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Original Research Article

Morphological spectrum of soft tissue tumours: experience of a cancer institute

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ABSTRACT

Background: Soft tissue tumours are defined as mesenchymal proliferations that occur in the extra skeletal nonepithelial tissues of the body, excluding viscera, brain coverings and lymphoreticular system. This study was undertaken to study the spectrum of soft tissue tumours in State Cancer Institute, Assam.
Methods: This is a cross-sectional study undertaken in the Department of Oncopathology, State Cancer Institute, Guwahati from January, 2021 to June, 2024. All cases of soft tissue tumours, biopsy, excised specimen and review cases were included in the study. Inadequate biopsy, non-mesenchymal and bone tumours were excluded.
Results: The overall prevalence of soft tissue tumours was 1.1% (104/9575). 46.15% cases were males while 53.85% cases were females with the male to female ratio of 1:1.17. 20.19% cases were benign, 16.35% intermediate and 63.46% malignant. Adipocytic tumours consisted of 14.42% cases, fibroblastic tumours 26.92%, vascular tumours 2.88%, perivascular tumours 0.96%, smooth muscle tumours 3.85 %, skeletal tumours 5.77%, nerve sheath tumours 18.27% and tumours of uncertain differentiation 26.92%.
Conclusions: Soft tissue tumours are rare and it is important for pathologists to identify them based on morphology, immunohistochemistry and molecular analysis for prognosis and proper management of patients.

Keywords: Benign, Histopathology, Malignant, Soft tissue tumours

INTRODUCTION

Soft tissue tumours are defined as mesenchymal proliferations that occur in the extraskeletal nonepithelial tissues of the body, excluding the viscera, coverings of the brain and lymphoreticular system and benign tumors are more common than malignant counterparts with a ratio of at least 100:1.[1] On one hand, benign tumours have low rate of local recurrence and are managed by conservative therapy; malignant tumours, on the other hand, have high rate of local recurrence and distant metastasis and hence require adjuvant therapy. Immunohistochemistry is of great value in soft tissue tumours and is extensively used to accurately classify these neoplasms.[2] Federation Nationale des Centres de Lutte Contre le Cancer (FNCLCC) grading is the standard grading system used for the morphological evaluation of sarcomas based on tumour differentiation score, mitoses and amount of tumour necrosis.[3] FNCLCC grading system was further reviewed by Coindre in 2006.[4] To study the spectrum of soft tissue tumours in State Cancer Institute, Assam.

METHODS

Study type

This is a cross-sectional study.

Study place

The study was undertaken in the Department of Oncopathology, State Cancer Institute, Guwahati.

Study duration

The study was conducted for a period of 42 months from January 2021 to June 2024.

Ethical approval

Institutional Ethical Committee approval was taken.

Inclusion criteria

All cases of soft tissue tumours, biopsy, excised specimen and review cases were included in the study.

Exclusion criteria

Inadequate biopsy, non-mesenchymal and bone tumours were excluded from the study. The total number of cases included in the study was 104 soft tissue tumours out of a total 9575 histopathological specimen spanning the study period of 42 months. The patient data were retrieved from pathological requisition forms and medical records and demographic data such as age, sex and relevant clinical history were recorded.

All the above cases were processed routinely in the Automated tissue processor Thermo Fisher Scientific, STP120 and stained with hematoxylin and eosin in the automated Stainer Thermo Fisher Scientific, Gemini AS model and examined, while immunohistochemistry (IHC) was performed in the automated IHC stainer Leica Bond Max as and when required. The various antibodies used were obtained from Biogenex.

Anti-PanCk (AMA46), Anti-EMA (AM057), Anti-Vimentin (AM074), Anti-Desmin (AM072), Anti-S100 (AMA15), Anti-CD99 (AN850), Anti-SMA (AM128), Anti-CD34 (AM236), Anti-Myogenin (AN789), Anti-CD117 (AM423), Anti-ALK (AN770), Anti-Bcl2 (AM287), Anti-NKX2.2 (AMC23), Anti-ERG1 (AN782), Anti-CD31 (AM232), Anti-MDM2 (D7) and Anti-Ki67 (AM410). Tumours were classified according to the WHO classification of soft tissue tumours 2020.

