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Original Article

Oncology Section

Primary Gastrointestinal Lymphomas in Adults: An Institutional Experience of 15 Years from Northern India

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ABSTRACT

Introduction: Primary Gastrointestinal Lymphomas (PGIL) are uncommon and distinct Gastrointestinal Tract (GIT) malignancies which vary in their epidemiologic and clinicopathologic features worldwide. Since gastrointestinal malignancies are commonest malignancies in Kashmir valley, we intended to study PGIL in our hospital set up.

Aim: To study the clinicopathological and demographic profile of PGIL

Materials and Methods: This combined retrospective (eight and a half years) and prospective (six and a half years) descriptive observational study of 15 years was performed at Sher-i-Kashmir Institute of Medical Sciences, Srinagar from April 1998 to March 2013. Total 93 cases were included as per Dawson's criteria. All the cases were reviewed and reclassified according to the World Health Organisation (WHO)-Revised European American Classification of Lymphoid Neoplasms (REAL). Statistical analysis was done using GraphPad Prism 8.

Results: Ninety-three patients (Male:Female ratio, 3:1) with a mean age of 47 years (age range=18-70 years) were studied. Patients mostly presented with non specific symptoms like abdominal pain (n=79) and anorexia (n=45); and small intestine (n=30), stomach (n=27) and large intestine (n=26) were the major sites affected. Histopathological and Immunohistochemical (IHC) studies revealed most of them to be Non Hodgkin's Lymphoma (NHL) of B-cell type (n=89) with Diffuse Large B-Cell Lymphoma (DLBCL), the commonest subtype (n=66) followed by Mucosa Associated Lymphoid Tissue (MALT) lymphoma (n=21). Stage distribution included 64 stage IE, 27 stage IIE and two stage IIIE patients. Surgical resection was performed in 53 patients along with chemotherapy (25), chemoradiotherapy (20) and anti-*Helicobacter pylori* (anti-*H. pylori*) treatment (2). Forty patients received chemotherapy without surgery, along with anti-*H.pylori* treatment (14) and radiotherapy (7). Mean survival of patients was 42 months.

Conclusion: Primary Gastrointestinal Lymphomas (PGIL), although uncommon GIT malignancy, can clinically mimic any GIT disease and can involve any part of GIT. A high degree of suspicion can pick up these lymphomas early and a judicial combination of surgery, chemotherapy and radiotherapy can be offered for better survival. Further, IHC studies including genetic and molecular studies along with long term follow-up studies, are required to have a better understanding of these lymphomas in our region.

Keywords: Diffuse large B-cell lymphoma, *Helicobacter pylori*, Mucosa associated lymphoid tissue lymphoma, Non hodgkin's lymphoma

INTRODUCTION

Lymphomas are the neoplastic lymphoproliferative disorders which besides developing in lymphoid organs like lymph nodes and spleen (Nodal Lymphomas), unusually can arise in other organs like GIT, brain or skin, which normally do not contain any lymphoid tissue. The later, called Extranodal Lymphomas (ENL) account for about 40% of all NHL and most of these lymphomas arise in the GIT [1,2].

Although, PGIL constitute 30-40% of ENL and 10-15% of all NHL, these are very rare tumours, even less frequent compared to primary nodal lymphomas with secondary involvement of GIT, and comprise only 1-4 % of all GIT malignancies [3-8]. The PGIL are heterogeneous lymphomas with regards to the incidence, patient characteristics, site of involvement, histologic subtypes, stage, and treatment results, which varies worldwide, with higher rates of incidence in Eastern countries than Western countries. However, their incidence has increased in Asia, United States and Europe over the past two decades. The PGIL often lack specific symptoms and typically present with non specific signs and symptoms like epigastric pain, dyspepsia, nausea, vomiting, anorexia, weight loss, attributable mainly to the site of involvement, extent and histological subtype of the disease. Due to this, these are easily misdiagnosed and some patients even present with fatal complications like perforation and massive haemorrhage [4,6,9-13].

Since gastrointestinal malignancies are commonest malignancies in Kashmir valley [14], the present study was done to assess the various clinicopathological characteristics and demographic features of PGIL in our hospital set-up.

MATERIALS AND METHODS

This combined retrospective (eight and a half years, from April 1998 to September 2006) and prospective (six and a half years, from October 2006 to March 2013) observational study was performed at Sher-i-Kashmir Institute of Medical Sciences, Srinagar, Jammu and Kashmir, over a period of 15 years. The study was approved by the Institutional Committee (Approval No. SIMS168 PG/06263-66 dated Nov 22, 2006). Consent was taken from patients. Ninety-three patients of PGIL were included in the study.

