

FREQUENCY OF TUMOR LYSIS SYNDROME IN PATIENTS
WITH HEMATOLOGICAL MALIGNANCIESShehir Bano^{*1}, Anum Khan², Aun Raza³^{*1,2}Postgraduate Trainee, Department of Internal Medicine, Shaukat Khanum Memorial Cancer Hospital and Research Centre, Lahore, Pakistan³Consultant, Infectious Diseases, Shaukat Khanum Memorial Cancer Hospital and Research Centre, Lahore, PakistanDOI: <https://doi.org/10.5281/zenodo.21273730>

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Abstract

Objective: To ascertain the incidence of tumor lysis disorder (TLS) and associated risk factors among individuals with hematological malignancies

Study Design: Cross-sectional study

Study setting and duration: Medicine department - Shaukat Khanum Memorial Cancer Hospital and Research Centre, Lahore, Pakistan (May 2025–July 2025).

Methodology: 145 patients with diagnosed hematological malignancies that were between the ages of 18-65 years old, using non-probability consecutive sampling. Data were collected and analyzed using SPSS (version 25). Descriptive statistics were used to summarize the demographic, disease, and treatment characteristics of patients (mean $\pm$ SD for continuous variables and frequency for categorical variables). Chi-square tests and an independent sample t-test were done to assess significant relationships using a p -value ≤ 0.05 as statistically significant.

Results: The mean age of study participants was 43.10 ± 14.11 . Overall (16.6%), 24 of 145 participants experienced TLS. Participants who experienced TLS were more likely to have acute lymphoid leukemias or chronic myeloid leukemias (p -value < 0.001). Participants experiencing TLS were found to correlate positively with receiving an advanced stage disease and use of chemotherapy (p -value < 0.001). Participants with TLS had a longer duration of disease before the finding of TLS but had a shorter duration of treatment for his/her hematological malignancy compared to patients without TLS (p -value < 0.001).

Conclusion: Tumor lysis syndrome occurs most frequently in patients diagnosed with hematologic cancers who are being treated with either chemotherapy or have reached the later stages of their illness.

INTRODUCTION:

Tumor Lysis Syndrome (TLS) is an acute oncological emergency that manifests with hyperkalemia, hyperphosphatemia, hypocalcemia, and hyperuricemia resulting from the large number of tumor cells being destroyed, most often within the context of hematological malignancies (such as acute leukemia and high-grade

lymphocytic/lymphoma). Internationally, TLS is on the rise in such patients, and the rate of TLS in the United States has increased from 31.63 to 54.75 per 100,000 discharges from 2016 to 2020 – the vast majority of cases are due to acute lymphoblastic leukemia (21.1%) or acute myeloid leukemia (20.9%) and are associated with an inpatient mortality rate of 22.1%(1,2). In the

pediatric hematology setting, TLS is present in approximately 15% of all cases of hematopoietic malignancy, and in many cases, leads to acute kidney injury(3).

In Pakistan, TLS has been seen in hematological malignancies in an estimated range of 19-25% in cross-sectional studies done at tertiary health care facilities located in Lahore and elsewhere(4). These rates are much higher than the rates found in smaller regional cohorts (e.g., 3.7%). In addition, the estimated number of patients with hematological malignancies is 90.2% of all adult malignancies(5,6); therefore, there is an urgent need for local investigations of TLS in hematological malignancies.

At the SKMCH&RC, this cross-sectional study aims to measure how often TLS occurs in patients with hematological malignancies; its main objective will be to determine whether or not the Cairo-Bishop criteria for TLS prophylaxis hold value in a time of increasing worldwide and local trends. The lack of site-specific data regarding the occurrence of TLS at the SKMCH&RC limits the effectiveness of TLS prophylaxis for an institution in Pakistan's high-prevalent population, in light of the fact that previous studies have recorded a frequency of TLS as 20%-62%, despite the provision of prophylaxis. Due to the recent worldwide increases in the frequency and the lack of institution-specific data in Pakistan, this cross-sectional study will allow the development of evidence-based TLS prevention and management protocols for use in developing countries.

Methodology:

The data for this cross-sectional study were collected from the Department of Medicine, Shaukat Khanum Memorial Cancer Hospital and Research Centre in Lahore, Pakistan. The study was conducted over a six-month period(May 2025 to July 2025) following approval of the study synopsis and had as its main objective to determine how frequently tumor lysis syndrome (TLS) will occur in patients diagnosed with hematological malignancies.

The total number of patients in the sample size was calculated to be 145 using the WHO sample

size calculator based on a 95% confidence interval, 5% margin of error and an expected prevalence of 10.5% in patients diagnosed with acute myeloid leukemia, chronic myeloid leukemia, acute lymphoblastic leukemia/lymphoma, diffuse large B-cell lymphoma, Hodgkin's lymphoma, multiple myeloma and associated disorders, who have been on therapy for longer than three months before study entry(7). A non-probability consecutive sampling method was used to recruit patients for the study.

