ADDIS ABABA UNIVERSITY

COLLEGE OF HEALTH SCIENCE SCHOOL OF MEDICINE

DEPARTMENT OF HEMATOLOGY ONCOLOGY

AND NUCLEAR MEDICINE

TREATMET OUTCOME AND PATTERN OF RADIOTHERAPY UTILIZATION OF PEDIATRICS RHABDOMYOSARCOMA AT TIKUR ANBESSA SPECIALIZED HOSPITAL; ETHIOPIA 5 YEAR RETROSPECTIVE STUDY

BY

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A THESIS SUBMITTED TO THE DEPARTMENT OF HEMATOLOGY ONCOLOGY AND NUCLEAR MEDICINE COLLEGE OF HEALTH SCIENCE ADDIS ABABA UNIVERSITY IN PARTIAL FULFILLMENT OF THE REQUIREMENTS FOR THE DEGREE OF SPECIALTY CERTIFICATE IN CLINICAL ONCOLOGY

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December, 2025

Addis Ababa, Ethiopia

Declaration

I, the undersigned declare that the research project entitled “Treatment outcomes and pattern of Radiotherapy utilization of pediatrics Rhabdomyosarcoma in TASH” is my original work and has not been presented for any degree in any other university and the source of materials used for this thesis have been acknowledged.

Declared by: Dr. Samson Zerihun

Signature ----------

Date----------

Statement of Certification

This is to certify that Samson Zerihun has done a study on the topic “Treatment outcomes and patter of Radiotherapy utilization of pediatrics RMS in TASH; under my supervision. this work is original and suitable for submission in the partial fulfillment of the requirement for the award of degree of specialty in clinical oncology

Dr. Adugna Fekadu (clinical oncologist)

Signatures ----------

Date ----------

Acknowledgment

I would like to express my deepest gratitude to my advisor Dr Adugna Fekadu for his encouragement and provision of constructive comments. And, I would like to acknowledge Addis Ababa University, college of Health Sciences Department of Hematology Oncology and Nuclear medicine for granting me the opportunity and permission to conduct this study.

Abstract

Background

Rhabdomyosarcoma is the most common pediatric soft tissue sarcoma. In low income countries RMS treatment is challenging unlike improved outcome in HICs. Unable to get timely Radiotherapy access and being higher stage presentation for surgery is main determinate factor for inferior outcome of pediatric RMS in sub-Saharan countries including Ethiopia. This study is expected to provide valuable insights about current pattern of RT utilization and treatment outcomes.

Objective

The study aim was to assess treatment outcomes and pattern of radiation therapy utilization, in pediatrics RMS at TASH between January 2021 and September 2025

Methods

Retrospective cohort study was conducted from January 2021 to September 2025 and 94 eligible patients were included. Data collected from the Radiotherapy system and chart of the patients. Analysis was performed using SPSS version 25 software and Kaplan-Meier method was used to estimate survival. COx proportional hazards regression analysis was done to identify independent prognostic factors associated to survival

Result all eligible 94 patients chart analyzed, this study showed majority of them are embryonal histology, head and neck site, 44.7% of patients received radiotherapy with 33% interruption and delayed interval from chemotherapy. Estimated 24-month survival time is 18% and EFS 35%. Surgery and Radiotherapy was significantly associated independent factor for Event free survival.

Conclusion Children with RMS present with locally advanced stage. There is low access of local treatment and RT is given after delayed time of recommendation and interruption. This result lower local control and poor survival**.**

Key word Rhabdomyosarcoma, Radiotherapy utilization, Treatment outcome

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List of acronyms and abbreviations

COG- Children's Oncology Group

DFS- Disease free survival

FFS - Failure-free survival

3DCRT – three dimensional conformal radiotherapy

EpSSG- European Pediatrics Soft Tissue Sarcoma Study Group

HMIS- Health management information system

IMRT – Intensity Modulated Radiotherapy

IRS- Intergroup Rhabdomayosarcoma Study

VMAT – Volumetric modulated arc therapy

LA- Locally advanced

LF- Local failure

LMICs- Low and middle income countries

LR- local recurrence

MDT – Multidisciplinary Team

OS - overall survival

OAR- organ at risk

RMS- Rhabdomyosarcoma

RT – radiotherapy

SIOP- International Society of Pediatric Oncology

TASH-Tikur Anbessa specialized Hospital

1. Introduction

1.1. Back ground of the study

Rhabdomyosarcoma is a malignancy of soft tissues specially arises from skeletal muscles. In the pediatrics age group it is the most common soft tissue sarcoma and account 4-5% of the total childhood malignancies. Annual incidence is 4.5 per million children below the age of 15 years (1)

There are four histologic subtypes of RMS. Embryonal subtype account (60-70%) followed by alveolar subtype and the rarer pleomorphic and sclerosing/spindle cell RMS. Head and neck is the most common site (2)

RMS treatment include chemotherapy, surgery and/or radiation therapy (RT) as a multimodality treatment. Stage of the disease, histology, post-surgery group and risk stratification determine mode of treatment. Radiotherapy is a key component for local control. Even if significant improvement in the last two decades' local control is challenging specially in LICs due to shortage of Machine and infrastructure (3)

In developed countries average survival is 70-80%.but it is 10 -50% reported for LMICs due to late presentation, lack of Radiotherapy and delay and treatment abandonment (4)

This LICs Burden is similar in our country but no survival study is done regarding Pediatrics RMS so this study is critical in terms of generating local evidence, evaluating the patterns of RT utilization, outcomes and informing context-relevant guidelines compatible with global practices and Ethiopia's infrastructural constraints

1.2 Statement of Problem

In developed countries advancement is increasing along with survival and account only 20% childhood cancer burden the remaining 80% burden is on LMICs due to late presentation, diagnosis and inaccessible treatment modality like radiotherapy all leads to lower cancer survival in the region (5)

In recent decades, the use of a multimodality treatment for RMS involving a combination chemotherapy and surgery and/or radiotherapy has improved the survival of RMS patients from 25% in the 1970 s to over 70% but in developing countries still less than <50% (6) Due to late presentation of patient that leads to inoperable and unable to get and delayed Radiotherapy

In Ethiopian there is a recent study at Tikur Anbessa Specialized Hospital found that just 52.1% of children with RMS got local treatment and only 24 % patients treated with RT out come and Detail of RT parameters was not studied. (7)

This result showed late presentation and access timely RT is challenge in our countries since it results poor local control and inferior survival)

So, this study helps to get accurate burden of RMS and patterns of RT for pediatric RMS patients at Tikur Anbessa from January 2021 to September 2025. It will also improve radiotherapy care for pediatric patients with RMS by guiding proper protocol, guideline and will be an opener for other researchers on these particular cases.

1.3 Significance of the study

The result from this study will provide valuable insights about current pattern of RT Utilization and Treatment outcomes.by analyzing deviations from international RT guidelines it will enhance **s**tandardization and improve local protocol concordance. It also supports hospital admins and policy makers understand the current status and support in planning and allocating resource for pediatric oncology and radiotherapy center.

Finally, the study will contribute to pediatric RMS management in Ethiopia and serves as reference for future clinical and radiation related research.