Inclusion criteria: All patients of PGIL aged more than 15 years were included in the study.

Exclusion criteria: All other patients of gastrointestinal lymphoma aged less than 15 years and those not fulfilling the Dawson's criteria [15] were excluded from the study.

All the cases were included as per Dawson's criteria which require the presence of following: 1). No enlargement of peripheral or mediastinal lymph nodes; 2). Normal white blood cell count; 3). Predominance of GIT lesions with only regional lymph node

involvement; and 4). No involvement of the liver and spleen [15]. The diagnostic work-up included history, physical examination, baseline investigations, bone marrow aspiration/biopsy, abdominal and pelvic ultrasound, chest X-ray, computed tomography scan, and upper, lower GI endoscopies with biopsies.

The tissue specimens were processed in 10% formalin and slides were made from paraffin embedded tissue blocks, and stained with Haematoxylin and Eosin (H&E) and reticulin stains. The IHC stains for CD45, CD20, CD3, Kappa (k) and lambda (λ) were performed. Kappa and lambda antibodies were used for demonstration of light chain restriction-a proof of monoclonality for distinguishing non neoplastic lymphoid infiltrates from neoplastic ones in some biopsy specimens only for confirmation of lymphoma. All the cases were reviewed and reclassified according to the WHO- Revised European American Classsification of Lymphoid Neoplasms (REAL). Patients were staged according to the Ann-Arbor classification modified by Musshoff K for GIT lymphomas [16].

STATISTICAL ANALYSIS

Statistical analysis was done using GraphPad Prism 8. All the data collected was entered in microsoft excel sheet and frequency (n) and percentages(%) were calculated.

RESULTS

Ninety-three patients of PGIL, 70 men (75.3%) and 23 women (24.7%), (M:F ratio=3:1) with a mean age of 47 years (range, 18-70 years) were diagnosed. Mean ages were similar in men (range 18-70 years) and women (range 25-70) 46.9 years and 46.4 years, respectively. Patients predominantly presented with non specific symptoms like abdominal pain (n=79, 85) and anorexia (n=45, 48.3%), however, some patients had complications like bleeding per rectum (n=12, 13%), peritonitis (n=4, 4.3%) and obstruction (n=2, 2.1%). The duration of illness varied from 1 week to 18 months (average, 4 months). Small intestine (n=30, 32.3%) followed by stomach (n=27, 29%) and large intestine (n=26, 28%) were the most common sites involved [Table/Fig-1,2].

Based on gross examination of resected specimens and/or endoscopic findings, these lymphomas presented as ulceroinfiltrative (43), ulcreoproliferative (25), proliferative (13) and ulcerative (12) lesions or masses [Table/Fig-3-6]. Histopathologically, except for two cases of Hodgkin's lymphoma, all cases (n=91) were NHL: B-cell lymphomas (n=89) which included DLBCL (n=66), MALT lymphoma (n= 21) and Immunoproliferative Small Intestinal Disease (IPSID) (n=2); and T-cell lymphomas (n=2), one being anaplastic large cell lymphoma and another peripheral T-cell lymphoma, not otherwise specified [Table/Fig-7-10].

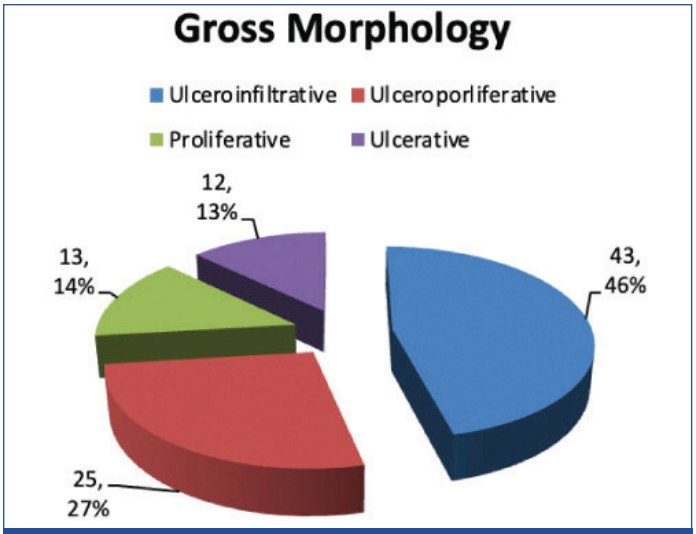
The DLBCL revealed destruction of mucosal lining with infiltration of large centro blast-like cells having irregular nuclear contours, vesicular nucleus, prominent nucleoli and scanty cytoplasm, admixed with variable number of centrocyte-like cells, multinucleate giant cells and macrophages, with many mitotic figures and apoptotic bodies, with or without a MALT component. The MALT lymphomas showed infiltration of small cleaved, centrocyte-like cells admixed