For accurate characterization of tumours, light microscopic examination was coupled with appropriate history and radiological investigations. Where possible, multiple slides from different representative sections were examined in case of large and heterogenous tumours.

Immunohistochemical tests were used as adjunct only in cases where there was significant morphological overlap and which required confirmation and differentiation from other differential diagnoses, especially in diagnosis of a common tumour in an uncommon location or an uncommon tumour in a common location. For FNCLCC grading, tumor differentiation and mitotic count were given a score from 1-3 and tumor necrosis was scored as 0-2.

The histologic grade is derived from the total score with 2-3 being grade 1, 4-5 being grade 2 and 6-8 being grade 3. Data was entered into excel spreadsheet and analysed with the help of the software SPSS version 27.

RESULTS

Demographic analysis

The overall incidence of soft tissue tumours was 1.1% (104/9575). 46.15% cases were males while 53.85% cases were females with the male to female ratio of 1:1.17. 0.96% cases belonged to age range 0-10 years, 6.73% to 11-20 years, 10.58% to 21–30 years, 18.27% to 31-40 years, 26.92% to 41-50 years, 21.15% to 51-60 years, 11.54% cases to 61-70 years and 3.85% cases to 71-80 years respectively. We received 10.58% biopsy cases, 70.19% excision specimen and 19.80% review cases. 11.54% cases were from head and neck, 10.58% from thorax, 19.23% from upper limb, 21.15% from abdomen and 37.5% from lower limb.

Pathological analysis

20.19% cases were benign, 16.35% intermediate and 63.46% malignant (Table 1). Out of the intermediate and malignant cases, most tumours were grade 3 (51.56%), followed by grade 2 (26.56%) and grade 1 (21.88%) (Table 2). Figure 4 shows a bar diagram with different types of soft tissue tumours and frequency of their FNCLCC grades.

Adipocytic tumours

Adipocytic tumours consisted of 14.42% (15/104) cases, of which 3.85% (4/104) were benign and 10.89% (11/104) were malignant. Lipoma was found with equal incidence in head and neck, abdomen, upper and lower limbs.

The most common malignant tumour was dedifferentiated liposarcoma, (Figure 1B to C) 4.81% (5/104) incidence in abdomen and 0.96% (1/104) in lower limb with 3.85% (4/104) FNCLCC grade 2 and 1.92% (2/104) FNCLCC grade 3.

Other malignant adipocytic tumours included Well differentiated liposarcoma FNCLCC grade 1, 2.88% (3/104), myxoid (Figure1A) and pleomorphic liposarcoma, 0.96% (1/104) each and both graded as 3.

Fibroblastic tumours

Fibroblastic tumours consisted of 26.92% (28/104) cases, of which 1.92% (2/104) were benign, 15.38% (16/104) intermediate and 9.6% (10/104) malignant. Dermatofibrosarcoma protuberans was the most common

intermediate type of tumour, 5.77% (6/104) followed by desmoid fibromatosis, 3.96% (4/104), inflammatory myofibroblastic tumour 2.88% (3/104) and fibromatosis, nodular fascitis and fibrohistiocytoma, 0.96% (1/104) each. High grade myxofibrosarcoma was the most common malignant tumour, 4.81% (5/104), with greatest incidence in lower limb 2.88% (3/104), followed by low grade myxofibrosarcoma 1.92% (2/104); Fibrosarcoma, malignant solitary fibrous tumour (Figure 1F & G) and myofibroblastic sarcoma of equal incidence, 0.96% (1/104).

All dermatofibrosarcoma protuberans cases, 5.77% (6/104) were given FNCLCC grade 1. Of the 7 myxofibrosarcoma cases, (Figure 1E) 1.92% (2/104) each were grade 1 and 2 and 2.88% (3/104) were in grade 3 respectively. 1.92% (2/104) cases of Inflammatory myofibroblastic tumour (Figure 1D) were graded 2 and 0.96% (1/104) was graded 1 with 0.96% (a single) case of Fibrosarcoma graded as 2.

Vasuclar tumours

Vascular tumours comprised 2.88% (3/104) cases of which all were malignant and included 1.92% (2/104) cases of Angiosarcoma and 0.96% (1/104) Hemangioendothelioma FNCLCC grade 1.

