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Original Research Paper

General Surgery

INCIDENCE AND DISTRIBUTION OF SOFT TISSUE SARCOMAS IN A TERTIARY HOSPITAL IN KARNATAKA

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ABSTRACT **Background:** Sarcomas are heterogenous group of malignancies linked by their common mesenchymal origin. They account for around 1% of malignancies in adults and 10- 20% of adolescents. We present a retrospective study depicting the incidence, distribution and management of soft tissue sarcomas in a tertiary hospital in South India. **Methods:** The study included histologically proven soft tissue sarcomas admitted in K.R hospital, Mysore from October 2021 to October 2022. The parameters studied were age distribution, gender distribution, histological subtype, site of the sarcoma and the treatment modality. **Results:** During the study duration, out of 8880 patients admitted for malignancies, 41 patients (0.16%) were diagnosed with soft tissue sarcomas. Maximum incidence (43.9%) was observed in the age group of 41-60. The incidence was found to be nearly equal in men and women. Liposarcoma was the most common histological subtype of soft tissue sarcoma (17.1%). Most of them were found to be arising from the thigh (34%). 70% of the patients were treated with a combination of surgery, chemotherapy and radiotherapy. **Conclusion:** The study throws light upon the diversity of soft tissue sarcomas and the increase in their incidence. The percentage of population presenting at advanced stages of the disease are high, this could be due to lack of awareness and non-availability of resources.

KEYWORDS : Soft tissue sarcoma, distribution, incidence, management

INTRODUCTION

Soft tissue sarcomas account for 1% of all adult tumours and 15% of all paediatric tumours [1, 2]. They comprise a heterogenous group of tumours. More than 50 histological subtypes of soft tissue sarcomas have been described, with each of them having unique clinical, prognostic and therapeutic features [1]. Most common histotypes include Undifferentiated Pleomorphic Sarcoma, Leiomyosarcoma and Liposarcoma [1]. The etiology is still unclear, risk factors include autoimmune conditions, exposure to radiation and chemicals, viral infections, certain genetic mutations and family cancer syndromes [4-6]. Family cancer syndromes include neurofibromatosis, Gardner syndrome, Li-Fraumeni syndrome, retinoblastoma and tuberous sclerosis [6]. Incidence of soft tissue sarcomas generally increases with age [2].

The management depends on several factors including histological type, size, grade, whether primary or recurrent, and treatment related factors- margins of clearance and use of adjuvant therapy. They are best managed by a multidisciplinary team of specialists to maximize survival, preserve the function, improve the quality of life and to prevent recurrences [1]. Clinical examination, tissue diagnosis and imaging (CT/MRI) are required for confirming the diagnosis and for staging of the disease. Surgical resection with clear margins is the mainstay of treatment of soft tissue sarcomas. Malignancy grade, tumour type and size, site, tumour resectability, surgical margins achieved and presence of metastases at diagnosis are important prognostic factors [7-10]. Patients with distant metastases have a poor prognosis despite chemotherapy/surgery [11]. Soft Tissue Sarcomas comprise a large proportion of paediatric malignancies and are an important cause of death in adolescents and young adults [12,13].

In the majority of patients who present with unresectable metastatic disease, the standard treatment is palliative and comprises of single-agent doxorubicin, dacarbazine, epirubicin, or ifosfamide or anthracycline-based combination regimens with doxorubicin/epirubicin plus ifosfamide and/or dacarbazine. Doxorubicin-based therapy has been shown to produce response rates of 12% to 24% in patients with locally advanced or metastatic disease [2,14,15].

Overall five-year survival rate of STSs in developed countries ranges from 55% to 78%.

While there is good published data on incidence and distribution of various subtypes of sarcomas in the developed nations, there is a paucity of data from India [16]. This study brings light to the incidence, different histological subtypes, site, age and gender distribution of soft tissue sarcomas reported in a tertiary hospital in Karnataka over one year.

Patients And Methods

A retrospective study was conducted in K.R Hospital, Mysore, Karnataka from October 2021 to October 2022. All patients, adults and paediatric, presenting with or being referred with soft tissue sarcoma to the Department of General Surgery were studied. These patients underwent routine blood investigations, chest x ray, biopsy and CT/MRI. Histologically and IHC proven cases of soft tissue sarcoma were included in this study. Patients refusing admission were excluded from the study. Among the total 8880 cases of malignancies admitted during the duration of the study, 41 cases were diagnosed with soft tissue sarcomas. The disease was staged and treated accordingly with surgery, radiation or chemotherapy.

