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PATTERN AND TREATMENT OUTCOME OF CHILDREN WITH ONCOLOGIC EMERGENCIES SEEN AT FIRST VISIT TO PEDIATRIC EMERGENCY UNIT, TIKUR ANBESSA SPECIALIZED HOSPITAL, ADDIS ABABA, ETHIOPIA

A RESEARCH THESIS TO BE SUBMITTED TO ADDIS ABABA UNIVERSITY, COLLEGE OF HEALTH SCIENCES; PEDIATRICS AND CHILD HEALTH DEPARTMENT IN PARTIAL FULFILMENT OF THE REQUIREMENT FOR THE SPECIALTY CERTIFICATE PROGRAM IN PEDIATRICS AND CHILD HEALTH

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Acronyms

MD.....	Medical Doctor
M.....	Male
F.....	Female
ARDS.....	Acute Respiratory Distress Syndrome
TLS.....	Tumor Lysis Syndrome
CVA.....	Cerebrovascular Accident
ICP.....	Intracranial Pressure
SVCS.....	Superior Vena cava Syndrome
SMS.....	Superior Mediastinal Syndrome
ALL.....	Acute Lymphoblastic Leukemia
AML.....	Acute Myelogenous Leukemia
CML.....	Chronic Myelogenous Leukemia
NHL.....	Non-Hodgkin Lymphoma
DLBCL.....	Diffused Large B-cell Lymphoma
HIV.....	Human Immunodeficiency Virus
CBC.....	Complete Blood Count
WBC.....	White Blood Cell
Hgb.....	Hemoglobin
LDH.....	Lactate Dehydrogenase
CI.....	Confidence Interval
TASH.....	Tikur Anbessa Specialized Hospital
DPCH.....	Department of Pediatrics and Child Health
ED.....	Emergency Department
SPSS.....	Statistical Package for Social Sciences
PI.....	principal investigator

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Abstract

Background:

Pediatric oncologic emergencies can occur at any time during a child's course of care for cancer; it can be either the initial manifestation of cancer or occur as a consequence. Pediatric oncologic emergencies may lead to acute and potentially life-threatening complications unless timely diagnosed and treated. Pediatric oncologic emergencies can be metabolic emergencies, neurological emergencies, thoracic emergencies, gastrointestinal emergencies, urogenital emergencies, acute respiratory distress syndrome (ARDS), and febrile neutropenia. To our knowledge, there is no study done in our country on the pattern and treatment outcome of oncologic emergencies in the pediatric emergency ward admission during the initial visit.

Objective: To determine the pattern and treatment outcome of children with oncologic emergencies seen at the first visit to the Pediatric Emergency Unit, TASH from January 2022 to January 2024

Method:

A hospital-based retrospective cross-sectional study was conducted in TASH with all selected 240 patients who attended the pediatrics emergency unit from January 2022 to January 2024. Data was collected by quota sampling method and analysis was done using SPSS version 25. Statistical significance was considered at a level of significance of 5%, and with a 95% confidence interval (CI) using a Chi-square to present the estimates of the association. The results were presented using text, tables, and charts.

Results:

There were 6,307 pediatric emergency admissions during the study period, and oncologic emergencies contributed to 3.8% of pediatric emergency unit admissions. A total of 240 pediatric patients were included in the study. Most of the patients; 80.8% were between the age of 1-9 years and 61.7% were male with a male-to-female ratio of 1.6:1. The major presenting symptoms were abdominal swelling (20.8%) followed by easy fatigability (17.5%), and neck swelling (13.3%). The most common oncologic emergencies in pediatric emergency visits were tumor lysis syndrome (42.5%), hyperleukocytosis (28.3%), and increased intracranial pressure (14.1%). About 44% of patients stayed at the ER for more than 1 week; 80% of the patients were admitted to the inpatient oncology ward, and 6.3% were linked to the outpatient oncology center. The most common childhood cancers were Acute Lymphoblastic Leukemia (40%), Brain tumors (15%), and non-Hodgkin's Lymphoma (12%). About 95% of the study patients survived, and 5% of the patients did not survive the oncologic emergency during their stay at the pediatric emergency unit. The duration of illness, vital sign status at admission, oxygen saturation, type of primary cancer, serum uric acid level, and electrolytes (potassium, phosphorous, Calcium) were significantly associated with the survival of patients with oncologic emergencies.

Conclusion: Our finding revealed that Tumor Lysis Syndrome was the most common oncologic emergency in children with cancer. The mortality rate in children with oncologic emergencies at the pediatric emergency unit was low in our setup.

Keywords: Cancer, pattern, Tikur Anbessa Specialized Hospital, Oncologic emergency, survival

1. Introduction

1.1. Background of the study

Survival in children with cancer has increased dramatically during the past five decades; this progress is due to advances in specific oncologic therapies as well as supportive care, and an improved ability to manage life-threatening complications. These oncologic emergencies can occur either as the initial manifestation of cancer or arise as a consequence of cancer therapy.¹ These oncologic emergencies may lead to acute and potentially life-threatening complications that directly or indirectly emerge due to the primary disease itself or the therapy. These oncologic emergencies can be further classified into metabolic emergencies, neurological emergencies, thoracic emergencies, gastrointestinal emergencies, urogenital emergencies, acute respiratory distress syndrome (ARDS), and febrile neutropenia.²

The most common metabolic emergencies include tumor lysis syndrome (TLS), hyperleukocytosis, hypercalcemia, and hyperkalemia. These tumor lysis syndromes frequently occur in highly proliferative and highly tumor-burden childhood cancers mainly acute leukemia or Burkitt-type non-Hodgkin lymphomas (NHL). Between 20 – 50% of patients eventually die unless the tumor lysis is appropriately diagnosed and treated.^{3,4}

