*Original Article*

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# Clinicopathological Study of Primary Small Intestine Lymphoma

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**Abstract**

*Background and Objectives:* Primary malignant tumors of the small intestine are rare and correspond to less than 2% of all tumors of the alimentary tract. Primary non-Hodgkin's lymphoma of small intestine(PLSI) represent 15-20% of small bowel malignant tumors. The objective of this study was to ascertain the anatomic distribution, macroscopic type and histological subtypes of PLSI. *Materials and Methods:* Present study is a prospective descriptive study. During the period 2011-2014 a total of 40 resected specimens of small intestine were received and subjected for detailed morphological examination, out of which 5 cases turned out to be PLSI. These 5 cases were analyzed and classified as per WHO classification. *Results:* Mean age of presentation was 32 years with male preponderance. Most common presenting complaint was abdominal pain. Most common site was ileum followed by jejunum. Macroscopically they presented diffusely followed by nodular growth. All the cases belonged to B-cell lineage and most common histological subtype was diffuse large B cell lymphoma(DLBCL) followed by MALT lymphoma. *Conclusion*: Due to its rarity and the lack of characteristic symptoms, PLSI is often not diagnosed until serious complications occur such as intestinal obstruction/ perforation. Hence detailed morphological evaluation is needed to understand the clinicopathological profile of PLSI .

**Keywords:** Small Intestine; Non-Hodgkin's Lymphoma; Intestinal Obstruction.

## Introduction

Primary malignant tumors of the small intestine are rare and correspond to less than 2% of all tumors of the alimentary tract [1]. The gastrointestinal tract(GIT) is the commonest site for extranodal non Hodgkin's lymphoma(NHL), which has increased in incidence in recent years. The most frequent primary sites are the stomach(50-60%) , small bowel(20-30%) followed by colon. The involvement of small and large bowel as the primary site is all the more rare [2]. Lymphomas represent 15-20% of small bowel malignant tumors [3]. The ileum is the most common site of involvement because of the greatest amount of gut associated lymphoid tissue [4].

Primary lymphoma of small intestine (PLSI) is defined as a tumor that predominantly involves the small intestine with lymph node confined to the drainage area of the primary tumor site, when there is no liver or spleen involvement or palpable lymph nodes, when the chest radiograph is normal and the peripheral white cells are normal [5].

Since the introduction of the REAL(Revised European and American classification) and its successor WHO classification of lymphomas, it is widely accepted that different lymphomas are not merely morphological variations of one disease but constitute individual diseases with diverse clinical behaviors. The modern lymphoma classification is based on morphological, immunophenotypic, genetic and clinical features. Making the correct diagnosis according to WHO classification is critical because treatment vary from a simple wait and watch approach to local radiation to surgery to high dose chemotherapy [6,7,8].

The majority of cases of primary intestinal NHL are B-cell type with T-cell type lymphoma comprising only

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10-25%. T-cell lymphomas tend to have a worse prognosis than B-cell tumors [9]. Increased risk for developing primary small bowel lymphomas has been reported in patients with celiac disease and immunodeficiency states (e.g., AIDS , 4).

Patients commonly present with fatigue, weight loss and abdominal pain whereas perforation, bleeding, obstruction or intussusceptions are less frequent [4]. Due to lack of characteristic symptoms and low incidence rate, PLSI is misdiagnosed until serious complications occur, such as perforation or bleeding. This study was undertaken to ascertain the anatomic distribution, histological subtypes and clinical aspects of this rare primary lymphoma of the small intestine.

## Material and Methods

The present research is a prospective descriptive study carried out at Vijayanagara Institute Of Medical Sciences, Ballari during the period 2011-2014. A total of 40 resected specimens of small intestine due to various causes like intestinal obstruction, perforation were collected from the department of histopathology. These specimens fixed in 10% formalin for 24 hrs and then subjected to detailed gross and microscopic examination. Total of 5 small intestinal specimens showing features of primary non-Hodgkin's lymphoma were included in the study. They are grossly examined and a minimum of 5 tissue bits were processed, sectioned and stained with Hematoxylin and eosin. These stained sections were subjected for detailed microscopic examination. Immuno-histochemical stains like CD 20, CD 3 were applied to categorize as B-cell or T-cell lymphoma as per WHO classification.

Generally small intestine lymphomas are usually large, with most larger than 7x5 cms; they may extend widely submucosally with or without regional lymph node involvement. Macroscopically tumors are classified as polypoid type, ulcerative type, polyposis type, diffuse infiltrating type or as mixed type [11].

