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Presentation, Biologic Behavior, and Short-Term Management Outcome of Gastrointestinal Stromal Tumors

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ABSTRACT: ***Background:*** The most common mesenchymal tumors of the gastrointestinal tract are called gastrointestinal stromal tumors (GISTs). They are thought to develop from the neoplastic transformation of intestinal pacemaker cells, which are often present in the intestine wall or their ancestors. One to three per cent of all GI neoplasms are GISTs. **Objectives:** To see the presentations, biological behaviour, and short-term management outcome of gastrointestinal stromal tumors. ***Methodology:*** The study is an observational study conducted from January to June 2018 in the Department of Surgery of Dhaka Medical College Hospital (DMCH), Bangabandhu Sheikh Mujib Medical University (BSMMU), Mitford Hospital, Suhrawardi Medical College Hospital, and BIRDEM. The study population includes patients admitted with GIST, and 30 respondents were interviewed through a structured questionnaire. ***Results:*** In the study, gastrointestinal stromal tumors (GISTs) commonly presented with generalized weakness (the most frequent symptom), followed by abdominal pain in 80% of cases. Other presentations included asymptomatic or incidentally diagnosed cases (50%), acute abdomen due to perforation (40%), upper GI bleeding (43.33%), palpable abdominal lump (36.67%), vomiting (23.33%), intestinal obstruction (10%), and per rectal bleeding (10%). The tumors varied in size, with eight cases ranging from 5 to 10 cm, and most tumors were larger than or equal to 10 cm. Risk assessment classified 13 cases as high risk and 7 as low risk. In terms of outcomes, 7 patients died, 43.33% lived with recurrent or metastatic disease, and 13.33% survived without recurrence or metastasis. Additionally, 6 patients were lost to follow-up after surgery. ***Conclusion:*** Common clinical features include anaemia, abdominal pain, upper gastrointestinal bleeding, palpable abdominal mass, and generalized weakness. The preferred treatment choices are immunotherapy and total resection from the surgical margins, with surgical resection being the most common approach.

Keywords: Gastrointestinal stromal tumor, short-term outcome, biologic behavior.

Article at a glance:
***Study Purpose*:** *To explore the clinical presentation, biological traits, and short-term treatment outcomes of gastrointestinal stromal tumors.*
Key findings: *Commonly present with generalized weakness, perforation, abdominal lump and pain. Immunotherapy with surgery is the common approach.*
Newer findings: *May present with GI bleeding and debulking surgery increase the mortality.*
Abbreviations: *GIST: Gastrointestinal Stromal Tumors, ICC: Interstitial Cells of Cajal.*

INTRODUCTION

A Gastrointestinal stromal tumor (GIST) is the most common malignant neoplasm of mesenchymal origin and a compelling clinical and biological model for the rational development of molecularly targeted agents.[1] Gastrointestinal stromal tumors (GIST) are malignant mesenchymal tumors deriving from lineage cells of interstitial cells of Cajal (ICC) with an annual incidence of approximately 135-155 per million individuals.[2] Most frequently observed locations are the stomach (60–65%), small intestine (20–35%), and rectum (3–5%).2 The mainstay of GIST therapy in the localized setting is surgery, whereby the main risk factors for relapse are tumor