The most common neurological emergencies include spinal cord compression, convulsions, cerebrovascular accidents, and increased intracranial pressure.⁵ Cardiothoracic oncologic emergencies include Vena cava superior syndrome (VCSS), massive pleural effusion, pericardial effusion, cardiac tamponade, massive hemoptysis, pneumothorax, and pneumomediastinum. Typhlitis, acute massive hepatomegaly, pancreatitis, and veno-occlusive disease are the commonest gastrointestinal emergencies in children with cancer.⁶ Hemorrhagic cystitis, oliguria/anuria, acute renal failure, and hypertension are the commonly encountered urogenital emergencies in children diagnosed with cancer.⁷ Infections are the leading cause of mortality and morbidity among children receiving cytotoxic chemotherapy, and patients get infected most commonly during the neutropenic intervals.⁸

2. Statement of the problem

Among pediatric oncology patients, oncologic emergencies are commonly encountered and usually require hospitalization. A large proportion of these patients will die unless they are diagnosed early and managed promptly and appropriately.

At the pediatric emergency unit, there are a huge number of children with oncologic emergencies who are either diagnosed in our hospital or referred from different institutions. Despite this high burden of patients, there is no proper working area; there is no adequate number of trained nurses

and physicians to take care of critically ill patients. There is no proper setup like unavailability of emergency drugs and ICU beds are not available most of the time.

According to a hospital based prospective Cohort study done at Tikur Anbessa Specialized Hospital, 29.5% of oncologic patients were found to have TLS. There were 11.5% laboratory TLS and 18.0% clinical TLS.⁹

Tikur Anbessa Specialized Hospital (TASH), which is the biggest hospital in the country and serves as the major comprehensive pediatric treatment facility, manages most patients who have access to health care and are diagnosed with Oncologic Emergencies and referred from all corners of the Country.

1.3. Significance of the study

Even though there are some studies done on specific oncologic emergencies such as Febrile Neutropenia and Tumor Lysis Syndrome there is not a single study done in our country on the pattern and treatment outcome of oncologic emergencies in general. Identifying the common types of oncologic emergencies, their main clinical presentation, treatment outcome, and associated factors are important for prevention, early identification, and prompt management of oncologic emergencies. Which in turn improves patient care and has a direct impact on the quality of life and long-term outcomes of oncology patients. Knowing the burden of the condition in our setup is also important to design a solution by involving different stakeholders. It is also important to compare the pattern and treatment outcome of oncologic emergency patients between developed and developing countries and to identify the associated factors. Hence this study will give us the pattern and treatment outcome of children with oncologic emergencies as compared to the outcome in developed and other developing countries. It will also determine the factors that affect the outcome in our setup so that it will add input to the existing knowledge and may help as a baseline for further prospective studies.

2. Literature Review

A prospective cohort study done in Turkey on admitted oncologic patients showed that tumor lysis syndrome, hyperleukocytosis, and convulsion were the most common oncologic emergencies. More than two-thirds had a primary oncologic disease, and the others had recurrent cancer. The most common presenting complaint was fever followed by breathing difficulties, and one-third of the patients died due the cancer and oncologic emergencies.¹⁰

A retrospective multicenter study done in China showed that children who had WBC counts above $50 \times 10^9/L$ were more prone to TLS. The incidences of hyperphosphatemia and hypocalcemia were significantly higher in TLS children with hyperleukocytosis.¹¹

A prospective cohort study conducted at Tikur Anbessa Specialized Hospital showed that tumor lysis syndrome was detected in 29.5 % of pediatric cancer patients, and 72.2% were spontaneous tumor lysis syndrome. A prospective cross-sectional study carried out at Jimma University Medical Center in Ethiopia showed neutropenic fever occurred in 23.4% of pediatric oncologic

patients. Among the oncologic patients who visited the emergency unit; 18.9% passed away, and patients with metastatic disease and comorbidities had a higher mortality rate.¹²

A retrospective study in Turkey on 41 children with mediastinal tumors showed that 19 of them had superior vena cava syndrome. Acute T-lymphoblastic leukemia, Hodgkin's, and non-Hodgkin's lymphoma were the most common mediastinal tumors.¹³

A retrospectively collected data from patients with newly diagnosed AML patients who had hyperleukocytosis at 12 institutions in the US, Spain, Germany, and France showed the median white blood cell count at presentation was $131.4 \times 10^9/L$; 63.0% of patients had a WBC of more than $100 \times 10^9/L$. Clinical leukostasis, DIC, and TLS were all observed in 25.7, 15.8, and 34.1% of patients, respectively.¹⁴

A retrospective study analysis done in South India showed that about 38.8% of the children had hyperleukocytosis, and 76.8% (n = 172) of the children had LDH levels greater than 2 ULN at the time of presentation. About 13.4% and 63% of the study participants had mediastinal mass and significant hepatosplenomegaly respectively.¹⁵

