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A study of serum uric acid concentration in leukemic patients before and after chemotherapy

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Abstract
Leukaemias are malignant disorders of the haematopoietic stem cell compartment, characteristically associated with increased numbers of white cells in the bone marrow and/ peripheral blood. Once the diagnosis of leukemia is suspected, a rapid evaluation and initiation of appropriate treatment is necessary because of its overwhelming impact on prognosis in terms of achieving complete remission or providing a better quality of life for a longer period of time. The study was being undertaken to study and correlate the serum Uric acid concentration in leukemic patients before and after 1 month of chemotherapy. And also to evaluate the utility of serum Uric acid concentration as a prognostic index. The present study was carried out among 30 patients admitted in different units of Medicine and Pediatrics department of Assam Medical College & Hospital, Dibrugarh, during a period of one year. The type of study done was a Case-Control Clinical Cross-over Study. The difference between the means of serum Uric acid concentration of leukemic patients and the corresponding means of controls have been found to be significant at Diagnosis and After 1 month of Chemotherapy. The difference in serum Uric acid concentration between CML and ALL patients before and after 1 month of chemotherapy was significant. Serum Uric acid concentration increases in leukemic patients and there is a significant reduction after chemotherapy. So the study concludes that biochemical alteration of serum Uric acid concentration can play an important role in the prognostic aspect of the disease.

Keywords: Uric acid, leukaemia, ALL, CLL, AML, CML

Introduction

Leukemias are malignant disorders of the haematopoietic stem cell compartment, characteristically associated with increased numbers of white cells in the bone marrow and/peripheral blood. The incidence of leukemias of all types in the general population is approximately 10/1,00,000 per annum, with males being more affected than females, the ratio being about 3:2 in acute leukemia, 2:1 in chronic lymphocytic leukemia (CLL) and 1.3:1 in chronic myeloid leukemia (CML) [1].

ALL is predominantly a disease of children, with highest incidence in children between the ages of 2 and 6. ALL has a second peak incidence in the elderly population. The incidence of AML increases with age, accounting for 80% of acute leukemias in adults and for 15% to 20% of acute leukemias in children. The rate of AML is somewhat higher in males than females [2].

Once the diagnosis of leukemia is suspected, a rapid evaluation and initiation of appropriate treatment is necessary because of its overwhelming impact on prognosis in terms of achieving complete remission or providing a better quality of life for a longer period of time. Haematological and bone marrow examination are the main parameters for the diagnosis of leukemia and also important indices for monitoring the prognosis of leukemia during and after treatment. In addition biochemical test such as serum lactate dehydrogenase activity and uric acid concentration have side by side gained importance in monitoring the prognosis of leukemia, especially during the phase of treatment [3].

Stephen P *et al* (2015) have found that the mean serum uric acid level in leukemic patients ranges from 8-16mg/dl after induction chemotherapy which declines after allopurinol administration [4].

Ching HP *et al* (1999) in a study of 88 cases of leukemia reported increase in the level of serum uric acid after induction chemotherapy which declines after 3-6 months of allopurinol administration [5].

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Hence, serum uric acid estimation, which is easily available and cost effective, have gained considerable appreciation as valuable prognostic markers of leukemia. So in order to evaluate serum uric acid concentration both in terms of clinical significance as well as in terms of possible use as a biochemical parameter of neoplastic activity in leukemic patients admitted in Assam Medical College & Hospital, Dibrugarh, the study is being undertaken with the following aims and objectives.

- To study the serum uric acid concentration in leukemic patients before and after chemotherapy.
- To study the correlation of serum uric acid concentration in leukemic patients before and after chemotherapy.
- To evaluate the utility of serum uric acid concentration as a prognostic index.

Material & Methods

The present study was carried out among 30 patients admitted in different units of Medicine and Pediatrics department of Assam Medical College & Hospital, Dibrugarh, during a period of one year. The type of study done was a Case-Control Clinical Cross-over Study.

Selection of cases and controls

Patients diagnosed as a case of leukemia, both male and female, irrespective of their age attending Out -Patient Department and admitted in various wards of Assam Medical College and Hospital, Dibrugarh were included in the study. 30 age and sex matched healthy controls were taken for comparison.