2. Literature review

2.1 Background and epidemiology

Rhabdomyosarcoma is the most common soft tissue sarcoma in children.it is arise from skeletal muscle lineage and found anywhere in the body, in a sites where striated muscles are normally found. (8)

RMS accounts almost half of pediatric soft tissue sarcoma and the incident is 4.7 per millions of children in the US. In LMIC, the RMS incidence is variable. According to African Cancer Registry Network estimation childhood RMS incidence rate in southern Africa ranged from 2.4 to 2.5 per million, 2.6 to 16.3 per million in Eastern Africa and 0.6 to 8.6 per million in western Africa. The peak age is early in childhood and a median age around 5 years. (8)

Histological subtypes of RMS, including embryonal, alveolar, spindle cell/sclerosing, and pleomorphic. (9) .The common primary sites are the head and neck (35%), genitourinary sites (31%) and extremities (13%) respectively .it has variable presentation depend on site which arise but most of the time present with painless and enlarging mass with disturbance of body normal function (9)

2.2 Radiotherapy utilization and outcomes

RMS needs multimodality treatment which includes chemotherapy, surgery and radiotherapy. Radiotherapy is one of main pillar of treatment with role of local control for patient with residual disease, unresectable and unfavorite histology. European Collaborative groups follow risk adapted RT protocol that include dose, timing and techniques to improve survival and local control (10)

RT is indicated for patient post-surgery with microscopic and macroscopic residual, involved LN, in location of limited surgery like head and neck and high risk histology. (10, 11)

According to international guidelines, for most of patient with localized RMS ideal time to receive RT is after 4cycle (12wk) of chemotherapy and after 7cycle (wk22) for metastatic disease. For a Patients with localized RMS who didn't take RT until 24 wk,

local recurrence is common. According to COG and SIOP the dose of radiotherapy mainly 36 to 50.4 gy depend of different parameters like chemotherapy response and residual disease status its delivered with different techniques IMRT/VMAT, proton therapy, electrons, brachytherapy, or other 3D conformal techniques. (10, 11)

Relapses are more common in unresectable disease, an unfavorable site, or metastatic disease at diagnosis. The prognosis for children or adolescents with rhabdomyosarcoma is related to the presence or absence of distant metastases, site, local treatment, histology and age. (12)

2.3 Empirical Evidence

Different international collaboration studies different parameter of Radiotherapy like indication, timing, dose outcome and adverse effects for baseline evidence of the guideline., the current recommendations Regarding the timing of RT is after four cycles (12 weeks) of chemotherapy most commonly a local failure occur in a patient received RT delayed beyond recommended time (13)

According to European study RT utilized based on risk group, and used 41.4 gy and 50.4 gy are using for microscopic residual and gross residual disease, remain effective for local control, use of advanced RT techniques like intensity-modulated radiation therapy (IMRT) are improving event-free survival to 75 to 80%. This European study also validated greater than 10years, greater size, unfavorable site and histology had inferior outcome.(14)

Regarding compliance of RT protocol children oncology group one report showed for a patient undergo surgery with microscopic residual 55% of patient present with operative bed recurrence didn't received RT group. The study was concluding that three-fourths of patients die due to regional disease was not controlled (15)

One retrospective cohort study done in Beijing Togren hospital, china from 2023 to 2019 RT improve the OS and EFS in a patient with Head and neck RMS by increasing local control. (16)

Uganda Cancer Institute studies done between 2016 and 2020 indicate 24.2% of the patients underwent surgery, and 28.1% took Radiation. 33.6%, was treatment completion rate and 46.1% of patient abandoned treatment. 19.5% only patients were alive at the time of the study, 50.8% had died, and patients with unknown status are 29.7 %.(17)

Another retrospective analysis at the Chris Hani Baragwaneth Academic Hospital (CHBAH), South Africa, showed that 40% of cases of pediatric RMS registered was RT used; the dose parameters ranged from 36 to 50 Gy. While in this study, RT did increase local control, survival of patient is inferior to HIC (18)

An Egyptian RMS study also showed that radiotherapy had significantly affected EFS and shown to be an independent prognostic factor for EFS in multivariate analysis (HR: 8.8; CI 95%: 2.5-31). (19)

In Ethiopia, at TASH, retrospective study on RMS 2017 to 2022 done by Yihenew et al. 96% of patients were received chemotherapy, 34% had surgery, and 24% patients were irradiated. (52.1%) had been treated with a combination of two or more types of treatment modalities (7) and it was not properly documented, and survival outcomes were not reported.

Since the existing study not addressed radiotherapy utilization, and treatment outcome for pediatrics RMS in Ethiopia These Finding fill the gap provides evaluation of protocol implementation, identification of practice obstacles and targeting intervention to improve outcomes. This retrospective hospital based analysis will therefore provide essential evidence to inform training and clinical practice

2.4 Conceptual Frame work

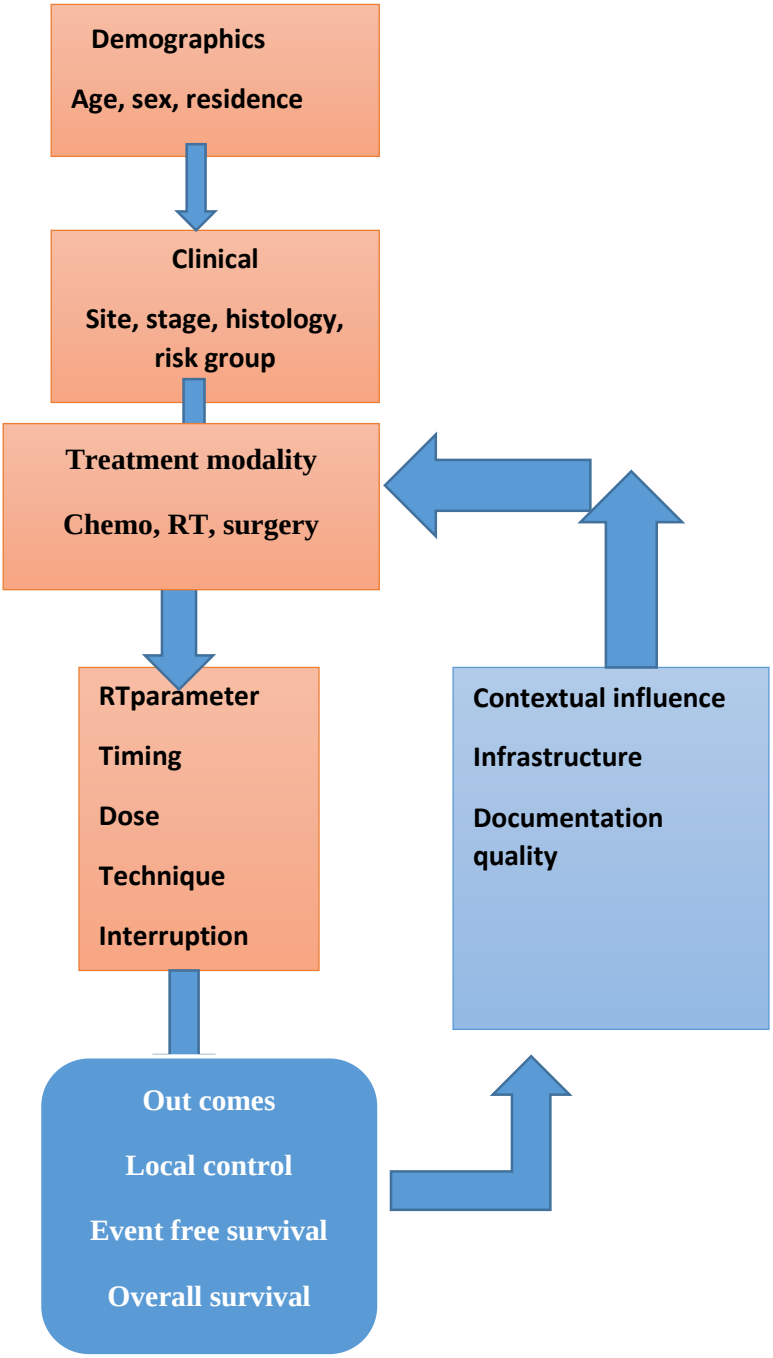

Figure 1 conceptual framework showing relationship between dependent and independent variables (developed by author)

