

## Original Research

### Clinicopathological Characteristics of Lymphomas of the Digestive Tract

Mehsa Bahram Shahri<sup>1</sup>, Saadat Eslami<sup>2\*</sup>

1. Department of Pathology, Shahid Sadoughi Teaching Hospital, Yazd Medical School, Shahid Sadoughi University of Medical Sciences, Yazd, Iran. **Orcid:** 0009-0008-8098-8771

2. MD, General Pathology, Department of Pathology, Shahid Sadoughi University of Medical Sciences and Health Services, Yazd, Iran. **Orcid:** 0000-0002-1831-0715.

**Corresponding Author:** Dr Saadat Eslami, Assistant Professor, Department of Pathology, Shahid Sadoughi University of Medical Sciences, Yazd, Yazd, Iran. Tel: 0098+9132578583. **Email:** saadateslami67@gmail.com

#### Abstract:

**Background:** About 40% of lymphomas occur in non-lymph nodes, most of which are in the digestive system. There are few studies on gastrointestinal lymphomas and their survival rate. Therefore, this study deals with the clinicopathological characteristics of gastrointestinal lymphomas in patients referred to the pathology ward of Shahid Sadoughi Hospital of Yazd, Iran, in 2016-2022.

**Method:** This descriptive-cross-sectional study was conducted on patients with gastrointestinal lymphoma who referred to Shahid Sadoughi Hospital in Yazd, Iran, in 2016-2022. The factors of age, gender, type of lymphoma, and anatomical location were evaluated. The researchers collected the information after receiving the code of ethics by referring to the data archive department of Shahid Sadoughi Hospital in Yazd. The data were analyzed using SPSS software version 16 and Chi-square and Fisher exact statistical tests.

**Results:** In this study, 29 patients were examined, of whom 51.2% (16) were men, and the average age was 49.3 years. Based on the location of lymphoma, one case (3.4%) was in the rectum, four cases (13.8%) were in the small intestine, four cases (13.8%) were in the colon, and 20 cases (69%) were in the stomach. Diffuse large B cell lymphoma was the most frequent, with a frequency of 18 cases (62.1%), followed by Maltoma, with six cases (20.7%). Abdominal pain, with a frequency of 13 cases (44.8%), followed by weight loss, with a frequency of nine cases (31%), was the most frequent. The frequency distribution of lymphoma types according to gender and anatomical location was insignificant.

**Conclusion:** Gastrointestinal lymphomas are often B cell phenotypes, most of which are diffuse large cell types. The anatomical location of more than half of the tumors was in the stomach. Primary tumors of the gastrointestinal tract do not have specific clinical symptoms. These patients' most frequent clinical symptoms were abdominal pain followed by B clinical symptoms (weight loss, weakness, and lethargy).

**Keywords:** Diffuse Large B Cell Lymphoma, Maltoma, Gastrointestinal Tract

Submitted: 12 May 2023, Revised: 4 June 2023, Accepted: 13: 21 June 2023 , Accepted: 28 June 2023

## Introduction

Lymphoma is divided into two subgroups, Hodgkin's and non-Hodgkin's, and 40% of them occur in areas other than lymph nodes, most of which are in the digestive system. The most common lymphoma in the WHO classification is MALTOMA (55%), followed by Diffuse large B cell lymphoma (40%), Burkitt lymphoma (3%), Follicular and Enteropathy type Tcell lymphoma (each less than 1%). The most common organs involved are usually the stomach and small intestine (1). Extranodal lymphomas occur in areas other than the lymph node, spleen, bone marrow, thymus, and Walder ring. Gastrointestinal lymphomas are cases in which the digestive tract is affected by lymphoma, with no involvement of the bone marrow, liver, or spleen. According to studies in Western societies, the prevalence of non-Hodgkin's lymphomas has increased in recent years compared to the previous decades. The rate of this increase has been faster than other types of malignancies except skin melanomas and lung cancer in women (2). The most common type of gastrointestinal lymphoma, B-cell lymphoma, has been reported in various studies. In Howell's study, diffuse large B-cell lymphoma was the most common type with 47%; in Song's study, diffuse large B-cell lymphoma was the most common type with 66% (3-4). Considering the limited studies on lymphomas of the digestive tract, this study aimed to evaluate the clinicopathological characteristics of the digestive tract in patients referred to the pathology department of Shahid Sadoughi Hospital, Yazd, Iran, from 2016 to 2022.