RESULTS

From October 2021 to October 2022 there were a total of 25,500 admissions in K.R Hospital in the Department of General Surgery out of which 8880 (34.8%) were cases of various malignancies. Out of the 8880 patients admitted with various malignancies, 41 of them were proven to have soft tissue sarcomas (0.16% of all inpatients in surgical ward and 0.46% of the total inpatients with malignancies).

In our study most common subtype was found to be Liposarcoma which accounted for 7 cases followed by dermatofibrosarcoma and leiomyosarcoma each accounting for 6 cases. Myxofibrosarcomas accounted for 5 cases and rhabdomyosarcomas accounted for 3 cases. Other soft tissue sarcomas observed were malignant round cell tumours,

myxoid fibrosarcoma and synovial sarcoma accounting for 2 cases each and epitheloid hemangioepitheilioma, fibromyxoid sarcoma, fibrosarcoma, hemangiosarcoma, malignant peripheral sheath tumour and myxoid liposarcoma account for 1 case each. Undifferentiated pleomorphic sarcoma accounted for 2 cases.

Table 1: Pattern Of Sarcomas In The Study Setting

Specific diagnosis	Frequency	Percentage
Liposarcoma	7	17.10%
Dermatofibrosarcoma	6	14.60%
Leiomyosarcoma	6	14.60%
Myxofibrosarcoma	5	12.20%
Rhabdomyosarcoma	3	7.30%
Malignant round cell tumour	2	4.90%
Myxoid fibrosarcoma	2	4.90%
Synovial sarcoma	2	4.90%
Epitheloid haemangioepithelioma	1	2.40%
Fibromyxoid sarcoma	1	2.40%
Fibrosarcoma	1	2.40%
Haemangiosarcoma	1	2.40%
Malignant peripheral sheath tumor	1	2.40%
Myxoid liposarcoma	1	2.40%
Undifferentiated pleomorphic sarcoma	2	4.90%
Total	41	100.0%

The average age at which soft tissues sarcoma was diagnosed was found to be 45.9. Majority of patients -18 cases out of 41, belonged to the age group of 41-60, 13 cases were in the age group of 21-40. 5 cases were above 60 years and 5 cases were below 20 years of age.

Table 2: Age Distribution Of Sarcoma Patients

Age group	Frequency	Percentage
≤ 20 years	5	12.2%
21 – 40 years	13	31.7%
41 – 60 years	18	43.9%
> 60 years	5	12.2%
Total	41	100.0%
Mean: 45.9 years		

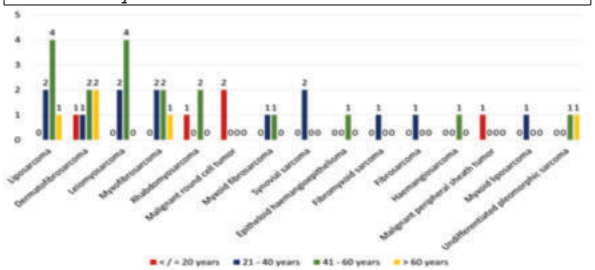

Fig 1: Distribution Of Sarcomas Across Various Age Groups

Liposarcoma, leiomyosarcoma and dermatofibrosarcoma were the predominant subtypes in all age groups except age group below 20. Cases of Malignant round cell tumour and Malignant peripheral sheath tumour were reported in patients below 20, which was not reported in other age groups.

In our study, we found almost equal incidence across genders with 21 of these cases occurring in women (51.2%) and the rest of the 20 cases (48.8%) in men.

Table 3: Distribution Of Sarcomas Across The Genders

Specific diagnosis	Gender	
	Female	Male
Liposarcoma	4 (57.1%)	3 (42.9%)
Dermatofibrosarcoma	3 (50.0%)	3 (50.0%)
Leiomyosarcoma	4 (66.7%)	2 (33.3%)
Myxofibrosarcoma	3 (60.0%)	2 (40.0%)
Rhabdomyosarcoma	1 (33.3%)	2 (66.7%)

Most common site of occurrence was found to be the thigh-with 14 cases being recorded, 6 cases were recorded in the arm,5 cases in the retroperitoneum and 3 over the abdominal wall. There were also patients who presented with lesions in the foot, adnexa, chest, gluteal region, paratesticular area, perianal region, upper back and uterus.

