

Epidemiological and Clinical Characteristics of Patients with Sarcoma in Erbil City

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Abstract

Sarcoma account for over 20% of all pediatric solid malignant cancers and less than 1% of all adult solid malignant cancers. The vast majority of diagnosed sarcomas will be soft tissue sarcomas, while malignant bone tumors make up just over 10% of sarcomas. This study is assigned to highlight the epidemiological and clinical characteristics of patients with sarcoma in Erbil city. A cross sectional study consisted of 151 diagnosed sarcoma patients who visited Rzgery teaching hospital – medical oncology unit from February 2018 to December 2020. Subjects of ≤ 14 -year-old are excluded from the study. The largest proportion of the sample (23.2%) were aged 10-19 years, and 21.9% were aged 20-29 years. More than half (58.3%) were males. Around (58.3%) of the patients had never smoked, and 18.5% were current smokers. Only 2% of patients used to drink alcohol, and 17.9% had family history of cancers. The most common site of sarcoma was limbs (43%), followed trunk (38.4%), and it was mainly (85.4%) a soft tissue tumor. The most common histo-pathological type was Ewing sarcoma of soft tissue (25.8%), followed by osteosarcoma (21.2%) and liposarcoma (18.2%). This study concluded that sarcoma is more common among people in the second decade of life, the limbs were the most common site of involvement and soft tissue sarcoma accounts majority of the cases.

Keywords: Sarcoma; Clinical Oncology; Ewing Sarcoma; Osteosarcoma; Liposarcoma.

1. Introduction

Sarcoma make up a broad group of malignant neoplasms of mesenchymal origin. Sarcomas account for over 20% of all pediatric solid malignant cancers and less than 1% of all adult solid malignant cancers. The vast majority of diagnosed sarcomas will be soft tissue sarcomas, while malignant bone tumors make up just over 10% of sarcomas [1].

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In addition, sarcomas represent multiple malignancies rather than a single cancer [2]. For example, more than 50 distinct histologic sarcoma subtypes exist. Furthermore, many of these subtypes can occur at any age and are not restricted to a specific location of the body. In order for the evaluation of the epidemiology and etiology of sarcomas to be feasible, this review will take a broad perspective, noting differences primarily between the two most common and distinct sarcoma groupings, malignant bone tumors and soft tissue sarcomas. Soft tissue sarcomas often form in the body's muscles, joints, fat, nerves, deep skin tissues, and blood vessels. As the name implies, malignant bone tumors such as osteosarcomas and Ewing's sarcomas are found throughout the bones of the body, but also can commonly be found in the cartilage [3]. According to the Surveillance, Epidemiology, and End Results Program of the National Cancer Institute, the incidence of STS is approximately 3.4 per 100,000 [4]. There is a slight male preponderance of 1.4:1.2. The median age at diagnosis is 59, with a bimodal distribution that peaks in the fifth and eighth decades [5]. STS occur most commonly on the extremities; upper and lower extremity STS account for 12% and 28%, respectively, of all STS. The thigh is the most common site of STS, accounting for 44% of all extremity STS. The most common type of extremity STS is liposarcoma (LPS). Visceral STS account for 22% of all STS and include gastrointestinal stromal tumors (GIST) and uterine leiomyosarcoma (LMS) [6]. Retroperitoneal sarcomas account for 16% of all STS, whereas trunk and other sites (including the head and neck) account for 10% and 12%, respectively. Retroperitoneal sarcomas are typically LPS and LMS. Overall, LPS is the most common type of STS, accounting for approximately 20% to 25% of all STS. LPS can be further subdivided into well-differentiated LPS (also called atypical lipomatous tumor), dedifferentiated LPS, myxoid LPS, and pleomorphic LPS. Other common STS histologic subtypes include LMS (14%) and undifferentiated pleomorphic sarcoma (14%), formerly known as malignant fibrous histiocytoma [2,4,6]. Bone sarcomas are even more uncommon, accounting for 0.2% of all new cancer diagnoses. This disease tends to affect the younger population, most frequently diagnosed in those 20 years or younger. The age at diagnosis also varies with the histologic subtype. Osteosarcoma is the most common bone sarcoma overall and is more frequently seen in adolescents than in adults. Similarly, Ewing sarcoma is more common in children and adolescents but can also be seen in adults. The median age at diagnosis is 15.8. Although any bone (or even soft tissue) can be involved, Ewing sarcoma is found commonly in the extremities. Ewing sarcoma is most common in Caucasians and is rare in African-American or Asian populations. Although bone sarcoma primarily affects the younger population, certain types have a predilection for the adult population. Chondrosarcoma is typically diagnosed between ages 30 and 60 and is the most common subtype of bone sarcoma in adults.

