWNRH‖, Bhutan, from January 2018 - June 2021 (*n*=98)

Variables	Total carcinoma	pT1+pT2 *n* (%)	pT3+pT4 *n* (%)	*p*-value
	98 (100%)	36 (36.7%)	62 (63.3%)	
1. Age in years (mean± SD)				0.474
≤ 40	7 (7.1%)	2 (28.6%)	5 (71.4%)	
41-60	39 (39.8%)	12 (30.8%)	287 (69.2%)	
> 60	52 (53.1%)	22 (42.3%)	30 (57.7%)	
2. Gender				0.737
Male	34 (34.7%)	21 (38.2%)	34 (61.8%)	
Female	64 (65.3%)	15 (34.9%)	28 (65.1%)	
3. Tumour site				0.508
Cardia	1 (1%)	0 (0.0%)	1 (100%)	
Body	13 (13.3%)	4 (30.8%)	9 (69.2%)	
Antrum	72 (73.5%)	29 (40.3%)	43 (59.7%)	
Pylorus	12 (12.2%)	3 (25.0%)	9 (75%)	
4. Tumour size (mean± SD)	(4.15±1.954)			0.003
<5 cm	58 (59.2%)	26 (44.8%)	32(55.2%)	
≥5cm	33 (33.7%)	5 (15.2%)	28 (84.8%)	
Not available	7 (7.1%)	5 (71.4%)	2 (28.6%)	
5. Gross finding				0.001
Ulcero-fungating mass	80 (81.6%)	22 (27.5%)	58 (72.5%)	
Polypoid mass	4 (4.1%)	3 (75.0%)	1 (25.0%)	
Mucosal flattening	9 (9.2%)	9 (100 %)	0 (00.0%)	
Wall thickening	5 (5.1%)	2 (40.0%)	3 (60.0%)	
6. Histological types				0.136
1. Tubular adenocarcinoma	80 (81.6%)	30 (37.5%)	50 (62.5%)	
2. PCC*, Signet ring cell type	10 (10.2%)	6 (60.0%)	4 (20.0%)	
3. PCC*, NOS†	2 (2.0 %)	0 (0.0%)	2 (100%)	
4. Mixed tubular and PCC*	4(4.1%)	0 (0.0%)	4 (100%)	
5. Mucinous adenocarcinoma	2 (2.0%)	0 (0.0%)	2 (100%)	
7. LVI‡				<0.0001
Yes	55 (56.1%)	9 (16.4%)	46 (83.6%)	
No	43 (43.9%)	27 (62.8%)	16 (37.2%)	
8. PNI§				<0.0001
Yes	68 (69.4%)	34 (50.0%)	34 (50.0%)	
No	30 (30.6%)	2 (6.7%)	28 (93.3%)	
9. Margin				0.082
Positive	5 (5.1%)	0 (0.0%)	5 (100%)	
Negative	92 (93.9%)	36 (38.7%)	57 (61.3%)	
10. Lymph node				<0.0001
Positive	55 (56.1%)	9 (16.4%)	46 (83.6%)	
Negative	40 (40.8%)	25 (62.5%)	15 (37.5%)	
Nx‖	3 (3.1%)	2 (66.7%)	1 (33.3%)	

**poorly cohesive carcinoma, †non-signet -ring cell type, ‡lympho-vascular invasion, §perineural invasion, ‖cannot be determined, ‖Jigme Dorji Wangchuck National Referral Hospital*

Tubular adenocarcinoma and PCC were predominantly seen in male patients. Three cases of mucinous adenocarcinoma were detected, two of which were in females and one in a male patient. Papillary and hepatoid adenocarcinomas were rare phenotypes with one instance each, all of which among females. All variants of gastric carcinoma were more frequent in elderly patient of > 60 years of age, while the single case of hepatoid adenocarcinoma was seen in a 30 year old woman. The age and sex distribution of histological phenotypes of gastric carcinoma is shown in Table 3.

