DOI: https://doi.org/10.53350/pjmhs2115124027

ORIGINAL ARTICLE

Clinico Pathologic Features and Prognostic Grouping of Gastrointestinal Stromal Tumors (GISTS) in Peshawar: an Institutional Perspective

MOHAMMAD MANZOOR[1], ASIM MUHAMMAD[2], ABDUL SALAM[3], MOHIBULLAH[4], INAM-U-LLAH[5], HINA MIR[6], SUMBAL JAMSHED[7], MUHAMMAD AWAIS[8], SUDHAIR ABBAS BANGASH[9]
[1]Pathology Department, Bacha Khan Medical College Mardan
[2]Assistant Professor Pathology, KMU-IMS, Kohat
[3]Lecturer, Institute of Pathology and Diagnostic Medicine, Khyber Medical University, Peshawar
[4]Assistant Professor Histopathology, Pak international Medical College, Peshawar
[5]PhD Health Management, Department of Food Science, The University of Haripur, KPK, Pakistan
[6]Department of Biochemistry, Shaheed Benazir Bhutto Women University, Peshawar
[7]Department of Allied Health Sciences, Iqra National University, Peshawar
[8]Department of Clinical Sciences, College of Veterinary and Animal Sciences, Jhang
[9]Faculty of Life Science, Department of Pharmacy, Sarhad University of Science and Information Technology, Peshawar
Corresponding author: Dr Mohammad Manzoor, Email: mohammadmanzoor418@gmail.com

ABSTRACT

Background: Gastrointestinal stromal tumours (GISTS) are uncommon gastrointestinal tumours. The prognosis is heavily influenced by the histopathologic features of resection specimens, which have not been investigated extensively in our community. Objective of the current study was to assess the histopathologic features of GISTs in our community, as well as how they affect their prognosis, based on what we found.

Methodology: In this study, 60 cases of GISTs were included that were found and treated at Peshawar's Khyber Teaching Hospital from Jan, 2018 to December, 2020.

Results: The patients' ages varied from 18 to 71 years. The stomach was the most common location for primary GISTs, accounting for 57.7% of cases.75% of the patients had spindle cell morphology, and 53.8 percent of them had a poor prognosis. It was shown that intestinal GISTs had a higher grade (70%) and were more likely to be in the elevated-risk prognosis groups than stomach gastrointestinal stromal tumor,(43 percent). However, there is no statistical difference found. Although GISTs are rare gastro-intestinal tumors, initial discovery and recognition of unfavorable histology properties are important for effective treatment. In stomach the GISTs is prevalent. However, intestinal gastrointestinal stromal tumors are shown to be more prevalent and more likely to be linked to poor prognostic factors. Moreover, further large-scale investigations are needed to confirm this conclusion.

Keywords: Intestinal-GISTs, Stomach-GISTs, Peshawar, Gastrointestinal stromal tumors,

INTRODUCTION

Account for a total of 1% of all the gastrointestinal carcinomas, gastrointestinal stromal tumors are considered to be the most prevalent one (Fülöp, Marcu, Milutin, & Borda, 2009).Because GISTs have common abdominal pain and cramps as clinical signs and symptoms, lead to delayed diagnosis and prognosis and eventually results in high morbidity and mortility rates. There are around 15 cases per million in the United States, whereas there are approximately 11 cases per million in Northern Europe. Although there is no evidence that GISTs existed prior to the year 2000, the increasing number of instances has motivated additional investigation into the subject. (Andersson and co-workers, 2006). We don't know how often GISTs occur in our nation since no large-scale investigations have been conducted.

Due to its physical similarities, GIST was originally classified as a leiomyoma or a leiomyosarcoma. 2004 (Bucher, Villiger, Egger, Buehler, and Morel). According to practically every piece of recent research, GISTs may arise anywhere in the digestive system, but the majority of GIST incidences are identified in the gastric region(Tryggvason, Gslason, Magnsson, & Jónasson),

The pathologicalproperties of GISTs during sectioning of the sample is crucial for guiding postoperative treatment and assessing patient prognosis, but they haven't been thoroughly investigated in our lab. Mushtaq et al. also classified 36 GIST patients as high or low risk. The study revealed the 7 patients were at low risk while ten individuals faced moderate risk and the remaining 19 were found at high risk. Furthermore, at the extremity of low risk there were no patient (Mushtaq and colleagues, 2009). Fewer studies are present on the GISTs in Pakistan. One of the study screens out 255 GIST cases and found that 62 patients of gastric GISTs, 81 patients of duodenal GISTs, 68 individuals of small intestine GISTs, 72 individuals of colorectal GISTs, and 89 individuals of colorectal GISTs were at high-risk (Bucher and colleagues, 2004).So far, the goal of this research was to assess clinic-pathological and prognostic factors of GISTs in the Peshawar community, that might aid in the development of customized therapy for localpopulations.