Perivascular tumours

Perivascular tumours comprised of only 0.96% (1/104) cases, a single benign case of cellular angiomyoma in the abdomen (Figure 1H and I).

Smooth muscle tumours

Smooth muscle tumours comprised 3.85% (4/104) cases, of which 2.88% (3/104) were Leiomyosarcoma, 1 each of FNCLCC grade 1, 2 and 3 respectively and 0.96% (1/104) was Pleomorphic leiomyosarcoma FNCLCC grade 3 (Figure 1J).

Skeletal muscle tumours

Skeletal muscle tumours comprised 5.77 % (6/104) cases, of which all were malignant with greatest incidence of Pleomorphic rhabdomyosarcoma (Figure 1K & L) 2.88% (3/104), all FNCLCC grade 3, followed by Embryonal, 1.92% (2/104) (1 each in FNCLCC grade 2 and 3) and spindle cell rhabdomyosarcoma, FNCLCC grade 2, 0.96% (1/104).

Nerve sheath tumours

Nerve sheath tumours consisted of 18.27% (19/104) cases, of which 13.46% (14/104) were benign and 4.81% (5/104) were malignant. Most benign cases were schwannoma 6.73% (7/104), followed by ancient schwannoma (Figure 2A) 3.85% (4/104) and neurofibroma 2.88% (3/104).

Malignant peripheral nerve sheath tumour (Figure 2B to E) was the only malignant type of tumour with 4.81% (5/104) cases.

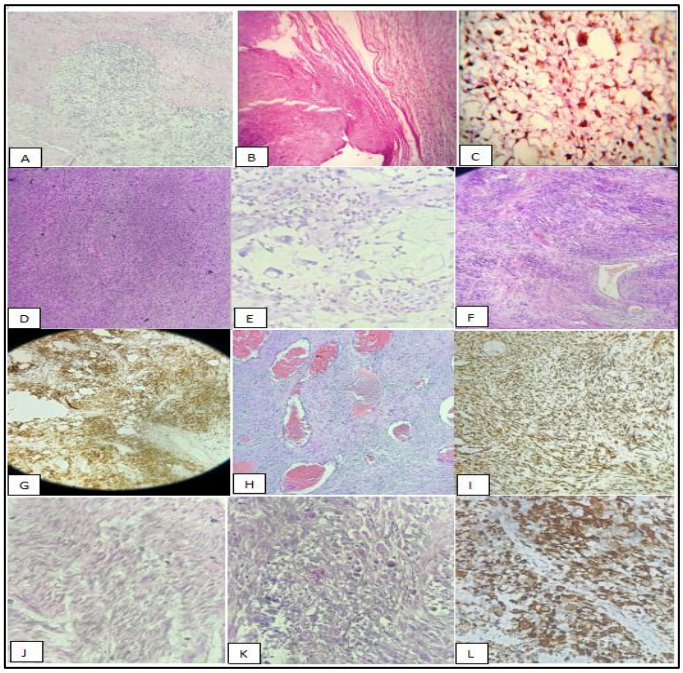

Figure 1: A) Myxoid Liposarcoma, B) Dedifferentiated Liposarcoma, C) Dedifferentiated Liposarcoma - MDM2, D) Inflammatory Myofibroblastic Tumour, E)Myxofibrosarcoma, F)Solitary Fibrous Tumour, G) Solitary Fibrous Tumour- CD34,H) Cellular Angiomyoma, I)Cellular Angiomyoma- SMA, J)Leiomyosarcoma, K)Pleomorphic Rhabdomyosarcoma, L) Pleomorphic Rhabdomyosarcoma -Desmin.

