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Clinical comparison of antioxidant for pregnant women with iron deficiency anemia

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***Abstract*---**The aim of this study was to study the evaluation of serum antioxidation in pregnant women with iron deficiency anemia by measuring to measure some antioxidant parameters including: ceruloplasmin (Cp), copper (Cu) and transferrin (Tf) levels in pregnant women with iron deficiency anemia. Blood samples were obtained from (80) pregnant women with anemia divided according to the stage of pregnancy and iron deficiency as follows: 1) Twenty patients in the second trimester with anemia without iron deficiency; 2) Twenty patients in the second trimester with anemia with iron deficiency; 3) Twenty patients In the third trimester with anemia without iron deficiency; 4) Twenty patients in the third trimester have anemia with iron deficiency. In addition, a control group of (40) healthy pregnant women was used. Twenty pregnant in the second trimester and 20 pregnant in the third trimester were divided into two groups. Results: The results show a presence of a significant increase in Cp, Cu and Tf in all groups of patients with Iron deficiency in comparison with control group.

***Keywords*---**pregnant women, antioxidation, anemia.

Introduction

Anemia is characterized by a reduction in the total number of red blood cells (RBCs) or hemoglobin in the blood continues to be a major public health issue. Anemia is characterized by a low hemoglobin concentration, which makes it difficult for tissues to meet their oxygen delivery demands. According to WHO, India has the highest prevalence of anemia among South Asian countries. Even more concerning is the fact that South Asian countries account for roughly half of all maternal deaths due to anemia worldwide; India accounts for roughly 80% of all maternal deaths due to anemia in South Asia [1].

Iron Deficiency Anemia

The most common nutrient deficiency is iron deficiency (ID). It has an impact on over 2 billion people all over the world. Iron deficiency anemia (IDA) is responsible for roughly half of all cases of anemia worldwide [1]. Iron deficiency anemia affects 1 to 18% of people in industrialized countries [2] compared to 30% to 51% in developing countries [3]. Iron deficiency anemia is more common in pregnant women, babies aged 4 months to 2 years, young women, vegetarians, and school-aged children [4]. Many studies on the relationship between IDA and neurological/behavioral development in children have discovered significant links between IDA and neurological/behavioral outcomes [5].

Ceruloplasmin

Ceruloplasmin (Cp) is a blue multi-copper oxidase that acts as a large copper ion carrier in the plasma. The protein is primarily synthesized as a single-chain polypeptide in the liver and secreted as α2-glycoprotein in the plasma [6]. It is a metal-associated protein. This consists of a 1046 amino acid peptide sequence in a single peptide and three amino-glucose molecules together with a side chain of several sugars and the molecular weight of the 132 KD peptide sequence and each Cp molecule has 6 to 8 copper atoms. The effectiveness of Cp is anti-oxidant depends on the amount of Cu^{+2} in the protein, since Cp acts to eliminate the radical $\bullet O^{-2}$ superoxide by reducing the protein's copper atom [7].

Copper

Copper (Cu) is an essential trace element for a variety of body functions. Free copper, on the other hand, is toxic due to the potential for the formation of reactive oxygen species (ROS). As a result, copper uptake, distribution, and excretion are all strictly regulated [8]. Copper is associated with Cp in 90-95 percent of human plasma, but only a trace of copper is present as free copper. Copper is only loosely bound to albumin and histidine in 5-10% of plasma [9]. Copper is involved in a variety of biochemical processes that are essential for normal growth, health, and development. Copper metabolism deficiencies cause Menkes and Wilson myeloneuropathy and cardiovascular disease, as well as other pathophysiological conditions [10]. Copper is a trace element that serves as a cofactor for a number of intermediate metabolism enzymes, most notably oxidae, and is required for hemoglobin synthesis by mobilizing ferrous iron [11].

Transferrin

Transferrin (Tf) is the most important protein carrying iron, a glycoprotein with a molecular weight of approximately 79.57 Daltons consisting of a single chain of 679 amino acids [12]. It is synthesized basically in the liver [13]. Iron levels, estrogen levels, and nutritional status all influence transferrin synthesis and storage [14]. Transferrin delivers ferric iron to

cells via receptor-mediated endocytosis, a unique mechanism that allows transferrin and its receptor to be reused in the delivery of iron [15].