METHODOLOGY

The research included 60 instances of GISTs identified and treated at Peshawar's Khyber Teaching Hospital between 2018 and 2020. The institutional ethical review committee approved the research before it could be carried out. All instances were biopsy-proven before the final resection. Following a preoperative workup, a definitive sectioning of specimenswas performed, and were processed in histopathology laboratory. Tumor size, location, tumour shape, grade, number of mitoses, and prognosis group were all documented according to (CAP) criteria, which

included tumour size, location, tumour shape, grades, counts of mitoses, and prognosis group.

Immunohistochemistry: Immunohistochemical markers such as ASMA, CKAE1/3, S100, CD117, and CD34 were carried out using the DAKO envisage methodology, and the slides examination was carried out by qualified histo-pathologists. DAKO supplied polyclonal rabbit anti-human CD117 and the c-kit antibody for CD117 IHC, and IHC was carry out using the DAKO envision technique.

Positive staining is defined as more than 10% of tumour cells with moderate to strong membranous staining. A FLEX monoclonal anti-human CD34 class II, clone QBEnd 10, a prepared antibodies were used for CD34. DAKO provided the FLEX polyclonal rabbit anti-S100 prepared antibody for S100 IHC. Similarly, a monoclonal antibody against human smooth muscle actin, clone 1A4, was used for ASMA IHC, which was done by following the manufacturer's instructions with the DAKO envision kit. For ASMA, S100, and CD34, cytoplasmic staining ranging from low to high in 10% of tumour cells was declared positive. For data analysis we used SPSS Version 25. A p value less than 0.05 will be considered significant.

RESULTS

The participants were between the ages of 20 and 71 years, with a male 32 (61.5%). The stomach was the most common location for primary GISTs, accounting for 57.7 percent of cases.As shown in Table 1, 75 % of patients had spindle cell shape, and 53.8 % had a poor prognosis.

Table 2 shows the comparison of GISTs in various parts of the digestive tract. Out of a total of 48 instances of primary gastrointestinal stromal turmors, 30 were identified in the gastral mucosa, 10 in the duodenum, and 8 in the large intestine. There were 20 GISTs in the above 50-year-old age group, 9 in the 31–50-year-old age group, and just one stomach gastrointestinal stromal tumor in the 31–50-year-old age group in the 30-year-old age group. Similarly, instances in the intestines are more usual in those over 50 years old.

Gender preponderance was overlooked since stomach GIST was found in similar proportions in both males and females. GISTs were found to be more common in the intestines of male, but this was non-significant.

Although the most of GISTs in the stomach were 5–10 cm in diameter, whilst the intestinal gastrointestinal stromal tumors are more likely bigger than 10cm in diameter. Spindle cell morphology was detected in 37 of the 48 instances. Twenty of the 30 cases with stomach GIST had a spindle cell morphology, 3 had an epitheloid morphology (Fig. 1), and 7 had a mixed morphology. Almost every occurrence of GIST in the small and large intestine was of the spindle cell type (Figure 1).

There were 29 instances in the elevated-risk group, five in the intermediate risk, 11 in the lower-risk category, and five in the lowest-risk category. Most of the patients had an overall mitotic activities of more than five/fifty HPF. CD34 positivity was found in 34 of the 46 tumours, while CD117 positivity was found in 46 of the 48 tumours. S100 was found in 12 of the 40 people tested, while ASMA was found in 19 of the 43. As a result, the majority of tumours tested positive for CD34 and CD117 but negative for S100 and ASMA, as shown in Figure 1.

