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Research Article

Tumor Lysis Syndrome, Frequency and Outcome Among Acute Leukaemia Paediatric Patients in Sudan

Alaa Atef Hamed Yasin[1], Mayasa Ibrahim Ali Mohamed[1], Mustafa Magbol[2, *], Ahmad Izzoddeen[1, 3]

[1]Medicine Program, Alfajr Collage for Sciences and Technologies, Khartoum, Sudan

[2]Faculty of Medicine, Al-Zaiem Al-Azhari University, Khartoum, Sudan

[3]Field Epidemiology Training Program, Federal Ministry of Health, Khartoum, Sudan

Abstract

Tumor lysis syndrome (TLS) is a haemato-oncological emergency syndrome characterized by metabolic and electrolyte imbalances that are associated with tumor cells. The syndrome is observed when starting chemotherapy for haematological malignancies, while the incidence of spontaneous tumor lysis prior to the start of tumor therapy is rare. A descriptive cross-sectional study conducted over a period of six months. A total of 91 patient records were totally covered from the University Diagnostic Center in Algezir, Sudan. For the determination of the frequency and outcome of TLS among acute leukemia paediatric patients. Of the total 91 leukemia cases retrieved from the hospital records, 60.4% were males while those from the center (Gezira, Sinar and Khartoum) represented 68.1% of the participants. ALL was found in 57.1% however, 51.6% had splenomegaly and lymphadenopathy. 18.7% of cases developed TLS. 5.5% of cases died while 4.4% had complete recovery. A considerable number of patients developed TLS. ALL was affecting more patients than AML. Males were affected more common in comparison to females, with all the cases reported in ALL. Additionally, clinically identified cases was far more than laboratory one. Also, a significant association was discovered between occurrence of TLS and comorbidities. Further future researches are highly recommended.

Keywords

Tumor Lysis Syndrome, Electrolyte Imbalances, Chemotherapy, Malignancy

1. Introduction

Tumor lysis syndrome (TLS) is an oncological emergency occurred due to the massive breakdown of malignant cells manifested clinically by renal failure, seizures, and arrhythmias that require early realizations and management [1]. TLS led to rapid releases of diverse intracellular components such as: (uric acid, potassium, and phosphate) [2]. The lysis of the malignant cells may happen spontaneously before the treatment or after induction with cytotoxic therapy and accordingly, it is called spontaneous or chemotherapy-induced TLS. Furthermore, classified as clinical or laboratory TLS [3]. According to Cairo and Bishop criteria, the laboratory TLS (LTLS), is existing if >two of the following abnormalities

*Corresponding author: mustafaaltyeb01236009@gmail.com (Mustafa Magbol)

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occur within three days before or up to seven days after chemotherapy, namely hyperuricemia (UA>8 mg/dl. Normal= 4_7 mg/dl), hyperphosphatemia (P>6.5 mg/dl. Normal= 2_5 mg/dl), hyperkalemia (K>6 meq/L. Normal= 3_5 mmol/l) and hypocalcaemia (calcium<7 mg/dl. Normal= 7_10 mg/dl). Clinical TLS (CTLS) is assigned by one of the clinical features like acute kidney injury (elevated serum creatinine > 1.5 times the upper limit of normal (Normal= .5_ 1.7 mg/dl) and oliguria for 6 hours), aspects of leukostasis (seizures, intracranial bleed), arrhythmias and death [1]. Hyperkalaemia is the most severe form and occurs within 6 to 72 hours after the start of treatment if not treated appropriately will lead to sudden cardiac death, Hyperuricemia occurs within 48 to 72 hours after the beginning of treatment and leads to acute kidney injury, Hyperphosphatemia occurs within 24 to 48 hours after treatment start may lead to tetanus and arrhythmia secondary to hypocalcaemia [4].

The reported incidence of TLS differs due to the invariability of the populations analysed in TLS studies and case reports. The prevalence Diverge among malignancies, used chemotherapies, and prophylactic measures [5]. It is highly linked to certain types of cancer; non-Hodgkin lymphoma 30%. Solid tumor 20%. AML 19% and ALL 13% [6]. additionally, overall occurrences of TLS in paediatric haematological malignancies fluctuate in a wide range from 4.4% to 53.6% [7].

The risk factors for TLS are set by multiple characteristics including Tumor, patients, and therapy-specific factors; tumor factors are: ALL with WBC count ≥ 100 × 109/L (Normal= 4000_ 7000) or less if the baseline elevation of LDH is twice the upper limit normal, AML with WBC count ≥100 × 109/L (high-risk patients). AML with a WBC amidst 25 × 109/l and 100 × 109/l or <25 × 109/L if the baseline elevation of LDH is twice ULN, ALL with WBC < 100 × 109/L and an LDH of less than twice ULN (intermediate risk). AML with WBC count <25 × 109/L and an LDH higher to less than twice ULN (low risk). Patient-related factors are dehydration, increasing age, large spleen, mediastinal mass, CNS, and Renal involvement. Therapeutic factors are intense polychemotherapy, corticosteroids, intracellular chemotherapy, radiotherapy, and interferon more commonly associated with TLS [4].

