Alpha Tocopherol, Bilirubin and Some Liver Enzymes in Sickle Cell Subjects

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Abstract: **Derangement in liver enzymes and hyperbilirubinemia in Sickle cell disease (SCD) has long been documented, generation of free radicals via Fenton's reaction results in oxidative stress. The serum levels of alphatocopherol, bilirubin and some liver enzymes were determined in forty-eight subjects (34 SCD and 14 apparently healthy age-sex matched controls). The serum levels of liver enzymes and bilirubin were significantly higher compared to the controls ($p<0.005$). Serum levels of Malondialdehyde (MDA) was significantly higher in sickle cell patients ($p<0.005$) than the controls. In conclusion, according to the findings of these results, SCD is associated with oxidative stress and deranged liver physiology. Supplementation and antioxidant and monitoring of liver physiology should be encouraged.**

Key Words: **Sickle cell disease, Free radicals, Oxidative stress, Bilirubin, Live enzymes**

I. INTRODUCTION

Sickle cell disease (SCD) is a genetic hereditary disorder found in tropical regions; particularly sub Saharan African, India and Middle East with three-quarter of the cases in Africa (Almeida and Roberts 2005). WHO reported an estimate of 2-3% newborns in Nigeria were affected by sickle cell anemia, accounting for 150,000 children every year (Elagouz *et al.,* 2010). Sickle cell anemia is characterized by reduction in amount of erythrocytes and their function in the body (Platt *et al.,* 1994), SCD is caused by point mutation at position six of β- chain of hemoglobin, this results when the hydrophilic glutamic acid is replaced with hydrophobic valine (Platt *et al.,* 1994; Steingberg *et al.,* 1994; Glover *et al.,* 1999). Sickle cell individuals are those that inherited mutated hemoglobin gene from both parent (Azubuike and Nkanginieme, 2007). In a low oxygen tension environment, the replaced valine can bind to a complementary hydrophobic site on a β subunit of another hemoglobin tetramer in a non covalent polymerization process which leads to sickling and decreased elasticity of erythrocytes (Serjean, 1997). The losses of sickle cell disease as normal erythrocytes are quite elastic, capable of deforming elastically (Azubuike and Nkanginieme, 2007). The sickle cell erythrocytes generate more than usual hydroxyl radicals through Fenton's reaction, these free radicals causes further sickling of the sickle cells, converting reversible sickle cells to irreversible ones (Rive-Evans *et al.,* 1986), thus loss of erythrocytes' function. The irreversible sickle cells usually undergo an adhesive event which leads to their clumping and results in vaso-occlusion; producing episodes of pain, hemolytic anemia, organ injury and early mortality (Deepa and Paul, 2013). Recurrent and unpredictable episodes of vaso-occlusion crises are the hallmark of sickle cell disease (Deepa and Paul, 2013). Hemolytic anemias are the major pathology of SCD and are mainly due to lyses of sickle erythrocytes by reticuloendothelial system (RES) consequently lead to low hemoglobin and hyperbilirubinemia (Dacie and Lewis, 2010). Biological enzymes such as catalase, superoxide dismutase and glutathione peroxidase and some essential vitamins specifically vitamin A, Vitamin C and alphatocopherol play a significant role in scavenging and morphing up of free radicals thereby preventing oxidative stress (Essien, 1995; Sies, 1995; Carl *et al.,* 2008).

Alphatocopherol is the most abundant, active and naturally occurring antioxidant vitamin within the biological system responsible for counteracting the negative effects caused by radicalized molecules in SCD (Satyaranayana, 2006). Liver disorder is a complication with SCD (Chukwu *et al.,* 2012; Gurkan *et al.,* 2005; Hassel *et al.,* 1994) caused by multiple factors such as vaso-occlussion, excess iron deposit, hemolysis, anemia, intra-hepatic sinusoidal sickling and bilirubin gallstone (Beutler *et al.,* 1999; Banerjee *et al.,* 2001; Kakarala *et al.,* 2004). Liver injury will be noticeable when there is an elevation of some of enzymes; Alanine-amino transferase (ALT), Aspartate-amino transferase (AST) and alkaline phosphatase (ALP) may indicate the status of the liver in both steady and crisis situations (Chukwu *et al.,* 2012). The present study is designed to determine the oxidative stress, erythrocytes depletion and liver involvement in sickle cell patients.