3. Conceptual Framework

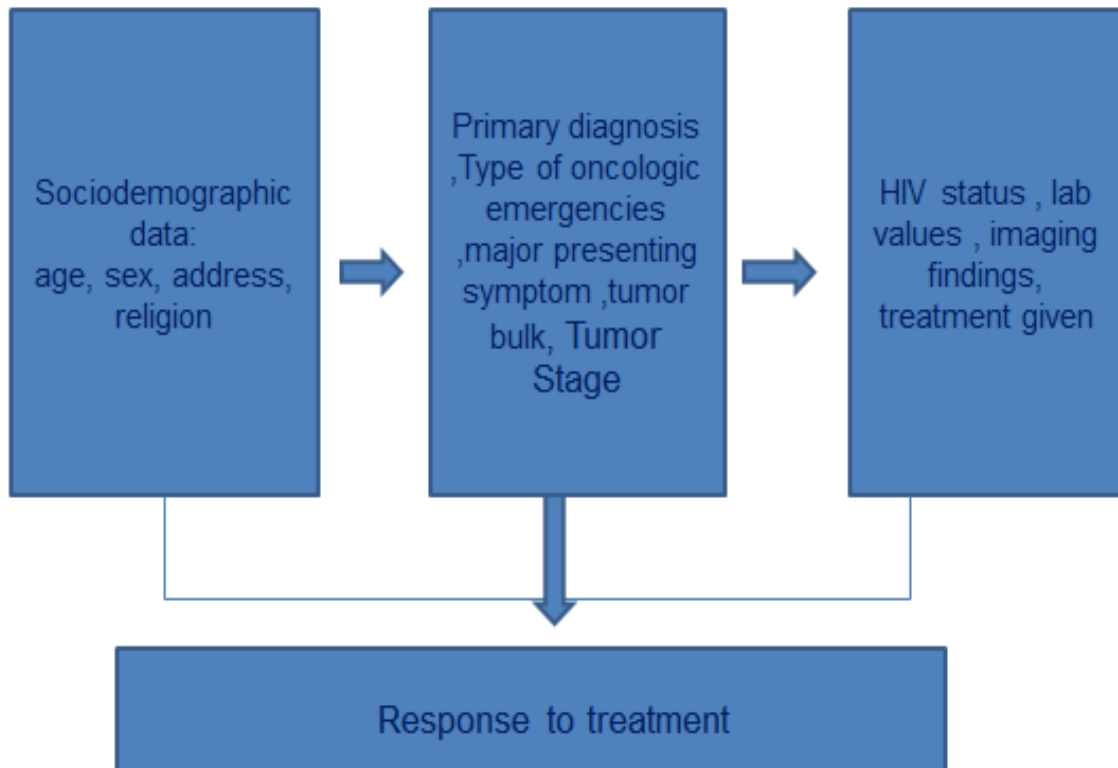


Figure 1. Conceptual framework of factors associated with treatment outcome of children with oncologic emergencies.

4. Objectives

4.1. General objectives

- To determine the Pattern and Treatment Outcome of children with Oncologic Emergencies seen at first visit to Tikur Anbessa Specialized Hospital Pediatric Emergency Unit.

4.2. Specific objectives

- To describe the demographic profile of children with oncologic emergencies seen at the pediatrics emergency unit
- To describe the pattern of oncologic emergencies in children in the pediatric emergency unit
- To determine the treatment outcome of children with oncologic emergencies at the pediatrics emergency unit during the emergency stay
- To identify factors that affect treatment outcomes of oncologic emergencies in children at the pediatric emergency unit

5. Methods and Materials

5.1. Study setting

The study was conducted in Tikur Anbessa Specialized Hospital at the Pediatric Emergency Unit, Addis Ababa, Ethiopia. Tikur Anbessa Specialized Hospital, established in 1974, is the largest tertiary hospital in the country. The hospital is administered by Addis Ababa University and is the largest and oldest teaching hospital among all in Ethiopia providing teaching for about 300 medical students and 350 Residents every year. Tikur Anbessa Hospital offers diagnosis and treatment for approximately 400,000 patients a year.

It was used as the only Hemato-oncology treatment unit in the county until recently. The pediatric hemato-oncology ward has 26 Beds the cancer center has 16 beds dedicated to pediatric patients and the Pediatric Emergency unit has 43 beds. Currently, there are 3 pediatric Hemato-oncologists and 6 Hemato-Oncology Fellows working in the pediatric unit. The unit renders both inpatient and outpatient services for more than 600 patients every month.

5.2. Study design

A hospital-based retrospective cross-sectional study design was conducted.

5.3. Study period

Two years of retrospective data collection from January 2022 to January 2024.

5.4. Population

5.4.1. Source population

All infants and children aged less than 15 years who were admitted to the pediatric emergency unit during the study period

5.4.2. Study population

All infants and children aged less than 15 years were diagnosed with oncologic diseases at the pediatric emergency unit during the study period.

5.4.3. Study subject -All infants and children aged less than 15 years who were diagnosed with an oncologic emergency at the pediatrics emergency unit during the study period.

5.5. Sample size

The sample size was determined using a single population proportion formula considering a confidence level of 95% and, a marginal error of 5%. The expected proportion of oncologic emergencies in children was taken from research done in Turkey in 2018 which showed a prevalence of 17.4%

$$\text{Sample size: } n = \frac{Z^2 P (1-P)}{d^2} = \frac{1.96^2 * 0.174 * (1-0.174)}{0.05^2} = 220$$

$$d^2 = 0.05^2$$

Where: n the minimum sample size

p=the expected prevalence of oncologic emergencies in children

d= the level of precision (margin of error)

z= the value at a 95% confidence level

Adding 10% of the calculated value for missing and incomplete data makes the final sample size required **242**

5.6. Inclusion and exclusion criteria

5.6.1. Inclusion criteria

- All infants and children less than 15 years of age who were diagnosed with oncologic emergency seen at the first visit to the Pediatric Emergency unit during the study period

5.6.2. Exclusion criteria

- Those patients with incomplete documentation
- Those patients only with Febrile Neutropenia
- Those patients with recurrent diseases

5.7. Data collection and measurements

A structured questionnaire was prepared after reviewing other literature with the same research topic and setup. All oncologic Patients who were admitted to the pediatric emergency unit in the study period were retrieved from the HMIS log book. All relevant data were collected from the medical records of study subjects.

