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Tumor Lysis Syndrome in Hematological Malignancies Presenting at a Tertiary Care Hospital in Pakistan

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ABSTRACT

Background: *Tumor lysis syndrome (TLS) is a group of metabolic derangements after the malignant cells die with treatment and leads to complications such as acute renal failure, cardiac arrhythmias, seizures, multiple organ failure, and sudden death. TLS is a common potentially preventable complication of hematological malignancies which are the most common cancers in our province. But the data about frequent complications in the course of their management such as TLS is rudimentary.* ***Objective:*** *The main objective of this study was to determine how frequently TLS occurs in our patients.* ***Design and methods:*** *A descriptive cross-sectional study was designed and conducted in Pathology Department, King Edward Medical University, Lahore (February 2014-July 2014). Newly diagnosed patients of hematological malignancies were enrolled in the study. The clinical parameters such as age, gender and laboratory parameters such as laboratory diagnosis, Complete Blood Count, Serum Potassium, Serum LDH, Serum Phosphate, Serum Uric Acid, Serum Calcium, and Serum Creatinine were evaluated.* ***Results:*** *A total of 130 patients were enrolled in the study. Eighty were males and 50 were females. Mean age was 47.02 ± 15 years. Thirty-two patients (25%) fulfilled the criteria for TLS in our setting. TLS was twice more common in females and in 61-80 year age group (36.67%). The frequency of TLS in each hematological malignancy was as follows: ALL 6.15%, AML 5.38%, NHL 5.38%, CML 4.62%, CLL 2.31% and HD 0.77%.* ***Conclusion:*** *TLS is not an uncommon complication of hematological malignancies in our part of the world. It usually occurs after treatment and can be diagnosed and monitored by routinely available biochemical tests. A high index of suspicion is required to optimize the oncology care as this can adversely affect the clinical outcome of these patients.*

Keywords: Tumor lysis syndrome, Hematological malignancies, Acute myeloid leukemia

Abbreviations: TLS: Tumor Lysis Syndrome; AML: Acute Myeloid Leukemia; ALL: Acute Lymphoblastic Leukemia; CML: Chronic Myeloid Leukemia; CLL: Chronic Lymphocytic Leukemia; HD: Hodgkin Disease; NHL: Non Hodgkin Lymphoma

INTRODUCTION

Tumor lysis syndrome (TLS) is a group of metabolic derangements caused by massive and abrupt release of potassium, phosphate and uric acid into the blood after the malignant cells die with treatment [1]. It occurs most often in hematological malignancies. The characteristic findings of TLS are hyperuricemia, hyperkalemia, hypocalcemia, hyperphosphatemia and uremia [2]. The signs and symptoms usually begin between one to five days after chemotherapy but it can occur spontaneously too [3]. Initially patients experience no symptoms but there are laboratory abnormalities which suggest progression of the condition. If untreated, it leads to complications such as acute renal failure, cardiac arrhythmias, seizures, multiple organ failure and sudden death [4]. However TLS is treatable if properly managed. Early detection of TLS is crucial for appropriate prophylaxis and treatment as it is one of the most common life-threatening oncological emergencies encountered [5].

During treatment, the patients should be assessed properly, with utmost importance given to patient's biochemical profile at the time of presentation and frequently thereafter for the risk of developing TLS. Once patient acquires

this complication, management is costly and time-consuming adding to the stress and financial burden on tertiary hospitals catering to a large population. Also these complications can affect the efficacy or further administration of the chemotherapy and hence increasing the mortality and morbidity [6]. Institution-based tumor registry from Punjab quotes hematological malignancies as the most common cancers in Punjab but the data for the incidence and outcomes of TLS in this area is understudied. This prompted us to conduct a study to generate our data about TLS and compare it with international statistics so as to guide the medical specialties with hematology, oncology, nephrology and accident and emergency background regarding the frequency of this life-threatening complication in our patients. This is expected to improve the standard of care to the oncology patients because it is potentially treatable and can be easily diagnosed and monitored by simple and routinely available biochemical tests, thus putting no additional financial burden on health resources economically deprived nations.

MATERIALS AND METHODOLOGY

A descriptive cross-sectional study was conducted in Pathology Department, King Edward Medical University, Lahore from 1st February 2014-31st July 2014. The sample size of 130 cases was calculated with 95% confidence level, 8% margin of error and taking expected frequency of TLS as 20%.

Patients of all ages and both genders presenting with tissue diagnosis of hematological malignancies were included in the study after taking informed consent. Patients who had already been under treatment for malignancies and patients receiving drugs that may affect metabolic status were not included in the study.

