

Research Article

Frequency of Tumor Lysis Syndrome in Acute Leukemia

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Abstract: Introduction: Acute leukemia is characterized by the presence of 20% or more blasts in peripheral blood and/or bone marrow biopsy. It includes both AML & Acute ALL. However the diagnosis of AML can also be made when the blast percentage in peripheral blood or bone marrow is < 20 % if there is an associated t (8;21), inv (16), or t (16;16) chromosomal abnormality or PML-RAR fusion gene [1-3]. Tumor lysis syndrome is the most common disease related emergency in patients with leukemia & requires immediate management.

Objective: To ascertain the Frequency of TLS in Acute Leukemia.

Study design: Cross sectional study.

Setting: NIBD & BMT, Karachi.

Duration of study: The duration of study was 6 months i.e. from May 2016 to November 2016.

Results: 111 patients were enrolled in this study. 41 (36.9%) patients were female & 70 (63.1%) were male, with mean age of 42.8±15.5 years. 66 (59.4%) patients were found to have AML & ALL was seen in 45 (40.6%) patients. Tumor lysis in AML was seen in 21 patients (18.9%) of which 15 patients (13.5%) had LTLS & 06 patients (5.4%) had CTLS. Tumor lysis in ALL was seen in 23 patients (20.7%) of which 16 patients (14.4%) had LTLS & 07 patients (6.3%) had CTLS.

Conclusion: TLS is a frequently common disease related complication in patients with acute leukemia. LTLS is found to be more common than CTLS both in AML & ALL.

Keywords: Tumor lysis (TLS), LTLS, CLTLS, Acute leukemia, AML, ALL.

INTRODUCTION

The tumor lysis syndrome (TLS) is the most common disease related emergency encountered in patients diagnosed with acute leukemia [4-6]. TLS takes place when tumor cells release their contents into the blood stream, causing electrolyte imbalance such as hyperuricemia, hyperkalemia, hyperphosphatemia & hypocalcaemia which can lead to clinically toxic effects, including renal insufficiency, cardiac arrhythmias, seizures & death due to multi organ failure [7, 8]. Clinically significant TLS occurs typically during induction chemotherapy but spontaneous TLS arising before the initiation of chemotherapy has also been documented [9, 10].

According to Cairo & Bishop classification system, TLS is classified as laboratory tumor lysis (LTLS) or clinical tumor lysis (CTLS) [11].

LTLS is considered as positive when any of the given two or more serum biochemical markers are positive within 03 days before or 07 days after the initiation of chemotherapy;

- Uric acid equal to or more than 8 mg/dl.

- Potassium equal to more than 6 Meq/L.
- Phosphorus equal to more than to 4.5 mg/dl.
- Corrected calcium equal to less than to 7 mg/dl.

CTLS is labelled once there is LTLS plus one or more of the following findings;

- Serum creatinine of more than 1.5 times upper limit of normal.
- Cardiac arrhythmias as defined by any abnormality in the heart rhythm as assessed by electrocardiography or sudden death.
- New onset seizures.

There is no age or sex predilection for TLS & the prevalence varies among different malignancies. Certain intrinsic tumor related factors such as large tumor burden with high proliferation rate, increased LDH levels & tumor chemo-sensitivity, are associated with an increased risk for the development.

After extensive search on international literature we found that the reported incidence of TLS in AML by Montesinos *et*

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al. is 17% (12% LTLS & 5% CTLS) [12]. The incidence of tumor lysis in ALL as reported by Truong *et al.* is 23% [13].

Although TLS is one of the most common oncological emergencies, no study has been conducted in Pakistan so far to see the frequency of this complication in acute leukemia. Incidence of leukemia ranges 10-18 per 100,000 persons per year worldwide & is highest among whites & lowest among American Indians/Alaskan natives. In Pakistani population, estimated incidence of acute leukemia is 11 per 100,000 per year. This study was designed to see the frequency of TLS in acute leukemia in Pakistan for the early identification of at risk patients for this life threatening complication so that appropriate prophylactic & therapeutic measures could be taken for its prevention.

MATERIAL & METHODS

Patients with acute leukemia meeting the inclusion criteria were enrolled in this study from inpatient department of NIBD, Karachi from May 2016 to November 2016. This was a cross sectional study and the purpose & procedure of the study were explained to the patients in detail. An informed consent was taken from patients above 18 years of age & from their parents or guardians for patients aged between 05 to 18 years. Bias was controlled by inclusion & exclusion criteria. Complete history, examination & base line ECG was done. Investigations including LDH, uric acid, potassium, calcium, phosphorus & creatinine were done. ECG was done during any rhythm abnormality. All information was collected on pre-designed Performa.

Statistical software SPSS version 17 was used for data analysis. Frequency & percentage was computed for categorical data like gender, type of acute leukemia, chemotherapy, TLS, LTLS & CTLS. Mean & SD was computed for numerical data like age & duration of acute leukemia.

RESULTS

111 patients were included in our study. 41 patients (36.9%) from them were female with mean age of 41.4 ± 15.43 years; 70 patients (63.1%) were male with mean age of 44 ± 15.33 years as presented in Fig. (1).

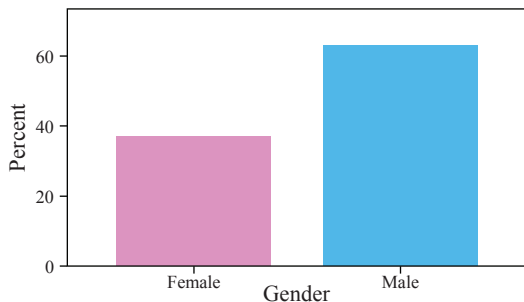


Fig. (1). Gender Distribution.