5.8. Data handling

Data completeness and cleanness were checked by the investigator. The hard copies were converted into soft copies, stored on the hard drive, and became ready for analysis, and the backup copy was stored on a separate drive.

5.9. Study variables

5.9.1. Independent variables

- Socio-demographic data: age, sex, address, residence, religion
- Major presenting symptom, Primary diagnosis, Oncologic Emergency type, tumor bulk, stage, HIV status, LDH, Uric Acid, K, P, Ca, Cr, Initial WBC, Tumor type, Type of treatment given.

5.9.2. Dependent variables

Treatment outcome

5.10. Data Quality Assurance

The primary investigator collected the data and its completeness was checked and coded. The converted soft copy was again cross-checked with the hard copy for neatness, Completeness, and consistency before carrying out the statistical analysis.

5.11. Data analysis

After a thorough cleaning and checking for its completeness data was entered into the Statistical Package for Social Sciences ver. 25 (SPSS) for subsequent descriptive analysis such as

Mean frequencies and percentages as appropriate. The chi-square test was used to analyze the association between variables. Statistical significance was taken for p values of <0.05 for all statistical tests.

6. Ethical considerations

Ethical clearance to conduct this study was obtained from the Pediatrics and Child Health Department's Research and Publications Committee of the School of Medicine, College of Health Sciences, Addis Ababa University. Confidentiality was fully maintained during the Data Collection and further analysis and dissemination of results.

7. Dissemination of findings

The result of the study will be submitted to Addis Ababa University, College of Health Sciences, School of Medicine, Department of Pediatrics and Child Health for the requirement of partial fulfillment of specialty certificate in pediatric and child health. The findings of the study will also be shared with other concerned bodies. Furthermore, the manuscript will be published in peer-reviewed journals.

8. Operational definitions (2)

1. **Laboratory TLS (LTLS):** The presence of two or more abnormal serum values at presentation (i.e., uric acid ≥ 8 mg/dl, potassium ≥ 6 mg/dl, phosphate ≥ 2.1 mmol/l, calcium ≤ 1.75 mmol/l).

2. **Clinical TLS (CTLTS):** Presence of LTLS and one or more of the following clinical complications: renal insufficiency, cardiac arrhythmias, seizures, or sudden death.

3. Bulky mass

Mediastinal mass in which the greatest diameter measures more than one-third the diameter of the chest measured at the level of the apex of the diaphragms on chest X-ray or A lymph node mass that measures >6 cm in the transverse (axial) diameter on CT scan.

4. **Hyperleukocytosis:** is defined as a peripheral leukocyte count exceeding 100,000/mL, but clinically significant hyperleukocytosis occurs with WBC counts of greater than 200,000/mL in AML, and greater than 300,000/mL in ALL and chronic myelogenous leukemia (CML)

5. **Supportive treatment:** Patients who were treated with O₂, Hydration, Allopurinol, given blood products, head elevation, and Manitol

6. **Unstable vital signs:** Patients whose vital signs are out of the normal range for their age

7. **Decreased level of consciousness:** Patients whose GCS is less than 15.

8. **Pediatric patient Survived:** Patients who survived during the pediatric emergency unit stay, including patients who were improved, transferred to the pediatric ward, or discharged.

9. **Pediatric patient non-survived:** Patients who are not alive at the time of discharge.

9. Result

9.1. Socio-demographic characteristics of the patient

There were 6,307 pediatric emergency admissions during the study period, of which 1,110 were oncologic patients and 719 of them were new and Oncologic Emergency contributed to 3.8% of ER admissions. Medical records of 242 subjects were retrieved and 2 were excluded due to incomplete documentation. Totally 240 study subjects were included. Most of the study subjects (80.8%) were in the age group of 1-9 years with a mean and SD of 5.55±3.28 years and 61.7% were male with M: F ratio of 1.6:1. Most of the subjects (38.3%) were from Oromia followed by Addis Ababa (18.8%). and 52.5% were urban in residency.

Table 1. The demographic characteristics of children with oncologic emergencies at the pediatric emergency unit, TASH

variable	frequency	Percent
Age in years		
<1	11	4.6
1-9	194	80.8
>10	35	14.6
Sex of the study participants		
Male	148	61.7
Female	92	38.3
Address of the study participants		
Addis Ababa	45	18.8
Oromia	92	38.3
Amhara	35	14.6
South Ethiopia	41	17.1
Tigray	2	0.8
Afar	4	1.7
Benishangul	9	3.8
others	12	5
Residence		
Urban	126	52.5
Rural	114	47.5

9.2. Clinical profile of the patients with an oncologic emergency at the pediatric emergency unit, TASH

The major presenting symptoms were abdominal swelling 20.8% (n=50) followed by easy fatigability 17.5% (n=42), neck swelling 13.3% (n=32), and nasal bleeding 9.2% (n=22). Other presenting symptoms were fever, cough, bone pain, abdominal pain, abnormal body movement, body weakness and headache Half of the study subjects had a duration of illness > 4 weeks. About 20% of the study subjects had unstable vital signs. Almost nine percent of the study participants required oxygen 6.3% had a decreased level of consciousness 15% had SAM and 8.7% had MAM the rest had normal nutritional status.

