Journal of Population Therapeutics & Clinical Pharmacology

RESEARCH ARTICLE
DOI: 10.53555/fhjtrr86

CYTO-HISTOPATHOLOGICAL STUDY OF SOFT TISSUE NEOPLASMS WITH RELEVANT IMMUNO-HISTOCHEMICAL STAINS.

Dr. Vishakha Vidyadhar Kothikar[1*], Dr. Vishal Sopanrao Kale[2]

[1*]Assistant professor at Department of Pathology, GMC Amravati, Maharashtra, India Email Id- vishakhakothikar1120@gmail.com
[2]Medical officer Municipal corporation Amravati, Maharashtra, India Email Id- vishal9423444341@gmail.com

***Corresponding Author:** Dr. Vishakha Vidyadhar Kothikar
*Department of Pathology, GMC Amravati, Maharashtra, India Email: vishakhakothikar1120@gmail.com

Declaration -
- Ethics approval and consent to participate – Patient's consent was taken completely.
- Consent for publication – All authors give permission for the publication
- Availability of data and materials – Data was made available by the corresponding author.
- Competing interests – No competing interest was recorded.
- Funding – There is no funding for the research.
- Authors' contributions - 1. Dr. Vishakha Vidyadhar Kothikar: Conceptualization, formal analysis, resources, Data curation
2. Dr. Vishal Sopanrao Kale: Validation, Writing original Draft, Methodology

ABSTRACT

Background: Soft tissue neoplasms (STNs) are a diverse group of tumors with varying behavior, ranging from benign to malignant. Due to overlapping features, accurate diagnosis can be challenging using cytology or histopathology alone. Immunohistochemical (IHC) staining helps in precise classification by identifying tumor origin and differentiation. This study highlights the role of combined cytohistopathological evaluation with relevant IHC markers in improving diagnostic accuracy of STNs.

Method: This four-year study (Jan 2012–June 2016) included both retrospective and prospective cases of benign and malignant soft tissue tumors diagnosed at a government tertiary care center in Maharashtra. Clinical, radiological, cytological, and gross findings were retrieved from histopathology records. FNAC was performed using 20–25G needles, and smears were stained with H&E, Pap, and Leishman stains. Gross specimens were evaluated for size, location, and morphological features. Tumors were classified and graded per WHO criteria. IHC was conducted on 3µm sections using enzyme-labeled antibodies and DAB chromogen. Data were analyzed using Primer of Biostatistics v7.0, with significance set at $p < 0.05$.

Results: In this study, out of 657 STTs, 93.6% were benign, 3.2% intermediate, and 3.2% malignant. STTs were most common in the 21–40 age group. Males were mainly affected in the third decade, females in the fifth. Adipocytic tumors were the most common subtype (67.28%),

followed by peripheral nerve sheath tumors (14.92%). Among malignant STTs, tumors of uncertain differentiation (33.33%) were most frequent. The extremities were the most common site (43.22%). FNAC showed high accuracy with 9 true positives, 112 true negatives, 1 false negative, and no false positives.

Conclusion: Benign soft tissue tumors were overwhelmingly more common than malignant ones, with adipocytic tumors being the most frequent subtype. STTs predominantly affected young to middle-aged adults, with extremities as the most common site. FNAC proved to be a reliable diagnostic tool, showing high accuracy in differentiating benign from malignant lesions.

Keywords: Soft Tissue Neoplasms; Neoplasms, Benign; Neoplasms, Malignant; Immunohistochemistry; Biopsy, Fine-Needle; Histological Techniques; Cytodiagnosis

INTRODUCTION

Soft tissue tumors (STTs) represent a diverse group of mesenchymal neoplasms arising in extraskeletal, non-epithelial tissues, excluding the viscera, brain coverings, and lymphoreticular system. Despite their often non-specific clinical presentation, these tumors exhibit a wide range of morphological differentiation. In many cases, histopathological examination alone is sufficient for diagnosis. However, in some instances, the complex and overlapping morphological features may leave the pathologist uncertain about the exact nature of the neoplasm, even after thorough evaluation [1].