## Methods

This descriptive-cross-sectional study was conducted on patients with gastrointestinal lymphoma referred to Shahid Sadoughi Hospital in Yazd in 2016-2022. The inclusion criteria were people diagnosed with lymphoma of the gastrointestinal tract who were referred to Shahid Sadouqi Hospital in Yazd in 2016-2022 with a lymphoma sample. The exclusion criteria included the incompleteness of the file to the

extent that the required information was unavailable. The present study was approved by the ethics committee of Shahid Sadoughi University of Medical Sciences, Yazd (ethics code: IR.SSU.MEDICINE.REC.1400.232). The required information was collected by a checklist designed by the researchers, including background information (age and sex factors) and laboratory and clinical information (type of lymphoma, anatomical location, and initial symptoms). The anatomical location of lymphomas, including the esophagus, stomach, small intestine, colon, and rectum, was considered. The researchers collected the information after receiving the code of ethics by referring to the data archive department of Shahid Sadoughi Hospital in Yazd. The data were imported into SPSS software version 16 after collection. Quantitative data were reported as mean, and standard deviation and qualitative data were expressed as numbers and percentages to provide descriptive information. The data were statistically analyzed using Chi-square and Fisher exact tests. Also, the significance level of the p-value was considered less than 0.05.

## Results

Generally, 30 patients with gastrointestinal lymphoma were included in the study. One of the cases had incomplete and completable information, which was excluded from the study. Finally, 29 patients were examined, of whom 44.8% (13) were women, and 51.2% (16) were men. The average age of the patients was 49.3, with a standard deviation of 20.4 years. The minimum and maximum ages were 4 and 77 years. Patients were divided into groups according to age with 10-year intervals. The frequency of patients in each category is shown in Table 1.

Of the seven observed findings, the most common was Diffuse large B cell lymphoma with a frequency of 18 cases (62.1%), followed by Maltoma with 6 cases (20.7%). For the rest of the cases, the frequency of each case was one (3.4%), as shown in Table 1.

Based on the anatomical location of lymphomas, one case (3.4%) was reported in the rectum, four cases (13.8%) in the small intestine, four cases (13.8%) in the colon, and 20 cases (69%) in the stomach. According to the primary clinical symptoms and the basis of disease diagnosis, abdominal pain was the most frequent, with a frequency of 13 cases (44.8%), followed by weight loss, with a frequency of nine cases (31%). Other symptoms included gastrointestinal bleeding with a frequency of six cases (20.7%), nausea and vomiting with a frequency of three cases (10.3%), and weakness and lethargy with a frequency of two cases (6.9%). In addition, three patients (10.3%) did not have clinical symptoms that were accidentally observed in endoscopy (Table 2).

Each Burkitt lymphoma, T cell lymphoma, and Maltoma tumor had only one person, and each was male. Classic Hodgkin lymphoma and Malignant lymphoma tumors each had one person, each female. Of 18 diffuse significant B cell lymphoma cases, 11 (61.1%) were women, and seven (38.9%) were men. All six of the six cases of Maltoma were men. Finally, the statistical test showed that this frequency distribution is insignificant ( $p$ -value=0.06) (Table 3).

Burkitt's lymphoma has a frequency of 1 case reported in the stomach in the study of the frequency distribution of tumor types according to anatomical location. Classic Hodgkin's lymphoma was reported in only one case observed in the colon. Out of 18 cases of diffuse large B cell lymphoma, 3 cases (16.7%) were in the small intestine, 2 cases (11.1%) were in the colon, and 13 cases (72.2%) were in the stomach. T-cell lymphoma was reported in only one patient, the small intestine.

Malignant lymphoma was the only case observed in the stomach. Maltoma was reported in 6 patients, one in the rectum, one in the colon, and four cases (66.7%) in the stomach. Mantle lymphoma was observed in one patient whose anatomical location was in the stomach, and the

patient presented with initial symptoms of abdominal pain (Table 4).