All cases				Site of tumour													
				Stomach		Small intestine		Large intestine		Ileocaecum		GE junction		Oesophagus		Multiple	
Age groups (in years)	Total (%)	M (%)	F (%)	M (%)	F (%)	M (%)	F (%)	M (%)	F (%)	M (%)	F (%)	M (%)	F (%)	M (%)	F (%)	M (%)	F (%)
≤20	3 (3.2)	3 (4.2)	0	-	-	1 (4)	-	2 (9.5)	-	-	-	-	-	-	-	-	-
21-30	11 (11.8)	7 (10)	4 (17.3)	-	2 (20)	3 (12)	1 (20)	3 (14.2)	1 (20)	-	-	-	-	-	-	1 (100)	-
31-40	13 (13.9)	11 (15.7)	2 (8.6)	2 (11.7)	-	4 (16)	-	5 (23.8)	-	-	1 (100)	-	1 (100)	-	-	-	-
41-50	32 (34.4)	21 (30)	11 (47.8)	2 (11.7)	5 (50)	11 (44)	3 (60)	6 (28.5)	2 (40)	1 (33.3)	-	-	-	1 (50)	-	-	1 (100)
51-60	20 (21.5)	17 (24.2)	3 (13)	8 (47)	2 (20)	2 (8)	-	4 (19)	1 (20)	2 (66.7)	-	-	-	1 (50)	-	-	-
61-70	14 (15)	11 (15.7)	3 (13)	5 (29.4)	1 (10)	4 (16)	1 (20)	1 (4.7)	1 (20)	-	-	1 (100)	-	-	-	-	-
71-80	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Total (100%)	93	70	23	17	10	25	5	21	5	3	1	1	1	2	-	1	1

[Table/Fig-1]: Distribution of cases according to age, gender and site of the tumour.
M: Male; F: Female; GE: Gastro-esophageal

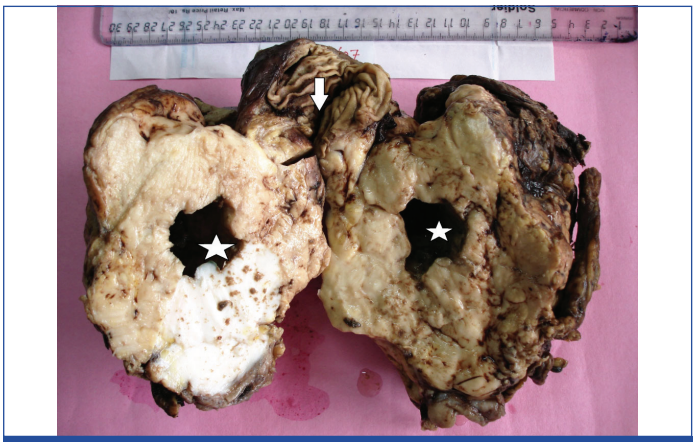
	All cases	Stomach	Small intestine	Large intestine	Ileocaecum	Oesophagus	GE junction	Multi-focal
Number (n)	93	27	30	26	4	2	2	2
Mean Age (years)	47	53	45	42	50	50	48	36
Range (Years)	18-70	28-70	19-65	18-70	39-60	41-60	32-65	30-42
Gender (M:F)	3:1	1.7:1	5:1	4:1	3:1	2:0	1:1	1:1
Presenting features								
Abdominal pain	79	24	26	21	4	-	2	2
Anorexia	45	19	15	7	2	-	1	1
Pallor	26	14	5	3	1	1	1	1
Weight loss	26	5	11	8	1	-	1	-
Abdominal mass	23	-	9	11	2	-	-	1
Vomiting	23	11	11	1	-	-	-	-
Constipation	16	3	2	10	1	-	-	-
Bleeding	12	2	1	9	-	-	-	-
Post prandial fullness	7	6	1	-	-	-	-	-
Peritonitis	4	-	4	-	-	-	-	-
Diarrhoea	3	-	3	-	-	-	-	-
Fever	3	-	3	-	-	-	-	-
Obstruction	2	-	-	2	-	-	-	-
Dysphagia	2	-	-	-	-	2	-	-

[Table/Fig-2]: Distribution of clinical features according to the site of involvement.