Microscopically there is often monotonus population of malignant lymphoid cells with diffuse infiltration of the intestinal wall [4]. After classifying the case into either B-cell or T-cell phenotypes, B-cell lymphomas were further subtyped as 1) Low grade lymphomas – marginal zone lymphoma of MALT type (MALT lymphoma), mantle cell lymphoma, follicular lymphoma 2) High grade lymphomas – diffuse large B-cell lymphoma, Burkitt lymphoma, lymphoblastic lymphoma [6].

Lymphomas may grow to large size before clinical symptoms present. Most small bowel lymphomas will be demonstrable on CT scan as a mass, bowel wall thickening, displacement of adjacent organs or luminal obstruction. Multiple lesions are present in 10-25% of patients. Tissue diagnosis requires biopsy of the submucosal lesion by endoscopy/CT guided biopsy or intestinal resection followed by histopathological examination [9].

## Results

A total of 40 resected specimens of small intestine due to various causes were received during the period 2011-2014, out of which 5 cases turned out to be primary Non-Hodgkins lymphoma of small intestine. These cases were analyzed under the following headings,

**Table 1:** Showing age and sex distribution of small bowel lymphoma

| Age group (years) | Male | Female | Total | Percentage |
|---|---|---|---|---|
| 1 – 20 | 1(20%) | - | 1 | 20% |
| 21 – 40 | 3(60%) | - | 3 | 60% |
| 41 – 60 | - | 1(20%) | 1 | 20% |
| | 4(80%) | 1(20%) | 5 | 100% |

**Table 2:** Showing site affected by lymphoma

| Site | No of cases | Percentage |
|---|---|---|
| Ileum | 4 | 80% |
| Jejunum | 1 | 20% |
| Total | 5 | 100% |

**Table 3:** Showing gross findings in lymphoma cases

| Microscopic type | No of cases | Percentage |
|---|---|---|
| Diffuse large B cell lymphoma(DLBCL) | 4 | 80% |
| MALT lymphoma | 1 | 20% |

**Table 4:** Showing microscopic findings in lymphoma cases

| Layers of intestine | Microscopic features | No of cases | Percentage |
|---|---|---|---|
| Mucosa | Normal | 3 | 60% |
| | Mucosal ulceration | 2 | 40% |
| | Tumor infiltration | - | - |
| Lamina propria | Tumor deposition | 5 | 100% |
| Submucosa | Tumor deposition | 5 | 100% |
| | Tumor emboli | 1 | 20% |
| Muscularis propria | Tumor infiltration | 5 | 100% |
| Subserosa | Tumor infiltration | 3 | 60% |
| Serosa | Tumor infiltration | 3 | 60% |
| Associated lymphadenopathy | Metastatic deposits | 2 | 40% |

**Table 5:** Showing microscopic type of lymphoma cases

| Microscopic type | No of cases | Percentage |
|---|---|---|
| Nodular | 2 | 40% |
| Ulcerative | 1 | 20% |
| Polypoidal | 1 | 20% |
| Polyposis | - | - |
| Diffuse infiltrative | 3 | 60% |

