ejpmr, 2021,8(4), 620-626

SJIF Impact Factor 6.222

EUROPEAN JOURNAL OF PHARMACEUTICAL AND MEDICAL RESEARCH

www.ejpmr.com

Research Article

ISSN 2394-3211

EJPMR

HISTOMORPHOLOGICAL SPECTRUM OF SOFT TISSUE TUMORS IN A TERTIARY CARE CENTER: A 5yr STUDY

Apoorva Saraswat*, Ashmeet Kaur, Kusum Mathur and Arpita Jindal

Villa No 86, Auric Villas Prime, Jaisinghpura, Bhankrota, Ajmer Road Jaipur Rajasthan India 302026.

***Corresponding Author: Dr. Apoorva Saraswat**

Villa No 86, Auric Villas Prime, Jaisinghpura, Bhankrota, Ajmer Road Jaipur Rajasthan India 302026.

Article Received on 15/02/2021 **Article Revised on 07/03/2021** **Article Accepted on 27/03/2021**

INTRODUCTION

Soft tissue refers to non-epithelial tissue excluding the skeleton, joints, central nervous system, hematopoietic and lymphoid tissues.[1] Tumors arising in soft tissue, form a varied and complex group that may show a wide range of differentiation.[2] There are more than 50 different tumor entities that make these tumors fairly complex and diagnostically challenging. These tumors account for <1% of all adult tumors and 15% of paediatric tumors.[3]

WHO has subsequently revised its classification of sarcomas thrice; the most recent classification was published in 2020.[4] The etiology of soft tissue tumors is still unclear, known risk factors include inherited syndromes, chemical and radiation exposures, viral infections and genetic mutations.[4,5,6]

Traditionally, the mainstay of treatment for STS has been surgical resection with tumor-free margins, adjuvant or neoadjuvant chemotherapy, and/or radiation therapy.[7,8] Tumor size, grade, stage, and surgical margin status are the most important prognostic factors in these tumors. To date, treatment strategy has been determined more by anatomical site than by histological subtype.[8,9] Only recently have investigators focused significantly on the influence of histology on prognosis.[8,10,11]

Due to their rarity, STSs are always outnumbered by carcinomas in many primary sites, therefore not reported in most researches categorizing cancers with the International Classification of Diseases.[6,12] This hinders the accurate diagnosis and appropriate treatment and at the same time makes it difficult to accumulate a sufficient number of cases of STS at a single institution for statistical analysis.[13] Thereby making the soft tissue tumor literature dominated by retrospective series. This is a single tertiary care center five year study of these soft tissue tumors correlating the demographics, anatomical site, histological features and immunohistochemistry at the same time.

MATERIALS AND METHODS

This is a 5year retrospective study conducted from July 2015-July 2020 in the Department of Pathology, Sawai Man Singh Medical College and Hospital, Jaipur. All the cases diagnosed as soft tissue tumors were analysed and correlated with clinical findings including age, sex and site. The gross and microscopic findings were evaluated in detail on hematoxylin and eosin stained sections. Histologic subtyping was done according to WHO classification of soft tissue tumors 2020. FNCLCC grading was done wherever possible. Immunohistochemistry was done where ever required to reach a final diagnosis.

RESULTS

Of the total 1388 cases included in the study, 1170cases (84.2%) were benign, 159 cases (11.4%) were malignant, and 59 (4.2%) were classified under intermediate category. Among the total STTs, adipocytic tumors formed the largest group of tumors (37.5%), followed by peripheral nerve sheath tumors (PNST) (21.6%) and vascular tumors (17.2%) (Table 2)

Soft tissue tumors were more commonly seen in 21-30yr and 31-40yr old patients. Soft tissue tumors showed a male preponderance with the male to female ratio of 1.2:1. (Figure 1). Individually benign, intermediate tumors showed maximum predilection for head and neck, (*n* = 406; 29.2%, n=18;1.29%), malignant tumors showed predilection for extremities (*n* = 125; 9.0%) (Table 1).