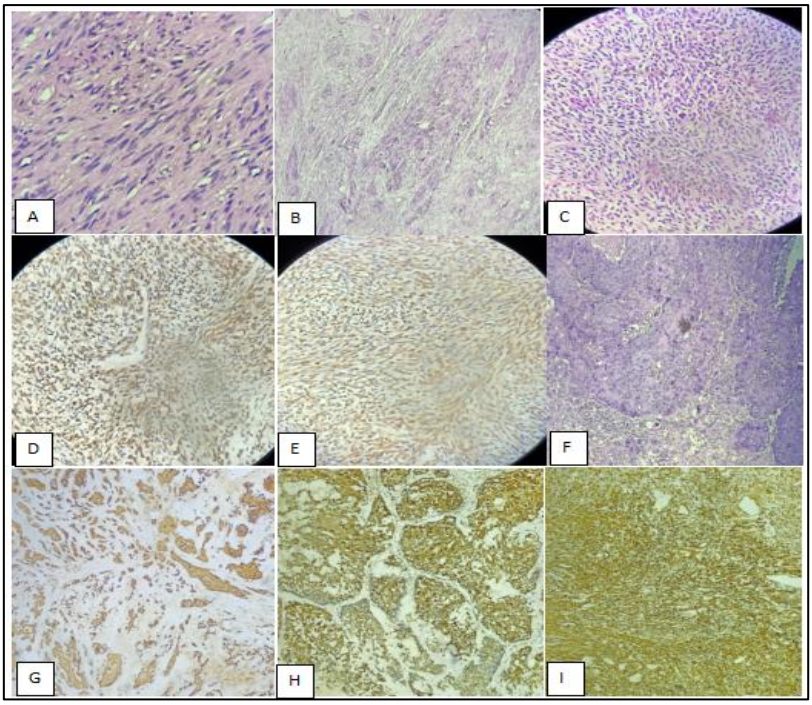

Figure 2: A) Schwannoma, B) Malignant peripheral nerve sheath tumour (MPNST), C) MPNST, D) MPNST-S100, E) MPNST-Bcl2, F) Malignant Mixed Tumour (MMT), G) MMT-PanCk, H) MMT- S100, I) MMT-Vimentin.

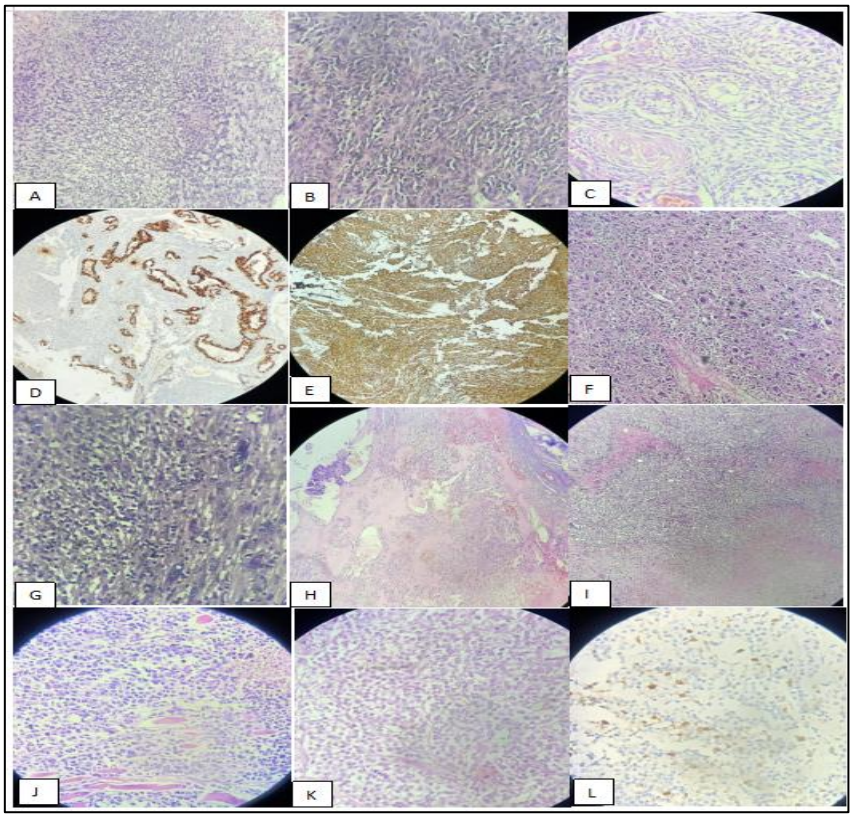

Figure 3: A) Extraskeletal myxoid chondrosarcoma, B) Synovial Sarcoma (SS)(Monophasic), C) Synovial Sarcoma (Biphasic), D) SS-PanCK, E) SS-Bcl2, F) Undifferentiated pleomorphic sarcoma (UPS), G) Spindle cell sarcoma H to J) Dedifferentiated chondrosarcoma, K) Clear cell sarcoma (CCS), L) CCS-S100.