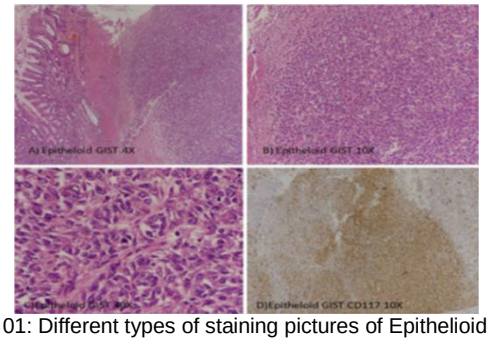

Figure. 01: Different types of staining pictures of Epithelioid GISTs

Table. 01. Characteristics of Gastrointestinal Stromal Tumor

Gender Male 32 (61.5%) Female 20 (38.51%) Age (years) Mean 53.4(18–71 years)	Size groups (cm) <2 1 (1.9%) 2–5 6 (11.5%) 5–10 20 (35.5%) >10 22 (42.3%)
Age groups (years) <30(5.8%) 31–50(34.61%) >50(59.6%)	Morphology Spindle 39(75%) Epithelioid 4(7.5%) Mixed 9(17.3%) Grade (mitotic activity) Low grade (<5/50HPFs) 23 (44.2%) High grade (>5/50HPFs)i29i(55.8%) Necrosis Present 10(19.2%)
Primary/metastatic Primary 48 (92.3%) Metastasis 4 (7.74%)	Absent 42 (80.8%) Prognostic groups Very low risk 5(9.63%) Low risk 11(21.2%) Moderate risk 5(9.6%) High risk 28 (53.8%
Site Stomach 30 (57.7%) Small intestine10 (19.2%) Large intestine 08 (15.4%) Liver 04 (7.7%) Size (cm) Mean 9.4(2–16)	

Table. 02: Location wise Comparison of Different Types of GISTs

Variables Age (years)	Stomach N(%)	Small intestine	Large Intestine	PiN(%)
Mean ± SD	54.50±11.99	52.10±15.53	55.25±14.29	0.852
≤30	1(3.3)	1(10)	0	0.785
31–50	9(30)	4(40)	3(37.5)	
>50	20 (66.7)	5(50)	5(62.5)	
Gender				
Male	15 (50)	8(80)	6(75)	0.159
Female	15 (50)	2(20)	2(25)	
Size				
Mean ± SD	8.96±3.94	10.20±4.75	10.28±3.11	0.570
≤i2	0	1(10)	0	0.287
2.1–5	4(13.3)	1(10)	1 (12.5)	
5.1–10	15(50)	2(20)	2(25)	
>i10	11(36.7)	6(60)	5(62.5)	
Morphology				
Spindle cell	20(66.7)	10(100)	7i(87.5)	0.318
Epithelioid	3(10)	0	0	
Mixed	7(23.3)	0	1(12.5)	
Prognostic group				
Very low risk	4(13.3)	1(10)	0	0.214
Low risk	10(33.3)	0	1(12.5)	
Moderate risk	3(10)	1(10)	1(12.5)	
High risk	13(43.3)	(80)	6(75)	
Grade (mitotic activity)				
Low grade (≤5/50HPFs)	15(50)	3(30)	5(62.5)	0.456
High grade (>5/50HPFs)	15(50)	7(70)	3(37.5)	

DISCUSSION

In this research, we compared preliminarily published literature to the general features of GIST in terms of location and histochemical labels (which proved helpful in gastrointestinal stromal tumor diagnosis). In this research of 48 individuals with primary GIST was only discovered in stomach, and both intestines in this research, despite the bulk of the literature mentioning GIST in the oesophagus, stomach, intestine, rectum, and mesentery. Stomachs accounted for 62.5 percent of the total in earlier research, lag by the small intestine (20.8 percent) and the large intestine (20.8 percent) (16.7 percent). This was in accordance with the bulk of previous Asian research's conclusions.

In rare instances, GISTs have been shown to be more frequent in young individuals under the age of 50, but they are exceedingly rare in those under the age of 30. The average age of the gastral as well as intestinal GISTs broadly variate among age groups categories. We may deduce from previous research that gastrointestinal stromal tumors is more prevalent in people under the age of 50, despite statistical evidence. Hasegawa, Matsuno, Shimoda, and Hirohashi (Hasegawa, Matsuno, Shimoda, and Hirohashi, 2002; Hou et al., 2002; Wang et al., 2014).

The majority of tumors (77%) are comprised of spindle cells organized in interlaced patterns to form spring like appearance with rich eosinophil cytoplasm.Despite the fact that epitheloid and mixed types were uncommon, the intermixed form dominate (10% and 35.8%, respectively), despite pre-virus research indicating that epitheloid was more common. (2011) (Fülöp et al.).Our results were in line with Asian research, which showed that mixed varieties predominated (Hou et al., 2002). Moreover, Spindle cells type is the most frequent one as evidenced from previous literatures. The stomach comprised of all three morphological patterns, with spindle cell morphology accounting for 100% of small intestine GISTs and spindle and mixed morphology accounting for 87.5 and 12.5 percent of large intestinal GISTs, respectively. (2011) (Fülöp and colleagues).Men were more likely than women to get GIST.