size, mitotic index, non-gastric site, and tumor rupture.[2] The most common symptoms are vague upper abdominal pain (50-70%), gastrointestinal hemorrhage (20-50%), and palpable abdominal mass (8-10%) and acute abdomen (10%). Most GISTs are immunohistochemically positive for c-kit protein (CD 117 in 97% and CD34 in 70% of cases). GISTs express a heterogenous clinical course not easily predicted by standard pathological means. The most important prognostic factors are tumor size >5 cm, tumor necrosis, infiltration and metastasis to other sites (mainly liver 65%, peritoneal cavity 21%, rarely lymph node 6%), mitotic count > 1-5 per 10 high-powered fields (hpf) and proliferation index greater than 10% and most recently mutation in the c-kit gene.[3] During the past few decades, there has been reasonable debate on the nomenclature, cellular origin, diagnosis, and prognosis of GISTs. Because of the almost similar appearance by light microscopy, GISTs were previously identified as smooth muscle neoplasm, and most were classified as leiomyosarcoma.[4] With the advancement through immunohistochemistry and electron microscopy, it became evident that GISTs possibly have myogenic features (smooth muscle GIST), neural attributes (gastrointestinal autonomic nerve tumor), or characteristics of both muscle and nerve (mixed GIST), or may lack differentiation (GIST not otherwise specified). Several studies have attempted to describe the criteria to distinguish benign GIST from malignant GIST. It has been found that tumor size and mitotic rate are the strongest predictors.[5] The treatment of choice for GIST is surgical resection. All GISTs should be approached with the intention of performing complete en block removal (Ro Resection) of the tumor and surrounding tissue. Benign GIST has an excellent prognosis after primary surgical treatment, with over 90% 5-year survival.[6] While recurrent or malignant, it had until recently an inferior prognosis even after surgical resection, with a median survival of 12 months. The development of a tyrosine kinase inhibitor has changed the management of unresectable malignant cases. This new tyrosine kinase inhibitor, imatinib mesylate, which inhibits the c-kit receptor, has proved highly effective against GIST and has improved survival in metastatic GIST and preventing recurrence.[7]

MATERIALS AND METHODS

This is an observational study conducted for six months period from January to June 2018 in the Department of Surgery of Dhaka Medical College Hospital (DMCH), Bangabandhu Sheikh Mujib Medical University (BSMMU), Mitford Hospital, Suhrawardi Medical College Hospital, and BIRDEM. The study population includes patients admitted with GIST and 30 respondents were interviewed through structured questionnaire. Information has been collected from patients who gave consent and participated in the study willingly. The duration of data collection was approximately 6 (six) months. Data has been collected from history; sign symptoms, laboratory investigation, preoperative findings, and postoperative follow-up. Findings of observation have been recorded on the prescribed data collection form. After collection, data editing and clearing have been done manually and prepared for data entry and analysis by using MS Excel. Most of the data has been presented in percentages. Descriptive univariant analysis of socio-demographic characteristics (such as age, religion and marital status) has been analyzed and presented using percentages, pie charts, frequency tables, bar charts, and histograms. In addition, analyses of functional outcomes have been presented using measures of distribution like frequency distribution tables, central tendency (mean, median and mode), and dispersions (range and standard deviation). Following chapter discusses data analysis in detail.

RESULTS

The mean age was 53.71 (±7.52) years, the majority (36.67%) of the cases belonged to the age group over 55 followed by age group 40 – 55 that accounts for 30%. It is seen that 63% of the cases are male and the remaining 37% cases are female (Table 1). It has been found that generalized weakness is common in all cases followed by abdominal pain in 80% of cases. Asymptomatic/ incidentally diagnosed and acute abdomen due to perforation accounted for 50% and 40%, respectively, upper GI bleeding 43.33%, palpable abdominal lump 36.67%, vomiting 23.33%, intestinal obstruction 10%, per rectal bleeding 10% cases (Figure I). The majority of the cases had signs of anemia (73.33%) and abdominal tenderness (53.33%), dehydration and abdominal lump 36.67% each, 10% of jaundice and 13.33% cases of acute hemorrhage due to tumor rupture (Figure II). Heterogeneous mass with core necrosis and cystic degeneration 13 (43.33%) is the main result, followed by enhancement 12 (40%). Seven cases (23.33%) had liver metastases, five cases (16.67%), four cases (13.3%), three cases (10%), and

two cases (6.67%) had ascites, solid mass, lymph node metastases, and omentum involvement, respectively (Table 2). It is evident that stomach 16 (53.33%) was the most common site of the tumor followed by small intestine 09 (30%), colorectal tumor 3(10%) and mesentery tumor were located in 02 (6.67%) cases (Table 3). Among the 30 cases of GIST, the size of the tumor is volatile ranging from small to large as shown in Figure III. Majority of the tumors (13 out of 30) were greater than or equal to 10 cm followed by 08 cases of tumor sized between 5 cm and 10 cm. 06 cases were found to have tumor sized between 2 cm and 5 cm. Only 03 cases were found with tumor size less than or equal to 2 cm (Figure III). In terms of medical management, 1 (3.3%) had radiotherapy, while 29 (96.67%) received immunotherapy or targeted therapy. Five (16.67%) underwent debulking surgery, and 15 (50%) had surgical margins that were completely respectable (Table-3). The study has been conducted over only 06 months period, long term outcomes cannot be provided. It is shown that 07 (23.33%) patients died, 43.33% the cases are alive with recurrent or metastatic disease, 13.33% are alive without recurrence or metastasis and 06 patients are lost to follow-up after surgery and therefore the outcome cannot be justified for those cases Table 5.