Table 2. The clinical profile of children with oncologic emergencies at the pediatric emergency unit,

variable	frequency	Percent
Duration of illness in weeks		
<2	39	16.3
2-4	79	32.9
>4	122	50.8
Duration from the time of referral to acceptance in weeks		
<1	163	85.3
1-4	28	14.7
The referral sheet was not found	49	20.4
Major presentation symptom		
Abdominal swelling	50	20.8
Easy fatigability	42	17.5
Neck swelling	32	13.3
Nasal bleeding	22	9.2
fever	18	7.5
Headache	15	6.3
Body weakness	10	4.2
Cough	9	3.8
Vomiting	9	3.8
Eye swelling	8	3.3
others	25	10.4
Vital sign		
Stable	194	80
Unstable	48	20
Types of vital sign derangement (n=48)		
bradycardia	3	6.3
fever	13	27.1
stage II HTN	19	39.6
tachycardia	4	8.3
tachypnea	9	18.8
require oxygen	21	8.7
Level of consciousness		
Conscious	225	93.7
Decrease level of consciousness	15	6.3
Nutritional status		
Unaffected	183	76.3
MAM	21	8.7
SAM	36	15

9.3. The patterns of Primary diagnosis among children with an oncologic emergency at the pediatric emergency unit, TASH

The finding of this study showed that the major pattern of primary diagnosis among oncologic emergency patients was ALL followed by NHL, AML, medulloblastoma, Wilms tumor, and neuroblastoma as shown in the figure below.

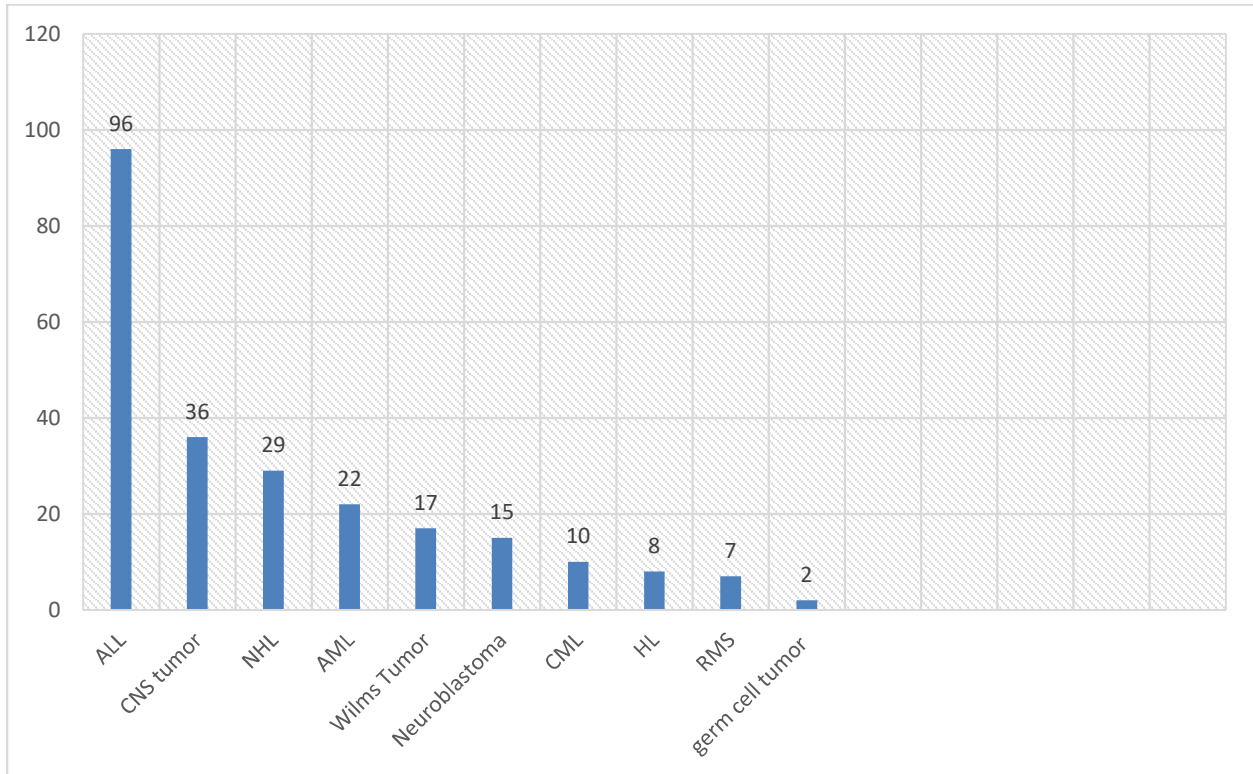


Figure 2. The pattern of primary diagnosis in children with an oncologic emergency at the pediatric emergency unit, TASH

9.4. Types of oncologic emergency among pediatric patients at the pediatric emergency unit, TASH

The study showed that the major oncologic emergency was tumor lysis syndrome (42.5%) followed by hyperleukocytosis (28.3%) and increased ICP (14.1%).

Table 3. The types of oncologic emergencies among pediatric patients at the pediatric emergency unit, TASH

Variable	frequency	Percent
Oncologic emergency (n=240)		
Tumor lysis syndrome	102	42.5
Type tumor lysis syndrome		
✓ Lab TLS	90	88.2
✓ Clinical TLS	12	11.8
Hyperleukocytosis	68	28.3
SVCS/SMS	16	6.7
Increased ICP	34	14.1
Seizure	3	1.3
Body weakness	9	3.8
Anuria/oliguria	3	1.3
Hypertension	24	10
Upper airway obstruction	5	2.1

9.5. Pretreatment laboratory profile of children with an oncologic emergency at the pediatric emergency unit, TASH

Twenty-eight percent of the study subjects had an initial WBC count of above 100K 66.3% of the participants had ANC of <500 and 22.9% had a hemoglobin level of <7g/dL. About 25% percent of the study subjects had <20K platelets and 33.3 % had >1000 LDH count. About 53% of the study subjects had a uric acid level of ≥ 8 and 20 percent of them had ≥ 6 potassium level.

