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Original Research Article

Clinico-Histopathological Characteristics and Immunohistochemical Analysis of Gastrointestinal Stromal Tumors: A Single Institution Experience

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Conflict of interest: Nil

Abstract:

Background: Gastrointestinal stromal tumors (GISTs) are the most common mesenchymal neoplasms of the gastrointestinal tract (GIT), originating from the interstitial cells of Cajal, which act as pacemaker cells in the muscularis propria. They are frequently associated with gain-of-function mutations in the KIT or PDGFRA genes, resulting in constitutive activation of receptor tyrosine kinases.

Objective: This study aims to evaluate the clinico-histopathological features of GIST variants with a focus on tumour size, site of origin, mitotic index, and immunohistochemical expression of CD117 and DOG-1.

Methods: A retrospective analysis was conducted on 12 Indian patients diagnosed with GIST at FAAMCH, Barpeta, between 2022 and 2024. Clinical data including age, gender, tumour site, and size were recorded. Histopathological examination and immunohistochemistry for CD117, DOG-1, S-100, Desmin, and SMA were performed.

Results: The stomach was the most frequent site of GISTs (41.67%), followed by the colon (33.33%). The spindle-cell variant was the most prevalent histological subtype (7/12 cases). All cases showed diffuse positivity for CD117 and DOG-1, with negative staining for S-100, Desmin, and SMA.

Conclusion: The immunoprofile supports the diagnosis of GIST, with the majority showing classical features. Observed differences from global data may reflect genetic or ethnic variations in the Indian population, highlighting the need for further multicentric studies to refine diagnostic and therapeutic strategies.

Keywords: Gastrointestinal stromal tumour, CD117, DOG-1, Spindle cell variant, Immunohistochemistry.

Introduction

Gastrointestinal stromal tumors (GISTs) are the most common mesenchymal neoplasms of the gastrointestinal tract, primarily driven by gain-of-function mutations in the KIT or PDGFRA receptor tyrosine kinases. These mutations are present in approximately 80% and 8-10% of GISTs respectively, making them essential diagnostic markers [1]. The development of targeted therapies based on molecular understanding has significantly improved patient outcomes [2]. Mesenchymal tumors constitute approximately 1% of all primary gastrointestinal tumors, with GISTs being the most prevalent [3]. These non-epithelial tumors arise from the interstitial cells of Cajal—specialized pacemaker cells located within the muscularis propria of the gastrointestinal wall [4]. GISTs most commonly occur in the stomach (approximately 60%), followed by the small intestine (35%) [5]. Colonic and rectal GISTs are less frequent, comprising about 5% of cases, with higher occurrence in the rectum [6,7]. Key pathological parameters include tumor size, anatomical site, mitotic index, histological pattern, and immunohistochemical profile. Histologically, GISTs are classified into spindle cell (70%), epithelioid (20%), or mixed types (10%). Immunohistochemically, CD117 (c-KIT) and DOG-1 expression serve as key diagnostic markers [8]. The spindle cell type

includes various subtypes such as sclerosing, palisaded-vacuolated, hypercellular, and sarcomatoid variants [9,10].

The incidence and histopathological spectrum of GISTs in the Indian population are not well-documented, with current treatment approaches largely based on Western studies [8]. Therefore, region-specific studies are essential to understand potential ethnic or genetic variations that could influence disease presentation and management. This study aims to analyze the clinical and histopathological spectrum of GISTs using conventional and immunohistochemical techniques, and to classify the tumors based on their histomorphological features in an Indian population.

Methodology

A retrospective, observational study was conducted from 2022 to 2024 in the Department of Pathology, Fakhruddin Ali Ahmed Medical College, and Barpeta, Assam, to analyze the clinico-histopathological characteristics of Indian patients histopathologically diagnosed with gastrointestinal stromal tumors. The study was approved by the Institutional Ethics Committee of FAAMCH, Barpeta, Assam, prior to data collection.

