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CLINICOPATHOLOGICAL ASSESSMENT OF GASTRIC CARCINOMA IN A SAMPLE OF IRAQI PATIENTS

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ABSTRACT

Introduction: Stomach cancer kills many people globally. Cancers dominate gastrointestinal malignancies. Gastric carcinoma is the fifth-most common and third-deadliest cancer. ы (age, gender, location, grade, gross features, endoscopical findings, clinical presentation, pathological stage and lymph node status). **Method:** A retrospective study including analysis of 100 randomly selected patients with gastric carcinoma collected from Teaching Laboratories of Al-Emamain Al-Kadhmain (AS) Medical City, Baghdad Medical City and private laboratories from October 2017 to January 2021and Regarding the type of specimen, (59.0%) were endoscopic biopsies, while (41.0%) were gastric resection specimens. **Results:** Age-wise, 68% of the sample aged 40-60. 1:1 male-female ratio. Epigastric discomfort was the main complaint (35.0%). The most frequent endoscopic presentation (20%) was ulcerative mass. Histological type was intestinal (53%), diffuse (47.0%). In 41 gastric resection patients, pT3 (68.3%) and pN2 (26.8%) were the most prevalent tumour sizes and nodal statuses. (57.0%) were badly differentiated, whereas 43.0% were moderately differentiated. **Conclusion:** Male to female ratio was 1:1; the majority of cases were between 40 and 60 years old; epigastric pain was the most frequent clinical presentation; both types of gastric carcinoma most frequently developed in the pylorus; lesions were more frequently 3 to 6 cm in size; and T3N2Mx was the most common stage.

KEYWORDS: Clinicopathological, gastric carcinoma, Iraqi patients.

INTRODUCTION

Gastric cancer is one of the leading causes of cancer-related fatalities globally. The most common kind of stomach cancer is carcinoma.[1] Third most lethal and fifth most common neoplasm overall is gastric cancer.[2] The diffuse and intestinal kinds of gastric adenocarcinomas are the two main histological subtypes according to the Lauren classification. For the diffuse type, tumour cells lack cell-to-cell connections and penetrate the stroma as single cells or small subgroups, resulting in a population of non-cohesive, dispersed tumour cells. The intestinal type is characterised by cohesive cells that form gland-like structures.[3] The intestinal type grows more quickly with age than the diffuse type and is more prevalent in men than females.[4] Diffuse lesions are more common in younger individuals and commonly occur against histologically "normal" stomach mucosa.[4] Hereditary diffuse gastric cancer may be caused by CDH1 germline mutations, which encode an aberrant version of Ecadherin, even if the underlying genetic processes are not usually recognised.[4] In addition to accumulating universal and particular genetic alterations, environmental factors also contribute to the development of gastric cancer, which typically affects older individuals due to prolonged atrophic gastritis. The average age of diagnosis for stomach cancer is 70.[5] Pernicious anaemia, hereditary diffuse gastric cancer, Helicobacter pylori infection, and a family history of gastric cancer are all risk factors.[6] Despite recent improvements in therapy, the prognosis is still dismal, with a 5-year death rate of 29% Signet ring cell cancer subtypes, which make up 11–37% of all stomach cancers, have been shown to be on the rise recently.[7] Signet ring cell carcinoma is described by the WHO as a weakly cohesive carcinoma made up mostly of tumour cells with significant cytoplasmic mucin and an eccentrically positioned crescent-shaped nucleus.[8] Esophagogastric junction cancer incidence has sharply increased in Western nations in recent years.[9] Western research has shown two forms of esophagogastric

adenocarcinoma: one linked to Helicobacter pylori (H. pylori) atrophic gastritis, similar to non-cardia gastric cancer, and the other to non-atrophic mucosa and GERD, similar to esophageal adenocarcinoma resulting from Barrett's oesophagus.[10] This research intends to analyse the kinds of gastric cancer in a sample of Iraqi patient in association with clinic-pathological factors (age, gender, location, grade, gross features, endoscopical findings, clinical presentation, pathological stage and lymph node status).

METHOD

A retrospective study including analysis of 100 randomly selected patients with gastric carcinoma collected from Teaching Laboratories of Al-Emamain Al-Kadhmain Medical City (AS), Baghdad Medical City and private labs from October 2017 to January 2021.