3 Objective of the study

3.1 General objective

- ✓ To assess Treatment outcome, pattern of radiation therapy utilization in pediatrics RMS at TASH between January 2021 and September 2025

3.2 Specific objective

- ✓ To describe socio demographic and clinical characteristics of pediatric RMS patient diagnosed at TASH, during study period
- ✓ To describe pattern of RT utilization in pediatrics RMS patients diagnosed at TASH, during study period
- ✓ To assess treatment outcome of pediatrics RMS patients diagnosed at TASH, during study period

4. Methods and material

4.1 Study design

A facility based retrospective cohort study was conducted at TASH from January 1 2021 to September 2025

4.2 Study area and setting

The study was conducted in pediatric hemato-oncology department and radiotherapy center of Tikur Anbessa Specialized Hospital in Addis Ababa which is the capital city of Ethiopia. Tikur Anbessa Specialized Hospital is the biggest tertiary hospital in Ethiopia and it is where one of the largest cancer center found.in the country, serving population of over 120 million. The Radiotherapy center was the only one in the country for 2 decades; previously service was given with cobalt machine for the last 5 years LINAC machine is giving service currently.

4.3 Study period

The study was conducted on patient diagnosed from January 2021 to September 2025 and data was collected from August 2025 to October 2025

4.4 Source population

All pediatric patient <18yrs histologically confirmed RMS between 2021 and September 2025

4.5 Study population

All pediatric RMS patients who fulfilled the inclusion criteria during the study period

4.6 Inclusion and Exclusion criteria

Inclusion criteria

Pediatric age less than 18 diagnosed

Histologically confirmed RMS in the study period

Medical records with at least diagnosis date, stage/risk group and histology document

Exclusion criteria

Patient with incomplete medical records (minimum of diagnosis date, stage/risk group, histology

Patient referred from other hospital for RT, but without minimum medical records

Patient not confirmed histologically but treated in line of RMS

4.7 Sample size and sampling techniques

Census was the sampling techniques and 94 eligible cases diagnosed with RMS and full fill the inclusion criteria in the study period were included in the study. Around 39 patients drops from study due to lack of biopsy, and unclear biopsy results inadequate documentation, misdiagnosis and lost old cards

4.8 Data collection procedure

The tool was prepared by reviewing related literature done in other areas. The data was collected by 2 oncology residents from the RT Planning software database and each patient medical chart by trained residents, under close supervision and facilitation by the principal investigator. Each day, the collected data was checked for accuracy and completeness. Data collection was done by Kobo toolbox application using mobile devices with safeguards in place to maintain patient confidentiality.

4.9 Variables

Independent variable

Demographic characteristics like Age, sex, place of residence and date of diagnosis

Disease related Tumor site, size, stage, histology and nodal status

Treatment modalities chemotherapy, surgery and Radiotherapy

RT parameters timing, indication, intent, dose techniques and interruption

Dependent variables

Local control

Overall survival time

Event free survival time

4.10 Operational Definition

Pediatric RMS: children less than 18 yrs. with histologically confirmed RMS from Jan 2021 –Sep 2025 at TASH.

Pattern of Radiation therapy utilization: extent in which how radiation therapy is applied in clinical practice in pediatric RMS patients encompass clinical indication, usage rate, Timing, dose, techniques and adherence to guideline.

Local Progression: worsening of primary site disease during or after treatment.

Local recurrence: reappear the disease after period of remission.

Complete response: disappearing of all target lesion.

Partial response: at least 30% decrease of target lesion without new lesion.

Stable disease: disease remain unchanged no decrement >30% and no increment >20%.

Local control: Absence of relapse or progression at primary site during follow-up.

Overall survival: time from first diagnosis to death from any cause.

Event free survival; time from first diagnosis to first event like progression, relapse.

Radiotherapy delay: initiation of RT later than 12 weeks for localized RMS and later than 22 weeks for metastatic according to SIOP and COG.

Treatment interruption: unplanned gap during Radiotherapy delivery >=1day after initiation.

Treatment Abandonment: unable to start or finish planned treatment despite medical advice without referral or death.

4.11 Data quality control

The data collection tool was reviewed by peers and mentors. More over a formal training was given to the data collectors on data collection tool to maintain consistency throughout the data collection. The collected data also checked by principal investigator every day. Missing values are coded as unknown retail cases that meet baseline criteria (histology, diagnosis date, and stage/risk) in survival analysis.

4.12 Data analysis and interpretation

Descriptive statistics used to summarize the demographic, clinical and treatment characteristics of the study population. Statistical analysis were performed using SPSS version 25 software. And Kaplan-Meier method with log-rank test used to estimate survival.

Cox proportional hazards regression analysis done to identify independent prognostic factors associated to survival and reported with hazard ratio and confidence interval. Association assessed using chi-square and P value of less than 0.05 will be significant statistically.

4.13 Ethical consideration

Ethical clearance and approval for the study was obtained from Institutional Ethics Review Board of Health Institute, Addis Ababa University. Permission was obtained from TASH administration and privacy will be maintained.

4.14 Dissemination plan and use of the result

The findings of this study will be presented to the department of Clinical Oncology for public defense. Summary report will be submitted to AAU. Effort will be made to publish the findings in peer reviewed journals

5. Result

A total of 133 pediatrics RMS cases extracted from HMIS, I care, RT book and pediatrics hemato oncology registration system then patient medical history assessed from retrieved card, I care and Mdt decision documents. Out of 133 patent cases 16 was misdiagnosed registration, 7 of them exclude by histology 9 cards lost with their documents since its old and another 7 patient card has inadequate documentation. A total of 39 patients excluded. A total of 94 patients were analyzed in this study.