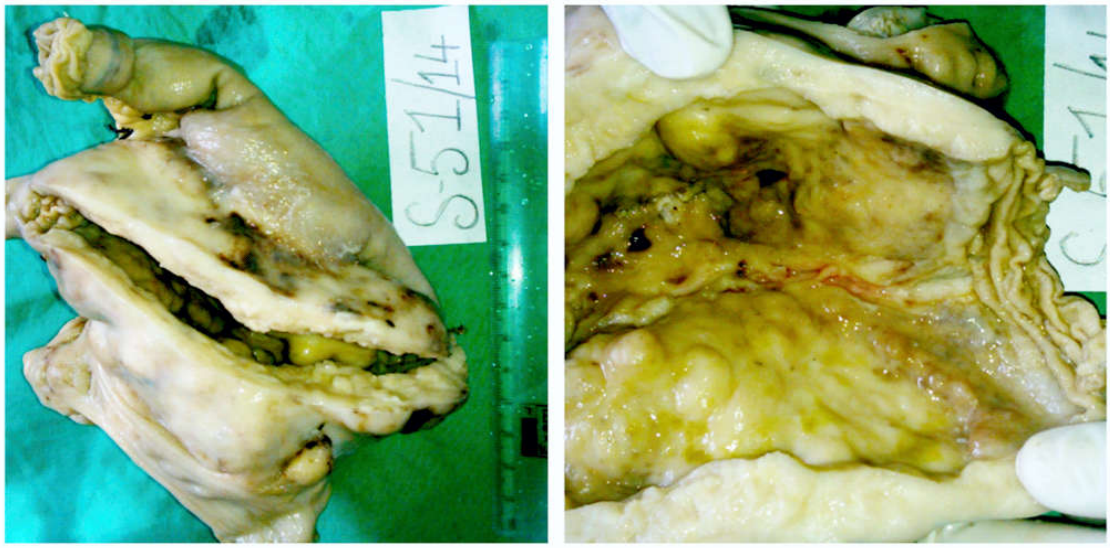
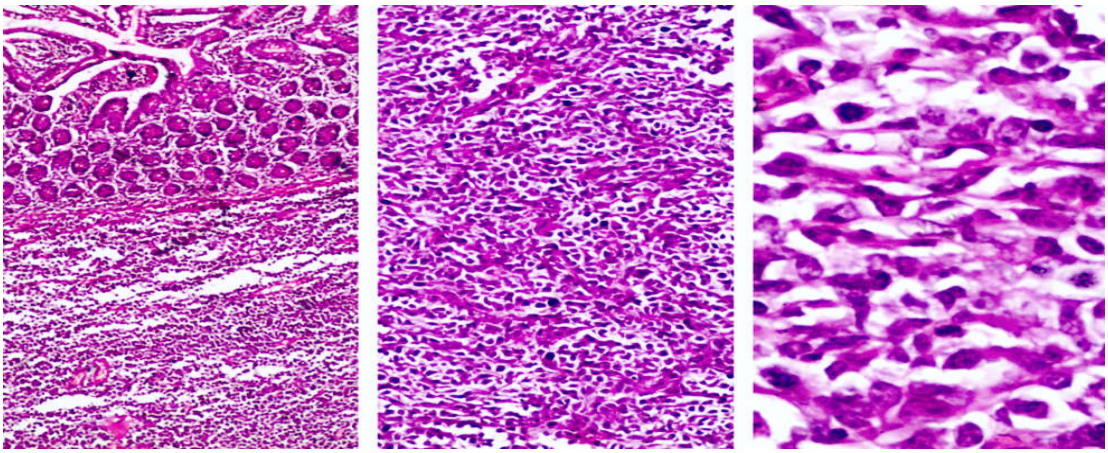
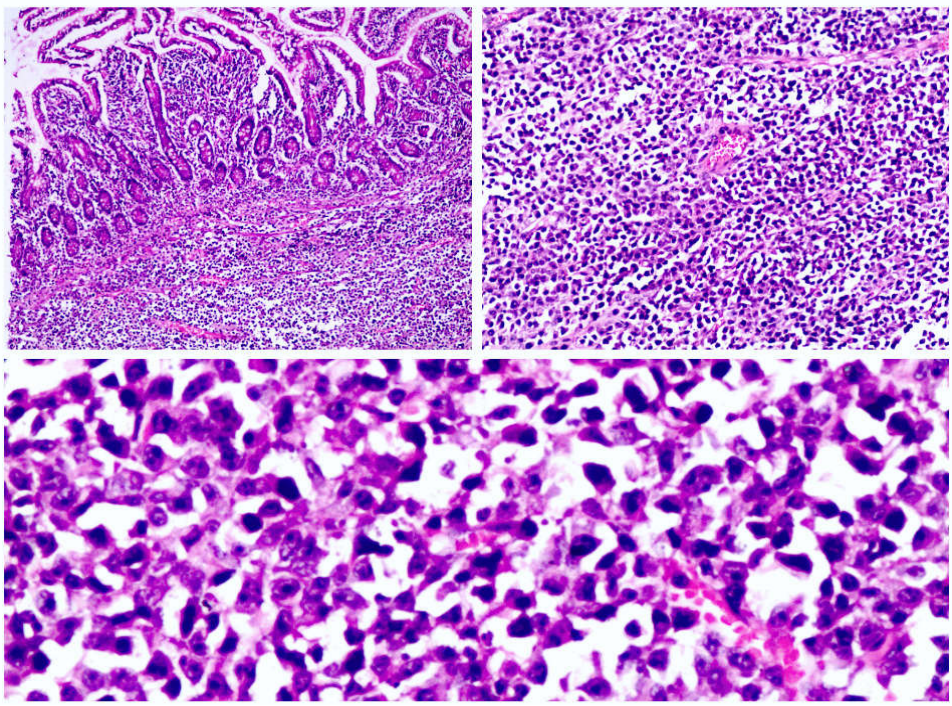



**Fig. 1:** Showing gross pictures of Lymphoma of small intestine **A:** External surface showing nodular appearance **B:** Cut section showing grayish white tumor mass involving the wall of intestine



**Microphotograph 1:** Microscopic images of Diffuse Large cell Lymphoma A:showing normal mucosa,with diffuse sheets of tumor cells in submucosa (H&E x4),B and C:showing large round to polygonal tumor cells with condensed nucleus with scant cytoplasm (H&E x10,x 40)



**Microphotograph 2:** Showing microscopic images of MALT lymphoma A: Showing normal mucosa with diffuse sheets of tumor cells B & C:Showing round tumor cells wuth condensed nucleus with scant cytoplasm( H&E 40X)

The youngest patient affected with small bowel lymphoma was 2years and oldest was 50years with a mean age of 32.4 years. Majority of the patients affected were males (80%) with male to female ratio of 4:1.