Table 1: Demographic Characteristics of The Respondents

Variables	Number	Percentage
Age group		
Below 18	01	3.33
18-25	03	10.00
25-40	06	20.00
40-55	09	30.00
Over 55	11	36.67
Mean ±SD	53.71 (±7.52)	
Sex		
Male	19.00	63.33
Female	11.00	36.67

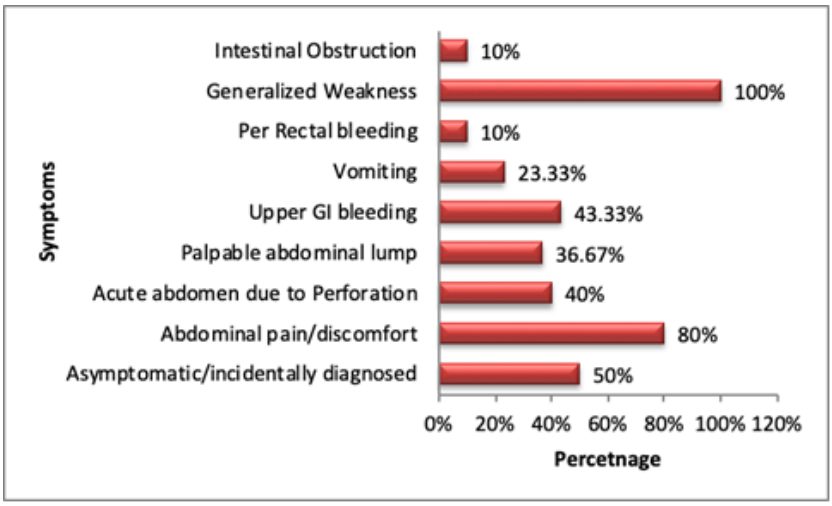

Figure 1: Symptoms of the Study Population (N=30)

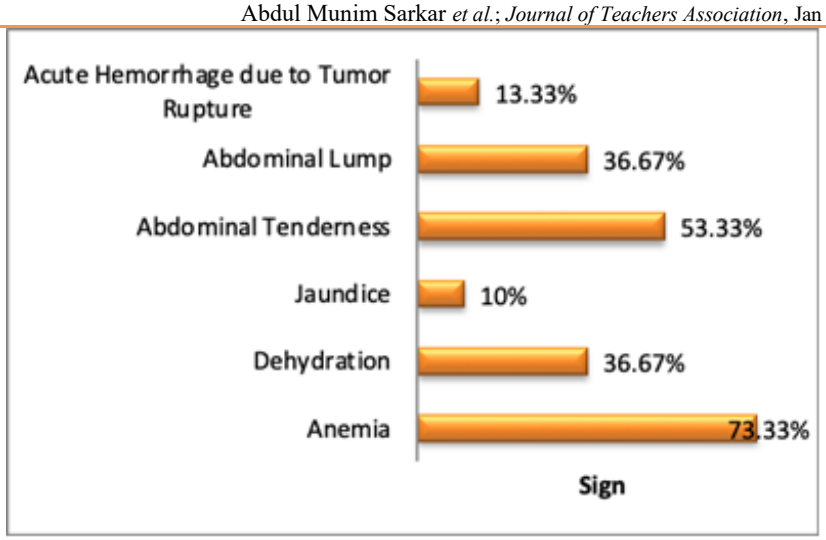

Figure 2: Signs of the Study Subjects

Table 2: CT scan Finding of the Study Subjects

Findings	Number	Percentage
Heterogeneous Mass with Central Necrosis & Cystic Degeneration	13	43.33%
Enhancement	12	40%
Liver Metastasis	07	23.33%
Ascites	05	16.67%
Lymph Node Metastasis	04	13.33%
Solid Mass	03	10%
Omental Involvement	02	6.67%