The advent of ancillary techniques, particularly immunohistochemistry (IHC), has significantly enhanced diagnostic accuracy by providing supportive information that aids in reaching a definitive diagnosis [2]. IHC has become an indispensable tool in the diagnostic workup of STTs, especially when routine hematoxylin and eosin (H&E) staining is inconclusive. It aids in identifying specific lineages of differentiation and detecting molecular alterations characteristic of certain tumor types [3,4]. In some cases, markers such as MDM2 and CDK4 are instrumental in diagnosing atypical lipomatous tumors, while STAT6 is specific for solitary fibrous tumors. Similarly, H3K27me3 loss is associated with malignant peripheral nerve sheath tumors, and DOG1 expression is indicative of gastrointestinal stromal tumors [5].

Recent advances have led to the development of novel immunohistochemical markers that correlate with underlying genetic alterations [6]. These include BCOR for BCOR-rearranged sarcomas, ALK for inflammatory myofibroblastic tumors and CAMTA1 for epithelioid hemangioendothelioma. The integration of these markers into diagnostic protocols has improved the precision of tumor classification and has prognostic and therapeutic implications [7].

However, using IHC also has its challenges. Variability in marker expression, antigen preservation, and interpretation can lead to diagnostic pitfalls. Therefore, a comprehensive approach that combines cytological, histological, immunohistochemical, and, when necessary, molecular analyses is essential for accurate diagnosis.

This study aims to evaluate the cytohistopathological features of soft tissue neoplasms, emphasizing the role of relevant immunohistochemical stains in enhancing diagnostic accuracy and contributing to effective patient management.

MATERIALS AND METHODS

This study included all benign and malignant soft tissue tumours diagnosed over a four-year period at a government-affiliated tertiary care centre in Maharashtra, comprising both retrospective cases (Jan 2012–June 2014) and prospective cases (July 2014–June 2016). Clinical, radiological, cytological, and gross findings were obtained from histopathology records. All incisional and excisional biopsies of soft tissue tumours were included, while pseudosarcomas and gastrointestinal soft tissue tumours were excluded.

Fine Needle Aspiration Cytology (FNAC) was performed using a 20–25G needle. Smears were fixed using a mixture of ether and 95% ethanol for H&E and Pap stains, and Leishman stain was used on unfixed smears. Gross specimens were assessed for location, size, borders, color, cut

surface, and features like necrosis, hemorrhage, and calcification. At least four sections per tumour, including the periphery and surrounding tissues, were processed with standard paraffin embedding and stained with haematoxylin and eosin.
Tumours were classified and graded based on WHO histopathological criteria. IHC was performed on 3µm sections using enzyme-labeled antibodies, involving antigen retrieval, blocking, staining with DAB chromogen, and counterstaining with haematoxylin. Positive and negative controls were included in each IHC batch to assess immunoreactivity.

Statistical Analysis:
Data were analyzed using the *Primer of Biostatistics* version 7.0 software. Frequencies and percentages were calculated for types of soft tissue tumours, their benign or malignant nature, demographic data, and site distribution. The Chi-square test was used to evaluate associations between tumour size and other variables. A p-value < 0.05 was considered statistically significant.

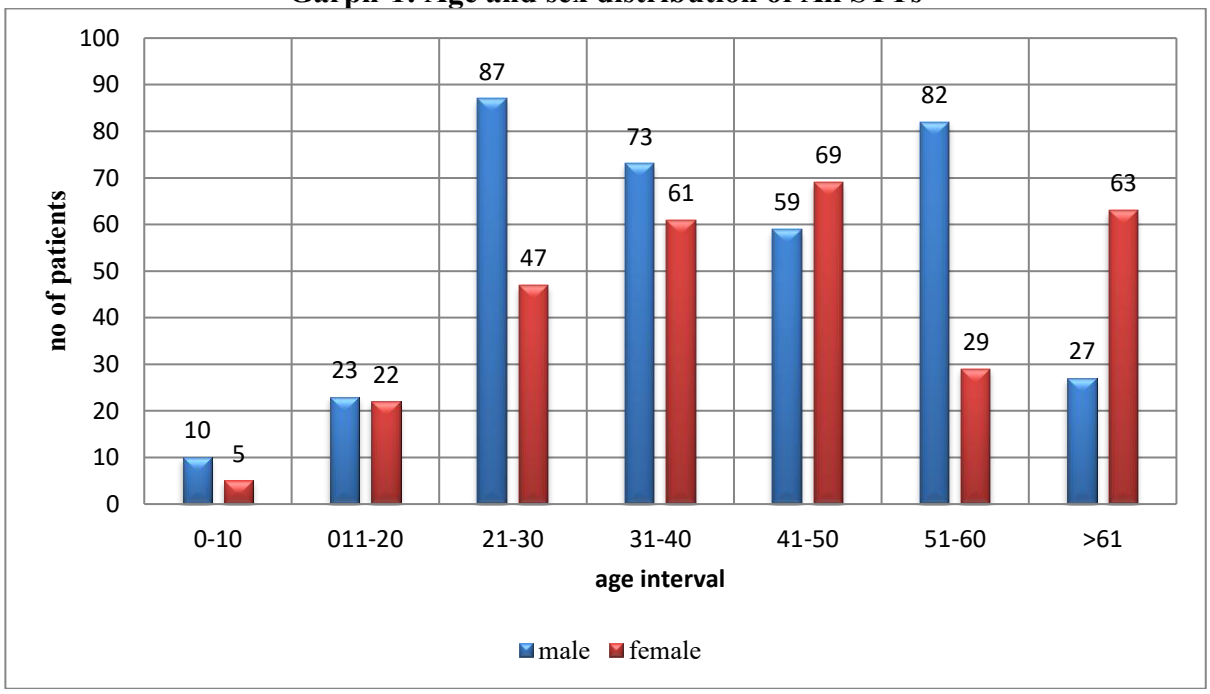
RESULTS:

Table-1: Distribution of All

Type	Total no. of STTs-(n=657)	Percentage
Benign	615	93.60%
Intermediate	21	3.20%
Malignant	21	3.20%
Total	657	100%

The above table 1 showed that the majority were benign, accounting for 615 cases or 93.60%. Both intermediate and malignant tumors were less common, with each category comprising 21 cases, representing 3.20% each. Overall, benign tumors were found to be overwhelmingly more prevalent than intermediate or malignant ones.

Garph-1: Age and sex distribution of All STTs



STT were found to be most common in young to middle-aged adults, particularly in the 21–30 and 31–40-year age ranges. A gender-based distribution indicated that males were more frequently affected in the third decade, while females showed a higher incidence in the fifth decade.

Table-2: Distribution of All STTs into histopathological subtypes

Tumour subtypes	Frequency	Percentage
Adipocytic tumours	442	67.28%
Fibroblastic/myofibroblastic tumours	22	3.35%
Fibrohistiocytic tumour	26	3.96%
Smooth muscle tumour	5	0.76%
Skeletal muscle tumour	2	0.30%
Vascular tumour	42	6.39%
Pericytic tumour	6	0.91%
Peripheral nerve sheath tumours	98	14.92%
Chondro osseous tumours	1	0.15%
Tumours of uncertain differentiation	9	1.37%
Undifferentiated/Unclassified sarcoma	4	0.61%
Total	657	100%

The above table showed that the adipocytic tumors were the most frequent, accounting for 67.28% of cases. Peripheral nerve sheath tumors followed at 14.92%, while vascular tumors made up 6.39%. Other subtypes, including fibroblastic/myofibroblastic, fibrohistiocytic, and tumors of uncertain differentiation, were less common. Rare cases included smooth and skeletal muscle tumors, pericytic tumors, chondro-osseous tumors, and undifferentiated sarcomas.

Table-3: Distribution of Malignant STTs into histopathological subtypes

Tumour subtype	Total no of cases.
Adipocytic tumours	01(4.76%)
Fibro/myofibroblastic tumours	01(4.76%)
Smooth muscle tumours	02(9.52%)
Skeletal muscle tumours	02(9.52%)
Vascular tumours	01(4.76%)
Peripheral nerve sheath tumours	03(14.29%)
Tumours of uncertain differentiation	07(33.33%)
Undiff /Unclassified sarcoma	04(19.05%)
Total	21(100%)

The above table showed that thetumors of uncertain differentiation were the most common, accounting for 33.33% of cases. Undifferentiated/unclassified sarcomas made up 19.05%, while peripheral nerve sheath tumors comprised 14.29%. Skeletal and smooth muscle tumors each represented 9.52% of the cases. Less frequent subtypes included adipocytic, fibro/myofibroblastic, and vascular tumors, each contributing 4.76% to the total.

