ORIGINAL RESEARCH

A Clinicopathological Study of Gastric Adenocarcinomas- A Two Year Retrospective Descriptive Study in a Tertiary Care Centre

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ABSTRACT

Background: Gastric carcinoma is the third most common cause of cancer related mortality worldwide. The present study is taken up to provide an overview of the spectrum of malignancies, age and sex incidence and risk factor such as tobacco usage, alcohol consumption, dietary intake and blood group analysis of gastric adenocarcinomas in South India.

Martial and Methods: The present study is a two year retrospective study that included all the cases received from 1st August, 2018 to 31st July 2020 in the department of pathology, Guntur Medical College and Government General Hospital, Guntur.

Results: A total of 49 cases were included in the study. The most common age group was sixth decade of life with male preponderance. Gastric outlet obstruction was the most common presenting symptom. Tubular type of gastric adenocarcinoma was the most common histopathological variant.

Conclusion: Regardless of growing understanding of the risk factors, phenotypic and genotypic alterations and diagnostic modalities, Gastric adenocarcinoma still linger to have poor prognosis due to limited treatment options.

Keywords: Carcinoma Stomach, Laurens Classification, WHO Classification.

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INTRODUCTION

Gastric carcinoma is the third most common cause of cancer related mortality worldwide.[1] These cancers are more common in elderly males with incidence increasing with progressing age. Since these cancers are diagnosed mostly in advanced stages, prognosis remains poor,[2] with 5-year relative survival below 30% in most countries.[3] Surgical resection is the only option for cure in these cancers;[2] so it is essential to detect them early for good patient outcome. Epithelial tumors predominate over the mesenchymal tumors.

The present study is taken up to provide an overview of the spectrum of malignancies, age and sex incidence and risk factor such as tobacco usage, alcohol consumption, dietary intake and blood group analysis of gastric adenocarcinomas in South India.

MATERIALS & METHODS

The present study is a two year prospective study that included all the cases received from 1st August, 2018 to 31st July 2020. Study involved the use of formalin fixed, paraffin embedded tissues of histopathologically diagnosed gastric malignancies which were obtained either from endoscopic biopsies or resection specimens. A total number 49 cases were included. Clinical and histopathological data obtained were recorded and tabulated. In the present study, WHO classification (2019) was followed to classify all the tumors. In case of resected specimens, Tumor, Nodal and Metastasis (TNM) staging was followed. Tumors were classified using TNM staging, AJCC 8th edition.

RESULTS

A total of 49 gastric adenocarcinomas were included in the study of which 36were endoscopic biopsies and 13 were resected specimens. Age distribution varied between 27 to 85 years. However, the most common age group was 6th decade (51-60years) of life amounting to 34.6% of cases. There was a male preponderance (M: F ratio- 2.26:1) in the incidence of gastric adenocarcinomas. The most common presenting symptom was gastric outlet obstruction constituting 18 cases (36.7%), followed by loss of appetite (24.4%) and pain abdomen (22.4%). Most common appearance on endoscopy was an ulcero-proliferative growth constituting 44.8% of cases. When personal habits of the patients were scrutinized, it was found that 32 cases had a history of alcohol consumption, 22 cases had a history of tobacco usage and 43 cases took mixed diet. The most common site for gastric carcinomas was pylorus/ antrum region (36 cases), making the distal stomach the most common site for malignancies. Histopathologically, the most common gastric carcinoma in the present study was Intestinal type of gastric carcinoma (as per Laurens Classification) and tubular adenocarcinoma (as per WHO classification 2019). Most tumors showed well differentiation. All tumors that occurred before 4th decade of life were well to moderately differentiated.[Table 1]

Table 1: Table depicting demographics, endoscopic findings, histopathological diagnosis and differentiation of the tumors in the present study

Clinical Characteristics	Number of males	Number of females	Total
Age Distribution (years)			
21-30	1	1	2
31-40	4	1	5
41-50	3	2	5
51-60	14	3	17
61-70	8	5	13
71-80	3	3	6
81-90	1	-	1
Presenting symptoms			
Hematemesis	1	-	1
Pain abdomen	6	5	11
Gastric outlet obstruction	12	6	18
Ascites	1	-	1
Cachexia	3	1	4
Loss of appetite	10	2	12
Weakness	1	1	2