2. Objective

This study is assigned to highlight the epidemiological and clinical characteristics of patients with sarcoma in Erbil city- Iraq.

3. Patients and Method

A cross sectional study consisted of 151 diagnosed sarcoma patients registered in Rzgary teaching hospital – medical oncology unit. The inclusion criteria were as follows: all patients of ≥ 14 -year-old. The exclusion criteria were: patients of ≤ 14 -year-old. An informed written consent was obtained from each patient or

caregiver, the study was consistent with the World Medical Association (WMA) Declaration of Helsinki medical research protocols and approved by the local KBMS ethical committee. Data were analyzed using the Statistical Package for Social Sciences (SPSS, version 25). Categorical variables were presented in the form of frequencies and percentages.

4. Results

Table 1: Basic characteristics of patients.

	No.	(%)
Age		
< 20	35	(23.2)
20-39	56	(37.1)
40-59	49	(32.5)
≥ 60	11	(7.3)
Gender		
Male	88	(58.3)
Female	63	(41.7)
Marital status		
Married	110	(72.8)
Unmarried	41	(27.2)
Ethnicity		
Kurdish	121	(80.1)
Arabs	26	(17.2)
Turkman	1	(0.7)
Others	3	(2.0)
Residency		
Rural	73	(48.3)
Urban	78	(51.7)
Educational level		
No formal education	51	(33.8)
Primary	36	(23.8)
Secondary	38	(25.2)
High school	13	(8.6)
University	13	(8.6)
Occupation		
Employee	69	(45.7)
Housewife	55	(36.4)
Retired	7	(4.6)
Unemployed	14	(9.3)
Others	6	(4.0)
Family income		
Low	25	(16.6)
Middle	123	(81.5)
High	3	(2.0)
Smoking		
Current	28	(18.5)
Ex-smoker	35	(23.2)
Never	88	(58.3)
Alcohol		
Yes	3	(2.0)
No	148	(98.0)
Family history		
Yes	27	(17.9)
No	124	(82.1)
Total	151	(100.0)

The total number of sarcoma patients was 151. Table 1 shows that the largest proportion of the sample (37.1%) were aged 20-39 years, and only 7.3% were aged ≥ 60 . More than half (58.3%) were males, and the majority (72.8%) of the patients were married. Around half (51.7%) of the patients were living in urban areas. Regarding the educational level, the table shows that one third (33.8%) of patients had no formal education (either illiterate or read and write), and only 8.6% were university graduates. Around half of the patients (45.7%) were working as employees, and 36.4% were housewives. The majority (81.5%) of the patients had middle income. More than half (58.3%) of the patients had never smoked, and 18.5% were current smokers. Only 2% of patients used to drink alcohol, and 17.9% had family history of cancers (Table 1).

It is evident in Table 2 that almost all (98.7%) of the patients were symptomatic, and the duration of sarcoma for around two thirds of patients was less than seven months. The most common site of sarcoma was the limbs (43%), and also the trunk (38.4%), and it was mainly (85.4%) a soft tissue tumor.

Table 2: Clinical characteristics of sarcoma.