Adipocytic tumors (*n* = 521, [37.5% of soft-tissue tumors])

Benign adipocytic tumors (*n* = 510) included mostly lipomas (*n* =497) and angiolipomas (*n* = 7) and were located superficially in the limbs, head, and neck. Benign variants were seen two decades earlier compared to intermediate variants (atypical lipomatous tumor; *n* = 5) and malignant ones which included, dedifferentiated liposarcoma and myxoid liposarcoma (*n* = 2), pleomorphic liposarcoma and mixed liposarcoma (*n* = 1 each).

Vascular tumors (*n* = 239, [17.20% of soft-tissue tumors])

Haemangioma (*n* = 206) and lymphangioma (*n* = 28) were seen in the head and neck in young patients, while angiosarcoma (*n* = 4) and epithelioid haemangioendothelioma (n=1) were seen in elderly (mean age 50 years) and involved extremities.

Peripheral nerve sheath tumors (*n* = 301 cases [21.6% of soft-tissue tumors])

Benign PNSTs (*n* = 297) included schwannoma (*n* = 222) and neurofibroma (*n* = 75). Benign PNST involved spine followed by the head and neck, whereas malignant PNST (MPNST) (n=4) was seen in extremities as large masses.

Fibroblastic tumors (*n* = 107(7.7%)

Benign cases (fibroma; *n* = 12, fibromatosis; n=10) showed a propensity for the head and neck and extremities, while intermediate tumors (dermatofibrosarcoma protuberance; *n* =33 and solitary fibrous tumor; *n* = 10) were seen in the extremities. Most common malignant fibroblastic tumor was fibrosarcoma (n=10) On IHC, vimentin positivity was a rule, and desmin, CD34, leukocyte common antigen (LCA), smooth muscle antigen (SMA) were negative.

Fibrohistiocytic tumors (*n* = 59; 4.2%)

Benign fibrous histiocytoma (BFH) and giant cell tumor of tendon sheath (GCTT) (*n* = 19 + 32 =51) and plexiform fibrous histiocytoma (MFH; *n* = 4) and giant cell tumor of soft tissue (n=4) showed propensity for extremities. IHC played a limited diagnostic role in MFH which was a diagnosis of exclusion.

Smooth muscle tumors (*n* = 25; 1.8%)

Leiomyosarcomas (LMS) formed the majority (*n* = 15; 1.08%). LMS involved the abdomen, retroperitoneum and lower limb. Dermal leiomyomas (*n* = 10;0.72%) involved the head and neck. On FNCLCC grading, Grade 2 (*n* = 4) and Grade 3 (*n* = 4) LMS were predominant.

Skeletal muscle tumors (*n* = 25; 1.80%)

These included embryonal rhabdomyosarcoma (RMS) (*n* = 18) which involved the head and neck region and were diagnosed in the first decade of life. On IHC, desmin, myogenin and vimentin were positive.

Tumors of pericytic differentiation (*n* = 11; 0.70%)

These included glomus tumor (*n* = 9) and myopericytoma and angioleiomyoma (*n* = 1).

Tumors of uncertain differentiation (*n* = 30; 2.10% of soft-tissue tumors)

Benign and intermediate tumors was not present, while malignant category (*n* = 30) included synovial sarcoma (*n* = 17), primitive neuroectodermal tumour [PNET (*n* = 5)], and epitheloid sarcoma(*n* = 4). Single case of alveolar soft part sarcoma, desmoplastic small round cell tumor, clear cell sarcoma of soft tissue and PECOMA was seen.

Unclassifiable (*n* = 44; 3.17%)

Maximum sarcoma were seen in the fifth decade of life, with a mean age of 45.4 years and involved lower limb followed by retroperitoneal. On IHC (*n* = 17), vimentin was universally positive in all [Table 3]. Few other markers such as SMA, desmin, S-100, myogenin, CD 31, CD34, CD117, CD99, CK, LCA showed negative results. The whole panel of markers was not done due to various reasons (scanty tissue, limited availability of markers, and financial constraints).

