

# A Multidisciplinary Team Approach in Gastrointestinal Stromal Tumour Management



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## Introduction

More than 90% of all cancers of the gastrointestinal (GI) tract arise from the epithelial cells, in contrast, gastrointestinal stromal tumors affect connective tissue of the GI tract. Gastrointestinal stromal tumors (GISTs) are rare tumours of the gastrointestinal tract arising from the mesenchyme (mesoderm). The actual cell of origin of GISTs is a pluripotent mesenchymal stem cell.[1]

Gastrointestinal stromal tumors express tyrosine kinase receptor – CD117 (KIT) and are KIT signaling driven mesenchymal tumors. Many GIST tumors have an activating mutation in either KIT or platelet-derived growth factor receptor alpha (PDGFR $\alpha$ ) [2]

The diagnosis and management of GISTs is challenging as most patients have non specific presentations and often present late in the disease. A variety of therapeutic options are available to manage GIST and the treatment has to be individualized to suit patient's needs. Hence a multidisciplinary team of physicians is essential to the successful treatment of GISTs. Evidence supports multi disciplinary team management with a gastroenterologist, surgeon, medical oncologist, pathologist and radiologist. The benefits of multidisciplinary disease management of patients include reducing recurrent disease, optimizing timing of surgery and organ preservation, prolonging survival for the patient and enhancing response to targeted therapies.



## Gastrointestinal stromal tumours

### Epidemiology [3–12]

GISTs account for 1-3% of all GI neoplasms. GISTs account for about 1-3% of gastric tumours, about 20% of small bowel tumours, and 1% or less of colorectal tumours. [1]

The population-based estimates (which count all cases in a defined region over time) vary between 9 per million to 19.6 per million in various studies. [3-9]

<b>Age</b>	<ul style="list-style-type: none"> <li>Commonly seen between the ages of 55 to 65 years</li> <li>May be seen in young adults</li> <li>Not common in children</li> </ul>
<b>Sex</b>	<ul style="list-style-type: none"> <li>A slight male preponderance is seen though many researchers have reported no sex predilection</li> </ul>
<b>Outcomes</b>	<ul style="list-style-type: none"> <li>Depend on the clinical presentation and the histopathological features of the tumour</li> <li>Long-term survival correlates inversely with tumor size and mitotic rate. Gastric GISTs carry a better prognosis than small bowel GISTs of similar size and mitotic rate. The 5-year overall survival rates for patients with GIST range from 28% to 45%.</li> </ul>

GISTs are the result of oncogenic mutations. Almost all GISTs are sporadic, i.e. mutations are random occurrences affecting a single individual.

- 85-90% of GISTs express KIT, a receptor tyrosine kinase encoded by protooncogene c-kit. In normal gastrointestinal wall, KIT is expressed by interstitial cells of Cajal (ICC), which are a pacemaker for autonomous gastrointestinal movement. GIST are considered to originate from ICC or their precursor cells.
  - Approximately 90% of the sporadic GIST have somatic gain-of-function mutations of the c-kit gene
  - Patients with familial and multiple GIST have germline gain-of-function mutations of the c-kit gene.
- About 3-5% of the remainder of KIT -negative GISTs contain platelet-derived growth factor receptor alpha (PDGFR  $\alpha$ ) mutations
- A few GISTs are normal or "wildtype" for both these genes
  - Mutations in the neurofibromatosis type 1 (NF1) gene, in NF1-associated GIST, B-Raf mutations and amplification of the insulin-like growth factor 1 receptor (IGF1R) may contribute to neoplastic transformation

### Pathology [15–17,101, 102, Fig 1]

<b>Site</b>	<ul style="list-style-type: none"> <li>Can occur in any part of the gastrointestinal tract. Seen in the oesophagus, stomach, duodenum, small intestines, colon, rectum, omentum and mesentery</li> </ul>
<b>Lesions</b>	<ul style="list-style-type: none"> <li>Usually Submucosal, grow parallel to the lumen.</li> <li>Typically solitary lesions, although in rare cases, multiple lesions can be found.</li> <li>The size may vary from 1cm to 40 cms</li> </ul>
<b>Spread</b>	<ul style="list-style-type: none"> <li>These tumors can grow intraluminally or extraluminally toward adjacent structures.</li> <li>Distant metastases tend to appear late in the course of the disease in most cases.</li> <li>The common metastatic sites of GISTs are the liver and peritoneum.</li> <li>Lymph node involvement is rare</li> </ul>

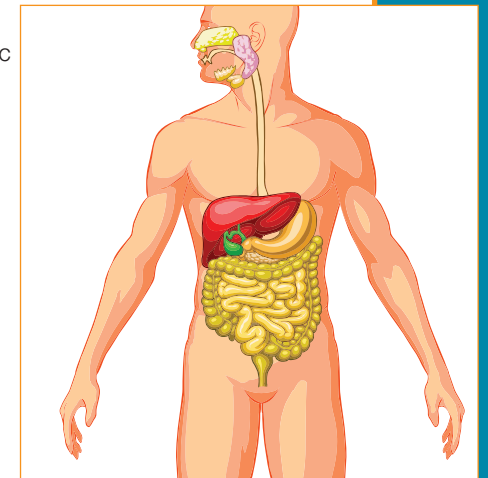
### Clinical features

The clinical picture varies from asymptomatic patients to abdominal pain and symptoms secondary to complications (Table 3).

#### Clinical presentations of GIST

- Asymptomatic
- Vague/ nonspecific abdominal pain
- Sense of satiety
- Abdominal fullness
- Abdominal mass
- Symptoms secondary to obstruction/ haemorrhage
  - GI bleeding - Malaise, fatigue, or exertional dyspnoea
  - Obstruction –
- Oesophageal GIST - Dysphagia
- Colorectal GIST - Constipation,
- Duodenal tumour- Obstructive jaundice

Clinical findings: Patients may not have any findings on clinical examination. Some of the patients present with findings related to hemorrhage, bowel obstruction or perforation. (Table 4).



**Fig.1:**  
**Sites of occurrence of GISTs [101]**