Number of patients: 12

Inclusion Criteria: All histologically confirmed cases of GIST with complete demographic details including age, sex, and tumor site were included. Cases were required to have complete immunohistochemistry results for CD117 and DOG-1, along with adequate tissue for histopathological evaluation.

Exclusion Criteria: Patients who did not provide informed consent for use of clinical data were excluded from the study. Cases with incomplete demographic of immuno-histochemical data, as well as those with inadequate tissue for evaluation, were also excluded.

Sample Processing and Analysis: Tissue specimens received in the pathology department were fixed in 10% neutral buffered formalin, processed routinely, sectioned at 4μm thickness, and stained with hematoxylin and eosin (H&E). Clinical details such as age, gender, tumor location, and size were recorded from medical records and relevant radiological investigations

Immunohistochemistry was performed using CD117 (c-KIT) and DOG-1 as primary markers, while S-100, Desmin, and SMA were used as exclusionary markers when required for differential diagnosis. Standard immunohistochemical protocols were followed with appropriate positive and negative controls.

Risk assessment was performed using the Armed Forces Institute of Pathology (AFIP) criteria based on tumor size, anatomical location, and mitotic rate per 50 high-power fields.

Statistical Analysis: Data were compiled using Microsoft Excel and analyzed using the Statistical Package for the Social Sciences (SPSS for Windows, version 21.0; Chicago, SPSS Inc.). Results were presented as frequencies and percentages in tabular format.

Results

Demographic Characteristics: The study included 12 patients with histologically confirmed GIST. The age range was 31-75 years, with a peak incidence in the 46-60 years age group (8/12 cases, 66.67%). A significant male predominance was observed with a male-to-female ratio of 3:1 (9 males, 3 females).

Anatomical Distribution: The stomach was the most common site of GIST occurrence (5/12 cases, 41.67%), followed by colon (4/12 cases, 33.33%) and small intestine (3/12 cases, 25%). No rectal GISTs were identified in this study.

Histopathological Characteristics

Morphologically, the spindle cell variant was most prevalent (7/12 cases, 58.33%), followed by mixed spindle and epithelioid type (5/12 cases, 41.67%). No purely epithelioid variants were identified in this cohort.

Table 1: Age and Gender Distribution

Age Group (years)	Male	Female	Total	Percentage
0-15	0	0	0	0%
16-30	0	0	0	0%
31-45	1	1	2	16.67%
46-60	7	1	8	66.67%
61-75	1	1	2	16.67%
Total	**9**	**3**	**12**	**100%**

Table 2: Anatomical Distribution of GISTs

Tumor Site	Number of Cases	Percentage

Stomach	5	41.67%
Small intestine	3	25%
Colon	4	33.33%
Rectum	0	0%
Total	**12**	**100%**

Table 3: Histopathological Distribution

Histological Type	Number of Cases	Percentage
Spindle cell type	7	58.33%
Epithelioid type	0	0%
Mixed type	5	41.67%
Total	**12**	**100%**

Risk Stratification: Based on AFIP criteria considering tumor size, site, and mitotic activity, risk stratification revealed that 6 cases (50%) showed low malignant potential, 2 cases (16.67%) demonstrated moderate malignant potential, and 4 cases (33.33%) exhibited high malignant potential.

Immunohistochemical Profile: All 12 cases (100%) demonstrated consistent and diffuse positivity for both CD117 and DOG-1.

Negative staining was observed for S-100, Desmin, and SMA in all cases, supporting the diagnosis of GIST and excluding other mesenchymal tumors.