Figure 2 Flow diagram of eligible patient's selection

5.1 Socio-demographic and clinical characteristics

Out of 94 analyzed patient cards the median age at diagnosis was 4years with slight male predominance male (53.2 %) and female (46.8%). Around 33(35.5%) of patients come from Oromia region and 18(19.1%) Amhara and 13% from AA. The yearly case pattern showed in the figure 1

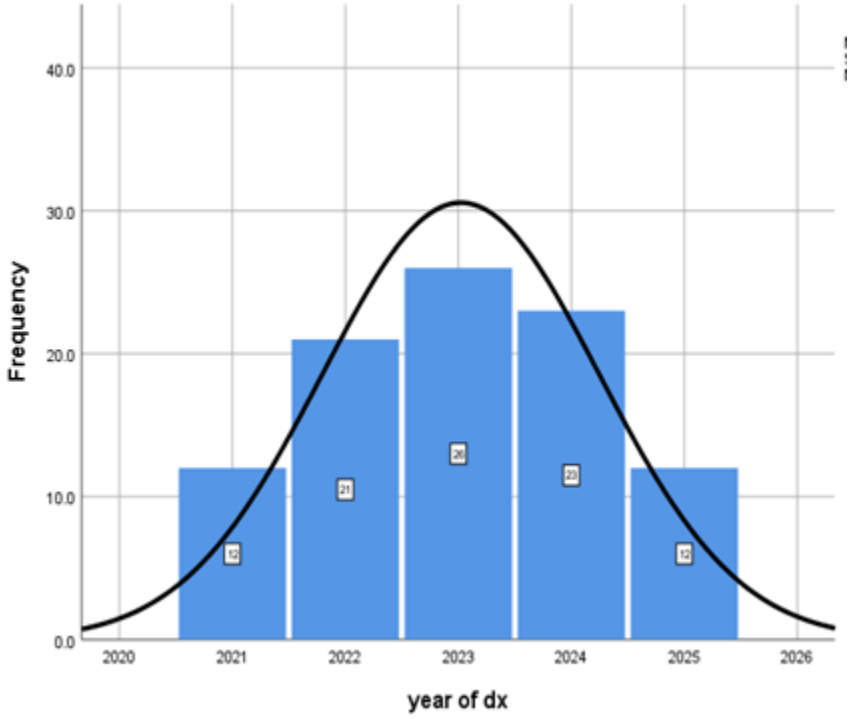

Figure 3 Yearly patterns of pediatric RMS cases at TASH from 2021 to 2025

As in the table 1 shown, the commonest primary site was head and neck comprising paramenegeal 12(12.8%) non paramengeal 21 (22.3%) and orbital cancer14 (14.9%). Histologically Embryonal and alveolar RMS accounted for 56(59.6%) and 28(29.8%) of the cases, respectively.

Majority of patients 65 (69.2%) are grouped under intermediate risk, and regarding stage 56.4 % are IRS stage III and 14.9% are metastatic at presentation.

Table 1 demographic and clinical characteristics of pediatrics RMS patient seen at TASH from 2021 to 2025

variable	category	frequency	percent
age	<1	7	7.4%
	1-5	50	53.2%
	5-10	27	30.9%
	>10	8	8.5%
sex	Male	50	53.2%
	Female	44	46.8%
Place of residence	Oromia	33	35.1%
	Amhara	18	19.1%
	AA	13	13.8%
	Central Ethiopia	11	11.7%
	Southern Ethiopia	10	10.6%
	other	9	9.6%
Primary site	orbital	14	14.9%
	Paramengeal	12	12.8%
	Non paramengeal	21	22.3%
	GU	26	27.7%
	Extremity	8	8.5%
	other	13	13.8%

Histology	embryonal	56	59.6%
	alveolar	28	29.8%
	Spindle sclerosing	4	4.3%
	other	6	6.4%
Nodal status	positive	32	34%
	negative	62	66%
IRS stage	I	13	13.8%
	II	14	14.9%
	III	53	56.4%
	IV	14	14.9%
Risk group	low	16	17%
	intermediate	65	69.2%
	high	13	13.8%
Metastatic disease at presentation	yes	14	14.9%
	no	80	85.1%

5.2 Treatment modality and pattern of Radiotherapy

Regarding mode of treatment, the majority of patient 92.6% received chemotherapy as one of the modalities of treatment; surgery was performed in 36.2% of patients and 44.7% of patients received radiotherapy. From local treatments overall, 21.3% surgery alone 30.9% RT alone, 13.8% had RT and surgery and 34% had no local treatment

Regarding indication of RT 22 (52.4%) out of 42 patient received definitive RT with incomplete response of chemotherapy, 14(33.3) adjuvant and 6(14.3%) received palliative R (see figure 2)

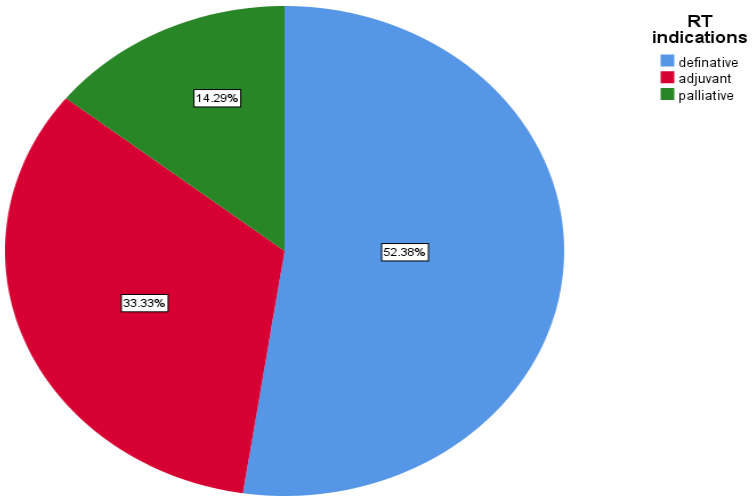

Figure 4 Radiotherapy indications among pediatrics RMS patients received radiotherapy at TASH from 2021 to 2025

35 out of 42 patient received RT with the intent of radical treatment and majority of treatment used dose of 41.4 or 50.4. The median dose is 45 gy and only 26.2% of patient from 42 patients who took RT contoured in two phase considering pre chemo and post chemo GTV

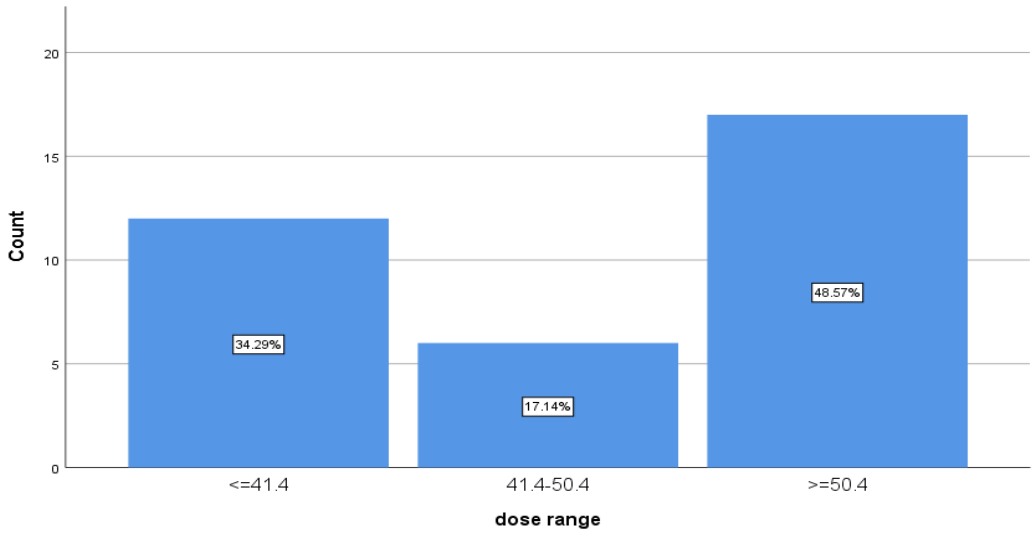

Figure 5 Graphic representation radiotherapy dose among pediatrics RMS patients received radiotherapy with radical intent at TASH from 2021 to 2025

For patients who receive Radiotherapy, the mean and median interval period between chemotherapy and Radiotherapy is 39wk and 35wk respectively. Out of 37 patients who took RT with radical intent only 5(13.8%) received before 24wk of chemotherapy. The most common RT technique used is 3DCRT accounts 78.6% followed by IMRT (16.7%) and VMAT (4.8%). Regarding RT toxicity in 90.5 % of patients no documented RT toxicity is found

From 42 patients received RT 33.3% has got interruption from this 14.5% of patient had got interruption of 1-3 days 7.1% for 4-7days and 11.9% for greater than 7days. It's showed in the figure 4.