## Discussion

The frequency of gastrointestinal lymphomas has increased in recent years in Asian, North American, and European countries (5-8). Among non-Hodgkin's lymphomas, gastrointestinal lymphomas have a frequency between 11% and 63% and are not considered a common disease (6, 9, 10).

A total of 29 patients were examined; 13 were women, 16 were men, and their average age was 49.3 years. A study in Pakistan (2023) showed that the average age of patients with non-Hodgkin's lymphomas was 47.7 years, half in the digestive system (11).

Gastrointestinal lymphomas are often B cell phenotypes, most of which are of the diffuse large cell type and include almost 70% of all gastric lymphomas (12, 13). The stomach, small intestine, and colon are the most frequent, respectively (14). In this study, diffuse large B cell lymphoma was the most common type of gastrointestinal lymphoma, and most of them were located in the anatomical location of the stomach, followed by the small intestine and colon.

Six patients with Maltoma were reported, four anatomically located in the stomach. Maltoma was the most common type in the study of gastric lymphomas (15). This study found that over half of Maltoma cases are in the stomach. Mantle cell lymphoma, or mature B cell carcinoma, comprises less than 4% of primary gastrointestinal lymphomas (16). Only one case of this lymphoma was reported, with a frequency of 3.4%. This mantle lymphoma is more frequent in the colon, and small intestine than in the stomach (17), but the mantle lymphoma reported in this study was located in the stomach. The type of lymphoma in the small intestine and colon sometimes manifests as mucosal polyps of the digestive system, which may go undiagnosed (18, 19), which may explain the low prevalence of this

lymphoma. Burkitt's lymphoma is one of the B-cell lymphomas with high invasiveness (20). This lymphoma comprises only 5% of all primary lymphomas of the gastrointestinal tract. In this study, only one case was reported in which the patient was a male, and the lymphoma was located in the stomach (7).

The anatomical location of more than half of the tumors was in the stomach. Koch et al. showed that the stomach (74.7%), followed by the intestine, is the most common site of involvement of this tumor, which was consistent with the present study (21). Studies have also stated that in the frequency distribution of this type of tumor, the stomach and intestine have relatively equal frequency (22, 23). On the other hand, in some studies, the frequency of these tumors was higher in the small intestines than in the stomach (24, 25). The lowest frequency of primary gastrointestinal lymphomas has been reported in the esophagus (26, 27); none were located there.

Primary tumors of the gastrointestinal tract do not have specific clinical symptoms, and even their manifestations may be misleading. Studies have shown that abdominal pain, clinical symptoms B, and nausea are the most common clinical symptoms (28, 29). These patients' most frequent clinical symptoms were abdominal pain followed by B clinical symptoms (weight loss, weakness, and lethargy).

Future studies should investigate gastrointestinal lymphomas in terms of radiological manifestations, laboratory results, and their relationship with patients' clinical symptoms. In addition, examination of these patients is recommended in terms of prognosis and response to treatment.

### Conclusion

Digestive tract lymphomas are often B cell phenotypes, most of which are diffuse large cell types. The anatomical location of more than half of the tumors was in the stomach.

Primary tumors of the gastrointestinal tract do not have specific clinical symptoms. Abdominal pain and clinical symptoms B (weight loss, weakness, and lethargy) were the most frequent clinical symptoms in these patients, respectively.

