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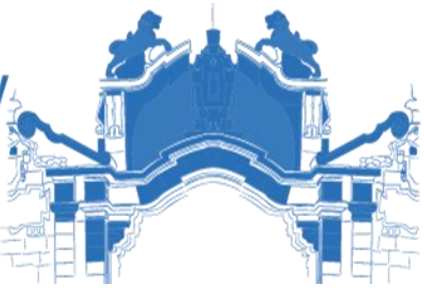

ADDIS ABABA UNIVERSITY

COLLEGE OF HEALTH SCIENCES

DEPARTMENT OF CLINICAL ONCOLOGY

Demographic, clinical, pathologic and treatment pattern of soft tissue sarcoma at Tikur Anbessa Specialized Hospital.

Ethiopia.

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A RESEARCH PAPER SUBMITTED TO ONCOLOGY DEPARTEMENT ADDISABABA UNIVERSITY SCHOOL OF MEDICINE IN PARTIAL FULFILLMENT OF THE REQUIREMENTS FOR CERITEFICATE OF SPECIALITY IN CLINICAL ONCOLOGY

February 14, 2022

Addis Ababa Ethiopia

DEPARTMENT OF CLINICAL ONCOLOGY, SCHOOL OF MEDICINE, COLLEGE OF HEALTH SCIENCES, ADDIS ABABA UNIVERSITY

APPROVAED BY THE EXAMING BOARD Signatures

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February 2022

Addis Ababa, Ethiopia

Abstract

Soft tissue sarcomas are an uncommon group of neoplasm that could be fatal, especially in the metastatic setting.

Late presentation, Missed Diagnosis and inadequate treatment may worsen clinical outcomes.

There is lack of evidence on the demographic, pathological, Clinical and treatment pattern of soft tissue sarcoma in developing countries like Ethiopia

Thus, this study is aimed to assess the demographic, pathological, Clinical and treatment patterns of soft tissue sarcoma in a single tertiary health institution in Ethiopia.

Objective:

The aim of this study is to assess demographic, pathologic, clinical and treatment pattern of soft tissue sarcoma at Tikur Anbesa Specialized hospital at four years duration.

Methods

This is a retrospective cross-sectional study that asses demographic, clinical,pathologic and treatment pattern of soft tissue sarcoma at the TASH between august 2017 and August 2021 G.C. This period was selected because most patient data before this are not available according to my pilot study.

Result:

A total of 320 patients were registered from August 2017 to August 2021 and 190 patients card were available for this study and 80 of patients were excluded according to exclusion criteria and 50 of patients' card were lost. The median age was 32 years of age and Male sex was commonly affected accounting 61.6% and female sex accounts 38.4%.

The commonest sites were extremities accounting for 48.9 % of cases. The Commonest presenting symptoms were mass and pain accounting for 93.2% and 77.9% of cases respectively.

The commonest histology subtypes were, undifferentiated sarcoma, rhabdomyosarcoma and synovial sarcoma accounting 50%, 15.8% and 6.3 % cases respectively.

The grade of the lesions was described in 67.3 % of patients. Of those lesions whose grade was described 56.8 % were high grade lesions.

From all cases 58.3% of the patients underwent surgery as a primary treatment modality. Only 50.5% of cases were started treatment with curative intent and 49.5% of the case started their treatment with palliative intent.

Conclusion:

The pattern of soft tissue sarcoma in this cross sectional study has shown different distribution in terms of demography, clinical presentation, treatment and pathological subtypes when compared to other studies. Advanced stage of initial clinical presentation and substandard work up according to standard text books and therapy makes it unique from cases reported from other parts of the world

Acknowledgment

I have a great gratitude to my advisor Dr Yonas Dandena, the oncology department staff and my friends Dr Amare, Dr Zerubabel and Mister Biruke for helping me in collecting data, for their comments on my research. I have also great gratitude to my wife W/Ro Feven Bazezew, my baby Benias Melsew and my sister Wubalem Netsaw for giving their patience and support while I was doing this research.

Abbreviations and Acronyms

FNAC:fine needle aspiration....16, 20, 34
GC:gregorean callender....20, 36
IAEA:international atomic energy agency....19
IHC:immunohistochemistry....24, 32, 34
MD:medical doctor 2, 36
MDT:multidiciplanary team 14
NCDB;national cancer data base 18
NF1:neurofibromatosis type 1....13
STS:soft tissue sarcoma....13, 14, 15, 16, 17, 18, 23, 29
TASH:tikur anbessa specialized hospital....4
WHO:world health organization....13

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Chapter one

1.1. Introduction

1.1.1. Background

Soft tissue sarcoma refers to cancer that begins in the muscle, fat, fibrous tissue, blood vessels, or other supporting tissue of the body.

Soft tissue sarcomas are a rare group of cancer accounting for 1% of all solid tumors(1).

The WHO recognizes approximately **70** histology subtypes(1).

There are less than 12,000 cases in the US for 2016 and soft tissue sarcoma represents ~ 1% of all cancers(2). Soft tissue sarcomas are a relatively uncommon group of malignancies. On average a general practitioner may only see one sarcoma in their career(3).

For the vast majority of cases, the etiology is unknown, although there are certain genetic associations.

The 10% lifetime risk of malignant peripheral nerve sheath tumor in individuals with familial neurofibromatosis, caused by mutations in the neurofibromatosis gene(4). There is an increased risk of sarcomas in patients who have had a familial retinoblastoma, caused by inherited mutations in the RB gene(5). Similarly, there is an increased risk of sarcomas, and other cancers in families with Li-Fraumeni syndrome who have inherited mutations in the TP53 tumor suppressor gene(6). There is also a small risk of sarcoma in areas of the body previously treated using radiotherapy, for example angiosarcoma following treatment for breast.

Due to the heterogeneous sites of origin of **STS**, it is difficult to clearly define the clinical features of the disease. However, a soft tissue lump exhibiting any of the following three clinical features should be considered to be malignant until proved otherwise(6).

- ✓ Increasing in size.
- ✓ Size more than 5 cm.
- ✓ Painful.

The more of these clinical features present, the greater the risk of malignancy with increasing size being the best individual indicator. In addition, deeper lying masses are more likely to be sarcomas. (7).

The standard approach to diagnosis of a suspicious mass is percutaneous core needle biopsy. several cores should be taken to maximize diagnostic yield. However, an incisional biopsy may be necessary on rare occasions, and excision biopsy may be the most practical option for small superficial lesions.

Histological diagnosis should be made according to the 2013 WHO Classification to determine the grade and stage of the tumor(3).

Pathologic diagnosis relies on morphology and immunohistochemistry. Increasingly it should be complemented by molecular pathology to confirm those diagnoses characterized by a specific genetic abnormality, such as an activating mutation, chromosomal translocation, or chromosomal amplification, using for example fluorescent in situ hybridization or reverse transcription polymerase chain reaction(8). It may have particular utility when the clinical pathologic presentation is unusual, or the histological diagnosis is doubtful. Molecular testing is now routine to confirm diagnoses such as Ewing sarcoma, rhabdomyosarcoma, synovial sarcoma, and to differentiate lipomas from atypical lipomatous tumors/well-differentiated liposarcomas.