Table 3: Location/ Site of the Tumor

Location/Site	No of Cases	Percentage
Stomach	16	53.33%
Small Intestine	09	30.00%
Colorectal	03	10.00%
Mesentery	02	06.67%

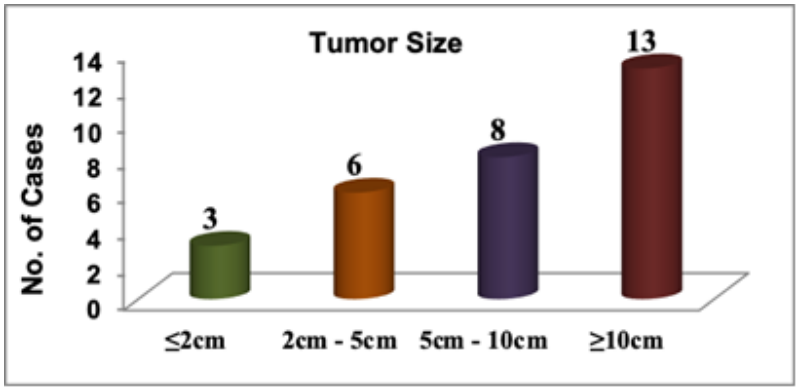

Figure 3: Size of the Tumor

Table 3: Management of the Respondent

	Number	Percentage
Medical Management		
Immunotherapy/ Targeted therapy	29	96.67%
Radiotherapy	1	3.33%

Surgical Management		
Completely resectable with Surgical Margin	15	50%
Laparoscopic resection	01	3.33%
Debulking surgery	05	16.67%

Table 4: Average Hospital Stay

Hospital Stay (in Days)	No. of Cases	Percentage
1-10	16	53.33%
11-20	06	20%
21-30	05	16.67%
More than 30	03	10%
Total	30	100%

Table 5: Short Term Outcome (within 6-month study period)

Outcome	Number	Percentage
Alive without recurrence/ metastasis	04	13.33%
Alive with recurrent/ metastatic disease	13	43.33%
Died	07	23.33%
Lost to follow up after surgery	06	20%
Total	30	100%

DISCUSSION

Before delving into the demographic profile and descriptive analysis of the 30 cases presented in previous chapters, it is evident that the presentation, biological behavior, and management of GISTs are primarily influenced by their nature following diagnosis. While the majority originate in the stomach, GISTs can develop anywhere along the gastrointestinal tract. The findings of this study are discussed in the context of prior research, incorporating both study objectives and observations from 30 cases over the past six months. This study found that the mean age of patients was 53.71 ± 7.52 years, with the majority (36.67%) over 55 years, followed by 30% in the 40–55 age group. Males accounted for 63% of cases, while females comprised 37%. These findings align with Al-Thani et al.[6] who reported a mean age of 48.4 ± 13.7 years and a male predominance (64.6%). Similarly, Parab *et al.*, observed a median age of 65 years (range: 10–100) with a 1:1 male-to-female ratio.[8] Data from an Italian study indicated a mean age of 60 years with equal gender distribution.[9] Sorour *et al.*, reported a mean diagnostic age of approximately 50 years, while Miettinen *et al.*, noted that GISTs are rare in individuals under 40 and exceptionally uncommon in children.[10, 11] These comparisons highlight the consistency of age-related trends in GIST presentation across different populations. Generalized weakness was the most common symptom, followed by abdominal pain in 80% of cases. Asymptomatic or incidental diagnoses accounted for 50%, while acute abdomen due to perforation was observed in 40%. Other clinical presentations included upper gastrointestinal bleeding (43.33%), palpable abdominal lump (36.67%), vomiting (23.33%), intestinal obstruction (10%), and per rectal bleeding (10%). The majority of cases exhibited signs of anemia (73.33%) and abdominal tenderness (53.33%). Dehydration and abdominal lumps were each present in 36.67% of cases, while jaundice was noted in 10%. Additionally, acute hemorrhage due to tumor rupture occurred in 13.33% of cases. Nearly half of the cases in the Egyptian study presented with gastrointestinal bleeding, followed by intestinal obstruction (30%), intraperitoneal hemorrhage (15%), and rupture with peritonitis (8%).[10] Abdominal pain was the most common symptom, affecting 85% of patients. Blood in stool and vomiting were reported in over half of the cases, while bowel obstruction was observed in fewer than 10%. Symptomatic patients often experience nonspecific symptoms such as nausea, vomiting, abdominal distension, early satiety, and abdominal pain, with a palpable mass being rare.[12-14] Larger tumors may obstruct the gastrointestinal lumen through endophytic growth or compress the GI tract via exophytic growth, leading to dysphagia, obstructive jaundice, or constipation, depending on tumor location. Perforated neoplasms typically

