ORIGINAL RESEARCH

Clinico pathological features and outcomes of gist: A five year retrospective data from a tertiary cancer care centre in south India

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ABSTRACT

Background and aims: Gastrointestinal stromal tumours (GISTs) are the most common mesenchymal neoplasms that arise in the gastrointestinal tract.They constitute about 0.1-3% of all GI tumours. Annual incidence is 1.2 per 10^5 individuals. Surgery remains the main stay of treatment. The use of adjuvant TKI Imatinib mesylate for 3 years reduce the frequency of disease recurrencefollowing complete resection.Five year survival for all stages combined is upto 83%.Here we present a five year retrospective data on the clinicopathological features and outcomes of GIST from a tertiary cancer care centre in south India.

Methods: This retrospective study was conducted in a tertiary cancer care centre in South India.Medical records of all consecutive patients with biopsy and IHC (Immunohistochemistry) proven GIST cases from January 2017 to December 2021 were collected, reviewed and analysed .

Results: 38 cases of biopsy and IHC proven GISTs were analysed. Median age was 54 years. 20 were males and 18 were females .The most common primary site was stomach(45%) followed by small intestine(39%).Majority of the patients were stage III at presentation (53%). 26 of cases were metastatic at presentation. Primary surgery was offered in 55% of the patients.68% of the patients received adjuvant treatment with Imatinib. 83 % of patients (10/12) who completed 3 years of adjuvant treatment remained disease free and 82% of all patients (31/38) are alive at the time of analysis. There was no progression in stage IV GISTs treated with Imatinib. 31% of patients developed GI toxicity with imatinib. Recurrence was seen in only 4 patients (14%) who received adjuvant TKI (Tyrosine kinase inhibitors). Common sites of recurrence was liver (50%) and omental and peritoneal secondaries.(50%).Progression on second line therapy with Sunitinib was seen only in one case of recurrent GIST.

Conclusion: Adjuvant Imatinib is efficacious and is well tolerated by our population.83% of the patients who completed adjuvant therapy are disease free at 2 years.5 year survival rate is about 82%.There is no grade 3 or 4 toxicity with Imatinib.

Key words: GIST, Pathology, TKIs, recurrence pattern

INTRODUCTION

Gastrointestinal stromal tumours (GISTs) are the most common mesenchymal neoplasms that arise in the gastrointestinal tract.[1] They constitute about 0.1-3% of all GI tumours. Annual

incidence is 1.2 per 10^5 individuals. [2] Most common sites include stomach (70%) followed by the small intestine (20-25%), colon and rectum (5%), and esophagus (< 5%) [3].
Molecular pathology lies in the activation of CKIT proto-oncogene.CD117 is an epitope that is expressed on the extra cellular domain of KIT receptor which helps in the diagnosis of GIST by IHC (Immunohistochemistry). CKIT is positive in 90% of cases and the remaining are considered as wild type GIST. [4]
Risk stratification is based on NIH-Flechter criteria which is different for different sites of the tumour. Surgery remains the main stay of treatment. The use of adjuvant TKI (Tyrosine kinase inhibitors) Imatinib mesylate for 3 years reduce the frequency of disease recurrence following complete resection.[5] Recent data recommends the use of adjuvant Imatinib for 5 years in patients with high risk of recurrence[6] . Second line treatment options include sunitinib and dasatinib. Avapritinib is used in PDGFRA (Platelet derived growth factor alpha) exon 18 and D842V mutation. Further lines of treatment include regorafenib, repretinib,cabozatinib etc.5 year survival for all stages combined is upto 83%.[7] Further increase in survival is expected with the use of risk adapted treatment approach at molecular levels.

MATERIALS AND METHODS:

This retrospective study was conducted in a tertiary cancer care centre in South India. Medical records of all consecutive adult patients with biopsy and IHC proven GIST cases from January 2017 to January 2022 were reviewed and relevant data were collected, reviewed and analysed .

RESULTS

38 cases of biopsy and IHC proven GISTs were analysed. Median age was 54 years (**Table 1)**. 20 were males and 18 were females. Abdominal pain was the most common presenting complaint (55%) followed by obstruction (21%) and bleeding (13%). Systemic symptoms like weight loss and fever was present in 10% of the individuals **(Table 2)**.
The most common primary site was stomach (45%) followed by small intestine (39%). Mesenteric GIST was seen in 11 % of the patients. 1 case of rectal GIST (3%) and 1 case of anal canal GIST (3%) were also present **(Table 3)(Figure 1)**.
The most common histology was spindle cell type (45%) followed by epithelioid type (18%). Mixed histology was found in 13% of the individuals and the remaining was unknown **(Table 4)**.
Majority of the patients were stage III at presentation (53%). 26% of cases were metastatic at presentation **(Table 5)**.
Primary surgery was offered in 55% of the patients. 4 cases (10%) received neoadjuvant TKI. 68% of the patients received adjuvant treatment with Imatinib. 46% of the patients completed the planned 3 years of adjuvant Imatinib at the time of analysis and remaining are continuing adjuvant treatment.
83 % of patients (10/12) who completed 3 years of adjuvant treatment remained disease free and 82% of all patients (31/38) are alive at the time of analysis. There was no progression in stage IV GISTs treated with Imatinib.
31% of patients developed GI toxicity with imatinib. Grade 1 and 2 GI toxicity was seen in 28% of the patients. Neutropenia (grade2) and thrombocytopenia (grade1) was seen in 2.6% of the patients.
Recurrence was seen in only 4 patients (14%) who received adjuvant TKI. Common sites of recurrence was liver (50%) and omental and peritoneal secondaries.(50%).Progression on second line therapy with Sunitinib was seen only in one case of recurrent GIST.