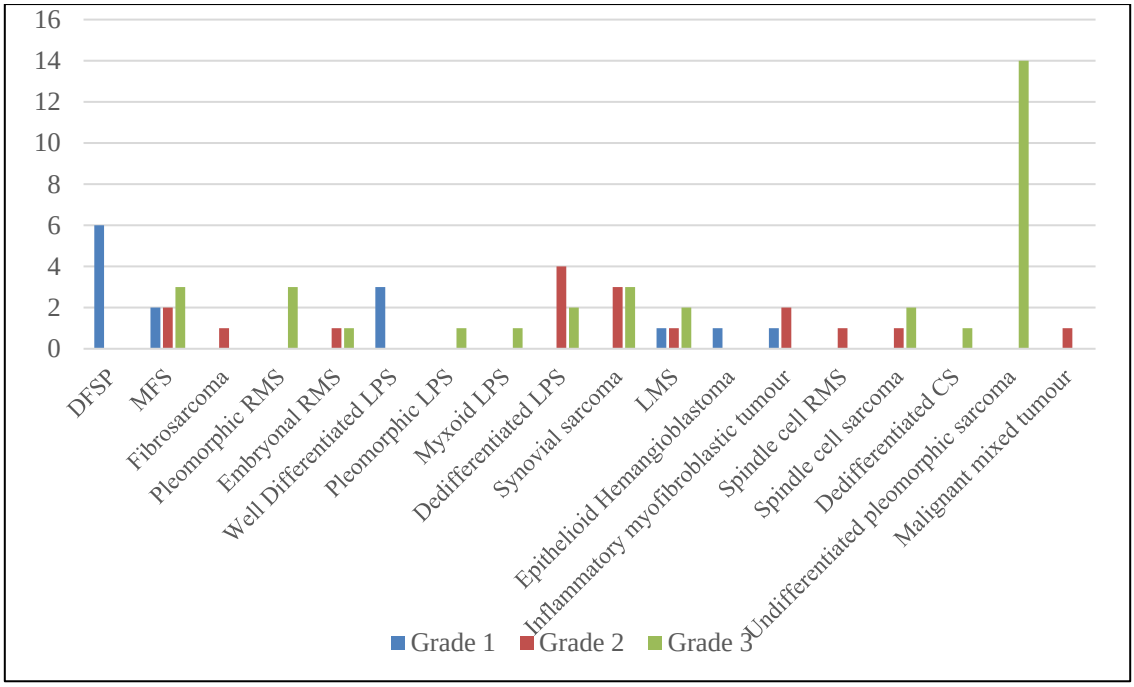

Figure 4: Different types of soft tissue tumours with the frequency of their respective FNCLCC grades.

Tumours of uncertain differentiation

Tumours of uncertain differentiation comprised of 26.92 % (28/104) cases, with 25.96% (27/104) malignant cases and only 0.96% (1/104) case of intermediate type tumour, Malignant mixed tumour (Figure 2F to I) FNCLCC grade 2.

The highest cases were of Undifferentiated pleomorphic sarcoma FNCLCC grade 3, (Figure 3F) 13.46% (14/104) with 11.54% (12/104) incidence in lower limb alone. It was followed by Synovial sarcoma, (Figure 3B to E) 5.77% (6/104) with equal incidence in upper and lower limb, 2.88% (3/104) each, with 2.88% (3/104) each in FNCLCC grade 2 and 3 respectively; Spindle cell sarcoma, (Figure 3G) 2.88% (3/104), 0.96% (1/104) in grade 2 and 1.92% (2/104) in grade 3 respectively; Clear cell sarcoma, (Figure 3K & L) 1.92% (2/104) and 0.96% (1/104) each of Dedifferentiated Chondrosarcoma FNCLCC grade 3 (Figure 3H to J) and extraskeletal myxoid chondrosarcoma (Figure 3A).

Immunohistochemical analysis

Adipocytic tumours

Immunohistochemical stains used for the diagnosis of Dedifferentiated liposarcoma were MDM2 (+), S100 (+).