The eventual outcome of TLS in ALL children was cure and event-free, on the other hand poor prognosis was demonstrated in TLS children with abnormality in karyotyping and a hydration period of shorter than 7 days [8]. Later studies found that mortality for TLS resulting from solid tumors is moderately high at 35% in comparison to the 1.9% rate reported for patients with ALL and NHL [9].

This study is centered on the fact that this vulnerable sector of the population is at high risk of exposure to TLS. It provides evidence of frequencies and Outcomes to enforce the system to establish preventive and management protocols. Up to researchers' knowledge, no studies conducted in Sudan addressing tumor lysis syndrome. The study aims to measure the frequency of TLS, patient's outcome and comorbidities association.

2. Methodology

A descriptive cross-sectional study was conducted over a period of six months. A total of 91 patients' records were covered from the University Diagnostic Center in Algezir, Sudan, for the determination of the frequency and outcome of TLS among children with acute leukaemia. Targeting patients below 17 years. We attempted to use the finite study formula at a confidence level of 95%, margin of error of 5%, and power of 80%:

$$n = z^2(p\ q) \div d^2$$

According to the initial estimation, the sample size was 385, unfortunately, the medical records that fulfill the selection criteria in this study were only 91 files, so we decided to make total coverage. The data was collected by reviewing patients' records by extraction forms to extract the data from patient files. The extraction form was converted to (Google form, manually prepared) in which written questions are presented and answered in written form. The data was analysed using the SPSS version 25 software program using descriptive statistics, descriptive data presented as frequency, proportion tables, and charts. Ethical approval was obtained from federal ministry of health and university diagnostic center.

3. Results

Of the total 91 leukemia cases retrieved from the hospital records, 60.4% were males while those from the center (Gezira, Sinar and Khartoum) represented 68.1% of the participants. ALL was found in 57.1% however, 51.6% had splenomegaly and lymphadenopathy. 18.7% of cases developed TLS. 5.5% of cases died while 4.4% had complete recovery (Table 1). Lab finding of TLS cases showed high WBC in 41% of the cases, while elevated potassium found in 11.8% of the cases. High serum Creatinine and Uric acid were reported in 23.5% (Table 2). A significant association was figured out between gender and occurrence of TLS where 11 cases took place on female while only 6 male developed TLS (Table 3). Another interesting finding was that 100% of the cases (17) occurred in patients with ALL with highly significant association (P=0.00) (Table 3).

Table 1. Descriptive analysis of variables, (n= 91).

Variable		Frequency	Percentage %
Sex	Female	36	39.6
	Male	55	60.4
Region of residence	Darfur	5	5.5
	Kurdufan	7	7.7
	Central	62	68.1
	Niles (White, Blue)	3	3.3
	Eastern	10	11
	River Nile state	4	4.4
Type of Malignancy			
	ALL	52	57.1
	AML	39	42.9
TLS	Non	74	81.3
	Clinical	11	12.1
	Lab	6	6.6
Reticuloendothelial system involvement	Splenomegaly and lymphadenopathy	47	51.6
	Splenomegaly	8	8.8
	None	13	14.3
	Lymphadenopathy	23	25.3
Treatment regimen			
	Slow induction chemotherapy	74	81.3
	Aggressive induction chemotherapy	8	8.8
	Not start chemotherapy	9	9.9
Comorbidities	Other malignant	5	5.5
	Other	4	4.4
	None	69	75.8
	Cardiac disease	9	9.9
	DM	4	4.4
Hospital stays			
	Missing variable	82	90.1
	> 7 days	9	9.9
Outcome	Complete recovery	4	4.4
	Death	5	5.5
	Missing	82	90.1

Table 2. Specific analysis for patients developed TLS (n= 17, only the cases with TLS).

Lab findings		Frequency	Percentage
Wbcs count:			
	Normal	1	5.9
	High	7	41.2
	Low	4	23.5
	No result	5	29.4
S. Creatinine level			
	Normal	4	23.5
	High	4	23.5
	Low	1	5.9
	No result	8	47.1
S. Potassium			
	Normal	3	17.6
	High	2	11.8
	Low	5	29.4
	No result	7	41.2
S. Calcium			
	Normal	4	23.5
	High	3	17.6
	Low	2	11.8
	No result	8	47.1
S. Phosphorus:			
	Normal	8	47.1
	High	2	11.8
	No result	7	41.2
	Low	0	0.0
S.Uric acid:			
	Normal	5	29.4
	High	4	23.5
	No result	8	47.1

Table 3. Association between TLS and specific variables (n= 86, dead cases excluded).