present with peritonitis or gastrointestinal bleeding, while intraperitoneal bleeding, whether indolent or massive, results from pressure necrosis and ulceration.[15, 16]

In this study, the stomach was the most common site of GISTs, found in 16 out of 30 cases, followed by the small intestine (9 cases). Colorectal tumors were observed in 3 cases, while mesenteric tumors were identified in 2 cases. Al-Thani *et al*. reported similar findings, with 56% of GISTs located in the stomach and 27% in the small bowel, while 18% (range: 5–40%) were discovered incidentally.[6] Other studies confirm the stomach as the most frequent site (56%), followed by the small bowel (32%), colon and rectum (6%), esophagus (0.7%), and other locations (5.5%).[12] A Jordanian study reported gastric GISTs in 41% of cases, while more than half of the cases in Saudi Arabian and Egyptian studies were also of gastric origin.[10-13] Notably, 20% of GIST patients in the Saudi Arabian study had tumors in the small bowel.[13] Between 10% and 30% of GISTs progress to malignancy, with non-gastric tumors demonstrating a higher malignant potential.[13] Exophytic growth is the most common pattern (79%), while intraluminal or mixed growth occurs less frequently.[17] In this study, most tumors (13 out of 30) were ≥10 cm, followed by 8 cases between 5–10 cm, 6 cases between 2–5 cm, and 3 cases ≤2 cm. Tumor size is crucial in the progression of the disease. The Chinese epidemiological study recorded mean diameter of 5.78 cm (0.3e25 cm).[18-20] An Egyptian study on gastric stromal tumors which included 16 GIST patients reported tumor sizes between 8.4 and 20 cm.[17] In the present study, the median tumor size was 8 cm ranging from 0.4 to 18 cm. H. Al-Thani *et al.*, study also shows 62% of the cases are with tumor size greater than 5 cm. GIST risk stratification systems are mainly based on tumor size that leads to assessment of the malignancy.[6] The study has been conducted over only 06 months period, long term outcome cannot be provided. It is shown that 07 (23.33%) patients died, 43.33% the cases are alive with recurrent or metastatic disease, and 13.33% are alive without recurrence or metastasis and 06 patients are lost to follow up after surgery and therefore the outcome cannot be justified for those cases. Al-Thani *et al.* alive without recurrence/metastasis 33 (68.5%), alive with recurrent/metastatic disease 7 (15%), died 2 (4%), lost to follow up after surgery 6 (12.5%).[6] Parab *et al*., Twenty-eight (49%) patients underwent surgical open laparotomy with resection with curative intent and the other 29 (51%) were treated post- surgically with imatinib for metastatic disease (n=26) or adjuvant therapy (n=3).[8] Seventy-nine percent (n=22) of the curative intent group had completely negative margins. Three patients had metastases that were completely resected with the tumor and two patients had successful resection after neoadjuvant imatinib therapy

CONCLUSION

Patients with GIST frequently exhibit acute abdomen from perforation, upper gastrointestinal bleeding, and a palpable abdominal mass, often accompanied by generalized weakness. Anemia, abdominal pain, and abdominal lumps are prevalent among cases. Gastric GIST is the most common, and affected patients tend to have shorter hospital stays. Surgical resection with clear margins remains the gold standard for treatment, with immunotherapy considered a beneficial adjunct.

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Conflict of interest: The authors have no conflicts of interest to disclose.

Ethical Approval

The study received ethical approval from the Ethical Review Committee of Dhaka Medical College, Dhaka. Informed consent was obtained from all participants, and all procedures followed relevant ethical guidelines and regulations.

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