Design of study

This study was conducted at Bint Al Hoda Maternity and Children Hospital Iraq, biochemistry laboratory at the period between 13/4/2022 and 31/5/2022. The study included (120) subjects, (80) patients with anemia (40 pregnant with anemia in second trimester and 40 pregnant with anemia in third trimester as well as 40 appearealy healthy pregnant to obtain the normal values of the studied parameterrs. With age range (18 - 40) years.

Table (1): The study included data from patients (pregnant women with anemia) and controls (healthy pregnant women)

Groups	No.	age range (years)
Controls	40	18 - 40
Second trimester anemia pregnant	40	18 - 40
Third trimester anemia pregnant	40	18 - 40

Collection of Blood Samples

About 5 mL of blood from pregnant women with anemia and controls was taken allowed to clot at room temperature in empty disposable tubes, centrifuged to separate it at 3000 rotor per minute (rpm) for 10 minutes, and the serum samples were separated.

Statistical Analysis

The results of this study's statistical analysis were calculated using Microsoft Excel 2010 and expressed as mean standard deviations (mean SD) using the LSD test. To compare parameters in different studied groups, the one-way ANOVA-test is used. The relationship between the current study parameters was determined using Pearson's correlation. P-values of less than 0.05 are regarded as statistically significant.

Results and Discussion

Serum Ceruloplasmin Concentrations

Table (2) shows a significant increase in serum CP concentrations in pregnant women with anemia when compared to the control group ($P \leq 0.05$). It was also discovered that there was a significant increase in 3rd groups compared to 2nd groups, as well as a significant increase in 3rd ID group compared to 3rd IN, and a significant increase in 2nd ID group compared to 2nd IN group. These findings corroborate each other [16]. In healthy pregnant women, levels of ceroplasmine in the third trimester of pregnancy are higher than in the second trimester of pregnancy,

ceruloplasmin which is a protein with antioxidant properties, it is possible that the chronic hypoxia associated with stage of pregnancy increases the level of ceruloplasmin. There is a relationship between cerloplasmin and iron, as the lower level of iron, the greater the level of ceruloplasmin. The biological purpose of Cp increased activity could be linked to Cp's role in iron balance. Cp induction will increase iron filling from storage depots, such as the liver, during dietary iron deficiency, thereby increasing iron delivery to the bone marrow for erythropoiesis to occur when the body's iron stores are depleted [17]. In previous studies, an increase in the levels of ceruloplasmin was observed in patients with iron deficiency, because ceruloplasmin is important for the release of iron from the tissues, and also when iron deficiency the level of copper increases, which enhance the deficiency of iron and because Cp is a transporter of copper, where the loading of copper in the liver leads to a significant increase in the protein of ceruloplasmin, which increases the level of Cp in pregnant women with iron deficiency anemia [17].

Table (2): Serum CP levels in all studied groups

Groups	No.	CP(mg/L) mean±SD
Second Trimester		
2nd Control	20	3.33 ± 1.03^{e}
2nd IN	20	5.19 ± 1.46^{cd}
2ndID	20	6.0 ± 0.99^{ab}
Third Trimester		
3rd Control	20	4.82 ± 0.84^{d}
3rd IN	20	5.68 ± 1.42^{bc}
3rd ID	20	6.66 ± 2.02^{a}
L.S.D		0.68

-The same letters to non-significant difference.
-The different letters refers to significant difference.
-No: Number of subjects.
-SD: Standard Deviation.
-LSD: Least Significant Difference.
-2nd control: Second trimester Control.
-2nd IN: Second trimester Iron Normal.
-2nd ID: Second trimester Iron deficiency.
-3rd Control: Third trimester Control.
-3rd IN: Third trimester Iron Normal.
-3rd ID: Third trimester iron deficiency.

Serum Copper Concentrations

Table (3) shows a significant increase in serum Cu concentrations in pregnant women with anemia when compared to the control group (P≤0.05). This is a close match to the result of [18]. There have been studies that show that the level of copper in pregnant women with