It is increasingly possible to tailor treatment according to the individual histology. The major therapeutic goals are long-term survival, avoidance of local recurrence, maximizing function, and minimizing morbidity. All

patients should have their care managed by a formally constituted sarcoma MDT. Decisions about surgery, chemotherapy, radiotherapy and the timing of all these modalities should be made by the Sarcoma MDT. For site specific STS (e.g. gynecological, head and neck) there should be a formal relationship between the sarcoma MDT and the site-specific MDT(9).

1.2 .Statement of the problem and Rationale

Cancer has become the second leading cause of death, behind cardiovascular disease, with more than 8.7 million attributable deaths worldwide in 2015.Low-income countries contribute up to 60% of this death toll. This is an alarming prospect, especially for LICs, where the weak health systems are severely resource constrained and already overwhelmed by the large burden of communicable diseases. Similar to other low income countries, the burden of non-communicable diseases (NCDs)is increasing in Ethiopia. Cancer has become the second leading cause of death in the adult population.

Local data on cancer epidemiology in Ethiopia are lacking. There is no reliable cancer registry anddata availability is scanty in our country, Ethiopia.

Soft tissue sarcoma is a rare disease whose management is challenging.

There are many histological sub types, anatomic sites and clinical Presentation which makes it a heterogeneous entity and difficult to have specific histologic diagnosis.

As a result of a lack of adequate diagnostics and therapy, most patients in low income countries present with advanced stages of disease. To my Knowledge there is no demographic, clinical, and pathologic and treatment pattern study done in Ethiopia.

1.3 Significance of study

The National Health Sector Transformation Plan (HSTP) 2015/16 in line with our country's second growth and transformation plan, has set ambitious goals to improve equity, coverage and utilization of essential health services, improve quality of healthcare, and enhance the implementation capacity of the health sector at all levels of the system. The plan outlines interventions to reduce the burden of cancer through changes in lifestyle, primary prevention, screening and early diagnosis, appropriate follow-up, treatment and provision of palliative care. In line with this, cognizance of the prominent characteristics of bladder cancer patients will greatly help stakeholders in beating cancer and salvage the overall health cost incurred by these neoplasms. Comprehensive knowledge of soft tissue sarcoma characteristics will be of irreplaceable help in early detection of these potentially fatal soft tissue sarcoma cases and allow oncology practitioners to make better clinical decisions for the best end of clients.

Furthermore, it will guide health policy makers and other concerned stakeholders to devise strategicprograms on inculcating evidence-based interventional protocol in candidate populations. Hence, the data collected from

this study can be a good input to the country's endeavor in handling the several formidable tasks: first, accurately measuring the scale of the national cancer burden and characterizing existing preventive, curative, and palliative care services available at each tier of the health system; second, identifying challenges to the improvement of cancer reporting and specialized oncology services; and finally, designing feasible interventions applicable in a low resource setting.

Finally, the findings obtained from this study will serve as a baseline for other researchers for further in-depth studies

Chapter two

2.1. Review on demographic pattern of soft tissue sarcoma

In a 5 year Retrospective cross sectional Study done in Jimma University Medical Center, Southwest Ethiopia in A total of 284patients, the commonest age of presentation was between **21-30** years with a median age of 31.00 years and regarding sex distribution there was a slight female predilection with M: F ratio of **1:1.01**(10)

There is retrospective cross sectional study on medical records of 108 patients who were diagnosed histologically as soft tissue sarcomas from 1999- 2001 in Uganda on demographic and histologic pattern and the peak age was 15-30 years. The male to female sex ratio was 1.5:1(11).

In a retrospective cross-sectional study done in India on clinical and pathological evaluation of soft tissue tumors in tertiary care center on total 360 cases, the highest prevalence of benign soft tissue tumors was in third decade while malignant tumors had in fifth decade and Soft tissue tumors had slightly male preponderance. Having male to female ratio was 1.3:1. Male to female ratio in benign tumors was 1.2:1 and among malignant tumors ratio was **2:1**(12)**.**

In a population based study done in Canada, the male to female ratio of STS was 1.5:1(13)**.**

In prospective cohort study done in Korea on from 2002 to 2015 on total of 7,813 patients, the most populous age group was 50-59 years (22.7%), about half were females (52.1%) and the initial diagnosis setting was a general hospital (94.1%). The average age of the advanced STS patients was 56.1±16.4 years, slightly higher than the localized STS patients (53.2±16.0 years)(14).

In retrospective study done in Europe STS was slightly more common in men. The typical patient with MFH was 70 years old and A leiomyosarcoma typically occurred in a patient of similar age but Patients with synovial sarcoma were typically young and the tumors were distally located(15).

In European setup ,a Population-Based Study from the Surveillance Epidemiology and End Results Database on Soft tissue Sarcoma across the Age Spectrum on 48012 patients was done, among all of the STS reported, 2,679 (5.6%) were among persons younger than age 20 years at diagnosis. The proportion of total malignancies that were STS was highest in individuals younger than age 30 at diagnosis. Males made up more than half of the cases for most tumor types among both pediatric and adult malignancies(16).In France each year, 3,526 people are diagnosed with STS and visceral sarcoma(17)

The gender ratio of soft tissue sarcoma in men and women is 1:1.25 ratio according to 2017 American statics(18)

2.2. Review on histopathology of soft tissue sarcoma

In retrospective cross sectional study done in **Jimma University** on five years patient's biopsy record of pathology department from September 2013 to August 2018 G.C. Benign tumors are three times more common than malignant. The most common soft tissue sarcomas were in children Rhabdomyosarcoma and in adults Malignant Fibrous Histiocytoma (10).

In **Uganda** descriptive records of patients who were diagnosed histologically as soft tissue sarcomas from 1999-2001 inclusive were retrieved and analyzed, there were 108 patients diagnosed with soft tissue sarcomas during the study period. The commonest type was fibrosarcoma, and the commonest grades were 1 and 3. The commonest site was the lower limb at the groin(11).

In **a 5-year retrospective** study between the period of 2010 to 2015 of all cancer patients diagnosed with soft tissue sarcoma, seen in the department of radiotherapy and oncology, a tertiary health center in **Sokoto Nigeria**, a total of 123 patients were reviewed: the commonest histological type in both the adult and pediatric age group was rhabdomyosarcoma (19).

In p**rospective study** done in **India**, carried out in the Department of Surgery, Mahatma Gandhi Institute of Medical Sciences, a total of 157 patients of soft tissue tumors who attended Surgery OPD were included in the study with informed consent. The main stay of diagnosis was clinical followed by ultrasonography and FNAC.

The diagnosis was confirmed by Histopathological examination if operated and by Tru Cut biopsy if inoperable, the most common malignant STS were Malignant Spindle cell Neoplasm, Liposarcoma, Malignant and Fibrous Histiocytoma and Leiomyosarcoma(20)

In **China** In 2017, they reported the epidemiology of STS using population-based cancer registry data from 339 cancer registries. Approximately **39,900** new STS cases occurred nationwide in China in 2014, accounting for **1.05%** of overall cancer incidence. **GIST was** the most common histological subtype, followed by nerve sheath tumor and malignant peripheral nerve sheath tumor, leiomyosarcoma, liposarcoma, and fibro sarcoma. (21).