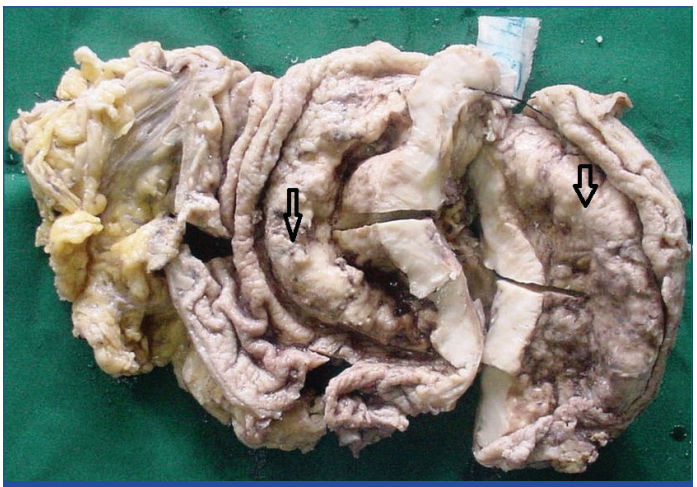


[Table/Fig-3]: Gross Morphology of GI Lymphomas based on Endoscopic and/Gross appearence.

[Table/Fig-4]: Gross morphology of an ileocaecal lymphoma.



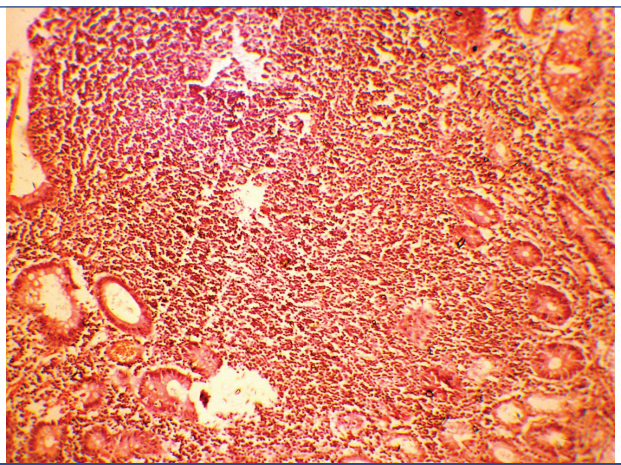
[Table/Fig-5]: Gross morphology of an ileal lymphoma.



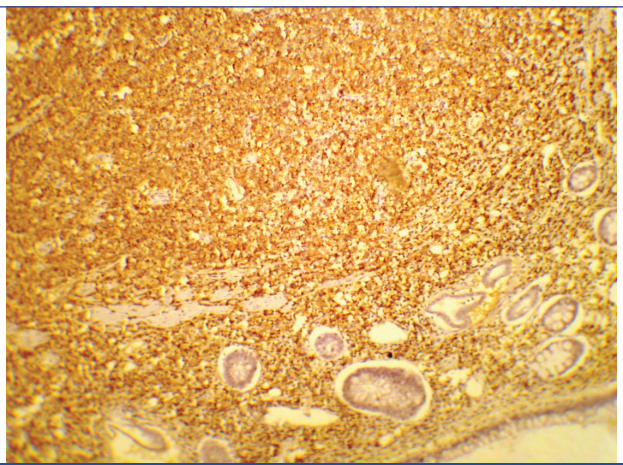
[Table/Fig-6]: Gross morphology of a stomach lymphoma.

Histological subtypes of lymphomas	All cases			Stomach		Small intestine		Large intestine		Ileocaecum		GE junction		Oesophagus		Multi-focal	
	T	M	F	M	F	M	F	M	F	M	F	M	F	M	F	M	F
NHL	91	68	23	15	10	25	5	21	5	3	1	1	1	2	-	1	1
B-cell	89	66	23	14	10	25	5	20	5	3	1	1	1	2	-	1	1
MALT	21	14	7	5	6	5	1	3	-	-	-	-	-	1	-	-	-
DLBL	66	50	16	9	4	18	4	17	5	3	1	1	1	1	-	1	1
IPSID	2	2	-	-	-	2	-	-	-	-	-	-	-	-	-	-	-
T-cell	2	2	-	1	-	-	-	1	-	-	-	-	-	-	-	-	-
HL	2	2	-	2	-	-	-	-	-	-	-	-	-	-	-	-	-
Total	93	70	23	17	10	25	5	21	5	3	1	1	1	2	-	1	1