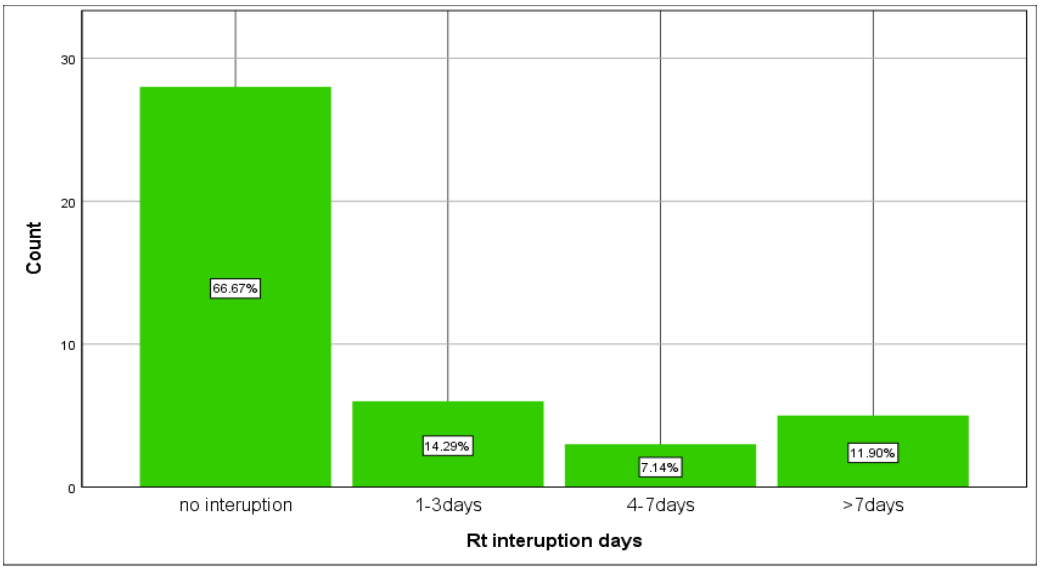

Figure 6 Radiotherapy interruption percentages among pediatrics RMS patient received Radiotherapy at TASH from 2021 to 2025

5.3 Treatment outcomes

Of the 94 patients analyzed, in the table 2 displayed treatment response showed that 31 (33%) had complete response followed by 19(20.2%) progressive disease, 17(18.1%) partial response 9(9.6%) stable disease and 19.1% were not assessed.

the most common first event occur was local progression 40.4%, followed by death 32.7%, distal metastasis and local recurrence. 48.9% of patient achieves local control.

Among 94 patients the most common site that achieve CR is orbital site 64,3% and the paramengeal site is commonest for disease progression 50%.

Table 2 Treatment outcomes among children with RMS treated at TASH, January 2021 to September 2025

variable	category	frequency	percentage
Treatment response	Complete response	31	33
	Partial response	17	18.1
	Stable disease	10	10.6
	Progressive disease	19	20.2
	Not assessed	17	19.1
Event occurred	yes	53	56.4
	no	34	36.2
	unknown	7	7.4
First event occurred	Local recurrence	6	11.5
	Local progression	21	40.4
	Distal mets	8	15.4
	death	17	32.7
Local control achieved	yes	31	33
	no	46	48.9
	unknown	17	18.1
Survival status	censored	54	57.4
	death	40	42.6

Among 94 patients orbital site is the commonest for both achieving complete treatment response (64.3%)and better survival outcome censored/alive 71.4%. while paramengeal site is with highest progression rate (50%), lowest rate of local control (33.3%) and highest mortality (58. 3%).regarding histology and outcome embryonal type had highest rate of complete response, better survival and local control while alveolar type had lowest complete response rate, highest progression rate and poor survival.

Of a total of 42 patients who took Radiotherapy 42.9% of them achieve complete response and 26.2% archive partial response. Patient who did not receive RT experience more disease progression (26.9%) Patient who receives RT achieved local control (69%) and had better survival rate (73.8%, alive/censored) and patient receive combine surgery and RT experience higher outcomes. As it is showed in the table 3 from patients who took Radiotherapy without interruption had better survival.

Table 3 frequency and percentage distribution of survival by clinical and treatment variables among children with RMS at TASH, January 2021 to September 2025

Independent variable	category	Survival status (death)	Event occurred yes
Tumor histology	embryonal	16(28.8%)	27(48.2%)
	alveolar	18(64.3%)	19(67.9%)
	Spindle sclerosing	1(25%)	2(50%)
	other	5(83.3%)	5(83.3%)
Age group	<1yr	3(42.9%)	2(28.6%
	1-5yr	20(40%)	25(50%)
	5-10yr	12(41.4%)	21(72.4%)
	>10yr	5(62.5%)	5(62.5%)
Primary site	orbital	4(28.6%)	6(42.9%)
	Paramengeal	7(58.3%)	8(66.7%)
	Non paramengeal	9(42.9%)	12(57.1%)
	GU	11(42.3%)	15(57.7%)
	Extremity	5(62.5%)	5(62.5%
	other	4(30.8%)%	7(53.8%)
Rt received	Yes	14(33.3%)	17(40.5%)
	no	26(50%)	36(69.2%)
Surgery done	Yes	12(35.3%)	18(52.9%)
	no	28(46.7%)	35(58.3%)
Local treatment received	Surgery	7(35%)	13(65%)
	RT alone	9(31%)	12(41.4%)
	Surgery+RT	5(38.5%)	5(38.5%)
	No local rx	19(59.4%)	23(71.9%)
Intent of RT	Radical	11(31.4%)	13(37.1%)
	palliative	3(42.9%)	4(57.1%)

Independent variable	category	Survival status (death)	Event occurred yes
RT interruption	No interruption	7(25%)	8(28.6%)
	1-3days	3(50%)	3(50%)
	4-7days	1(33.3%)	1(33.3%)
	>7days	3(60%)	5(100%)

Regarding local control, its varies depend on which local treatment the patient received. This study shows that patients receive both surgery and Radiotherapy achieved 76.9% local control as it is shown in figure 7 in contrast patient without local treatment have poor local control but significant number of patient 40.6% were classified unknown this imply majority will be from treatment abandonment group

