THE PREVALENCE OF GASTROINTESTINAL STROMAL TUMOUR AS SEEN IN THE JOS UNIVERSITY TEACHING HOSPITAL (JUTH), JOS, NORTH CENTRAL NIGERIA

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ABSTRACT

Background: Gastrointestinal stromal tumours (GIST) represent 1% of all malignant tumours of the gastrointestinal tract (GIT). However, it is the most common Mesenchymal tumour of the GIT with majority (40 to 60%) arising from the stomach.

Objective: To determine the prevalence of GIST among patients in Jos University Teaching Hospital between 2005 and 2012.

Methodology: Five (5) antibodies were used on the Mesenchymal tumours (CD117, CD34, Desmin, SMA and S100). Diagnosis of specific Mesenchymal tumours was based on histological patterns of the tumours on H and E stained slides and immunostaining characteristics of the tumours.

Results: Seven Mesenchymal tumours seen within the study period. This comprises of 6 GIST and 1 Leiomyosarcoma.

Conclusions: This study shows that even though GIST is a rare tumour, it is the commonest Mesenchymal tumour of the stomach. It also shows that they are commonly positive for both CD117 and Cd34.

Keywords: GIST, Mesenchymal Tumour, Gastrointestinal Tract, Stomach

INTRODUCTION

Gastrointestinal stromal tumours represents only 1% of all malignant tumours of the gastrointestinal tract (GIT).[1] It is however the most common mesenchymal tumour of the GIT with majority arising from the stomach.[1,2] GIST accounts for 2.2% of malignant gastric tumours in SEER data . It occurs most frequently in individuals over the age of 55 years, but the peak age of diagnosis is 60years, with far less than 10% occurring in individuals under the age of 40years.[3] The mean age of diagnosis in a study by Abdulkareem et al.[1] in Lagos, South western Nigeria, was 45.4 years, while that of Gillian Baker et al. in South Africa was 56 years**.** Kim et al. and Chan et al. recorded mean ages of 56.3 and 66 years respectively in a similar study in Asia.Studies in Europe by Ahmed et al. in the United Kingdom and Rbio et al in Spain showed mean age of 64 and 63 years respectively. Thomas et al in the USA also recorded a mean age 63 years which was similar to what was seen by Rbio in spain[4]. Several other studies showed mean age between 50 and 65.8 years. There is no gender predominance (M: F 1.1:1).[5]The male to female ratio seen by Kim et al. and Chan et al. were 1:1 and1:1.2 respectively, while that of Ahmed et al and Rbio et al were 1:0.9 and 1:1.0. The Studies by Thomas et al and Gillian Baker et al showed a male to female ratio of 1.2:1 and 1.25:1 respectively[4].

Histologically, GISTs are composed of either spindle cells, round (polygonal or epithelioid) cells or a mixture of the two. Pure spindle cells tumours are composed of elongate cells with scant, eosinophilic, fibrillar cytoplasm and blunt or sharp ended nuclei with or without paranuclear vacuoles. These cells are separated by variable amount of stroma that may undergo myxoid change or hyalinization. There is usually dense cellularity, but nuclear pleomorphism, cytologicatypia and mitotic figures are rare.[6] According to Corless et al, GISTs are mostly composed of spindle-shaped cells (70%), but some are dominated by epithelioid cells (10%- 20%) or may contain a mixture of both spindloid and epithelioid cells (10%-20%)[7].In a study by Sherif et al 68.5% of the tumors were composed of spindle cells, 10.5% were epithelioid cell tumours, 10.5% have both spindle and epithelioidcells, while 10.5% were unclassified.In

this same study, most of the tumours (42.1%) were seen in the upper 1/3 of the stomach, 31.5% in the middle 1/3 and 26.3% in the lower 1/3.[8] Matthews et al also had similar findings with the proximal stomach being involved in about two thirds of the patients.[9]

