



## International Journal of Chemistry and Pharmaceutical Sciences

IJCPS, 2013: Vol. 1(4): 263-265

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### Oxidative imbalance in Sickle Cell Disease

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#### Abstract

Oxidative defense imbalance in Sickle Cell Disease was evaluated using enzymatic (Lactate Dehydrogenase) and nonenzymatic (Uric acid and Ascorbic Acid (vit C)) indicators. The study was carried out using eight patients with sickle cell disease in steady state, seven patients with Sickle Cell Disease in crisis. Twenty patients with AS haemoglobin and another twenty of normal haemoglobin (AA) served as Control. All groups have age range between 10-30 years comprising of both sex. All analysis was based on calorimetric assay. Both serum uric acid and LDH concentrations were significantly higher in sickle cell patients in crisis compared to patients with sickle cell disease in steady state and the healthy patients. ( Lactate Dehydrogenase (U/L) AA 288.05 ± 8.53, Sicklers 383.88 ± 12.59 and Sicklers In crisis 511.44 ± 14.56., Uric acid (uMol/L). AA 321.80 ± 2.75 Sicklers 339.48. ± 4.60 Sicklers in crisis 470.66. ± 9.23 (P<0.05). However, the level of Ascorbic Acid (vit C) was remarkably reduced in Sicklers cell patients in crisis (P<0.05). This study has stressed further the importance of antioxidant in the management of sickle cell disease.

**Key words:** Lactate Dehydrogenase, Uric acid, Ascorbic Acid, Sickle Cell Disease

#### Introduction

Sickle cell disease refers to a collection of genetic blood disorders characterized by hemoglobin variant called HbSS. Individuals who are affected with sickle cell anemia have two copies of this beta globin variant, and the primary hemoglobin present in their red blood cells is HbSS. This disease is particularly common among people whose ancestors come from sub-Saharan Africa, Spanish-speaking regions (South America, Cuba, Central America), Saudi Arabia, Oman, India, and Mediterranean countries such as Turkey, Greece, and Italy (Familusi and Adeyokuma 1975) Sickle cell disease is diagnosed most frequently in the peditric age prior to the age of six. Two defective haemoglobin mutant (HbSS) inherited from each parent produce pathogenic mechanism that manifest clinically as hyperhaemolysis, tissue or organ damage, abdominal, bone, joint and chest pains .Others are myocardial infarction and a drop in Hb level (Bum1997 Kim, 1999, Thomas 2003). Stressful conditions such as [wheather (cold) or emotional, acidosis and infections may precipitate crisis in persons with sickle cell disease. Hyperheamolysis occur when these sickle cell enter the circulation because there are fragile to withstand the mechanical components of circulation (Thomas 2003). Splenomegaly and hypovolaemic shock occur in childhood (Mba *et al*, 2004, Ocheni and Aken'Ova, 2006).

Sickle cell gene carrier with those with hemoglobin HbAs are said to be protected from malaria attack. The mechanism by which this selective protection is achieved is unclear. However, it is attributed to the fact that these cells sickle in the circulation and are removed by the spleen before the parasite can develop into Schizonts. (Fleming *et al*, 1979, Luzzatto, 1979, Young *et al*, 1990, Cheesbough, 2003). Sickle cell trait is not usually regarded as a disease state because it has complications that are either uncommon or mild. Nevertheless, under unusual circumstances, serious morbidity or mortality can result from complications related to polymerization of deoxy-hemoglobin S. Moreover, sickle cell traits present with varied problems including increased urinary tract infection in women, gross

hematuria, complications of hyperhema, splenic infarction with altitude hypoxia, life-threatening complications of exercise etc. Renal medullary carcinoma in the young, early onset of end stage renal, as well as disease from autosomal dominant polycyst (Barry et al, 1977). Hyperuricemia of unknown etiology has been associated occasionally with sickle cell anemia (SS). It should be noted however that excessive production and accumulation of uric acid leads to a type of arthritis known as gout characterized by acute joint pains. In view of this Hyperuricemia and other metabolic derangement that we decided to evaluate the levels of Lactate Dehydrogenase, Uric acid and Ascorbic Acid (vit C) in Sickle Cell patients.