IN EUROPE IN A TERTIARY REFERRAL INSTITUTIONS, THE MOST COMMON SOFT TISSUE SARCOMA SUBTYPES IN ADULTS ARE LIPOSARCOMA ,LEIOMYOSARCOMA, UNDIFFERENTIATED PLEOMORPHIC SARCOMA, AND GIST(22).

In European setup, a Population-Based Study from the Surveillance Epidemiology and End Results Database on Soft Tissue Sarcoma across the Age Spectrum on 48012 patients was done, Individuals less than 20 years of age represented 5.6%, with rhabdomyosarcoma being the most common subtype. In adults, the most common types were Kaposi sarcoma, fibro histiocytic tumors, and leiomyosarcoma(16)

2.3. Review on clinical presentations of soft tissue sarcoma

The patient with extremity soft-tissue sarcoma typically presents with a painless, enlarging mass(23). Symptoms of compression may be reported including new onset edema and/or new or worsening paresthesia(24).

The anatomic distribution of soft tissue sarcomas in 4550 adults as reviewed by the American College of Surgeons:

It was **46%** on the thigh, buttock, and groin ,**13%**Upperextremity,`**18%**Torso,**13%**Retroperitoneum ,**9%**Head and neck (25).

According to Kotilingam.et.al,the commonest site of body affected by soft tissue sarcoma is extremity accounting 80% of the cases(26).

There was a descriptive retrospective review of pediatric patients aged between 0 to 18 years with a histopathologically confirmed diagnosis of either an STS or bone sarcoma at MNH Pediatric Oncology Unit in Tanzania from January 2011 to December 2016,41 % of patients were diagnosed as stage IV disease(27).

EUROPEAN JOURNAL OF CANCER, A retrospective review of an orthopedic oncology database identified **1170** patients with newly diagnosed STS during a 7.5-year period (1996–2004). The patient demographics,

tumor type, size, depth, histology grade and presence of metastatic disease at presentation were studied, the incidence of metastases at diagnosis was 10% (116 patients), 8.3% (96 patients) had lung metastases on chest CT and 1.7% (20 patients) had metastases elsewhere.
The risk of having lung metastases at diagnosis was 11.8% in high grade tumors, 7% in intermediate grade and 1.2% in low grade tumor(28).

2.4. Review on treatment pattern of soft tissue sarcoma

In **a retrospective cohort** study done in Nigeria on sub-Saharan African experience in the surgical management of soft tissue sarcomas in an oncology unit: the study was done on 596 cases of STS were seen over the ten-year period. The resection margin was negative in 88% of the cases and patients who benefitted from definitive surgical treatment for STS were found to be the young and middle age group(29).

There was a retrospective review of 382 patients with localized extremity or truncal STS who underwent limb-sparing surgery and RT from 1983 to 2010, in Oxford university and analyzed marigin status in which Surgical margins were positive in 18% patients and negative in 82% patients(30).

A population based cohort study was done in Canada on treatment pattern of STS, the combination of surgery and radiation therapy was the most common treatment regimen for Stage 1 and 2 patients which accounts 69%of the cases and 39.5% of the cases were given adjuvant radiotherapy after surgery(13).

In a Systematic review done on different Asian countries on 1,822 patients and 32studies, nearly all patients undergo surgery, and more studies used adjuvant radiotherapy than chemotherapy (24 vs 17 studies)(31).

The American College of Surgeons Commission on Cancer and the American Cancer Society was doing retrospective study on NCDB 7,752 soft tissue sarcoma patients on treatment pattern of soft tissue sarcoma management. The study shows 57.3%, 41%, 33.6% and 19.4% of stage I.II.III and IV patients were undergone surgery and it also shows 22.1% of the cases were given chemotherapy only. 26.8%,33.6%,34.5% and 8% of stage I,II,III and IV patients were given surgery and radiotherapy respectively(32).

A Retrospective Medical Record review in the United Kingdom, Spain, Germany, and France to describe real-world treatment patterns and outcomes for patients with advanced soft tissue sarcoma not amenable to surgery or radiotherapy .the study was done 807 patients and Overall, 57% of patients received only 1 line of therapy,

32% received 2 lines of therapy, and 11% received ≥3 lines of therapy. The most common first-line regimens were doxorubicin alone (41%), doxorubicin plus ifosfamide (19%), docetaxel plus gemcitabine (9%), paclitaxel alone (4%), and ifosfamide (4%).

Conclusions. advanced STS is most commonly treated with older therapies in the United Kingdom, Spain, Germany, and France(33).

A retrospective cohort study was done on 555 patients to see the treatment patterns among patients with metastatic soft tissue sarcoma in the US, among the metastatic STS study cohort, 41.3% had 2 LOTs, 15.9% had 3 LOTs, and 5.0% had 4 LOTs during the study period. Across all LOTs, the most frequently prescribed agent (in either mono- or combination therapy) was gemcitabine (43%), followed by doxorubicin (36%), docetaxel (35%), and pazopanib (21%)(34).

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3.0. Research questions

3.1. What is the four year demographic, clinical, and pathologic and treatment pattern of soft tissue sarcoma patients at Tikur Anbessa hospital?

Chapter three

4.0. Objectives

4.1. General objectives:

*T*he aim of this study is to assess demographic, pathologic, and clinical and treatment pattern of soft tissue sarcoma at TikurAnbesa Specialized hospital at four years duration.

4.2. Specific objectives

. To determine the demographic pattern of soft tissue sarcoma patients.

. To assess patients stage pattern.

. To assess the commonest histologic subtypes

Chapter four

5. Methods and materials

5.1 Study area and setting

The study was conducted in TikurAnbessa Specialized Hospital Radiotherapy center.

It was established 27 years back with the help of International Atomic Energy Agency (IAEA).

The center currently has one LINAC units. Six full time consultant oncologists, three medical physicists and 5 radiotherapists are currently working in the center.

The center has started training of clinical oncology in 2013 and currently 36 residents are enrolled.

Activities include inpatient admission for chemotherapy and outpatient clinics for new patient evaluation and simulation for radiotherapy and contouring.

There are two chemotherapy centers one in black lion and newly opened center few years ago which is called Amstegna health center.

5.2 Study design

This is a retrospective cross sectional study that evaluates the four year demographic, pathologic, and clinical and treatment pattern of soft tissue sarcoma patients that were seen from august 2017 to august 2021 GC

5.3. Source population

All the soft tissue sarcoma patients that were registered at the oncology department of TikurAnbessa hospital between August 2017 to August 2021 G.C are included

5.4. Study population

All cases of histopathology confirmed soft tissue sarcoma patients seen in TikurAnbassa Specialized Hospital Radiotherapy center and whose files were available during the study period**.**

5.5 Inclusion criteria

- Pathologically confirmed disease at presentation by biopsy or FNAC
- Patients of any stage.
- All age groups

5.6 Exclusion criteria

Inadequate data which lacks 3 or more of the following variable

- ✓ histology types,
- ✓ treatment pattern,
- ✓ marigin status,
- ✓ grade,
- ✓ age,
- ✓ sex

sample size calculation

- ✓ $N= Z^2 P(1-P) / W^2$
- ✓ P=0.5 Z=1.96 W=0.05
- ✓ $N=1.96^2 0.5(1-0.5)/0.05^2$
- ✓ N=384
- ✓ Sample size adjustment=384/1+384/320)=175

In this study all of cases were equal with the adjusted sample size and they were includded

5.7. Sampling procedure

HMIS logbooks were used to identify all cases of soft tissue sarcoma that were documented after evaluation at the oncology department. And every case that fulfills the inclusion criteria was included in the study.