Among the soft tissue sarcomas occurring in the thigh, majority of them were either liposarcomas or myxofibro-sarcomas with 4 cases each. Dermatofibro-sarcomas, myxoid fibrosarcomas, synovial sarcomas, hemangiosarcomas, rhabdomyosarcomas and undiffe-rentiated pleomorphic sarcomas accounted for one case each.

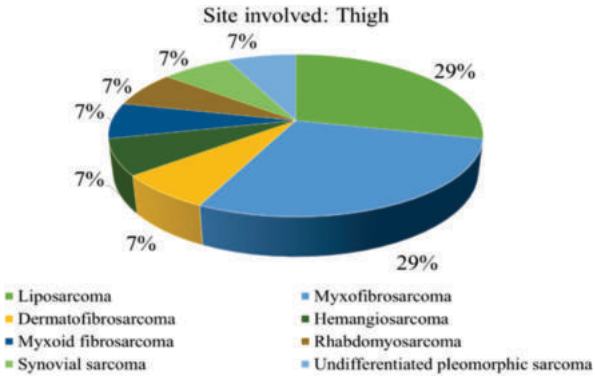

Fig 2: Histological Subtype Of Soft Tissue Sarcoma In Thigh

There was a case each of Dermatofibrosarcoma, Malignant peripheral nerve sheath tumour, Rhabdomyosarcoma, Liposarcoma, Myxoid fibrosarcoma and Synovial sarcoma reported in the arm.

Among retroperitoneal soft tissue tumours, 60% were liposarcomas and 40% were leiomyiosarcomas. 34% of soft tissue sarcomas arising from the arm were fibromyxoid sarcomas and myxoid liposarcomas and malignant round cell tumours accounted for 33% each.

In our study, 70% of patients ended up being treated with all three modalities, that is, surgery, chemotherapy and radiotherapy. 13% underwent chemoradiation and 17% were considered for palliative care because of the advanced stage at presentation.

DISCUSSION

As our population increases, the incidence of malignancies including sarcomas also increases. In a study conducted in Europe, the age adjusted sarcoma incidence was 7.4 (men) and 6.6 (women) per 100,000 inhabitants. In contrast in a study conducted in Asia, the crude incidence rate of sarcoma was found to be 2.50/100,000 (2.27/100,000 in men and 2.73/100,000 in women) [2,17]

Analysis of age distribution showed a peak incidence of STS around the age of 60 years and a second, modest peak in early childhood (0–5 years). The median age at diagnosis for all sarcomas was 67.4 years for men and 67.7 for women [2,17]. In our study we found that patients presenting with soft tissue sarcomas were much younger than the worldwide average with the mean age of diagnosis being just 45.9 years. Soft tissue sarcomas are known to affect men and women equally with slight predilection for women.

The most commonly encountered histological subtypes were liposarcoma, dermatofibrosarcoma and leiomyosarcoma. The differences in the distribution of subtypes in various studies have been analysed, showing nonuniform results.

In a study conducted in China, GIST was the most common histological subtype. However, GIST is no longer considered a

soft tissue sarcoma as per MSKCC hence we have not included GIST in our study. According to a study conducted in Europe, complex mixed and stromal neoplasms, non-uterine leiomysarcomas and fibrosarcomas were the most common in women while in men fibrosarcomas and liposarcomas were found to be most common. In current literature, complex neoplasia group is not categorized as an individual entity, hence we have not grouped them separately. Common subtypes in United States were fibrohistiocytic tumors (30.4%) and leiomyosarcoma (27.4%) [18]. In Japan, leiomyosarcoma (28.1%) was the most prevalent subtype, followed by liposarcoma (9.6%), and malignant fibrous histiocytoma (9.0%) [19]. Leiomyosarcoma was found to be the prevailing subgroup in all nations. Nerve sheath tumour and MPNST is far more prevalent in China, representing more than 12% of all STS, compared with 3.5% in Japan and 4.6% in United States and 2.4% in our study [2,17-19].