Ileum was the most common site (80%) involved in 4 cases followed by jejunum (20%) in one cases.

Grossly diffuse grayish white solid mass was seen in 3 cases, out of which one case showed focal grey white area, polypoidal in one case, nodular appearance in 2 cases and one case showed variegated appearance with solid and friable necrotic and ulcerated areas. On cut section the mass appears grayish white and homogenous in all the cases and necrosis was seen in only one case.

Microscopy showed normal mucosa in 3 cases and surface ulceration in 2 cases. The lamina propria and the submucosa showed complete replacement by diffuse monotonous sheets of tumor cells. The cells have normal round to oval shape appear polygonal and plasmacytoid in one case with scant cytoplasm and condensed hyperchromatic nucleus. The muscularis propria, subserosa and serosa show diffuse infiltration of these tumor cells. In one case tumor emboli was seen with in the lymphatics in submucosal layer. Associated mesenteric lymphadenopathy was seen in two out of five cases showing metastatic deposits of the primary tumor.

All the 5 cases were of B cell lymphoma out of which diffuse large B cell lymphoma type being the most common histological type seen in 4 cases(80%) and MALT lymphoma in one case(20%). DLBCL microscopically showed diffuse infiltrate of large lymphoid cells with oval to round nuclei, condensed chromatin, 1-2 nucleoli and MALT lymphoma showed diffuse infiltrate of small centrocyte like cells with lymphoepithelial lesions.

## Discussion

Gastrointestinal tract is one of the most frequent sites of extranodal malignant lymphoma, the occurrence of primary small intestinal lymphoma is relatively uncommon accounting for 15-20% of small bowel malignancies. In the present study of 40 intestinal resected specimens, 14 malignant tumors have been reported and out of which 5 cases were primary Non-Hodgkins lymphoma of small intestine.

The mean age of presentation in the present study was 32.5 years where as in studies by Yaranal PJ et al [2], Cardona DM et al[12], Yin L et al [13] and Tereda T et al [14] the mean age affected were high with 43yrs, 60years, 59years and 74 years respectively.

The sex ratio showed a highest incidence in male in our study but in studies of Cordona DM et al and Tereda T et al female predominance was seen.

In present study all the patients presented with abdominal pain and obstruction(100%) in accordance with the study done by Nakamura S et al(11) where abdominal pain was the presenting symptom in 78% and bowel obstruction was noted in 28.7%. Similar other studies by Yin L et al and Cordona DM et al also stated abdominal pain to be the most common presenting symptom.

**Table 5:** Showing Macro and micro scopic type of lymphoma in various studies

| Parameters | Cordona DM et al(12) | Yin L et al (13) | Nakamura S et al(11) | Present study |
|---|---|---|---|---|
| Most common site | - | Ileum | Ileum | Ileum |
| Ulcerative | 1.4% | - | 54% | 20% |
| Nodular | 86.7% | - | Not mentioned | 40% |
| Polypoidal | - | - | 25% | 20% |
| Diffuse | 8.4% | - | 6% | 60% |
| Most common histological type | DLBCL | DLBCL | DLBCL | DLBCL |

The ileum was the most common site affected in our study (80%) and one case had tumor mass in the duodenojejunal junction (20%). This was similar to findings in Yin L et al study where site distribution was ileum (58%), followed by jejunum (26.5%) and duodenum (17.6%).

In our study all the cases were of B-cell lineage and DLBCL(80%) was the commonest subtype followed by MALT lymphoma which was similar to the other reports[15,16]. Many studies have shown that intestinal lymphoma had poor survival than gastric lymphoma probably due to a higher proportion of aggressive lymphomas such as DLBCL seen in this area [17].

## Conclusion

Primary small intestinal lymphoma is a heterogenous entity with varied morphological features. High grade tumors are more common than low grade. Our data clearly demonstrates that most common primary site was ileum followed by jejunum. Most patients presented with abdominal pain followed by intestinal obstruction for which intestinal resection was done. Macroscopically majority showed diffuse growth and histologically DLBCL being the commonest subtype followed by MALT lymphoma. However large-scale prospective investigation of PSIL is difficult due to its low incidence and complicated histological subtypes and hence need for further multicenter prospective study to create a database large enough to rationalize the treatment of such patients.