Table 4: Risk Stratification by AFIP Criteria

Site/Size/Mitotic Rate	Gastric GISTs	Colonic GISTs	Small Intestine GISTs
Low Risk			
>2≤5cm, ≤5/50HPFs	0	2	1
>5≤10cm, ≤5/50HPFs	3	0	0
Moderate Risk			
>10cm, ≤5/50HPFs	1	0	0
>5≤10cm, ≤5/50HPFs	0	0	1
High Risk			
>5≤10cm, >5/50HPFs	0	1	1
>10cm, >5/50HPFs	1	0	0
>5≤10cm, >5/50HPFs	0	1	0

Table 5: Immunohistochemical Expression Profile

IHC Marker	Positive Cases	Negative Cases	Percentage Positive
CD117	12	0	100%
DOG-1	12	0	100%
S-100	0	12	0%
Desmin	0	12	0%
SMA	0	12	0%

Case Example 1: A 65-year-old female presented with complaints of abdominal pain, nausea, and vomiting.

Radiological Findings:

Ultrasonography (USG) revealed a hypoechoic lesion with multiple cystic spaces, measuring approximately 92 × 62 mm in the epigastric region, along with minimal pelvic ascites.

Contrast-enhanced CT (CECT) demonstrated a well-defined, midline, heterogeneously enhancing soft tissue mass measuring approximately 77 × 63 × 97.2 mm. The lesion was located in the gastrohepatic region, between the left lobe of the liver and the lesser curvature of the stomach. These findings were suggestive of a gastrointestinal stromal tumor (GIST) of gastric origin.

Gross Examination: The excised specimen measured 10.2 × 6.3 × 4.0 cm (Figure 1). On cut section, the tumor displayed partially cystic and partially solid areas (Figure 2).

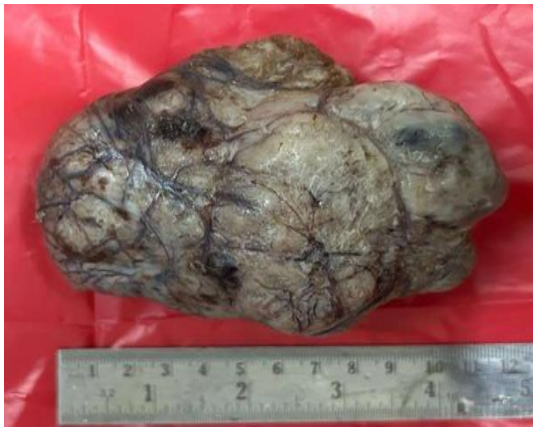

Figure 1: Gross Picture of the Specimen

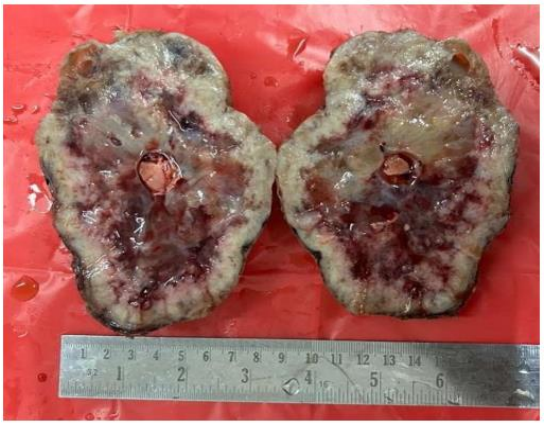

Figure 2: On cut section of the Specimen

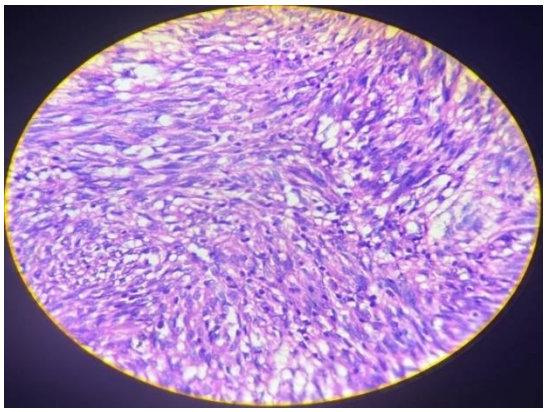

Figure 3: Microscopic Examination (40X)