anemia increases when compared to healthy pregnant women, making it important in free radical scanning and oxidation-reducing reactions (oxidation). There was also a significant increase in 3rd groups compared to 2nd groups, as well as a significant increase in 3rd ID group compared to 3rd IN, and a significant increase in 2nd ID group compared to 2nd IN group. These findings are consistent with previous research such as [19]. Copper is required for the conversion of ferrous to ferric iron, as well as its incorporation into hemoglobin, which results in microcytic, hypochromic anemia. Increased copper levels in iron-deficient anemic mothers may be an offsetting mechanism to combat anemia, which is complemented by an increase in ceruloplasmin synthesis, which has ferroxidase activity. Several human and animal studies have found that increased iron intake is linked to lower serum copper concentrations and activity of copper enzymes, and vice versa, most likely due to competitive absorption mechanisms for iron and copper a rise in copper levels during pregnancy. Several human and animal studies have found that increased iron intake is linked to lower serum copper concentrations and activity of copper enzymes, and vice versa, most likely due to competitive absorption mechanisms for iron and copper. Copper metabolism is intricately intertwined with iron metabolism. Ferroxidase I and II, two copper-containing enzymes, have the ability to convert ferrous (Fe^{2+}) to ferric (Fe^{3+}) forms of iron. The transport of iron is done in ferric form. Copper is an important trace element. Iron deficiency causes an increase in copper levels in the mother's liver. This is linked to a rise in the mother's serum copper levels and the activity of maternal serum ceruloplasmin [20]. Various studies comparing with incremental increase in trimesters. There is a study that indicates that the placental transport system changes during the last stages of development, which leads to higher copper values being transferred at the end of pregnancy than early pregnancy copper. The third is higher than the first third [21]. Because copper is an indispensable nutrient required for fetal development and its deficiency may affect fetal growth, and the chances of complications in pregnancy and childbirth. Copper is necessary in order to share life in the functions of many mineral enzymes. This micronutrient is delivered to the developing fetus by specific vectors in the placenta [22].

Table (3): Serum Cu levels in all studied groups

Groups	No.	Cu(umol/L) mean±SD
Second Trimester		
2nd Control	20	132.18 ± 37.63[a]
2nd IN	20	142.87 ±37.22[ab]
2nd ID	20	145.44 ± 31.21[ab]
Third Trimester		
3rd Control	20	136.35 ± 28.95[a]
3rd IN	20	148.49 ± 29.39[ab]
3rd ID	20	153.58 ± 28.52[b]
L.S.D		16.44

Serum Transferrin Concentrations:

Table (4) shows a significant increase in serum Tf concentrations in pregnant women with anemia when compared to the control group (P≤0.05). There was also a significant increase in the 3rd groups compared to the 2nd groups, as well as a significant increase in the 3rd ID group compared to the 3rd IN group, and a significant increase in the 2nd ID group compared to the 2nd IN group. These findings are consistent with previous research, such as [23]. Tranferrin is a glycoprotein, β globulin synthesized in liver and carries two atom of iron, in the ferric state. Decreased saturation of transferrin by iron enhances the release of iron from intestinal mucosal cells. In the iron requiring cells, transferrin is taken by transferrin receptor–mediated endocytosis. In antenatal women, due to the elevated steroid levels, the concentration of transferrin increase which represents an increased rate of production for its functional capacities along with no changes in its degradation rate The clearance time of transferrin bound iron from circulation is mostly affected by the plasma iron level and activity of erythroid marrow. The serum levels of transferrin where highly elevated in the patients under study in all the three trimesters. The rate of erythropoesis also increases from first to third trimester as the pool of erythroid cells requiring iron increases which leads to progressive decrease in the clearance time of tranferrin from circulation. Consequently, estimation of serum transferrin can be considered an early biochemical marker to correct iron deficiency anemia in prenatal women, wherever there is a decrease in iron levels there is an increase in levels of transferrin [24]. When the body's iron supply is low, transferrin synthesis increases. The transfer-rin receptor binds the iron-transferrin complex to cell membranes, and the iron is then internalized [25]. Various studies have shown that transferrin receptors in the blood are increased in cases of iron deficiency or under conditions of increased cellular iron requirements. The rise in Tf with advancing pregnancy was attributed firstly to increased stimulation of erythropoiesis, and secondly to increased iron requirements due to non-independent cell proliferation. It is not known whether inhibition of erythropoiesis in early pregnancy has a negative effect on detection of concomitant iron deficiency through Tf determination [26].

Table (4): Serum Tf levels in all studied groups

Groups	No.	Tf (mg/L) mean ±SD
Second Trimester		
2nd Control	20	2.27 ± 0.33^{c}
2nd IN	20	2.41 ± 0.40^{bc}
2nd ID	20	3.62 ± 0.29^{a}
Third Trimester		
3rd Control	20	2.25 ± 0.32^{c}
3rd IN	20	2.50 ± 0.44^{b}
3rd ID	20	3.70 ± 0.36^{a}
L.S.D		0.18

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