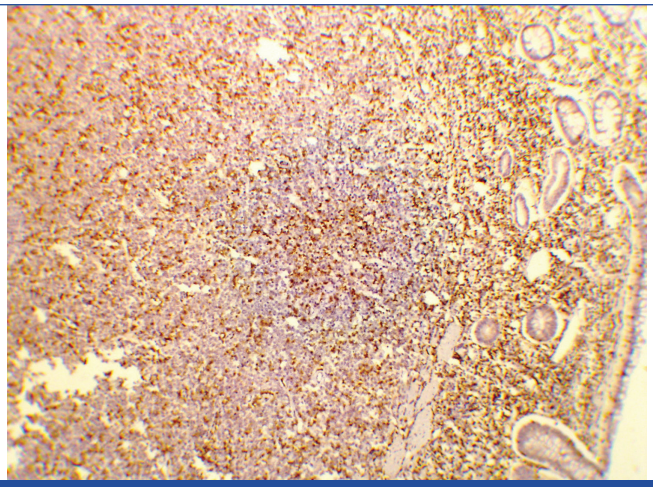
[Table/Fig-7]: Distribution of histopathological subtypes in relation to site of involvement.
NHL: Non hodgkins lymphoma; GE: Gastro-esophageal; MALT: Mucosa associated lymphoid tissue; DLBL: Diffuse large b-cell lymphoma; IPSID: Immunoproliferative small intestinal disease; HL: Hodgkin's lymphoma



[Table/Fig-8]: Haematoxylin & Eosin (H&E) stained section from gastric Mucosa Associated Lymphoid Tissue (MALT) lymphoma (x10).



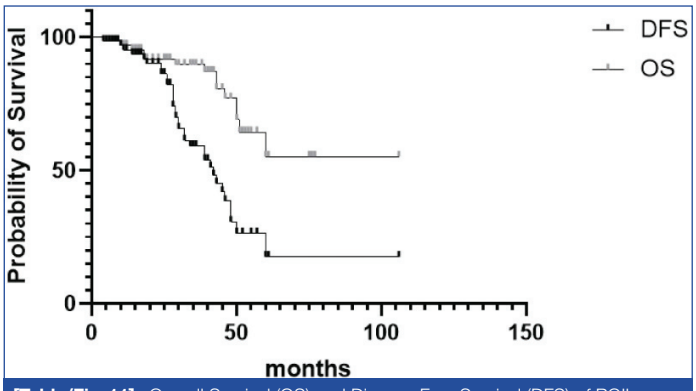
[Table/Fig-9]: CD20 stain of the caecal Diffuse Large B-Cell Lymphoma (DLBCL) highlighting neoplastic B- cells (x10).



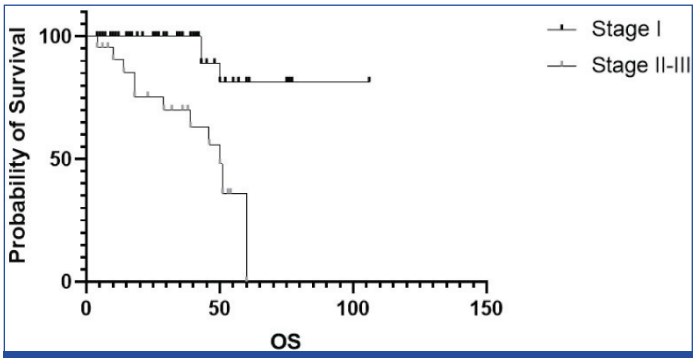
[Table/Fig-10]: CD3 stain shows non neoplastic T-cells at the periphery and scattered in between the neoplastic cells (x10).

with plasma cells and some eosinophils with destruction of glands and formation of lymphoepithelial lesions. Two cases IPSID showed marked lymphoplasmacytic infiltrate with formation of lymphoid follicles and lymphoepithelial lesions. Sixty-four patients belonged to stage IE, 24 patients to stage IIE1, three patients to stage IIE2 and two patients to stage IIIE.

Treatment modalities used for these patients were surgery or chemotherapy alone or in combination, with or without radiotherapy. Antibiotic therapy for eradication of *Helicobacter pylori* was given to 14 patients of MALT lymphoma and two patients of IPSID. Initial surgical resection was performed in 53 (57%) patients: 16 patients underwent total or subtotal gastrectomy; 13 had ileocaecal resection with right hemicolectomy; 10 had ileocaecal resection; three had tumour resection; two each had ileocaecal resection with extended right hemicolectomy, extended right hemicolectomy, right hemicolectomy and palliative or debulking surgery; and one each had transverse colectomy with colo-colic anastamosis, left hemicolectomy and oesophagectomy. Of these patients, 25 received chemotherapy alone; 20 received chemotherapy and radiotherapy in addition; and surgery alone was done in eight patients along with anti-*H. pylori* treatment in two of them. Rest of the patients (40) patients were treated without surgery: 33 patients received chemotherapy alone, with anti-*H. pylori* treatment in 14 of them; while as seven patients received chemotherapy plus radiotherapy. Cyclophosphamide, Doxorubicin, Vincristine, and Prednisolone (CHOP) and other anthracyclin-containing regimens were the most frequently used regimens for chemotherapy. Seventy-one patients including 49 stage IE patients, 21 stage IIE patients and one stage IIIE patient, were followed up for a period ranging from 4-106 months (mean 42 months). Overall Survival (OS) and Disease Free Survival (DFS) were calculated [Table/Fig-11]. Fourteen patients (10 stage IIE, three stage IE and one stage IIIE patients) died within a period of 4-60 months following initial treatment; and 26 patients (13 stage IE and 13 stage IIE patients) relapsed after a period of 11-60 months after initial treatment [Table/Fig-12].Twenty-two patients diagnosed during the initial five years of retrospective period (April 1998-March 2003), could not be followed because of the unavailability of record.