Variable	TLS		P value
	No	Yes	
Sex			
Male	47	6	.007
Female	22	11	

Variable	TLS		P value
	No	Yes	
Comorbidity			
None	51	9	
Other malignancies	8	3	.72
Cardiac disease	7	2	
DM	3	3	
Treatment regimen			
Slow induction chemotherapy	54	16	
Aggressive induction chemotherapy	8	0	.19
Not start chemotherapy	7	1	
Type of malignancy			
ALL	28	17	.00
AML	41	0	

4. Discussion

Extensive review of hospital records demonstrated a considerable number of reported TLS cases among leukemia patients. In line with literature finding, males were predominantly affected [10]. ALL found in the most of the records 57.1% while AML recognized in 42.9% this finding agrees with Annemans L et al study's showed the same distribution of cases [11]. Furthermore, many studies reported a favorable prognosis among ALL cases in the recent past years with a cure rate reaching up to 80% as a consequence of [12-15].

A will know complication of hematological malignancies that strongly linked to unfavorable prognosis, increasing morbidity and mortality rate is TLS, that reported in up to 40% of cases in several studies [16, 17]. The study figured out 17 cases of TLS (18.7%), this is considered a low percentage in comparison with a multicenter cohort study reported 30.7% incidence of TLS among leukemia patients [18]. The observed finding could be attributed to the differences in disease prevalence among the study populations. In addition, methodological variations inform of study design and sample size thought to be a considerable contributor. All the discussed cases were reported among ALL patients 100%. Generally, higher occurrence of TLS among ALL had been reported globally [19]. The observed finding could be explained through oncological characteristics; including higher mitotic activity, larger cell size, in addition to rapid cells turnover [20]. The syndrome could be identified either clinically or through lab investigations, with the former reported in most of the cases [21-23]. Interestingly in this study the clinically reported cases were far exceeding the lab one. In completeness of the data as missing of some lab results and furthermore low resource sittings are thought to be a contributory factor for the observed finding. Moreover, it has been reported that limited resource sittings were associated with increasing number of patients that develop clinical TLS [24].

Consequently, to the liberation of intracellular contents that accordingly resulted in serious metabolic and electrolyte disturbances TLS considered as a life-threatening condition [25]. For more illustration of this point analysis of lab finding were carried out that demonstrate; elevated WBC counts in around half of the cases while high creatinine and uric acid were reported in quarter of the cases however, minority of the patients reported elevated potassium level. The mentioned lab findings were unique and extraordinary in contrast to the average finding among TLS patients [26]. limitations of data and missing of many lab records had led to the extraordinary finding. In regard to hospital stay, 9 patients were figured out to have more than seven days, however due to limitation of data entry in this regard, data were only obtained from this section of patients that accordingly limited further analysis. Another scanty of data was figured out in concern to patients' outcome when only 9 cases were reported within whom 4 had complete recovery while 5 were dead.

The study represent a considerable data and findings regarding TLS in Sudan that could help guiding other future researches. However, inability to achieve the targeted sample size as a consequence of incomplete records limited the overall utility of the findings. In proper documentation of lab

investigations, hospital stays and patient's outcome affected the study negatively and moreover, withhold further valuable statistical analysis and interpretations. Further future researches are highly recommended to address the study subject in a deeper manner.

5. Conclusion

A considerable number of patients developed TLS. ALL was affecting more patients than AML. Males were affected more common in comparison to females, with all the cases reported in ALL. Additionally, clinically identified cases was far more than laboratory one. Also, a significant association was discovered between occurrence of TLS and comorbidities.

Our findings suggest that TLS is a serious event in childhood leukemia in the university diagnostic center. Although rates of occurrence are very low, there is a significant difference in the occurrence of TLS with all the cases reported among ALL patients. Additionally, death reported on five cases while, others reported complete recovery of TLS. However, further prospective studies with a larger sample size are highly recommended.

Abbreviations

TLS Tumor Lysis Syndrome

Author Contributions

Alaa Atef Hamed Yasin: Conceptualization, Data curation, Software

Mayasa Ibrahim Ali Mohamed: Project administration, Resources, Software

Mustafa Magbol: Resources, Writing – review & editing

Ahmad Izzoddeen: Supervision

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Data Availability Statement

The data used in this study are available from the corresponding author on reasonable request.

Conflicts of Interest

The authors declare no conflicts of interest.

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