Inclusion criteria

- All newly diagnosed leukemia cases irrespective of their age and sex.
- No history of taking any chemotherapeutic drugs

Exclusion criteria

- Patient on treatment excluded from the study.
- Patient who did not give consent for the study

Collection of blood sample

Selected subject's blood samples were collected with all aseptic and antiseptic precautions. 3ml of blood was collected from antecubital vein without application of tourniquet in a sterile empty vial (SEV). The blood collected in SEV was allowed to clot for 30 minutes in a clean dry test tube and was subjected to centrifugation in a clinical centrifuge machine at 3000 rpm for 3 minutes to separate the serum. The separated serum was used to estimate serum uric concentration.

Estimation of serum uric acid by Uricase/PAP method [6]

Principle: Enzyme uricase hydrolyses uric acid to allantoin and hydrogen peroxide. The hydrogen peroxide formed further reacts with a phenolic compound and 4 aminoantipyrineby the catalytic action of peroxidase to form a purple quinoneimine dye complex. Intensity of the colour formed is directly proportional to the amount of uric acid present in the sample.

Results

In the Table 1 it was found that maximum number of cases (60%) were seen in the range of 7-9mg/dl followed by 23.3% of cases in the range of >9mg/dl at diagnosis. After 1

month of chemotherapy maximum number of cases (66.6%) were seen in the range of 2.6-7 mg/dl followed by 30% of cases in the range of 7-9mg/dl. Serum Uric Acid in control group maximum number of cases (93.4%) were seen in the range of 2.6-7mg/dl and 6.6% of cases in the range of7-9mg/dl both at diagnosis and after 1 month of chemotherapy.

Table 1: Serum Uric acid Concentration at Diagnosis and after chemotherapy

Serum Uric Acid (mg/dl)	At Diagnosis	After Chemotherapy	Control
2.6-7	5(16.6%)	20(66.6%)	28(93.4%)
7-9	18(60%)	9 (30%)	2(6.6%)
>9	7(23.4%)	1(3.4%)	

In the Table 2 it was found that the difference between the means of serum uric acid concentration of Leukemic patients at diagnosis and the corresponding means of controls have been found to be very highly significant($p<0.0001$). It was also found that the difference between the means of serum uric acid concentration of Leukemic patients after 1 month of chemotherapy and the corresponding means of controls have been found to be significant ($p<0.01$).

Table 2: Mean serum Uric acid Concentration of Leukemic patients and the controls at Diagnosis and After Chemotherapy.

Number	Serum Uric ACID (mg/dl)	
	At Diagnosis Mean ± SD	After Chemotherapy Mean ± SD
CASE (30)	8.47 ± 1.47	6.67 ± 1.5
CONTROL (30)	5.1 ± 0.98	5.1 ± 0.98
P-value	$p<0.001$	$p<0.001$

In the present study it was found the following observations
(1) The percentage distribution of samples were in CML-56.67%, ALL- 30%, AML and CLL-6.67%.
(2) Maximum rise in serum uric acid concentration before chemotherapy was seen in AML followed by CML.
(3) In AML patients, 50% of cases was seen both in the range of 7- 9mg/dl and >9 mg/dl at diagnosis. After chemotherapy, 50% of cases was seen both in the range of 2.6-7mg/dl and >9mg/dl.
(4) In ALL patients, maximum number of cases (88.8%) was seen in the range of 7-9mg/dl and 11.1% of cases in the range of 2.6- 7mg/dl at diagnosis. After chemotherapy, maximum number of cases (88.8%) was seen in the range of 2.6-7mg/dl and 11.1% of cases in the range of 7-9mg/dl.
(5) In CML patients, the maximum number of cases (52.9%) was seen in the range of 7-9mg/dl followed by 35.2% of cases in the range of >9mg/dl at diagnosis. After chemotherapy, maximum number of cases (52.9%) was seen in the range of 2.6-7mg/dl and 47% of cases in the range of 7-9mg/dl.
(6) In CLL patients, 100% of the cases were seen in the range of 2.6- 7mg/dl before and after chemotherapy.

