



ORIGINAL ARTICLE

## Oxidant-antioxidant status in Egyptian children with sickle cell anemia: a single center based study<sup>☆</sup>

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### KEYWORDS

Antioxidants;  
Nitrite;  
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### Abstract

**Objective:** the present study was conducted to investigate the oxidant-antioxidant status in Egyptian children with sickle cell anemia.

**Methods:** the serum levels of total antioxidant capacity (TAO), paraoxonase (PON), vitamin E, nitrite, and malondialdehyde (MDA) were measured in 40 steady state children with homozygous sickle cell anemia (24 males and 16 females) and 20 apparently healthy age- and gender-matched controls.

**Results:** mean serum TAO, PON, vitamin E, and nitrite levels were significantly lower in the group with sickle cell anemia, whereas mean serum MDA was significantly higher in these children compared to controls. No significant differences in mean levels of TAO, PON, nitrite, vitamin E, and MDA were found in sickle cell anemia patients receiving hydroxyurea when compared with those not receiving hydroxyurea. A significant negative correlation between serum nitrite and the occurrence of vaso-occlusive crises (VOC) was observed ( $r = -0.3$ ,  $p = 0.04$ ). PON level was found to be positively correlated with patients' weight and BMI ( $r = -0.4$ ,  $p = 0.01$ ;  $r = -0.7$ ,  $p < 0.001$ , respectively), but not with frequency of VOC. The area under the curve of serum nitrite in predicting occurrence of VOC was 0.782, versus 0.701 for PON, and 0.650 for TAO ( $p = 0.006$ ). Serum MDA was not correlated with nitrite, PON, TAO, or vitamin E levels. No significant correlations were detected between serum nitrite and hemoglobin or antioxidant enzymes.

**Conclusion:** children with sickle cell anemia have chronic oxidative stress that may result in increased VOC, and decreased serum nitrite may be associated with increases in VOC frequency. A novel finding in this study is the decrease in PON level in these patients, which is an interesting subject for further research.

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**PALAVRAS-CHAVE**

Antioxidantes;  
Nitrito;  
Paraoxonase;  
Malondialdeído;  
Anemia falciforme;  
Crianças

**Estado oxidante-antioxidante em crianças egípcias com anemia falciforme: estudo baseado em um único centro****Resumo**

**Objetivo:** o presente estudo foi realizado com o objetivo de investigar o estado oxidante-antioxidante em crianças egípcias com anemia falciforme.

**Métodos:** dosamos os níveis séricos da capacidade antioxidante total (CAT), paraoxonase (PON), vitamina E, nitrito e malondialdeído (MDA) em 40 crianças estáveis com anemia falciforme homozigótica (24 meninos e 16 meninas), e 20 controles pareados por idade/sexo aparentemente saudáveis.

**Resultados:** os níveis séricos médios da CAT, PON, vitamina E e nitrito foram significativamente menores, ao passo que o nível sérico médio de MDA foi significativamente maior em crianças com anemia falciforme (AF), em comparação aos controles. Não foram encontradas diferenças significativas nos níveis médios de CAT, PON, nitrito, vitamina E e MDA em pacientes com AF em tratamento com hidroxiureia, em comparação aos que receberam hidroxiureia. Encontramos uma correlação negativa significativa entre o nitrito sérico e a ocorrência de crises vaso-oclusivas agudas (CVO) ( $r = -0,3$ ,  $p = 0,04$ ). Descobrimos que o nível de PON está correlacionado positivamente com o peso e o IMC dos pacientes ( $r = -0,4$ ;  $p = 0,01$ ;  $r = -0,7$ ;  $p < 0,001$ , respectivamente), porém não com a frequência de CVO. A área sob a curva (ASC) do nitrito sérico na previsão da ocorrência de CVO foi 0,782, em comparação a 0,701 para PON e 0,650 para CAT ( $p = 0,006$ ). O MDA não está correlacionado a nitrito, PON, CAT ou vitamina E. Não foram detectadas correlações significativas entre nitrito sérico e hemoglobina ou enzimas antioxidantes.

**Conclusão:** crianças com AF apresentam estresse oxidativo crônico que pode resultar em aumento das CVO. Em crianças com AF, a redução nos níveis de nitrito sérico pode estar associada a aumentos da frequência de CVO. Um novo achado neste estudo é a redução no nível de PON em pacientes com AF, que é um campo interessante de novas pesquisas.

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**Introduction**

Sickle cell anemia (SCA) is one of the most common monogenic disorders in the world, predominantly observed in Africa and Southeast Asia. It is a multi-system disease, associated with episodes of acute illness and progressive organ damage.<sup>1</sup> SCA results from a p mutation in the genetic code such that glutamic acid is replaced by valine in the globin chain of hemoglobin. This substitution transforms normal adult hemoglobin (HbA) into sickle hemoglobin (HbS). When deoxygenated, HbS polymerizes, and when a critical amount of HbS polymer accumulates within a sickle erythrocyte, cellular injury occurs. A sufficient number of damaged erythrocytes cause the phenotype of sickle cell disease (SCD), characterized by hemolytic anemia and vasoocclusion.<sup>2</sup>

SCD is emerging as an important model of oxidative stress. Since red blood cells (RBCs) carry oxygen to the body tissues, they are already rich in oxidative fuel. Their distinctive structural features make them susceptible to an oxidant assault. Chronic oxidative stress resulting from an imbalance between the production of reactive oxidant species (ROS) and antioxidant enzymes constitutes a critical factor in endothelial dysfunction, inflammation, and multiple organ damage in SCD. In addition, the disease is characterized by damage to the cell membrane due to increased lipid peroxidation products, such as malondialdehyde (MDA) and the increased consumption of nitric oxide (NO).<sup>3,4</sup>

Increased ROS production is caused by intrinsic mechanisms of disease, such as increased activity of several oxidases (NADPH oxidase and endothelial xanthine oxidase),<sup>5</sup> auto-oxidation of HbS, release of heme iron, increased asymmetric dimethylarginine,<sup>6</sup> uncoupling of NO synthase activity, and decreased NO levels.<sup>7</sup> This enhanced production of free radicals in SCA and subsequent decreased NO bioavailability inactivate NO-mediated vascular relaxation.<sup>8</sup> Impaired vascular relaxation and increased endothelial adherence contribute to the vaso-occlusive phenomena.<sup>9</sup>

Several reports indicate that SCA patients have lower levels of antioxidants such as NO, total antioxidant capacity (TAO), and vitamin E as compared to normal healthy controls.<sup>10-13</sup> Moreover, one study showed a significantly enhanced lipid peroxidation in SCA patients when compared to controls.<sup>14</sup> However, limited studies have evaluated the role of oxidants and antioxidant status in children with SCA. To the authors' knowledge, none have been conducted in patients with SCD in Egypt. The present study aimed to evaluate the oxidant-antioxidant status in Egyptian children with SCA in a steady state through the estimation of serum levels of the lipid peroxidation product MDA, nitrite, PON, vitamin E, and TAO.

**Material and methods**

This was a prospective case-control study conducted at the New Children's Hospital of Cairo University, Egypt, and at

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