Table 4 Pretreatment laboratory profile of children with an oncologic emergency at the pediatric emergency unit, TASH

Variable	frequency	Percent
WBC		
<10k	82	34.2
10-50k	81	33.7
50-100k	9	3.8
>100k	68	28.3
ANC		
<500	159	66.3
500-1000	23	9.6
>1000	58	24.2
HGB		
<7	55	22.9
7-10	78	32.5
>10	107	44.6
PLT		
<20K	59	24.6
20-100K	71	29.6
>100K	110	45.8
LDH		
<1000	160	66.7
≥1000	80	33.3
Uric acid		
<8	113	47.1
≥8	127	52.9
K		
<6	192	80.0
≥6	48	20.0
P		
<6.5	185	77.1
≥6.5	55	22.9
Calcium		
>7	185	77.1
≤7	55	22.9
Creatinine		
≤0.5	167	69.6
>0.5	73	30.4
Urea		
≤20	144	60.0
>20	96	40.0

9.6 Mode of treatment and treatment outcome of pediatric oncologic patients at the pediatric emergency unit during the emergency stay.

Ninety-five percent of the study subjects had received treatment and all of them had received supportive treatment. About 18% were treated with hydroxyurea and 6.7% with steroids. Of those who were treated with steroid/hydroxyurea, 70% were received within 24 hours. About 44% of patients stayed at the ER for more than 1 week. About 80% of the patients were admitted to the ward 6.3% were linked to the oncology center while 5.4% died. Of those who died at the emergency unit, 61.5% were due to oncology-related causes.

Table 5 Mode of treatment and treatment outcome of children with an oncologic emergency at the pediatric emergency unit during the emergency stay.

Variable	frequency	Percent
Treatment received		
Yes	235	95.3
No	5	2.6
Types of treatment at emergency (n=235)		
Supportive	235	100
steroid	16	6.7
hydroxyurea	44	18.3
Time of enrolment to steroid/hydroxyurea initiation (n=60)		
<24hrs	42	70
24-48hrs	15	25
48-72hrs	3	5
Duration at ER in days		
1	31	12.9
2-7	103	42.9
>7	106	44.2
Status of the patient after oncologic treatment		
admitted to ward	191	79.6
admitted to ICU	4	1.7
died	13	5.4
abandoned the treatment	7	2.9
transfer to another facility	10	4.1
link to the oncology center	15	6.3
Reason for death (n=13)		
Oncology related	8	61.5
Not oncology related	5	38.5

9.7. Chi-square relation between independent variables and oncologic emergency treatment outcome during emergency stay

The finding of the study revealed that duration of illness ($p=0.010$), vital sign status at admission ($p=0.002$), oxygen saturation level ($p<0.001$), the pattern of primary diagnosis ($p<0.024$), Uric acid ($p=0.005$), and electrolytes (K, P, Ca) were statistically significant at p -value <0.05 with the treatment outcome of oncologic emergency pediatric patients using chi-square test. While socio-demographic profile, supportive treatment, treatment with steroid or hydroxyurea, initial white cell count, and creatinine values are not statistically significant.

Table 6 The Chi-square relation between independent variables and oncologic emergency treatment outcome during emergency stay

variable	The outcome of an oncologic emergency		Chi-square	p-value
	Not survived	survived		
Age in years			3.26	0.196
<1	0	11		
1-9	13	181		
≥ 10	0	35		
Sex of the study participants			0.74	0.992
Male	8	140		
Female	5	87		
Residence			0.45	0.502
Urban	8	118		
rural	5	109		

Variable	The outcome of an oncologic emergency		Chi-square	p-value
	Not survived	Survived		
Duration of illness			4.59	0.010
<2wk	4	35		
2-4wk	6	73		
>4wk	3	119		
vital sign			9.84	0.002
stable	6	186		
unstable	7	41		
require oxygen			15.19	0.000
yes	5	16		
no	8	211		
Received supportive treatment			0.29	0.589
Yes	13	222		
no	0	5		
Received steroid treatment			1.7	0.195

Yes	2	14		
No	11	213		
Received hydroxyurea			0.21	0.649
Yes	3	41		
no	10	189		
Primary diagnosis			27.59	0.024
ALL	4	92		
AMY	2	20		
anaplastic oligo dendro-glioma	1	0		
brain stem glioma	0	3		
craniopharyngioma	0	2		
CML	0	10		
ependymoma	0	2		
germ cell tumor	0	2		
high-grade glioma	0	2		
HL	1	7		
medulloblastoma	3	19		
neuroblastoma	0	15		
NHL	0	29		
Pilocytic astrocytoma	0	2		
RMS	0	7		
Wilms tumor	2	15		
WBC			1.92	0.589
<10K	3	79		
10-50K	4	69		
50-100K	0	9		
>100K	6	70		
<7	3	53	7.69	0.021
7-10	0	78		
>10	10	97		
Creatinine			1.35	0.354
≤0.5	10	157		
>0.5	3	70		
Uric acid			7.71	0.005
<8	11	102		
≥8	2	125		
k			3.44	0.044
<6	13	179		
≥6	0	48		
p			4.08	0.043
<6.5	13	172		
≥6.5	0	55		
Ca			11.61	0.001
>7	5	180		
≤7	8	47		

10. Discussions

This study was a retrospective hospital-based cross-sectional study, conducted at the Pediatrics Emergency Unit, Tikur Anbessa Specialized Hospital, Addis Ababa, Ethiopia, involving Two hundred forty records from January 2022 to January 2024.