Gain of function mutation of the gene coding the tyrosine kinase c-KIT is seen in 75– 80% of GISTs. CD117 or c-KIT is a receptor for stem cell factor (SCF).[10] Another 8% have mutations that activate a Platelet derived growth factor receptor (PDGFR). They may show membrane, diffuse cytoplasmic or a peri-nuclear accentuation pattern for c-KIT.[10] True smooth muscle tumours and Schwannomas are consistently negative for c-KIT (CD117) and are distinguished from GISTs by positive staining for muscle and neural markers respectively.[11] Thus, with rare exception the term GIST should be reserved for those tumours that are immunohistochemically positive for c-KIT (CD117).[11] CD34 positivity is seen in 70 – 80% of GISTs (membrane pattern).[12] But unlike c-KIT, CD34 is also noted in Solitary fibrous tumours and Kaposi sarcoma. CD34 has been shown to be associated with a malignant phenotype. The expression of CD44 has been demonstrated to correlate with a better prognosis. 30 – 40% show focal or diffuse positivity for Smooth muscle actin (SMA), while very few show reactivity for Desmin (<5%) and S100 protein (<5%).[13]

Abdulkareemet al.[1] in Lagos, South western Nigeria, studied Gastrointestinal mesenchymal tumours using five antibodies; CD117, CD34, S100, Desmin and Smooth muscle actin (SMA). 41% of the tumours seen were GIST, all positive for c-KIT (CD117) and CD34. Only 30.7% of these were suspected to be GIST by routine H & E staining.From available literature, 5% of GISTs are negative for c-KIT (CD117) by immunohistochemistry.[6] These tumours have either c-KIT wild-type or harbour PDGFRA mutations. Because of that, some GISTs will be misdiagnosed without doing genetic analysis.

New gene markers discovered on gene expression arrays are now been studied to improve the diagnostic accuracy for GIST, especially for c-KIT-negative GISTs. These include DOG1 (Discovered on GIST 1), PKC-θ (protein kinase C theta) and CA II (carbonic anhydrase II).[6] DOG1 is also known as ANO1 (anoctamin 1, calcium-activated chloride channel), TMEM161A and FLJ10261. Recent studies have shown that the overall sensitivity of DOG1 Staining in GIST ranges from 75% to 100% depending on the type of antibody used.[14]

MATERIALS AND METHOD

The study was an eight year hospital based retrospective analysis of tissue blocks and slides of Gastric specimens received at the histopathology department of the Jos University Teaching hospital (JUTH) between January 2005 and December 2012. The materials for this study included hospital histopathology investigation request forms, patient case notes, duplicated copies of all despatched results, blocks and archival slides of gastric specimens received between January 2005 and December 2012.

Paraffin wax embedded tissue blocks and corresponding archival routine haematoxylin and eosin (H&E) stained slides of all gastric cancer cases were retrieved and reviewed. Fresh sections were taken from blocks for all cases that required immunohistochemical staining and where original slides were missing or damaged.

Relevant information such as age, hospital numbers, laboratory numbers and clinical details including extent of the disease was extracted from the departmental cancer registry, duplicated copies of despatched results and patient's folders from JUTH and referring hospitals.

Five (5) antibodies were used on the Mesenchymal tumours (CD117, CD34, Desmin, SMA and S100). Diagnosis of specific mesenchymal tumours was based on histological patterns of the tumours on H and E stained slides and immunostaining characteristics of the tumours. Criteria for the diagnosis of GIST are based on histology and positivity for CD117 and CD34. Positivity for Desmin and Smooth muscle actin was the criteria for the diagnosis of smooth muscle tumours.