The clinic-pathological data that were collected from patients pathology reports included:

- Age
- Gender
- Clinical presentation
- Tumor site
- Endoscopic finding for biopsy specimens
- Gross findings, pathological stage and nodal status for resection specimens
- Histological type and grade of the tumor
- Exclusion Criteria:
  - Patients diagnosed with benign or malignant neoplasms other than gastric carcinoma (intestinal type, diffuse type)
  - Incomplete clinical or pathological data or endoscopy reports from referring physicians.

Formalin-fixed paraffin-embedded tissue blocks were collected. Then, sections 4-6 microns stained routinely with Hematoxylin & Eosin and the diagnosis was revised by two pathologists. All statistical analyses were performed utilizing SPSS, version 23 and including mean, standard deviation, frequency and percentage using Yates Chi square with p. value <0.05 regarded as statistically significant.

RESULTS

Regarding age, most of the studied sample cases were in the age group 40-60 years (68%). As for gender, the male to female ratio was 1:1; as illustrated in table.[1] The clinic-pathological characteristics of the studied sample are illustrated in table.[2] Epigastric pain was the most common presenting symptom (35.0%). During endoscopy, ulcerative mass was the most common endoscopic appearance (20.0%). The gastric pylorus was the most common tumor site (19.0%). As for histological type, intestinal type was found in (53.0%), whereas diffuse type was detected in (47.0%). Concerning tumor characteristics among 41 cases that underwent gastric resection, pT3 was the most common tumor size (68.3%), and pN2 was the most common nodal status (26.8%).

Table (1): Sociodemographic characteristics of the studied sample.

Sociodemographic characteristics	Frequency	Percentage
Age		
<40	7	7.0
40-49	22	22.0
50-59	22	22.0
60-69	26	26.0
≥70	23	23.0
Total	100	100.0
Gender		
Male	50	50.0
Female	50	50.0
Total	100	100.0
Clinical characteristics	Frequency (Total =100)	Percentage (%)
Presentation (Total = 100)		
Epigastric pain	35	35.0
Ascites	7	7.0
Malena	8	8.0
Dyspepsia	6	6.0
Dysphagia	6	6.0
Hematemesis	7	7.0
Constitutional symptoms (anemia, weight loss)	11	11.0
Mass	6	6.0
Metastasis	8	8.0
Vomiting	6	6.0
Type of specimen (Total = 100)		

Endoscopic biopsy	59	59.0
Gastric resection	41	41.0
Endoscopic appearance (Total = 100)		
Ulcerative mass	20	20.0
Fungating mass	19	19.0
Flat lesion	19	19.0
Ulcer	3	3.0
Polypoid lesion	1	1.0
Not assessed	38	38.0
Gross appearance (Total = 41)		
Wall thickening	18	43.9
Fungating mass	10	24.4
Ulcerative mass	9	22.0
Wall thickening and mass	3	7.3
Polyp	1	2.4
Tumor site (Total = 100)		
Pylorus	22	22.0
Cardia	5	5.0
Antrum	11	11.0
Body	9	9.0
Lesser curvature	4	4.0
Greater curvature	3	3.0
Entire stomach	10	10.0
Body and antrum	8	8.0
Body and cardia	2	2.0
GEJ	4	4.0
multiple sites	3	3.0
Not assessed	19	19.0%
Size (Total = 41)		
<3 CM	4	9.8
3-6 CM	20	48.8
>6 CM	17	41.5
Histological type (Total = 100)		
intestinal	53	53.0
diffuse	47	47.0
pT (Total = 41)		
T1a	1	2.4
T2	4	9.8
T3	28	68.3
T4a	6	14.6
T4b	2	4.9
pN (Total = 41)		
Nx	1	2.4
N0	9	22.0
N1	7	17.1
N2	11	26.8
N3a	8	19.5
N3b	5	12.2
Tumor grade (Total = 100)		
Moderately differentiated	43	43.0
Poorly differentiated	57	57.0

A significant association was detected between histopathological type and age (p value= 0.006). No significant association was detected between histopathological type and gender (p value= 0.229); as illustrated in table (2).

Table (2): Relationship between histopathological type and age and gender.

