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Research Article

Hyperurecimia in Sickle cell Disease

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Abstract

Background: Sickle cell disease is an inherited blood disorder that affects red blood cells. People with sickle cell disease have red blood cells that contain mostly hemoglobin S, an abnormal type of hemoglobin. Hyperuricemia is a common feature of homozygous sickle cell (SS) disease. In this study we have estimated the serum uric acid concentration in sickle cell disease subject and the reason behind the abnormal results are interpreted. **Materials and Methods**: To evaluate biochemically, the patients with sickle cell disease (n=100) from medicine and pediatrics wards/OPD were included in the study. 100 age matched healthy individuals were also selected as controls. **Result**: Serum uric acid levels are significantly higher in sickle cell disease patient as compared to healthy subjects. Discussion: Increased nucleic acid breakdown results in increased production of uric acid. There is increased hemolysis which leads to increased break down of the nucleic acid that leads to overproduction of uric acid this could be the possible explanation for the higher uric acid level observed in our study. **Conclusion**: From this study it has been seen that elevated levels of uric acid in sickle cell disease patient is quite a common finding. The increased levels of uric acid has been attributed either to overproduction due to increased breakdown of purine or due to decreased clearance from the body due to impaired renal function.

Keywords: Purine Metabolism, Creatinine, Red cell, Renal

Introduction

Sickle cell disease is an inherited blood disorder that affects red blood cells. People with sickle cell disease have red blood cells that contain mostly hemoglobin S, an abnormal type of hemoglobin. Sickle cell hemoglobinopathies are hereditary disorders involving primarily the β chain of HbA and forms HbS in the red cells. Sickle cell hemoglobin is produced by substitution of valine for glutamic acid at position 6 of β chain of normal hemoglobin. In the steady state, the patient has moderate to severe anemia. The patients get easily fatigued and cannot undertake strenuous activity. Hyperuricemia is a common feature of homozygous sickle cell (SS) disease. (1,2) In this study we have estimated the serum uric acid concentration in sickle cell disease subject and the reason behind the abnormal results are interpreted.

Materials and Methods

The present study was carried out during the period of December 2007 - September 2009 in the Department of Biochemistry, Indira Gandhi Government Medical College, Nagpur. The study protocol was approved by the Institutional Ethical Committee. To evaluate biochemically, the patients with sickle cell disease (n=100) from medicine and pediatrics wards/OPD were included in the study. 100 age matched healthy individuals were also selected as controls. An informed written consent was obtained from all the study subjects who were enrolled in the study. The estimation of serum uric acid was done by Transasia Erba XL 300 fully automated analyzer with dedicated reagents.

Statistical Analysis

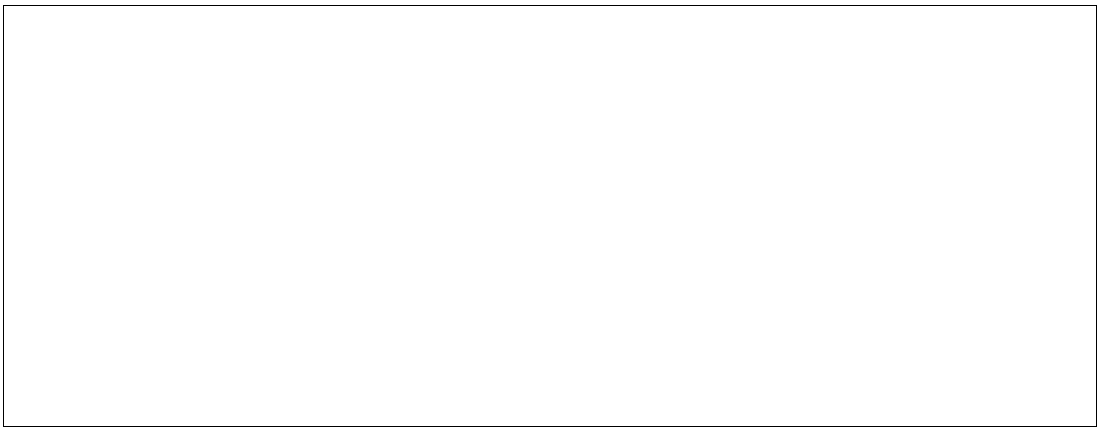
All values were reported as mean ± SD. The unpaired two tailed Student's t test was used to assess the significance of the difference in the values in the sickle cell disease subjects and in healthy controls. The differences were considered as statistically significant at a probability value, $P < 0.05$. All statistical analyses were performed by using statistical software Graph Pad Prism.

Results

The results obtained after estimating serum uric acid in healthy subject and disease subjects are tabulated.

Table 1:Showing Mean and Standard Deviation of Serum Uric Acid in Cases and Control.