Table-4: Site distribution of benign STTs

Tumours	Extremities	Head and neck	Back and shoulder	Trunk and abdomen	Others	Total
Adipocytic	166	111	110	41	5	433
Fibro/myofibroblastic	5	3	1	0	2	11
Fibrohistiocytic	20	0	4	0	0	24
Smooth muscle	2	0	0	1	0	3
Skeletal muscle	0	0	0	0	0	0
Vascular tumours	14	21	4	0	1	40
Pericytic tumours	5	1	0	0	0	6
PNST	47	27	15	5	1	95
Chondro osseous tumours	1	0	0	0	0	1
Tumours of uncertain dif	0	0	0	0	2	2
Total	260	163	134	47	11	615
Percentage	-42.11%	-26.50%	-21.79%	-7.64%	-1.79%	-100%

The above table showed that themost were located in the extremities (42.11%), followed by the head and neck (26.50%) and back and shoulder regions (21.79%). Adipocytic tumors were the most frequent subtype across all major sites. Peripheral nerve sheath tumors were mainly found in the extremities and head and neck, while vascular tumors were more common in the head and neck region. Other subtypes such as fibrohistiocytic and pericytic tumors occurred primarily in the extremities.

Table-5: Distribution of soft tissue tumours according to the site and biologic potential.

Sr no	Site	Benign	Intermediate	Malignant	Total
1	Extremities	260	12	12	284(43.22%)
2	Head and neck	163	3	2	168(25.57%)
3	Back and shoulder	134	2	4	140(21.31%)
4	Trunk and abdomen	47	4	3	54(8.22%)
5	Others	11	0	0	11(1.67%)
6	Total	615	21	21	657(100%)

The above table 5 showed that the extremities were the most common site, accounting for 43.22% of cases. This was followed by the head and neck region with 25.57%, and the back and shoulder with 21.31%. The trunk and abdomen comprised 8.22%, while other locations made up only 1.67% of the total. Benign tumors predominated across all regions, with malignant and intermediate tumors appearing less frequently.

Table-6: Cytohistopathological correlation of soft tissue tumours

	HISTOPATHOLOGY			**Total**
		Malignant	**Benign**	
FNAC	**Malignant**	09(TP)	0(FP)	9
	Benign	1(FN)	112(TN)	113
	Total	10	112	122

In this analysis of 122 cases compared by FNAC and histopathology, FNAC correctly identified 9 malignant cases (true positives) and 112 benign cases (true negatives). There was 1 false negative, where a malignant tumor was misclassified as benign and no false positives. This indicated a high accuracy of FNAC in distinguishing between benign and malignant soft tissue tumors.

DISCUSSION

In the present study, benign STTs were overwhelmingly the most prevalent, accounting for 93.60% of all cases. In contrast, both intermediate and malignant tumors were significantly less common, each representing only 3.20% of the total. This suggests that most STTs affecting the lower extremities in our study population are non-aggressive in nature, with malignant transformation being relatively rare.

This finding aligns with the study by **Chandralekha J et al. [8] (2015)**, who reported a higher prevalence of benign STTs (62.5%) compared to malignant ones (37.5%) in a series of 320 cytologically evaluated cases. However, the proportion of malignant tumors in their study was notably higher than in the current study, indicating a greater representation of malignant lesions in their cohort.

Regarding histopathological subtypes, our study found that adipocytic tumors were the most common, constituting 67.28% of all STTs, followed by peripheral nerve sheath tumors (14.92%), vascular tumors (6.39%), and fibrohistiocytic tumors (3.96%). Less frequently observed were fibroblastic/myofibroblastic tumors (3.35%), skeletal muscle tumors (0.30%), and chondro-osseous tumors (0.15%), while tumors of uncertain differentiation and undifferentiated sarcomas together accounted for 1.98%. This distribution confirms the predominance of adipocytic tumors, especially

