Significance of malondialdehyde in Iraqi women patients with iron deficiency anemia

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Abstract. Evidence from previous epidemiological and clinical studies suggests a possible relationship between antioxidant stress and anemia. Our study was conducted from February 2021 to May 2021 and the aim of the study is to evaluate oxidative stress by studying lipid peroxidation for women only in Najaf Governorate / Iraq with iron deficiency anemia compared to healthy controls. A case-control study was designed to evaluate malondialdehyde (MDA). The number of samples was 180, 90 of whom were IDA patients and the other 90 were normal control subjects. Serum levels of Malondialdehyde were assessed using enzyme-linked immunosorbent assay (ELISA). The results showed a statistically significant increase in malondialdehyde (MDA) levels (8.54 ± 2.5 (nmol/ml) versus 4.39 ± 0.83 (nmol/ml); P<0.001), in addition to an increase in lipid peroxidation in women with iron deficiency anemia.

1 Introduction

Anemia is most commonly caused by iron deficiency [1]. In children, women and the elderly, iron deficiency anemia is an important health concern. It is also common in kidney disease [2] and comorbidity among a wide range of medical conditions. Iron deficiency anemia (IDA) is relatively common in aging populations [3]. Menstrual loss, pregnancy, or abnormal uterine bleeding in women puts them to evolving iron deficiency which leads to severe fatigue, reduced exercise capacity, and poor work performance [4]. The pathophysiology of IDA involves many different pathways. Oxidative stress (OS) is one of these metabolic pathways that play a main role in the pathogenesis of IDA [5]. The imbalance between the antioxidant defense system and the generation of oxygen species is called the OS [6]. Reactive oxygen species (ROS), released by a variety of external and internal cell activities, may cause serious oxidative damage to important compounds such as DNA, proteins and lipids, leading to cell dysfunction. [7]. Lipid peroxidation's final product is malondialdehyde (MDA), The products of lipid peroxidation have a remarkable effect on cell functioning by affecting the structure and activity of a protein [8]. In IDA, lipid peroxidation rises and anti-oxidant defenses decline [9]. The action of free radicals on phospholipids or polyunsaturated fatty acids(PUFA) in cellular or organelle membranes causes lipid peroxidation [10]. The PUFA in cell membranes are prime targets of ROS,
which cause lipid peroxidation, that can disrupt the cell structure and function [11]. Malondialdehyde (MDA) is a biomarker widely used to evaluate lipid peroxidation [12]. MDA, a byproduct of lipid peroxidation (LPO) and a byproduct of PUFA breakdown by free radicals, can cause lipid, protein, and nucleic acid crosslinking. All of these factors may have an impact on the survival of red blood cells (RBCs). The purpose of this study was to evaluate oxidative stress by investigating lipid peroxidation of Najaf women with iron deficiency anemia as comparison to healthy controls.

2 Materials and Methods

2.1 Ethical Consideration

It was approved by the Scientific Research Committee in the Najaf Health Department, in addition to the Scientific Research Ethics Committees in the College of Medicine at the University of Kufa.

2.2 Patients

The study was conducted from February 2021 to May 2021 and a case-control study was designed on ninety subjects and ninety control. A case-control study of 180 randomly selected individuals (90 IDA and 90 control) was performed to investigate the oxidative status with IDA. The Participants aged (67-18) years with a mean ± SD of 35.1 ± 10.2 years. All patients were diagnosed by specialist doctors as having IDA.

2.3 The inclusion criteria and exclusion criteria

Microcytic hypochromic erythrocytes are the description criterion for IDA, serum iron concentration less than 45 g/dL, serum ferritin concentration less than 15 ng/ml, and T.I.B.C (total iron-binding capacity) more than 250 Mg/dl. Iron-deficient anemic (IDA) women were included in the study group. In women, IDA is defined as a hemoglobin concentration of less than 10.5 g/dl. This is inclusion criteria. And the exclusion criteria include: 1. Acute bleeding. 2. A history of blood transfusions within the previous 6 months prior to the study. 3. Those suffering from diabetes, hypertension, liver diseases, renal dysfunction, coronary artery disease, systemic or local infection, cancer, and rheumatoid arthritis. 4. Alcohol abuse, and smoking. 5. Using vitamin and mineral supplements or taking birth control pills. 6. Subjects with a medical history of thalassemia and sickle cell anemia.