Pathological evaluation of the gastrectomy specimens

Of 494 cases studied, 396 (80.2%) had undergone endoscopic biopsy and only 98 (19.8%) cases had undergone gastrectomy in Bhutan. Gross examination revealed ulcero-fungating growth in 81.6%, mucosal flattening in 9.2%, and circumferential wall thickening without a definite mass in 5.1% of the cases. The size of the tumor ranged from 1 cm to 10 cm in the greatest dimension. Both lymphovascular invasion and regional lymph node metastasis were seen in 56.1% of the cases. Perineural invasion was found in only 30.6% of cases.

Serosal invasion (pT4) was seen in 32.7% of the cases, followed by invasion of subserosal connective tissue (pT3) in 30.6%, and invasion of muscularis propria (pT2) in 20.4%. The summary of frequency of depth of invasion is illustrated in Figure 1.

We assessed the correlation of tumor extent with age, gender and pathological variables by grouping the results of tumor extent as (pT1+pT2) and (pT3+ pT4). The study showed significant association of higher tumor stage with tumor size, gross nature of tumor, histological types, and presence of lymphovascular and perineural invasion; and lymph node metastasis. The pathological findings of gastrectomy specimens and the correlation with tumor extent is summarized in Table 4.

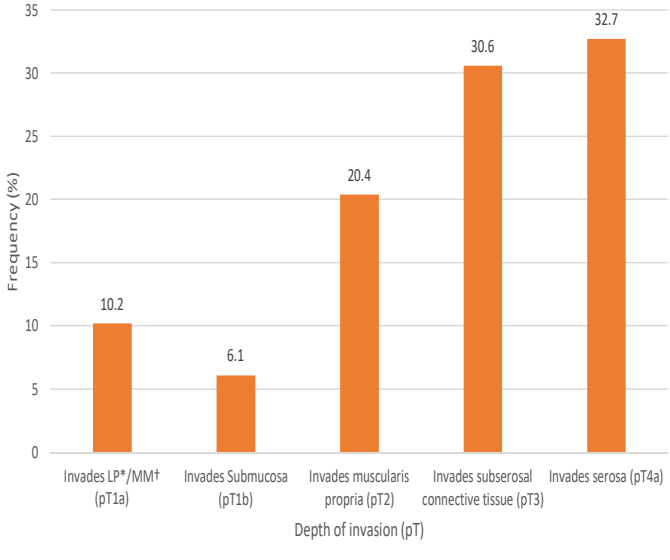

Figure 1. Frequency of depth of invasion (pT) of primary tumor in gastrectomy specimens of patients with gastric carcinoma at JDWNRH‡, Bhutan, from January 2018 - June 2021

**Lamina propria, †Muscularis mucosa, ‡Jigme Dorji Wangchuck National Referral Hospital*

DISCUSSION

We conducted a retrospective analysis of histopathological characteristics of gastric carcinoma in the Bhutanese population for three and half years. Most patients with gastric cancers are usually between 60 to 80 years of age at the time of diagnosis9. More than half of our patients (67.6%) were over 60 years of age, while only 4.9% of our patients were ≤40 years of age. Gastric cancer is more prevalent in male patients[10-12]. Our study also showed male predominance (60.7%). In general, incidence and mortality rates in men are approximately double to those in women[9].

H. pylori was found as a strong risk factor for non-cardia gastric cancer but is inversely associated with the risk of gastric cardia cancer[13]. The higher prevalence and more virulent H. pylori could be the reason for the preponderance (76.5%) of the antral location of gastric cancer in our study. We also discovered a significant association between H. pylori infection and tumor site, with increased H. pylori positivity in non-cardia gastric cancer. A Japanese study done by Yamagata et al. showed a significant association of H. pylori infection with subsequent development of gastric cancer in men[14]. Our study showed higher H. pylori infection rate in males (64.6%) as compared to female patients (35.4%). Although previous studies[6,15] reported a very high prevalence of H. pylori infection in the Bhutanese population, our study showed a comparatively lesser prevalence rate of only 16.6% (82/494). This could be because, prior to gastric biopsy, our patients are routinely treated for H. pylori based on the results of a urease breath test. Moreover, this study evaluated H. pylori status only of gastric carcinoma patients.