	No.	(%)
Symptoms		
Symptomatic	149	(98.7)
Asymptomatic	2	(1.3)
Duration of sarcoma		
< 1 month	6	(4.0)
1-6 months	98	(64.9)
7-12 months	39	(25.8)
1-3 years	6	(4.0)
> 5 years	2	(1.3)
Site of sarcoma		
Head and neck	28	(18.5)
Trunk and abdomen	58	(38.4)
Limbs	65	(43.0)
Type of sarcoma		
Soft tissue	129	(85.4)
Bone	15	(9.9)
Others	7	(4.6)
Total	151	(100.0)

The most common histo-pathological type was Ewing sarcoma of soft tissue (25.8%), then comes the osteosarcoma (21.2%) and the liposarcoma (18.2%). The majority of the patients were of grades III and IV (55.6% and 29.8% respectively). The same pattern is observed for grading, where it is evident that 54.3% of patients were of grade III and 7.9% were of grade IV (Table 3).

Table 3: Histopathological characteristics of sarcoma.

Histopathological type		
Ewing sarcoma of soft tissue	39	(25.8)
Osteosarcoma	32	(21.2)
Liposarcoma	28	(18.5)
Fibrosarcoma	18	(11.9)
Leiomyosarcoma	11	(7.3)
Ewing bone sarcoma	7	(4.6)
Others	16	(10.6)
Stage		
I	2	(1.3)
II	20	(13.2)
III	84	(55.6)
IV	45	(29.8)
Grade		
I	21	(13.9)
II	36	(23.8)
III	82	(54.3)
IV	12	(7.9)
Total	151	(100.0)

Surgery was performed for 80.1% of patients, and chemotherapy was given for 72.8% of patients, while radiotherapy was given for 57.6% of patients (Table 4).

Table 4: Modes of management of sarcoma.

	No.	(%)
Surgery		
Yes	121	(80.1)
No	30	(19.9)
Chemotherapy		
Yes	110	(72.8)
No	41	(27.2)
Radiotherapy		
Yes	87	(57.6)
No	64	(42.4)
Total	151	(100.0)

Note: More than one mode of management is possible for each patient.

It is evident in Table 5 that there was no significant association between age and site of sarcoma ($p = 0.429$), and stage of sarcoma ($p = 0.669$). The table shows that 14.3% and 16.1% of patients aged < 20 years and 20-39 years respectively had bone sarcoma, while none of the patients aged 40-59 had bone sarcoma. One patient (9.1%) of those aged ≥ 60 years had bone sarcoma ($p = 0.003$). Regarding the histopathological types, the table shows that 54.5% of patients aged ≥ 60 years had Ewing sarcoma of soft tissue compared with 17.1% of those aged less than 20 years, while 42.9% of the young aged patients had osteosarcoma compared with 9.1% of the patients aged ≥ 60 years. The other comparisons are presented in the table, and the differences were significant ($p = 0.011$).

Table 5: Association between age with site, type, histopathological types and grade of sarcoma.

	Age (years)				p
	< 20	20-39	40-59	≥ 60	
	No. (%)	No. (%)	No. (%)	No. (%)	
Site of sarcoma					
Head and neck	5 (14.3)	16 (28.6)	6 (12.2)	1 (9.1)	0.429*
Trunk and abdomen	15 (42.9)	18 (32.1)	21 (42.9)	4 (36.4)	
Limbs	15 (42.9)	22 (39.3)	22 (44.9)	6 (54.5)	
Type of sarcoma					
Soft tissue	29 (82.9)	47 (83.9)	43 (87.8)	10 (90.9)	0.003*
Bone	5 (14.3)	9 (16.1)	0 (0.0)	1 (9.1)	
Others	1 (2.9)	0 (0.0)	6 (12.2)	0 (0.0)	
Histopathological type					
Ewing sarcoma of soft tissue	6 (17.1)	15 (26.8)	12 (24.5)	6 (54.5)	0.011†
Osteosarcoma	15 (42.9)	11 (19.6)	5 (10.2)	1 (9.1)	
Liposarcoma	2 (5.7)	9 (16.1)	15 (30.6)	2 (18.2)	
Fibrosarcoma	4 (11.4)	5 (8.9)	7 (14.3)	2 (18.2)	
Leiomyosarcoma	1 (2.9)	8 (14.3)	2 (4.1)	0 (0.0)	
Ewing bone sarcoma	3 (8.6)	1 (1.8)	3 (6.1)	0 (0.0)	
Others	4 (11.4)	7 (12.5)	5 (10.2)	0 (0.0)	
Stage					
I	0 (0.0)	2 (3.6)	0 (0.0)	0 (0.0)	0.669*
II	3 (8.6)	7 (12.5)	7 (14.3)	3 (27.3)	
III	23 (65.7)	30 (53.6)	27 (55.1)	4 (36.4)	
IV	9 (25.7)	17 (30.4)	15 (30.6)	4 (36.4)	
Total	35 (100.0)	56 (100.0)	49 (100.0)	11 (100.0)	