Common subtypes in adolescents and young adults include rhabdomyosarcoma, malignant round cell tumour, dermatofibrosarcoma and malignant peripheral sheath tumour. In a study conducted in the United States predominant subtypes in the adolescent and young adult population included rhabdomyosarcoma, synovial sarcoma, neurogenic sarcoma, epithelioid sarcomas and alveolar soft parts sarcoma [20].

Soft tissue sarcomas commonly occur in the extremities and the retroperitoneum. These results are concurrent with existing studies which say that 40-50% of soft tissue sarcomas occur in the extremities and 13% in the trunk [1,21,22]. While fibrosarcomas and angiosarcomas were the most predominant types in the head and neck, fibrosarcomas, liposarcomas and non-uterine leiomyosarcoma were most prominent in the limbs and trunk.

Management of soft tissue sarcomas depend on several factors like grade, histological subtype, size, site, tumour resectability, surgical margins achieved and presence of metastases. In our study a large proportion of patients required palliative care due to high grade of tumour and presence of distant metastasis at presentation. We attribute the presentation in the terminal stage to the lack of awareness among people and the healthcare community about cancers.

Soft tissue sarcomas often present a clinical dilemma to the surgeon due to their diversity in terms of cell of origin, rapid growth, possibility of occurrence in any anatomical site and the aggressive tumour biology [1]. Their high recurrence rates warrant frequent long term follow up and counselling for repeat interventions whenever necessary. Optimal management of soft tissue sarcomas need a combined effort from the surgeon, pathologist, radiologist, medical and radiation oncologist.

In a developing country like India there is a general lack of awareness about cancers resulting in delayed presentation. There is a lack of specialists and limited diagnostic and therapeutic options especially in the rural setting. These are the main deterrents to early diagnoses and management of malignancies. Another factor that adds to the mortality and morbidity is the poor compliance to chemotherapy/ radiotherapy and regular follow up. There is a need for specialised centres for oncology with multidisciplinary teams of primary care physicians, pathologists, medical and surgical oncologists, radiologists, radiation oncologists and pain specialists. Ancillary services including good nursing care, physiotherapy and rehabilitation also improve the outcome and survival rates. There is a need for awareness programmes to educate the public about cancers. Better understanding of the disease leads to presentation in the early stages, better compliance and better outcomes.

This study is one of the first in India to report the incidence of soft tissue sarcomas as well as the distribution of histological subtypes. Available evidence is limited, more number of studies need to be done on soft tissue sarcoma. The disease varies greatly depending upon the histological subtype. Survival rates vary tremendously (48.0%-99.5%) between subtypes [23].

It is imperative we understand the biologies and behaviours of the various histological subtypes of soft tissue sarcomas, and targeted therapies become available.

Currently the treatment guidelines for each subtype are less established. They tend to be region-specific, depending on resource availability and infrastructure within each country. Expanding our knowledge of the behaviour and sensitivities of the various subtypes, in conjunction with results from an increasing collection of retrospective reviews and prospective randomized studies, is crucial in treating the disease [24].

Due to association of soft tissue sarcomas with certain autoimmune conditions and familial syndromes, screening of the population at risk would go a long way in early detection of the disease.

Limitations

Recruitment of patients was challenging due to rarity of the disease. The true incidence of STS remains uncertain to some degree. The lack of knowledge and limited access to healthcare results in underreporting of the disease. There are no cancer registries so it becomes difficult to estimate the true burden of the disease. Changing of classification of soft tissue sarcomas over time also leads to confusion – earlier entities like GIST, Kaposi's sarcoma and complex neoplasms were included under soft tissue sarcomas. It is difficult to come to a conclusion from our study due to the small sample size. More studies need to be done to understand the disease better and form treatment guidelines for the various subtypes.