In this study, most (80.8%) of the study participants were in the age group of 1-9 years with mean and SD of 5.55 ± 3.28 years and 61.7% were male and 38.3% were female with male to female ratio of 1.6:1. This is comparable to a study done at Tikur Anbessa Specialized Hospital from October 2016 - July 2017 at the pediatric hematology-oncology unit that showed 63.9% of the study subjects were males with Male to female ratio was 1.77:1. (9). A study was done in Turkey on oncologic emergency patients, except for febrile neutropenia, between July 2014 and December 2015, where males accounted for 67.1% and females accounted for 32.9%, with a male-to-female ratio of 2:1. (10). This study is inconsistent with a study done in China between 2015 to 2018 which showed Children older than 10 years and younger than 1 year had a higher risk of TLS than children of 1–10 years old. (11)

Regarding distribution by regions, 38.3% were from Oromia 18.8% from Addis Ababa and 17.1% from SNNPR, and 52.5% were urban in residency. In the previous study at TASH, 42.6% of the children were from the Oromia region, followed by the Southern Nation Nationality Peoples Region at 19.7%. 72.1% of the study participants were from the rural area of the country. (9). This is because the Oromia region is the largest regional state in Ethiopia and the nearest region to the Capital Addis Ababa.

Out of 240 pediatric oncology patients 191(80%) had hematologic and lymphoid malignancy and solid tumors account for 49 (20%). The majority of hematologic and lymphoid malignancies in our study were ALL 40% (n=96), NHL 12% (n=29%), AML 9.1% (n=22), and the majority of solid tumors were Medulloblastoma 9.1% (n=22), Wilms tumor 7% (n=17), Neuroblastoma 6.2% (n=15). This is Comparable to the previous study done in TASH 65.9% had hematologic malignancy, while the rest 34.4% had solid malignancy. The majority of the hematologic malignancies in that study were ALL, 34.4% followed by NHL, 13.1%, AML, 11.5%. (9)

The major presenting symptom was abdominal swelling 20.8% (n=50) followed by easy fatigability 17.5% (n=42), nasal bleeding 9.2% (n=22), and fever 7.5% (n=18). This is different from the Turkish study where the major presenting complaints of the oncologic emergency

patients were, fever (n=21; 23.3%) and breathing difficulties (n=20; 22.2%) were the most commonly encountered ones. (10). In the previous study in TASH Easy fatigability, abdominal pain, and prolonged fever were the most prevalent complaints by the study participants. (9)

In this study, the major oncologic emergency was a tumor lysis syndrome (42.5%) followed by hyperleukocytosis (27.9%) and increased ICP (10.4%). The majority of cases with TLS in this study were patients with a primary diagnosis of ALL, NHL, or AML. This is similar to the study done in Turkey where TLS was the most commonly encountered oncologic emergency condition during their study (33.3%) The majority of the cases with TLS in their study were the patients with a primary diagnosis of ALL or NHL. (10). This supports that ALL is a highly proliferative tumor NHL is highly proliferative with high tumor turn and the risk of having a bulky tumor is high.

In this study, Clinical TLS prevailed within the Cases of RMS whereas the majority of ALL patients developed Lab TLS. This is inconsistent with the Turkish study where for the cases with TLS, clinical TLS prevailed within the NHL group; whereas, the majority of ALL patients developed laboratory TLS. (10)

Considering the pretreatment laboratory profile of patients, about 53% had Hyperuricemia, 22.9% had both Hyperphosphatemia and Hypocalcemia and 20% had Hyperkalemia. This is consistent with the previous Turkish study where All patients with TLS had hyperuricemia, followed by hypocalcemia and hyperphosphatemia. (10). In the previous Chinese study hyperphosphatemia occurred with the highest frequency (68.8%) and hyperkalemia occurred with the lowest frequency (35.4%) (11)

Among patients with clinical TLS AKI was present in all 12 patients but sudden death, arrhythmia or convulsion did not occur in any patient. In the Turkish study among the manifestations to establish the diagnosis of clinical TLS, AKF was present in (88.9%, and sudden death occurred in 11.1%; whereas convulsion did not occur in any patient. (10). In the Previous Chinese study arrhythmia was observed in 7.5%, seizure in 3.8%, and AKI in 41.7% of the cases. (11)

About 98% of patients received supportive treatment of these, 18.3% received hydroxyurea and 6.7% received steroids. About 70% of these started hydroxyurea and steroids within 24 hours of admission. In the Turkish and Chinese studies, in addition to hydration & Allopurinol patients had received Rasburicase, Alkalinization, and Hemodialysis. (10,11)

In our study, 95% (n=227) of the study subjects had survived while 5% (n=13) had not survived after treatment of the oncologic emergency during their stay at the pediatric emergency unit.

After oncologic emergency treatment, 79.6% of patients were admitted to the ward 6.3% were linked to the Oncology center 4.1% were transferred to another facility 2.9% abandoned treatment, and 5.4% died. 61.5% of the deaths are linked to Oncologic causes.

The chi-square relation between oncologic emergency outcome and independent variable study revealed that duration of illness ($p=0.010$), vital sign status at admission ($p=0.002$), oxygen saturation level ($p<0.001$), pattern of primary diagnosis ($p<0.024$), uric acid ($p=0.005$), and electrolytes (K, P, Ca) were statistically significant at p -value <0.05 with the survival emergency oncologic outcome pediatric patients.