5.8. Data collection tools and procedures

Medical record charts was collected based on the HMIS record and all the cards that are not in accordance with the inclusion criteria was returned by the primary investigator/supervisor.

The supervisor discussed the goal and purpose of the study as well as the questionnaire with the other data collectors.

Before data collection, orientation was given to supervisors and data collectors on the purpose of the study and how to fill the information on structured (formulated) questionnaire so that there will be common understanding of the objectives of each of the questions. This could minimize the personal variation on interpretation.

The data collection process was supervised by the principal investigator and data collectors' supervisor

5.9. Variables

- ✓ sex
- ✓ age
- ✓ histology
- ✓ marigin status
- ✓ treatment type

5.9.2 Operational definitions

Staging is a way to describe how much cancer is in the body and where it is located in the body.

In the TNM system, the overall stage is determined after the cancer is assigned a letter or number to describe the tumor **(T),** node **(N),** and metastasis **(M)** categories according to the 8th edition AJCC.

This is done by cross sectional imaging in this study. This imagings include MRI of the affected site and CT scan of the affected sites.

- **T** describes the original (primary) tumor size.
- **N** tells whether the cancer has spread to the nearby lymph nodes.
- **M** tells whether the cancer has spread (metastasized) to distant parts of the body.

Soft tissue sarcoma: is a broad term for cancers that start in soft tissues (muscle, tendons, fat, lymph and blood vessels, and nerves).

6. Data management and quality assurance

The principal investigator was training on the relevance of the study to the data collectors and followed closely the data collection procedures and keep hard copy of the completed forms in a protected place.

6.1 Data analysis

Data was entered and analyzed using SPSS version 25. The main findings were described by using frequencies, percentages, and summary statistics**.**

6.2. Ethical consideration

Ethical clearance was obtained from the Ethical review board of Addis Ababa University College of Health Sciences (AAU

Chapter five: **Results**

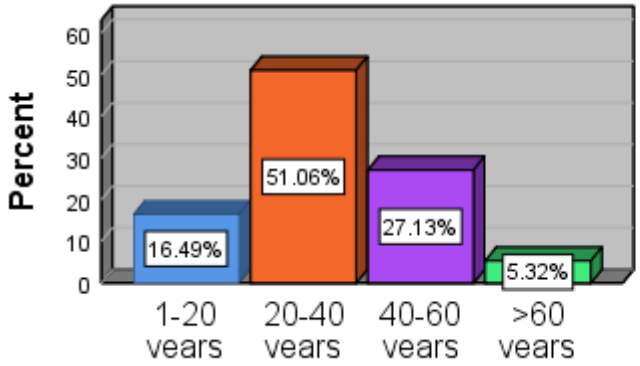
In the years August 2017 to August 2021 a total of 320 soft tissue sarcoma patients were registered. Of these 190 charts were found. The summary of the findings in these study is presented as follows.

6.1 Demography

Considering age, the age group **20- 40** is the commonest age group accounting for **50.5%** of the population. The age range in this study was from **8 to 75** years old.

The median age was **32** years old. Figure 1 demonstrates the age distribution in this study.

In respect to gender of the 190 patients, **117 (61.6%)** were male patients.



0-1 age in interval

Variable		Frequency	Percentage (%)
Age (in years)	1-20	31	16.5
	20-40	96	51.1
	40-60	51	27.1
	>60	12	5.3
sex	male	117	61.6
	female	73	38.4
Marital status	married	107	56.3
	single	60	31.6
	divorced	5	2.6
	widow	2	1.1
	unreported	16	8.5
Religion	orthodox	109	57.4
	Muslim	42	22.1
	protestant	37	19.5

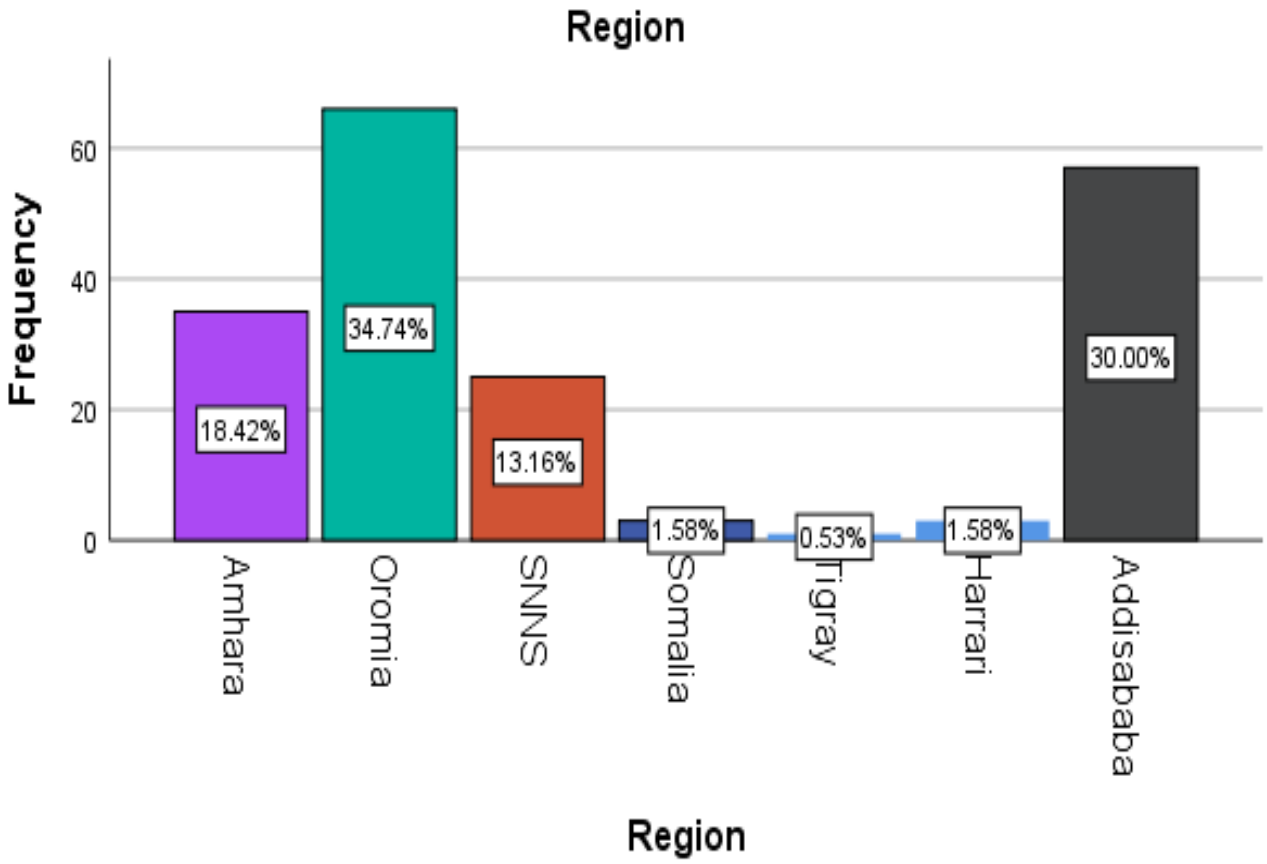
2/9/2022 27

0-2 sociodemographic data

6.2. Region

With regard to region in Ethiopia, patients coming from Oromia Region were most common accounting **34.7%** of the cases followed by Addis Ababa city.

