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Research Article

New Insights of Oxidative Stress and Thalassemia May Lead to Antioxidant Therapy

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ABSTRACT

Background: Because of chronic hemolysis, thalassemic patients are under oxidative cell injury caused by secondary iron overload. This provokes oxidative damage to the cellular membranes of organs that accumulate excess iron. Several researchers studied the oxidative stress in patients with thalassemia during chelation therapy and repeated blood transfusion periods, and they found that β-thalassemia patients are under oxidative stress, but they did not focus on before the chelating therapy period. **Objective**: To evaluate the total antioxidant capacity (TAOC) and oxidative stress (OS) in newly diagnosed patients with β-thalassemia before chelating therapy. **Methodology**: In the present case-control study, twenty patients newly diagnosed with β-thalassemia before receiving chelating agents, and another 30 healthy individuals, sex-matched with patients, considered as a control, were included in the study. Total antioxidant capacity (TAOC) and Malondialdehyde (MDA) were assessed in the studied groups. **Results**: The TAOC values of the thalassemic group (35±0.11 u/ml) were significantly (p<0.001) lower than that of the control group (79±7.2 u/ml). MDA values of the thalassemic group (7.9 ±2.35nmol/l) were significantly (p<0.001) more than that of the control group (0.57±0.25 nmol/l). **Conclusion**: The present study demonstrated that patients with β thalassemia have decreased values of TAOC, and increased values of MDA when compared with the control group.

Keywords: Thalassemia, Oxidative stress, Antioxidants.

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INTRODUCTION

Thalassemia is a genetic disease of abnormal hemoglobin moieties of red blood cells (RBCs)[1], resulting of abnormal and unpaired α-globin chain, or by abnormal globin molecules synthesis leading to fragility of RBCs membrane, with subsequent easily broken down of erythrocytes, resulting in chronic hemolytic anaemia.[2-4] Moreover, the formed severe anaemia resulted in lifelong dependence on blood transfusions to sustain life[5], a therapy that causes additional iron overload, with its complications and toxic effects.[6]

Accumulation of iron lead to elevation of free toxic ferrous in plasma.[7] Moreover, the accumulated ferrous form induces production of reactive oxygen species (ROS) including hydroxyl radicals ($OH^{\bullet}$).[8-10] this dualistic impact of acculated unpaired globin chain and LPI facilitate the oxidant load on erythrocyte consequently reducing erythrocytes lifespan[11] increasing the chance of membrane lipid peroxidation[4], increased lipid peroxidation processes with subsequent consumption of antioxidants. This consumption of antioxidants is responsible for constant intracellular oxidative stress, although oxidative stress is not the primary cause of thalassemia, it mediates several of its pathologies. It aggravates the disease condition including increased hemolysis, and release of free (non-heme) iron[12], defects in red blood cell synthesis and functional insufficiency of important organs like the heart and liver.[13]

SUBJECTS AND METHODS

A case-control study included 20 newly diagnosed β-thalassemic patients 5 (25.%) males and 15 (75%) females. with age range between 1-4 years, diagnosed according to clinical signs and symptoms, and haemoglobin electrophoresis attended the thalassemia centre at Ibn- Alatheer-Teaching-Hospital, Mosul city-Iraq, from November 2021 to April 2022.

Thirty healthy children matched for age and gender with the patients group, were kept as a control group. Participation agreement were signed by all participants before recruiting for the study, weight and height measured and BMI calculated.

Biochemical analysis of TAOC, and serum MDA level, were measured using Colorimetric Assay Kit Elabscience®. (USA).[14]

RESULTS

The demographic parameters of the enrolled subjects are represented in Table 1. A non-significant statistical difference in age existed between patients (2.25±0.97), and the control group (1.97±10) (p>0.05). The number of patients in to control group and male-to-female numbers were not matched, although as a ratio were similar. A non-significant statistical difference in BMI existed between the patients (16.5±2.1) and control groups (16.35±2.27) (p>0.05).

Table 2 shows the comparison of antioxidant/oxidant parameters in the control group versus thalassemia patients. TAOC plasma concentration of the patient group (35±11 u/ml) was significantly lower than the control group (79±7.2u/ml). Conversely, the MDA plasma concentration of the patient group (7.9±2.35 mmol/ml) was significantly higher than the control group (0.57±0.25 mmol/ml) (p<0.05).

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Table 1. The demographic parameters of both groups.

Parameter	Patients n= 20	Control n=30
Age (in years)	2.25±0.97	1.97±10
Sex(M/F)	5/10	10/20
BMI	16.5±2.1	16.35±2.27

Table 2. The serum levels of TOAC and MDA of thalassemia patients and control groups.

Parameter	Patients n= 20	Control n=30
TAOC(U/ml)	35±11	79±7.2
MDA(nmol/ml)	7.9±2.35	0.57±0.25

Data expressed as mean±SD, t-test conducted for statistical analysis, *p<0.05 denotes the statistical differences between groups.