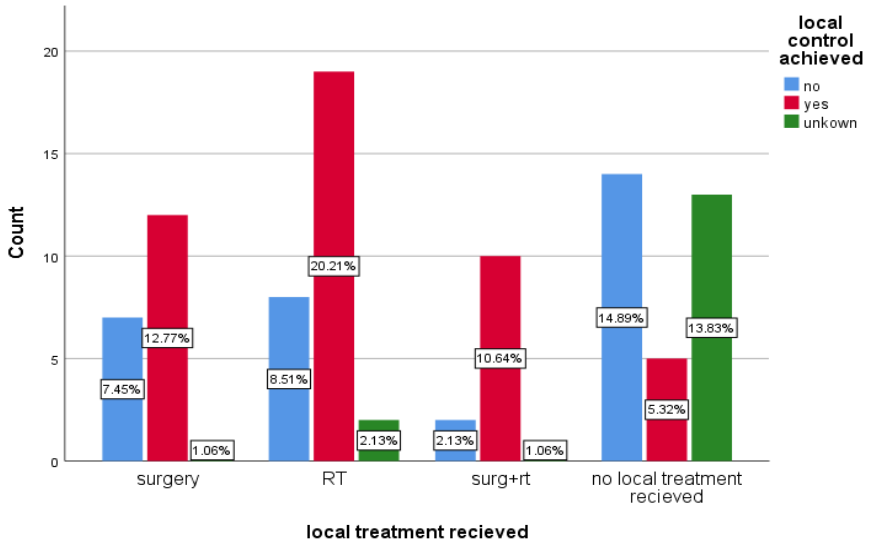

Figure 7 Clustered bar graph shows relationship between local treatment modality with local control in pediatric RMS patients at TASH

5.4 Survival analysis

The estimated mean survival time was 12.46 month (95%CI; 9.72 to 15.2months) and mean survival time was 10 months (95CI; 7.4 to 16.2month) the 24-month survival estimation is near 18%. The survival curve is shown in the figure 4

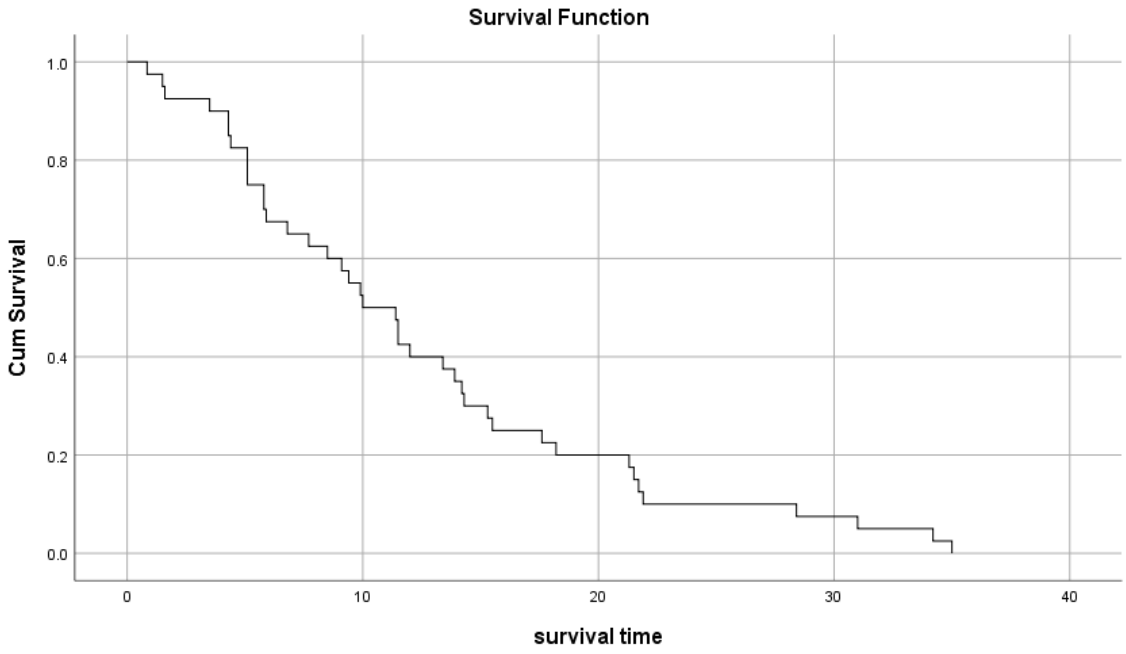

Figure 8 Cumulative overall survival probabilities of pediatric RMS patients at TASH from 2021 to 2025

The estimated mean event free survival time was 22.77 month (95%CI; 18.36 to 27.19months) and median event free survival time was 14.20 month (95CI; 7.08 to 21.32month) the 24 month EFS estimation is near 35%.

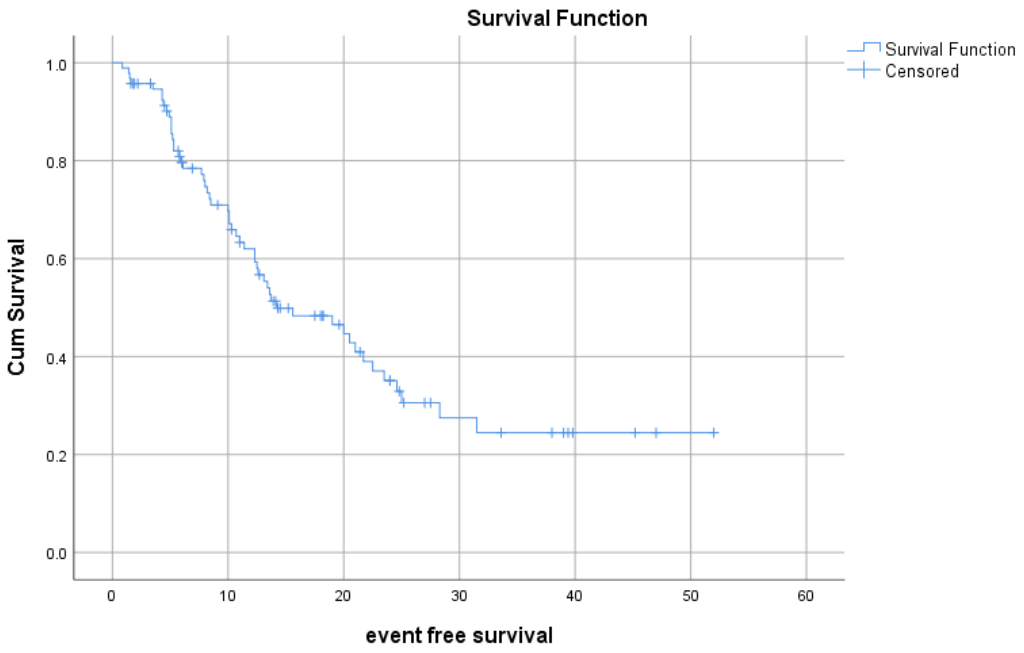

Figure 9 Event free survival probabilities of pediatric RMS patients at TASH from 2021 to 2025

The estimated mean and median survival time with respect to tumor histology the longer is for embryonal which is 11.5 month and 14.4 month but statically it's not significant. The estimated EFS time difference between tumor histology is longer for embryonal and statistical significant compared by log rank test (p value 0.004) which is the median and mean is 21.7 month and 27.3 month

Further survival comparison was done by local treatment received or not. Patient receiving Radiotherapy has longer os time and EFS time than not received group. Median EFS for received group 28.3 month and 10 months for not received group. The survival curves for the two groups are displayed in the figure 6