Inclusion criteria: Participants eligible for inclusion were those aged 18-65 years, of either sex, diagnosed with hematologic malignancy (including acute myeloid leukemia, chronic myeloid leukemia, acute lymphoblastic leukemia/lymphoma, diffuse large B-cell lymphoma, Hodgkin's lymphoma, multiple myeloma, and other related disorders), who had been receiving treatment for longer than three months before they visited the hospital.

Exclusion criteria: Excluded from eligibility under these criteria were patients with hypocalcemia due to bisphosphonate therapy and patients with known metastatic disease.

The data collected from the hospital information system was collected retrospectively using medical record numbers. Patient confidentiality was upheld through the anonymization of all data collected, which included both demographic variables (i.e., age and gender) as well as clinical characteristics (i.e., type and stage of malignancy, and duration of their disease) and details regarding treatment (i.e., type and duration of therapy) using a structured proforma.

Tumor lysis syndrome was defined using laboratory criteria for the values of serum uric acid $\geq 476 \mu\text{mol/L}$; potassium $\geq 6.0 \text{ mmol/L}$; phosphorus $\geq 2.1 \text{ mmol/L}$ in children or $\geq 1.45 \text{ mmol/L}$ in adults; and calcium $\leq 1.75 \text{ mmol/L}$, or by having a change in value compared to baseline of $\geq 25\%$. Patients meeting this laboratory definition were labeled as having TLS.

Statistical analysis was performed using SPSS version 25. The means and standard deviations were calculated for continuous variables, as the data were normal using the Shapiro-Wilk test. Age, disease duration, and treatment duration were considered to exhibit a normal distribution. The qualitative variables were considered in terms of gender, type of malignancy, stage of malignancy, treatment type, and presence of tumor lysis syndrome (TLS), and are represented in terms of frequency and percentage. Effect modifications were accounted for through stratification. Continuous variables were compared with

independent sample t-tests, and categorical variables were compared with chi-square tests. p-values ≤ 0.05 are considered statistically significant.

Results:

Table 1 includes descriptive statistics of continuous variables ($n = 145$) for this study population, revealing a mean age of 43.10 ± 14.11 (range: 14 - 72) years; the mean disease duration of 7.82 ± 5.16 months; and an average treatment duration of 6.22 ± 2.49 days - both showing moderate variability.

Table I: Descriptive statistics of continuous variables($n=145$)

Variable	Mean $\pm$ SD
Age (years)	43.10 ± 14.11
Duration of disease (months)	7.82 ± 5.16
Duration of Treatment (days)	6.22 ± 2.49

Values are presented as mean $\pm$ standard deviation.

Table 2 presents the frequency and percentage of categorical variables. Of the sample, 77 (53.1%) females; 68 (46.9%) males; the majority (38 (26.2%)) have a diagnosis of acute lymphoblastic leukemia (ALL); chronic myeloid leukemia (CML) in 31 (21.4%), with most having an advanced stage

of disease (Stage III, 43 (29.7%), Stage IV, 39 (26.9%)). The most common form of treatment received was chemotherapy (46.2%); Twenty-four (16.6%) patients experienced tumor lysis syndrome (TLS).

Table II: Frequency distribution of categorical variables($n=145$)

Variable	Category	n (%)
Gender	Female	77 (53.1%)
	Male	68 (46.9%)
Type of Malignancy	ALL	38 (26.2%)
	AML	20 (13.8%)
	CML	31 (21.4%)
	DLBCL	23 (15.9%)
	HL	20 (13.8%)
Stage of Disease	MM	13 (9.0%)
	I	35 (24.1%)
	II	28 (19.3%)
	III	43 (29.7%)
Type of Therapy	IV	39 (26.9%)
	Chemotherapy	67 (46.2%)
	Radiotherapy	43 (29.7%)
Tumor Lysis Syndrome	Both	35 (24.1%)
	Present	24 (16.6%)
	Absent	121 (83.4%)

Values are presented as frequency (percentage)

Table 3 presents the results of the chi-square analysis of categorical variables with tumor lysis syndrome (TLS). The results show a statistically significant relationship between type of malignancy and TLS ($p < 0.001$), with acute lymphoblastic leukemia or leukemia (ALL) and chronic myelogenous leukemia (CML) having the highest number of cases of TLS. There was also a

statistically significant relationship between stage of disease and TLS ($p < 0.001$), with all of the cases being in stage III or IV disease. There was a statistically significant relationship between the type of therapy and TLS ($p < 0.001$), with all of the cases of TLS being among patients receiving chemotherapy.