The distribution is described in the following figure



0-3 resident by region

6.3 Clinical Presentation

When it comes to site of primary disease extremity is the commonest site (**48.9 %)** followed by trunk **(24.7%)** and head and neck (**15.8 %).**

Retroperitoneum (4.2%) and other sites accounted for the remaining 6.4%.

Site	Frequency	Percent (%)

Lower extremity	65	34.2
Upper extremity	28	14.7
Trunk	47	24.7
Intraabdominal	2	1.1
Retroperitoneal	8	4.2
Head and neck	30	15.8
Scrotal	3	1.6
par testicular	3	1.6
Vaginal	3	1.6
Breast	1	0.5
Total	190	100

Table 1 origin by site

When it comes to presenting symptom, mass and pain are the commonest presenting symptoms **(77.9%)** followed by painless mass **21.6%.**

Out of the 190 patients, 38(20%) presented with cough from lung metastasis.

Table 2 symptoms from primary disease in soft tissue sarcoma diagnosed in August 2017-August 2021

Presenting symptoms	Number	Percentage
Mass	177	95.2 %
Pain	148	77.9 %
Cough	38	20 %
Bleeding	27	14.2 %

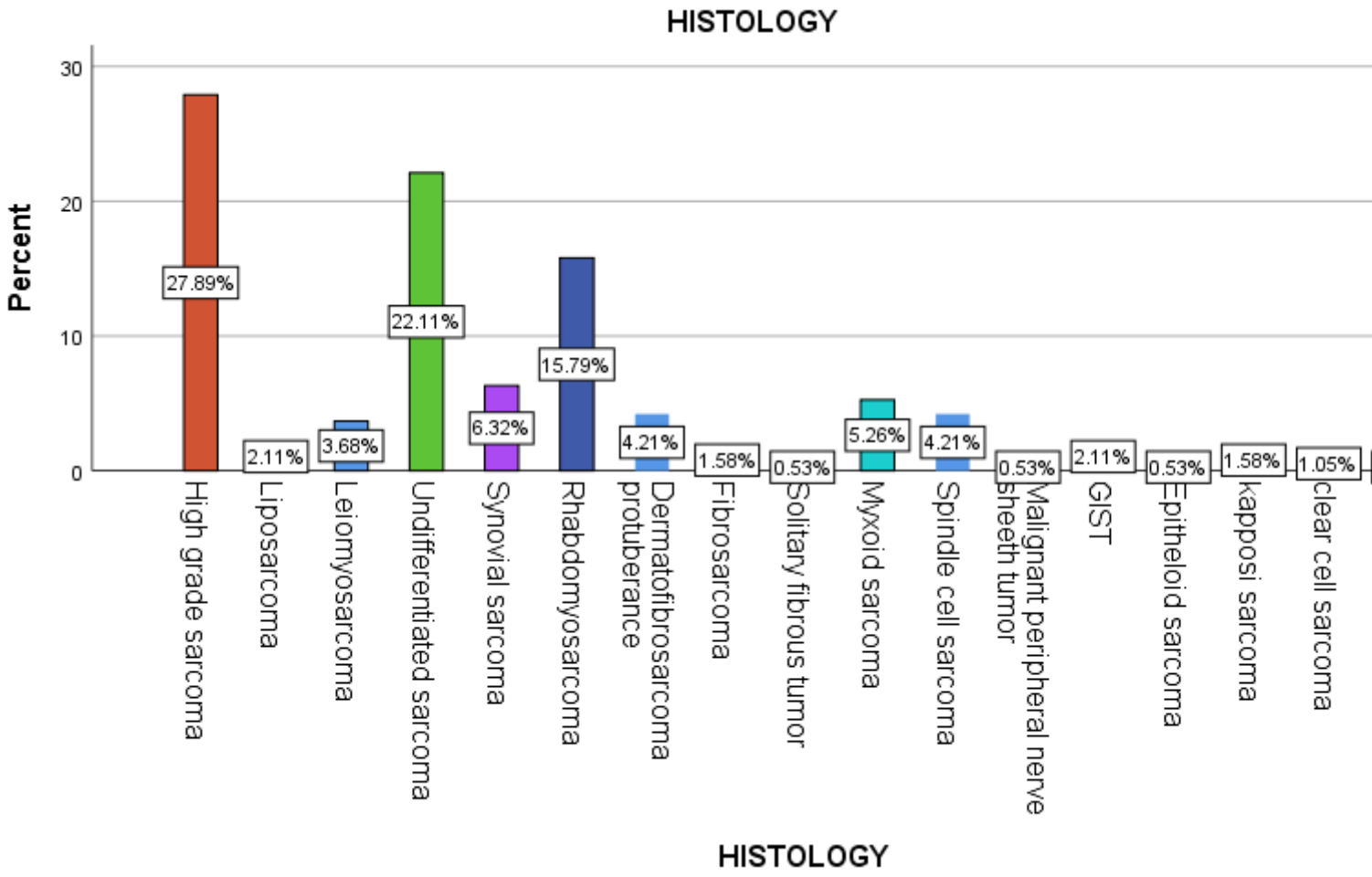
Table 2 clinical presentation

6.4. Histological Diagnosis and types of histology

For histological diagnosis at oncology department 3.2 % came with FNA result alone and 96.8 % came with biopsy results and none of patients had IHC at time of initial presentation.

6.4.1. Histology subtypes

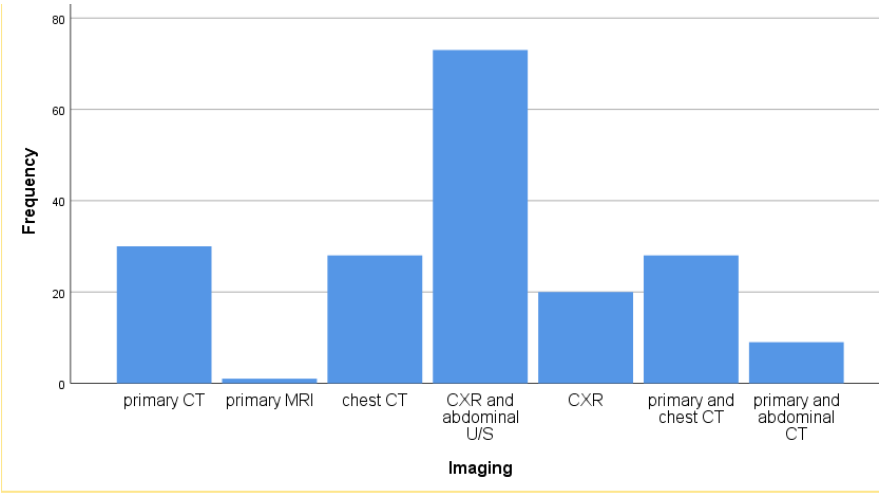
The commonest histology type was undifferentiated sarcoma accounting **(50%)** followed rhabdomyosarcoma accounting **(15.8 %)** and the third most common histology is synovial sarcoma accounting 6.3% of the cases.