Despite prior Asian research (Miettinen, Majidi, & Lasota, 2002) revealing a modest male-female dominance, there was no statistical significance in this study (P = 0.159). In most situations, GISTs damage the whole thickness of the gut wall. (Fülöp et al., 2011; Fenoglio-Preiser, Lantz, Michael, Listrom, & Rilke, 1989; Fenoglio-Preiser, Lantz, Michael, Listrom, & Rilke, 1989; Fenoglio-Preiser, Michael, Michael, Michael, Michael, Listrom, & Rilke, 1989;This is due to the fact that they are often bigger, as shown by the fact that the majority of the tumours in this research were more than 10 cm in diameter and hardly less than 5 cm. The tumor's tremendous development might be attributed to its brief clinical history. Hou and colleagues (Hou et al., 2002).

The average size of the stomach tumour was 8.96 cm, and the small and large intestines were 10.20 and 10.28 cm, respectively. The majority of stomach tumours had a diameter of 5 to 10 cm, whereas the majority of intestinal tumours had a diameter of more than 10 cm. The majority of stomach tumours were between 5 and 10 cm in diameter, which was not statistically significant (P = 0.570). Other Asian research has shown that the average tumour size is greater than 5 cm. (Rauf, Bhurgri, & Pervez, 2007; Fülöp et al., 2011).

According to Asian research, the majority of GISTs were low-grade tumours with high-risk traits (Hasegawa et al., 2002), lagged by moderate and lower-risk features (Kim et al., 2004; Rauf et al., 2007). The majority of stomach GISTs in our study were classified as elevated-risk (43.3%), with lower- risk, lowest-risk, and intermediate risk following closely behind. The small (80%) and large (80%) intestines, on the other hand, had the highest percentage of high-risk cancers (75%).

Researchers used two types of antibodies to investigate the immunohistochemical features of GISTs: one with elevated specificity for gastrointestinal stomal cell tumor, such as CD117 and CD34, and another with a higher specificity for muscle and neural tumours (ASMA and S-100), as these are the two types of tumours most frequently misdiagnosed as GISTs. In 12 instances, S-100 was positive, in 28 individuals it was negative, and in eight instances it was not done. In 19 instances, ASMA was positive, in 24 specimens it was negative, and in 5 instances it was not done. CD34 was found to be positive in 34 of the instances, negative in 12 of the instances, and untested in two others. CD117 was found to be positive in 46 of the instances and negative in 46 of the instances. (Wolfe et al., 2012; F.-Y. Liu, Qi, Xu, & Wu, 2006).

When Liu et al. analysed 300 patients with gastric GISTs, they discovered that duodenal GISTs were highly associated with poorer prognostic features. (Z. Liu and colleagues, 2018). Zhu et al. evaluated colorectal and stomach GISTs in similar research. They observed that rectal GISTs were associated with a higher overall survival rate, but intestinal gastrointestinal stromal tumors were related with a higher mortality rate (Zhu et al., 2018).

While the vast majority of stomach GISTs (70.8%) and S-100 (64.3%) were negative for ASMA and S-100 but positive for CD34 and CD117 (as were the vast majority of small intestine tumors), the vast majority of large intestine GISTs (26.3%) were positive for ASMA but negative for CD34 (41.7%). Majority, of spindle cell types were negative for ASMA and positive for CD34, whereas most epithelioid and mixed types were positive for ASMA (10.5 and 26.3 percent, respectively), and mostly epithelioid types were negative for CD34.The majority of high-risk tumours tested negative for ASMA, whereas the majority of low-risk tumours tested positive. positive for the tumor's location (P = 0.013).CD34 positivity in the tumour was statistically significant (P = 0.024); other results, however, were and CD117 positivity in the morphology was not statistically significant.