11. Limitations of the study

Due to the incomplete registration of patient information and data management system in the study hospital, some other variables were not included in the study. Lack of previous research studies on the same topic in our setup for comparison. Loss of patient charts as a whole or some part of the chart is common.

12. Conclusions

The finding of this study showed that most cases of oncologic emergency in children occurred in those 1-9 years of age. It is more common in males than females. Most of the study subjects were from Oromia followed by Addis Ababa. More than half of the cases were from urban areas. The major presenting symptom was abdominal swelling followed by easy fatigability, neck swelling, and nasal bleeding. Oncologic emergency is more common in hematologic and lymphoid malignancies like ALL, NHL, and AML than solid tumors. The major oncologic emergency was Tumor lysis syndrome followed by Hyperleukocytosis and increased ICP. Hyperuricemia is the commonest laboratory abnormality followed by hyperphosphatemia and hypocalcemia. Acute kidney injury is the most common parameter in clinical tumor lysis syndrome. Duration of illness, vital sign status at admission, oxygen saturation, level of consciousness, the pattern of primary diagnosis, uric acid, and electrolytes (K, P, Ca) were statistically significant at p-value <0.05 with the survival of children with an oncologic emergency during their stay at the pediatric emergency unit.

13. Recommendations

This study showed that oncologic emergencies are common in children on their first visit to health facilities. We recommend that there should be a separate area for these patients the staff should be trained on how to diagnose, manage, and follow specific types of oncologic emergencies and the necessary medications should be easily available. All children who are diagnosed with an oncologic emergency should start treatment as promptly as possible and should be followed closely with clinical and laboratory parameters. Proper documentation and chart placement should be practiced.

14. References

1. Lanzkowsky P, Lipton JM, Fish JD, editors. Lanzkowskys Manual of Pediatric Hematology and Oncology. 6. Edition. Amsterdam, Boston, Heidelberg, London, New York, Oxford, Paris, San Diego, San Francisco, Singapore, Sydney, Tokyo: Elsevier; 2016. 751 p.
2. Pizzo PA, Poplack DG, Adamson PC, Blaney SM, Helman L, editors. Principles and practice of pediatric oncology. Seventh edition. Philadelphia: Wolters Kluwer; 2016.
3. Li HCW, Chung OKJ, Tam CJ, Chiu SY. Effective Prevention and Management of Tumor Lysis Syndrome in Children With Cancer: The Important Contributions of Pediatric Oncology Nurses. *J Pediatr Oncol Nurs*. 2015 Jul;32(4):209–18.
4. Bose P, Qubaiah O. A review of tumor lysis syndrome with targeted therapies and the role of rasburicase: *TLS with targeted therapies and role of rasburicase*. *J Clin Pharm Ther*. 2011 Jun;36(3):299–326.
5. Sandberg DI, Bilsky MH, Kushner BH, Souweidane MM, Kramer K, Laquaglia MP, et al. Treatment of Spinal Involvement in Neuroblastoma Patients. *Pediatr Neurosurg*. 2003;39(6):291–8.
6. Davila ML. Neutropenic enterocolitis: *Curr Opin Intern Med*. 2006 Apr;5(2):194–7.
7. Stillwell TJ, Benson RC. Cyclophosphamide-induced hemorrhagic cystitis: A review of 100 patients. *Cancer*. 1988 Feb 1;61(3):451–7.
8. Hughes WT, Armstrong D, Bodey GP, Bow EJ, Brown AE, Calandra T, et al. 2002 Guidelines for the Use of Antimicrobial Agents in Neutropenic Patients with Cancer. *Clin Infect Dis*. 2002 Mar 15;34(6):730–51.
9. Micho H, Mohammed Y, Hailu D, Genet S. Evaluation and characterization of tumor lysis syndrome before and after chemotherapy among pediatric oncology patients in Tikur Anbessa specialized hospital, Addis Ababa, Ethiopia. *BMC Hematol*. 2018 Dec;18(1):22.
10. Çiftçi AÇ, Küpeli S, Sezgin G, Bayram İ. Evaluation of pediatric patients with an oncologic emergency: single center experience. *Turk J Pediatr*. 2018;60(6):660.
11. Xue Y, Chen J, Gao S, Zhai X, Wang N, Gao J, et al. Clinical characteristics of tumor lysis syndrome in childhood acute lymphoblastic leukemia. *Sci Rep*. 2021 May 6;11(1):9656.

12. Workina A, Habtamu A, Zewdie W. Reasons for Emergency Department Visit, Outcomes, and Associated Factors of Oncologic Patients at Emergency Department of Jimma University Medical Centre. *Open Access Emerg Med*. 2022 Oct; Volume 14:581–90.
13. Özcan A. Vena Cava Superior Syndrome in Children With Mediastinal Tumors: Single Center Experience. *North Clin Istanb* [Internet]. 2019 [cited 2023 Jun 25]; Available from: <http://www.kuzeyklinikleri.com/jvi.aspx?pdirenci&plng=eng&un=NCI-46354>
14. Shallis RM, Stahl M, Wei W, Montesinos P, Lengline E, Neukirchen J, et al. Patterns of care and clinical outcomes of patients with newly diagnosed acute myeloid leukemia presenting with hyperleukocytosis who do not receive intensive chemotherapy. *Leuk Lymphoma*. 2020 Apr 15;61(5):1220–5.
15. Gopakumar KG, Seetharam S, Km JK, Nair M, Rajeswari B, Cs G, et al. Risk-based management strategy and outcomes of tumor lysis syndrome in children with leukemia/lymphoma: Analysis from a resource-limited setting. *Pediatr Blood Cancer*. 2018 Dec;65(12):e27401.