*By Fisher's exact test. †By Chi square test (not enough computer memory to use Fisher's test).

5. Discussion

This cross-sectional study of 151 diagnosed sarcoma patients in Rzgary teaching hospital – medical oncology unit. To the extent of our knowledge, this is the first epidemiological study in our region. In addition, sarcoma is rare type of cancer worldwide, in addition it is also rare in our region, this study could be used as a reference for future upcoming studies on this subject in our locality. The study revealed that the largest proportion of the overall sample (23.2%) were aged 10-19 years, and 21.9% were aged 20-29 years. The median age of soft tissue sarcoma was 55 years, almost the same finding is concluded in *Howlader N* and his colleagues [8]. More than half (58.3%) were males, which is in parallel of the same results of *Howlader N* and his colleagues in-SEER cancer statistics review [8]. In our study, the most common site of sarcoma was limbs (43%), and thigh was the most common site of Soft Tissue Sarcoma. The same finding is concluded in *Brennan* and his colleagues [9]. The most common type of sarcoma in our study was STS (91.1%), followed by bone sarcoma (9.9%), this finding was concluded in *Howlader N* and his colleagues [10]. The most common histopathological type of STS in our study was Ewing soft tissue sarcoma (25.8%) followed by LPS (18.5%), the same results are concluded in *Brennan* and his colleagues [11]. In our study, osteosarcoma is the most common bone sarcoma overall, followed by Ewing bone sarcoma, and they are more frequently seen in adolescents than in adults. This finding is in parallel with the same finding of *ESMO/European Sarcoma Network Working Group* and his colleagues [12]. In this study, other rare types of sarcoma include cutaneous sarcomas (mainly Kaposi sarcoma and dermatofibrosarcoma) accounting only (10.6%) of sarcoma cases. The same finding was concluded in *Rouhani*

and his colleagues [13]. In SEER data (1973–2008), we observed that soft tissue sarcomas currently occur much more frequently than malignant bone tumors [14]. In 2008, soft tissue sarcomas accounted for nearly 87% of all sarcomas diagnosed, while the remaining 13% of the diagnoses were malignant bone tumors [14]. Osteosarcomas and chondrosarcomas were the most commonly diagnosed malignant bone tumors, accounting for over half of all the malignant bone tumor diagnoses. According to SEER, “other specified soft tissue sarcomas” accounted for roughly 51% of all sarcomas diagnosed in 2008, and clearly lead soft tissue sarcoma occurrence. Age is an important determinant of sarcoma occurrence. Based on current statistics provided by the NCHS and SEER, from 2004–2008, the mean age at diagnosis for soft tissue sarcomas and malignant bone tumors was 58 and 40 years of age, respectively [15]. Young adults experience the lowest incidence of soft tissue sarcomas, but occurrence steadily increases until the age of 50. At ages greater 50 years and above, incidence of soft tissue sarcomas increases much more dramatically. 16, 17, 18, 19. Malignant bone tumors, generally have a fairly stable rate of incidence across all ages. However, noticeable increase in rates often occur in adolescents and young adults due to osteosarcoma and Ewing’s sarcoma. 20, 21, 22. Our study has a limitation which was a single-center study; the number of participants is relatively small in epidemiologic terms, which suggests that there may not have been sufficient numbers of patients representing the whole range of sarcoma.