lipomas, consistent with the findings of **Dash AK et al. [9] (2019)**, who reported that lipomas made up 48.7% of their 463 soft tissue lesions, with benign lesions comprising 74.9% of their cohort.
In terms of tumor location, our study observed that the extremities were the most frequently affected site (43.22%), followed by the head and neck (25.57%), back and shoulder (21.31%), and the trunk and abdomen (8.22%), with other sites being rare (1.67%). These results are comparable to those reported by **Atram et al. [10] (2023)**, who also found a predominance of benign STTs and noted a benign-to-malignant ratio ranging from 10:1 to 100:1. Notably, our study had a relatively lower benign-to-malignant ratio of 3:1, suggesting a slightly higher proportion of malignant cases than typically observed. A similar trend was seen in the study by **Nayak et al. [11](2019)**, who reported a ratio of 4.7:1.
Cytohistopathological correlation in our study demonstrated a high diagnostic accuracy for Fine Needle Aspiration Cytology (FNAC). Among 122 cases, FNAC correctly identified 9 malignant tumors as true positives and 112 benign tumors as true negatives. There were no false positives, but one benign tumor was misclassified as malignant, resulting in a single false negative. These findings underscore the high sensitivity and specificity of FNAC in diagnosing STTs.
Comparable results were seen in the study by **Dash AK et al. [9] (2019)**, where FNAC correctly identified 344 benign and 114 malignant cases, with only 3 false negatives and 2 false positives, indicating strong concordance with histopathological findings. Similarly, **Atram MA et al. [10] (2023)** reported a sensitivity of 87.21%, specificity of 96.69%, positive predictive value (PPV) of 89.92%, and negative predictive value (NPV) of 95.71%, with a statistically significant correlation between cytology and histopathology ($P < 0.05$). These findings, together with ours, reinforce the utility of FNAC as a reliable, minimally invasive, and cost-effective diagnostic tool for initial evaluation of STTs.

CONCLUSION

The diagnosis of STTs relies on a multimodal approach. Routine haematoxylin and eosin (H&E) staining remains fundamental for identifying key histological features. FNAC is a minimally invasive, cost-effective tool for initial assessment. Gross examination and proper tissue sampling are essential for diagnostic accuracy. Immunohistochemistry and special stains assist in resolving complex cases, though their use may be limited by cost and availability.
Immunocyto histopathological evaluation, which integrates cytology, histology, and immunohistochemistry, is considered the gold standard. A resource-sensitive, combined diagnostic strategy ensures the best outcomes in managing soft tissue tumours.

REFERENCES

1. Maiti B, Bhattacharya S, Banerjee U, Bhattacharya SK, Mondal K. Immunohistochemical approach to diagnosis of soft tissue tumors of lower extremities with its possibilities and limitations. *Int J Med Res Prof*. 2017; 3(3):254–61.
2. Choi JH, Ro JY. The Recent Advances in Molecular Diagnosis of Soft Tissue Tumors. *International Journal of Molecular Sciences*. 2023; 24(6):5934.
3. Wei S, Henderson-Jackson E, Qian X, Bui MM. Soft Tissue Tumor Immunohistochemistry Update: Illustrative Examples of Diagnostic Pearls to Avoid Pitfalls. *Arch Pathol Lab Med*. 2017; 141(8):1072-1091.
4. Cordier F, Ferdinande L, Hoorens A, Van de Vijver K, Van Dorpe J, Creytens D. Soft Tissue and Bone Tumor Diagnostics: Harnessing the Power of Molecular Techniques. *Genes*. 2023; 14(12):2229
5. Anderson WJ, Jo VY. Diagnostic Immunohistochemistry of Soft Tissue and Bone Tumors: An Update on Biomarkers That Correlate with Molecular Alterations. *Diagnostics (Basel)*. 2021; 11(4):690.
6. Schaefer IM, Hornick JL. Diagnostic Immunohistochemistry for Soft Tissue and Bone Tumors: An Update. *Adv Anat Pathol*. 2018; 25(6):400-412.

7. PDQ Pediatric Treatment Editorial Board. Childhood Soft Tissue Sarcoma Treatment (PDQ®): Health Professional Version. 2025 Apr 21. In: PDQ Cancer Information Summaries [Internet]. Bethesda (MD): National Cancer Institute (US); 2002-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK65923/
8. Chandralekha J, Bhagya Lakshmi A, Vijaya Bharathi I, Rajagopal M. Cytohistopathological and immunohistochemical correlation of soft tissue tumors. Int J Res Med Sci 2015; 3:475-83.
9. Dash AK, Tripathy M, Mohanty S, Tripathy K, Nanda SN, Mishra DP. Cytohistopathological and Immunohistochemical Correlation of Soft Tissue Lesions. *Int J Med Res Prof.* 2019;5(4):81–88.
10. Atram MA, Ghongade P, Gupta A, Gangane NM. Cytohistopathological and Immunohistochemicalcorrelation of soft tissue tumors: A retrospective study at a tertiary care rural hospital in central India.Chron Dis J 2023; 11(3): 134-44.
11. Nayak S, Dutta G, Mohapatra K, Agarwal KC. FNAC of soft tissue tumor with histopathological correlation in western odisha-a 7years prospective and retrospective study. Global Journal for Research Analysis. 2019; 8(2): 20-2.