Table III: Association of categorical variables with tumor lysis syndrome(n=145)

Variable	Study Groups		p-value
	TLS Present n (%)	TLS Absent n (%)	
Type of Malignancy			<0.001
ALL	12 (31.6%)	26 (68.4%)	
CML	12 (38.7%)	19 (61.3%)	
Others	0 (0%)	76 (100%)	
Stage of Disease			<0.001
I	0 (0%)	35 (100%)	
II	0 (0%)	28 (100%)	
III	12 (27.9%)	31 (72.1%)	
IV	12 (30.8%)	27 (69.2%)	
Type of Therapy			<0.001
Chemotherapy	24 (35.8%)	43 (64.2%)	
Radiotherapy	0 (0%)	43 (100%)	
Both	0 (0%)	35 (100%)	

Chi-square test was applied for categorical variables. A p -value ≤ 0.05 was considered statistically significant.

Table 4 reports the mean values of continuous variables comparing TLS versus non-TLS patients. There was a statistically significant difference in the mean duration of disease between TLS (15.75 ± 5.07 months) and non-TLS groups (6.25 ± 3.45

months) with $p < 0.001$. However, there was also a statistically significant difference in the mean duration of treatment between TLS (2.38 ± 0.50 days) and non-TLS patients (6.98 ± 1.96 days); $p < 0.001$.

Table IV: Comparison of continuous variables with tumor lysis syndrome(n=145)

Variable	Study Groups		p-value
	TLS Absent (Mean $\pm$ SD)	TLS Present (Mean $\pm$ SD)	
Duration of disease (months)	6.25 ± 3.45	15.75 ± 5.07	<0.001
Duration of Treatment (days)	6.98 ± 1.96	2.38 ± 0.50	<0.001

An independent sample t -test was used for comparison of continuous variables between groups. A p -value ≤ 0.05 was considered statistically significant.

Discussion:

We report on a cross-sectional study performed at a tertiary care cancer hospital in Lahore, Pakistan, in which we identified 24 (16.6%) of 145 patients with hematological malignancies who had developed TLS who were mainly adults with acute lymphoblastic leukemia (ALL; 26.2%) and chronic myeloid leukemia (CML; 21.4%) and many patients were advanced-stage (29.7% stage III, 26.9% stage IV) and statistically liable to receive chemotherapy (46.2%). There is a statistically significant relation between the development of TLS and specific types of malignancies (100% of all cases were ALL or CML), advanced stage of disease (100% of all cases had been diagnosed with stage III or IV malignancies), and chemotherapy-based therapies (100% of all cases were being treated with chemotherapy). The TLS-positive patients had a significantly longer mean duration of disease (15.75 ± 5.07 months) but a significantly shorter mean duration of treatment (2.38 ± 0.50 days) compared to the TLS-negative patients ($p < 0.001$ for both). Our results indicate that there is a considerable burden of TLS among adults with ALL and CML in Lahore and that the burden of TLS in that population is higher than has been reported in the laboratory-focused studies identified in Western countries, and that this finding is consistent with the emerging data from other resource-limited settings and the known risk factors associated with the use of chemotherapy directed toward ALL and CML.

The rates of TLS in people with blood cancers are widely distributed throughout the world. Some studies have revealed that the incidence of laboratory-detected TLS is between 9 % and 21 %, while that of clinical TLS (defined as 5 %) reflects the intensity of treatment and underlying tumor type(8). Based on an analysis studies, the incidence of TLS hovers between approximately 30 and 55 cases per 100,000 discharges, with ALL accounting for 21.1 percent of these patients and CML accounting for only 3.45 percent, given the relatively higher growth rate and better response to chemotherapy of ALL(9,10). However, our 16.6 percent incidence of TLS in our recently reported, single-center cohort (N=145) suggests either a

higher underlying risk in this population, or a more aggressive patient mix, particularly with respect to the evident predominance of ALL and advanced stage disease in the cohort. A recent 2024 review from *Frontiers in Oncology* on pediatric patients with hematologic malignancies also reported TLS rates of between 3 percent and 30 percent in patients with either acute or non-hodgkin lymphoma, and that approximately 20 percent to 40 percent of these patients ultimately progress to clinical TLS; in an adult based analysis of TLS in 138 ALL patients those investigators noted that 30.4 percent of patients developed TLS when treated with induction chemotherapy and that one half of these patients met criteria for the diagnosis of clinical TLS(11). The strong correlation between TLS and ALL and CML in our cohort is consistent with the known predominance of these leukemias in TLS-prone cohorts. Studies have found that ALL was among the top three causes of TLS, accounting for 21.1% of all TLS-related discharges, while CML only amounted to 3.45%, due to lower levels of tumor cell turnover and the different chemotherapeutic regimens used(12,13). Conversely, our data show that half of all patients (47.6%) with TLS had ALL or CML, thus having a different risk profile from that expected based on national databases, which may be due to treatment intensity choices, advanced stage of disease presentation, or delayed referral patterns typical to tertiary care centers in Pakistan. A 2025 review of TLS in hematologic and solid tumors similarly notes that ALL and other acute leukemias compose the most prevalent underlying diagnoses for TLS-related hospitalizations, and that bulky and rapidly proliferating tumors represent the greatest risk for developing TLS(14). Therefore, our present finding that BOTH ALL/CML represent the leading sources of TLS despite a significantly smaller percentage of CML cases in the national-level databases suggests that in Pakistan, TLS is primarily caused by the local epidemiology of ALL/CML rather than the global distribution of lymphoma/AML as causes of TLS.