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REFERENCES

1. Gamboa AC, Gronchi A, Cardona K. Soft tissue sarcoma in adults: an update on the current state of histiotypespecific management in an era of personalized medicine. CA Cancer J Clin 2020;70(3):200-29.
2. 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(3):565.
3. Beauchamp, Evers, Mattox: Sabiston Textbook of Surgery. 17th Ed. Elseveir vol. 1:805, 2007.
4. 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.
5. Fletcher CDM, Bridge JA, Hogendoorn P, Mertens F. WHO classification of tumours of soft tissue and bone. 4th ed. Lyon, France: IARC Press; 2013.
6. Quek RH, Farid M, Wang E, et al. Epidemiology, treatment (tx) patterns and outcomes in Asian soft tissue sarcoma (STS) patients: Results from the Soft Tissue Sarcoma in the Asia Pacific Region (STAR) study. J Clin Oncol 2015;33:10549.
7. Casali PG, Abecassis N, Bauer S, et al. Soft tissue and visceral sarcomas: ESMO-EURACAN Clinical Practice Guidelines for diagnosis, treatment and follow-up. Ann Oncol 2018.
8. TNM Classification of Malignant Tumours, 8th edition. Oxford: John Wiley & Sons, Inc., 2016.
9. Zagars GK, Ballo MT, Pisters PW, et al. Prognostic factors for patients with localized soft-tissue sarcoma treated with conservation surgery and radiation therapy: an analysis of 1225 patients. Cancer 2003;97:2530-43.
10. Koea JB, Leung D, Lewis JJ, et al. Histopathologic type: an independent prognostic factor in primary soft tissue sarcoma of the extremity? Ann Surg Oncol 2003;10:432-40.
11. Data from Surveillance, Epidemiology and End Results (SEER) Programme: SEER 9 Regs Public Use, Nov 2001 Sub [1973–1999]
12. Ferrari A, Sultan I, Huang TT, Rodriguez-Galindo C, Shehadeh A, Meazza C, et al Soft tissue sarcoma across the age spectrum: a population-based study from the surveillance epidemiology and end results database. Pediatr Blood Cancer. 2011;57:943–9.
13. 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.
14. Linch M, Miah AB, Thway K, Judson JR, Benson C. Systemic treatment of soft-tissue sarcoma-gold standard and novel therapies. Nat Rev Clin Oncol. 2014; 11: 187- 202.

15. Bramwell VH, Anderson D, Charette ML. Doxorubicin-based chemotherapy for the palliative treatment of adult patients with locally advanced or metastatic soft-tissue sarcoma: a meta-analysis and clinical practice guideline. Sarcoma. 2000; 4: 103- 112.
16. Quek RH, Farid M, Wang E, et al. Epidemiology, treatment (tx) patterns and outcomes in Asian soft tissue sarcoma (STS) patients: Results from the Soft Tissue Sarcoma in the Asia Pacific Region (STAR) study. J Clin Oncol 2015;33:10549.
17. Ressing M, Wardelmann E, Hohenberger P, Jakob J, Kasper B, Emrich K, Eberle A, Blettner M, Zeissig SR. Strengthening health data on a rare and heterogeneous disease: sarcoma incidence and histological subtypes in Germany. BMC Health Serv Res. 2018;18(1):1-1.
18. Ferrari A, Sultan I, Huang TT, RodriguezGalindo C, Shehadeh A, Meazza C, Ness KK, Casanova M, Spunt SL. Soft tissue sarcoma across the age spectrum: a populationbased study from the surveillance epidemiology and end results database. Pediatric blood & cancer. 2011 1;57(6):943-9.
19. Nomura E, Ioka A, Tsukuma H. Incidence of soft tissue sarcoma focusing on gastrointestinal stromal sarcoma in Osaka, Japan, during 1978–2007. Japan J Clin Oncology. 2013 1;43(8):841-5.
20. Herzog CE. Overview of sarcomas in the adolescent and young adult population. J Pediatr Hematol Oncol. 2005 1;27(4):215-8.
21. Blay JY, Honore C, Stoeckle E, et al; Surgery in reference centers improves survival of sarcoma patients: a nationwide study. Ann Oncol. 2019; 30: 1143-1153
22. Brennan MF, Antonescu CR, Moraco N, Singer S. Lessons learned from the study of 10,000 patients with soft tissue sarcoma. Ann Surg. 2014; 260: 416-421; discussion 421-422.
23. Trautmann F, Schuler M, Schmitt J Burden of soft-tissue and bone sarcoma in routine care: estimation of incidence, prevalence and survival for health services research. Cancer Epidemiol. 2015;39:440–6.
24. Martín Broto J, Le Cesne A, Reichardt P. The importance of treating by histological subtype in advanced soft tissue sarcoma. Future Oncology. 2017;13(1s):23-31