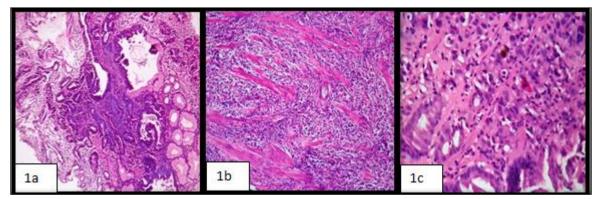| **Alcohol Consumption**			
Never consumed	4	13	17
Occasional consumption	13	2	15
Regular consumption	17	-	17
History of smoking			
Never smoked	14	13	27
Previously smoking	9	1	10
Currently smoking	11	1	12
Type of diet			
Vegetarian	2	4	6
Mixed	32	11	43
Blood group			
A group	12	10	22
B group	8	1	9
AB group	5	2	7
O group	9	2	11
Site of tumor			
Cardiac	1	-	1
Fundus/body	4	2	6
pylorus/Antrum	24	12	36
Diffuse	5	1	6
Site of tumor			
Proximal stomach	5	2	7
Distal stomach	24	12	36
Diffuse	5	1	6
Endoscopic findings			
Fungating growth	3	1	4
Ulcerative growth	10	8	18
Ulceroproliferative growth	17	5	22
Diffuse growth	3	1	4
Strictural growth	1	-	1
Laurens Classification			
Intestinal type	24	8	32
Diffuse type	9	6	15
Mixed Type	1	1	2
WHO Classification			
Tubular adenocarcinoma	20	6	26
Papillary adenocarcinoma	3	-	3
Tubulopapillary adenocarcinoma	1	-	1
Poorly cohesive carcinoma	9	6	15
Mucinous Carcinoma	1	1	2
Mixed Carcinoma	-	2	2
Glandular Differentiation			
Well differentiated	14	3	17
Moderately differentiated	7	2	9
Poorly differentiated	4	4	8

Figure 1: Laurens classification: 1a:10X: Intestinal type of gastric adenocarcinoma. 1b: 10X: Diffuse type of gastric adenocarcinoma. 1c: 40X: Mixed type of gastric adenocarcinoma
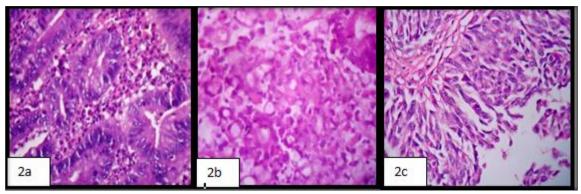

Figure 2: WHO classification: 2a:40X: Tubular gastric adenocarcinoma. 2b: 40X: Poorly cohesive gastric adenocarcinoma (signet ring cell variant). 2c: 40X: Papillarygastric adenocarcinoma

DISCUSSION

During this twenty four month of study period, we received a total of 36 endoscopic biopsies and 13 were resected specimens. Endoscopic biopsies posea diagnostic challenge to histopathologists, as criteria of malignancy are over shadowed by other non-specific features. In the present study, we faced difficulty in diagnosing malignancies as features like inflammation; fibrosis and necrosis obscured the hallmarks of malignancy. This finding was similar to that found by Geisinger et al.[4] Pathologists are often confronted with small biopsies that show architectural and cytological atypia with no evidence of infiltration into the underlying stroma. These features lead to ambiguous diagnoses that lead to intra and inter observer variability and lack of reproducibility.

Of the 49 gastric cancer reported in this two year period, 17 cases (34.7%) occurred in 6th decade of life. The youngest patient in the cohort was diagnosed as diffuse gastric carcinoma at an age of 27 years. On enquiring about his family history, it was found that his father also died with gastric carcinoma. Based on clinical criteria of International Gastric Cancer Linkage Consortium (1999),[5] this case was diagnosed as Hereditary Diffuse Gastric Cancer Syndrome. However, genetic confirmation by germline mutation analysis for E-Cadherin (CDH1) gene was not performed due to financial constraints. Male to female ratio in gastric carcinomas of the current analysis was 2.26:1. This observation is in parallel to several studies,[6,7,8] which ranged between 1.9:1 to 3.07:1. In the present study 65.3% were alcoholics and 44.9% of patients were known to use tobacco in various forms, concluding that there was an association of upper gastrointestinal tract malignancies with alcoholism and tobacco usage. Moy et al,[9] in there study quoted that tobacco usage was more common than

alcoholism in their study cohort. Blood group a constituted 48.8% of cases and these findings correlate with Edgren et al,[10] study.

Pylorus / antrum region constituted the most common site for malignancies in stomach in the current analysis. This observation is similar to that observed by Vidhyavathi et al.[11] However, cardiac and body regions constituted about 12% each, which is much lesser than the observations of MH Derakhshan et al,[12] who quoted an incidence of 44.5% in cardiac region and Inoue M et al,[13] who quoted an incidence of 32.6% in fundus/body region. According to the WHO Classification 2019, all the cancers that were formerly called tumors of gastric cardia, are now included in the tumors of esophagogastric junction. Tumors of the esophagogastric junction include all adenocarcinomas that straddle the junction of esophagus and stomach. However, it is to be noted that squamous cell carcinomas are not included in this group even if the bulk of the tumor is located in this area.