Regarding histological phenotype, adenocarcinoma was the most predominate type in our country constituting 98% of stomach malignancies, while GIST and lymphoma constituted only 1.2% and 0.8%, respectively. Tubular adenocarcinoma is the most common histological type, followed by papillary and mucinous adenocarcinoma[16]. Even in this study, 81.6% of gastric carcinoma was tubular adenocarcinoma, predominantly affecting patients >60 years of age (69.2%). Similar to our findings, a much higher frequency (72.4%) has been reported in elderly patients in Japan[3]. However, papillary, mucinous and other specialized subtypes were very rare in our cohort. Squamous cell carcinoma, adenosquamous carcinoma, undifferentiated carcinoma, gastroblastoma, and neuroendocrine neoplasms are other malignant epithelial tumors of the stomach that were not seen in this study.

The second most common subtype of adenocarcinoma in our study was PCC, signet ring cell type (12.8%) and third was PCC, NOS (3.6%). PCC accounts for 20-54% of gastric

carcinoma with a higher frequency reported in Japanese patients[3]. Similar to tubular adenocarcinoma, we found more males (57.1% and 77.8% for PCC, signet ring cell type and PCC, NOS respectively) and patients over 60 (61.9% and 44.4% for PCC, signet ring cell type, and PCC, NOS respectively) being affected.

The pTNM staging system is currently the single most important factor for prognosis in patients with gastric cancer. The 5 year survival rate in patients with pTis is > 90%, and the survival decreases in stepwise fashion with increasing in pT category[3]. Similar to a study in Malaysia and Iran, most of our patients were at advanced stages (32.7% of pT4 and 30.6% of pT3) at the time of diagnosis[17,18]. We found significant association of tumor extent (pT) with tumor size, gross nature of tumor, histological types, and presence of lympho-vascular invasion, lymph node metastasis; and perineural invasion. Grossly, tumors presenting as ulcero-fungating mass (73.8%) and tumor size of ≥5cm (87.9%) had higher pT stages (pT3+ pT4). More lympho-vascular invasion (83.6%) and lymph node metastasis (83.6%) were noted in tumor with higher pT stage (pT3+ pT4).

Some of our patients with gastric cancer were referred abroad for further management due to limited facility available in our country. Therefore, we could not get the details of surgical resections done abroad. We could not present the molecular status of gastric carcinoma in this study due to limited resources in our laboratory and lack of financial support. Moreover, the prognosis of each histological phenotype of gastric cancer could not be presented as this is a retrospective study. These are the main limitations of this study.

CONCLUSIONS

The basis for preponderance of distal location of tumor and tubular adenocarcinoma being the most common subtype of gastric carcinoma in Bhutanese population could be attributed to higher prevalence and more virulent H. pylori. The histopathological pathological characteristics of gastric carcinoma in Bhutanese population were similar to regions with high gastric cancer incidence (Asia, Central and South America and Eastern Europe). As established in other regions, gastric carcinomas were more prevalent among males and patients over 60 years in Bhutan.