	Cases (mean ± S.D.) (n=100)	Control (mean ± S.D.) (n=100)	P value
Sr. Uric Acid (mg %)	6.82±0.93	4.89±0.89	<0.001(HS)



Graph1: Bar Diagram Showing Mean & SD of Uric Acid level in study group.

Table 2: Showing distribution cases and controls according to Sr. Uric Acid level.

Sr. No.	Sr. Uric Acid (mg %)	Cases(n=100)	Controls(n=100)
1.	2.8-6.4	30	100
2.	>7.0	70	00

Table. 3: Showing serum uric acid level in various studies.

Sr. No.	Uric Acid (mg %)	Herbert S et al (3) (1979) (n=67) %	K De Ceulaer et al (4) (1981) (n=44) %	U P Isichei (5) (1985) (n=69) %	A. K. ALI et al (6)(1995) (n=71) %	Present Study (n=100) %
1.	Normal	61	59	72	59	30
2.	Above normal	39	41	28	41	70

Discussion

In present study the normal range for serum uric acid in control was 2.8-6.4 mg%. Out of 100 patients 70% have increased uric acid level as compared to normal healthy subject. A. K. ALI (1995) et al estimated the serum uric acid, creatinine, urea levels in patients with glucose 6 – phosphate deficiency (n=20), and sickle cell disease (n=29) and compare them with normal subjects. Hyperuricemia has been reported as a feature of homozygous sickle cell disease, occurring in 41% of patients. Values of creatinine were found to be lower than in normal subjects ($p<0.05$) the difference in serum urea level in patients with sickle cell disease when compared to the normal subject was found to be insignificant. (6) U P Isichei (1985) et al studied the serum uric acid level of 69 children below the age of 11 years with homozygous sickle cell disease, determined by the uricase method. The values were compared with those seen in normal children in the same age group who were used as a control. A statistically significant difference was seen in their mean values; 28% of children with sickle cell disease exceeded the upper normal limit of the control group. The implications of the comparatively high uric acid levels are discussed.(5) K DE Ceulaer (1981) et al estimated serum and urinary urate concentrations in 44 patients with homozygous sickle cell (SS) disease, and in 27 controls with normal hemoglobin. Hyperuricemia (> 0 39 mmol/l (6-5 mg/100 ml)) occurred in 41 % of SS patients and inversely correlated with renal urate clearance but not with indices of bone marrow turnover. Higher serum urate concentrations occurred in patients with proteinuria, probably due to associated tubular damage. Higher serum urate concentrations and lower urate clearance occurred in males compared to females. (4) AL-Naama Lamia M. (1996)et al determined the levels of serum uric acid, urea and creatinine in subjects with sickle cell disease and compare them to those reported in literature. Plasma uric acid, urea and creatinine were estimated by Varley's method, group of 65 sickle cell patients (35 Hb AS, 30 Hb SS) aged between 2-11 years. The results were compared with those obtained in a group of 45 age and sex-matched controls with normal hemoglobin (Hb AA). The uric acid level was elevated in sickle cell patients as compared with the normal control group. The 95% confidence intervals for differences in the mean of the two groups: Hb AA vs. Hb AS was 4.22 (0.3), while for Hb AA for Hb SS was 3.4 (0.06), both being statistically highly significant [$p<0.0001$]. (7) Diamond HS, (1979) et al studied serum uric acid and uric acid excretion in 95 patients with sickle cell anemia ranging in age from 17 months to 45 years to ascertain the natural history of urate overproduction. Hyperuricemia was infrequent in children with sickle cell anemia, but was found in 26 of 67 adults (39%). (8) Barry R. Walker (1971) et al observed that, hyperuricemia of unknown etiology has been associated occasionally with sickle cell anemia (SS). Asymptomatic SS patients were compared to normal volunteers, with the former showing a significant increase in the ratio of total uric acid to creatinine excretion suggesting increased purine synthesis. (9) Gene V. Ball, (1970) et al in their study reported patient with sickle cell disease complicated by gouty arthritis. Theoretically hyperuricemia may result from increased production of uric acid, decreased excretion, or a combination of both. Studies of red cell survival and endogenous carbon monoxide production during the steady state in SS disease have suggested that the marrow is functioning at about six times the normal rate. (10) Increased nucleic acid breakdown results in increased production of uric acid. (11) There is increased hemolysis which leads to increased break down of the nucleic acid that leads to overproduction of uric acid this could be the possible explanation for the higher uric acid level observed in our study.

Conclusion

From this study it is been seen that elevated levels of uric acid in sickle cell disease patient is quite a common finding. The increased levels of uric acid has been attributed either to overproduction due to increased breakdown of purine or due to decreased clearance from the body due to impaired renal function.

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