6. Conclusion

This study concluded that sarcoma is more common among people in the second decade of life, the limbs were the most common site of involvement and finally, soft tissue sarcoma accounts majority of the cases.

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7. List of Abbreviations

Table 6

Abbreviation	Stands for
ES	Ewing Sarcoma
LMS	Leiomyosarcoma
LPS	liposarcoma
STS	Soft Tissue Sarcoma
GIST	Gastrointestinal Stromal Tumor

References

- [1]. Surveillance, Epidemiology, and End Results (SEER) Program (<http://www.seer.cancer.gov>).
- [2]. Lahat, G., Lazar, A., & Lev, D. (2008). Sarcoma epidemiology and etiology: potential environmental

and genetic factors. *Surgical Clinics of North America*, 88(3), 451-481.

- [3]. A Snapshot of Sarcoma. <http://www.cancer.gov/aboutnci/servingpeople/cancer-statistics/snapshots>, National Cancer Institute. Sept 2010.
- [4]. Howlader, N. N. A. K. M., Noone, A. M., Krapcho, M., Garshell, J., Miller, D., Altekruse, S. F., ... & Cronin, K. A. (2014). SEER cancer statistics review, 1975–2012. National Cancer Institute.
- [5]. Bauer, H. C., Trovik, C. S., Alvegård, T. A., Berlin, Ö., Erlanson, M., Gustafson, P., ... & Wiklund, T. (2001). Monitoring referral and treatment in soft tissue sarcoma: study based on 1,851 patients from the Scandinavian Sarcoma Group Register. *Acta Orthopaedica Scandinavica*, 72(2), 150-159.
- [6]. Brennan, M. F., Antonescu, C. R., Moraco, N., & Singer, S. (2014). Lessons learned from the study of 10,000 patients with soft tissue sarcoma. *Annals of surgery*, 260(3), 416.
- [7]. ESMO/European Sarcoma Network Working Group. (2014). Bone sarcomas: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. *Annals of oncology: official journal of the European Society for Medical Oncology*, 25, iii113-iii123.
- [8]. Howlader, N. N. A. K. M., Noone, A. M., Krapcho, M., Garshell, J., Miller, D., Altekruse, S. F., ... & Cronin, K. A. (2014). SEER cancer statistics review, 1975–2012. National Cancer Institute.
- [9]. Brennan, M. F., Antonescu, C. R., Moraco, N., & Singer, S. (2014). Lessons learned from the study of 10,000 patients with soft tissue sarcoma. *Annals of surgery*, 260(3), 416.
- [10]. Howlader, N. N. A. K. M., Noone, A. M., Krapcho, M., Garshell, J., Miller, D., Altekruse, S. F., ... & Cronin, K. A. (2014). SEER cancer statistics review, 1975–2012. National Cancer Institute.
- [11]. Brennan, M. F., Antonescu, C. R., Moraco, N., & Singer, S. (2014). Lessons learned from the study of 10,000 patients with soft tissue sarcoma. *Annals of surgery*, 260(3), 416.
- [12]. ESMO/European Sarcoma Network Working Group. (2014). Bone sarcomas: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. *Annals of oncology: official journal of the European Society for Medical Oncology*, 25, iii113-iii123.
- [13]. Rouhani, P., Fletcher, C. D., Devesa, S. S., & Toro, J. R. (2008). Cutaneous soft tissue sarcoma incidence patterns in the US: an analysis of 12,114 cases. *Cancer: Interdisciplinary International Journal of the American Cancer Society*, 113(3), 616-627.
- [14]. Surveillance, Epidemiology, and End Results (SEER) Program (www.seer.cancer.gov) SEER*Stat Database: Incidence - SEER 9 Regs Research Data, Nov 2010 Sub (1973–2008) <Katrina/Rita Population Adjustment Linked To County Attributes - Total U.S., 1969–2009 Counties, National Cancer Institute, DCCPS, Surveillance Research Program, Cancer Statistics Branch, released April 2011, based on the November 2010 submission.
- [15]. Howlader N, Noone AM, Krapcho M, Neyman N, Aminou R, Waldron W, Altekruse SF, Kosary CL, Ruhl J, Tatalovich Z, Cho H, Mariotto A, Eisner MP, Lewis DR, Chen HS, Feuer EJ, Cronin KA, Edwards BK (eds). SEER Cancer Statistics Review, 1975–2008, National Cancer Institute. Bethesda, MD, http://seer.cancer.gov/csr/1975_2008/, based on November 2010 SEER data submission, posted to the SEER web site, 2011.
- [16]. Che-Jui Lee, Agnieszka Wozniak, Thomas Van Cann, Iris Timmermans, Jasmien Wellens, Ulla Vanleeuw, Inge H. Briaire-de Bruijn, Christian Britschgi, Judith V. M. G. Bovée, Inti Zlobec, Raf Scot, Patrick Schöffski, Establishment of an Academic Tissue Microarray Platform as a Tool for Soft