Immunohistochemistry correlation was done in 110 specimen, 95 malignant and 15 intermediate tumors. A definite diagnosis was reached in 78/95 malignant tumors and 15/15 intermediate tumors.

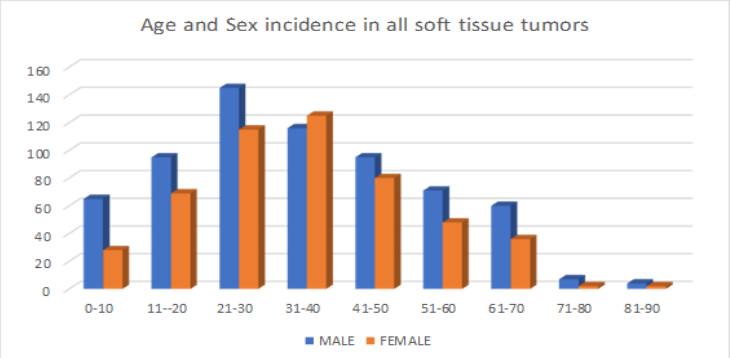

Figure 1.

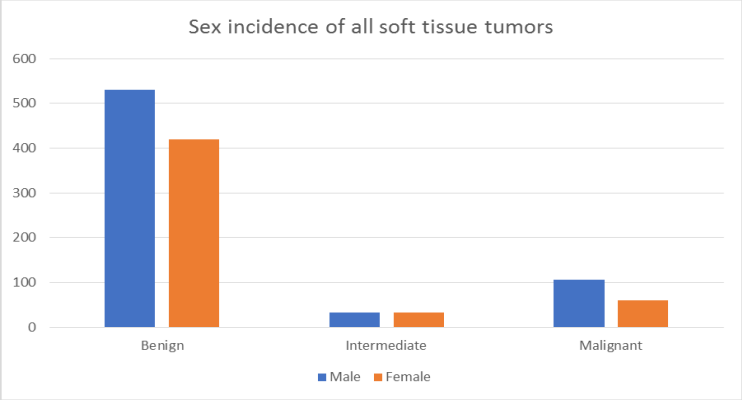

Figure 2.

Table 1: Site distribution of all soft tissue tumors.

Site	Benign	Intermediate	Malignant	Total
Extremity	293 (21.1)	16 (1.15)	125 (9.0)	434(31.2%)
Head and Neck	406 (29.2)	18 (1.29)	82 (5.9)	506(36.4%)
Shoulder and Back	215 (15.4)	12 (0.86)	10 (0.72)	237(17.07%)
Trunk and Abdomen	109 (7.8)	9 (0.64)	45 (3.24)	163(11.7%)
Others	9 (0.64)	14 (1.0)	25 (1.8)	48(3.4%)
Total	1032(74.3%)	69(4.9%)	287(20.6%)	1388

Table 2: Distribution of cases.

	Benign	Intermediate	Malignant
Adipocytic tumors	510 (36.74)	5 (0.3)	6 (0.43)
Fibroblastic/myofibroblastic tumors	27 (1.94)	55 (3.9)	25(1.8)
Fibrohistiocytic tumors	51 (3.67)	8 (0.57)	
Vascular tumors	234 (16.8)		5 (0.3)
Pericytic/perivascular tumors	11 (0.7)		
Nerve sheath tumors	297 (21.3)		4 (0.2)
Smooth muscle tumors	10 (0.72)		15 (1.08)
Skeletal muscle tumor			25 (1.8)
Gastrointestinal stromal tumors	22 (1.5)		2 (0.1)
Tumors of Uncertain differentiation			30 (2.16)
Chodroosseous tumors			3 (0.2)
Undifferentiated Sarcoma	5 (0.3)		44 (3.17)
Total cases	1170 (84.2)	68 (4.8)	159 (11.4)

Table 3: Distribution of benign tumors.