[Table/Fig-11]: Overall Survival (OS) and Disease Free Survival (DFS) of PGIL.



[Table/Fig-12]: Overall Survival (OS) in months, of early- and advanced-stage PGIL.

DISCUSSION

The PGIL are uncommon tumours, although time-trend analyses have demonstrated an increase of 2.7% per annum in the incidence for gastric (6.3%) and small bowel diseases (5.9%) [17]. The definition of PGIL proposed by Isaacson PG is an operational modification of Dawson's criteria which requires that the lymphoma be limited to the GIT and its contiguous lymph nodes with main bulk of disease in the GIT, necessitating direction of treatment to that site [18].

The PGIL is often clinically misdiagnosed as carcinoma and the duration of symptoms is long until a histologic diagnosis is established, because of the non specific symptoms and signs [7,8,13]. Abdominal pain followed by anorexia and weight loss were the predominant symptom in the present study and average duration of illness was about four months, which is comparable to the reports of others [5,11,12]. In this study, men significantly outnumbered women (M:F ratio; 3:1) and the mean age of presentation was 47 years (age range, 18-70 years), consistent with other studies [4,5,19,20]. Sites from which PGIL most commonly arise in the Western population are in the descending order of frequency: stomach, small intestine, ileocaecal region and colon whereas in the Middle East and North Africa, small intestine is the dominant site [19,20].

Although, stomach has no mucosal lymphoid tissue in its normal state, it is the predominant site of extranodal NHL representing between 30% and 40% of all ENL and 55% and 65% of all GIT lymphomas. Primary gastric lymphoma, however, is a rare tumour, with an incidence of 4%-20% of NHL and approximately 5% of primary gastric neoplasms [12,13]. Here, stomach (n=27, 29%) was the second commonest site affected following small intestine (n=30, 32.3%), similar to some studies [9,21] and contrary to other studies [11,19,20,22]. Most of the gastric lymphoma patients are over 50 years of age with a relative predilection in men [3,13]. Likewise, most of the gastric lymphoma patients in the present study were men (n=17, 63%; M:F ratio=1.7:1) with a mean age of 53 years.

Lymphoma is the most common malignancy of the small bowel accounting for 15%-20% of all small intestine neoplasms; and small intestine is the second commonest site affected by PGIL, accounting for 20-30% of all GIT lymphomas [3,7]. In addition, with population migration and an increasing incidence of Human Immunodeficiency Virus (HIV) infection, the incidence of small intestine involvement has increased in the Western series [19]. Small intestines was the most common part of GIT affected (n=30, 32.3%) in patients of the present study and ileum, which is classically thought to be the commonest site of small bowel lymphoma because of the greater amount of lymphoid tissue, was the most common area (n=18; 60%) involved followed by duodenum (n=9, 30%) [3,12].

Primary lymphoma of large intestine is very rare, constituting only 0.2% of all malignant tumours of large intestine and 6%-12% of all GIT lymphomas; often affects the caecum, ascending colon and rectum

[3,7,8,23]. Large intestine was involved in significant number of patients in this study (n=26; 28%), and caecum (n=11, 42%) was the commonest site affected followed by ascending colon (n=10, 38.5%) which is comparable to the results of other studies [19,24]. Like other studies, some unusual sites of involvement by PGIL like oesophagus (two cases) and rectum (one case) were also identified in this study [3,8,20].

Theoretically, with the exception of cutaneous cerebriform T-cell lymphoma, any of the lymphomas may arise in GIT; however, majority being NHL (mainly, B-cell lymphomas of MALT type; DLBCL, with or without the components of MALT; Mantle cell lymphoma; and Burkitt's or Burkitt-like lymphoma,) while Hodgkin's lymphoma is extremely rare in the GIT [3,8,12,13,18,20]. Consistently, except for two cases of Hodgkin's lymphoma of stomach, majority of cases of this study (98%) were NHL. DLBCL was the commonest histological subtype (n=66, 72.5%) followed by MALT lymphoma (n=21, 23%) [19,21,22]. In contrast, Papaxoinis G et al., study from Greece and Shirsat HS and Vaiphei K study from India, reported MALT lymphomas as the most common subtype followed by DLBCL [10,20].