*Ethical Clearance*

Taken from ethical committee VIMS Ballari

*Source of Funding*

From the department of pathology

*Conflict of Interest*

NIL

## References

1. Ojha A, Zacherl J, Scheuba C, Jakesz R, Wenzl E. Primary small bowel malignancies: single center results of three decades. J Clin Gastroenterol. 2000; 30: 289-93.
2. Yaranal PJ, Harish SG, Purushotham B. Primary intestinal lymphoma: A clinicopathological study. Indian J Cancer. 2016; 51(3): 306-08.
3. Weiss NS, Yang CP. Incidence of histological types of cancer of the small intestine. J Natl Cancer Inct. 1987; 78: 653-6.
4. Evers BM. Small intestine. 18th ed. In: Sabiston Textbook of surgery: The biological basis of modern surgical practice, Townsend CM Jr, Beauchamp RD, Evers BM, Mattox KL, eds. Philadelphia: Saunders Elsevier; 2008.
5. Arora N, Manipadam MT, Pulimood A, Ramakrishna BS, Chacko A, Kurian SS, et al. Gastrointestinal lymphomas: Pattern of distribution and histological types: 10years experience in a tertiary centre in south india. Indian J Pathol Microbiol. 2011; 54: 712-9.
6. Harris NL, Jaffe ES, Stein H, Banks PM, Chan JK, Cleary, et al. A revised European-American classification of lymphoid neoplasms: A proposal from the international lymphoma study group. Blood. 1994; 84: 1361-92.
7. Unassigned. A clinical evaluation of the international lymphoma study group classification of non Hodgkins lymphoma. The Non-Hodgkins lymphoma classification project. Blood. 1997; 89: 3909-18.

8. Cardona DM, Layne A, Lagoo AS. Lymphomas of the gastrointestinal tract- Pathophysiology, pathology and differential diagnosis. Indian J Pathol Microbiol. 2012; 55(1): 1-16.

9. Scott G Houghton, Antonio Ramos De la Medina, Michael G Sarr.Bowel obstruction. 11th ed.Chapter 17. In: Maingot'sAbdominal operations, Michael J Zinner, Stanley W Ashley, eds. New York: McGraw-Hill Medical; 2007.

10. Vallicelli C, Coccolini F, Catena F, Ansaloni F, Montori G, Salomone DS, et al. Small bowel emergency surgery:literature's review. World Journal of Emergency Surgery. 2011; 6(1): 1-8.

11. Nakamura S, Matsumoto T, Takeshita M, Kurahara K, Yao T, Tsuneyoshi M, et al. A clinicopathological study of primary small intestine lymphoma. Prognostic significance of Mucosa associated lymphoid tissue derived lymphoma. Cancer. 2000; 88(2): 286-94.

12. Diana M. Cardona, Amanda Layne, Anand S. Lagoo, Lymphomas of the gastro-intestinal tract – Pathophysiology, pathology, and differential diagnosis ; Review Article;Indian Journal of Pathology and Microbiology. 2012 January-March; 55(1): 1-16.

13. L Yin, Cq Chen, Ch Peng, Gm Chen, Hj Zhou, Bs Han And Hw Li ,Primary Small-bowel Non-Hodgkin's Lymphoma: a Study of Clinical Features,Pathology, Management and Prognosis ; The Journal of International Medical Research. 2007; 35: 406-415.

14. Tadashi Terada,Malignanttumors of the small intestine: A histopathologic study of 41 cases among 1,312 consecutive specimens of small intestine, Int J ClinExpPathol. 2012; 5(3): 203-209.

15. Wang GB, Xu GL, Luo GY, Shan HB, Li Y, Gao XY, et al. Primary intestinal Non-Hodgkins lymphoma:A clinicopathological analysis of 81 patients. World J Gastroenterol. 2011; 17: 4625-31.

16. Li B, Shi YK, He XH, Zou SM, Zhou SY, Dong M, et al. Primary non-Hodgkins lymphomas in the small and large intestine: Clinicopathological characterstics and management of 40 patients. Int J Hematol. 2008; 87: 375-81.

17. Koch P, del valle F, Berdel WE, Willich NA, Reers B, Hiddemann W, et al. Primary non-Hodgkins lymphoma: Anatomic and histologic distribution, clinical features and survival data of 371 patients registered in the German multicenter study GIT NHL 01/92. J Clin Oncol. 2001; 19: 3861-73.