The overall mean age is 42.8 ± 15.5 years. 15 patients (13.5%) were between 06-10 years of age, 06 patients (5.4%) were between 16-20 years of age, 16 patients (14.4%) were between 40-45 years of age, 30 patients (27%) were between 46-50 years of age, 44 patients (39.6%) were between 51-55 years of age as presented in Fig. (2).

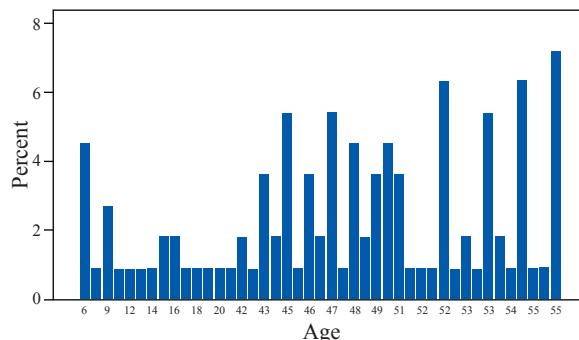


Fig. (2). Age Distribution.

The mean duration since the diagnosis of acute leukemia was found to be 5.14 ± 0.87 days. In 108 patients (97.3%) induction chemotherapy was given, whereas in 03 patients (2.7%) it was not given.

Of 111 patients included in our study 66 patients (59.4%) were diagnosed to have AML whereas ALL was seen in 45 patients (40.6%).

Overall, 44 (39.6%) patients were observed with tumor lysis out of which 31 (70.5%) patients developed LTLS and 13 (29.5%) patients developed CTLS (Table 1). Out of 111, 45 (40.6%) and 66 (59.4%) patients were diagnosed as ALL and AML respectively.

Table 1. LTLS & CTLS according to type of Leukemia (n = 111).

	Total	Non-Tumor lysis (%)	^a Tumor lysis (%)	^b LTLS (%)	^c CTLS (%)
ALL	45 (40.6%)	22 (48.9)	23 (51.1)	16 (69.6)	7 (30.4)
AML	66 (59.4%)	45 (68.2)	21 (31.8)	15 (71.4)	6 (28.6)
Total	111	67 (60.4)	44 (39.6)	31 (70.5)	13 (29.5)

ALL = Acute Lymphoblastic Leukemia, AML = Acute Myeloid Leukemia, LTLS = Laboratory Tumor Lysis Syndrome; CTLS = Clinical Tumor lysis Syndrome. **b** and **c** are breakup of **a**.

Tumor lysis in AML was seen in 21 patients (31.8%), of which 15 patients (71.4%) had LTLS & CTLS was seen in 6 patients (28.6%).

Tumor lysis in ALL was seen in 23 patients (51.1%), of which 16 patients (69.6%) had LTLS & CTLS was seen in 7 patients (30.4%).

DISCUSSION

Our study showed that TLS is a one of the common complication in patients diagnosed with acute leukemia especially observed during induction chemotherapy. We divided TLS into CTLS & LTLS, and found that only one third of our patients who met LTLS criteria developed CTLS and development of CLTLS was associated with higher induction mortality. In spite of the current preventive & therapeutic measures the observed TLS-related mortality was 2%. We found that increased incidence of CTLS was associated with raised pretreatment LDH, uric acid, WBC & creatinine levels and they were significant independent risk factors. In our study 66 patients (59.4%) were found to have AML & ALL was seen in 45 patients (40.6%). Tumor lysis in AML was seen in 21 patients (18.9%), of which 15 patients (13.5%) had LTLS & 06 patients (5.4%) had CTLS. Tumor lysis in ALL was seen in 23 patients (20.7%), of which 16 patients (14.4%) had LTLS whereas CTLS was seen in 07 patients (6.3%) as compared to Montesinos *et al.* study [14, 15] in which TLS was observed in 130 patients (17%) of AML of whom 38 (5%) had CTLS and 92 (12%) had LTLS.

We found that the median day of onset of TLS was day +2 after the initiation of chemotherapy (range, -3 to +7). In 32 patients (25%) (Eight with CTLS & 24 with LTLS) TLS was present before starting chemotherapy and in the remaining 98 patients (75%) it was induced by chemotherapy. The most common laboratory features of TLS were increased potassium and creatinine. Higher death rate during induction therapy, mostly due to sudden cardiac arrest was significantly associated with CTLS. Conversely the development of isolated LTLS was not associated with a high mortality during induction. We also found correlation of increased incidence of CTLS with raised pretreatment LDH, uric acid; WBC & creatinine levels and they were significant independent predictors of TLS which is also previously reported as well [16, 17]. Therefore early identification of at risk patient with daily monitoring of serum biomarkers along with clinical signs and symptoms especially during first 7 days of induction will be helpful in early management of tumor lysis syndrome through prophylaxis treatment with allopurinol and rasburicase [18-20].

CONCLUSION

From our study we concluded that in patients with acute leukemia tumor lysis syndrome is one of the frequently encountered disease related emergency which can be effectively managed with early recognition of serum biomarkers and clinical signs and symptoms. Of all the patients diagnosed with LTLS only one third of patients with LTLS developed CTLS, that is, the form of TLS which was associated with higher mortality.

CONFLICT OF INTEREST

Declared none.

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