Fibroblastic tumours

Immunohistochemical stains used for the diagnosis of myxofibrosarcoma were CD34 (+), SMA (+/-), vimentin (+/-), S100 (-). Inflammatory myofibroblastic tumour were Vimentin (+), ALK (+), S100 (-), CD117 (-), Malignant solitary fibrous tumour CD34 (+), Cd99 (+), Bcl2 (+), S100 (-), PanCK (-).

Vascular tumours

Immunohistochemical stains used for the diagnosis of Angiosarcoma were CD31 (+), CD34 (+), ERG (+).

Perivascular tumous

Immunohistochemical stains used for the diagnosis of Cellular Angiomyoma were SMA (+), Vimentin (+), CD117 (-), CD34 (-), S100 (-) and Ki67 2%.

Smooth muscle tumours

Immunohistochemical stains used for the diagnosis of Leiomyosarcoma were SMA (+), CD34 (-), S100 (-).

Skeletal muscle tumours

Immunohistochemical stains used for the diagnosis of Rhabdomyosarcoma were Desmin (+), Myogenin (+) and Vimentin (+).

Nerve sheath tumours

Immunohistochemical stains used for the diagnosis of Malignant Peripheral nerve sheath tumour were S100 (patchy +), Vimentin (+), Bcl 2 (+), CD34 (-), SMA (-), Neurofibroma S100 (+) and CD34 (+) and Schwannoma S100 (diffuse +).

Tumours of uncertain differentiation

Immunohistochemical stains used for the diagnosis of Malignant mixed tumour were PanCk (+), SMA (+), Vimentin (+) and S100 (+); Synovial sarcoma were CD99 (+), PanCK (+), EMA (+), Vimentin (+), Bcl2 (+) and S100 (-), CD34 (-) and Clear cell sarcoma S100 (+), SMA (-), Desmin (-).

Table 1: Distribution of cases according to WHO Classification of Soft tissue tumours 2020.

Categories			(N)	(N)	(%)
Adipocytic (15)	Benign (4)	1. Lipoma	4	H - 1 A - 1 L - 1 U - 1	3.85
	Malignant (11)	1.Well Differentiated Liposarcoma	3	A - 1 L - 1 U - 1	2.88
		2.Myxoid liposarcoma	1	L - 1	0.96
		3.Pleomorphic liposarcoma	1	A - 1	0.96
		4.Dedifferentiated liposarcoma	6	A - 5 L - 1	5.77
Fibroblastic (28)	Benign (2)	Angiofibroma	2	A - 1 L - 1	1.92
	Intermediate (LA) (13)	1.Fibromatosis	1	U - 1	0.96
		2. Desmoid fibromatosis	4	T - 1 L - 3	3.85
		3.Nodular Fascitis	1	A - 1	0.96
		4.Fibrous histiocytoma	1	T - 1	0.96
		5.Dermatofibrosarcoma protuberans	6	H - 2 T - 1 U - 2 L - 1	5.77
	Intermediate (RM) (3)	1.Inflammatory myofibroblastic tumour	3	T - 1 A - 2	2.88
	Malignant (10)	1.Myxofibrosarcoma low grade	2	U - 1 A - 1	1.92
		2.Myxofibrosarcoma high grade	5	T - 1 U - 1 L - 3	4.81
		3.Myofibroblastic sarcoma	1	L - 1	0.96
		4.Fibrosarcoma	1	T - 1	0.96
		5.Malignant Solitary Fibrous tumour	1	A - 1	0.96
Vascular (3)	Malignant (3)	1.Epithelioid hemangioendothelioma	1	T - 1	0.96
		2.Angiosarcoma	2	A - 1 L - 1	1.92
Perivascular (1)	Benign (1)	1.Cellular angiomyoma	1	A - 1	0.96
Smooth muscle (4)	Malignant (4)	1.Leiomyosarcoma	3	A - 2 U - 1	2.88
		2.Pleomorphic Leiomyosarcoma	1	L - 1	0.96
Skeletal muscle (6)	Malignant (6)	1.Pleomorphic rhabdomyosarcoma	3	U - 1 L - 2	2.88
		2.Embryonal rhabdomyosarcoma	2	H - 1 L - 1	1.92
		3.Spindle cell rhabdomyosarcoma	1	U - 1	0.96
Nerve sheath tumours (19)	Benign (14)	1.Schwannoma	7	H - 5 U - 1 T - 1	6.73

Continued.