	No.of cases
Adipocytic tumors	
Lipoma	497
Lipoblastoma	2
Angiolipoma	7
Angiomyolipoma	2
Spindle cell lipoma	2
Fibroblastic/myofibroblastic tumors	
Nodular fasciitis	2
Myositis ossificans	1
Fibromatosis coli	10
Fibroma of tendon sheath	12
Calcifying fibrous tumor	1
Angiofibroma	1
Fibrohistiocytic tumors	
Tenosynovial giant cell tumor	32
Benign fibrous histiocytoma	19

Smooth muscle tumors	
Leiomyoma	10
Pericytic tumors	
Glomus tumors	9
Myopericytoma	1
Angioleiomyoma	1
Vascular tumors	
Hemangioma	206
Lymhangioma	28
Nerve sheath tumors	
Schwannoma	222
Neurofibroma	75
Gastrointestinal stromal tumors	22
Benign mesenchymal lesion	5

Table 4: Distribution of intermediate tumors.

	No. of cases
Adipocytic tumors	
Atypical lipomatous tumor	3
Liposarcoma	2
Fibroblastic/myofibroblastic tumors	
Desmoid type fibromatosis	1
Dermatofibrosarcoma protuberance	33
Solitary fibrous tumor	10
Inflammatory myofibroblastic tumor	3
Low grade myofibroblastic sarcoma	7
Infantile fibrosarcoma	1
Fibrohistiocytic tumors	
Plexiform fibrohistiocytic tumor	4
Giant cell tumor of soft tissue	4

Table 5: Distribution of malignant tumors.

	No. of cases
Adipocytic tumors	
Dedifferntiated liposarcoma	2
Myxoid liposarcoma	2
Pleomorphic liposarcoma	1
Pleomorphic myxoid liposarcoma	1
Fibroblastic/myofibroblastic tumors	
Fibrosarcoma	10
Myxofibrosarcoma	9
Low grade fibromyxoid sarcoma	5
Sclerosing epitheloid fibrosarcoma	1
Smooth muscle tumors	
Leiomyosarcoma	15
Skeletal muscle tumors	
Embryonal rhabdomyosarcoma	18
Alveolar rhabdomyosarcoma	4
Pleomorphic rhabdomyosarcoma	2
Spindle cell rhabdomyosarcoma	1
Vascular tumors	
Epitheliod hemangioendothelioma	1
Angiosarcoma	4
Gastrointestinal stromal tumors	2
Chondroosseous tumors	
Mesenchymal chondrosarcoma	3
Nerve sheath tumors	
MPNST	4

Tumors of uncertain differentiation	
Synovial sarcoma	17
Epitheloid sarcoma	4
Alveolar soft part sarcoma	1
Clear cell sarcoma of soft tissue	1
Desmoplastic small round cell tumor	1
PNET	5
PECOMA	1
Undifferentiated Sarcoma	
Undifferentiated spindle cell sarcoma	9
Undifferentiated pleomorphic sarcoma	24
Undifferentiated sarcoma,NOS	11