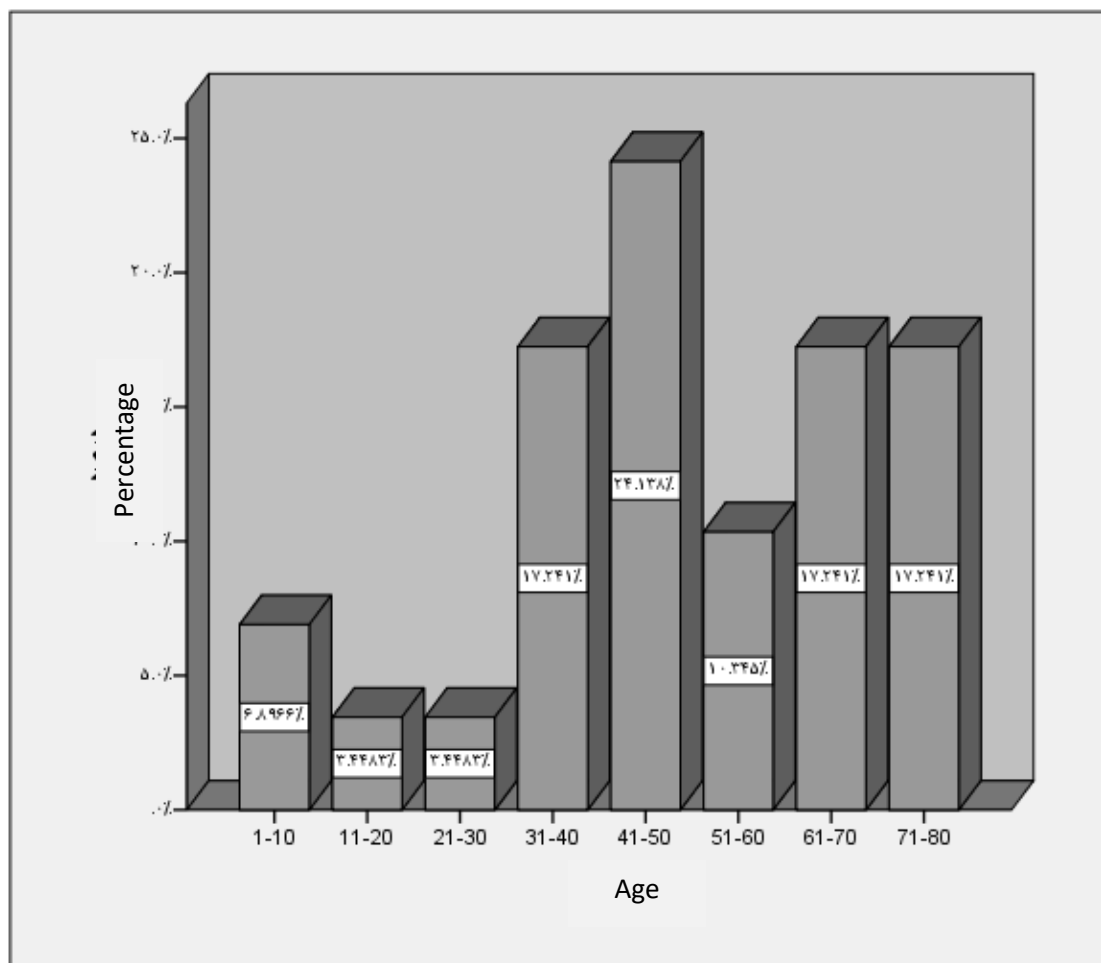
### References

1. Willemze R, Jaffe ES, Burg G, Cerroni L, Berti E, Swerdlow SH, et al. WHO-EORTC classification for cutaneous lymphomas. *Blood*. 2005;105(10):3768-85.
2. d'Amore F, Brincker H, Grønbaek K, Thorling K, Pedersen M, Jensen M, et al. Non-Hodgkin's lymphoma of the gastrointestinal tract: a population-based analysis of incidence, geographic distribution, clinicopathologic presentation features, and prognosis. Danish Lymphoma Study Group. *Journal of clinical oncology*. 1994;12(8):1673-84.
3. Howell JM, Auer-Grzesiak I, Zhang J, Andrews CN, Stewart D, Urbanski SJ. Increasing incidence rates, distribution and histological characteristics of primary gastrointestinal non-Hodgkin lymphoma in a North American population. *Canadian Journal of Gastroenterology*. 2012;26(7):452-6.
4. Song L-N, Cen X-N, Ou J-P, Liang Z-Y, Qiu Z-X, Wang W-S, et al. Clinical and prognostic analysis of 101 cases of primary gastrointestinal non-Hodgkin's lymphoma. *Zhongguo shi yan xue ye xue za zhi*. 2013;21(2):387-91.
5. Yin WJ, Wu MJ, Yang HY, Zhu X, Sun WY. [Clinicopathological features and prognostic factors of 216 cases with primary gastrointestinal tract non-Hodgkin's lymphoma]. *Zhonghua Xue Ye Xue Za Zhi*. 2013;34(5):377-82.
6. Papaxoinis G, Papageorgiou S, Rontogianni D, Kaloutsi V, Fountzilias G, Pavlidis N, et al. Primary gastrointestinal non-Hodgkin's lymphoma: a clinicopathologic study of 128 cases in Greece. *A Hellenic Cooperative*