Venous blood samples were taken in Ethylene diamine tetraacetic acid (EDTA) vial for Complete blood count (CBC), lithium heparin-coated vacutainers for the levels of serum phosphate, uric acid, potassium, calcium, creatinine, lactate dehydrogenase (LDH). Peripheral smears were made and stained by Giemsa. Bone marrow aspirate and trephine biopsies were performed for all patients.

Internal quality controls were run along with patient samples to maintain precision. The samples were run on Sysmex Kx-21 for CBC. Samples for serum uric acid, creatinine and LDH were analyzed on Beckman CX-5 auto analyzer, while samples for serum potassium, calcium and phosphorus were analyzed on ROCHE Potentiometer 9180. The levels of serum phosphate, uric acid, potassium, calcium, creatinine, LDH were measured at presentation and then daily from the day before starting chemotherapy till day 5. The data was analyzed on SPP version 16.0.

RESULTS

A total of 130 cases recruited in the study. Mean age of the patients was 47.02 ± 15 years (range 20-73 years). Most of the patients were young (between 20-40 years followed by 41-60 years of age). The demographic characteristics of enrolled patients are shown in Table 1. Majority of patients were male constituting 61.54% (Figure 1).

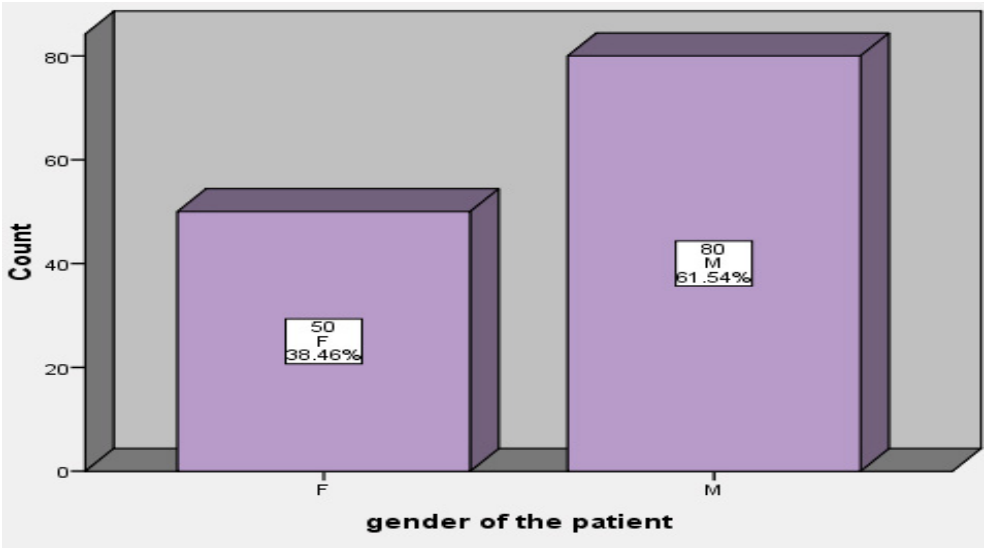

Figure 1 Gender distribution of the study population

Table 1 Demographic characteristics of study population

Characteristics	Number of patients	Percentage of patients
Gender		
Male	80	61.54%
Female	50	38.46%
Age distribution		
20-40 years	52	40%
41-60 years	48	37%
61-80 years	30	23%
Diagnosis		
ALL	37	28.46%
AML	32	24.60%
CML	25	19.23%
NHL	23	17.69%
CLL	11	8.46%
HD	2	1.54%

The most frequent diagnosis in our study group was Acute Lymphoblastic Leukemia ALL (28.46%), followed by Acute Myeloid Leukemia AML (24.6%), Chronic Myeloid Leukemia CML (19.23%), Non Hodgkin Lymphoma NHL (17.69%), Chronic Lymphocytic Leukemia CLL (8.46%) and Hodgkin disease HD (1.54%). of 130 patients, TLS was present in 32 patients (25%). Median day of onset of TLS was day +2 post-chemotherapy. Four patients (12.5%) developed TLS spontaneously while most of the patients developed TLS after initiation of chemotherapy (87.5%). Most common presentation was hyperkalemia and hyperuricemia followed by elevated creatinine levels. 6 of our patients (19%) died due to renal and cardiac complications.