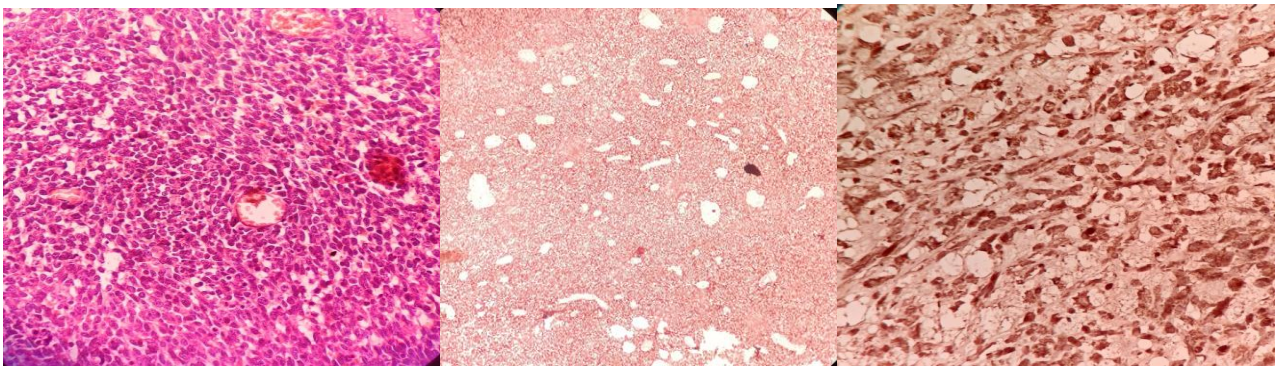

Fig. 3: Case of Rhabdomyosarcoma (a) H&E stained section of tumor which showed diffuse positivity for desmin (b) and myogenin(c) on IHC.

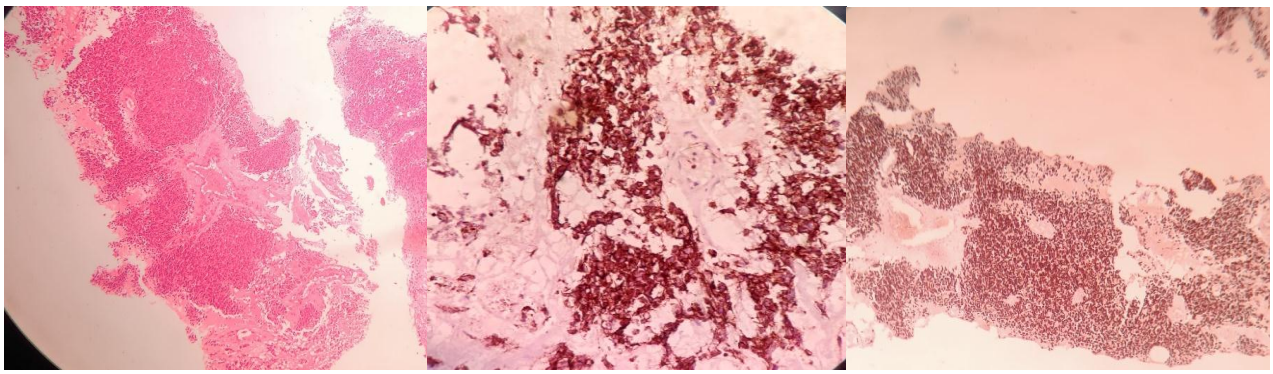

Fig. 4: Case of extraskeletal ewings sarcoma (a) showing diffuse and strong positivity for CD 99 (b) and NKX 2.2 (c).

DISCUSSION

Out of the total 1388 soft tissue tumors analysed. Benign were maximum followed by malignant and intermediate tumors this is in concordance with studies conducted by Heena Paul Singh et al, Agravat et al and stout.[14,15,16]

Benign Soft tissue tumors were common in younger population (mean age 40 years) as compared to malignant soft tissue tumors which were more numerous in 61-70 years of age group (15.70%) these findings are in concordance with the studies conducted by Heena Paul Singh et al, Agravat et al and Vimber et al[14,16,17] The male to female ratio is 1.2:1 which is similar to Heena Paul Singh et al

Most common sight of predilection of these benign and intermediate soft tissue tumor is head and neck (29.2% and 29%) while the malignant tumor shows predilection for extremities. These findings are similar to makino[16,18] and trojani et al.[19]

Previous studies showed benign soft tissue tumors outnumbered malignant tumors by the margin of 100. In our study 74.3% of soft tissue were benign (n=1032) and 20.6% (n=287) cases were of malignant soft tissue tumors. These findings are similar to studies done by Myhera Jainson Et al,[20] Lazxim Et al[21] and Kransdolf et al[22,23] where benign tumor predominated malignant tumors. The relative frequency of benign to Malignant tumors appear difficult to estimate clearly because most benign tumor are asymptomatic and all benign tumors are not surgically removed.