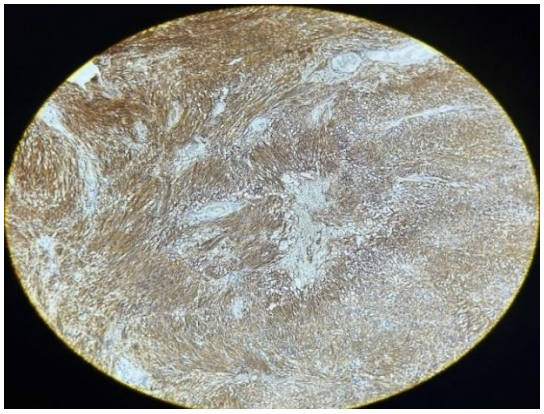

Figure 4: IHC with CD117 Positivity

Microscopic Examination: Histological sections from the tumor revealed interlacing bundles and fascicles of spindle-shaped cells with elongated, blunt-ended nuclei and moderate eosinophilic cytoplasm (Figure 3). Nuclear pleomorphism and mitotic activity were minimal.

Immunohistochemistry (IHC): The tumour cells exhibited diffuse and strong positivity for CD117 (c-KIT) and DOG-1, confirming the diagnosis of GIST. IHC staining was negative for S-100, Desmin, and SMA, thereby excluding neural and smooth muscle differentiation (Figure 4).

Case Example 2: A 74-year-old male presented with abdominal discomfort, loss of appetite, and unintentional weight loss.

Radiological Findings: Imaging revealed a large, partly solid and partly cystic/necrotic lesion measuring approximately 173 × 122 × 90 mm, located in the region of the pancreatic tail and extending toward the greater curvature of the stomach. The radiological impression was suggestive of a large gastrointestinal stromal tumour (GIST) likely of gastric origin.

Figure 5: Gross Picture of the Specimen

Figure 6: On Cut Section of the Specimen

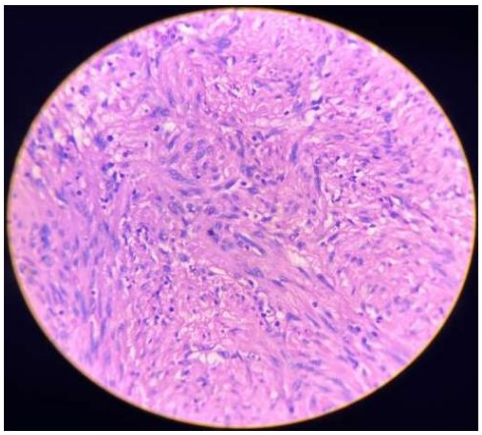

Figure 7.1: Microscopic Examination (40X)

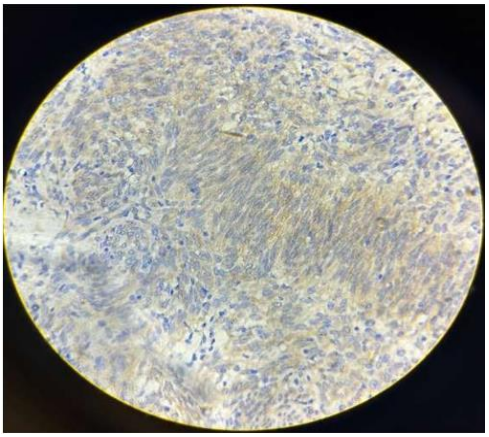

Figure-7.2: IHC with DOG-1showing Positivity

Gross Examination: The excised mass measured 15 × 12 × 7 cm (Figure 6.1). On cut section, the tumour showed solid and cystic components with areas of haemorrhage and necrosis (Figure 6).

Microscopic Examination: Histopathology showed interlacing bundles of spindle-shaped cells with elongated, blunt-ended nuclei and eosinophilic cytoplasm. There were large areas of necrosis and hemorrhage, and the tumor exhibited increased mitotic activity (Figure 7.1).