DISCUSSION

In β-thalassemia, excess iron accumulation is a great issue in both transfusion-dependent- thalassemia (TDT) caused by repeated blood transfusion, and non-transfusion-dependent thalassemia (NTDT) due to hemolysis, and is considered as the main cause of morbidity and mortality in thalassemia patients. Iron deposition occurs in visceral organs causing tissue injury and finally organ dysfunction.[4]

Previous researchers have assessed the antioxidant/ oxidant status of thalassemia patients. Nonetheless, previous researches focused on chronic cases of thalassemia patients who are on chronic repeated blood transfusion and subsequently on iron chelating agents rather than the newly diagnosed patients. Therefore, the present study focused on evaluating the oxidative stress status of the patients who are newly diagnosed thalassemic patients not on iron therapy

However, most studies have studied the chronic cases of patients who are on chronic repeated

The study involved 20 newly diagnosed patients and 30 healthy kept as a control group. The groups were matched regarding demographic parameters. This matching may exclude the influences of these factors on the outcome of the study. The removal of the factors that influence with results of studies concerning the antioxidant field was done in the majority of other studies [15]

A review of the literature provided limited studies dealing with antioxidants/oxidant status in newly diagnosed patients with thalassemia, with the majority focusing on patients with blood transfusion and chelating therapies. Regarding the measurement of TAOC, most studies advise to measure to TAOC in plasma, because it is more useful than measuring antioxidants individually. After all, there are synergistic interactions that could be determined[16], and because it reflects precise marker of the relationship between antioxidants and disease.[17]

Our study shows a significant decrease in the TAOC value of β-thalassemic patients when compared with control. This finding is by a study done by Ghone et *al.*,[18] and Nahla *et al.*,[19] who found that serum TAOC and CAT in the β-thalassemic group were significantly decreased. Tsamesidis *et al.*,[20] measured TAOC in different nations in medeterians regions with beta-thalassemia, and found decreased values in all patients. Garelnabi *et al.*,[21]; Wassem *et al.*,[12] and Nafadya *et al.*,[5], assessed the values of individual antioxidants, they found that antioxidant levels were significantly lower in β thalassemic patients as than the control group. Low levels of vitamin E in thalassaemic patients were found in studies done by Naser *et al* .,[2]; Simsek *et al.*,[23]. Allen *et al.*,[10] found a decrease in TAS and Vitamins C and E were markedly deficient in all β –thalassemia.

The decrease in TAOC, low levels of vitamin E and other antioxidant enzymes in thalassemic patients might be due to its consumption of antioxidant defence mechanisms for counterbalancing the effects of excess generation ROS caused by iron overload and suppressing their harmful oxidative stress effects and protecting against oxidative hemolysis.[20,24] In this study, there was a significant increase in serum level of MDA a marker for the presence of oxidative stress in the patients group as compared with control. Our results were from previous studies, that showed higher MDA levels in the patient group than control group. [25-27] Allen *et al.*,[10] found that MDA was elevated in approximately 75% of β-thalassemic patients.

Lipid peroxidation due to oxidative stress as a result of hemolysis of RBCs results in elevated MDA levels due to abnormal type of hemoglobin, free haemoglobin (Hb) and the accumulation of alpha globulin in the plasma resulted in their oxidation resulting in more free radicals oxidizing heme and iron which results in further toxicity. Insufficient antioxidant molecules results in cellular membrane damage thereby cellular damage of blood vessels and endothelium.[10,11]

CONCLUSION

The present study demonstrated that the newly diagnosed patients with β thalassemia before blood transfusion and chelating therapies have lower levels of TAOC, and higher levels of MDA than the control group due to hemolysis and increased iron concentration resulting in the generation of ROS and oxidative stress. This result may give a new insight that antioxidant therapy may have value in the management of thalassemia.

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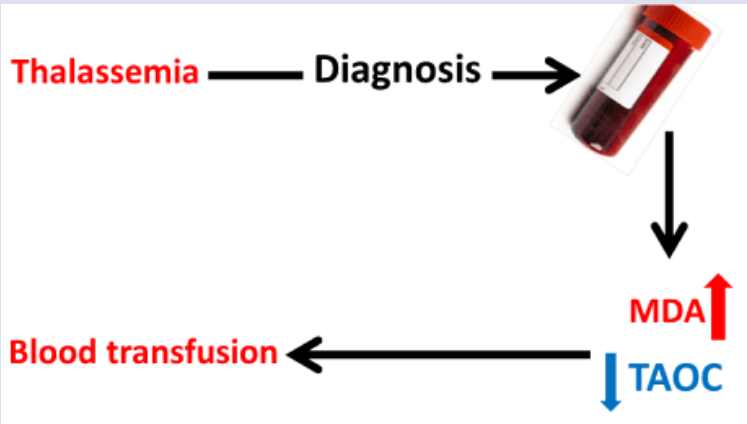
GRAPHICAL ABSTRACT



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