Adipocytic tumors were the most common tumors constituting 37.5% of all tumors these findings were similar to the study conducted by like Agravat et al[14] and Heena Paul et al.[16] The most common adipocytic tumor was lipoma constituting 95.3% of the adipocytic tumor. Dedifferentiated Liposarcoma, Myxoid Liposarcoma were common among the malignant adipocytic tumor. Liposarcoma was sixth most common of all the malignant soft tissue tumor. With the peak incidence in the 4th decade and affecting males predominantly. Studies done by Ahmed et al,[24] Stout[15] and Heena Paul Singh[16] et al also showed similar findings.

Nerve Sheath tumors (21.3%) comprising of schwannoma (n=222, 74.7%), neurofibroma (n=75, 25.3%) were the second largest benign soft tissue tumors followed by vascular tumors (16.8%) and fibrohistiocytic tumors (3.67%).

These findings are consistent with Heena Paul Singh[16] et al

Malignant soft tissue tumors were 11.4% of all the soft tissue tumors. Majority were seen in elderly males (--%). -% were of these tumors were located in the extremities. These findings are similar to the findings of Navya Narayan et al. [23]

Fnclcc grading system was used to grade these malignant soft tissue tumors. It is based mainly on degree of differentiation, cellular pleomorphism, number of mitotic figures per high power field and presence or absence of necrosis.

Intermediate soft tissue tumors constituted 4.8% (n=68) of all the soft tissue tumors. These showed repeated local recurrences and also showed low to moderate risk of metastasis. Fibroblastic tumors constituted the largest tumors of this group. Dermatofibrosarcoma protuberance, Solitary Fibrous tumor, low grade myofibroblastic sarcoma were the most common among these. These findings are similar to the studies done by peterson et al[25] and Navya Narayan et al. [23]

CONCLUSION

Soft tissue tumors form a vast and heterogenous group of neoplasm which require an integrated diagnostic approach of clinical histological and immunohistochemical techniques. These tumors form a significant specimen load in the histopathological section. Benign tumors form the major bulk of these tumors. Lipoma is the most common benign soft tissue tumor. Most of the fibroblastic tumor belong to the intermediate category and as seen in the extremities malignant tumors were common in the elderly and located commonly in the extremities.

This series may had a limited sample size and selection bias in favour of advanced, recurrent, or otherwise complicated sarcomas, but such studies and their compilation is necessary to study the survival and other treatment outcomes in heterogeneous group of these tumors.