TLS was seen most frequently in ALL where 6.15% patients developed this complication, while 5.38% patients of AML and NHL, 4.62% patients of CML, 2.31% patients of CLL and 0.77% patient of HD developed TLS. TLS was most common in 61-80 year age group (36.67%), followed by 20-40 year age group (23.08%) while it was seen least commonly in 41-60 year age group (18.75%). For unexplained reasons, there was a female predominance in patients of ALL, AML and CML in contrast to CLL, and NHL where mostly males were a victim of this complication.

DISCUSSION

The results of our study showed that TLS occurred in 25% of our patients. Variability in the frequency of TLS has been quoted in literature. Our result is consistent with the figure of 20% in a study conducted in Karachi and 23% according to a study conducted on pediatric population by Tony, et al. [7,8]. Another study by Darmon, et al., quoted the frequency of TLS in hematological malignancies to be 30.7% [9]. Possible explanations to these subtle differences could be several factors such as application of different criteria for diagnosis of TLS, variation in age of the study population, differences in chemotherapeutic regimens in different centers, underlying malignancy, and stage of the disease. The most common presentation was hyperkalemia and hyperuricemia followed by elevated creatinine levels. Hyperkalemia is reported to be the first abnormality in TLS in literature [10].

Mean age of our patients was 47 years which relates to 43 years in a study by Ansari, et al. [7]. This minor difference can be attributed to the late access of the patients to the tertiary care centers either due to lack of awareness, mishandling by quacks or hakeems or financial constraints. In our set up, overall TLS was observed most frequently in female patients; 14 females and 7 male patients developed TLS. Probably there may be a role of some non-modifiable risk factors in this regard such as genetic makeup, polymorphism of urate transporters or poor tolerance of female patients to electrolyte imbalances [11]. This has yet to be established.

In our study, TLS was seen most frequently in ALL (6.15%), followed by NHL and AML (5.38% each), CML (4.62%) and CLL (2.31%) and least commonly in Hodgkin's disease (0.77%). Variable figures for the incidence of TLS have been mentioned by other researchers. In AML, it varies from 3.4% to 10% to 17% [12,13]. In ALL, it varies widely from 5.2% to 25% [7,14]. Similarly in NHL, figures of 4.4%, 6.1% and 42% have been quoted [7,15,16]. In a study of CLL patients, TLS was seen in 46% [17]. The exact incidence for CML is not known; there are few case reports only. In general it is believed to be low [18].

Our results are comparable for ALL, AML and NHL but differences do exist for CLL and CML. This difference can be attributed to segregation of the patients in different hospitals, stage of the disease at presentation, pre-existing medical illness, lack of awareness on part of the referring and treating physicians, less effective prophylactic measures adopted beforehand and failure to report all cases. Another possible reason could be the difference in prevalence of the diseases between western countries and ours.

Our results showed a higher occurrence of TLS in females as compared to males in ALL, AML and CML. This is in contrast with a study by Mato, et al., which reported male gender as a risk factor for TLS in AML [19] as well as another study which quoted that there is no association of gender with the risk of TLS in AML [13]. Again this effect can be due to genetic background or comorbidities or a higher number of patients of a particular gender in the study population.

It was reported that female gender is associated with a high risk of developing TLS in CLL but our data showed that males are affected more in CLL [17]. In our study, gender had no effect on developing TLS in NHL. This is consistent with a study on pediatric population with NHL by Alavi, et al. [20]. In our study, TLS was seen more frequently in 61-80 years age group (36.67%) followed by 20-40 year age group (23.08%) and least commonly observed in 40-60 year age group (18.75%). The literature search also shows that elderly people are more vulnerable to TLS on account of multiple factors: increased incidence of cancers in elderly people, cardiac and renal senescence, co-morbidities and poor tolerance to the treatment [21].

CONCLUSION

TLS is a potentially preventable but life-threatening complication of aggressive malignancies such as hematological malignancies. So it is of crucial importance to recognize the risk factors for developing TLS, biochemical changes and clinical features indicative of TLS in view of the increased morbidity and mortality related to this complication. Usually it occurs after initiating chemotherapy when massive cell lysis occurs. During treatment, patients should be closely monitored by simple biochemical tests at the time of presentation to frequently thereafter in order to diagnose TLS as appropriate risk assessment and management can make difference between life and death. In view of the lack of data on incidence of TLS in hematological malignancies in Pakistan and the results of our study showing a significant frequency, we recommend further studies from other tertiary centers of the country as well in order to get a clear incidence of TLS in hematological malignancies in Pakistan.

DECLARATIONS

Conflict of Interest

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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