Chronic inflammation, particularly, infection with *Helicobacter pylori* usually causes MALT lymphoma [3,4]. Stomach was the most common site for MALT lymphomas in the present study (n=11, 52.4%) with presence of characteristic lymphoepithelial lesions in all of them, and most of them (n=7, 64%) were positive for *H. pylori* on histology, similar to what has been reported in the literature [3-5]. The IPSID, a variant of MALT lymphoma which arises in the small bowel and is common in the Middle-east countries, was also seen in present study (two cases), suggesting that, with lower incidence, IPSID exists in India [19,20]. Majority of present cases belonged to stage IE (64) followed by IIE (27), similar to the stage distribution of other studies [10,20].

Treatment plans for PGIL include a combination of surgical resection, radiation therapy, chemotherapy, and antibiotics. However, controversy exists regarding the indications and efficacy of surgical resection and the issue whether chemotherapy alone or combined with radiotherapy can replace surgery. Traditionally, surgical treatment was considered the cornerstone of the therapeutical strategy showing impressive results in terms of long DFS and OS, particularly, in patients with completely resectable early-stage disease, where surgery has more of an advantage but could delay the use of chemotherapy, could be associated with some morbidity, and may also have a mortality rate of up to 10%. Even some controlled trials couldn't find any benefit from surgery. Others support conservative approach in the treatment of PGIL. Now, the management of PGIL has been extensively revised and is centered on systemic treatments such as chemotherapy and radiotherapy for localised as well as advanced disease [5,11,17].

The current National Comprehensive Cancer Network (NCCN) guidelines suggest chemotherapy mainly for the gastric MALT lymphoma and *H.Pylori* eradication therapy in the early disease. For complications, like bleeding or perforation or obstruction, surgery is advocated. Preventive surgery is sometimes advocated to prevent life threatening complications when rapid tumour necrosis occurs due to chemoradiotherapy [17]. Among 22 patients of stage, IE gastric PGIL, surgery was performed in 11 patients, along with chemotherapy in seven patients and anti-*H. pylori* treatment in two patients; chemotherapy (without surgery) was offered in 11 patients, along with radiotherapy and anti-*H. pylori* treatment in one patient each. Rest of the five, stage IIE patients were treated with surgery along with chemoradiotherapy.

For intestinal lymphoma, surgical resection is indicated in stage I bulky disease, in the case of suspected residual mass after chemotherapy and in life-threatening complications like occlusion, bleeding and perforation [5,17]. Many of patients of this study with small and large bowel lymphomas had bulky tumours, hence, surgery was performed in 16 patients of small bowel lymphoma (nine stage IE and seven stage IIE) along with chemotherapy in 15 patients and anti-*H. pylori* treatment in one patient; and 15 patients of large bowel lymphoma with chemotherapy in 12 and chemoradiotherapy in six of them. Chemotherapy alone was offered to 14 patients of the small bowel lymphoma patients along with radiotherapy in two patients and anti-*H. pylori* treatment in five patients; and 11 patients of large bowel lymphoma along with radiotherapy in two patients.

Limitation(s)

The present study had certain limitations like only few IHC markers were used instead of a panel of IHC markers for subtyping of PGIL as germinal center/non germinal center type and identification of rare entities. Also, a detailed follow-up of all patients was not available.

CONCLUSION(S)

In this study, PGIL was more commonly seen in males. The PGIL are a distinct and heterogeneous group of GI neoplasms which, generally, are uncommon but affects many patients in our region too and can be missed, particularly in early stages due to lack of specific signs and symptoms or until patients present with complication like obstruction and haemorrhage. Thus, a high degree of suspicion is required to pick up these lesions and a judicial combination of surgery, chemotherapy and radiotherapy can be offered to patients depending on stage, bulk of disease, residual disease and other factors for better survival. Further, IHC studies including genetic and molecular studies and long term follow-up studies, are required to have a better understanding of these lymphomas in our region.