- Oncology Group study (HeCOG). Leuk Lymphoma. 2006;47(10):2140-6.
7. Howell JM, Auer-Grzesiak I, Zhang J, Andrews CN, Stewart D, Urbanski SJ. Increasing incidence rates, distribution and histological characteristics of primary gastrointestinal non-Hodgkin lymphoma in a North American population. *Can J Gastroenterol*. 2012;26(7):452-6.
  8. Liu S, Semenciw R, Mao Y. Increasing incidence of non-Hodgkin's lymphoma in Canada, 1970-1996: age-period-cohort analysis. *Hematol Oncol*. 2003;21(2):57-66.
  9. Gou HF, Zang J, Jiang M, Yang Y, Cao D, Chen XC. Clinical prognostic analysis of 116 patients with primary intestinal non-Hodgkin lymphoma. *Med Oncol*. 2012;29(1):227-34.
  10. Li YY, Hu DZ, Wang YF, Zhao ZG, Cao Z, Zhang YZ, et al. [Clinical Characteristics of 219 Patients with Primary Gastrointestinal Non-Hodgkin's Lymphoma]. *Zhongguo Shi Yan Xue Ye Xue Za Zhi*. 2020;28(3):849-54.
  11. Saleem R, Chughtai A, Zafar G, Chughtai O, Javeed S, Chughtai AS. Clinicopathological Spectrum of B-Cell Non-Hodgkin Lymphoma in Pakistan Population: A Single-Center Study. *Cureus*. 2023;15(1):e34298.
  12. Juárez-Salcedo LM, Sokol L, Chavez JC, Dalia S. Primary Gastric Lymphoma, Epidemiology, Clinical Diagnosis, and Treatment. *Cancer Control*. 2018;25(1):1073274818778256.
  13. Ramachandran P, Sahni S, Wang JC. De novo CD5+ primary gastrointestinal diffuse large B-cell lymphoma: challenges with treatment and clinical course. *Journal of Investigative Medicine High Impact Case Reports*. 2019;7:2324709619893546.
  14. Erkurt MA, Aydogdu I, Kuku I, Kaya E, Basaran Y. Clinicopathologic characteristics and therapeutic outcomes of primary gastrointestinal non-Hodgkin's lymphomas: 10 years of experience from a single center in eastern Anatolia. *Medical Principles and Practice*. 2009;18(5):399-406.
  15. Ishikawa E, Nakamura M, Satou A, Shimada K, Nakamura S. Mucosa-Associated lymphoid tissue (MALT) lymphoma in the gastrointestinal tract in the modern era. *Cancers*. 2022;14(2):446.
  16. Wang GB, Xu GL, Luo GY, Shan HB, Li Y, Gao XY, et al. Primary intestinal non-Hodgkin's lymphoma: a clinicopathologic analysis of 81 patients. *World J Gastroenterol*. 2011;17(41):4625-31.
  17. Vetro C, Bonanno G, Giulietti G, Romano A, Conticello C, Chiarenza A, et al. Rare gastrointestinal lymphomas: The endoscopic investigation. *World J Gastrointest Endosc*. 2015;7(10):928-49.
  18. Lambrechts C, Van der Wijst E, Bries G, Bogaert J, De Schepper H, Van Hauthem P, et al. Endoscopic diagnosis of a colonic localization of a mantle cell lymphoma. *Acta Gastroenterol Belg*. 2022;85(4):632-4.
  19. Oña-Ortiz FM, Sánchez-Del Monte J, Ramírez-Solís ME, de la Mora-Levy JG, Alonso-Larraga JO, Lino-Silva LS, et al. Mantle cell lymphoma with involvement of the digestive tract. *Rev Gastroenterol Mex (Engl Ed)*. 2019;84(4):434-41.
  20. Sabattini E, Bacci F, Sagrmoso C, Pileri SA. WHO classification of hematopoietic and lymphoid tissue tumors in 2008 :an overview. *Pathologica*. 2010;102(3):83-7.
  21. Koch P, del Valle F, Berdel WE, Willich NA, Reers B, Hiddemann W, et al. Primary gastrointestinal non-Hodgkin's lymphoma: I. Anatomic and histologic distribution, clinical features, and survival data of 37 patients registered in the German Multicenter Study GIT NHL 01/92. *J Clin Oncol*. 2001;19(18):3861-73.
  22. Wang T, Gui W, Shen Q. Primary gastrointestinal non-Hodgkin's lymphoma:



- clinicopathological and prognostic analysis. *Med Oncol*. 2010;27(3):661-6.
23. Ge Z, Liu Z, Hu X. Anatomic distribution, clinical features, and survival data of 87 cases of primary gastrointestinal lymphoma. *World Journal of Surgical Oncology*. 2016;14(1):85.
24. Koniaris LG, Drugas G, Katzman PJ, Salloum R. Management of gastrointestinal lymphoma. *J Am Coll Surg*. 2003;197(1):127-41.
25. Nakamura S, Matsumoto T, Iida M, Yao T, Tsuneyoshi M. Primary gastrointestinal lymphoma in Japan: a clinicopathologic analysis of 455 patients with special reference to its time trends. *Cancer*. 2003;-2462(10)97.
26. Peng JC, Zhong L, Ran ZH. Primary lymphomas in the gastrointestinal tract. *J Dig Dis*. 2015;16(4):169-76.
27. Alvarez-Lesmes J, Chapman JR, Cassidy D, Zhou Y, Garcia-Buitrago M, Montgomery EA, et al. Gastrointestinal Tract Lymphomas: A Review of the Most Commonly Encountered Lymphomas. *Archives of Pathology & Laboratory Medicine*. 2021;145(12):1585-96.
28. Huang J, Jiang W, Xu R, Huang H, Lv Y, Xia Z, et al. Primary gastric non-Hodgkin's lymphoma in Chinese patients: clinical characteristics and prognostic factors. *BMC Cancer*. 2010;10(1):358.
29. Hu C, Yi C, Dai X. Clinical study of 31 patients with primary gastric mucosa-associated lymphoid tissue lymphoma. *J Gastroenterol Hepatol*. 2006;21(4):722-6.

**Table & Figure:****Figure 1. Frequency distribution of patients based on the age category****Table 1. Frequency distribution of samples based on tumor type**

Type of lymphoma	Number	Percentage
Burkitt lymphoma	1	%4. 3
Classic Hodgkin lymphoma	1	%4. 3
Diffuse large B cell lymphoma	18	%1. 62
T cell lymphoma	1	%4. 3
Malignant lymphoma (unknown type)	1	%4. 3
Maltoma	6	%7. 20
Mantle lymphoma	1	%4. 3

**Table 2. Frequency distribution of masses according to clinical factors**

<b>Clinical factors</b>	<b>Number</b>	<b>Percentage</b>
<b>Anatomical location</b>		
Stomach	20	%69
Small intestine	4	%8. 13
Colon	4	%8. 13
Rectum	1	%4. 3
<b>Symptoms or basis of primary diagnosis</b>		
Evidence of a mass at endoscopy	4	%3. 10
digestive bleeding	6	%7. 20
stomach ache	13	%8. 44
Weakness and lethargy	2	%9. 6
nausea and vomiting	3	%3. 10
Weight Loss	9	%31
Indigestion (dyspepsia)	2	%9. 6

**Table 3. Frequency distribution of tumor types based on gender**

<b>Type of finding</b>	<b>Gender (number (%))</b>	
	<b>Female</b>	<b>Male</b>
Burkitt lymphoma	0	1 (100%)
Classic Hodgkin lymphoma	1 (100%)	0
Diffuse large B cell lymphoma	11 (61.1%)	7 (38.9%)
T cell lymphoma	0	1 (100%)
Malignant lymphoma (unknown type)	1 (100%)	0
Maltoma	0	6 (100%)
Mantle lymphoma	0	1 (100%)
<b>P-value: 0.06</b>		