Age	Histopathological type		Total	P value
	Intestinal	diffuse		
<40	1	6	7	**0.006**
	1.9%	12.8%	7.0%	
40-49	6	16	22	
	11.3%	34.0%	22.0%	
50-59	13	9	22	
	24.5%	19.1%	22.0%	
60-69	17	9	26	
	32.1%	19.1%	26.0%	
≥70	16	7	23	
	30.2%	14.9%	23.0%	
Total	53	47	100	
	100.0%	100.0%	100.0%	
Gender	**Histopathological type**		**Total**	**P value**
	Intestinal	**diffuse**		
Male	30	20	50	0.229
	56.6%	42.6%	50.0%	
Female	23	27	50	
	43.4%	57.4%	50.0%	
Total	53	47	100	
	100.0%	100.0%	100.0%	

A significant association was detected between histopathological type and presentation (p value= 0.011). A statistically significant association was detected between histopathological type and gross features (p value<0.001). A significant association was detected between histopathological type and endoscopic appearance (p value<0.001). No significant association was detected between histopathological type and tumor size (p value= 0.439). A significant association was detected between histopathological type and tumor site (p value= 0.011). A significant association was detected between histopathological type and tumor site (p value< 0.001). No significant association was detected between histopathological type and pT staging (p value= 0.095). No significant association was detected between histopathological type and pN staging (p value= 0.165); as illustrated in table (3).

Table (3): Relationship between histopathological type and study variables.

Type of specimen	Histopathological type		Total	P value
	Intestinal	diffuse		
Epigastric pain	14	21	35	**0.011**
	26.4%	44.7%	35.0%	
Ascites	2	5	7	
	3.8%	10.6%	7.0%	
Melena	7	1	8	
	13.2%	2.1%	8.0%	
Dyspepsia	3	3	6	
	5.7%	6.4%	6.0%	
Dysphagia	6	0	6	
	11.3%	0.0%	6.0%	
Hematemesis	4	3	7	
	7.5%	6.4%	7.0%	
Constitutional symptoms (anemia, weight loss)	9	2	11	
	17.0%	4.3%	11.0%	
Mass	1	5	6	
	1.9%	10.6%	6.0%	
Metastasis	4	4	8	
	7.5%	8.5%	8.0%	
Vomiting	3	3	6	
	5.7%	6.4%	6.0%	

Total	53	47	100	
	100.0%	100.0%	100.0%	
Gross features	**Histopathological type**		**Total**	**P value**
	Intestinal	**diffuse**		
fungating mass	10	0	10	**<0.001**
	45.5%	0.0%	24.4%	
polyp	1	0	1	
	4.5%	0.0%	2.4%	
wall thickening	4	14	18	
	18.2%	73.7%	43.9%	
wall thickening and mass	1	2	3	
	4.5%	10.5%	7.3%	
ulcerative mass	6	3	9	
	27.3%	15.8%	22.0%	
Total	22	19	41	
	100.0%	100.0%	100.0%	
Type of specimen	**Histopathological type**		**Total**	**P value**
	Intestinal	**diffuse**		
Fungating mass	17	2	19	<0.001
	50.0%	7.1%	30.6%	
Ulcer	3	0	3	
	8.8%	0.0%	4.8%	
Polypoid lesion	1	0	1	
	2.9%	0.0%	1.6%	
Flat lesion	3	16	19	
	8.8%	57.1%	30.6%	
Ulcerative mass	10	10	20	
	29.4%	35.7%	32.3%	
Total	34	28	62	
	100.0%	100.0%	100.0%	
Size	**Histopathological type**		**Total**	**P value**
	Intestinal	**diffuse**		
<3 CM	1	3	4	0.439
	4.5%	15.8%	9.8%	
3-6 CM	12	8	20	
	54.5%	42.1%	48.8%	
>6 CM	9	8	17	
	40.9%	42.1%	41.5%	
Total	22	19	41	
	100.0%	100.0%	100.0%	
Tumor location	**Histopathological type**		**Total**	**P value**
	Intestinal	**diffuse**		
pylorus	14	8	22	0.011
	30.4%	22.9%	27.2%	
cardia	4	1	5	
	8.7%	2.9%	6.2%	
antrum	9	2	11	
	19.6%	5.7%	13.6%	
body	6	3	9	
	13.0%	8.6%	11.1%	
lesser curvature	0	4	4	
	0.0%	11.4%	4.9%	
greater curvature	1	2	3	
	2.2%	5.7%	3.7%	
entire stomach	2	8	10	
	4.3%	22.9%	12.3%	
body and antrum	4	4	8	
	8.7%	11.4%	9.9%	