Discussion

Age distribution: In the present study maximum number of leukemic patients i.e. 8 patients (26.67%) were in the age group of 0— 10 years followed by 7 patients (23.33%) in the age group of 41—50 years. If the different leukemic

types were considered separately, it was seen that the maximum number of patients in case of ALL were in the age groups of 0—10 constituting 6 patients (66.6%); in case of CML in the age groups of 41—50 constituting 5 patients (29.4%); in case of AML in the age group of 31—50 constituting 2 patients and in case of CLL in the age group of 41 and above constituting 2 patients. The distribution of age in this study is similar to the studies done by AK Siraj *et al* (2003) [7], S Ghosh *et al* (2003) [8], M Wakui *et al* (2008) [9].

Sex distribution: In the present study it was seen in leukemia as a whole, the male patients constitute 56.67% and the female patients constitute 43.33% with a male to female ratio of 1.3:1. If the different leukemic types were considered separately, in case of ALL male patients constitute 66.6% and female patients constitute 33.3%; in case of CML male patients constitute 58.8% and female patients constitute 41.1%; in case of AML both male and female patients constitute 50%; in case of CLL female patients constitute 100%.

Serum Uric acid concentration in the study group and control at diagnosis
In the present study, it was seen that 83.3% of cases with leukemia have serum uric acid concentration above the normal range with the mean uric acid level being 8.92 mg/dl and 16.6% of cases towards the higher normal range with the mean uric acid level being 6.16mg/dl at diagnosis. The probable cause of increase serum uric acid level in the study group is due to increased nucleic acid catabolism due to increase turnover of malignant cells resulting in increased purine catabolism. Maximum number of cases (93.4%) in the control group was seen within the normal range (2.6-7mg/dl) and only 6.6% of cases in the range of 7-9mg/dl. The mean serum uric acid in leukemic patients at diagnosis was 8.47 mg/dl whereas the mean in the control group was 5.1 mg/dl. A very highly significant difference (elevation) in the mean value of serum uric acid concentration has been found between the leukemic patients at diagnosis and control group ($p<0.001$).

Serum Uric acid concentration in the study group and control after 1 month of chemotherapy: In the present study, it was seen that 33.3% of cases with leukemia have serum uric acid concentration above the normal range with the mean uric acid level being 7.52 mg/dl and 66.6% of cases within the normal range with the meanuric acid level being 5.79 mg/dl after 1 month of chemotherapy. Maximum number of cases (93.4%) in the control group was seen within the normal range (2.6-7mg/dl) and only 6.6% of cases in the range of 7-9mg/dl. The mean serum uric acid in leukemic patients after chemotherapy was 6.6mg/dl whereas the mean in the control group was 5.1mg/dl. A significant difference (elevation) in the mean value of serum uric acid concentration has been found between the leukemic patients after chemotherapy and controls ($p<0.01$) but the difference have been substantially reduced which means on complete follow up of the chemotherapy regimen there would be statistically no significant difference between the cases and controls.

Serum uric acid concentration in the study group at diagnosis and after 1 month of chemotherapy: In the present study, if the different leukemic types were considered separately, it was seen that in case of ALL and

CML at diagnosis the mean serum uric acid was 7.72 mg/dl and 8.98 mg/dl whereas the mean after chemotherapy was 6.21 mg/dl and 6.91 mg/dl. A highly significant difference (lowering) in serum uric acid level has been observed between the ALL and CML patients at diagnosis and after chemotherapy ($p<0.001$).
Hartmut D *et al* (2015) have found that the mean serum uric acid level in leukemic patients ranges from 8-16mg/dl after induction chemotherapy which declines after allopurinol administration [10].
Jacob F. *et al* (1994) in a study of 88 cases of leukemia reported increase in the level of uric acid after induction chemotherapy which declines after 3-6 months of allupurinol administration [11].
Miroljub Petrovi and Miodrag Raji (2002) in a study of 60 patients with acute leukaemia observed that the difference in serum uric acid concentration after chemotherapy was statistically significant [12].

Conclusion
Leukemias still remains a challenge for the treating physicians, both in adults and children because of high mortality and morbidity. Early therapy may prolong the life expectancy to some extent provided the case has been detected at the earliest, investigated and treatment initiated. In the present study it has been observed that serum uric acid concentration increases in leukemic patients and there is a significant reduction after chemotherapy. So the study concludes that biochemical alteration of serum uric acid concentration can play an important role in the prognostic aspect of the disease.

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