### Material and methods

Eight patients with sickle cell disease in steady state, seven patients with Sickle Cell Disease in crisis. Twenty patients with AS haemoglobin and another twenty of normal haemoglobin (AA) served as Control. All groups are within the age range of 10-30 years and comprised of both sex and they have been attending Nnamdi Azikiwe University Teaching Hospital, Nnewi, Nigeria. Their hemoglobin type was confirmed by haemoglobin electrophoresis. They were subjected to the assay of Lactate Dehydrogenase, Uric acid and ascorbic acid. The Lactate Dehydrogenase(LDH), was determined using the method of Henry, Cannon and Winkelmann, 1974, Uric acid level was estimated using fortress diagnostic kit. While the Ascorbic Acid (vit C) Level was assayed using Roe and Kuther, 1943 method. All analysis was based on calorimetric assay. The statistical analysis used was the one-way analysis of variance ANOVA.

### Result and Discussion

Table Lactate Dehydrogenase(LDH), Uric acid and Ascorbic Acid (vit C) Levels in Sickle Cell Disease.

Parameters	LDH (U/L)	Uric acid (uMol/L).	Ascorbic Acid (vit C) (uMol/L).
AA (Control)	288.05 ± 8.53,	321.80 ± 13.75	15.60 ± 7.20
Carrier AS	307.00 ± 9.14*	325.00 ± 14.6*	12.50 ± 6.80*
Sicklers Without crisis	383.88 ± 12.59**	339.48 ± 16.8**	10.00 ± 4.10**
Sicklers in crisis	511.44 ± 14.56.***	470.66 ± 9.23***	5.80 ± 3.00.***

\*Significant difference P < 0.05

The results obtained from the study indicated a marked increase in Lactate Dehydrogenase activity, Uric acid levels in both sickle cell patients in crisis and sickle cell disease in steady state compared to control. However, the level of Ascorbic Acid (vit C) was remarkably reduced in Sicklers cell patients in crisis (Ascorbic Acid (vit C) (uMol/L) AA. 15.60 ± 7.20 vs 5.80 ± 3.00 (P < 0.05) (Table). The increased uric acid levels observed in our study collaborates with other studies where they attributed the high uric acid level to metabolic production of urate and the way in which it is excreted by the Kidneys. It should be noted that Erythrocytes contain mainly haemoglobin "S" and this have a short life span leading to remarkable reduction in the number of the blood cells. This however, is the basis of anaemia. Again, it would be expected that during erythropoiesis increased Synthesis of nucleic acid might occur, thus the destruction of red blood cells lead to increased nucleic acid degradation. This means that lysis of red cells in person with sickle cell disease liberates the uric acid content in the cell leading to hyperuricemia. It was also postulate that the higher uric acid level is due to the oxidative damage to cells causing an increase in cell turnover and muscle wasting (Wayner, 1987).

Furthermore, it was suggested that there could be an excessive level of uric acid pool due to an increased marrow activity and turnover of nucleic acids. These conditions were associated with many diseases including hemolytic anaemia and certain haemoglobinopathies. Another reason given was a decrease in excretion of uric acid resulting from impaired tubular function. (Al-Ali et al, 1995, TNduk et al, 1995). Jarvis, 1996 Williams et al, 1996). Equally, suggested was that hyperuricemia in SS patients occurs when defective renal function is superimposed on the excessive purine synthesis. It is not known whether the hyperuricemia or uricosuria plays any role in sickle cell nephropathy. A study by Barry et al, (1977) revealed that there was enhanced lipid peroxidation along with imbalance in the pro-oxidant and antioxidant status in patients with sickle cell anaemia. Although available reports suggested that sickle cell erythrocytes are susceptible to endogenous free radical mediated oxidant damage, there remains some discrepancy in the status of antioxidant enzymes and antioxidant vitamins in these patients. (Uzoegwu and onwurah 2003).

In our study the levels of ascorbic acid were significantly depleted in sickle cell anaemic patients. The results were indicative of enhanced lipid peroxidation along with imbalance in the pro-oxidant and antioxidant status in patients with sickle cell anaemia. It is not surprising that lactate dehydrogenase activity is highest in Sicklers in crisis. LDH

as known is used for the assessment of tissue breakdown particularly when there are no other indicators of hemolysis. Also it is used to follow-up cancer (especially lymphoma) patients, as cancer cells have a high rate of turnover with destroyed cells leading to an elevated LDH activity. Red cells destruction is highest in sicklers in crises compared to others hence the activity of this enzymes is highest in this group .It is therefore important that uric acid and ascorbic acid should be monitored continually to check oxidative stress in sickle cell patients as to minimize crisis.

### Acknowledgment

The authors are grateful to the management and staff of Excellence Diagnostic laboratory for their technical assistance.

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