body and cardia	0	2	2	
	0.0%	5.7%	2.5%	
GEJ	3	1	4	
	6.5%	2.9%	4.9%	
multiple sites	3	0	3	
	6.5%	0.0%	3.7%	
Total	46	35	81	
	100.0%	100.0%	100.0%	
Tumor grade	**Histopathological type**		**Total**	**P value**
	Intestinal	**diffuse**		
Moderately differentiated	43	0	43	
	81.1%	0.0%	43.0%	
Poorly differentiated	10	47	57	
	18.9%	100.0%	57.0%	<0.001
Total	53	47	100	
	100.0%	100.0%	100.0%	
pT staging	**Histopathological type**		**Total**	**P value**
	Intestinal	**diffuse**		
T1a	0	1	1	
	0.0%	5.3%	2.4%	
T2	2	2	4	
	9.1%	10.5%	9.8%	
T3	17	11	28	
	77.3%	57.9%	68.3%	
T4a	3	3	6	
	13.6%	15.8%	14.6%	0.095
T4b	0	2	2	
	0.0%	10.5%	4.9%	
Total	22	19	41	
	100.0%	100.0%	100.0%	
pN staging	**Histopathological type**		**Total**	**P value**
	Intestinal	**diffuse**		
Nx	0	1	1	
	0.0%	5.3%	2.4%	
N0	6	3	9	
	27.3%	15.8%	22.0%	
N1	6	1	7	
	27.3%	5.3%	17.1%	
N2	6	5	11	
	27.3%	26.3%	26.8%	0.165
N3a	3	5	8	
	13.6%	26.3%	19.5%	
N3b	1	4	5	
	4.5%	21.1%	12.2%	
Total	22	19	41	
	100.0%	100.0%	100.0%	

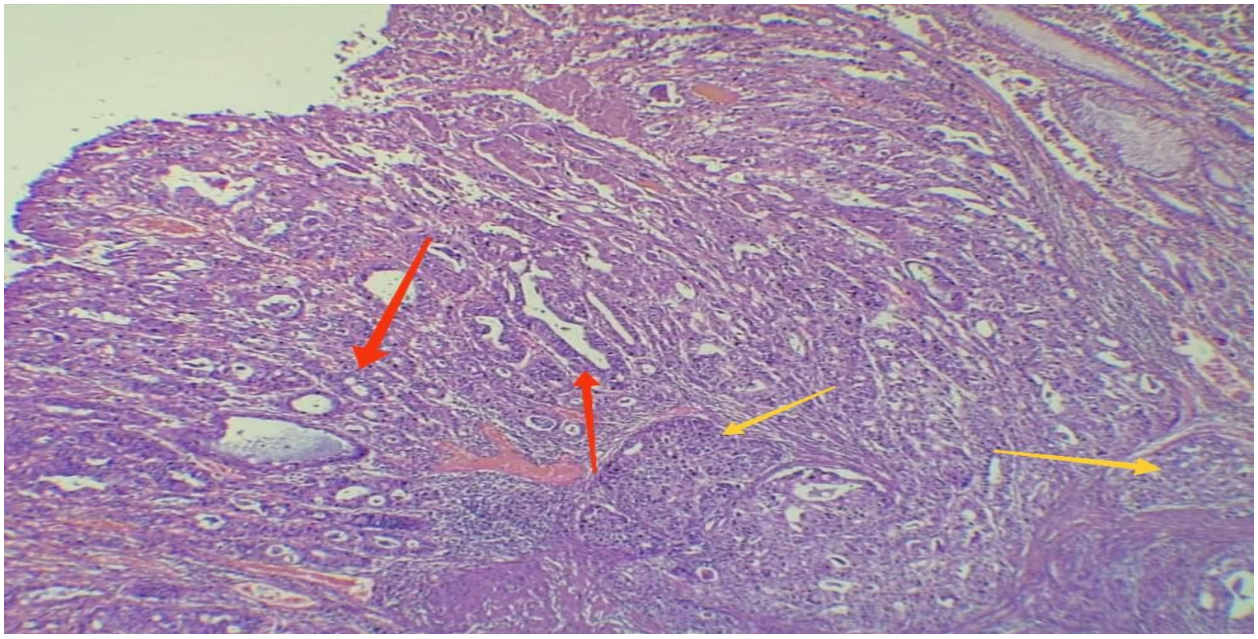

Fig. 1: Intestinal type adenocarcinoma, moderately differentiated. A section from the stomach shows surface ulceration and invasion of underlying tissue by malignant cells forming tubules (red arrows) and loose clusters (yellow arrows). H&E 4x.