RESULTS

Seven mesenchymal tumours were seen within the study period. This comprises of 6 GIST (Table 1) and 1 Leiomyosarcoma (2 of the GISTs were diagnosed prior to this work, without immunohistochemistry as Leiomyosarcoma). The entire GISTs comprising of 4 spindle cell variant and 2 epithelioid variant, were all positive for CD117/c-KIT, 5 were positive for CD34 while all were negative for SMA and Desmin. One of the GIST, a spindle cell variant washowever positive for S100. All the GISTs were seen in male patients within the age range of 32 to 65 years and mean age

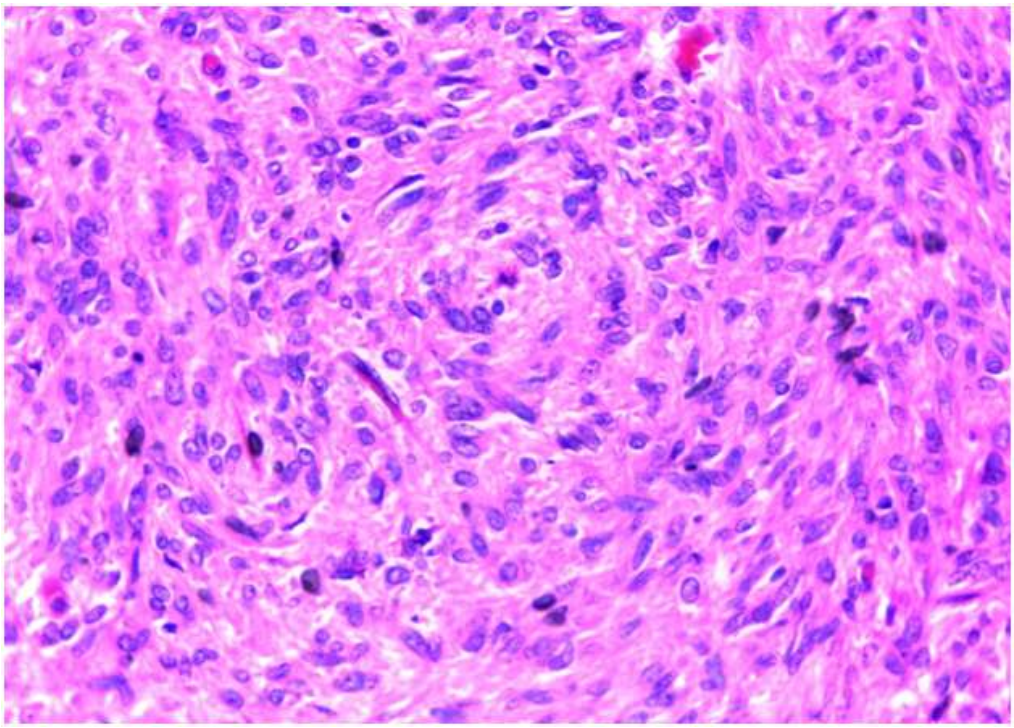
of 52.2 years. 4 out of 6 GISTs seen were located in the Gastric Antrum, while the remaining two were seen at the Gastric Corpus. The diagnosis of the Leiomyosarcoma seen in the study was based on histology on H & E and immunopositivity for Desmin and Smooth muscle Actin (SMA). This same tumour was negative for CD117, CD34 and S100.

Table 1Histopathological subtypes of gastric mesenchymal malignancies seen in J.U.T.H, Jos