Categories			(N)	(N)	(%)
		2.Ancient schwannoma	4	H- 2 T - 1 A - 1	3.85
		3.Neurofibroma	3	T - 1 A - 1 U - 1	2.88
	Malignant (5)	1.Malignant peripheral nerve sheath tumour	5	U - 1 L - 2 A - 1 H - 1	4.81
Uncertain differentiation (28)	Intermediate (RM) (1)	1.Malignant mixed tumour	1	L - 1	0.96
	Malignant (27)	1.Synovial sarcoma	6(3/3)	U - 3 L - 3	5.77
		2.Undifferentiated pleomorphic sarcoma	14	T - 1 U - 1 L - 12	13.46
		3. Spindle cell sarcoma	3	U - 1 L - 2	2.88
		4.Extraskeletal myxoid chondrosarcoma	1	A - 1	0.96
		5.Clear cell sarcoma	2	U - 1 L - 1	1.92
		6.Dedifferentiated Chondrosarcoma	1	T - 1	0.96
Total			104	H - 12 T - 11 A - 22 U - 20 L - 39	100

Abbreviations: H-Head and Neck, T-Thorax, A-Abdomen, U-Upper limb, L-Lower limb, LA-Locally Aggressive, RM-Rarely Metastasizing

Table 2: Distribution of soft tissue tumours according to FNCLCC grading system.

	Grade 1	Grade 2	Grade 3	Total
Dermatofibrosarcoma protuberans	6	0	0	6
Myxofibrosarcoma	2	2	3	7
Inflammatory myofibroblastic tumour	1	2	0	3
Fibrosarcoma	0	1	0	1
Spindle cell rhabdomyosarcoma	0	1	0	1
Embryonal rhabdomyosarcoma	0	1	1	2
Pleomorphic rhabdomyosarcoma	0	0	3	3
Well Differentiated Liposarcoma	3	0	0	3
Myxoid liposarcoma	0	0	1	1
Pleomorphic liposarcoma	0	0	1	1
Dedifferentiated liposarcoma	0	4	2	6
Leiomyosarcoma	1	1	2	4
Epithelioid hemangioendothelioma	1	0	0	1
Malignant mixed tumour	0	1	0	1
Synovial sarcoma	0	3	3	6
Spindle cell sarcoma	0	1	2	3
Undifferentiated pleomorphic sarcoma	0	0	14	14
Dedifferentiated Chondrosarcoma	0	0	1	1
Total	14	17	33	64

Table 3: Comparison of frequency of benign and malignant soft tissue tumours.

S. no.	Author	No. of cases	Benign (N)	Benign (%)	Malignant (N)	Malignant (%)	Benign: Malignant ratio
1	Myhre et al (1981)[5]	1403	1331	94.6	72	5.4	18.5:1
2	Kransdorf (1995)[6]	31047	18677	60.2	12370	39.8	1.5:1
3	Baig MA (2005)[7]	137	113	82.48	24	17.52	4.7:1
4	Agravat et al, (2010)[8]	92	86	93.5	6	6.5	14.4:1
5	Bashar et al (2010)[9]	93	70	75.2	23	24.8	3:1
6	Vikas et al (2012)[10]	154	138	89.6	16	10.4	8.6:1
7	Kinjal et al (2015)[11]	131	122	93.13	9	6.87	13.5:1
8	Umarani et al (2015)[12]	220	204	92.73	11	5	18.5:1
9	Chakrabarti et al (2015)[13]	150	140	93.3	9	6	15.6:1
10	Narayanan (2016)[14]	291	273	93.8	8	2.8	34.1:1
11	Baste et al (2017)[15]	70	67	95.72	3	4.28	22.3:1
12	Damani et al (2020)[16]	235	225	95.75	6	2.55	37.5:1
13	Raasi et al (2022)[17]	100	50	50	39	39	1.3:1
14	Present study	104	21	20.19	66	63.46	1:3.14

Table 4: Comparison of site wise distribution of soft tissue tumours.