The fact that all TLS events in our current report occurred in patients who were diagnosed with

Stage III or IV also supports existing data showing that the risk of experiencing TLS increases dramatically with both tumor burden and advancement of disease. The systematic literature reviews and large cohort studies demonstrate that bulky ("corpus bulk") tumors, high-grade non-Hodgkin lymphoma, and advanced-stage leukemia make up the three most common TLS risk factors, with spontaneous TLS being more frequent in older children than in adults, while treatment-induced TLS is more common in adults than in children(15). A pediatric nephrology study published in future issues of Pediatrics evaluating children with hematologic malignancies indicates that TLS-associated acute kidney injury (AKI) occurs in 5–40% of cases and in excess of 75% of high-bulk tumor cases; this further illustrates the significant relationship between disease stage/bulk and the development of renal/metabolic complications(16,17).

There is also significant evidence to support the temporal relationship between the length of disease and how long the patient has been treated for TLS. In TLS, the average length of time a person has had their disease is significantly longer than for individuals without TLS (15.75 ± 5.07 months of disease vs. 6.25 ± 3.45 months of disease), while the length of time spent receiving treatment is comparatively less for TLS (2.38 ± 0.50 days vs. 6.98 ± 1.96 days). This pattern is consistent with a "late presenter" model, which is a common finding in resource-poor countries; there is significant accumulation of disease burden before initiation of intensive chemotherapy, and therefore results in prolonged untreated disease and a short, aggressive treatment course. Similar observations have also been reported in a cohort of young people with TLS who received treatment for CTLS early after starting therapy (usually within 72 hours of beginning treatment) and demonstrate that patients with CTLS had extremely short treatment durations compared to patients without CTLS(18,19). However, there is currently no evidence to show that adults with all leukemias in high-resource countries experience CTLS as a result of having bouts of longer disease course than CLL and thereby having a greater

likelihood of developing TLS. Rather, a large cohort of individuals treated for ALL from resource-rich environments reports that TLS generally occurs during induction without much emphasis placed on the length of time untreated prior to initiation of treatment, and instead focuses primarily on conventional risk factors associated with TLS, such as LDH and white cell counts(20,21).

Because all the TLS cases occurred in patients receiving chemotherapy in our database, this supports the well-established concept that cytotoxic chemotherapy is the most significant catalyst for TLS to occur in patients diagnosed with hematologic cancers. The report prepared from 2022 to 2025 by an expert group studying TLS in solid and hematologic tumors shows that the majority of TLS cases are secondary to therapy, typically occurring within a few days after chemotherapy begins, and that hydration, allopurinol, and rasburicase, while effective in reducing the number of TLS cases happening in high-risk patients, do not completely prevent TLS from occurring.

Limitations of the study:

The methodology of this study has its limitations because it used a cross-sectional method to collect information on all patients during the relevant timeframe. Because the sample size was very small ($n=145$), the study was underpowered to detect small associations. The data were also limited due to the patient population being selected as a tertiary-referral center and therefore subject to referral bias (the sample size includes significant numbers of patients with more advanced and complicated presentations). Finally, and perhaps most significantly, it is important to consider how practice differences (such as hydration, use of allopurinol, and availability of rasburicase) between the high-income and Pakistani settings may modulate TLS rates differentially, so that the perception of "higher" TLS rates may not only reflect biological entities but rather service gaps.

Conclusion:

This paper concludes that there is an association between tumor lysis syndrome and patients diagnosed with hematologic cancers. The percentage of patients diagnosed with hematologic malignancies that develop tumor lysis syndrome is 16.6%. Tumor lysis syndrome occurs more often in patients with certain types of malignancies, including acute lymphoblastic leukemia and chronic myeloid leukemia; advanced stages of disease; or who have received chemotherapy for treatment. Additionally, patients who had longer disease duration and shorter treatment duration were at higher risk for developing tumor lysis syndrome. The data presented here indicate that early assessment of risk factors, close observation of patients after starting chemotherapy, and administering prophylactic measures appropriately can help improve outcomes for high-risk patients.

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