



# International Journal of Surgery Science

E-ISSN: 2616-3470

P-ISSN: 2616-3462

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2022; 6(1): 21-23

Received: 16-11-2021

Accepted: 18-12-2021

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## Gastrointestinal stromal tumours: A single institution study

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**DOI:** <https://doi.org/10.33545/surgery.2022.v6.i1.a.812>

### Abstract

**Background and Objectives:** Gastrointestinal stromal tumours (GIST) are the most common mesenchymal tumours of the gastrointestinal tract arising from the interstitial cells of Cajal with an increasing incidence. It can occur anywhere from the esophagus to the anus. It has a few works of literature to its credit in India. Hence we conducted the study to evaluate the epidemiology, clinical and histopathological findings, management and survival pattern of gastrointestinal stromal tumours treated in our surgical setup.

**Methods and Methodology:** A retrospective cross-sectional study conducted at the department of general surgery/ surgical oncology between 2011 and 2016. Data were collected according to demographic characteristics, clinical pattern, investigations, treatment and therapeutic variable and was analysed and reviewed.

**Results:** On analysing, we found that among 32 patients diagnosed with GIST had a median age of 56.5 years and a sex ratio of 1.4:1. Non-specific abdominal pain was the most common symptom. 18 of the tumours was found in the stomach, 11 in the small bowel and 2 in the rectum and 1 in the colon. All were confirmed by the positivity of CD 117. All underwent surgical resection with adjuvant Imatinib. The overall survival was 71% in one year.

**Conclusion:** The size of the tumour and the mitotic index were identified as the prognostic factors. GISTs managed by aiming to complete surgical resection combined with targeted chemotherapy had a good prognosis.

**Keywords:** gastrointestinal stromal tumours, GIST, CD 117, prognostic factor

### Introduction

Gastrointestinal Stromal Tumour (GIST) is the most common mesenchymal tumours originating in the gastrointestinal tract. Approximately 5,000 new cases get diagnosed each year with an increasing prevalence <sup>[1]</sup>. It is a rare type of sarcoma accounting for less than 1% of all gastrointestinal tumors <sup>[2]</sup>. They can be benign or malignant in nature and forms a distinct histopathological group of intestinal neoplasms of mesenchymal origin. Historically, these lesions were classified as leiomyomas or leiomyosarcomas. They arise either from Interstitial cells of Cajal (ICC) or from less differentiated stem cells/precursor cells that can develop into ICC. These are primarily caused by gain-of-function mutations in *KIT* or platelet-derived growth factor receptor alpha (*PDGFRA*) genes with characteristic morphology <sup>[3]</sup>. The diagnosis of GIST is by histology but confirmed by immuno-histochemical (IHC) staining <sup>[4]</sup>. The most important IHC staining method is c-Kit (CD117). Others are CD 34, DOG1 (discovered on GIST). It can occur anywhere from the oesophagus to the anus. Most commonly occur in the stomach (60%) or small intestine (30%) and rarely in extra-gastrointestinal locations such as the omentum, mesentery, pelvis, rectum and retroperitoneum <sup>[5]</sup>. It can occur anywhere from the esophagus to the anus. GIST being uncommon has a few works of literature to its credit in India.

### Aims and Objectives

To evaluate the epidemiology, clinical and histopathological findings, management and survival pattern of gastrointestinal stromal tumours treated in our surgical setup.

### Methods and Methodology

A retrospective cross-sectional study was conducted of patients treated for GIST between 2011 and 2016. Institutional ethical clearance was sought before conducting this study.

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Data were collected according to demographic characteristics, clinical patterns, relevant investigations, intra-operative findings. All these cases were confirmed by the positivity of CD 117. These patients were followed up for about 1 year. Data were analysed using descriptive statistics, multivariate analyses,  $X^2$ -test, log-rank analyses, and cox regression models.

## Results

Among 32 patients who were diagnosed to have GIST, the median age was found to be 56.5yrs (range 32–79) (Fig 1). Out of which, 19 (59.38%) were male and 13 (40.62%) were female with the sex ratio of 1.4:1.

Non-specific abdominal pain or abdominal discomfort was the most common presentation followed by gastrointestinal bleed and vomiting (Fig. 1). The most common site of the tumour was found to be stomach with small intestine being next (Fig. 2). The mean tumour size was 10.9 cm (range 4–30 cms).