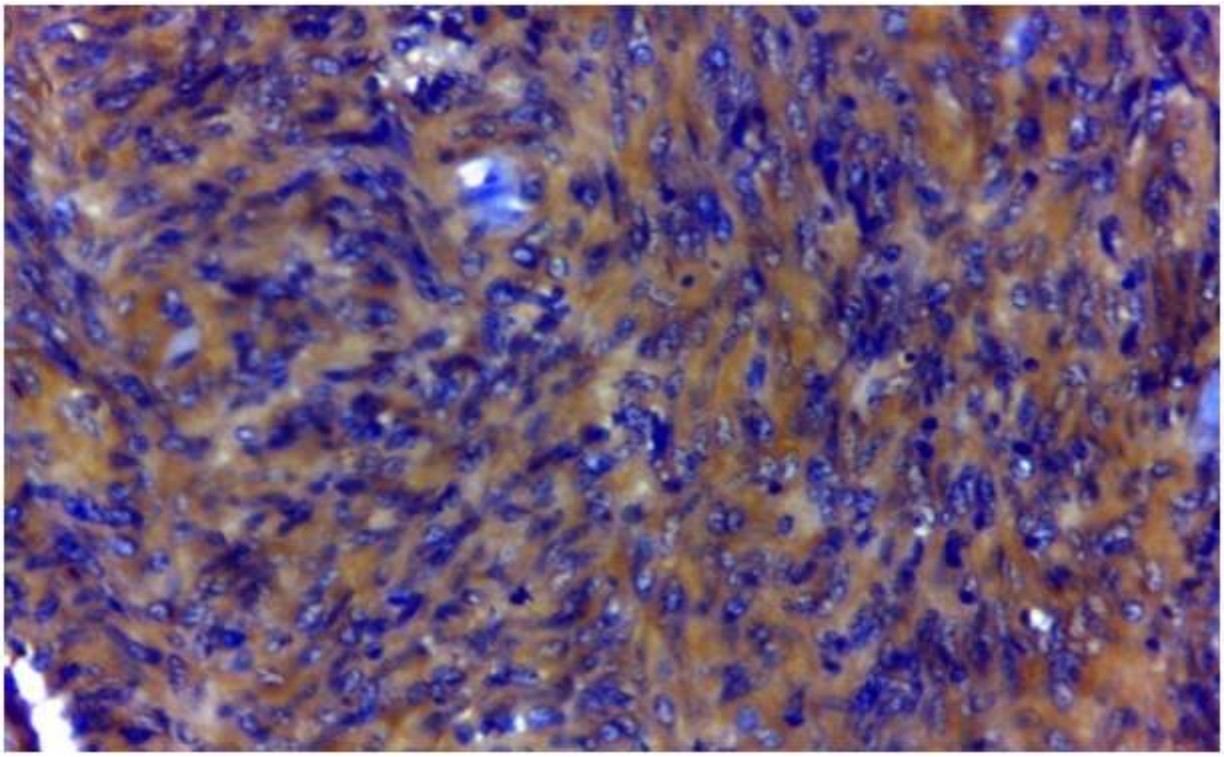
Tumour type	Frequency	Percent (%)
GIST	6	85.7
Leiomyosarcoma	1	14.3
Total	**7**	**100**

Table 2 Histopathological subtypes of gastric mesenchymal malignancies seen in J.U.T.H, Jos