REFERENCES

1. Robbins S, Aster J, Perkins J, Abbas A, Kumar V. Robbins Basic Pathology. Tenth edition. Philadelphia: Elsevier, 2018.
2. Fletcher Christopher.Tumors of Soft Tissue Diagnostic Histopathology of tumors Fourth edition Philadelphia: Elsevier, 2013.
3. Ramaswamy A, Rekhi B, Bakhshi S, Hingmire S, Agarwal M. Indian data on bone and soft tissue sarcomas: A summary of published study results. South Asian J Cancer, 2016; 5: 138-45.
4. Fletcher CD, Bridge JA, Hogendoorn P, Mertens F. WHO classification of tumours of soft tissue and bone. 4th ed. Lyon, France: IARC Press, 2013
5. Dangoor A, Seddon B, Gerrand C, Grimer R, Whelan J, Judson I. UK guidelines for the management of soft tissue sarcomas. Clin Sarcoma Res, 2016; 6: 20.
6. Yang Z, Zheng R, Zhang S, Zeng H, Li H, Chen W. Incidence, distribution of histological subtypes and primary sites of soft tissue sarcoma in China. Cancer Biol Med, 2019; 16: 565-74
7. Lewis JJ, Leung D, Woodruff JM, et al. Retroperitoneal softtissue sarcoma: Analysis of 500 patients treated and followed at a single institution. Ann Surg, 1998; 228: 355.
8. Gutierrez Juan C, Perez Eduardo A, Franceschi Dido, Moffat Frederick L., Livingstone Alan S, Koniaris Leonidas G. Outcomes for Soft-Tissue Sarcoma in 8249 Cases from a Large State Cancer Registry. Journal of Surgical Research, 2007; 141: 105–114.
9. Linehan DC, Lewis JJ, Leung D, et al. Influence of biologic factors and anatomic site in completely resected liposarcoma. J Clin Oncol, 2000; 18: 1637.
10. Singer S, Antonescu CR, Riedel E, et al. Histologic subtype and margin of resection predict pattern of recurrence and survival for retroperitoneal liposarcoma. Ann Surg, 2003; 238: 358-370.
11. Perez EA, Franceschi D, Livingstone AS, et al. Truncal and retroperitoneal sarcoma: Prognosis depends upon tumor type not location. Ann Surg Oncol, 2007; 14: 11-14.
12. Stiller CA, Trama A, Serraino D, Rossi S, Navarro C, Chirlaque MD, et al. Descriptive epidemiology of sarcomas in Europe: report from the RARECARE project. Eur J Cancer, 2013; 49: 684-95.
13. Ogura Koichi, Higashi Takahiro, Kawai Akira. Statistics of soft-tissue sarcoma in Japan: Report from the Bone and Soft Tissue Tumor Registry in Japan. Journal of Orthopaedic Science, 2017; 22: 755-64
14. Agravat AH, Dhruva GA, Parmar SA. Histopathology study of Soft Tissue Tumours and

Tumour like Lesions. J Cell Tissue Res, 2010; 10: 2287–92.
15. Stout AP. Atlas of Tumour Pathology. 1st ed. Washington, D.C: Armed Forces Institute of Pathology, 1953.
16. Singh Hena Paul , Grover Sumit, xGarg Sumit, Sood N. Histopathological Spectrum of Soft-Tissue Tumors with Immunohistochemistry Correlation and FNCLCC grading: A North Indian Experience.Niger Med J, 2017; 58(5): 149–155.
17. Wibmer C, Leithner A, Zielonke N, Sperl M, Windhager R. Increasing incidence rates of soft tissue sarcomas? A population based epidemiologic study and literature review. Annals of Oncology, 2010; 21: 1106–11.
18. Makino Y. A clinicopathological study on Soft Tissue Tumours of the head and neck. Pathology International, 1979; 29: 389–408.
19. Trojani M, Contesso G, Coindre JM, Rouesse J, Bui NB, Mascarel AD, et al. Soft tissue Sarcomas of adults: study of Pathological Prognostic Variables and Definition of a Histopathological Grading System. Int J Cancer, 1984; 33: 37–42.
20. Myhre-Jensen O; A consecutive 7-year series of 1331 benign soft tissue tumors. Clinicopathologic data. Comparison with sarcomas. Acta Orthop Scand., 1981; 52(3): 287-293.
21. Lazim AF, Bedoor AK, Al-Irhayim; Soft tissue sarcomas in Mosul: a pathologic evaluation. Ann Coll Med Mosul., 2008; 34(2): 152-160.
22. Kransdorf MJ; Benign soft-tissue tumors in a large referral population: distribution of specific diagnoses by age, sex, and location. AJR Am J Roentgenol, 1995; 164(2): 395-402.
23. Narayanan Navya OA, M Sapna, B Sumangala.Spectrum of soft tissue tumors in a tertiary care centre- A 5year study.Niger Med J, 2017; 58(5): 149–155.
24. Amhad Z, Qureshi A, Idrees R. Epidemiological data of common Soft tissue Sarcomas as seen in our practice. J Clin Pathol, 2010; 63: 375–76.
25. Petersen I, Gunther B, Mildner K, Subhi F, Knosel T, Altendorf-Hofmann A, Katenkamp D; Update from the soft tissue tumor registry in Jena. Pathologe, 2011; 32(1): 40-46.