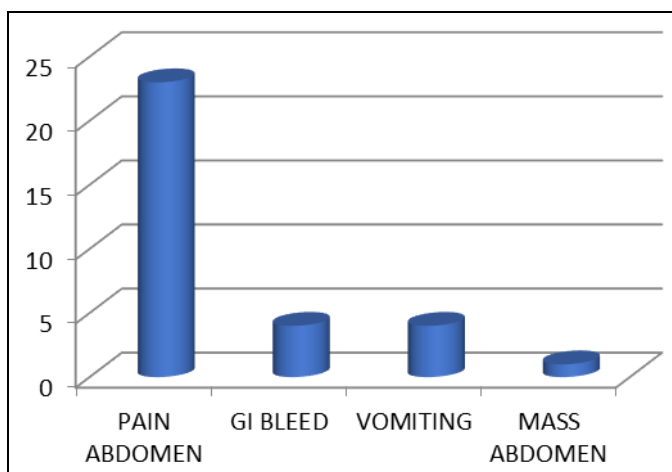


Fig 1: Clinical presentation

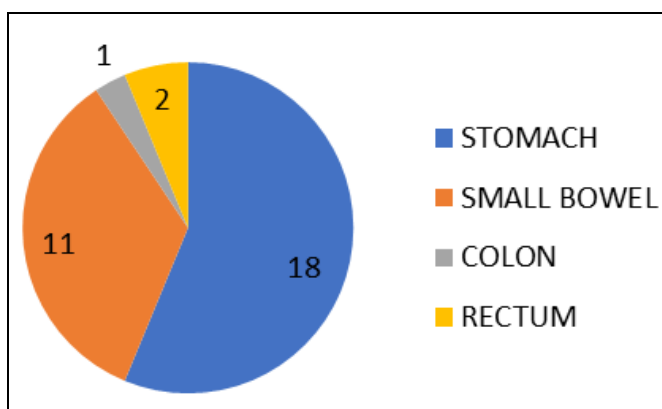


Fig 2: Site of tumour

All 32 patients underwent surgical resection. The specimen was sent for histopathological examination. All indicative cases were positive for CD 117. They were put on Imatinib 400mg once daily. These cases were followed up for 1 year and were found to have an overall disease-free survival of 71%. The recurrence was seen in 9 of the patients with larger tumour sizes with a high mitotic rate and it was in the form of hepatic and peritoneal recurrence.

## Discussion

Gastrointestinal Stromal Tumours represent the most common mesenchymal neoplasms of the GIT with an annual overall

incidence of 14.5 per million people and they form 0.1%-3.0% of gastrointestinal malignant tumours [6, 7]. Historically, GISTs were considered to be originating from smooth muscle and was named as 'gastric leiomyosarcomas'. But with the advent of electron microscopy and immune-histochemistry, it was demonstrated that they differ from leiomyosarcomas, and then termed it as GISTs [8]. They arise either from Interstitial cells of Cajal (ICC) or from less differentiated stem cells/precursor cells that can develop into ICC. They are primarily caused by gain-of-function mutations in *KIT* (80-85%) or platelet-derived growth factor receptor alpha (*PDGFRA*; 5%-7%) genes [3]. In our study, the mean age at diagnosis is 56.5 years, similar findings were observed in a study conducted by Lakshmiaiah *et al.* [2]. There is usually no predilection for either gender but some series suggest a slight male predominance [9] as was seen in our study too.

GISTs can develop anywhere along the Gastrointestinal tract from the esophagus to the rectum; however, stomach (60%) and small intestine (30%) are the most common locations for GIST. Only 10% of GISTs are found in the esophagus, mesentery, omentum, colon or rectum [5]. The most frequent clinical manifestations are occult gastrointestinal bleeding, fatigue due to anemia, anorexia, vomiting, dyspepsia, a palpable mass and mild abdominal pain [7]. GISTs with indolent (low-risk) behaviour are typically found as small submucosal lesions, [10] whereas 30% of GISTs exhibit high-risk (malignant) behaviour such as metastasis and infiltration [1]. The metastasis is predominantly intra-abdominal- peritoneal and liver metastasis. Lymph nodal invasion is rare [11].

Computed Tomography (CT) and Magnetic Resonance Imaging (MRI) are the most frequent diagnostic imaging studies for the detection and staging of a primary GIST. They demonstrate a mass lesion, organ invasion and distant metastases. [12] GISTs arise within muscularis propria of the stomach or intestinal wall with an exophytic growth pattern, which are exhibited as dominant masses outside the organ of origin. Dominant intramural and intraluminal masses are less common radiologic manifestations. Small tumours tend to appear homogeneous whereas larger tumours (>6 cm) show central areas of necrosis or hemorrhage. [13] Endoscopic ultrasound helps in identifying intramural masses, to evaluate whether mucosal ulceration is due to sarcoma or due to a non-stromal tumour, and also to assess pancreatic involvement if any [14]. All the patients underwent a CT scan of the abdomen and pelvis and most of them had exophytic growth from the organ of origin with necrosis and haemorrhage. The mean tumour size was 10.9 cm (range 4–30 cms), similar results were found in the study conducted by Lakshmiaiah *et al.* [2]. All the patients underwent complete surgical resection, which is the treatment of choice for localised GISTs.

The pathological diagnosis of GIST is mainly by histology. There are three different histologic subgroups; spindle cell GISTs (70%), epithelioid GISTs (20%) and the mixed type (10%) with spindle and epithelioid cells. But the diagnosis is confirmed by immune-histochemical (IHC) staining [4]. The most important IHC staining method is c-Kit (CD117), positive in 94-98% of cases. Others are CD 34, DOG1 (discovered on GIST). CD34 is positive in 60%-80% of all GISTs whereas DOG1 was reported to be positive in 85%-95% of c-Kit–positive GISTs and 30%-36% of c-Kit–negative GISTs [15]. Detection of *KIT* or *PDGFRA* mutation can also be used to diagnose GIST, even though they are negative for both c-Kit and DOG1. All 32 of our study cases were positive for CD117.

Generally, recurrences occurred in the liver and peritoneum within 2 years of surgery, before the introduction of adjuvant chemotherapy [16]. Hence adjuvant therapy was introduced in

patients predicted to have a moderate to high risk of recurrence, to reduce or delay the growth of microscopic tumours after complete resection of a GIST. Imatinib, a tyrosine kinase inhibitor (TKI) is widely used for this purpose. It is the treatment of choice for unresectable and/or metastatic GISTs. The disease-free survival period has been radically lengthened with the effective usage of Imatinib treatment, while conventional chemotherapy and radiotherapy are solely indicated to Imatinib-resistant cases, as adjuvant or palliative treatment after surgical resection of primary and recurrent GISTs [17]. All our patients were put on Imatinib 400 mg once daily and were followed up for 1 year and were found to have overall disease-free survival of 71%. The recurrence was seen in patients with larger tumour size with high mitotic rate and spillage /incomplete resection. Limitations of our study included the lack of long term follow up.

### Conclusion

The size of the tumour and the mitotic index were identified as the prognostic factors. GISTs managed by aiming complete surgical resection combined with targeted chemotherapy had a good prognosis.

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