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REFERENCES

1. Dendup T, Richter JM, Yamaoka Y, Wangchuk K, Malaty HM. Geographical distribution of the incidence of gastric cancer in Bhutan. World J Gastroenterol. 2015;21(38):10883-9. [PubMed | Full Text | DOI]
2. International Agency for Research on Cancer. GLOBOCAN 2020. New Global Cancer Data [Internet]. 2020. [Full Text]
3. Fukayama M, Rugge M, Washington M. WHO Classification of Tumours. Digestive System Tumours (5th edition): Lyon, France: International Agency for Research on Cancer; 2019. 50-104 p. [Full Text]
4. Zali H, Rezaei-Tavirani M, Azodi M. Gastric cancer: prevention, risk factors and treatment. Gastroenterol Hepatol Bed Bench. 2011;4(4):175-85. [PubMed | Full Text]
5. Hundahl SA, Phillips JL, Menck HR. The National Cancer Data Base Report on poor survival of US gastric carcinoma patients treated with gastrectomy: American Joint Committee on Cancer staging, proximal disease, and the "different disease" hypothesis. Cancer. 2000;88(4):921-32. [PubMed]
6. Barad AK, Mandal SK, Harsha HS, Sharma BM, Singh TS. Gastric cancer—a clinicopathological study in a tertiary care centre of North-eastern India. J Gastrointest Oncol. 2014;5(2):142. [PubMed | Full Text | DOI]
7. Uemura N, Okamoto S, Yamamoto S, Matsumura N, Yamaguchi S, Yamakido M, et al. Helicobacter pylori infection and the development of gastric cancer. N Engl J Med. 2001;345(11):784-9. [PubMed | Full Text | DOI]
8. Eslick GD. Helicobacter pylori infection causes gastric cancer? A review of the epidemiological, meta-analytic, and experimental evidence. World J Gastroenterol. 2006;12(19):2991-9. [PubMed | Full Text | DOI]
9. Brenner H, Rothenbacher D, Arndt V. Epidemiology of stomach cancer. Methods Mol Biol. 2009;472:467-77. [PubMed | Full Text | DOI]
10. Liu S, Feng F, Xu G, Liu Z, Tian Y, Guo M, et al. Clinicopathological features and prognosis of gastric cancer in young patients. BMC cancer. 2016;16(1):1-7. [Full Text]
11. Rawla P, Barsouk A. Epidemiology of gastric cancer: global trends, risk factors and prevention. Prz Gastroenterol. 2019;14(1):26-38. [PubMed | Full Text | DOI]
12. Mandal SK, Suman PK. A Retrospective Study to Find Correlation Between Clinical and Pathological Factors of Gastric Cancer. International Journal of Pharmaceutical and Clinical Research. 2021; 13(3); 141-49. [Full Text]
13. Kamangar F, Dawsey SM, Blaser MJ, Perez-Perez GI, Pietinen P, Newschaffer CJ, et al. Opposing risks of gastric cardia and noncardia gastric adenocarcinomas associated with Helicobacter pylori seropositivity. J Natl Cancer Inst. 2006;98(20):1445-52. [PubMed | Full Text | DOI]
14. Yamagata H, Kiyohara Y, Aoyagi K, Kato I, Iwamoto H, Nakayama K, et al. Impact of Helicobacter pylori infection on gastric cancer incidence in a general Japanese population: the Hisayama study. Arch Intern Med. 2000;160(13):1962-8. [PubMed | Full Text | DOI]
15. Dorji D, Dendup T, Malaty HM, Wangchuk K, Yangzom D, Richter JM. Epidemiology of H elicobacter pylori in Bhutan: The Role of Environment and Geographic Location. Helicobacter. 2014;19(1):69-73. [PubMed | Full Text | DOI]

16. Hu B, El Hajj N, Sittler S, Lammert N, Barnes R. Meloni-Ehrig. Gastric cancer: Classification, histology and application of molecular pathology. J Gastrointest Oncol. 2012;3(3):251-61. [PubMed | Full Text | DOI]
17. Chong SY, Ang SF. The Clinicopathological Features and Staging at Presentation of Gastric Cancer: A Single-Center Retrospective Study. Asian Journal of Oncology. 2020;6(03):120-6. [Full Text]
18. Safaee A, Moghimi-Dehkordi B, Fatemi S, Ghiasi S, Pourhoseingholi M, Zali MR. Clinicopathological features of gastric cancer: A study based on cancer registry data. Iranian Journal of Cancer Prevention. 2009;2(2):67-70. [Full Text]

AUTHORS CONTRIBUTION

Following authors have made substantial contributions to the manuscript as under:

SC: Concept, design, data collection and analysis, manuscript writing and review.

CW: Concept, design, data analysis, manuscript review

Author agree to be accountable for all respects of the work in ensuring that questions related to the accuracy and integrity of any part of the work are appropriately investigated and resolved.

CONFLICT OF INTEREST

None

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