REFERENCES

[1] Isaacson PG. Extranodal lymphomas: The mucosa-associated lymphoid tissue concept. Verh Dtsch Ges Pathol.1992;76:14-23. PMID: 1283245.
[2] Mishra P, Das S, Kar R, Jacob SE, Basu D. Primary extranodal non Hodgkin lymphoma: A 3-year record-based descriptive study from a tertiary care center in Southern India. Indian J Pathol Microbiol. 2015;58(3):296-300.
[3] Ghimire P, Wu GY, Zhu L. Primary gastrointestinal lymphoma. World J Gastroenterol. 2011;7(6):697-707.
[4] Shirwaikar Thomas A, Schwartz M, Quigley E. Gastrointestinal lymphoma: The new mimic. BMJ Open Gastro. 2019;6:e000320. Doi: 10.1136/ bmjgast-2019-000320.
[5] Radman I, Kovacevic-Metelko J, Aurer I, Nemet D, Zupancic-Salek S, Bogdanic V, et al. Surgical resection in the treatment of primary gastrointestinal Non Hodgkin's lymphoma: Retrospective study. Croat Med J. 2002;43(5):555-60.
[6] Chen Y, Chen Y, Chen S, Wu L, Xu L, Lian G, et al. Primary gastrointestinal lymphoma. a retrospective multicenter clinical study of 415 cases in Chinese province of guangdong and a systematic review containing 5075 Chinese patients. Medicine. 2015;94(47):e2119.
[7] Peng JC, Zhong L, Ran ZH. Primary lymphomas in the gastrointestinal tract. J Dig Dis. 2015;16(4):169-76.
[8] Lo Re G, Federica V, Midiri F, Picone D, Tona GLa, Galia M, et al. Radiological features of gastrointestinal lymphoma. Gastroenterol Res and Pract. 2016;2016:2498143.
[9] Li M, Zhang S, Gu F, Xiao W, Yao J, Chao K, et al. Clinicopathological characteristics and prognostic factors of primary gastrointestinal lymphoma: A 22-year experience from South China. Int J Clin Exp Pathol. 2014;7(5):2718-28.
[10] Papaxoinis G, Papageorgiou S, Rontogianni D, Kaloutsi V, Fountzilas 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):2140-46.
[11] 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. Med Princ Pract. 2009;18:399-406. Doi: 10.1159/000226295. Epub 2009 Jul 31.
[12] Ge Z, Liu Z, Hu X. Anatomic distribution, clinical features, and survival data of 87 cases primary gastrointestinal lymphoma. World J Surg Oncol. 2016;14:85. Doi: https://doi.org/10.1186/s12957-016-0821-9.
[13] Jua´rez-Salcedo LM, Sokol L, Chavez JC, Dalia S. Primary gastric lymphoma, epidemiology, clinical diagnosis, and treatment. Cancer Control. 2018;25(1):01-12.
[14] Rasool MT, Lone MM, Wani ML, Afroz F, Zaffar S, Mohib-ul Haq M. Cancer in Kashmir, India: Burden and pattern of disease. J Can Res Ther. 2012;8(2):243-46.
[15] Dawson IM, Cornes JS, Morson BC. Primary malignant lymphoid tumours of the intestinal tract. Report of 37 cases with a study of factors influencing prognosis. Br J Surg. 1961;49:80-89. Doi: 10.1002/bjs.18004921319.
[16] Musshoff K. Clinical staging classification of non Hodgkin's lymphomas. Strahlentherapie. 1977;153(4):218-21.
[17] Cirocchi R, Farinella E, Trastulli S, Cavaliere D, Covarelli P, Listorti C, et al, Surgical treatment of primitive gastrointestinal lymphomas: A systematic review. World J Surg Oncol. 2011;9:145. https://www.ncbi.nlm.nih.gov/books/NBK91864/.
[18] Isaacson PG. Gastrointestinal lymphoma. Hum Pathol. 1994;25(10):1020-29.
[19] Arora N, Manipadam MT, Pulimood A, Ramakrishna BS, Chacko A, Kurian SS, et al. Gastrointestinal lymphomas: Pattern of distribution and histological subtypes: 10 years experience in a tertiary centre in South India. Indian J Pathol Microbiol. 2011;54(4):712-19.

[20] Shirsat HS, Vaiphei K. Primary gastrointestinal lymphomas- A study of 81 Cases from a tertiary healthcare centre. Indian J Cancer. 2014;51(3):290-92.
[21] Warrick J, Luo J, Robirds D, Branson J, Frater JL, Kreisel F, et al. Gastrointestinal lymphomas in a North American population: clinicopathologic features from one major Central-Midwestern United States tertiary care medical center. Diag Pathol. 2012;7:76. https://doi.org/10.1186/1746-1596-7-76.
[22] Terada T. Gastrointestinal malignant lymphoma: A pathologic study of 37 cases in a single Japanese institution. Am J Blood Res. 2012;2(3):194-200.
[23] Maguire LH, Geiger TM, Hardiman KM. Surgical management of primary colonic lymphoma: Big data for a rare problem. J Surg Oncol. 2019;120(3):431-37.
[24] Yaranal PJ, Harish SG, Purushotham B. Primary intestinal lymphoma: A clinicopathological study. Indian J Cancer. 2014;51(3):306-08.

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