2.4 Measuring the indicators under study

**Determination of Body Mass Index (BMI)** : 

\[ \text{BMI} = \frac{\text{Wt (Kg)}}{\text{Ht (m}^2\text{)}} \]

**Determinations of IDA** : Serum ferritin level was estimated by (VIDAS), serum iron was determined, and serum TIBC capacity was estimated, by the method Directions were carried out according to the manufacturer's instructions (BIOLABOSAS, France). Malondialdehyde (MDA) was determined by ELISA.

2.5 Statistical analysis

Data analysis (calculating the mean, standard deviation, and percentages) was performed using the statistical package SPSS version 26, the P value is less than 0.05. [13,14].
3 Results

The results were obtained as shown in Figure (1) and Tables (1, 2, 3, 4, and 5).

![Figure 1](https://example.com/fig1.png)

**Fig. 1.** Distribution of age in iron deficiency anemia patients and healthy controls.

**Table 1.** Anthropometric characteristics of study groups.

<table>
<thead>
<tr>
<th></th>
<th>Healthy Controls (n=90)</th>
<th>IDA Patients (n=90)</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, (mean ±SD)</td>
<td>34.95 ± 10.00</td>
<td>35.06 ± 10.19</td>
<td>0.939</td>
</tr>
<tr>
<td>Under 45 years NO. (%)</td>
<td>46 (51%)</td>
<td>48 (53%)</td>
<td>------</td>
</tr>
<tr>
<td>Over 45 years NO. (%)</td>
<td>44 (49 %)</td>
<td>42 (47%)</td>
<td>------</td>
</tr>
<tr>
<td>BMI, (kg/m²), (mean ±SD)</td>
<td>25.25 ± 2.88</td>
<td>25.58 ± 3.99</td>
<td>0.511</td>
</tr>
</tbody>
</table>

**Table 2.** MDA serum levels and their ratios in IDA patients as compared to healthy controls.

<table>
<thead>
<tr>
<th>Study parameters (mean ± SD)</th>
<th>Healthy Controls (n=90)</th>
<th>IDA Patients (n=90)</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>MDA (nmol/ml)</td>
<td>4.39 ± 0.83</td>
<td>8.54 ± 2.5</td>
<td>&lt;0.001***</td>
</tr>
</tbody>
</table>

**Table 3.** Biochemical & hematological characteristics of study groups.

<table>
<thead>
<tr>
<th>Study parameters (mean ± SD)</th>
<th>Healthy Control (n=90)</th>
<th>IDA Patient (n=90)</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Biochemical parameters:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Iron (μg/dl)</td>
<td>81.52 ± 11.45</td>
<td>29.88 ± 9.15</td>
<td>&lt;0.001***</td>
</tr>
<tr>
<td>TIBC (μg/dl)</td>
<td>370.45 ± 24.59</td>
<td>507.60 ± 60.85</td>
<td>&lt;0.001***</td>
</tr>
<tr>
<td>TS (%)</td>
<td>22.12 ± 3.63</td>
<td>6.05 ± 2.20</td>
<td>&lt;0.001***</td>
</tr>
<tr>
<td>Study parameters (mean ± SD)</td>
<td>Pre-menopausal women &lt; 45 years</td>
<td>Post-menopausal women ≥ 45 years</td>
<td>P-Value</td>
</tr>
<tr>
<td>-----------------------------</td>
<td>---------------------------------</td>
<td>---------------------------------</td>
<td>---------</td>
</tr>
<tr>
<td>Healthy Control</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MDA (nmol/ml)</td>
<td>4.38 ± 0.95</td>
<td>4.32 ± 1.02</td>
<td>0.792</td>
</tr>
<tr>
<td>IDA Patient</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MDA (nmol/ml)</td>
<td>8.28 ± 2.33</td>
<td>9.00 ± 10.13</td>
<td>0.619</td>
</tr>
</tbody>
</table>

Table 4. MDA serum levels and their ratios in the study participants according to different age subgroups.