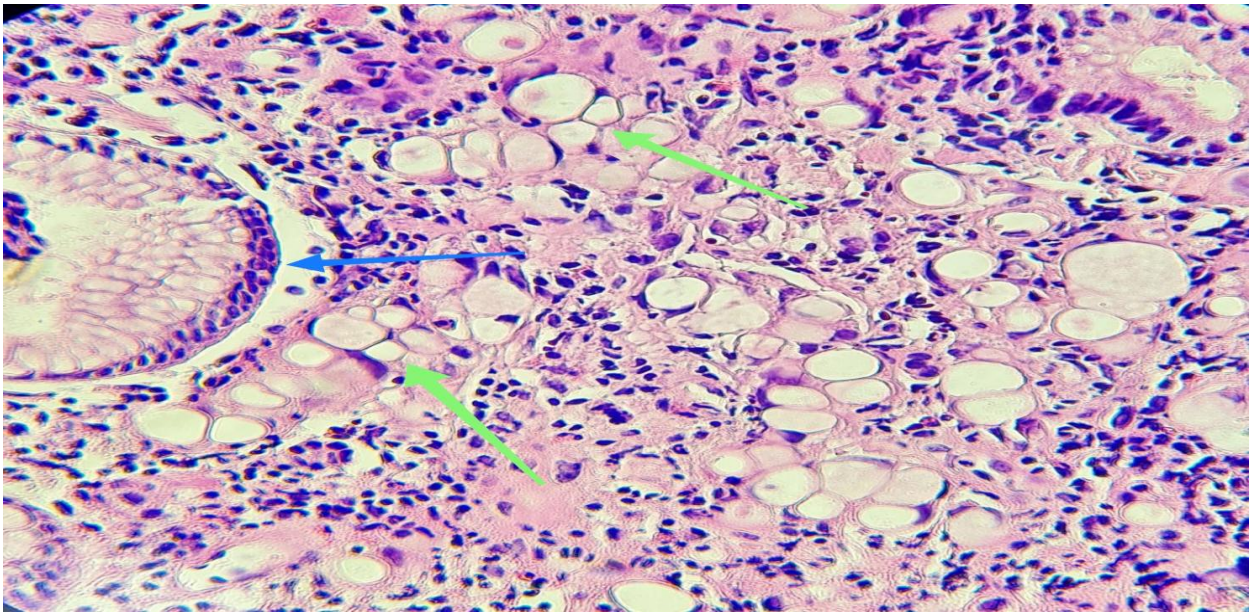

Fig. 2: Diffuse type gastric carcinoma, signet ring type .A section from the antrum and body showing infiltration by malignant signet ring cells with eccentric hyperchromatic nuclei (green arrows), singly and in loose clusters with permeation among mucosal glands (blue arrow). (H&E, 40X).

DISCUSSION

Elderly gastric cancer patients have a better prognosis due to their clinico-pathological characteristics. Gastric cancer is infrequent in adults under 50. Men are two to three times more likely than women to acquire stomach cancer, which peaks between 55 and 80.[11] This research found 26% of instances in the 60-69 age range, the most common, and 68% in the 40-60 age group. Murugesan et al. (2018) found that 85.15% of Indians were above 70.[12] Similar to Sun et al. (2020), 74.3% of patients were over 60.[13] In this study, 62.3% of patients over 60 years old were diagnosed with intestinal type gastric carcinoma, and 51% of cases were diffuse type before 60 years old. This is consistent with a 2005 study by Tavares et al., Portugal, which found that 65.2% of patients under 40 years old had diffuse type, while 70.8% of those over 40 had intestinal type with a P value < 0.05. (0,0001).[4] and comparable to another Taiwanese research by Chen et al., 2016, which found that diffuse type was more prevalent before 65 and intestinal type after 65 with a P value <0.001.[14] This research had a 1:1 male-to-female ratio, comparable to a 2020 US study by Sun et al. that found 57.4% male and 42.5% female