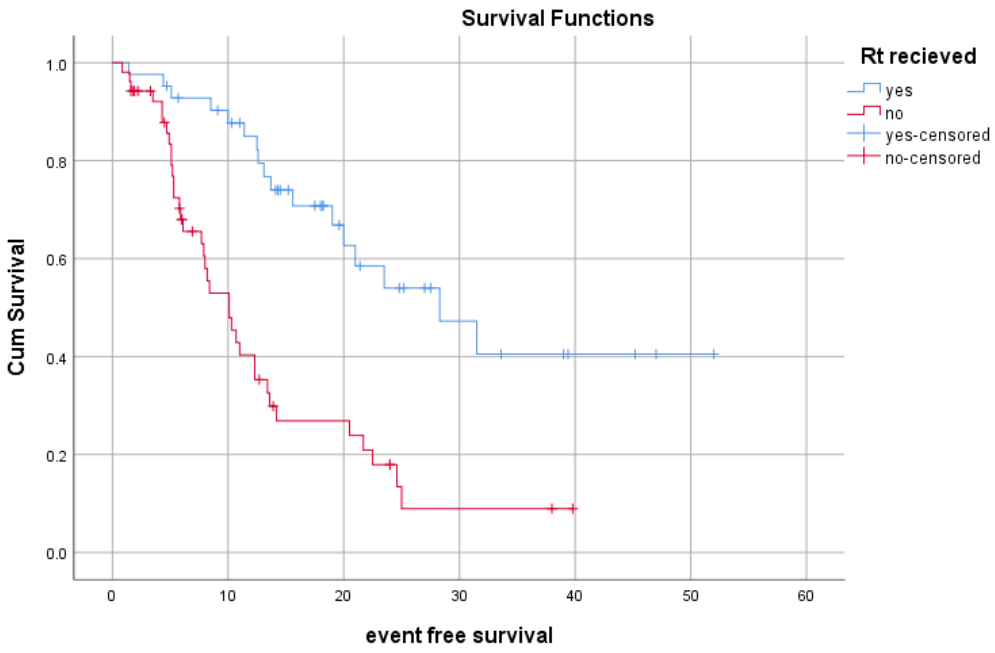

Figure 10 Event free survival probabilities of pediatric RMS received RT group at TASH from 2021 to 2025

Previously reported clinical and treatment variables were compared between groups by univariate analysis with Kaplan-Meier method and log rank test. The result show in the table 3

Survival time was associated with local treatment RT and surgery, and EFS time affected by statistically significantly by primary site, histology and by patient received Radiotherapy and undergoes surgery.

By variant analysis patient received RT and surgery, embryonal histology and favorable primary site are all statistically significant good independent predictors of better EFS.

Table 4 Univarate analysis of independent variables for survival among Pediatric RMS patients at TASH, from 2021 to 2025

VARIABLES	Overall survival			EFS		
	HR	P value	95%ci	HR	P value	95%ci
Rt received Yes no	 Ref 2.041	 0.04	 1.019-4.089	 3.433	 <0.001	 1.908-6.174
Histology embryonal Non embryology	 Refe 1.19	 1.19	 0.86-1.672	 1.574	 0.002	 1.179-2.101
Surgery done Yes No	 Refe 2.08	 0.04	 1.034-4.183	 2.082	 0.013	 11.168-3.709
Site Favorable unfavorable	 Ref 1.043	 0.901	 0.539-2.019	 3.781	 <0.001	 2.042-7.000
Age <1 1-5 6-10 >10	REF 0.513 0.358 0.842	 0.381 0.189 0.866	 0.115-2.284 0.077-1.658 0.115-6.164	 0.856 1.135 0.784	 0.800 0.837 0.766	 0.257-2.856 0.340-3.793 0.157-3.907
RT interruption No interruption 1-3 4-7 >7	 Refe 0.847 0.392 0.376	 0.819 0.389 0.226	 0.205-3.502 0.046-3.310 0.077-1.833	 2.685 0.762 4.437	 0.168 0.798 0.013	 0.659-10.939 0.095-6.107 1.361-14468

Cox proportional hazard model was used for multivariate analysis and all statistically significant variables were included. The result was expressed as HR with 95%CI for each variable and a variable with p value <0.0s considered as independent prognostic factor. The result reported in the table 4.

Patients received RT and surgery were shown statistically significant improvement in EFS time but for survival time it's not significant and show strong trend toward improve survival time.

Table 5 Multivariate analysis of patient RT received and underwent surgery for survival

variables	Overall survival			Event free survival		
	HR	P value	95%CI	HR	Pvalue	95%CI
Rt received Yes no	 Ref 1.930	 0.065	 0.960-3.877	 5.401	 <0.001	 2.824-10.327
Surgery done Yes no	 Ref 1.969	 0.058	 0.976-3.971	 3.688	 <0.001	 1.933-7.037

6. Discussion

This retrospective study evaluated the treatment outcomes and pattern of RT utilization among pediatric RMS patient treated from Jan 2021 to September 2025.This study show, slight predominant of male, most of the patient in the 1 to 5 age group (53.2%)and with the median age group of 4 yr is consistent with global data (1)

Regarding to primary site, this study found that head and neck RMS is the most common site (50%), Compared to European countries data from SIOP the commonest site is trunk and others and accounts 30% and head and neck account 20 %(6)

The most common histology found in this study is embryonal account 59.6% and alveolar histology is the next (29.8%) compared to US data Report from the Children's Oncology Group in the International radiation oncology journal. This relatively higher alveolar histology may contribute for lower outcome in our setup (11)

Regarding dose parameters and target volume 35 out of 42 patient received RT with the intent of radical treatment and majority of treatment used dose of 41.4 or 50.4. the median dose is 45 gy. This is consistent and concordance with guidelines likes SIOP. And only 26.2% of patient from 42 patients who took RT contoured in two phase considering pre chemo and post chemo GTV, according to SIOP and COG RT volume must cover GTV of prechemo by fusing pre chemo image and by assisted by IMRT and IGRT Like in developed counties since its one cause of local frailer (11,14)

Most of our RMS patients in this study are belonged to IRS stage III (56.4%) and based on risk stratification intermediate risk (69.2%), this make more advanced disease presentation and has difference from US data documented in the COG also from study done Uganda. (17) this may infer most of our patient had late presentation, limited access of early treatment and make the treatment more difficult since it need intensive multimodality treatment, this will affect the survival of the patient.

Regarding treatment modality, this study reveals most of the patient 92% took chemotherapy, 36.2% had surgery, and 44.7% received radiation and of patient receive

both surgery and RT. It's better than from Uganda single institution study done 2016 to 2020 published at 2025, 28.1% were received RT. (17) and treatment abandonment also 18.1% of our study and around 40% in the Uganda study. This may impact of MDT activities which is working more on giving RT priority for pediatrics despite infrastructure problem of our countries.

Compared to retrospective study done at TASH from 2017 to 2022 by Yihenew, almost by half which was 24 %. RT getting rate increased despite the study didn't cover outcome. (7) This improvement may have explained by due to the new linac machine for the last 5yr and Improvement in the multidisciplinary team discussion to give Priority of pediatric cases explain remarkable development of RT receiving patient rate.