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Healthy Controls (n=90) R</th>
<th>IDA Patients (n=90) R</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>MDA (nmol/ml) p-value</td>
<td>MDA (nmol/ml) p-value</td>
</tr>
<tr>
<td>Iron (μg/dl)</td>
<td>0.024-</td>
<td>0.093-</td>
</tr>
<tr>
<td>Ferritin (ng/ml)</td>
<td>0.049 -</td>
<td>0.059-</td>
</tr>
<tr>
<td>TIBC (μg/dl)</td>
<td>0.074</td>
<td>All p&gt;0.05</td>
</tr>
<tr>
<td>Hb (g/dl)</td>
<td>0.054</td>
<td>0.150</td>
</tr>
<tr>
<td>PCV (%)</td>
<td>0.043</td>
<td>0.036</td>
</tr>
<tr>
<td>MCV(fl/cell)</td>
<td>- 0.138</td>
<td>0.145-</td>
</tr>
</tbody>
</table>

Table 5. Correlation of malondialdehyde (MDA) serum levels with biochemical and hematological parameters of the studied groups.

4 Discussion

This study showed a significant increase (P < 0.05) in the marker of lipid peroxidation in women with IDA compared to age and BMI matched healthy women, which was in favor of the hypothesis of higher oxidative stress in IDA. These results are consistent with earlier reported results by other investigators. For example, Sharif Usman [15] study have showed that in both iron deficiency anemia patients and those with inadequate iron reserves, lipid peroxidation was considerably elevated. Based on the results of the [16] study, according to their findings, anemic women are more likely to the develop free radicals, abnormalities, and peroxidation of critical body molecules, implying an elevated risk for
anemic women, based on the findings of their study. In the literatures of [17-20], Microcytic red blood cells were more susceptible to oxidants and produced more malondialdehyde. Similarly, the current study results have indicated that serum MDA levels were elevated in women with IDA than in healthy controls. Moreover, Madhikarmi and his colleagues have been indicated that elevated of lipid peroxidation and depletion of antioxidant system could be improved oxidation stress state. that affecting the status of IDA patients [21] have been observed that MDA generation lead to increase in the serum of IDA patients, indicating an increased quantity of auto-oxidizable lipids under oxidative stress. This disparity in results could be attributable to differences in methods used in each of these investigations. Ferrous is a well-known ion that contributes to Habar Weiss and Fenton reactions in vivo by converting less potent O$_2$ species such as superoxide anion radical and H$_2$O$_2$ to hydroxyl radical, which is the most effective and dangerous free radical that damages directly proteins, lipids, and nucleic acids [24-28]. In contradiction with the current study has proved a higher serum MDA levels, which appear to be a sign of lipid peroxidation in anemic women despite iron deficiency. It's possible that this is because lipid peroxidation occurs in a hydroperoxide–superoxide–dependent mechanism, bypassing the Fenton and Habar-Weiss reactions [18, 24-32]. Unfortunately, the mechanism that increases lipid peroxidation in this manner is not fully understood [18]. A second explanation of the reported high lipid peroxidation product in the present study was that the deficiency of iron might induce nitrous oxide (NO) production, which showed to be a feature of iron deficiency anemia [33] and may contribute to lipid peroxidation [34]. In iron-deficiency anemia, decrease erythrocyte survival has been reported as a result of increased susceptibility to oxidant damage. MDA elevation has been formally linked to decreased deformability of RBC [18, 30, 32]. Erythrocyte membrane injury, osmotic fragility, and cell death result from increasing lipid peroxidation [35], and as part of oxidative stress was reported in the pathogenesis of IDA [28], membrane sulfhydryl group inhibition, increased membrane rigidity, and reduced deformability were observed to increase vulnerability to erythrocyte hemolysis in IDA [36]. In addition to what was mentioned, increased Hb oxidation and ROS generation may shorten the lifespan of red blood cells or be removed from the blood circulation [37]. Iron deficiency along with the resulting DNA damage, early apoptosis, and poor repair systems, maybe the pathophysiological basis for a variety of disorders [38].

5 Conclusions

In Iraq - Najaf Governorate - the finding of the current study has been signified an increase in oxidative stress in women of Najaf governorate with iron deficiency anemia represented by a high level of MDA in IDA cases but not in healthy control.

Acknowledgement

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References