patients.[13] In this research, 56.6% of intestinal type patients were male and 57.4% of diffuse type cases were female, comparable to Henson et al., United States, 2000, which found that intestinal type is more frequent in men and Zheng et al., Japan, 2006, found that intestinal-type cancer was widespread in aged males and diffuse-type carcinoma in young women.[14,16] Gastric cancer symptoms include stomach discomfort, anorexia, dyspepsia, and weight loss. Proximal gastric and gastroesophageal junction tumours may cause dysphagia or regurgitation. Bleeding tumours may cause anaemia. Upon diagnosis, symptoms are frequently advanced and incurable.[17] Epigastric pain was the most prevalent presenting symptom (35%), but Fuchs and Mayer, 1995, found that weight loss was the most common clinical presentation followed by stomach discomfort.[18] Epigastric pain was the most prevalent clinical manifestation for both intestinal and diffuse types, comparable to Medina-Franco et al., Mexico City, 2000, which found that gastric carcinoma's most common symptom was abdominal pain (70%).[19] In this study, most intestinal type cases presented as fungating mass endoscopically in biopsy specimens (50%) and grossly in surgical resection specimens (30%), while diffuse type cases most frequently appeared endoscopically and grossly as flat lesions and second most frequently as ulcerative lesions, which differs from Zhao et al., 2020, which showed that (80.5%) cases of both types appeared as depressed mass.[20] Nevertheless, Chen et al., Taiwan, 2016 found that most intestine cases were superficial lesions and most diffuse cases were ulcerations and flat lesions with a p value <0.001. Western nations have more proximal stomach tumours. Obesity and gastroesophageal reflux syndrome may be raising proximal gastric cancer rates. The East is likewise embracing this trend.[21] Warsinggih, et al., Taiwan, 2022 found that the corpus (43.8%) was the most common tumour location, while this research found the pylorus (22%). Research demonstrated that both kinds were more often found in the mid and distal stomach sections. p (0.076).[23] Kim et al., Korea, 2019, found that most intestine type cases were distal whereas diffuse type cases were mid gastric, P value < 0.05. (0.001). Nevertheless, tumour size is not an independent factor in multivariate analysis, whereas lymph node metastasis, depth of invasion, and tumour location are more important.[25] In the current research, 44.8% of cases measured (3-6 cm) and 26.8% were N2, 22% N0, which is comparable to Tachibana et al., 1999, which revealed that 27% of cases were less than 2 cm and 49% measured 2-5 cm.[26] In this analysis, 54.5% of intestinal carcinomas were 3-6 cm, whereas 42.1% of diffuse type cases were 3-6 cm and 42.1% were >6 cm. A 2015 research by Liu et al., China, found that 60% of stomach cancer for both kinds measured <5 cm with a P value of 0.05. (0.851). Our country's absence of screening programmes may explain this disparity. And comparable to Chen et al Taiwan research, which found that intestinal type cases mainly measured < 4 cm while diffuse type cases mostly measured 4-8 cm. P value (<0.001).[14] In the current study, 68.3% of cases were T3 in depth and 26.8% were N2, which is in contrast to a study by Bando et al., Japan, 2018, which showed that 30% of cases were T4 and only 6.8% were T3 and (72.8%) were N0 (28), and similar to a study by Murugesan et al., India, 2018, which showed that 85.4% of subtotal and 85.8% of total gastrectomy specimens were T3.[12] 77.3% of intestinal cases and 57.9% of diffuse type were T3 in depth in this investigation. Bando et al. (2018) found that 50% of both categories were Ta and 58.9% were N0 in Japan.[29] Another Chinese research by Qiu et al., 2013, found that intestinal type patients were more often N0 and diffuse type were N3 (30) and a Taiwanese research by Chen et al. found that 52.8% of intestinal type patients were T1 and 34% of diffuse type cases were T3 with a P value <0.001.[14] Gastric cancer's Laruen classification predicts survival. Henson et al. found that 76% of cases were intestinal type and 13% were diffuse type.[15] while Chen et al. found that intestinal type recurrence rate was 54.9 % and diffuse type 59.6 %, with a P value of 0.013.[14] The present research found that 57% of instances were poorly differentiated and the rest were moderately differentiated, comparable to a 2013 Chinese study by Qiu et al., which found 62% of cases were poorly distinguished.[30] Another 2011 research by Hass et al., Germany, found that 50% of patients were poorly distinguished, p = 0.011.[31] Korea, 2017, found that 94.8% of intestinal type cases were well distinguished and moderately differentiated with a P value <0.05. (0.001) (32). Another research by Chen et al. found that 81.7% of intestine type cases were moderately differentiated with a P value <0.05. (0.001).[14]

CONCLUSION

Whereas diffuse type gastric cancer is more prevalent in younger age groups and females, intestinal type is more prevalent in older age groups and men. The most prevalent clinical symptom was epigastric pain, the pylorus was the most common tumour location, intestinal type cases were more common than diffuse type cases, and T3N2Mx was the most common stage, according to the TNM staging method. There was a substantial correlation between the histological type and (age, clinical presentation, endoscopic appearance, gross features, tumour site and tumour grade).

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