II. METHODOLOGY

Study Population:

The study consisted of forty-eight subjects, 34 sickle cell patients and 14 apparently healthy aged-sex match attending Rasheed Shekoni teaching Hospital Dutse, Jigawa-Nigeria.

Current research includes Sickle cell Patients under crises only.

Specimen Collection:

Five mills (5mls) of blood specimens were collected and delivered into ethylinediaminetetra acetic acid (EDTA) and serum container for the hematological parameters and biochemical determinations respectively.

Biochemical determination:

Vitamin E; Estimation was performed using the method of Neil and Pearson (1963). ALT, AST and ALP were determined using Chemistry anlyser; SELECTRA PRO.

Statistical Analysis:

The statistical analysis was done using SPSS Software version 16. The results were expressed as Mean±SD. The differences between the groups were analyzed using Student's "t"-test and one way analysis of Variance (ANOVA).

Ethical Clearance:

Informed consent and ethical clearance was sought for and acquired before the commencement of the research.

III. RESULTS

Table1.0: Serum levels, Vitamin E and Packed cell volume among the test and control subjects.

Parameters	SC Patients(n=34)	Controls(n=14)
Bilirubin (mg/dl)	1.92±0.50	0.31±0.27
Vitamin E (mg/dl)	0.31±0.07	0.73±0.07
PCV (%)	25.1±2.72	38.4±2.6

KEY

SC=Sickle cell; n=number of subjects.

Table 2.0: Serum Transaminases and Alkaline Phosphatase levels in Sickle cell Patients and Controls.

Parameters	Sickle cell Subjects (n=34)	Controls (n=14)
ALP (UI/)	173.1±43.1	132.6±24.0
AST(U/I)	67.1±5.6	33.6±6.1
ALT(U/I)	54.0±6.9	11.8±3.2

KEY

SC=Sickle cell; n=number of subjects.

IV. DISCUSSION

Insufficient oxygen supply in SCD patients is one of the primary causes leading to sickle cell crisis; brought about by abnormal red cells function and destructions. Based on the results obtained, low packed cell volume (PCV) was observed in sickle cell patients when compared to the control subjects. The findings are in agreement with those of Bhoi *et al.*, (2014) and Manfredini *et al.*, (2008) which demonstrated low hemoglobin and PCV among the study subjects. The decreased could be due to erythrocyte destruction of the abnormal red cells by RES. Pandey *et al.,* (2012) and Bhoi *et al.,* (2014) documented an increased bilirubin in patients with SCD. Elevation of serum bilirubin is proportional to the degree of hemolysis. Significantly higher ($p<0.005$) serum bilirubin was found in the study subjects compared to the controls, the effect of RES upon the sickle erythrocytes and inability of liver to conjugate the bilirubin may be the reason for hyperbilirubinemia. The study also revealed a statistical decrease ($p<0.005$) of alpha tocopherol in SCD patients compared to the control which may be as due to generation of free radicals in the thereby increase utilization of alpha tocopherol to counteract the oxidative damage. Yeldu *et al.,* (2014) and Tukur *et al.,* (2015) also reported deficiency of alpha tocopherol in sickle cell subjects. Increased levels of liver transaminases are associated with liver injuries in SCD. The present research revealed an elevated levels of ALT in sickle cell subjects, this is in line with previous work of Pandey *et al.,* (2012) and Chukwu *et al.,* (2012) who documented high levels of ALT among patient with SCD. According to the results obtained from this study, Both AST and ALP were statistically high ($p<0.005$) when compared to the control subjects. Gurkan *et al.,* (2005), Pandey *et al.,* (2012) and Chukwu *et al.,* 2012 all reported an deranged levels of AST and ALP in sickle cell patients. Therefore, monitoring of liver enzymes in SCD is of paramount importance.

V. CONCLUSION

SCD still remains common and deadly in our society, anemia and liver problems are associated with the diseases. In conclusion, low PCV and hyperbilirubinemia were observed in SCD patients, these painted out anemia and hemolysis respectively. Decreased serum alpha tocopherol and elevated levels of ALT, AST and ALP were also recorded.

Recommendations

Having established the decreased vitamin E and deranged liver enzymes accompanying low PCV and dietary improvement of food containing rich vitamin E substances should be encouraged. Pre-marital screening of hemoglobin genotype for all intending couples and the general public should be enlightened about SCD and its complications.

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