Table 1: Age Distribution

Sample size	38
Lowest value	25.0000
Highest value	75.0000
Arithmetic mean	52.0000
95% CI for the Arithmetic mean	47.8332 to 56.1668
Median	54.5000
95% CI for the median	48.9936 to 57.0000
Variance	160.7027
Standard deviation	12.6769
Relative standard deviation	0.2438(24.38%)
Standard error of the mean	2.0565
Coefficient of Skewness	-0.3261(P=0.3747)
Coefficient of Kurtosis	-0.5743(P=0.4235)
D'Agostino-Pearson test for Normal distribution	accept Normality (P=0.4896)

Table 2: Presenting Complaints

Abdominal pain	21
Obstruction	8
Bleeding	5
Perforation	0
Systemic symptoms	4

Table 3: Primary Site

Stomach	17
Small intestine	15
Colon	0
Rectum	1
Esophagus	0
Mesentery	4
Anal canal	1

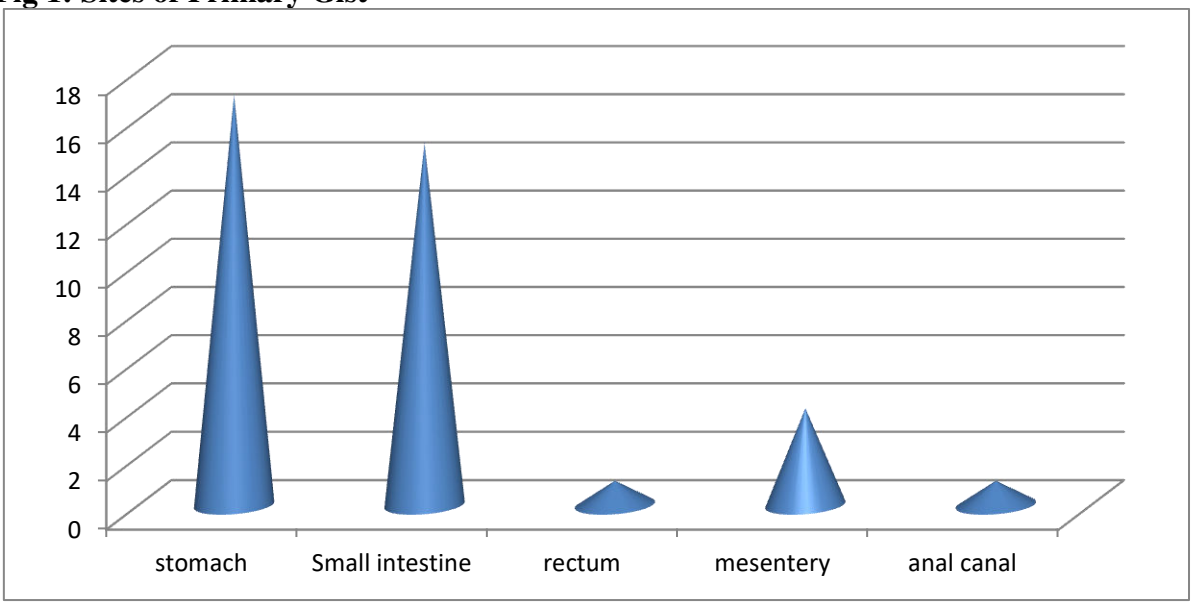
Table 4 Histology Type

Spindle	17
Epetheliod	7
Mixed	5
Unknown	9

Table 5: Stage at Presentation

STAGES	No.	%
Stage I	1/38	0.02
Stage II	7/38	18.4
Stage III	20/38	52.6
Stage IV	10/38	26.3

Fig 1: Sites of Primary Gist



DISCUSSION

Our results were consistent with those of other published datas on GIST. Median age of diagnosis is 52 years. GIST was more common in males than females. The common Site involved is stomach.Most of the patients are either stage 11 or 111 at presentation and surgery is the primary modality of treatment. Adjuvant Imatinib is efficacious and is well tolerated by our population. 83% of the patients who completed adjuvant therapy are disease free at 2 years.5 year survival rate is about 82%.There is no grade 3 or 4 toxicity with Imatinib. There was no progression of stage 1V patients treated with Imatinib

CONCLUSION

This retrospective data from a tertiary cancer care centre in South India highlights the clinico-pathological features and treatment outcomes in GIST.

FUTURE PERSPECTIVE

Many changes are under way to risk stratifying the GIST cases on basis of molecular pathology and treatment may be risk adapted at molecular level. Further studies are required to know the molecular pathology which may guide in treatment and may improve treatment outcomes

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CONFLICT OF INTEREST

The authors declare that they have no conflict of interest.

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