In the present study, intestinal type of gastric adenocarcinoma constituted the most common histopathological entity when Lauren's Classification was used. This result correlates with the findings of Yan SY et al,[8] and Warneke VS et al.[14] However, Chinese literature,[7,13] report a higher incidence (15 to 17%) of mixed/ unclassified type when compared to the current analysis (2%).Tumors were classified as intestinal type [Figure 1a] when tumors were grossly polypoidal and microscopy revealed tumor cells predominantly arranged in glandular, papillary or mixed patterns with varying differentiation. Tumors were typed as diffuse [Figure 1b] when grossly tumors were plaque like with infiltrating margins and histopathology revealed cords of tumor cells against a mucoid stroma, infiltrating into the layers of the stomach, with almost no gland formation. Individual tumor cells were round to oval with hyperchromatic nucleus and scant to moderate amount of eosinophilic cytoplasm. Some cases showed predominance of signet ring cell morphology. Some cases showed cells resembling lymphocytes and histiocytes. Tumors with mixed patterns were grouped as mixed/unclassified. [Figure 1 c]

Out of 32 intestinal types of gastric adenocarcinomas, 17 showed intestinal metaplasia in the adjacent mucosa. Our findings correlate well with that of Berlth F et al,[15] who also reported evidence of intestinal metaplasia and Helicobacter pylori infection in intestinal type of gastric adenocarcinoma.

Of the 15 cases reported as diffuse, five cases were predominantly or almost exclusively composed of signet ring cells. These cases were associated with a deeper invasion when compared to the other types. This observation was similar to that observed by Bozzetti C et al.[6]

When gastric adenocarcinomas were classified based on WHO 2019 classification, tubular adenocarcinoma constituted the most common type, followed by poorly cohesive adenocarcinoma. These observations are in parallel to those of Dewan et al.[16]

In their review, Berlth F et al,[15] stated that Laurens Intestinal type of gastric carcinomas include tubular, papillary carcinomas of WHO classification, and Lauren's Diffuse type of gastric carcinomas is equivalent to poorly cohesive adenocarcinomas including signet ring cell variant of WHO classification.

Tumors were categorised as tubular adenocarcinomas when the tumor was composed of cells arranged in dilated and branching tubules and in acinar and slit- like patterns [Figure 2a]. Individual cells were cuboidal to columnar with mild to severe pleomorphism. Desmoplastic stroma may or may not be present.

Tumors were grouped under papillary when they were predominantly exophytic with cells arranged as finger like projections along a fibrovascular core [Figure 2b]. Cells tend to maintain their polarity and are columnar to cuboidal.

Poorly cohesive carcinomas were composed of cells arranged in cords, nests and singly scattered infiltrating into the adjacent layers [Figure 2c]. Individual cells can be signet ring cell like, lymphocyte like, histiocyte like or a mixture of all.

In the present study, we classified intestinal and mixed types of adenocarcinomas as well differentiated when greater than 95% of tumor was composed of glands, as moderately differentiated when 50% to 95% of the tumor was composed of glands and poorly differentiated when 49% or less of the tumor was composed of gland. Of the 35 cases, well differentiated category constituted the largest group, while moderately differentiated were more common in the study of Yan SY et al,[8] and poorly differentiated tumors constituted the most common group in Shan et al[7] and Dewan et al,[16] studies.

Of the 13 gastrectomies we received, 6 showed infiltration of the tumor upto muscularis propria and 7 showed infiltration upto serosa, with lymph nodal metastasis ranging from 0 to 11 in different cases. Based on Laurens Classification, 7 cases were diagnosed as intestinal type, 5 cases were diagnosed as diffuse type, and one was mixed type. Based on WHO classification, 7 were tubular type, 4 were poorly cohesive, one was mucinous carcinoma and one was diagnosed as tubulopapillary carcinoma. Case that was diagnosed as mucinous carcinoma showed metastasis in 11 lymph nodes.

The highest stage that was diagnosed was $T_4 N_3 M_x$.

Transition zone in these specimens showed changes ranging from non-specific superficial gastritis to intestinal metaplasia to atrophy and necrosis and our finding correlated with several other studies.[17]

CONCLUSION

Regardless of growing understanding of the risk factors, phenotypic and genotypic alterations and diagnostic modalities, Gastric adenocarcinoma still linger to have poor prognosis due to limited treatment options. The most common predisposing factors such as *Helicobacter pylori* infection, Epstein-Barr virus infection, high salt intake and smoking are avoidable. Thus, primary prevention should be our goal.

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