This retrospective study showed the estimated mean survival time was 12.46 month (95%CI; 9.72 to 15.2months) and mean survival time was 10 months (95CI; 7.4 to 16.2month and the 24-month survival estimation is near 18%. The estimated mean event free survival time was 22.77 month (95%CI; 18.36 to 27.19months) and median event free survival time was 14.20 month (95CI; 7.08 to 21.32month) the 24 month EFS estimation is near 35%. this suggest inherently poor outcome This figure is significantly lower than the 3-year predicted survival was 60.2 % (95 % CI 73.2–47.2) and the 5-year survival was predicted to be 55.0 % (95 % CI 68.8–41.2) reported from Chris Hani Baragwaneth Academic Hospital, South Africa. (18) The estimated mean event free survival time was 22.77 month (95%CI; 18.36 to 27.19monthsThis is attributed to late and advanced presentation, low RT access and less resection chance due advancement.

The RT utilization has significant improvement compared to previous study done at TASH, by yihenew which was 24 % of patient was taking RT from 2017 to 2022. (16) And

During study period Out of 94 patient included in this study 33(35.1%) of them were alive, 38(40.4%) dead and 24.5 % were unknown their status.19.1 % were abandoned their treatment. Another suboptimal trend seen in the study of Uganda, of the 128 patients analyzed, only 25 (19.5%) could be confirmed to be alive, 65 (50.8%) had died, and 38 (29.7%) had been lost to follow-up, and their status could not be ascertained this is even

lower than our study. (17) It is suggesting that lack of multimodality treatment, late presentation still is challenge in developing countries

Using Kaplan– Meier Survival curves, significant differences in survival were seen patient who receive RT, Surgery favorable site and embryonal RMS, had longer survival time. In the multivariable analysis pediatrics patient who took RT (95%CI HR 5.401 P value <0.001) and surgery (95%CI 1.933-7.037 HR 3.668 P value <0.001 were associated with longer event fee survival time. RMS incidence using data from U.S. Cancer Statistics (USCS) and survival trends, unfavorable site, age <1 and >10, alveolar histology are associated histology. This is due to in US nearly all complete multimodality treatment and <5% of treatment abandonment rate and the independent prognostic facto manly clinical and molecular characteristics of tumor unlike our study which is lack of local treatment is independent prognostic factor (17)

7. Strength and Limitations of the study

7.1 Strength

- This study is the first to assess both the outcome and Radiotherapy utilization among Pediatrics RMS so it will fill evidence gap and will be baseline for further study.

7.2 Limitations

- As its retrospective the study was chart based the finding is limited by completeness of charts, missing documentations that limit the ability to provide reliable data.
- The study is done only at TASH, so the findings have limitation to generalize as a national level.
- Even all eligible patients are included its small sample size and leads to limitation in subgroup analysis with decrease statistical power.
- The other limitation is patient lost from follow up are significant and it underestimate the survival estimation.
- For Patient diagnosed in the last months of the study period, there outcome is not assesse reliably

8. Conclusion and Recommendation

8.1 Conclusion

This retrospective study showed, from 94 RMS patient review chart majority of them are embryonal histology, head and neck histology, IRS stage III and included under intermediate risk group that imply more late presentation.

This study concludes that 44.7% of pediatrics RMS patients received radiotherapy I the study period and from patients received with radical intent all received beyond 12 weeks and 86.2 % took beyond 24weeks after chemotherapy.

This study indicated that only 33% of pediatric RMS patient achieve local control. Estimated 24-month survival time is 18% and EFS 35% which is significantly poor survival this may result from advanced and late presentation, inadequate local treatment like in access for RT and getting after significantly prolonged interval from recommended time and incomplete surgery.

The Radiotherapy dose parameters concordance with international guideline despite given with significant delay, 33% interruption and without documentation of toxicity that leads to disease progression and lower survival

Finally, it’s concluded that patient with incomplete Surgery and patient didn’t receive Radiotherapy was significantly associated independent factor for Event free survival

8.2 Recommendation

To Healthcare Professionals/Hospitals

- Ensure timely and appropriate patient referral for biopsy, imaging, and advanced treatment to reduce late presentation of patients
- Maintain standardized documentation and patient record-keeping

To department of oncology

- Strength MDT and establish constant clinical audit to provide radiotherapy with priority for pediatrics and to identify challenges
- Improve documentation specially RT toxicity and strength supportive treatment.

To Hospital administration

- Expand radiotherapy infrastructure like additional machine, treatment planning system to decrease delay and interruption

To ministry of health

- Increase the Number of of radiotherapy machine to reduce treatment delays
- Develop national oncology guideline tailored to Ethiopian setting

To Researchers and Academic Institutions

- To conduct further study like prospective cohort studies to better analyses survival

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Annex

Questionaries'

Patterns of Radiation Therapy utilization dose parameters and treatment Outcomes in pediatrics RMS at Tikur Anbessa Specialized Hospital: A Retrospective Study Between January 2021 and September 2025

PART I: Patient & Demographics

1. Study ID: _____

2. Age at diagnosis: ___ years

3. Sex: Male Female

4. Place of residence: _____

5. Date of diagnosis: //____

PART II: Disease Characteristics and treatment

6. Primary site: **A**. Orbit B Para meningeal, **C** Non-Para meningeal H&N,

D GU–bladder–prostate **E**. GU–non-bladder–prostate, F Extremity, G Other

7. Tumor size (cm): _____

8./Stage (IRS/COG): A. I, B.II, C.III, D. IV

RISK A.Low B. INTERMEDIATE C. HIGH

Group after surgery I II III IV

9. Nodal status: A. Negative Positive Unknown

10. Metastatic disease at diagnosis: Yes / No

11. Histology: **A** Embryonal, **B** Alveolar, C Spindle Sclerosing, Other

13. Surgery done : **A** yes B no

14. Margin status: **A** R0, B.R1, **C**. R2, **D**.Not recorded

15. Chemotherapy received A yes B No

16 Date of start: //____ □ Cycles completed: ___

Part III: Radiotherapy – Utilization

19. RT indication for who took Radiotherapy

20. Timing Date of RT start: //____

22. Interval chemo start → RT start (weeks): ___

23. Interval surgery → RT start (weeks): ___

24. RT delay (>12 weeks from chemo start): Yes / No

25. Technique: A. 2D, B.3D-CRT, C. IMRT, D.VMAT, , Other

26. Total prescribed dose (Gy): ___ □ Dose per fraction (Gy): ___ □ No. of fractions: ___

27. Overall treatment time (days): ___

□ Boost given: Yes / No → Dose: ___ Gy, Volume: _____

28. RT dose level vs indication:

I. Adjuvant Microscopic residual (36–41.4 Gy) → Delivered: ___ Gy

II. Node positive 41.4gy delivered -------- Gy

III. Gross disease (50.4 Gy) → Delivered: ___ Gy

IV. Palliative RT Delivered dose-----Gy

29. Treatment interruptions: A. Yes B. No → If yes , duration (days): ___ and reason: _____

30. Target Volumes Pre-chemo GTV covered: A. Yes B. No

31. Nodal coverage included: Yes / No

35. Any toxicity documented toxicity yes or No or not documented if yes ---- _____

Part iv: Outcomes

36. Treatment response A CR B PR C SD D PD E Unknown

37. Local control achieved A. Yes B. No →

38. Event occur: A yes B.no Date of event: //____

39. IF Yes what is the event. A local progression B. Recurrence C distant mets D. death

40 Overall survival status: A. Alive B. Dead → C unknown Date of last follow-up: //____

41 RT omission despite indication: A. Yes B. No

42. RT delay beyond window: A. Yes, B No

43. Survival status during study A. alive B Death C unknown