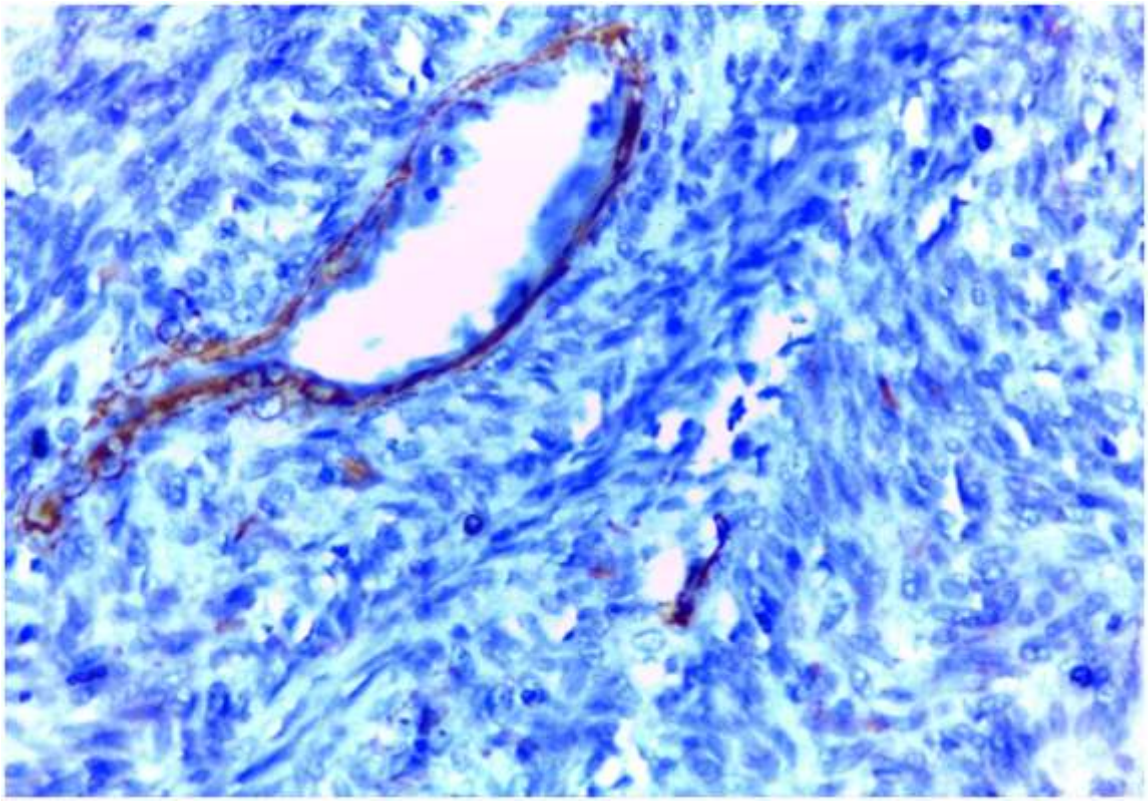
S/N	AGE(YEARS)	SEX	SITE	TUMOUR VARIANTS
1	32	Male	Corpus	Spindle
2	43	Male	Antrum	Epitheloid
3	50	Male	Antrum	Spindle
4	58	Male	Corpus	Epitheloid
5	65	Male	Antrum	Spindle
6	65	Male	Antrum	Spindle



GIST showing proliferating spindle cells with nuclear atypia and mitotic figures (H & E X 20)



Diffuse intense cytoplasmic c-KIT/CD117 staining in a case of Gastrointestinal stromal tumour (GIST) (Immunoproxidase x 40)



SMA staining only the cytoplasms of blood vessel pericytes while Gastrointestinal stromal tumour (GIST) cells has no staining (negative) (immunoperoxidase technique x 40)

DISCUSSION

There were 7 cases of malignant mesenchymal tumours seen within the study period. These comprise of 6 gastrointestinal stromal tumours (GISTs) and a Leiomyosarcoma. This is in line with other studieswhich show that GISTs are the commonest gastrointestinal mesenchymal tumours. The mean age in our study is 52.2 years. This value is similar to 56 and 56.3 years seen by Gillian et al. and Kim et al. in their studies. However, this is much higher than the 45.4 years seen by Abdulkareem et al. in her study and lower than 63, 64 and 66 years seen by Thomas et al. ,Rbio et al.,Ahmed et al. and Chan et al. in their respective studies. All the cases reported in our study were male patients. This did not correspond to most reported studies were no sex predominance was noted. 4 of the GISTs cases were of the spindle cell variant, while two were epithelioid variant. This correspond well with findings in other Studies were the spindle cell variant predominates. In our work, most tumours are located in the antrum. This does not correspond with the findings of Sherif et al. and Mathews et al who reported majority of cases to be located in the upper gastric portion.All the GISTs seen in our study were positive for c-KIT/CD117, 1 was negative for CD34 while one was positive for S100. These are all seen in most studies.

CONCLUSION

In conclusion, the commonest gastric mesenchymal tumour is the Gastrointestinal stromal tumour (GIST) and itsaccurate diagnosismay require the use of immunohistochemistry. All GISTs seen in our work were positive for c-KIT. This confirms that most GISTs are positive for c-KIT, with few exceptions where the PDGFR mutation may be involved.This work has also concurred with other studies for showing the commonest variant to be the spindle cell type and that it is a disease of people around the age of 50 to 60 years

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