0-1 histology type

6.5. Imaging

Different imaging modalities were used to evaluate the primary and metastatic sites. Primary CT,CXR and abdominal U/S were the commonest imaging modality used for primary site and metastasis work up accounting (38.4%) of the cases followed by primary and chest CT accounting 16.3% of the cases. It is illustrated in the following figure

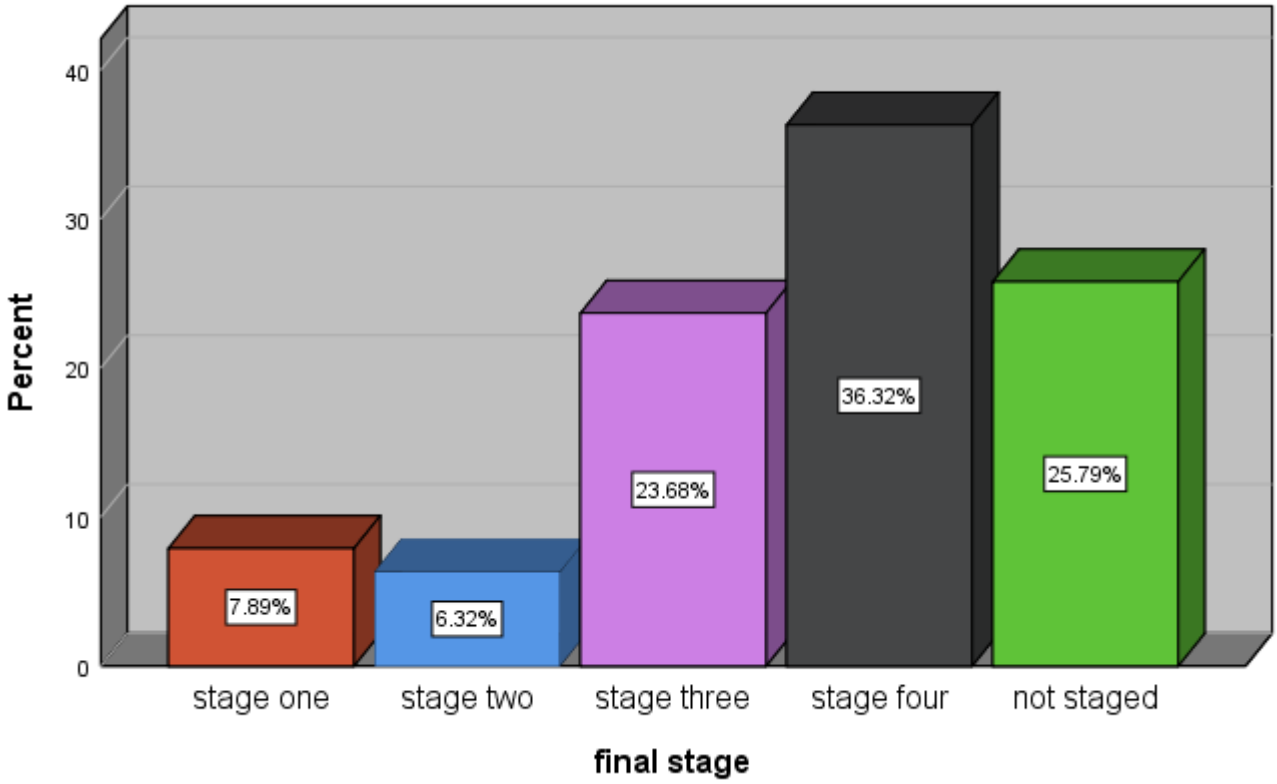


0-2 imaging modality

6.6. Stage

The commonest stage at presentation in this study was stage IV accounting (**36.3%)** of the cases followed by stage III accounting (**23.7 %)** of the cases.

It is described in the following figure

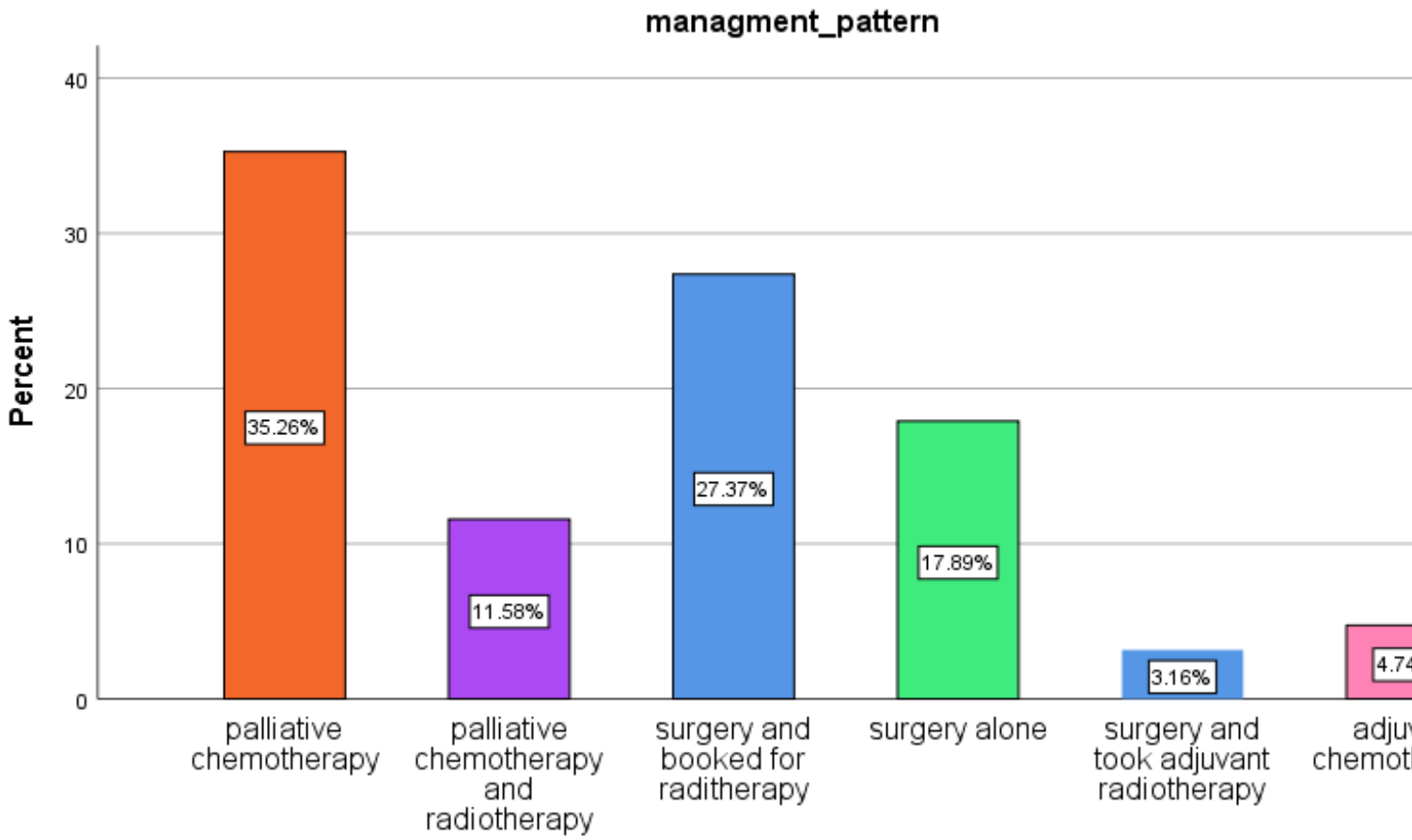


0-3 group staging

6.7. Treatment

Near to half of patients **(48.5 %)** had undergone surgery. Of these **4.7 %** had received adjuvant chemotherapy. Only 3.2% received adjuvant radiotherapy and for **17.9 %** of patients surgery alone was sufficed. **35.3** % of patients were given palliative chemotherapy and 1l.6 % of patients were given both palliative chemotherapy and palliative radiotherapy

It is illustrated in the following figure below



0-11 treatment pattern

6.7.1 Adjuvant Chemotherapy

When it comes to adjuvant treatment of the 101 patients who underwent surgery 15(14.9%) took adjuvant treatment. 6(5.9%) patients took adjuvant chemotherapy and radiation.