Immunohistochemistry (IHC): The tumor cells showed strong diffuse positivity for CD117 (c-KIT) and DOG-1, consistent with a diagnosis of GIST. Staining for S-100, Desmin, and SMA was negative, excluding neural or smooth muscle differentiation (Figure 7.2).

Case Example 3: A 54-year-old male was clinically diagnosed with a growth in the proximal terminal ileum.

Gross Examination: The excised mass measured 9 × 7 × 5 cm^3 (Figure 8.1). On cut section, the tumour appeared solid with focal areas suggestive of necrosis (Figure 8.2).

Microscopic Examination: Histological evaluation revealed tumour cells arranged in sheets, with focal areas of necrosis. The predominant cells were epithelioid, round to oval in shape, with moderate eosinophilic cytoplasm. In some areas, fascicles of spindle cells with blunt-ended nuclei were also observed. The tumour showed high mitotic activity, with more than 50 mitoses per 5 mm^2, suggesting a high-grade malignancy.

Figure-8.1: Gross Picture of the Specimen

Figure-8.2: On Cut Section of the Specimen

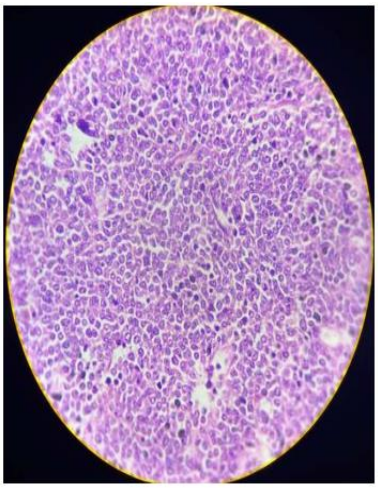

Figure-9.1: Microscopic Examination Area of Epitheliod Type Cell (40x)

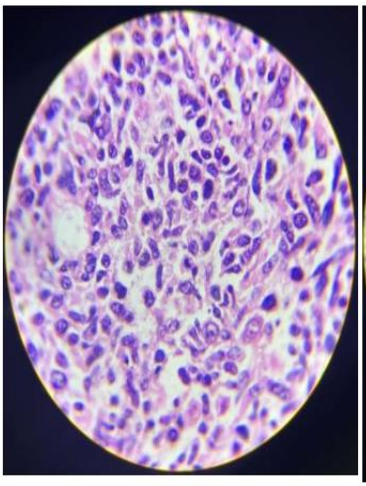

Figure-9.2: Microscopic Examination Mixed Type with Mitotic Figures (100x)

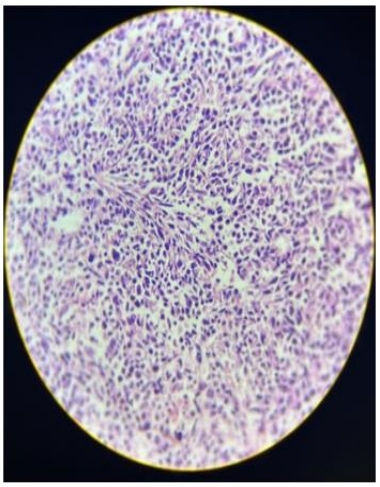

Figure-9.3: Microscopic Examination Epitheliod Type Cells With Focal

Discussion

This retrospective study analyzed 12 cases of gastrointestinal stromal tumors diagnosed at our institution between 2022 and 2024. The demographic profile showed a mean age of 59.08 years with peak incidence in the 50–65 years age group, consistent with previous studies [11]. The clear male predominance (3:1 ratio) aligns with findings by Enodéan B and Hendie D [12].

Present study revealed the stomach as the most common site (41.67%), followed by small intestine (25%), which is consistent with global literature. However, a notable finding was the high frequency of colonic GISTs (33.33%) compared to the typically reported 5-10% [6,7]. This significant discrepancy may be attributed to ethnic or regional genetic differences within the Indian population, a potential rising trend in colonic GIST incidence, or selection bias due to referral patterns. This finding warrants larger population-based studies for validation and could have implications for screening strategies in the Indian subcontinent.