S. no.	Study	Benign	Malignant
1	Kransdorf et al (1995)[6,20]	Upper extremity	Lower extremity
2	Baig et al (2005)[7]	Head & neck, Trunk	Lower extremity
3	Narhire et al (2012)[10]	Upper extremity	-
4	Batra et al (2013)[18]	Upper extremity	Lower extremity
5	Janaki et al (2014)[19]	Extremities	Lower extremity
6	Bera et al (2015)[11]	Trunk	Lower extremity
7	Raasi et al (2022)[17]	Upper extremity	Lower extremity
8	Present study	Upper extremity, Trunk	Lower extremity

Table 5: Comparative study of grading of soft tissue sarcomas by FNCLCC system.

S. no	Study	Grade 1 (%)	Grade 2 (%)	Grade 3 (%)
1	Hashimoto et al (1992)[21]	15.52	27.76	56.71
2	Aydin et al (1999)[22]	20	34.3	45.7
3	Raasi et al (2022)[17]	21	37	42
4	Present study	21.88	26.56	51.56

DISCUSSION

The present study was undertaken to analyze the histopathological spectrum of soft tissue tumours and their prevalence in relation to age, sex and site in our set up. The present study consisted of 104 soft tissue tumours, which constituted only about 1.1% of all neoplasms during the study period. Malignant tumours were the most common in our study as the institute is a dedicated cancer facility. Benign tumours constituted about 20.19% (21/104) of cases, intermediate grade tumours about 16.35% (17/104) and malignant tumours about 63.46% (66/104). The age range of soft tissue tumours was 7 to 80 years and the most common age group involved was 41-50 years. Soft tissue tumours were slightly more common in females (53.85%) than males (46/15%) with male to female ratio of 1:1.17.

The sites of predilection were upper extremity and trunk for benign tumours and lower extremities for malignant tumours. Most common soft tissue tumours were fibroblastic tumours and tumours of uncertain differentiation (26.92%) each followed by peripheral nerve sheath tumours (18.27%). Most common malignant soft tissue tumour was undifferentiated pleomorphic sarcoma (13.46%) followed by myxofibrosarcoma (6.73%) and malignant peripheral nerve sheath tumour

(4.81%). In FNCLCC grading, most of the sarcomas were grade 3 (51.56%), followed by grade 2 (26.56%) and grade 1 (21.88%) (Table 2).

The results of this study are similar to those of Kransdorf MJ et al.[6,20] Narhire et al, Batra et al, Bera et al and Raasi et al, when comparing the frequency of common site of benign and malignant tumours (Table 4).[10,11,17,18] Also, this study has striking resemblance to those of Hiroshi Hashimoto et al, Aydin et al and Raasi et al, on comparison of the frequency of different grades of soft tissue tumours by the FNCLCC grading system (Table 5).[17,21,22]

However, the ratio of benign to malignant tumours in this study is 1:3.14 which is in sharp contrast to the other similar studies by Myhre-Jensen et al, Kransdorf et al, Baig et al, Agravat et al, Bashar et al, Narhire et al, Kinja et al, Umarani et al, Chakrabarti et al, Narayanan et al, Baste et al, Damani et al, Raasi et al, where the ratio is reversed with greater percentage of cases being benign (Table 3).[5-17] This could be attributed to the fact that the present study was being conducted in a dedicated tertiary cancer set up which facilitates that majority of cases being admitted or referred here are invariably malignant.

This study is one of its kind showing the varied spectrum with site specificity in a distinct region of India. However, it is not a true representation of the actual incidence of benign and malignant soft tissue tumours as it shows the scenario in a tertiary cancer centre, which as the name suggests, receives a greater load of malignant cases. Having said that, this study is equally significant as it shows such a great spectrum of malignant soft tissue tumours.

Most cases were diagnosed on the histopathological examination as it is the gold standard and the first test that should guide further ancillary investigations. Molecular test to further confirm each case is not an essential tool given the current clinical demographics but the same may be done in the future as an extension to the current study. Another important area to work is the prognostics which could be done in a longitudinal study in the future, this study could not highlight that owing to its cross-sectional nature.

CONCLUSION

Though soft tissue tumours are rare, the incidence of intermediate and malignant soft tissue tumours are increasing due to early detection and diagnosis aided by immunohistochemistry and molecular testing. FNCLCC grading and TNM staging helps to prognosticate and guide therapeutic interventions leading to improved outcomes and overall survival.

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Ethical approval: The study was approved by the Institutional Ethics Committee

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