6.7.2 Palliative chemotherapy

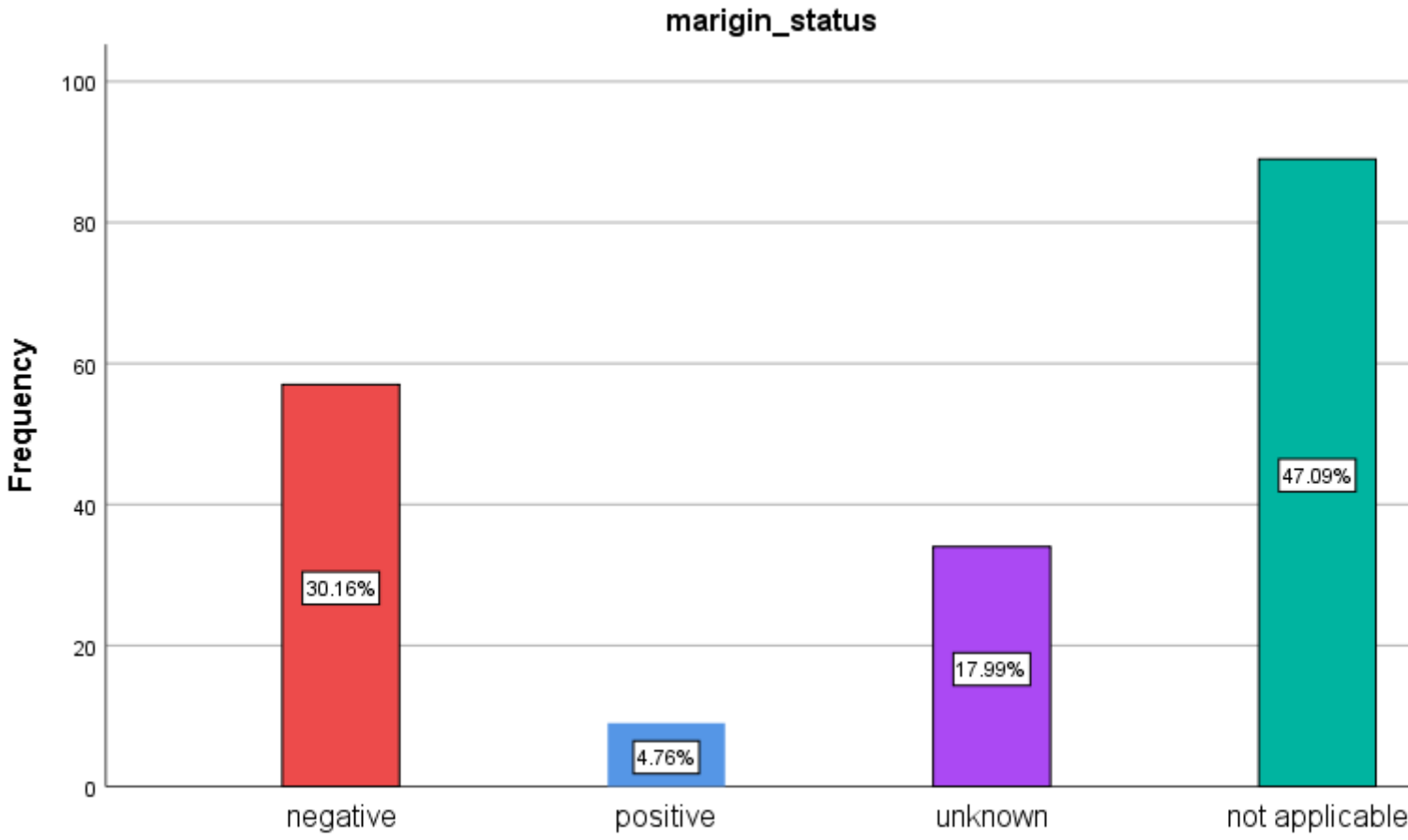
Of the total 190 patients 89(46.9%) took palliative chemotherapy from these patients 22(11.6%) took both palliative chemotherapy and palliative radiotherapy

6.7.3 Radiotherapy

When it comes to radiation treatment: 29 patients (15.2%) took radiation treatment for different indications. From this 22 patients (75.9%) took palliative radiotherapy and only 6(21%) took adjuvant radiation

6.7.4 Post operative pathologic review

When it comes to post operative pathologic review, of the 190 of patients 30 % had negative margin and 4.7% had positive and 17.9% status was unknown and 46.8% were unapplicable for assessing al status. Marginal status in these pathologic reviews are shown in the figure below