The predominance of spindle cell variant (58.33%) is consistent with global literature and previous Indian studies [8,12]. However, the proportion of mixed spindle-epithelioid cases (41.67%) was higher than typically reported, potentially indicating genetic diversity in our population.

The distribution of risk categories (50% low-risk, 16.67% intermediate-risk, 33.33% high-risk) reflects the referral pattern to our tertiary center, with a tendency toward more advanced cases. The mitotic index proved valuable for risk stratification, with 75% of cases showing <5/50 HPF and 25% showing ≥5/50 HPF.

The universal positivity for CD117 and DOG-1 in our cohort confirms their reliability as diagnostic markers, consistent with studies by Lakshmaiah KC et al. [13] and Lopes LF et al. [14]. The complete absence of S-100, Desmin, and SMA positivity supports the diagnostic specificity of our immunohistochemical panel [15].

Clinical Implications

The study highlights several important clinical considerations for GIST diagnosis and management in the Indian population. The universal positivity for CD117 and DOG-1 in our cohort supports their continued use as primary diagnostic markers for GIST, with 100% concordance reinforcing their reliability in clinical practice. The higher frequency of colonic GISTs observed in our study (33.33%) compared to global literature (5-10%) may necessitate adjusted surveillance strategies and heightened clinical suspicion for GIST in colonic masses within the Indian population.

The AFIP risk stratification criteria remain applicable and valuable for prognostic assessment in our population, supporting their continued use in clinical decision-making. These findings emphasize the importance of comprehensive immunohistochemical evaluation in suspected mesenchymal tumors and highlight potential regional variations that may influence diagnostic approaches.

Limitations

This study has several limitations that should be considered when interpreting the results. The relatively small sample size of 12 cases limits the statistical power and generalizability of our findings. The retrospective design introduces potential selection bias, as cases were identified from a single tertiary care center which may not be representative of the general population. Additionally, the lack of molecular genetic analysis limits our understanding of the underlying genetic mechanisms that may contribute to

the observed regional variations. Long-term follow-up data were not available, precluding survival analysis and assessment of treatment outcomes.

Future Research Directions

Based on our findings, several research priorities emerge for advancing GIST research in the Indian population. Large-scale, multicentric prospective studies are essential to validate the higher frequency of colonic GISTs observed in our cohort and to determine whether this represents a true regional variation or a sampling artifact. Molecular genetic analysis, including KIT and PDGFRA mutation profiling, should be incorporated to investigate potential genetic factors contributing to regional variations in GIST presentation. Long-term follow-up studies are needed to assess treatment outcomes, survival patterns, and factors affecting prognosis in the Indian population. Additionally, population-based epidemiological studies could provide valuable insights into the true incidence and characteristics of GISTs across different regions of India, potentially informing targeted screening and diagnostic strategies.

Conclusion

This study provides valuable insights into the clinico-histopathological characteristics of GISTs in the Indian population. While most features align with global literature, the significantly higher frequency of colonic GISTs (33.33% vs. typical 5-10%) and increased mixed histological patterns represent important findings that may reflect genetic or ethnic variations specific to this population. The universal positivity for CD117 and DOG-1 in our cohort confirms their diagnostic utility and reliability as primary diagnostic markers, while the complete absence of other mesenchymal markers supports their diagnostic specificity. The predominance of spindle cell morphology and the applicability of AFIP risk stratification criteria are consistent with international studies. These findings contribute significantly to understanding GIST characteristics in the Indian context and highlight important regional variations that may warrant adjusted diagnostic and surveillance strategies. The results emphasize the need for larger, multicentric studies to validate these observations and potentially develop region-specific diagnostic and therapeutic approaches tailored to the Indian population.

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