REFERENCES

1. Andersson, J., Bümming, P., Meis–Kindblom, J. M., Sihto, H., Nupponen, N., Joensuu, H., . . . Nilsson, B. J. G. (2006). Gastrointestinal stromal tumors with KIT exon 11 deletions are associated with poor prognosis. *130*(6), 1573-1581.
2. Bucher, P. A. R., Villiger, P., Egger, J.-F., Buehler, L. H., & Morel, P. J. S. m. w. (2004). Management of gastrointestinal stromal tumors: from diagnosis to treatment. *134*(11-12), 145-153.
3. Fenoglio-Preiser, C. M., Lantz, P. E., Michael, D., Listrom, M. B., & Rilke, F. O. (1989). Gastrointestinal pathology an

atlas and text. In *Gastrointestinal pathology an atlas and text* (pp. 892-892).
4. Fülöp, E., Marcu, S., Borda, A., Moldovan, C., Fülöp, E., Loghin, A., & Pávai, Z. J. R. J. M. E. (2011). Histopathological and immunohistochemical features of gastrointestinal stromal tumors. *52*(2), 555-562.
5. Fülöp, E., Marcu, S., Milutin, D., & Borda, A. J. R. J. M. E. (2009). Gastrointestinal stromal tumors: review on morphology, diagnosis and management. *50*(3), 319-326.
6. Hasegawa, T., Matsuno, Y., Shimoda, T., & Hirohashi, S. J. H. p. (2002). Gastrointestinal stromal tumor: consistent CD117 immunostaining for diagnosis, and prognostic classification based on tumor size and MIB-1 grade. *33*(6), 669-676.
7. Hou, Y., Wang, J., Zhu, X., Du, X., Sun, M., & Zheng, A. J. Z. B. l. x. z. z. C. J. o. P. (2002). A clinicopathologic and immunohistochemical study on 76 cases of gastrointestinal stromal tumors. *31*(1), 20-25.
8. Kim, M. K., Lee, J. K., Park, E. T., Lee, S. H., Seol, S. Y., Chung, J. M., . . . Yoon, H. K. J. T. K. J. o. G. T. S. H. c. (2004). Gastrointestinal stromal tumors: clinical, pathologic features and effectiveness of new diagnostic criteria. *43*(6), 341-348.
9. Liu, F.-Y., Qi, J.-P., Xu, F.-L., & Wu, A.-P. J. W. j. o. g. W. (2006). Clinicopathological and immunohistochemical analysis of gastrointestinal stromal tumor. *12*(26), 4161.
10. Liu, Z., Zheng, G., Liu, J., Liu, S., Xu, G., Wang, Q., . . . Feng, F. J. B. c. (2018). Clinicopathological features, surgical strategy and prognosis of duodenal gastrointestinal stromal tumors: a series of 300 patients. *18*(1), 1-13.
11. Miettinen, M., Majidi, M., & Lasota, J. J. E. J. o. C. (2002). Pathology and diagnostic criteria of gastrointestinal stromal tumors (GISTs): a review. *38*, S39-S51.
12. Mushtaq, S., Mamoon, N., Hassan, U., Iqbal, M., Khadim, M. T., & Sarfraz, T. J. J. o. g. c. (2009). Gastrointestinal Stromal Tumors—A Morphological and Immunohistochemical Study. *40*(3), 109-114.
13. Rauf, F., Bhurgri, Y., & Pervez, S. J. I. J. o. G. O. J. o. t. I. S. o. G. (2007). Gastrointestinal stromal tumors: a demographic, morphologic and immunohistochemical study. *26*(5), 214-216.
14. Tryggvason, G., Gíslason, H. G., Magnússon, M. K., & Jónasson, J. G. J. I. j. o. c. (2005). Gastrointestinal stromal tumors in Iceland, 1990–2003: The Icelandic GIST study, a population-based incidence and pathologic risk stratification study. *117*(2), 289-293.
15. Wang, M., Xu, J., Zhang, Y., Tu, L., Qiu, W.-Q., Wang, C.-J., . . . Cao, H. J. B. s. (2014). Gastrointestinal stromal tumor: 15-years' experience in a single center. *14*(1), 1-10.
16. Wolfe, C. M., Green, W. H., Hatfield, H. K., Shakar, T. J., Baniahmad, O., & Cognetta, A. B. J. A. j. o. d. (2012). Multiple secondary cutaneous tumours following electron beam radiotherapy for cutaneous malignancies of the scalp. *53*(3), 233-238.
17. Zhu, R., Liu, F., Grisotti, G., Pérez-Irizarry, J., Cha, C. H., Johnson, C. H., . . . Zhang, Y. J. J. o. G. O. (2018). Distinctive features of gastrointestinal stromal tumors arising from the colon and rectum. *9*(2), 231.