0-21 marigin status

Margin	Frequency	Percentage
Negative	57	30%
Positive	9	4.7%

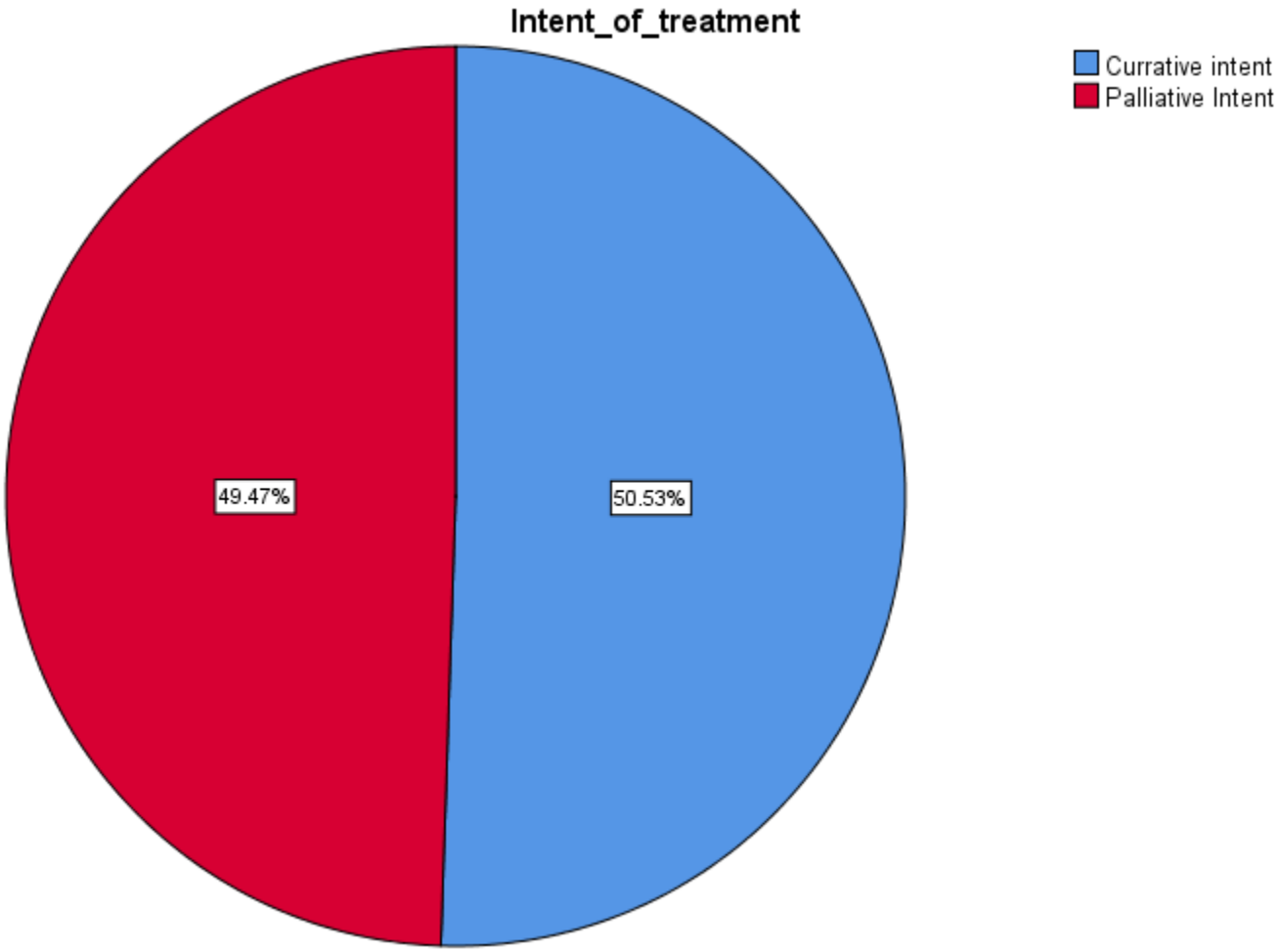
Unknown	34	17.9%
Not applicable	89	46.8%
Low grade	11	5.8%
Intermediate grade	9	4.7%
High grade	108	56.8%
Unspecified	61	32.1%

Table 3 marigin status

6.7.5. Intent of treatment

With regard to treatment intent, near half of patients were treated with palliative intent accounting 49.5%

It is illustrated in the following figure



0-31 treatment intent

Chapter 6 Discussion

The male to female ratio in this study is 1.6:1 and the commonest age of presentation in this study is 20-40 years of age and the median age is 32 years between men and women which is almost similar with Uganda study in which the male to female sex ratio was 1.5:1. It is also accordance with Canadian study having male to female ratio of 1.5:1((11)(20)

The Indian study having male to female ratio in benign tumors was 1.2:1 and among malignant tumors ratio was 2:1 is also similar with this study where as it is 1:1.25 in American cancer society data from the 2017(19).

With regard to age the commonest age of presentation in this study is 20-40 years of age and the median age is 32 years. This result is almost similar to the previous study done in Jimma University which was between 21-**30** years with a median age of 31.00 years(10). It is also almost similar with Ugandian study in which the peak age was 15-30 years(11).

But the commonest and median age of presentation in this study is younger compared to the Korea study in which the most populous age group was 50-59 years(14). This difference may be due to long life expectancy in developed country.

Mass and pain are the commonest presenting symptoms (77.9%) followed by painless mass 21.6%. Out of the 190 patients, 38(20%) presented with cough from lung metastasis. This study has also similar outcome compared with retropspective study on clinical presentation of soft tissue sarcoma(23).

With regard to site of primary disease, the extremity is the commonest site (48.9 %) followed by trunk (24.7%) and head and neck (15.8 %) and it is almost similar to the review done by the American College of Surgeons which was **46%** on the thigh, buttock, and groin ,**13%** Upperextremity,`**18%**Torso,**13%**Retroperitoneum ,**9%**Head and neck (25).

This is also similar with other American study done by (26) with the commonest site of body affected by soft tissue sarcoma is extremity accounting 80% of the cases.

With regard to the types of histology, the commonest histology type was undifferentiated pleomorphic sarcoma (50%) followed by rhabdomyosarcoma (15.8%) and the third most common histology subtype was synovial sarcoma (6.3%) in this study. The result of this study shows our histology reporting system is not adequate to specify the type of histology and it is not enough reporting to compare with the other studies.

The commonest stage at presentation in this study was stage IV accounting (36.3%) of the cases followed by stage III accounting (23.7 %) of the cases. This study almost has similar stage of presentation with Tanzanian study in which 41 % of patients were diagnosed as stage IV disease even if the type of histology was predominantly rhabdomyosarcoma in this study(27).

In contrast to our study EUROPEAN JOURNAL OF CANCER, A retrospective review of an orthopedic oncology database identified **1170** patients with newly diagnosed STS ,the incidence of metastases at diagnosis was 10% (116 patients), 8.3% (96 patients) had lung metastases on chest CT and 1.7% (20 patients) had metastases elsewhere(29). **This difference may be due to late presentation in our set up in developing countries like Ethiopia.**

This study 35.3%, 11.6% of the total cases was treated with palliative chemotherapy and both palliative chemotherapy and radiotherapy respectively about 48.5% of patients had undergone surgery. Of these 27.7% of patients had underwent surgery and booked for radiotherapy and 17.9% had undergone surgery alone. The other 3.2% of the cases were given adjuvant radiotherapy. The study has also has less surgical treatment pattern compared with other Canadian and European studies in which around 69% of the cases were treated with surgery. And also in this study only 3.2% of the cases were given adjuvant radiation in contrast to Canadian study in which 39.5% of the cases were given adjuvant radiation after surgery(13)(31)(30). This difference may be due to inadequate availability of radiotherapy in our country and late presentation of our cases.

The marigin status was done for patients undergoing surgery in which it was negative in 57% of patients, it was positive 9% of the cases and 34% of the cases the marigin status was unknown. This study has contradictory result compared with Nigerian study which has most cases were done with surgery and the resection margin was negative in 88% of the cases(29). This study has also contradictory result in contrast to Oxford university result in which 18% of patients were positive and 82% of patients were negative and non of the patients were unknown(30). In contrast to Nigerian and European studies many of our patients' marigin status was not reported. This may be due to lack of multidisciplinary discussion.

Chapter 7: conclusions and recommendation

The pattern of soft tissue sarcoma in this cross sectional study has shown different distribution in terms of demography, clinical presentation, treatment and pathological subtypes when compared to other studies.

Advanced stage of initial clinical presentation and substandard work up and therapy makes it unique from cases reported from other parts of the world..

We recommend the government should increase radiotherapy centers so that we can treat patients with radiotherapy

We recommend Pathologists to report as much as possible the type of histology other than grade and marigin status

We recommend multidisciplinary management has to be practiced on the management of soft tissue sarcoma

Strength

- ✓ It includes all age groups and both sexes
- ✓ It has well defined inclusion and exclusion criteria

Weakness

- ✓ The pediatric age group is not well represented.
- ✓ Most of the histology subtype was not histologically diagnosed
- ✓ The treatment pattern and follow up was not well documented on the chart

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