Tissue Sarcoma Research, Sarcoma, 10.1155/2021/6675260, 2021, (1-12), (2021).

- [17]. S. Foersch, M. Eckstein, D.-C. Wagner, F. Gach, A.-C. Woerl, J. Geiger, C. Glasner, S. Schelbert, S. Schulz, S. Porubsky, A. Kreft, A. Hartmann, A. Agaimy, W. Roth, Deep learning for diagnosis and survival prediction in soft tissue sarcoma, *Annals of Oncology*, 10.1016/j.annonc.2021.06.007, (2021).
- [18]. Serena Pillozzi, Andrea Bernini, Ilaria Palchetti, Olivia Crociani, Lorenzo Antonuzzo, Domenico Campanacci, Guido Scoccianti, Soft Tissue Sarcoma: An Insight on Biomarkers at Molecular, Metabolic and Cellular Level, *Cancers*, 10.3390/cancers13123044, **13**, 12, (3044), (2021).
- [19]. Ilse van Eck, Dide den Hollander, Ingrid M.E. Desar, Vicky L.M.N. Soomers, Michiel A.J. van de Sande, Jacco J. de Haan, Cornelis Verhoef, Ingeborg J.H. Vriens, Johannes J. Bonenkamp, Winette T.A. van der Graaf, Winan J. van Houdt, Olga Husson, Unraveling the Heterogeneity of Sarcoma Survivors' Health-Related Quality of Life Regarding Primary Sarcoma Location: Results from the SURVSARC Study, *Cancers*, 10.3390/cancers12113083, **12**, 11, (3083), (2020).
- [20]. Gamboa, A. C., Gronchi, A., & Cardona, K. (2020). Soft-tissue sarcoma in adults: An update on the current state of histiotype-specific management in an era of personalized medicine. *CA: a cancer journal for clinicians*, 70(3), 200-229.
- [21]. Blay, J. Y., Le Cesne, A., & Demetri, G. D. (2020). The current reality of soft tissue sarcomas: advances, controversies, areas for improvement, and promising new treatments. *Expert review of anticancer therapy*, 20(sup1), 29-39.
- [22]. Annovazzi, A., Rea, S., Zoccali, C., Sciuto, R., Baldi, J., Anelli, V., ... & Ferraresi, V. (2020). Diagnostic and Clinical Impact of 18F-FDG PET/CT in Staging and Restaging Soft-Tissue Sarcomas of the Extremities and Trunk: Mono-Institutional Retrospective Study of a Sarcoma Referral Center. *Journal of Clinical Medicine*, 9(8), 2549.